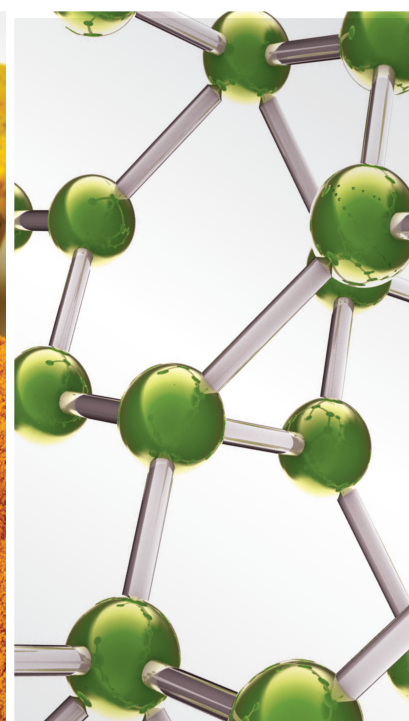


# Herbal Medicines and Natural Products for Genitourinary Cancer Treatment

Lead Guest Editor: Alamgeer Yuchi

Guest Editors: Muhammad Wasim Khan and Muhammad Nadeem Khan





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# **Herbal Medicines and Natural Products for Genitourinary Cancer Treatment**



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Muhammad Nadeem Khan



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


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Xu Liu, Jianyun Ge, Jiejie Zhang, and Boxiang Du 

Research Article (6 pages), Article ID 2102618, Volume 2021 (2021)

## Retraction

# Retracted: PTPN18 Stimulates the Development of Ovarian Cancer by Activating the PI3K/AKT Signaling

### Evidence-Based Complementary and Alternative Medicine

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

- (1) Discrepancies in scope
- (2) Discrepancies in the description of the research reported
- (3) Discrepancies between the availability of data and the research described
- (4) Inappropriate citations
- (5) Incoherent, meaningless and/or irrelevant content included in the article
- (6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

### References

- [1] N. Mao, H. Li, H. Yang, J. Su, Z. Liang, and G. He, "PTPN18 Stimulates the Development of Ovarian Cancer by Activating the PI3K/AKT Signaling," *Evidence-Based Complementary and Alternative Medicine*, vol. 2022, Article ID 1091042, 7 pages, 2022.



## Retraction

# Retracted: Effect of Combined Spinal-Epidural Anesthesia and Total Intravenous Anesthesia on Hemodynamics and Pregnancy Outcomes of Severe Preeclampsia Pregnant Patients Undergoing Cesarean Section

### Evidence-Based Complementary and Alternative Medicine

Received 18 July 2023; Accepted 18 July 2023; Published 19 July 2023

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- [1] G. Wang, P. Zhang, M. Li, X. Wu, and H. Li, "Effect of Combined Spinal-Epidural Anesthesia and Total Intravenous Anesthesia on Hemodynamics and Pregnancy Outcomes of Severe Preeclampsia Pregnant Patients Undergoing Cesarean Section," *Evidence-Based Complementary and Alternative Medicine*, vol. 2022, Article ID 2655858, 6 pages, 2022.

## Research Article

# Efficacy of Modified Qingre Jiedu Decoction Combined with Three-Dimensional Conformal Radiotherapy in Treating Moderate to Advanced Ovarian Carcinoma and Its Effect on Levels of Serum Carcinoembryonic Antigen and Carbohydrate Antigen 125

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**Objective.** To explore the efficacy of modified Qingre Jiedu decoction combined with three-dimensional conformal radiotherapy (3D-CRT) in treating moderate to advanced ovarian carcinoma (OC) and its effect on patients' serum carcinoembryonic antigen (CEA) and carbohydrate antigen 125 (CA125). **Methods.** The clinical data of 84 patients with moderate to advanced OC treated in the gynecology department of Changqing District People's Hospital of Jinan from February 2017 to February 2018 were selected for retrospective analysis, and the patients were divided into the single chemotherapy group (taxol + carboplatin,  $n = 42$ ) and the combined group (modified Qingre Jiedu decoction + 3D-CRT,  $n = 42$ ) according to the parity of their admission numbers. By measuring their levels of serum CEA and CA125 after treatment, the cellular immune levels of the two groups were compared. **Results.** Compared with the single chemotherapy group after treatment, the combined group obtained significantly higher total clinical effective rate and 1-year, 2-year, and 3-year survival rates ( $P < 0.05$ ), significantly higher CD4<sup>+</sup>/CD8<sup>+</sup> and NK cell level values ( $P < 0.001$ ), significantly lower serum CA125 and CEA level values ( $P < 0.001$ ), and significantly lower total incidence rates of toxic and side effects ( $P < 0.05$ ). **Conclusion.** The abovementioned results show that the combined treatment modality has a significant effect on prolonging the survival of patients with moderate to advanced OC and can effectively reduce the levels of tumor markers and improve the body's immunity. Further study will be conducive to establishing a better solution for OC patients.

## 1. Introduction

Ovarian carcinoma (OC) is a malignant tumor that occurs in the ovary, which has diverse histologic types and is mainly of epithelial origin. As a gynecological malignant tumor with high mortality, patients who suffer from the disease only have a 5-year survival rate of about 30% [1, 2]. Due to the insidious onset and lack of typical clinical manifestations at an early stage of the tumor, most patients have entered the middle to late stages when diagnosed, and without timely

treatment or processing, they will suffer from different degrees of complications, such as tumor rupture, twisting of the pedicle, and severe infections, endangering their life and health. Cytoreductive surgery plus postoperative systemic chemotherapy is currently the main therapeutic modality for patients with moderate to advanced OC [3], which will improve the short-term efficacy of patients, but has a high recurrence rate caused by resistance to chemotherapy, with more than 70% of patients relapsing within 1-2 years. Therefore, how to prolong the survival time and reduce the

recurrence rate of such patients has been a challenge for gynecologic oncologists [4].

With the development of imaging and linear accelerator technology, adjuvant radiotherapy has been widely used in treating gynecological diseases. It has been documented that [5] extracorporeal conformal radiotherapy is a common radiation treatment for a variety of tumor diseases, and three-dimensional conformal radiotherapy (3D-CRT) is currently the most frequently used one, which can reduce the irradiated dose to the surrounding organs, reduce the damage to the surrounding tissues, and achieve the effect of precise radiation therapy while ensuring efficacy [6, 7]. Traditional Chinese medicine (TCM) is experienced in treating gynecological diseases. The modified Qingre Jiedu decoction is prepared based on the famous antitumor formula “Lichong decoction” and has a proven antitumor effect. It contains peach seed, dandelion, tuckahoe, Mongolian milkvetch root, and other herbs and can exert efficacy such as promoting blood circulation and detoxication, invigorating the spleen, and replenishing qi [6]. Relevant clinical reports in recent years have shown [8] that the combination of TCM and Western medicine has significant advantages in improving the efficacy and reducing the mortality rate of patients with gynecological tumors. Currently, few reports focus on the efficacy of combining the two, and the results of the combination therapy were reported as follows.

## 2. Data and Methods

**2.1. General Information.** The clinical data of 84 patients with moderate to advanced OC treated in the gynecology department of *Changqing District People's Hospital of Jinan* from February 2017 to February 2018 were selected for retrospective analysis, and the patients were divided into the single chemotherapy group and the combined group according to the parity of their admission numbers, with 42 cases each. See Figure 1 for the specific study process.

**2.2. Inclusion and Exclusion Criteria.** The inclusion criteria were as follows: ① the patients who met the diagnosis criteria for OC in the 4<sup>th</sup> edition of *Guidelines for the Diagnosis and Management of Ovarian Malignancies* [7] and were diagnosed after histopathological diagnosis, and the clinical manifestations included lower abdominal distending pain, abdominal mass, and hesitancy in urination; ② their KPS scores were not less than 60 points, and the estimated survival was over 6 months; ③ they met the indications of 3D-CRT; and ④ the study met the *World Medical Association Declaration of Helsinki (2013)* [8] and was approved by the Ethics Committee of *Changqing District People's Hospital of Jinan*.

The exclusion criteria were as follows: ① the patients who had other malignant tumors; ② the patients who suffered from serious cardiovascular and cerebrovascular diseases; ③ the patients who were at least 65 years old or under the age of 18; and ④ the patients who had diseases in the immune system, blood system, nervous system, etc., were allergic to the drugs used in the study, or had poor compliance.

**2.3. Methods.** Taxol + carboplatin therapy was performed on patients in the single chemotherapy group with the following specific steps: 135 mg/m<sup>2</sup> of taxol (manufactured: Beijing Union Pharmaceutical Factory Co., Ltd.; NMPA approval no. H20083786; specification: 10 ml: 60 mg) was dissolved in 500 mL of normal saline for intravenous drip, 1 h after that, 200 mg/m<sup>2</sup> of carboplatin (manufactured: Yangtze River Pharmaceutical (Group) Co., Ltd.; NMPA approval no. H20044616; specification: 100 mg) was added to normal saline and administered via intravenous drip within 2 h [9, 10]. Before chemotherapy, it was necessary to use antiallergic drugs and prepare first aid equipment to ensure the safety of patients. The chemotherapy was conducted once every four weeks as one course, with 6 consecutive courses totally.

The modified Qingre Jiedu decoction combined with 3D-CRT treatment was carried out on patients in the combined group.

The formula of the modified Qingre Jiedu decoction was 28 g of tuckahoe, 30 g of largehead atractylodes rhizome, 30 g of dandelion, 8 g of liquorice root, 15 g of oriental water plantain tuber, 15 g of safflower, 10 g of peony root, 10 g of peach seed, 10 g of heterophylly false starwort root, 10 g of Mongolian milkvetch root, and 10 g of Sichuan lovage rhizome. The decoction was decocted with the TCM decoction machine (manufactured: Zhengzhou Xinyao Mechanical Equipment Co., Ltd.; model: XY-BC1 + 1W). After boiling, it was extracted and filtered through the solution machine and packed with the microcomputer packaging machine according to the patients' oral dose, with 200 ml per pack. The patients took 1 pack in the morning and in the evening for 6 consecutive weeks. Patients in both groups accepted regular clinical follow-up visits.

3D-CRT treatment: contrast-enhanced computed tomography (CECT) was adopted for sequential scanning positioning, 5-mm slice thickness scanning, and delineating gross tumor volume and expanding by 0.5–1.0 cm as the planning target area. Four cophase radiation fields were selected and surrounded by a 90% isodose curve, and the optimal treatment regimen was evaluated by dose volume histograms. The external irradiation dose of the linear accelerator four-field box 3D-CRT was 45 Gy, and the afterload treatment was the intracavitary dose of 25–30 Gy.

**2.4. Observation Indicators.** The clinical efficacy after treatment of all patients was evaluated by the response evaluation criteria in solid tumors (RECIST 1.1) [11]. Complete response (CR): disappearance of lesion for over one month; partial response (PR):  $\geq 50\%$  decrease volume of measurable lesion; stable disease (SD):  $< 50\%$  decrease volume of measurable lesion and  $< 25\%$  enlarged lesion; and progression disease (PR):  $\geq 25\%$  increase volume of measurable lesion or new lesions. The objective remission rate (ORR) = CR + PR.

After treatment, 5 ml of fasting elbow venous blood was drawn from patients of both groups to take the serum after anticoagulation and centrifugation. The cellular immune levels, including the level values of CD4<sup>+</sup>, CD8<sup>+</sup>, and natural killer (NK) cells, were measured with the flow cytometer (manufactured: Shanghai 3V Medical Equipment Co., Ltd.;

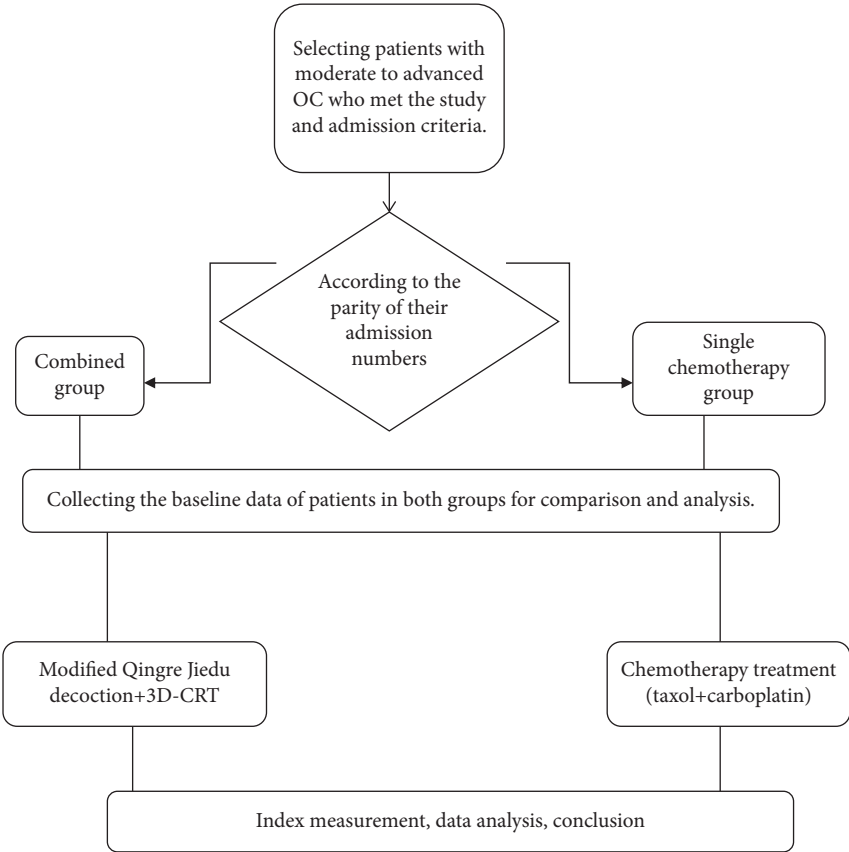


FIGURE 1: Study technical process.

model: FACSVia), and the level values of CD4<sup>+</sup>/CD8<sup>+</sup> were calculated.

The serum CEA and CA125 level values were measured by enzyme linked immunosorbent assay (ELISA) with the kits purchased from Shanghai Jingkang Bioengineering Co., Ltd., and the operation was carried out in strict accordance with the specifications on the kits.

By 3 years of follow-up, the postoperative 1-year, 2-year, and 3-year survival rates and the incidence rates of toxic and side effects (including gastrointestinal reactions, neutropenia, radiodermatitis, renal dysfunction, and leukopenia) after treatment were compared between the two groups.

**2.5. Statistical Methods.** In this study, the data processing was conducted by the professional statistical software SPSS 23.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), the enumeration data were examined by the  $\chi^2$  test and expressed by (n(%)), the measurement data were examined by the  $t$ -test and expressed by mean  $\pm$  SD, and differences were considered statistically significant at  $P < 0.05$ .

3. Results

**3.1. Comparison of Baseline Data between the Two Groups.** The clinical data such as mean age, BMI value, pathological type, and degree of differentiation were not significantly different between the two groups ( $P > 0.05$ ) (Table 1).

**3.2. Comparison of Clinical Efficacy between the Two Groups.** The total clinical effective rate of the combined group was significantly higher than that of the single chemotherapy group ( $P < 0.05$ ). See Table 2.

**3.3. Comparison of Cellular Immune Level after Treatment between the Two Groups.** After treatment, the level values of CD4<sup>+</sup>/CD8<sup>+</sup> and NK cells were significantly higher in the combined group than in the single chemotherapy group ( $P < 0.001$ ) (see Figure 2).

**3.4. Comparison of Level Values of Serum Tumor Markers between the Two Groups.** After treatment, the CA125 and CEA level values of the combined group were significantly lower than those of the single chemotherapy group ( $P < 0.001$ ) (Figure 3).

**3.5. Comparison of Survival Rates at Different Moments between the Two Groups.** The 1-year, 2-year, and 3-year survival rates of the combined group were significantly higher than those of the single radiotherapy group ( $P < 0.05$ ) (Table 3).

**3.6. Comparison of Toxic and Side Effects between the Two Groups.** The total incidence rate of toxic and side effects was significantly lower in the combined group than in the single chemotherapy group ( $P < 0.05$ ) (Table 4).

TABLE 1: Comparison of baseline data between the two groups ( $n=42$ ).

Item	Single chemotherapy group	Combined group	$\chi^2/t$	$P$
Mean age (mean $\pm$ SD, years)	47.42 $\pm$ 4.17	47.48 $\pm$ 4.03	0.067	0.947
BMI (mean $\pm$ SD, kg/m <sup>2</sup> )	21.26 $\pm$ 0.83	21.30 $\pm$ 0.76	0.230	0.818
Pathological type				
Serous cystadenocarcinoma	26 (61.90%)	24 (57.14%)	0.198	0.657
Clear cell carcinoma	12 (28.57%)	10 (23.81%)	0.398	0.528
Hybrid cystadenocarcinoma	4 (9.52%)	8 (19.05%)	1.556	0.212
Tumor stage			0.233	0.629
III	29 (69.05%)	31 (73.81%)		
IV	13 (30.95%)	11 (26.19%)		
Degree of differentiation				
Poor differentiation	6 (14.29%)	7 (16.67%)	0.091	0.763
Moderate differentiation	26 (61.90%)	27 (64.29%)	0.051	0.821
Well differentiation	10 (23.81%)	8 (19.05%)	0.283	0.595
Marital status				
Married	33 (78.57%)	35 (83.33%)	0.309	0.578
Unmarried	5 (11.90%)	2 (4.76%)	1.403	0.236
Divorced	4 (9.52%)	5 (11.90%)	0.124	0.724
Educational degree				
College	9 (21.43%)	11 (26.19%)	0.263	0.608
High school	25 (59.52%)	21 (50.00%)	0.769	0.381
Primary school	8 (19.05%)	10 (23.81%)	0.283	0.595
Place of residence			0.429	0.513
Urban area	19 (45.24%)	22 (52.38%)		
Rural area	23 (54.76%)	20 (47.62%)		

TABLE 2: Comparison of clinical efficacy between the two groups ( $n(\%)$ ).

Group	$n$	CR	PR	SD	PD	ORR
Combined group	42	22 (52.38)	14 (33.33)	4 (9.52)	2 (4.76)	85.71% (36/42)
Single chemotherapy group	42	16 (38.10)	11 (26.19)	9 (21.43)	6 (14.29)	64.29% (27/42)
$\chi^2$						4.200
$P$						<0.05

#### 4. Discussion

In recent years, the increasing work pressure on women has led to more and more new OC cases every year and shows a younger trend of the disease, which has a mortality rate up to more than 65% [12], ranking the first in female reproductive malignancies. OC is often overlooked for its insidious onset at an early stage, so most patients are at the middle to late stage when they visit the clinic. Survey data have shown [13] that about 75% of patients who present to the hospital with lesions that have involved one or both ovaries are accompanied by abdominal metastasis, with clinical manifestations such as abnormal pain, menstrual disorder, and abnormal vaginal bleeding. In advanced stages, the disease can involve the thoracic cavity, liver, kidney, and other organs and show cachexia signs such as obvious ascites, edema of the lower extremities, and anemia, which are life-threatening. At present, cytoreductive surgery or chemoradiotherapy is mainly adopted for treatment, but clinical investigations have found [14–16] that tumor cells in patients treated in these ways can still rapidly spread into the blood and lymphatic system, leading to a higher recurrence rate. With the stronger toxic and side effects of chemoradiotherapy, most patients will have

vomiting, diarrhea, and other intestinal reactions, and some will even have liver and kidney injury, and cytoreductive surgery can only reduce the tumor volume but does not have the ability of radically curing the tumor, which affects their prognosis and rehabilitation [14, 17]. In this study, according to the summary of long-term clinical experience, the modified Qingre Jiedu formula was applied on the basis of 3D-CRT for treating patients with moderate to late OC.

Relevant studies have confirmed [15] that radical radiotherapy has the same effect as surgery. As a radiotherapy technique applied in the clinic for a long time, conformal radiotherapy can reduce the irradiation dose to the surrounding tissue by adjusting the morphology of the irradiated X-ray [16, 18, 19]. Computer and imaging technology are continuously developing, and as an advanced technology of modern radiotherapy, 3D-CRT is based on the principle of controlling the strength of the subrays in each beam, which then controls the dosage distribution, improving the tumor control rate and reducing the damage to normal tissues and organs to the greatest extent. However, 3D-CRT results in significant radiation to normal tissue outside the irradiated area, in addition to universal and equal intensity irradiation within



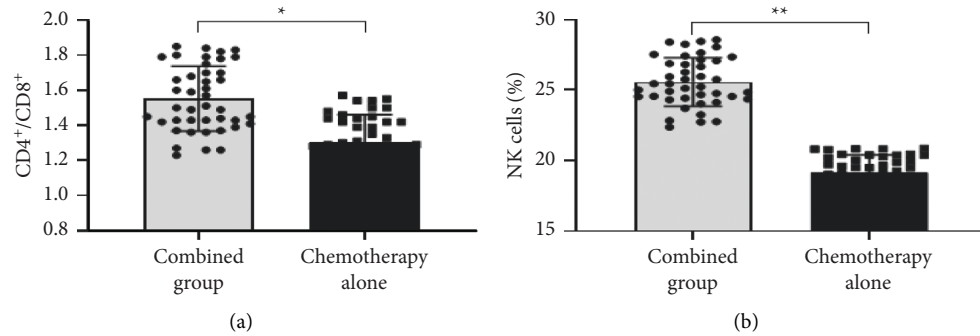


FIGURE 2: Comparison of cellular immune levels after treatment between the two groups (mean  $\pm$  SD,  $n=42$ ). (a) Comparison of the CD4<sup>+</sup>/CD8<sup>+</sup> level values after treatment between the two groups. The horizontal axis indicates the combined group and the single chemotherapy group, and the vertical axis indicates the values. The mean CD4<sup>+</sup>/CD8<sup>+</sup> level values of the combined group and the single chemotherapy group after treatment were  $1.55 \pm 0.19$  and  $1.30 \pm 0.16$ , respectively. \* indicates a significant difference in the mean CD4<sup>+</sup>/CD8<sup>+</sup> level values after treatment between the two groups ( $t=6.523$ ,  $P<0.001$ ). (b) The comparison of the NK cell level values after treatment between the two groups. The horizontal axis indicates the combined group and the single chemotherapy group, and the vertical axis indicates the values in %. The mean NK cell level values of the combined group and the single chemotherapy group after treatment were  $25.56 \pm 1.72\%$  and  $19.13 \pm 1.27\%$ , respectively. \*\* indicates a significant difference in the mean NK cell level values after treatment between the two groups ( $t=19.490$ ,  $P<0.001$ ).

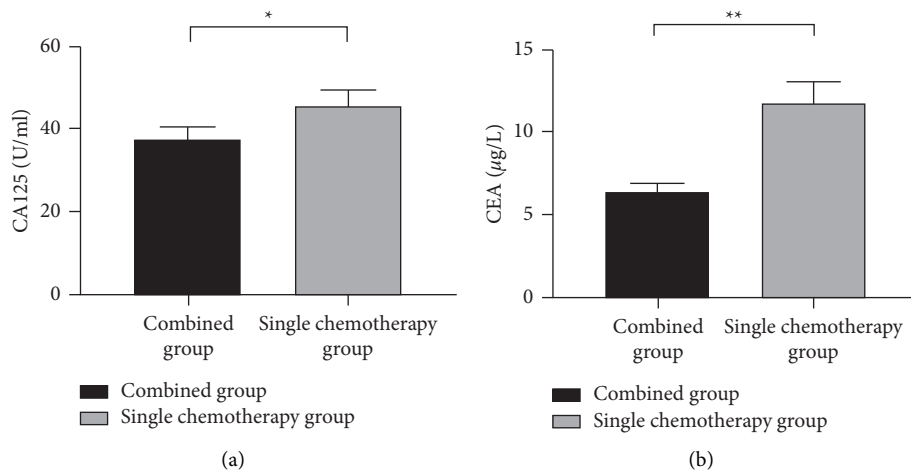


FIGURE 3: Comparison of level values of serum tumor markers between the two groups (mean  $\pm$  SD,  $n=42$ ). (a) The comparison of the CA125 level values after treatment between the two groups. The horizontal axis indicates the combined group and the single chemotherapy group, and the vertical axis indicates the values in U/ml. After treatment, the CA125 level values of the combined group and the single radiotherapy group were  $37.39 \pm 3.07$  and  $45.34 \pm 3.07$ , respectively. \* indicates a significant difference in CA125 level values after treatment between the two groups ( $t=11.867$ ,  $P<0.001$ ). (b) The comparison of the CEA level values after treatment between the two groups. The horizontal axis indicates the combined group and the single chemotherapy group, and the vertical axis indicates the values in  $\mu\text{g/L}$ . After treatment, the CEA level values of the combined group and the single radiotherapy group were  $6.31 \pm 0.58$  and  $11.74 \pm 1.24$ , respectively. \*\* indicates a significant difference in CEA level values after treatment between the two groups ( $t=25.706$ ,  $P<0.001$ ).

the irradiated area [20]. With the rapid development of TCM, its application jointly with chemoradiotherapy in treating tumors has gradually become a research hotspot. TCM holds that [21] OC belongs to the category of “amassment and accumulation,” which causes severe loss of vital qi, blood flow and fluid, and deficiency of both yin and yang, and then leads to the formation of coagulated phlegm, blood stasis, and internal stagnation, which may easily result in tumor recurrence if not promptly eliminated. Modified Qingre Jiedu decoction has efficacy in clearing heat and eliminating toxins, removing stasis, supporting

healthy energy, and invigorating qi and nourishing yin, and among its formula, Mongolian milkvetch root can invigorate qi and spleen, induce diuresis for removing edema, and so on; tuckahoe has the effects of diuresis and diffusing dampness, invigorating the spleen and regulating the stomach, and tranquilizing the mind, and therefore it can enhance body immunity, resist tumors, and protect the liver; Sichuan lovage rhizome can promote blood circulation to remove blood stasis, relieve pain, and reduce swelling; peony root has the function of dissipating blood stasis and relieving pain as well as clearing heat and cooling

TABLE 3: Comparison of survival rates between the two groups ( $n(\%)$ ).

Group	1-year survival rate	2-year survival rate	3-year survival rate
Combined group	38 (90.48%)	32 (76.19%)	26 (61.90%)
Single chemotherapy group	30 (71.43%)	23 (54.76%)	14 (33.33%)
$\chi^2$	4.941	4.266	6.873
$P$	<0.05	<0.05	<0.05

TABLE 4: Comparison of toxic and side effects between the two groups.

Group	Gastrointestinal reaction	Neutropenia	Radiodermatitis	Renal dysfunction	Leukopenia	Total incidence rate
Combined group	2 (4.76)	1 (2.38)	1 (2.38)	1 (2.38)	2 (4.76)	16.67% (7/42)
Single radiotherapy group	5 (11.90)	3 (7.14)	0 (0.00)	3 (7.14)	4 (9.52)	35.71% (15/42)
$\chi^2$						3.941
$P$						<0.05

blood. In modern pharmacology, this formula can accelerate the apoptosis of tumor cells and promote the secretion of immune factors, and its therapeutic efficacy has been demonstrated in advanced cervical cancer [22].

CA125, a glycoprotein detected from OC antigen, is mainly derived from the coelomic epithelium in the embryonic development period and is mostly highly expressed in the serum of OC patients [23]. CEA is a broad-spectrum tumor marker, with a level elevated in the middle to late stages of OC [24, 25]. In this study, the results proved that after treatment, the serum CA125 and CEA levels were significantly lower in the combined group than in the single chemotherapy group ( $P < 0.001$ ), indicating that the combined treatment could effectively kill the tumor cells and reduce tumor burden. In addition, the study also found that the survival rates were significantly better in the combined group than in the single chemotherapy group, indicating that the combined treatment could greatly prolong the survival time of patients with moderate to advanced OC.

The innovations of this study are as follows: ① the comparative analysis between the modified Qingre Jiedu decoction plus 3D-CRT and single chemotherapy was conducted to explore the feasibility of the combination therapy; ② by comparing the total clinical effective rate, survival rate, and toxic and side effects, the advantages of combined treatment in treating moderate to advanced OC were discussed, the application value and clinical meaning of the combined treatment for OC were generally evaluated, and the prospect of clinical application was revealed. The limitations of this study are as follows: ① due to the limited clinical conditions and other factors, only 84 research objects were enrolled in the study, and they were all treated in the local hospitals, so the source of cases lacked diversification; ② only the chemotherapy regimen of taxol plus carboplatin was adopted, and the comparative study with other regimens was lacking; therefore, the completeness of clinical data requires further support from multicenter and large-sample studies. Further confirming that the combined application of modified Qingre Jiedu decoction and 3D-CRT can create a new field for the treatment of OC.

## Data Availability

Data used to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Application Effect of Bladder Function Training Combined with Kangaiping Pills on Permanent Bladder Stoma after Radical Prostatectomy

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**Objective.** To investigate the application effect of bladder function training combined with Kangaiping pills on permanent bladder stoma after radical prostatectomy (RP). **Methods.** The clinical data of 80 patients with a permanent bladder stoma after RP in our hospital from December 2018 to December 2019 were retrospectively analyzed, and they were equally split into the experimental group (EG) and control group (CG) according to the odd and even hospitalization numbers. EG received bladder function training combined with Kangaiping pills while CG received routine nursing for permanent bladder stomas to compare the urodynamic indexes and quality of life (QOL) scores after intervention between the two groups. **Results.** Compared with CG, EG after intervention achieved an obviously higher number of patients with bladder function grade I (\*), higher urodynamic indexes ( $P < 0.001$ ), a higher SF-36 score ( $P < 0.001$ ), a lower LUTS score ( $P < 0.001$ ), and a lower total incidence of postoperative adverse reactions ( $P < 0.05$ ). **Conclusion.** Bladder function training combined with Kangaiping pills is a reliable method to improve the bladder function of patients with a permanent bladder stoma after RP. This intervention method greatly enhances the QOL of patients and reduces the risk of postoperative adverse reactions, which is recommended for clinical application.

## 1. Introduction

Prostate cancer (PC) is a common malignant tumor disease in men, with morbidity and mortality ranking second and sixth in all male malignant tumors worldwide [1, 2]. In recent years, with the acceleration of population aging in China, the harm of PC to Chinese men has been increasing [3]. With the continuous improvement of clinical surgical techniques in China, radical prostatectomy (RP) has become a common surgical approach in clinical practice, as well as a gold standard of surgery for PC [4, 5]. Since RP has changed the normal urination, a permanent bladder stoma is necessary to protect renal function and maintain normal water-electrolyte metabolism and homeostasis.

Cystostomy is mainly used in patients with prostatic hyperplasia who are unable to undergo surgery, urethrostenosis, urethrectomy due to urethrophyma, neurogenic bladder, and other diseases that require urine drainage

[6]. Since patients with a permanent bladder stoma need to carry a fistula device for a long time and are prone to postoperative complications such as urinary tract infection and cystospasm, the implementation of necessary postoperative intervention measures is particularly critical to improving the prognosis of patients [7]. A study [8] has confirmed that effective bladder function training can make detrusor constantly move, which increases the flushing effect of urine, shortens the stay of bacteria, decreases the risk of infection, and plays a positive role in reducing postoperative adverse reactions. In recent years, the intensive research of traditional Chinese medicine (TCM) in cancer has found that the pathogenesis of PC is closely related to the kidney [9]. The combination of internal and external wind, cold, and toxins causes phlegm turbidity and cold coagulation to block blood vessels. Phlegm turbidity, blood stasis, cold coagulation, and cancer toxins mix with each other and cannot be eliminated, eventually leading to diseases after

long-time accumulation. TCM is the treasure of Chinese medicine, which is of great value in the clinical treatment of a variety of diseases, with significant advantages in regulating human organ function and quality of life. Kangaiping pills, composed of more than ten herbs such as loosestrife and herba sarcandrae, can relieve stasis, remove pain, and clear away heat and toxic material [10], thus fighting against tumors and increasing body immunity, which has been confirmed in gastrointestinal tumors such as rectal cancer and gastric cancer [11]. At present, few reports have been found on the clinical efficacy of bladder function training combined with Kangaiping pills. In this study, eighty patients with a permanent bladder stoma after RP in our hospital were selected as the research subjects to explore the effect of this intervention method on the patients, reported as follows.

## 2. Materials and Methods

**2.1. General Information.** Eighty patients with a permanent bladder stoma after RP in our hospital were selected as the research subjects, and all patients completed relevant clinical examinations after admission. It was a retrospective analysis, the provision of patients' informed consent was waived upon the review of the hospital, and the trial met the Declaration of Helsinki (as revised in 2013) [12].

### 2.2. Inclusion and Exclusion Criteria

**2.2.1. Inclusion Criteria.** The inclusion criteria were as follows: (1) patients who met the PC diagnostic criteria and were confirmed by pathological examinations, with an age  $\leq 75$  years; (2) patients who had clear consciousness, could move freely, and were willing to cooperate; and (3) patients who had no distant metastasis and no other serious complications.

**2.2.2. Exclusion Criteria.** The exclusion criteria were as follows: (1) patients with other types of cancer; (2) patients who were discharged during the study; (3) patients suffering from serious chronic diseases; and (4) patients who were delirious and unable to express subjective wishes on their own.

**2.3. Methods.** Routine nursing for permanent bladder stomas was performed to the 40 patients in CG. The surgeons determined the patients' degree of recovery by observing their stoma status for the physicians to prepare medication and rehabilitation plans. The nurses explained the preoperative preparation, the importance, and specific steps of permanent cystostomy and introduced the characteristics and usage of different urostomy pouches and other auxiliary supplies to the patients and their families. The nurses instructed the patients to choose suitable stoma care supplies and carefully explained and demonstrated the replacement of urostomy pouches and precautions. They also carried out clinical health education, with diet and discharge guidance to the patients [13, 14].

Bladder function training combined with Kangaiping pills was performed to the 40 patients in EG. Bladder function training was implemented as follows. The patients were told to drink enough water to ensure the daily water intake of 1.5–2.0 L, and personalized programs for drinking water were formulated according to the daily eating habits of patients. In terms of trigger point urination training, the patients were instructed to separate their legs and imagine the sensation of urination while their inner thigh and suprapubic region were stimulated, and their feedback of the urination stimulation points was timely recorded. The stimulation was strengthened to promote detrusor contraction and activate autonomous urination reflex, and the training was performed once a day, five times a week, and consecutively for 4 weeks. According to the physician's prescription, the pharmacists gave patients the Kangaiping pills (manufacturer: Hebei Hongri Yaodu Pharmaceutical Co., Ltd.; NMPA approval no. Z46020009; specification: 1 g \* 18 bottles), with the dosage of 0.5–1.0 g each time and 3 times a day, and the dose could be controlled within 0.5 g at the first-time administration and then could be added gradually, and if patients felt distention in the stomach, the dose could be reduced appropriately. With 3 weeks as a course of treatment, the patients took 2 courses continuously.

### 2.4. Evaluation Indexes

**2.4.1. Classification of Bladder Function.** The residual urine volume under B ultrasound after extubation was recorded in both groups, with the volume  $< 50$  ml as grade I, 50–100 ml as grade II,  $> 100$  ml as grade III, and severe dysuria as grade IV.

**2.4.2. Urodynamic Indexes.** The urodynamic equipment (manufacturer: Shanghai Hanfei Medical Device Co., Ltd.; model: Nidoc 970A) was used to measure the Valsalva leak point pressure (LPP) and maximum urethral closure pressure (MUCP) of both groups after intervention. The international lower urinary tract symptom score (LUTS) [15] was used to evaluate the urination status of both groups after the intervention, including 7 items, with each item scoring 5 points and a total score of 35 points. A higher score represented worse urination function. The SF-36 scale [16] was used to evaluate the quality of life (QOL) of both groups after the intervention, including physical pain, physiological function, and emotional function, with a total score of 100 points. A higher score demonstrated better QOL. The incidence of postoperative adverse reactions in both groups was recorded.

**2.5. Statistical Methods.** The data were processed by the professional statistical software SPSS26.0 and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The enumeration data were tested by  $\chi^2$  and expressed as  $n$  (%), while the measurement data were tested by  $t$ -test and expressed as Mean  $\pm$  SD. When  $P < 0.05$ , the differences were statistically significant.

TABLE 1: Comparison of clinical data ( $n = 40$ ).

Items	EG	CG	$\chi^2/t$	$P$
Average age (mean $\pm$ SD, years)	65.83 $\pm$ 3.46	65.79 $\pm$ 3.52	0.051	0.959
BMI (mean $\pm$ SD, kg/m <sup>2</sup> )	21.72 $\pm$ 1.35	21.76 $\pm$ 1.42	0.129	0.898
Hypertension			0.202	0.653
Yes	17 (42.50%)	19 (47.50%)		
No	23 (57.50%)	21 (52.50%)		
Diabetes			0.219	0.640
Yes	11 (27.50%)	13 (32.50%)		
No	29 (72.50%)	27 (67.50%)		
Family income			0.205	0.651
$\geq 3000$ yuan/(month/person)	16 (40.00%)	18 (45.00%)		
$< 3000$ yuan/(month/person)	24 (60.00%)	22 (55.00%)		
Residence ( $n$ (%))			0.453	0.501
Urban area	17 (42.50%)	20 (50.00%)		
Rural area	23 (57.50%)	20 (50.00%)		
Education ( $n$ (%))				
College degree or above	2 (5.00%)	3 (7.50%)	0.213	0.644
Senior high school	6 (15.00%)	4 (10.00%)	0.457	0.499
Junior high and below	32 (80.00%)	33 (82.00%)	0.082	0.775

TABLE 2: Comparison of changes in bladder function classification ( $n$  (%)).

Group	$n$	Grade I	Grade II	Grade III	Grade IV
EG	40	27 (67.50)	11 (27.50)	2 (5.00)	0 (0.00)
CG	40	18 (45.00)	13 (32.50)	6 (15.00)	3 (7.50)
$\chi^2$		4.114	0.219	2.222	3.117
$P$		$< 0.05$	0.640	0.136	0.077

TABLE 3: Comparison of urodynamic indexes after intervention (mean  $\pm$  SD, kPa).

Group	$n$	LPP	MUCP
EG	40	11.82 $\pm$ 1.35	37.64 $\pm$ 3.27
CG	40	9.26 $\pm$ 1.17	29.29 $\pm$ 3.31
$T$		9.063	11.350
$P$		$< 0.001$	$< 0.001$

### 3. Results

**3.1. Clinical Data.** No notable differences were observed in the average age, family income, and residence of patients between the two groups ( $P < 0.001$ ) (see Table 1).

**3.2. Comparison of Changes in Bladder Function Classification.** After intervention, the numbers of cases with bladder function grade I, II, III, and IV were, respectively, 27, 11, 2, and 0 in EG and were, respectively, 18, 13, 6, and 3 in CG. The numbers of cases with bladder function grade I were significantly different between the two groups ( $P < 0.05$ ), as presented in Table 2.

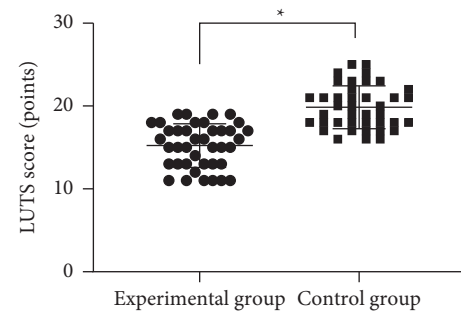


FIGURE 1: Comparison of LUTS scores between the two groups after intervention (mean  $\pm$  SD). *Note.* The abscissa represented EG and CG, and the ordinate represented the LUTS score (points). The average LUTS scores of EG and CG after intervention were (15.23  $\pm$  2.63) and (19.85  $\pm$  2.59), respectively. \*represents a notable difference in the average LUTS scores after intervention between the two groups ( $t = 7.916$ ,  $P < 0.001$ ).

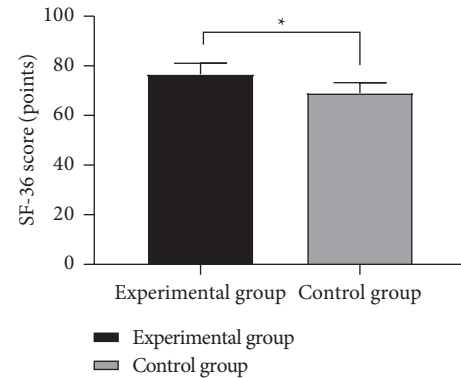


FIGURE 2: Comparison of SF-36 scores between the two groups after intervention (mean  $\pm$  SD). *Note.* The abscissa represented EG and CG, and the ordinate represented the SF-36 score (points). The SF-36 scores of EG and CG after intervention were (76.60  $\pm$  4.44) and (69.00  $\pm$  4.21), respectively. \*represents a notable difference in the SF-36 scores after intervention between the two groups ( $t = 7.856$ ,  $P < 0.001$ ).

**3.3. Urodynamic Indexes.** Table 3 presented obviously higher LPP and MUCP values in EG than in CG after intervention ( $P < 0.001$ ).

**3.4. LUTS Scores.** In terms of urinary function, the average LUTS score in EG after intervention was remarkably lower compared with CG ( $P < 0.001$ ) (see Figure 1).

**3.5. QOL.** In terms of QOL, after intervention, the total QOL score in EG was notably higher compared with CG ( $P < 0.001$ ) (see Figure 2).

**3.6. Incidence of Postoperative Adverse Reactions.** Peristomal skin infection is a common type of postoperative complication in patients undergoing RP. After surgery, 1 case in EG had peristomal skin infection, and there were 2 cases with urinary tract obstruction, 1 case with cystospasm, and 3 cases with peristomal skin infection in CG. Compared with CG, EG achieved a lower total incidence of postoperative adverse reactions ( $P < 0.05$ ), as shown in Table 4.



TABLE 4: Comparison of occurrence of postoperative adverse reactions ( $n$  (%)).

Group	$n$	Urinary tract obstruction	Cystospasm	Skin infection around the stoma	Total incidence
EG	40	0 (0.00)	0 (0.00)	1 (2.50)	2.50% (1/40)
CG	40	2 (5.00)	1 (2.50)	3 (7.50)	15.00 (6/40)
$X^2$					3.914
$P$					<0.05

#### 4. Discussion

In China, prostate cancer (PC) has become one of the malignant tumors with the fastest rising morbidity and mortality in recent years due to the gradual aging of population structure, westernization of living and eating habits, and the application and promotion of prostate-specific antigen (PSA) screening [17]. PC progresses rapidly and can easily pose a threat to the life safety of patients without timely treatment. With the advantages of the open surgical field and easy operation, radical prostatectomy (RP) is currently one of the most effective methods for PC treatment and can complete pelvic lymphadenectomy via the same approach, which is favored by doctors and patients. Permanent cystostomy is the surgical treatment for urethral obstruction with suprapubic cystostomy to achieve permanent urinary diversion, which is clinically applicable to many diseases such as total urinary tract resection of urethral tumors and neurogenic bladder [18]. However, many adverse effects such as blocked stoma tube and skin infection around the stoma can occur after cystostomy. Combined with the inconvenience to the patients' mobility caused by a permanent bladder stoma, these effects seriously affect QOL of the patients and arouse their resistance to treatment, thus hindering postoperative rehabilitation.

A study [19] has confirmed that early bladder function training after surgery can enhance the pressure of the sphincter, pelvic floor muscle, and urethra, promote the recovery of bladder function, improve urination, and help patients return to normal life as soon as possible. With the continuous development of modern Chinese medicine, traditional Chinese medicine (TCM) has been widely used in treating various types of malignant tumors. Kangaiping pills, composed of loosestrife, barbed skullcup herb, hedyotis, Indian mock strawberry, actinidia chinensis planch, toad venom, all-grass of Bluecalyx Japanese Radosia, sarcandra, common bluebeard herb, and herba selaginellae doederleinii, conform to the TCM concept of strengthening the body and restoring normal function in clinical treatment [20]. The pills can effectively activate the anticancer factors of the human body, which plays an important role in improving the autoimmunity of patients with malignant tumors, and are often used to treat the digestive system malignant tumors such as gastric cancer, esophageal cancer, and rectal cancer [21, 22].

In this study, the number of cases with bladder function grade I was markedly higher in EG than in CG after intervention ( $P < 0.05$ ), suggesting that bladder function training combined with Kangaiping pills can effectively improve the bladder function of patients with a permanent bladder stoma after RP. The reason may be that bladder

function training adopted in this study can stimulate the inner thigh and suprapubic region to find the urination stimulation points, promote detrusor contraction, and activate spontaneous micturition reflex by strengthening stimulation, while the application of Kangaiping pills can effectively inhibit the metastasis and proliferation of tumor cells, protect the hematopoietic function of patients, improve clinical symptoms, and indirectly accelerate the improvement of bladder function [23]. In terms of urodynamic indexes and voiding condition, patients who received bladder function training combined with Kangaiping pills intervention had more significant results, because bladder function training can effectively stimulate the recovery of bladder function, help regulate the periodic contraction rhythm of the bladder, train the awareness of urination, and maintain the maximum capacity and pressure of the bladder, and Kangaiping pills can better promote the reverse differentiation of tumor cells, control the continued spread of metastases, reduce symptoms, improve the functional condition of the body, and promote the improvement of urination function. In the clinical education of cystostomy, bladder function training should be actively carried out in addition to increasing water intake, keeping stoma clean and dry, and timely replacing bladder fistula. The stoma left in the bladder and open to the outside world provides the possibility for bacteria to enter the bladder [24]. In addition, as a foreign body, the fistula remaining in the bladder for a long time greatly damages the normal bladder environment. Therefore, the patients are prone to various adverse reactions. This study demonstrated that EG had a notably lower total incidence of adverse reactions after intervention compared with CG ( $P < 0.05$ ), illustrating that the bladder function training combined with Kangaiping pills can effectively reduce the incidence of postoperative adverse reactions in patients. It is speculated that bladder function training can effectively stimulate detrusor activity, enhance the flushing effect of urine, and greatly shorten the stay of bacteria in the bladder, thereby reducing the possibility of bacterial infection, avoiding the spasm due to the stimulation of fistula to the bladder mucosa to a certain extent, and promoting urination [25]. In addition, in terms of QOL, the SF-36 score in EG after the scientific intervention was obviously higher than that in CG ( $P < 0.001$ ), demonstrating that the implementation of bladder function training for patients with a permanent bladder stoma can help improve urination, reduce the occurrence of adverse reactions, and enhance QOL. This study also has some inadequacies, such as a small sample size and a lack of research about the effect of age and bladder function before treatment on the findings of this study due to the limitations of research conditions. Therefore, in future treatment, the bladder function of such

patients should be evaluated, and more scientific and systematic postoperative intervention measures should be formulated to reduce the adverse reactions after colostomy, alleviate the pain, relieve the economic burden, and improve QOL of patients.

## Abbreviations:

EG:	Experimental group
CG:	Control group
RP:	Radical prostatectomy
QOL:	Quality of life
PC:	Prostate cancer
TCM:	Traditional Chinese medicine
MUCP:	Maximum urethral closure pressure
LPP:	Valsalva leak point pressure
LUTS:	Lower urinary tract symptom score
PSA:	Prostate-specific antigen.

## Data Availability

The data to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Kefu Sha1 and Yue Zhao contributed equally to this article.

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## Retraction

# Retracted: PTPN18 Stimulates the Development of Ovarian Cancer by Activating the PI3K/AKT Signaling

### Evidence-Based Complementary and Alternative Medicine

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

- (1) Discrepancies in scope
- (2) Discrepancies in the description of the research reported
- (3) Discrepancies between the availability of data and the research described
- (4) Inappropriate citations
- (5) Incoherent, meaningless and/or irrelevant content included in the article
- (6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

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- [1] N. Mao, H. Li, H. Yang, J. Su, Z. Liang, and G. He, "PTPN18 Stimulates the Development of Ovarian Cancer by Activating the PI3K/AKT Signaling," *Evidence-Based Complementary and Alternative Medicine*, vol. 2022, Article ID 1091042, 7 pages, 2022.

## Research Article

# PTPN18 Stimulates the Development of Ovarian Cancer by Activating the PI3K/AKT Signaling

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**Objective.** To illustrate the functions of protein tyrosine phosphatase nonreceptor type 18 (PTPN18) in the progression of ovarian cancer and the potential molecular mechanism. **Methods.** Differential PTPN18 expression in ovarian cancer samples was determined. Following PTPN18 knockdown, changes in proliferation and migration in ovarian cancer cells were detected. Nude mice with ovarian cancer were used to uncover the effects of PTPN18 on ovarian cancer growth in vivo. **Results.** PTPN18 was significantly upregulated in ovarian cancer samples and linked to pathological staging and metastasis rate. PTPN18 displayed prognostic and diagnostic potentials in ovarian cancer. Knockdown of PTPN18 and treatment of the PI3K inhibitor could inhibit proliferative and migratory abilities in ovarian cancer cells. Moreover, PTPN18 was capable of inactivating PI3K/AKT signaling. In vivo knockdown of PTPN18 suppressed ovarian cancer growth in nude mice. **Conclusions.** PTPN18 is upregulated in ovarian cancer, which stimulates the malignant development by activating PI3K/AKT signaling. The PTPN18 level is also associated with pathological staging and metastasis in ovarian cancer patients, which may be utilized as a hallmark predicting the malignant level.

## 1. Introduction

Ovarian cancer (OC) is one of the most common gynecological malignancies [1, 2]. Most patients are diagnosed as the advanced ovarian cancer or ovarian cancer accompanied by intraperitoneal implantation and metastasis, leading to a high mortality rate [1, 3]. Despite improvements achieved in surgical techniques and chemotherapy, the effective treatment rate of advanced OC is only 15–20% [4–6]. The Wnt, Notch, Hedgehog, and PI3K signaling are believed to influence the development of ovarian cancer [7–10]. At present, targeted therapy of ovarian cancer is well concerned. Clarifying ovarian cancer-associated signaling contributes to block the recurrence and metastasis, thus improving the clinical outcomes [11, 12].

Protein tyrosine phosphatase nonreceptor type 18 (PTPN18) is the first discovered specific tyrosine phosphatase of human epidermal growth factor receptor 2 (HER2), which is closely linked to tumor development [13, 14]. Protein tyrosine phosphatases influence cell growth

and other cellular functions under external stimuli [13]. PTPN18 has a strict substrate specificity, and it can only dephosphorylate the phosphorylated tyrosine residues of HER2 [13, 15]. PTPN18 negatively regulates HER2 tyrosine kinase activity mainly through selectively dephosphorylating the tyrosine phosphorylation site of HER2, thereby effectively regulating cell function [13]. Previous evidence reported the expression of PTPN18 in kinds of tumor cell lines [13, 14]. In addition, it is able to inhibit the progression of chronic myeloid leukemia and to influence functions of hematopoietic stem cells [13, 14, 16].

As a vital pathway, the phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signaling is of significance in regulating cell activities [17, 18]. During tumor development, the PI3K/AKT signaling is overactivated, which is responsible for mediating malignant phenotypes of tumor cells [17–20]. Here, we explored the functions of PTPN18 and its potential mechanism in the malignant development of ovarian cancer.

## 2. Patients and Methods

**2.1. Ovarian Cancer Patients Enrolled in the Study.** Ovarian cancer tissues and paracancerous ones were collected from 44 patients without anticancer treatment. This study was approved by the Ethics Committee of Guangzhou Panyu Central Hospital (16GZ-EC403). Informed consent was also obtained from each subject before the study.

**2.2. Cell Lines and Reagents.** Six human-derived OC cell lines (SKOV3, OVCAR3, PEO1, A2780, 3AO, and CAO3) and a human ovarian surface epithelial cell line (HOSEPICs) were obtained from American Type Culture Collection (ATCC) (Manassas, VA, USA). Dulbecco modified Eagle medium (DMEM) supplemented with 10% fetal bovine serum (FBS) (Gibco, Rockville, MD, USA), 100 U/mL penicillin, and 100 µg/mL streptomycin DMEM (Gibco, Rockville, MD) was used for cells culture in an incubator with 5% CO<sub>2</sub> at 37°C.

**2.3. Transfection.** Cells with 30–40% confluence were transfected with transfection plasmids, GenePharma (Shanghai, China), via Lipofectamine 2000 reagent (Invitrogen company, Carlsbad, CA, USA).

**2.4. Cell Counting Kit-8 (CCK-8) Assay.** The cells were seeded in 96-well plates with  $2 \times 10^3$  cells in each well. The absorbance value of each sample at 490 nm was recorded using the Cell Counting Kit-8 (CCK-8) (Dojindo Laboratories, Kumamoto, Japan) at the specified time point to plot the survival curve.

**2.5. Transwell Migration.** 700 µL medium containing 10% FBS and 200 µL suspension ( $5.0 \times 10^5$ /ml) was added to the upper and bottom of the transwell chamber (Millipore, Billerica, MA, USA), respectively. 48 h later, the fixed cells at the bottom were stained with crystal violet for 20 min. Finally, the number of migrating cells was calculated in 5 randomly selected regions in each sample.

**2.6. qRT-PCR.** RNA extracted with TRIzol reagent (Invitrogen, Carlsbad, CA, USA) was purified by the DNase I using PrimeScript RT reagent (TaKaRa, Otsu, Japan) and was reversely transcribed into cDNA. Quantitative real-time polymerase chain reaction (QRT-PCR) was performed on the obtained cDNA using SYBR® Premix Ex Taq™ (TaKaRa, Otsu, Japan). The  $2^{-\Delta\Delta C_t}$  method was used for the analysis of the relative level of PTPN18 normalized to glyceraldehyde-3-phosphate dehydrogenase (GAPDH). PTPN18: forward: 5'-TTAATGGCAACTTCATCCG-3', reverse: 5'-TCACCTTGACCCCAAACTC-3'; GAPDH: forward: 5'-TGACTTCAACAGCGACACCA-3', reverse: 5'-CACCTGTTCGTAGCCAAA-3'.

**2.7. Western Blotting.** Cells were lysed to separate proteins. Protein was loaded on polyvinylidene fluoride (PVDF) membranes (Millipore, Billerica, MA, USA). Then,

membranes were blocked in 5% skim milk for 2 hours. After being incubated with primary and secondary antibodies, the band exposure and analysis were performed.

**2.8. Nude Mice Tumorigenicity Assay.** The animal ethics and use committee approved the experimental procedures for the in vivo xenograft model of ovarian cancer in nude mice. Ten male nude mice were randomly divided into two groups ( $n = 5$ ) and were injected subcutaneously with A2780 cells transfected with sh-NC and sh-PTPN18#1, respectively. Tumor size was recorded weekly. Mice were sacrificed after 6 weeks to collect tumor tissue. Ovarian cancer tissue sections from nude mice were blocked and incubated with anti-PTPN18.

**2.9. Statistical Analyses.** SPSS 19.0 software (IBM, Armonk, NY, USA) was used for data analyses. Comparison between multiple groups was done using the one-way ANOVA test followed by the post hoc test (least significant difference) (with 95% confidence interval). Percentage (%) was used to express the enumeration data, and the chi-square test was used for data analysis. Kaplan–Meier and ROC curves were depicted for analyzing the prognostic and diagnostic potentials of PTPN18 in ovarian cancer, respectively.  $P < 0.05$  was considered as statistically significant.

## 3. Results

**3.1. Upregulation of PTPN18 in Ovarian Cancer Samples.** We found higher level of PTPN18 in OC tissues than paracancerous tissues (Figure 1(a)). Identically, PTPN18 was highly expressed in OC cell lines (Figure 1(b)).

The median level of PTPN18 was calculated in 44 included OC tissues. Subsequently, patients were divided into the high PTPN18 group or low PTPN18 expression group, respectively. It showed that PTPN18 level was positively linked to pathological staging, lymphatic metastasis, and distant metastasis in OC patients (Table 1). In addition, survival analysis demonstrated that PTPN18 was a risk factor of prognosis in OC (Figure 1(c)). ROC curves confirmed the diagnostic potential of PTPN18 in ovarian cancer (Figure 1(d)).

**3.2. Knockdown of PTPN18 Attenuated Proliferation and Migration in OC.** Transfection of either sh-PTPN18#1 or sh-PTPN18#2 could significantly decrease PTPN18 in A2780 and CAO3 cells (Figure 1(e)). Knockdown of PTPN18 decreased viability in ovarian cancer cells (Figure 2(a)). Moreover, the number of migratory cells was lower in A2780 and CAO3 cells with sh-PTPN18#1 or sh-PTPN18#2 than those of controls (Figure 2(b)).

**3.3. Knockdown of PTPN18 Inactivated PI3K/AKT Signaling in Ovarian Cancer.** Transfection with sh-PTPN18#1 or sh-PTPN18#2 decreased p-PI3K, p-AKT, and p-mTOR in A2780 and CAO3 cells (Figure 3(a)). To further explore the interaction between PTPN18 and PI3K/AKT pathways, LY294002 (inhibitor of PI3K) was applied. LY294002

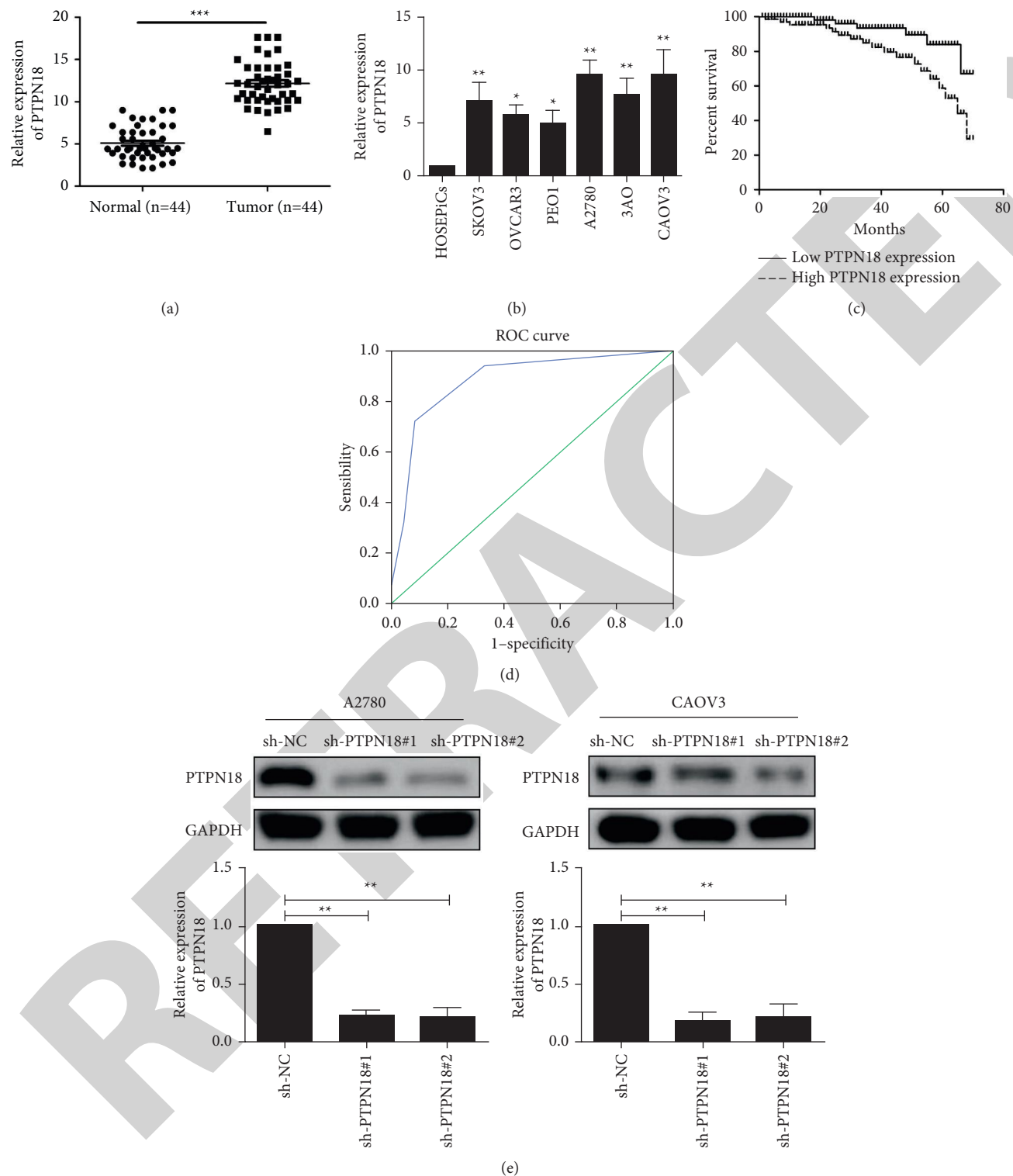


FIGURE 1: Upregulation of PTPN18 in ovarian cancer samples. (a) Differential expression of PTPN18 in OC tissues and paracancerous ones. (b) PTPN18 level in ovarian cancer cell lines. (c) Overall survival in ovarian cancer patients based on their PTPN18 level. (d) ROC curves showing specificity and sensitivity in diagnostic potential of PTPN18 in ovarian cancer. (e) Transfection efficacy of sh-PTPN18#1 and sh-PTPN18#2 in A2780 and CAOV3 cells. Data are expressed as mean  $\pm$  SD. \*\* $P < 0.05$ , \*\*\* $P < 0.001$ .

TABLE 1: Clinicopathologic characteristics of the enrolled patients with ovarian cancer in low and high PTPN18 groups.

Indexes	N	PTPN18		P
		Low (n = 24)	High (n = 20)	
Age (y)				0.956
<60	20	11	9	
≥60	24	13	11	
T staging				0.047
T1/T2	26	17	9	
T3/T4	18	7	11	
Lymph node metastasis				0.040
No	25	17	8	
Yes	19	7	12	
Distance metastasis				0.019
No	28	19	9	
Yes	16	5	11	

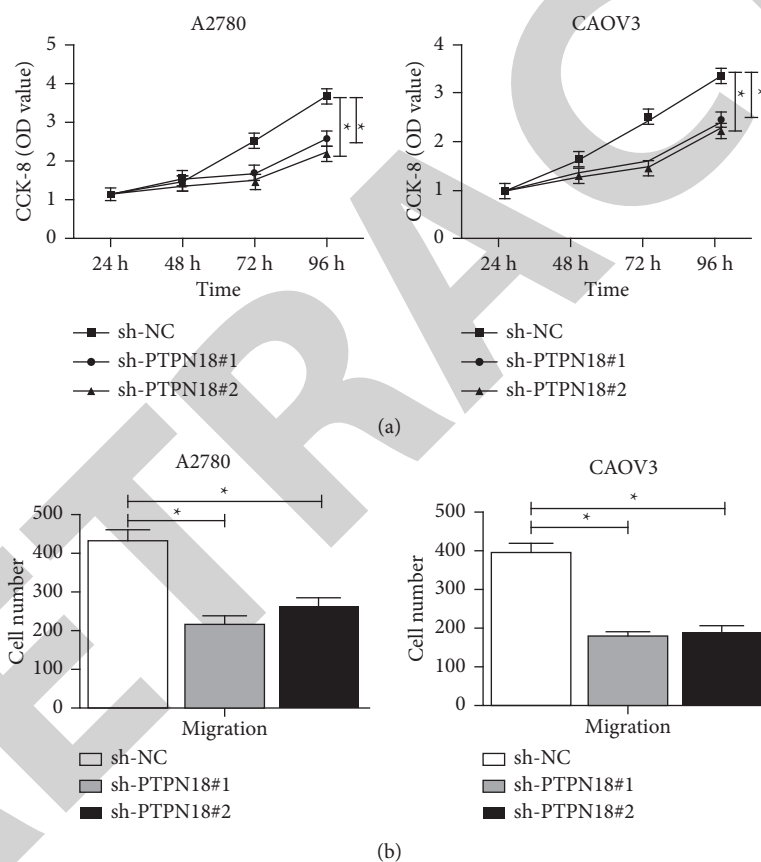


FIGURE 2: PTPN18 knockdown inhibited proliferation and migration of OC. (a) Viability in A2780 and CAOV3 cells transfected with sh-NC, sh-PTPN18#1, or sh-PTPN18#2, respectively. (b) Migration in A2780 and CAOV3 cells with sh-PTPN18#1, sh-PTPN18#2, or sh-NC, respectively (magnification: 40×). \*  $P < 0.05$ .

induction decreased protein level of PTPN18 in ovarian cancer cells (Figure 3(b)). Viability and migratory cell number in A2780 and CAOV3 cells were also reduced following LY294002 treatment (Figures 3(c), 3(d)).

**3.4. Knockdown of PTPN18 Inhibited Tumorigenesis of Ovarian Cancer.** A2780 cells with sh-NC or sh-PTPN18#1 were administrated into the left armpit of nude mice.

Apparently, tumor volume was significantly smaller in OC tissues of mice with PTPN18 knockdown ( $P < 0.05$ ) (Figure 4(a)). As expected, knockdown of PTPN18 markedly decreased the weight of harvested ovarian cancer ( $P < 0.001$ ) (Figure 4(b)). Both Western blot and IHC results showed significantly lower level of PTPN18 in ovarian cancer tissues harvested from mice administrated with sh-PTPN18#1 than those of controls ( $P < 0.001$ ) (Figures 4(c), 4(d)).

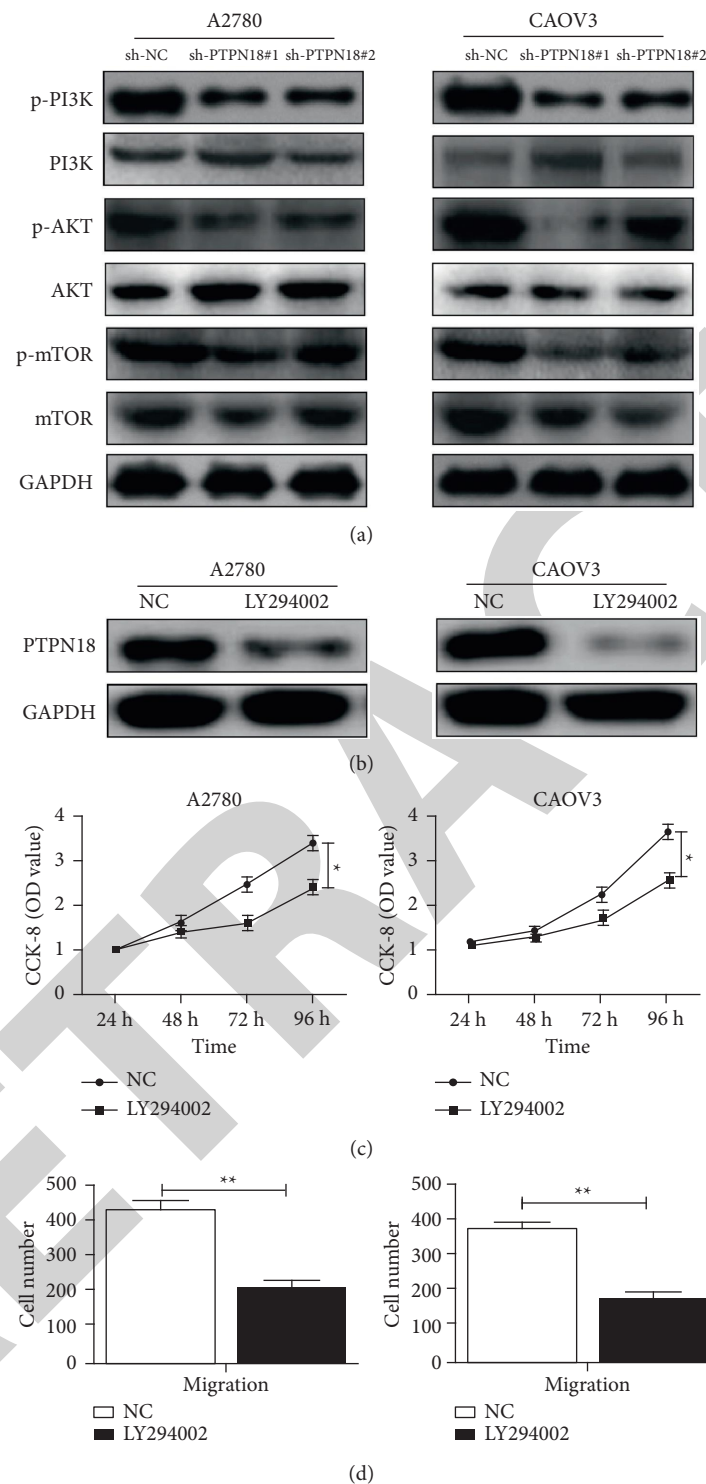


FIGURE 3: Knockdown of PTPN18 inactivated PI3K/AKT signaling in ovarian cancer. (a) Protein levels of p-AKT, AKT, p-mTOR, p-PI3K, PI3K, and mTOR in A2780 and CAOV3 cells transfected with sh-NC, sh-PTPN18#1, or sh-PTPN18#2, respectively. (b) Protein level of PTPN18 in A2780 and CAOV3 cells induced with LY294002. (c) Viability in A2780 and CAOV3 cells induced with LY294002. (d) Migration in A2780 and CAOV3 cells induced with LY294002. \* $P < 0.05$ , \*\* $P < 0.01$ .



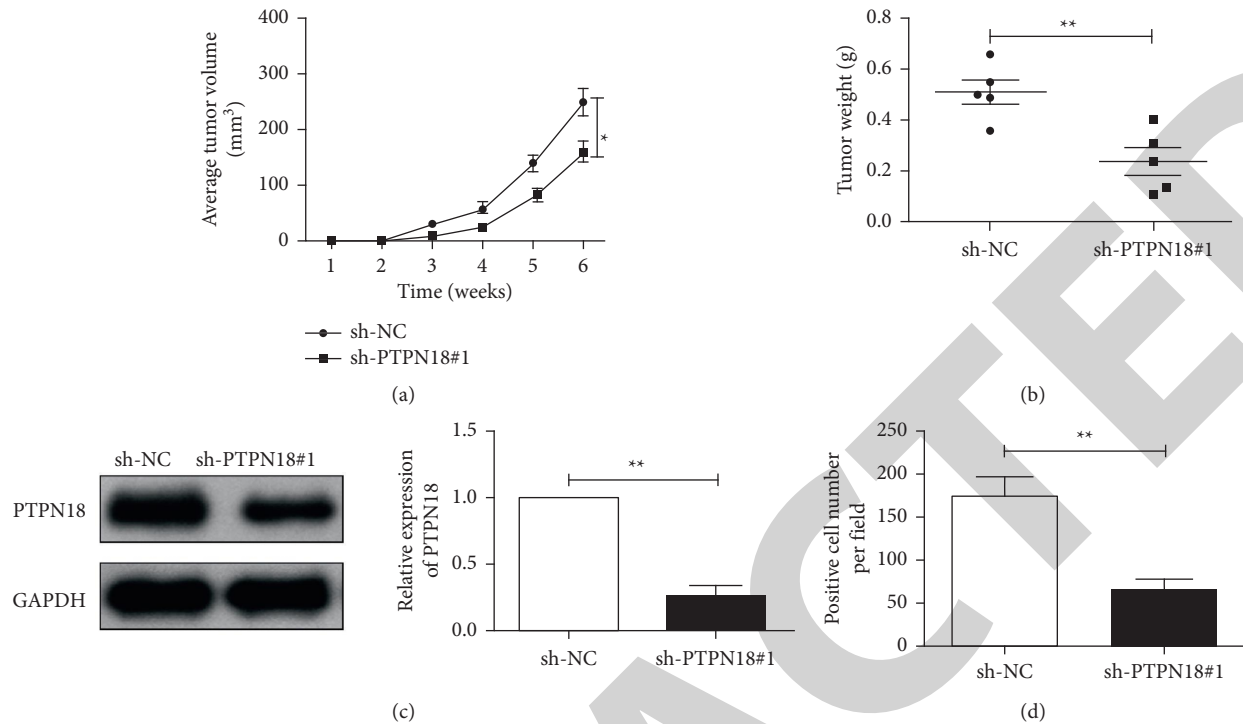


FIGURE 4: PTPN18 knockdown inhibited tumorigenesis of ovarian cancer. (a) Tumor volume that was weekly recorded in nude mice administrated with A2780 cells transfected with sh-NC or sh-PTPN18#1. (b) Tumor weight in nude mice administrated with A2780 cells transfected with sh-NC or sh-PTPN18#1. (c) Protein level of PTPN18 in ovarian cancer tissues collected from nude mice administrated with A2780 cells transfected with sh-NC or sh-PTPN18#1. (d) Positive level of PTPN18 in ovarian cancer tissues collected from nude mice administrated with A2780 cells transfected with sh-NC or sh-PTPN18#1. \* $P < 0.05$ , \*\* $P < 0.01$ .

#### 4. Discussion

Ovarian cancer is featured by high malignant level, fast growth, and high metastasis rate. Metastasis and recurrence are the two major events resulting in poor prognosis in ovarian cancer patients. In addition, endocrine therapy, TCM therapy, target drugs, and immunity treatment are also beneficial to ovarian cancer patients. Early discovery and diagnosis of cancer are of great significance. It is urgent to seek for effective hallmarks and therapeutic targets of ovarian cancer.

PTPN18 has been identified to regulate tumor cell behaviors. Our findings uncovered that highly expressed PTPN18 was associated with pathological staging and metastasis in ovarian cancer patients. Silence of PTPN18 remarkably suppressed proliferation and migration in OC cells. Moreover, in vivo knockdown of PTPN18 inhibited tumorigenesis in nude mice bearing ovarian cancer, manifesting as smaller tumor size and lower tumor weight than those of controls. It is demonstrated that PTPN18 was an oncogene in ovarian cancer.

Abnormally activated PI3K/AKT signaling is capable of stimulating tumor cell growth and metastasis [17, 18]. PI3K can specifically phosphorylate the 3-hydroxy group in inositol phosphate ring [17, 19]. Akt, also known as PKB, is the downstream target of PI3K [18–20]. Knockdown of PTPN18 decreased p-mTOR p-PI3K and p-AKT in OC cells. Application of LY294002, the PI3K/AKT inhibitor, achieved

the same results as PTPN18 knockdown in ovarian cancer cells. Collectively, PTPN18 contributed to ovarian cancer deterioration by activating PI3K/AKT signaling. There are very obvious deficiencies in this study. For example, we simply tested the role of PTPN18 in several ovarian cancer cell lines. The effects of knockdown or overexpression of PTPN18 in mice models should be further explored. Additionally, the sample of the OC patients was small, which seriously weakened the evidence level of our conclusions. In the future, we plan to enlarge the sample size and also to further perform the in vivo experiments, thus to deeply investigate the biofunctions PTPN18 in OC and to elucidate the potential underlying molecular mechanism in the process.

#### 5. Conclusions

PTPN18 is upregulated in ovarian cancer, which stimulates the malignant development by activating PI3K/AKT signaling. The PTPN18 level is also associated with pathological staging and metastasis in ovarian cancer patients, which may be utilized as a hallmark predicting the malignant level.

#### Data Availability

The datasets used and analyzed during the current study are available from the corresponding author upon request.



## Retraction

# Retracted: Effect of Combined Spinal-Epidural Anesthesia and Total Intravenous Anesthesia on Hemodynamics and Pregnancy Outcomes of Severe Preeclampsia Pregnant Patients Undergoing Cesarean Section

### Evidence-Based Complementary and Alternative Medicine

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- [1] G. Wang, P. Zhang, M. Li, X. Wu, and H. Li, "Effect of Combined Spinal-Epidural Anesthesia and Total Intravenous Anesthesia on Hemodynamics and Pregnancy Outcomes of Severe Preeclampsia Pregnant Patients Undergoing Cesarean Section," *Evidence-Based Complementary and Alternative Medicine*, vol. 2022, Article ID 2655858, 6 pages, 2022.

## Research Article

# Effect of Combined Spinal-Epidural Anesthesia and Total Intravenous Anesthesia on Hemodynamics and Pregnancy Outcomes of Severe Preeclampsia Pregnant Patients Undergoing Cesarean Section

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**Objective.** The purpose of the study was to investigate the effect of combined spinal-epidural anesthesia (CSEA) and total intravenous anesthesia (TIVA) on hemodynamics and pregnancy outcomes of severe preeclampsia pregnant patients undergoing cesarean section. **Methods.** 126 patients with severe preeclampsia admitted to Zhangqiu District People's Hospital from August 2018 to August 2019 were selected as the study subjects and randomly divided into the experimental group ( $n = 63$ ) and control group ( $n = 63$ ). After undergoing cesarean section, the patients in the experimental group received CSEA, while those in the control group were given TIVA. After that, the effect of different anesthesia methods on the hemodynamics and pregnancy outcomes of pregnant women was compared. **Results.** There were no significant differences in age, BMI value, weight, height, gestational weeks, SBP, DBP, and residence between the two groups ( $P > 0.05$ ). The operation duration, the onset time of anesthesia, and delivery time in the experimental group were significantly shorter than those in the control group, with less intraoperative blood loss in the experimental group than that in the control group ( $P < 0.001$ ). In both groups, MAP and  $SpO_2$  during delivery were significantly lower than those before anesthesia, and HR was significantly higher than that before anesthesia ( $P < 0.001$ ). In the experimental group, MAP and HR during delivery were significantly lower than those in the control group, and  $SpO_2$  was significantly higher than that in the control group ( $P < 0.001$ ). The total effective rate of anesthesia in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ). The Apgar scoring of the newborns in the experimental group was significantly higher than that in the control group ( $P < 0.001$ ), and the total incidence of postoperative adverse reactions in the experimental group was significantly lower than that in the control group ( $P < 0.05$ ). **Conclusion.** CSEA is a reliable anesthesia method for improving the hemodynamics indicators in pregnant patients with severe preeclampsia; such strategy greatly increases the Apgar score of newborns and shortens the anesthesia onset time. Further research will be conducive to establishing a better anesthesia plan for such patients.

## 1. Introduction

Preeclampsia, a common pregnancy complication mostly occurring after 20 weeks of gestation, is mainly manifested by elevated blood pressure and proteinuria. With the progress of the disease, severe preeclampsia will further develop into eclampsia, which results in convulsions or coma of puerperae and induces some complications such as heart failure, retinal detachment, and placental abruption, seriously threatening maternal and infant health [1, 2]. The latest data from the World Health Organization showed that the incidence of severe preeclampsia was 3.2–5% and the death rate was 4.3–5.6% [3]. At present, cesarean section is a common treatment for severe preeclampsia, and the selection of anesthesia methods has become the research focus of current medical community. CSEA has the advantages of the rapid onset time, good blocking effect, and obvious analgesic effect, which have been proven in patients with pregnancy-induced hypertension syndrome undergoing cesarean section [4]. TIVA refers to the adoption of multiple short-acting intravenous anesthetics after the induction of routine intravenous anesthesia to maintain anesthesia in the form of intermittent or continuous intravenous injection, with the effect that has been confirmed in elderly patients undergoing abdominal operation [5]. However, prolonged TIVA easily causes drug accumulation in the body and extends awakening time and has the possibility of triggering circulatory depression, leading to conduction disturbances in the heart and susceptibility to arrhythmias. Different anesthesia methods bring different effects to pregnant women and pregnancy outcomes [6]. Whether the abnormal changes of hemodynamics in blood pressure during anesthesia aggravates pregnant patients' conditions and adversely affects surgery becomes an important issue for anesthesiologists to take into account [7]. Currently, there are few reports exploring the application of CSEA and TIVA in severe preeclampsia pregnant patients undergoing cesarean section. Based on that, in this study, with the purpose of further exploring the effect of CSEA and TIVA on hemodynamics and pregnancy outcomes of severe preeclampsia pregnant patients undergoing cesarean section, 126 pregnant patients with severe preeclampsia admitted to Zhangqiu District People's Hospital from August 2018 to August 2019 were selected as the study subjects, and the summary report is as follows.

## 2. Materials and Methods

**2.1. General Information.** 126 patients with severe preeclampsia admitted to Zhangqiu District People's Hospital from August 2018 to August 2019 were selected as the study subjects and randomly divided into the experimental group ( $n = 63$ ) and control group ( $n = 63$ ). The study met the World Medical Association Declaration of Helsinki [8].

**2.2. Inclusion Criteria.** The inclusion criteria were as follows: patients met the diagnostic criteria for severe preeclampsia, i.e., systolic blood pressure  $\geq 160$  mmHg, diastolic blood

pressure  $\geq 110$  mmHg, platelet count  $< 1 \times 10^6$ , or the occurrence of kidney function impairment, pulmonary edema, and visual disorder, and their clinical manifestations included dizziness, vomiting, abdominal distention, and palpitation; patients met the indications of cesarean section and had single birth; and patients had no other pregnancy complications. This study was approved by the Ethics Committee of Zhangqiu District People's Hospital, and pregnant patients and their families were informed of the purpose and process of this study and signed the informed consent.

**2.3. Exclusion Criteria.** The exclusion criteria were as follows: patients had organic lesions in the brain, heart, lungs, and kidneys; patients had abnormal systemic coagulation; patients had contraindications to surgery or anesthesia; and patients had cognitive impairment such as mental disorders or refused to cooperate with the study.

**2.4. Methods.** In the control group, the patients received TIVA with the intravenous injection of 1.5 mg/kg of propofol (State Food and Drug Administration approval number: H20093542; manufacturer: Hebei Yipin Pharmaceutical Co., Ltd.; specification: 10 ml: 0.1 g). When the onset of anesthesia was observed, the patients were injected intravenously with 0.6 mg/kg of rocuronium bromide (State Food and Drug Administration approval number: H20100069; manufacturer: Hebei Baiqi Pharmaceutical Co., Ltd.; specification: 5 ml: 50 mg) and 1.0  $\mu$ g/kg of remifentanyl (State Food and Drug Administration approval number: H20030197; manufacturer: Yichang Humanwell Pharmaceutical Co., Ltd.; specification: 1 mg). Before delivery, the patients underwent pump infusion of propofol at 2.5 mg/kg per hour and remifentanyl at 0.05 mg/kg per minute at the same time. After the birth of the newborns, the continuous pump infusion of 0.05 mg/kg of midazolam (State Food and Drug Administration approval number: H10980026; manufacturer: Jiangsu Nhwa Pharmaceutical Co., Ltd.; specifications: 3 ml: 15 mg) and 0.3 mg/kg of sufentanil (State Food and Drug Administration approval number: H20054172; manufacturer: Yichang Humanwell Pharmaceutical Co., Ltd.; specification: 2 ml: 100  $\mu$ g) were performed at 3–4 mg/kg per hour, and 0.2 mg/kg of rocuronium was also added to maintain anesthesia [9].

In the experimental group, the patients were treated with CSEA. Epidural puncturing was carried out in pregnant patients' intervertebral space from L<sub>2</sub> to L<sub>4</sub>, and lumbar puncture was performed with puncture needles by routine techniques of needling. After cerebrospinal fluid flowed out, the patients were injected with 1.2 ml of 0.75% levobupivacaine (State Food and Drug Administration approval number: H20050403; manufacturer: Zhuhai Rundu Pharmaceutical Co., Ltd.; specification: 5 ml: 37.5 mg) for 10 s. After withdrawing the needles, tubes were inserted in epidural space, and then, the patients took supine positions. Subsequently, the intravenous injection with 5 ml of 2% lidocaine hydrochloride

injection (State Food and Drug Administration approval number: H44023825; manufacturer: Guangzhou Baiyunshan Mingxing Pharmaceutical Co., Ltd.; specification: 2 ml: 40 mg) was conducted to the patients; if the signs of subarachnoid space anesthesia were not observed after 5 minutes of injection, the patients were injected with 5 ml of bupivacaine hydrochloride injection (State Food and Drug Administration approval number: H37022107; manufacturer: Shandong Hualu Pharmaceutical Co., Ltd.; specification: 5 ml: 37.5 mg) and 5 ml of 2% lidocaine. When the anesthesia was maintained at level T8, the cesarean section was carried out.

**2.5. Evaluation Indexes.** The operation duration, the onset time of anesthesia, delivery time, and intraoperative blood loss were recorded in both groups.

Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation (SpO<sub>2</sub>) before anesthesia and at delivery were measured in both groups. MAP = (systolic blood pressure + 2 × diastolic blood pressure)/3; the HR value was measured by the electronic sphygmomanometer (manufactured: Nanjing Vedeng Medical Co., Ltd.); and SpO<sub>2</sub> was measured by the fingertip photoelectric sensor (manufactured: Guangzhou Sichuang Hongyi Electronic Technology Co., Ltd.), during which the pregnant patients were told to keep the body relaxed while the sensor was clamping to their fingertips.

The condition that after anesthesia, with appropriate muscle relaxation, the patients had no adverse reactions during the surgery which was carried out smoothly was excellent; the condition that after anesthesia, with good muscle relaxation, the patients had slight tremors during the surgery, which did not affect the surgery was effective; the condition that after anesthesia, with poor muscle relaxation, the patients had significant tremors after the surgery, and they should be given analgesic and sedative drugs to finish the surgery and was ineffective. The total effective rate = (number of excellent cases + number of effective cases)/total number of cases × 100%.

The newborns' physical conditions in both groups were evaluated by referring to the Apgar scoring [10], with the total score of 10 points. 7–10 points represented normal condition, 4–7 points represented mild asphyxia, and 4 points and below represented severe asphyxia. The scoring items included color of the skin, breathing, reflexion, heartbeat rate, muscle tone, and movement.

Postoperative adverse reactions were recorded in both groups, including hypotension, pulmonary edema, and traction reaction.

**2.6. Statistical Methods.** The data in the study were statistically analyzed and processed by SPSS 21.0 software. GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw pictures of the data. Measurement data were expressed by ( $\pm s$ ) and tested by the *t*-test. Enumeration data were expressed as (*n* (%)) and tested by the  $\chi^2$  test. The differences had a statistical significance when  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Clinical Data between the Two Groups.** There were no significant differences in age, BMI value, weight, height, gestational weeks, SBP, DBP, and residence between the two groups ( $P > 0.05$ ), which were comparable, as given in Table 1.

**3.2. Comparison of Surgical Conditions between the Two Groups.** The operation duration, the onset time of anesthesia, and delivery time in the experimental group were significantly shorter than those in the control group, and the intraoperative blood loss in the experimental group was significantly less than that in the control group ( $P < 0.05$ ), as given in Table 2.

**3.3. Comparison of Hemodynamic Indexes at Different Time Points between the Two Groups.** In both groups, MAP and SpO<sub>2</sub> at delivery were significantly lower than those before anesthesia, and HR at delivery was significantly higher than that before anesthesia ( $P < 0.05$ ). MAP and HR at delivery in the experimental group were significantly lower than those in the control group, and SpO<sub>2</sub> in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), as given in Table 3.

**3.4. Comparison of the Anesthetic Effect between the Two Groups.** The total effective rate of anesthesia in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), as given in Table 4.

**3.5. Comparison of Apgar Scoring between the Two Groups.** The Apgar scoring of newborns in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), as shown in Figure 1.

The Apgar scoring of the newborns in the experimental group was ( $9.28 \pm 0.33$ ) points, while that in the control group was ( $8.41 \pm 0.86$ ) points.

\*Significant difference in Apgar scoring between the two groups ( $t = 7.497$ ,  $P < 0.001$ ).

**3.6. Comparison of Adverse Reactions after Surgery between the Two Groups.** The total incidence of postoperative adverse reactions in the experimental group was significantly lower than that in the control group ( $P < 0.05$ ), as given in Table 5.

### 4. Discussion

Preeclampsia is one of the peculiar diseases of pregnancy, characterized by disorders of uterine spiral artery remodeling, endothelial damage, and local ischemia as the basic pathological changes [11]. Parturient presents with preeclampsia present systemic inflammatory response, mainly manifesting clinically as edema, hypertension, and proteinuria. Severe eclampsia is severe and sudden in onset, and affected women generally experience headaches with syncope and unconsciousness, which can lead to generalized

TABLE 1: Comparison of clinical data between the two groups.

Types	Experimental group ( $n = 63$ )	Control group ( $n = 63$ )	$\chi^2$ ( $t$ )	$P$
Average age (years old)	28.17 $\pm$ 0.63	28.14 $\pm$ 0.65	0.263	0.793
BMI (kg/m <sup>2</sup> )	21.53 $\pm$ 1.25	21.55 $\pm$ 1.26	0.089	0.929
Weight (kg)	69.21 $\pm$ 2.43	69.24 $\pm$ 2.45	0.069	0.945
Height (cm)	162.45 $\pm$ 3.65	162.52 $\pm$ 3.67	0.107	0.915
Gestational weeks (weeks)	34.85 $\pm$ 1.25	34.86 $\pm$ 1.28	0.044	0.965
SBP (mmHg)	174.25 $\pm$ 2.43	174.27 $\pm$ 2.42	0.046	0.963
DBP (mmHg)	125.24 $\pm$ 2.21	125.26 $\pm$ 2.24	0.050	0.960
Residence			0.032	0.858
Urban area	28 (44.44%)	29 (46.03%)		
Rural area	35 (55.56%)	34 (53.97%)		

TABLE 2: Comparison of surgical conditions between the two groups ( $\pm s$ ).

Group	$n$	Operation duration (min)	The onset time of anesthesia (min)	Delivery time (min)	Intraoperative blood loss (ml)
Experimental group	63	42.14 $\pm$ 7.64	6.25 $\pm$ 1.85	12.32 $\pm$ 5.78	142.54 $\pm$ 18.77
Control group	63	51.55 $\pm$ 7.58	11.58 $\pm$ 1.69	25.44 $\pm$ 5.49	185.31 $\pm$ 18.64
$t$		6.940	16.884	13.063	12.833
$P$		0.001	0.001	0.001	0.001

TABLE 3: Comparison of hemodynamic indexes at different time points between the two groups ( $\pm s$ ).

Group	$n$	Time	MAP (mmHg)	HR (time/min)	SpO <sub>2</sub> (%)
Experimental group	63	Before anesthesia	123.25 $\pm$ 4.26	78.77 $\pm$ 1.65	95.21 $\pm$ 2.08
		At delivery	97.43 $\pm$ 3.18	80.32 $\pm$ 1.73	93.18 $\pm$ 1.28
Control group	63	Before anesthesia	123.28 $\pm$ 4.29	78.79 $\pm$ 1.69	95.24 $\pm$ 2.06
		At delivery	105.22 $\pm$ 3.15*	87.22 $\pm$ 1.83*	90.63 $\pm$ 1.32*

Each hemodynamic index at delivery in both groups was significantly lower than that before anesthesia; \* comparison between the experimental group and the control group,  $P < 0.001$ .

TABLE 4: Comparison of the anesthetic effect between the two groups ( $n$  (%)).

Group	$n$	Excellent	Effective	Ineffective	Total effective rate
Experimental group	63	24 (38.10%)	37 (58.73%)	2 (3.17%)	96.83% (61/63)
Control group	63	19 (30.16%)	35 (55.56%)	9 (14.29%)	85.71% (54/63)
$\chi^2$					4.881
$P$					<0.05

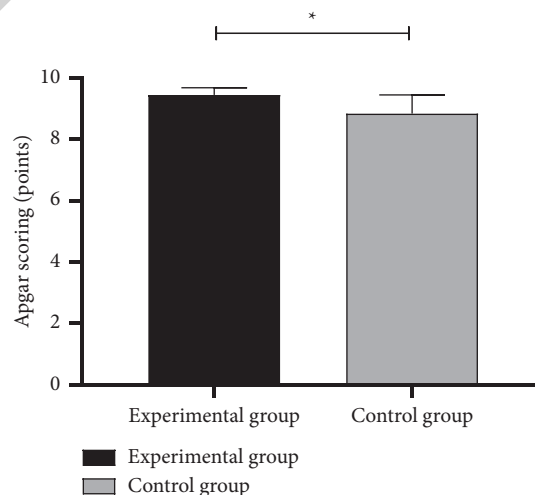


FIGURE 1: Comparison of Apgar scoring between the two groups ( $\pm s$ ). The abscissa represents the experimental group and control group, while the ordinate represents Apgar scoring.

TABLE 5: Comparison of adverse reactions between the two groups ( $n$  (%)).

Group	$n$	Hypotension	Pulmonary edema	Traction reaction	Total incidence
Experimental group	63	1 (1.59%)	0 (0.00%)	2 (3.17%)	4.76% (3/63)
Control group	63	3 (4.76%)	3 (4.76%)	4 (6.35%)	15.87% (10/63)
$\chi^2$					4.203
$P$					0.040

arteriolar spasms, local ischemia, endothelial damage, and resultant blood supply deficiency of tissue and organs, and in severe cases, maternal and fetal death [12]. Research investigations have shown [13] that the number of maternal deaths from eclampsia greatly exceeds 100,000 per year in China. As severe preeclampsia can easily progress to eclampsia and its condition is difficult to control, the pregnant patients have to receive cesarean section immediately to terminate pregnancy; thus, the selection of anesthesia methods is essential for the implementation of surgery [14, 15]. Generally speaking, the hospitals mostly carry out CSEA for cesarean section because it can quickly make the pregnant patients enter anesthesia states, with longer time of blocking and a better therapeutic effect [16, 17]. TIVA is a type of anesthesia that completely relies on intravenous injection or infusion of anesthetics to finish surgery, which easily leads to respiratory depression and circulation inhibition, greatly increasing the surgical risks. Besides, propofol, rocuronium, and other drugs used in anesthesia will increase the patients' pains, adversely affecting surgery [18, 19].

Clinical studies have confirmed that CSEA can make the human body enter optimal anesthesia states without large doses of anesthetics. During the process of anesthesia, drug doses can be adjusted appropriately according to maternal delivery conditions [20]. Severe preeclampsia is mostly caused by the imbalance of the maternal immune system, placental calcium deficiency, or ischemia; hence, the implementation of effective anesthesia can further improve maternal physical health and increase the neonatal survival rate. This study confirmed that the total effective rate of CSEA in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), which was presumably related to the lower dosage of this anesthesia, leading to the surgical requirements for muscle relaxation and the less impact on its hemodynamics. This study found that the incidence of adverse reactions in the experimental group was significantly lower than that in the control group ( $P < 0.05$ ). Clendenon et al. [21] pointed out that the incidence of adverse reactions in patients undergoing cesarean section was 4.53%, which was significantly lower than 16.03% in the reference group ( $P < 0.05$ ), demonstrating that the purpose of this study was to show that CSEA could significantly reduce the adverse reactions after cesarean section and improve maternal and infant health. It was speculated that the results might be correlated with the administration methods of CSEA, where the administration was performed in external cavity and lumbar puncture was conducted with fine puncture needles, effectively reducing the clinical adverse reactions of pregnant patients after surgery. Academic studies have also revealed that CSEA can maintain the stability of maternal hemodynamics, reduce heart rate fluctuation, improve blood supply, and reduce surgical risks

[22, 23]. The limitations of the study: based on the limited study area, the sample size selected was only the patients within our region and did not include those from other regions, so the results obtained may be affected by factors such as the small sample size and region.

In conclusion, CSEA can make the hemodynamics of severe preeclampsia pregnant patients undergoing cesarean section in stable states, improve the delivery outcomes, and reduce the adverse reactions after surgery, with a better anesthetic effect, which is worthy of application and popularization.

### Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Irisin Activates M1 Macrophage and Suppresses Th2-Type Immune Response in Rats with Pelvic Inflammatory Disease

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**Objective.** To investigate the mechanism of irisin to treat rats with acute pelvic inflammatory disease (APID). **Methods.** Female rats were established as APID. Firstly, the content of IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa$ B was tested in rats' serum by enzyme linked immunosorbent assay (ELISA). Interferon- $\gamma$  (IFN- $\gamma$ ) and IL-4 in the supernatant of pelvic homogenates were also detected. The mRNA expression of the inducible nitric oxide synthase (iNOS), TNF- $\alpha$ , chemokine ligand 1 (CXCL1), arginase-1 (Arg1), and chitinase-3-like-3 (Chi313) genes in the pelvic cavity was detected by quantitative reverse transcription polymerase chain reaction (RT-qPCR). IFN- $\gamma$  and IL-4 secreted by spleen CD4<sup>+</sup>T cells and CD8<sup>+</sup>T cells were counted by flow cytometry, and the ratio of IFN- $\gamma$ /IL-4 in CD4<sup>+</sup>T cells and CD8<sup>+</sup>T cells in the spleen was also detected by flow cytometry. **Results.** Irisin reduced the levels of IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa$ B in serum. Compared with the APID group, the expression level of IL-4 in the APID + Irisin group was reduced in the homogenate. At the same time, Irisin promotes the activation of M1 macrophages in the uterus, ovaries, and uterine tubes of rats with APID. Irisin also inhibited Th2-type immune response. **Conclusions.** Irisin activates M1 macrophage and suppresses Th2-type immune response in APID rats.

## 1. Introduction

Acute pelvic inflammatory disease (APID) is one of the gynecological diseases with high incidence and great harm in clinic. APID is a type of gynecological disease that refers to pelvic cavity reproductive organs such as the uterus, uterine tubes, and pelvic inflammation [1, 2]. The main reason is the anaerobic bacteria infection. People with poor hygiene during the menstrual period, irregular reproductive tract infections, sexual life, etc. are prone to anaerobic bacteria infection, which in turn causes APID [3]. Patients usually experience lower abdominal pain and increased leucorrhea, often accompanied by dizziness, high fever, loss of appetite, and other phenomena, and improper treatment may lead to chronic pelvic inflammatory disease, leading to pelvic effusion, causing pelvic adhesions, etc., which will have a greater impact on menstruation and pregnancy [4]. In addition, studies have confirmed that PID is associated with an increased risk of borderline ovarian tumors, particularly among women

who had had multiple episodes of PID [5]. Therefore, APID should arouse our attention.

APID can induce innate immune response and adaptive immune response [6]. The former is the body's first line of defense against pathogen invasion and plays an important role in the early removal of pathogens and infection control. Among them, macrophages are the most important innate immune cells. Macrophages are dynamic heterogeneous cells with heterogeneity. Under different microenvironments and different inducing signals in the body, macrophages can change their morphology and physiological characteristics and differentiate into different activation states to deal with the external environment. According to the difference in the activation mode, phenotype, and secretion of cytokines of macrophages, macrophages can be divided into two types: classically activated macrophages (CAMs or M1) and alternatively activated macrophages (AAMs or M2). Under normal circumstances, in the process of inflammatory response, the balance of M1 and M2 macrophages is constantly changing due to the regulation of



different cell signals [7, 8]. If the balance shifts to either side, the final outcome of the inflammatory response may be changed. Therefore, if the activation of M1 macrophages is promoted in the early stages of infection, it will help the body eliminate pathogens. At present, studies have confirmed that lipopolysaccharide, IFN- $\gamma$ , and so on can activate M1. Also, IL-4, IL-10, IL-13, and so on can promote the activation of M2-type macrophages.

Although innate immunity can fight infection at an early stage, the body's complete and thorough elimination of pathogens mainly depends on adaptive immunity [9]. The main pathogen of APID is aerobic bacteria, followed by ureaplasma urealyticum, chlamydia trachomatis, and anaerobic bacteria. Studies have found that patients with impaired humoral immunity are prone to chronic infection after infection, indicating that antibodies have a certain role in preventing pathogen infection, but the protective effect is not complete [10]. Therefore, cellular immunity plays an important role in eliminating intracellular pathogens and preventing chronic and persistent infections. The cellular immune response is mediated by T lymphocytes [11], including CD4+T cells and CD8+T cells. CD4+T cells mainly include T-helper cell type 1 (Th1), Th2, Th3, and Th17 and regulatory T cells [12]. Th1 cells mainly secrete cytokines such as IFN- $\gamma$ , TNF- $\alpha$ , and IL-2, which mediate cellular immune responses and play an important role in the complete elimination of pathogens [13]. If immune regulation can promote Th2 immunity to Th1-type immunity, it can promote the killing and elimination of pathogens by the body's immune system.

Irisin is a soluble peptide consisting of 112 amino acids [14]. Irisin promotes the browning of white fat by activating uncoupling protein 1 (UCP 1) to increase energy metabolism and is, therefore, considered to play a key role in metabolic diseases [14]. In recent years, more and more studies have shown that irisin has anti-inflammatory, antioxidative stress, and antiapoptotic effects in the physiological and pathological processes of lung injury and brain injury [15, 16]. Also, some studies have suggested that irisin and UCP2 work synergistically to improve alveolar epithelial cell damage in acute lung injury [17]. Irisin has different effects on the proliferation and apoptosis of tumor cells in breast cancer, lung cancer, and liver cancer through various mechanisms. We all know that proliferation and apoptosis of tumor cells are very important for tumor development, suggesting that irisin may have a similar effect with genitourinary cancers [18]. However, there is still a lack of research on the role of irisin in the pathophysiological process of APID.

This study intends to make a rat model of APID by injecting mixed bacteria into the uterus to study the anti-inflammatory mechanism of irisin on APID in rats and to provide a more adequate basis for the clinical application of irisin in the treatment of APID.

## 2. Materials and Methods

**2.1. Animal.** 30 female SD rats, weighing 200–240 g and 8 weeks old, were provided by Beijing Weitonglihua Experimental Animal (Beijing, China). Five rats in each cage were

raised in the Experimental Animal Center of Yangtze University. The rearing temperature was 20–25°C, and the humidity was 50%–70%. During the feeding period, they were given free access to food and drinking water. All animal feeding and experiment procedures meet the requirements of the Animal Experiment Ethics Committee of Yangtze University.

**2.2. Bacteria Preparation.** *Staphylococcus aureus* (strain number: 26001) and *Escherichia coli* (strain number: 44138), after biochemical identification, were cultured with ordinary meat intestine broth medium at 37°C, and  $1 \times 10^9$  bacteria/mL were taken in the logarithmic growth stage and mixed in 1 : 1 for use. A special medium for mycoplasma was used, and *Ureaplasma urealyticum* was cultured in an 85% nitrogen-containing incubator.  $1 \times 10^6$  pieces/mL were taken and mixed with the abovementioned mixed bacterial solution for modeling.

**2.3. Construction of the APID Rat Model.** Of the 30 rats, 10 rats were randomly selected as the sham operation group, and the remaining 20 rats were used for modeling and were randomly divided into the model group and irisin treatment group, with 10 rats in each group. Among them, rats in the irisin treatment group were injected intraperitoneally at a concentration of 100  $\mu$ g/kg irisin, once a day, for 14 consecutive days, and then, the model was made. Experimental rats were weighed, routinely disinfected, and anesthetized by intraperitoneal injection of 1% pentobarbital sodium (5 mg/100 g). After the anesthesia took effect, 0.2 mL of 3 billion/mL of mixed bacterial fluid was extracted. The needle of the syringe (the tip of the needle was cut off) was used to carefully enter one side of the uterine cavity at the bifurcation of the cervix at the bottom of the vagina. Then, the bacterial fluid was injected towards the ovary, and 0.1 mL was injected into each side of the uterus. After the injection, the absorbent gelatin sponge was placed on the cervix at the bottom of the vagina to prevent leakage of the medicine. In the sham operation group, the operation was the same as above, and the same amount of 0.9% saline was injected. After the operation, the animals were not given any treatment, drinking water was restored, and the animals were kept clean and kept for another 10 days.

**2.4. Sample Collection.** Rats anesthetized with 1% pentobarbital sodium (5 mg/100 g) were intraperitoneally injected and fixed on the operating table. A central abdominal incision was made to open the abdominal cavity and chest cavity. Blood samples were collected by rapid heart puncture in a 1.5 mL EP tube. At the same time, the uterus, ovaries, hoses, and spleen tissues of the rats were quickly removed. The collected tissue was placed in a 1.5 mL cryopreserved tube and stored in a refrigerator at –80°C for subsequent experiments.

**2.5. Enzyme Linked Immunosorbent Assay (ELISA).** The rat pelvic tissue was homogenized and centrifuged at 12,000 rpm at 4°C for 5 min, and the supernatant was



transferred to a new EP tube and stored at  $-80^{\circ}\text{C}$ . Indirect ELISA (Yi Fei Xue, Nanjing, China) was used to detect the expression levels of IFN- $\gamma$  and IL-4 in the uterus, ovaries, and transfusion tube homogenate supernatant. Besides, ELISA was also used to detect the expression levels of proinflammatory cytokines IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa\text{B}$  in the serum. We repeated all the experiments three times.

**2.6. Quantitative Reverse Transcription Polymerase Chain Reaction (RT-qPCR).** About 20 mg of pelvic tissue was cut into an EP tube prefilled with 1 mL of TRIzol reagent (R&D, Minneapolis, MN, USA), then a homogenizer was used to homogenize the tissue, and it was left for 5 min at room temperature and centrifuged at  $4^{\circ}\text{C}$ , 12,000 rpm for 10 min, and the supernatant was aspirated. Next, 0.2 mL of chloroform was added to the EP tube, shocked for 15 sec, allowed to stand at room temperature for 5 min, and centrifuged at 12,000 rpm for 15 min at  $4^{\circ}\text{C}$ . Next, the RNA in the water phase was transferred to a new EP tube. At the same time, 1 mL of isopropanol was added to it, pipetted to mix, and allowed to stand at room temperature for 10 min. The RNA pellet was centrifuged at  $4^{\circ}\text{C}$  at 12,000 rpm for 10 min, the supernatant discarded, and 1 mL of 75% ethanol was used to wash the RNA pellet. After centrifugation, the RNA pellet was dissolved with 50  $\mu\text{L}$  RNase-Free ddH $_2\text{O}$ . Next, the reverse transcription system mixture was configured according to the instructions, and reverse transcription was performed at  $55^{\circ}\text{C}$  for 15 minutes and  $85^{\circ}\text{C}$  for 5 seconds. Then, fluorescence staining RT-qPCR was used to detect the mRNA transcription level of macrophage activation marker genes. With GAPDH as the internal reference gene, the data were relatively quantitatively analyzed by the  $2^{-\Delta\Delta\text{Ct}}$  method. Primers are shown in Table 1. We repeated all the experiments three times.

**2.7. IFN- $\gamma$  and IL-4 were Detected by FCM in T Lymphocytes of Rat Spleen.** The fresh spleen tissues of rats were placed in 5 mL EP tubes, 2 mL precooled Hank's solution (Camilo Biological, Nanjing, China) was added to it, homogenized by using a homogenizer, and centrifuged at 1200 rpm for 5 min, and the supernatant was discarded. Next, 3 mL erythrocyte lysate was used for resuspended precipitation, and it was allowed to stand for 5 min. Then, 5 mL PBS solution was used to stop the cleavage reaction and centrifuged at  $4^{\circ}\text{C}$  and 1200 rpm for 5 min, and the supernatant was discarded. 5 mL 1640 incomplete medium was used to add resuspended precipitation, which was centrifuged at 1200 rpm for 5 min at  $4^{\circ}\text{C}$ . The precipitation was retained and repeated to wash away the remaining red blood cell lysates. The cells were resuspended with 1640 complete medium (Thermo Fisher Scientific, Waltham, MA, USA), the cell density was adjusted to  $2 \times 10^6/100 \mu\text{L}$ , and they were transferred to a 96-well plate with 100  $\mu\text{L}$  per well. After incubating the IL-4 and IFN- $\gamma$  antibodies (Life Technology, China) at  $4^{\circ}\text{C}$  in the dark for 30 minutes, 300  $\mu\text{L}$  staining solution was used to resuspend the pellet. Flow cytometry was used to detect cytokines, and the data were analyzed using Flow Jo software. We repeated all the experiments three times.

**2.8. Statistical Analysis.** In this experiment, GraphPad Prism 8.0 software (La Jolla, CA, USA) was used to analyze the experimental data by one-way ANOVA and the Duncan test, and the experimental data were expressed as mean  $\pm$  standard deviation ( $\bar{X} \pm \text{SD}$ ).  $P < 0.05$  indicates a significant difference.

### 3. Results

**3.1. Effect of Irisin on Rat Serum Cytokines.** In order to detect the level of inflammation in rats, we drew rat serum and used ELISA to detect the level of cytokines of rats. The results showed that compared with the sham group, the levels of IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa\text{B}$  in the APID group were increased, and the difference was statistically significant, suggesting that the rat model of APID was successfully made. Compared with the APID group, the content of IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa\text{B}$  in the irisin treatment group was reduced, and the difference was statistically significant (Figures 1(a)–1(d)), indicating that irisin treatment has a curative effect on the rat model of APID. However, irisin cannot completely restore IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa\text{B}$  levels. The abovementioned results indicate that irisin can reduce the level of inflammation in rats with APID.

**3.2. Changes of IL-4 and IFN- $\gamma$  Expression in Rat Uterus, Ovaries, and Uterine Tube Homogenates.** The indirect ELISA method was used to detect the expression levels of IL-4 and IFN- $\gamma$  in the supernatant of the uterus, ovaries, and uterine tube tissues on the 10th day of the model. Compared with the sham group, the expression level of IL-4 in the APID + irisin group was reduced in the homogenate (Figure 2(a)). However, there was no significant difference in the expression level of IFN- $\gamma$  in the two groups of tissues (Figure 2(b)).

**3.3. Level Detection of Macrophage Activation Marker Genes.** RT-qPCR detection showed that the relative transcription level of M1 macrophage activation marker iNOS gene mRNA in the uterus, ovaries, and uterine tube homogenates in the APID + irisin group was dramatically higher than that in the APID group. The relative transcription level of TNF- $\alpha$  and CXCL 1 gene mRNA was also higher than that of APID group (Figures 3(a)–3(c)), while the relative expression level of M2 macrophage activation marker Arg 1 gene mRNA was lower than that of APID group. At the same time, the relative transcription of Chi3l3 gene mRNA was also dramatically lower than that of the APID group (Figures 3(d) and 3(e)). The abovementioned results indicate that irisin promotes the activation of M1 macrophages in the uterus, ovaries, and uterine tube of rats with APID.

**3.4. Irisin Inhibits Th2-Type Immunity in Rats with APID.** On the 10th day after the infection of rats with APID, the ratio of CD4 $^{+}$ T cells secreting IL-4 in the spleen of rats in the APID + irisin group was lower than that in the APID group

TABLE 1: Real-time PCR primers.

Gene name	Forward (5'>3')	Reverse (5'>3')
iNOS	GTTCTCAGCCCAACAATACAAGA	GTGGACGGGTCGATGTCAC
TNF- $\alpha$	CCCTCACACTCAGATCATCTTCT	GCTACGACGTGGGCTACAG
CXCL1	CTGGGATTACACCTCAAGAACATC	CAGGGTCAAGGCAAGCCTC
Arg1	CTCCAAGCCAAAGTCCTTAGAG	AGGAGCTGTCATTAGGGACATC
Chi313	CAGGTCTGGCAATTCTTCTGAA	GTCTTGCTCATGTGTGTAAGTGA
GAPDH	GGAGCGAGATCCCTCCAAAAT	GGCTGTTGTCATACTTCTCATGG

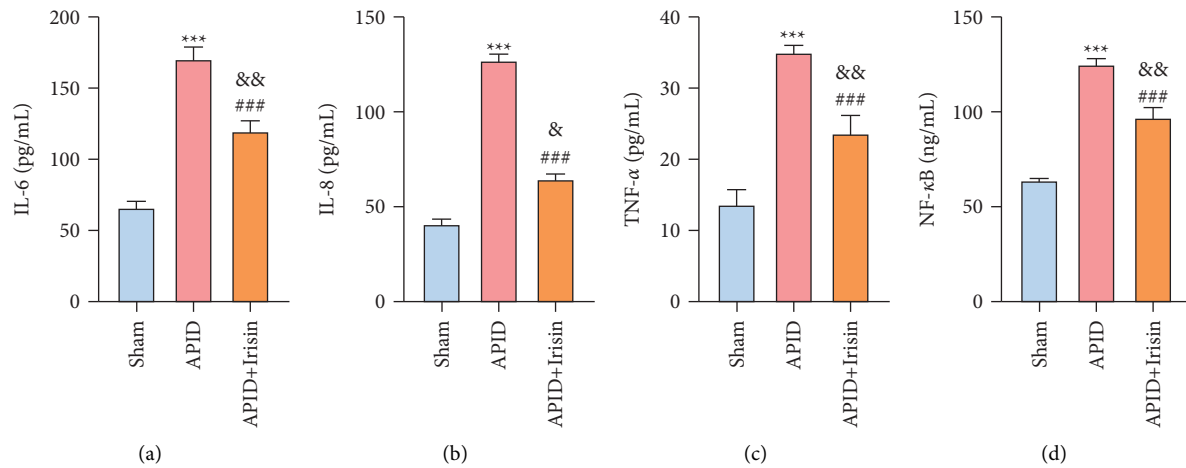


FIGURE 1: Effect of irisin on rat serum cytokines. (a ~ d) Levels of IL-6, IL-8, TNF- $\alpha$ , and NF- $\kappa$ B in the rat serum were determined by ELISA (“\*\*\*” indicates a statistical difference from the sham group,  $P < 0.001$ ; “###” indicates a statistical difference from the APID group,  $P < 0.001$ . “&” indicates a statistical difference from the sham group,  $P < 0.05$ ; “&&” indicates a statistical difference from the sham group,  $P < 0.01$ ).

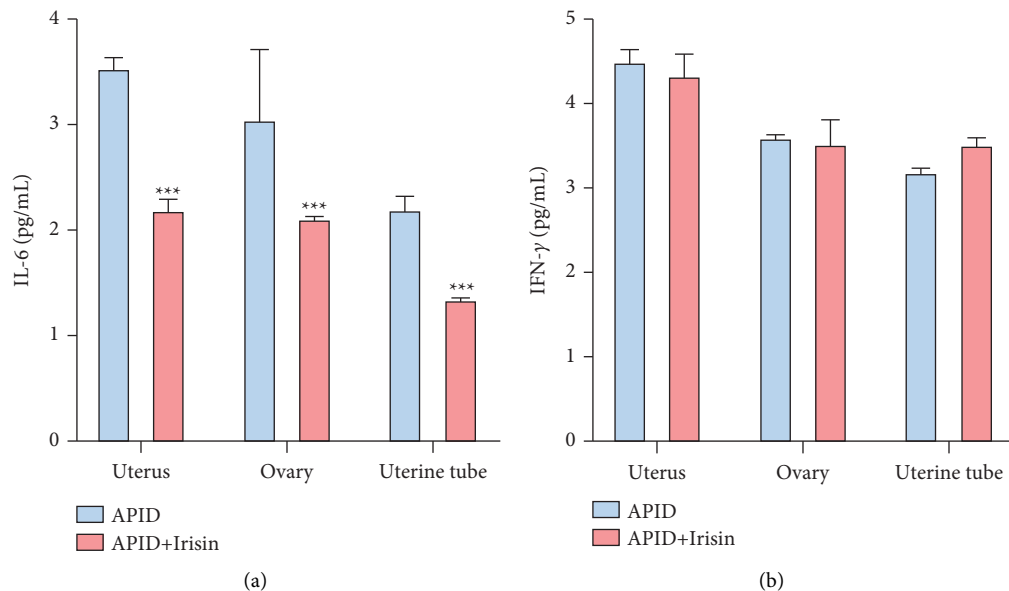


FIGURE 2: Changes of IL-4 and IFN- $\gamma$  expression in rat uterus, ovaries, and uterine tube homogenates. (a), (b) Levels of IL-4 and IFN- $\gamma$  in rat uterus, ovaries, and uterine tube were determined by ELISA (“\*\*\*” indicates a statistical difference from the APID group,  $P < 0.001$ ).

and the ratio of CD8<sup>+</sup>T cells secreting IL-4 in the spleen of rats in the APDI + irisin group was lower than that in the APID group (Figure 4(a)), while the ratio of CD8<sup>+</sup>T cells

secreting IFN- $\gamma$  in the spleen of rats in the APDI + irisin group was higher than that in the APID group. However, there was no significant difference in IFN- $\gamma$  secreted by

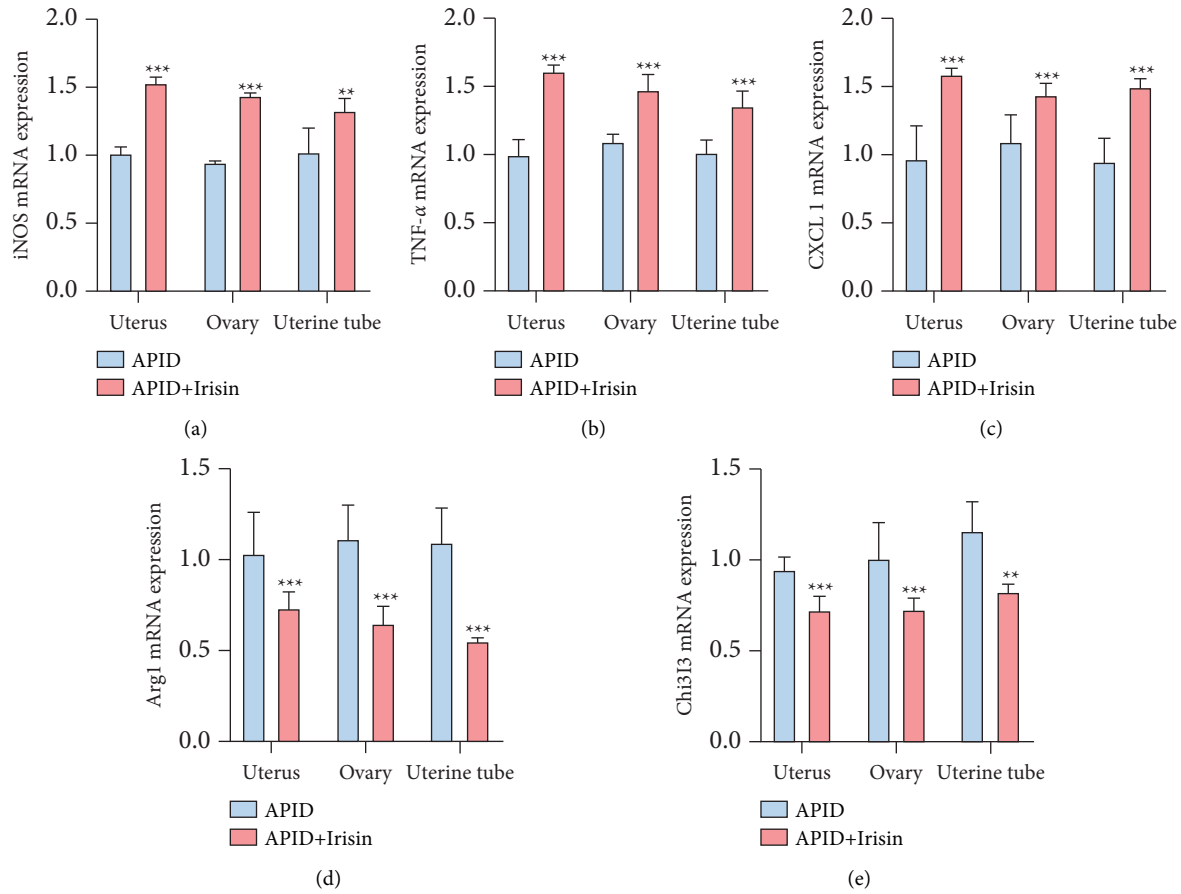


FIGURE 3: Level detection of macrophage activation marker genes. (a ~ e) The mRNA expressions of iNOS, TNF- $\alpha$ , CXCL1, Arg1, and Chi3l3 in rat uterus, ovaries, and uterine tube were determined by RT-qPCR (\*\*\*\* indicates a statistical difference from the APID group,  $P < 0.001$ ).

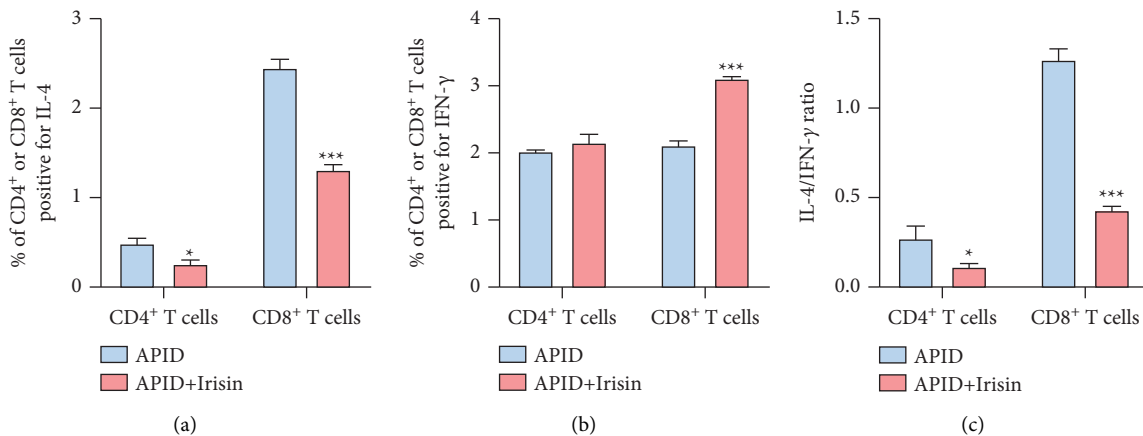


FIGURE 4: Irisin inhibits Th2-type immunity in rats with APID. (a, b) IFN- $\gamma$  and IL-4 were detected by FCM in T lymphocytes of rat spleen (\*\*\*\* indicates a statistical difference from the APID group,  $P < 0.001$ ).

CD4<sup>+</sup> T between the two groups (Figure 4(b)). Next, the rat spleen was taken to prepare lymphocytes, and the ratio of IL-4 to IFN- $\gamma$  in CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells was detected by flow cytometry. The results showed that compared with the APID group, the ratio of IL-4/IFN- $\gamma$  in CD4<sup>+</sup> T cells of the

APID + irisin group was lower and the ratio of IL-4/IFN- $\gamma$  in CD8<sup>+</sup> T cells of the APID + irisin group was also lower than that of the APID group (Figure 4(c)). The abovementioned results indicate that irisin inhibits Th2-type immunity in APID rats.

## 4. Discussion

The results of this experiment show that irisin can promote the clearance of acute pelvic inflammatory pathogens in rats and reduce the inflammation of rat pelvic tissue caused by infection. At the same time, irisin can promote the activation of M1 macrophages and inhibit Th2 immunity in infected rats.

At present, most studies believe that APID is mostly a mixed infection, and it is caused by two sources: (1) endogenous pathogen, from the original bacteria residing in the vagina; (2) exogenous pathogen, mainly the pathogen of sexually transmitted diseases. However, the clinical treatment is mostly the combined application of antibiotics, and the use of sensitive antibiotics is the key to treatment. However, there is currently no better method other than antibiotics for treating APID. Long-term use of antibiotics can easily lead to the production of drug-resistant bacteria and double infections, resulting in prolonged illness and repeated attacks. Studies have shown that, during acute lung injury, irisin protects alveolar epithelial cells from damage by maintaining mitochondrial function and improving oxidative stress [19]. In addition, in the research of brain injury and type 2 diabetes, the effects on antioxidative stress, antiapoptosis, and anti-inflammatory are also described [20, 21]. In this study, we first detected serum cytokine levels and found that irisin dramatically reduced the level of inflammation in rats with APID.

Phagocytes are the main cells involved in the innate immune response and play an important role in the early killing and elimination of pathogens. We found that compared with the APID group, the expression level of IL-4 in the pelvic tissue of the irisin group was reduced, and there was no significant difference in the expression level of IFN- $\gamma$ . The mRNA transcription level of M1 macrophage activation marker iNOS increased, and the mRNA transcription levels of TNF- $\alpha$  and CXCL 1 genes also increased, while the mRNA transcription levels of M2 macrophage activation markers Arg 1 and Chi3l3 decreased. The abovementioned results indicate that irisin can reduce the expression of IL-4 in the pelvic tissues of rats after infection, promote the activation of M1 macrophages after infection, and weaken the activation of M2 macrophages.

We also demonstrated that irisin can inhibit the infection of Th2-type immunity. The reduction and inhibition of the differentiation of Th2 cells were seen [22]. Moreover, when the expression of uncleared pathogen antigens in pelvic tissues is reduced, Th1-biased immunity will continue to be induced, and the positive feedback regulation formed will continue to increase the clearance of pathogens and shorten the course of infection.

## 5. Conclusions

This article explores the effect of irisin on APID and preliminarily explores the remote regulation mechanism of irisin on macrophage activation and specific immunity after infection, which will help to understand the host's regulation and mechanism of inflammation caused by infection.

## Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Conflicts of Interest

The authors declare no conflicts of interest.



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## Research Article

# Root Extract of a Micropropagated *Prunus africana* Medicinal Plant Induced Apoptosis in Human Prostate Cancer Cells (PC-3) via Caspase-3 Activation

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Prostate cancer is one of the major causes of cancer-related deaths among men globally. Medicinal plants have been explored as alternative treatment options. Herein, we assessed the *in vitro* cytotoxic effects of 70% ethanolic root extracts of six-month-old micropropagated *Prunus africana* (PIR) on PC-3 prostate cancer cells as an alternative to the traditionally used *P. africana* stem-bark extract (PWS) treatment. *In vitro* assays on PC-3 cells included annexin-V and propidium iodide staining, DAPI staining, and caspase-3 activity analysis through western blotting. PC-3 cells were exposed to PWS and PIR at different concentrations, and dose-dependent antiprostata cancer effects were observed. PC-3 cell viability was determined using CCK-8 assay, which yielded IC<sub>50</sub> values of 52.30 and 82.40 µg/mL for PWS and PIR, respectively. Annexin-V and PI staining showed dose-dependent apoptosis of PC-3 cells. Significant ( $p < 0.001$ ) percent of DAPI-stained apoptotic PC-3 cells were observed in PWS, PIR, and doxorubicin treatment compared with the negative control. PWS treatment substantially elevated cleaved caspase-3 levels in PC-3 cells compared with the PIR treatment. These results provide evidence for the antiprostata cancer potential of PIR and sets a basis

for further research to enhance future utilization of roots of young micropropagated *P. africana* for prostate cancer treatment as an alternative to stem bark. Moreover, micropropagation approach may help provide the required raw materials and hence reduce the demand for *P. africana* from endangered wild population.

## 1. Introduction

Prostate cancer is one of the most common nonskin cancers, affecting 9%–11% of men worldwide [1, 2], and one of the leading causes of cancer deaths in men [3–6]. Prostate cancer develops due to uncontrolled prostate cell division, which in turn causes abnormal cell growth and spreads to other parts of the body [1]. During the initial stages, prostate cancer is androgen-dependent, and trans-activation of target genes occurs due to androgens binding to the androgen receptor [7, 8]. Under normal conditions and in the case of cancer androgens and androgen receptor-mediated signaling play pivotal roles in prostate functioning and development [9]. Therefore, downregulation of androgens through anti-androgenic agents is vital in prostate cancer treatment [6, 7, 10]. Typically, this cancer is treated using numerous conventional methods, including radiation therapy, surgery, hormone therapy, and cryosurgery [11]; however, these methods are frequently associated with various adverse side effects [12]. Thus, other avenues with fewer adverse effects are being continuously tested for effective treatment of prostate cancer. One such approach is the use of medicinal plants [13–15].

Many medicinal plants such as African cherry (*Prunus africana* (Hook f.) Kalkman; Rosaceae family) exert strong antiprostata cancer effects [9]; further, in previous ethnomedicinal studies, *P. africana* bark decoction was used to treat cancers, including prostate cancer [1, 16]. Many scientific studies have confirmed the significant antiprostata cancer effects of *P. africana* stem bark, whereby its use as an antiprostata cancer agent has in fact already been patented [17]. In an *in vivo* study, transgenic adenocarcinoma of the mouse prostate (TRAMP) mice fed on *P. africana* (synonym *Pygeum africanum*) showed a significant reduction ( $p = 0.034$ ) in prostate cancer incidence compared with casein-fed mice [18]. Similarly, in an *in vitro* study, the bark extract of *P. africana* was observed to induce about 50% growth inhibition of human prostate cancer (PC-3) and also induced significant apoptosis in the PC-3 cell line [18]. PC-3 is one of the main cell lines in *in vitro* studies on human prostate cancer [19].

The anticancer activity of the stem bark of *P. africana* has been attributed to numerous novel bioactive compounds, including  $\beta$ -sitosterol, ferulic acid,  $\beta$ -sitosterol-3-O-glucoside, lauric acid, oleanolic acid, ursolic acid, atraric acid,  $\beta$ -amyrin, and N-butylbenzene-sulfonamide [9, 20].

Moreover, the stem bark of *P. africana* has also been used in traditional medicine to treat several other diseases, such as benign prostatic hyperplasia, epilepsy, hemorrhage, arthritis, hypertension, and diarrhea [20, 21]. Unfortunately, the continued use of this plant constitutes a serious threat to wild populations. Indeed, the species was recently classified as an endangered species and, as such, the supply of stem

bark is not sufficient to meet global demand [22]. To meet the global demand, we previously developed a micropropagation protocol for *P. africana* [23]. In this study, however, we examined the antiprostata cancer potential of the micropropagated juvenile six-month-old *P. africana* plants based on our protocol as an alternative to the use of the stem bark of wild *P. africana* plants using PC-3 cell line. In addition, we compared the chemical profiles of the different parts of the six-month-old plants and that of the bark of a mature wild *P. africana* plants using Fourier transform near-infrared (FT-NIR) spectrometry, gas chromatography-mass spectrometry (GC-MS), and high-performance liquid chromatography (HPLC). Thus, our study provides basis for the potential use of micropropagated *P. africana* in future drug development for prostate cancer treatment.

## 2. Material and Methods

**2.1. Chemicals.** Analytical-grade chemicals were used for HPLC analysis, including trifluoroacetic acid (Sigma-Aldrich, St. Louis, MO, USA), acetonitrile (Thermo Fisher Scientific, Oxford, UK), and ultrapure water produced using a Milli-Q system (Millipore, Burlington, MA, USA).

**2.2. Plant Material Collection and Extract Preparation.** Plant material used in this study consisted of stem bark samples (500 g) of wild *P. africana* provided by the Natural Chemotherapeutics Research Institute, Ministry of Health, Uganda. A voucher (specimen number KIOM201901022377) was deposited at the Korean Herbarium of Standard Herbal Resources (Index Herbarium code: KIOM) at the Korean Institute of Oriental Medicine (KIOM), Herbal Medicine Resources Research Center, South Korea.

The following sample types were used: wild *P. africana* stem bark (PWS) (Figure 1(a)), stem of a six-month-old micropropagated *P. africana* plant (PIS) (Figure 1(b)), roots of a six-month-old micropropagated *P. africana* plant (PIR) (Figure 1(c)), leaves of a six-month-old micropropagated *P. africana* plant (PIL) (Figure 1(d)), and *P. africana* calluses generated from leaf explants (PIC) (Figure 1(e)). Each sample was ground to a fine powder (Figure 1(g)–1(j)) and then extracted and concentrated as previously described [24]. Vacuum dried extracts were used for antiprostata cancer assays.

**2.3. High-Performance Liquid Chromatography (HPLC) Analysis of *P. africana*.** Powdered PWS, PIS, PIR, PIL, and PIC samples (500 mg, each) were sequentially extracted twice for 30 min using 50 mL methanol and an ultrasonicator. Each extract was concentrated *in vacuo* using an evaporator, followed by dissolving the extract in methanol at 50  $\mu$ g/mL and





FIGURE 1: *Prunus africana* samples used in the experiment: (a) wild *P. africana* stem bark (PWS); (b) juvenile stem bark from cloned *P. africana* plant (PIS); (c) juvenile roots from cloned *P. africana* plant (PIR); (d) juvenile leaves from cloned *P. africana* plant (PIL); (e) in vitro callus from leaf explant (PC); (f) wild stem bark powder; (g) juvenile stem bark powder from cloned *P. africana* plant; (h) juvenile root powder from cloned *P. africana* plant; (i) juvenile leaves powder from cloned *P. africana* plant; (j) callus powder.

filtration through a 0.22  $\mu\text{m}$  membrane filter (Whatman International Ltd., Maidstone, UK). Samples were then stored at 4°C until use. HPLC was performed using a Dionex UltiMate 3000 system (DAD; Thermo Fisher Scientific, CA, USA). Output signals from the detector were processed using Chromeleon software (v. 7). A total of 10  $\mu\text{L}$  of each sample was injected using an autosampler. Chromatographic separation was achieved using a Gemini C<sub>18</sub> column (4.6  $\times$  250 mm, 5  $\mu\text{m}$ ; Phenomenex, Torrance, CA, USA) with the following mobile phases: 0.1% trifluoroacetic acid in water (v/v) as solvent A and acetonitrile as solvent B at a flow rate of 1 mL/min with a total run time of 50 min. HPLC elution conditions were optimized as follows: 0–2 min, 0%–3% B; 2–30 min, 3%–35% B; 30–31 min, 35%–50% B; 31–35 min, 50% B; 35–40 min, 50%–100% B; 40–45 min, 100% B; 45–50 min, 3% B; column oven temperature was 40°C, and detection wavelengths were 203, 254, 280, and 320 nm.

**2.4. Gas Chromatography-Mass Spectrometry (GC-MS) Analysis of *P. africana*.** Powdered PWS, PIS, PIR, PIL, and PIC samples (50 mg, each) were extracted using 1 mL 100% methanol and sonication for 30 min, followed by filtration through a 0.2  $\mu\text{m}$  syringe membrane filter (Whatman International Ltd). Analysis was performed using a 7890B GC-MS system (Agilent Technologies, Atlanta, GA, USA) coupled with a 7977B model mass detector (Agilent Technologies) and using a DB-5 MS capillary column (30 m  $\times$  0.25 mm  $\times$  0.25  $\mu\text{m}$ ). Briefly, 1  $\mu\text{L}$  extract was injected in split mode at a ratio of 1/20 under the following chromatographic conditions: 250°C injection temperature and 50°C initial oven temperature, which was increased to 110°C over the next 5 min and then to 300°C at 7°C/min. A mass analyzer was used for scanning from 30 to 600 amu. Peaks were distinguished by

comparison with experimental mass spectra at the National Institute of Standards and Technology (NIST) and Wiley GC-MS libraries.

**2.5. Fourier Transform Near-Infrared (FT-NIR) Analysis of *P. africana*.** Powdered PWS, PIC, PIR, PIL, and PIS samples (3 g, each) were placed in 22 mm vials and analyzed as previously described by Komakech et al. [23] using a TANGO FT-NIR spectrometer (Bruker Optics, Billerica, MA, USA).

**2.6. Cancer Cell Line and Cell Culture Conditions.** The PC-3 cell line was subcultured in tissue culture flasks containing Dulbecco's Modified Eagle Medium supplemented with 1% penicillin-streptomycin, 10% fetal bovine serum, and 1% nonessential amino acids. Cells were incubated in a CO<sub>2</sub> incubator at 5% CO<sub>2</sub> and 95% relative humidity. After trypsinization, cell counts were performed and cell viability was assessed using trypan blue staining and a hemocytometer. A known number of cells ( $2 \times 10^3$  cells/well in 100  $\mu\text{L}$  medium) were seeded in 96-well microtiter plates for the methyl tetrazolium bromide (MTT) assay.

**2.7. Treatment and MTT Cell Viability Assay of PC-3 Cells.** Antiprstate cancer effects of PWS, PIC, PIR, PIL, and PIS extracts were determined *in vitro* using an MTT assay with PC-3 cells. To enhance cell attachment, the PC-3 cells were seeded at a known density in 96-well microtiter plates and incubated at 37°C at 5% CO<sub>2</sub> and 95% relative humidity for 24 h. After incubation, extracts were added to the cells at concentrations of 0, 10, 30, 60, 90, or 270  $\mu\text{g/mL}$ . Doxorubicin was used as a positive control, and a blank control was included to which the same concentrations of fresh



medium were added. The plates were incubated in a CO<sub>2</sub> incubator for 48 h before aspirating the medium from each well. The cells were then washed using phosphate-buffered (PBS) solution before adding a fresh medium. A 30  $\mu$ L aliquot of MTT (5 mg/mL in PBS) was added to each well, followed by incubation at 37°C for 4 h. The medium was then aspirated, and dimethyl sulfoxide (DMSO) was added to solubilize any formazan crystals formed. After incubation with cell-counting kit solutions for 1 h, absorbance was measured at 450 nm using a microplate reader (Versa Max), and cell growth inhibition caused by each extract was expressed as the corresponding IC<sub>50</sub> value.

**2.8. Apoptosis and Viability Assays.** Apoptosis induced by PWS and PIR extracts was determined by staining PC-3 cells with fluorescein isothiocyanate annexin-V and propidium iodide (PI) stains using the FITC Annexin V Apoptosis Detection Kit II (BD Biosciences, San Jose, CA, USA), according to manufacturer instructions. Cells were stained for 20 min on ice using the appropriate antibodies in a binding buffer (PBS with 2% FBS and 1 mM EDTA); analysis was performed using a fluorescence-activated cell sorter (FACS Canto II; BD Biosciences). Cell viability was determined using Cell Counting Kit-8 (CCK-8; Dojindo Molecular Technologies, Rockville, MD, USA). Briefly,  $2 \times 10^4$  cells/100  $\mu$ L were seeded in a 96-well plate, treated with PWS and PIR extracts at concentrations of 10, 30, 60, 90, and 270  $\mu$ g/mL and incubated at 37°C for 48 h. Then, 10  $\mu$ L CCK-8 was added to each well, and absorbance was measured at 450 nm using the SpectraMax i3x Multi-Mode Microplate Reader (Molecular Devices, San Jose, CA, USA).

**2.9. Western Blot Analysis of PC-3 Cells after Treatment with *P. africana* Extracts.** Proteins were extracted from PC-3 cells treated with different concentrations (0, 10, 30, 60, 90, and 270  $\mu$ g/mL) of PWS and PIR extracts using RIPA buffer (50 mM Tris-HCl, pH 7.4, 150 mM NaCl, 1% Triton X-100, 0.5% sodium deoxycholate, 0.1% SDS) (GenDEPOT, Baker, TX, USA). The cell lysate was separated on 8%–15% SDS-PAGE gels and transferred to PVDF membranes (Millipore, Bedford, MA, USA) treated with primary antibodies against cleaved caspase-3 (9661; Cell Signaling Technology, Danvers, MA, USA) and actin (sc-47778; Santa Cruz Biotechnology, Dallas TX, USA). After incubation with peroxidase-conjugated anti-rabbit or anti-mouse IgG (Jackson ImmunoResearch, West Gove, PA, USA), signals were detected using SuperSignal West Pico Chemiluminescent Substrate (Pierce). Western blots were visualized using WSE-6100 LuminoGraph (ATTO, Tokyo, Japan).

**2.10. 4',6-Diamidino-2-Phenylindole (DAPI) Staining.** PC-3 cells were maintained in Roswell Park Memorial Institute (RPMI) 1640 medium supplemented with 10% (v/v) fetal bovine serum and antibiotics. Cells were seeded on an eight-well slide and incubated overnight. After 24 h, cells were treated with respective IC<sub>50</sub> concentrations of PWS (52.30  $\mu$ g/mL) and PIR (82.40  $\mu$ g/mL), negative control cells were treated with DMSO (0.1%), and positive control cells

treated with doxorubicin (1.13  $\mu$ M) and incubated for 48 h. Incubated cells were washed with PBS, fixed with 2% paraformaldehyde and stained with DAPI (1  $\mu$ g/mL), and incubated for 5 min. Cells placed on slides were observed under a fluorescence microscope (Olympus CKX53; Olympus, Tokyo, Japan). The criteria defining apoptosis of DAPI staining, such as nuclear pyknosis and fragmentation, were applied as described in a previous study [25]. The number of nuclei showing these morphological characteristics was counted as DAPI positive cells under the immunofluorescence microscope at 40 $\times$  magnification. For each sample, three independent areas of interest with at least 1000 total nuclei per area were counted using Image J software and DAPI positive cells were showed as % of total cells. Statistical analyses were performed using a one-way analysis of variance (ANOVA) with GraphPad Prism 8.4.3.

**2.11. Statistical Analysis.** Means, standard error of the means, and proportions were determined. LC<sub>50</sub> values were determined using linear regression. The data were analyzed by ANOVA, and differences were tested using Bonferroni's post hoc test implemented in GraphPad Prism software (ver. 5.03). Statistical significance is reported at  $p < 0.05$ . FT-NIR spectroscopy multivariate statistical analyses were performed, and Ward's algorithm was calculated using OPUS TANGO-R software for homogeneity cluster analysis.

### 3. Results

**3.1. High-Performance Liquid Chromatography Analysis of *P. africana*.** Finger-printing analysis results of *P. africana* extract are shown in Figure 2. Sufficient selectivity and separation were recorded at 254 and 320 nm, respectively. Relative to PWS, sample PIS showed comparable component patterns at 15–20 min (Part I) and 40–45 min (Part II), although peak intensities differed. The components of sample PIC were comparable to those of sample PIR; in particular, these profiles appeared to be quite similar in Part I and Part II of the chromatogram at 320 nm. Among the five different *P. africana* sample types, sample PIL showed the most complex pattern, with various component profiles at all applied UV wavelengths.

**3.2. Gas Chromatography-Mass Spectrometry Analysis of *P. africana*.** Based on mass spectra, retention times, and quality ratio analysis, GC-MS analysis results for PWS extract indicated 32 components (Figure 3 and Table 1). Identified compounds included benzoic acid (14.02%),  $\beta$ -sitosterol (8.37%), 13-docoseamide (6.49%), and n-hexadecanoic acid (4.95%). Comparative analyses of the other extracts were performed based on the chemical composition of PWS extract. According to mass spectra and retention times (Table 1), 4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl- (4), benzoic acid (5), 5-hydroxymethyl-2-furaldehyde (8), n-hexadecanoic acid (23), 9,12-octadecadienoic acid (Z, Z)- (24), octadecanoic acid (26), 9-octadecenamide, (Z)- (28), 13-docosenamide, (Z)- (30), and  $\beta$ -sitosterol (32) were present in all extracts. Among these nine components, (5) represented

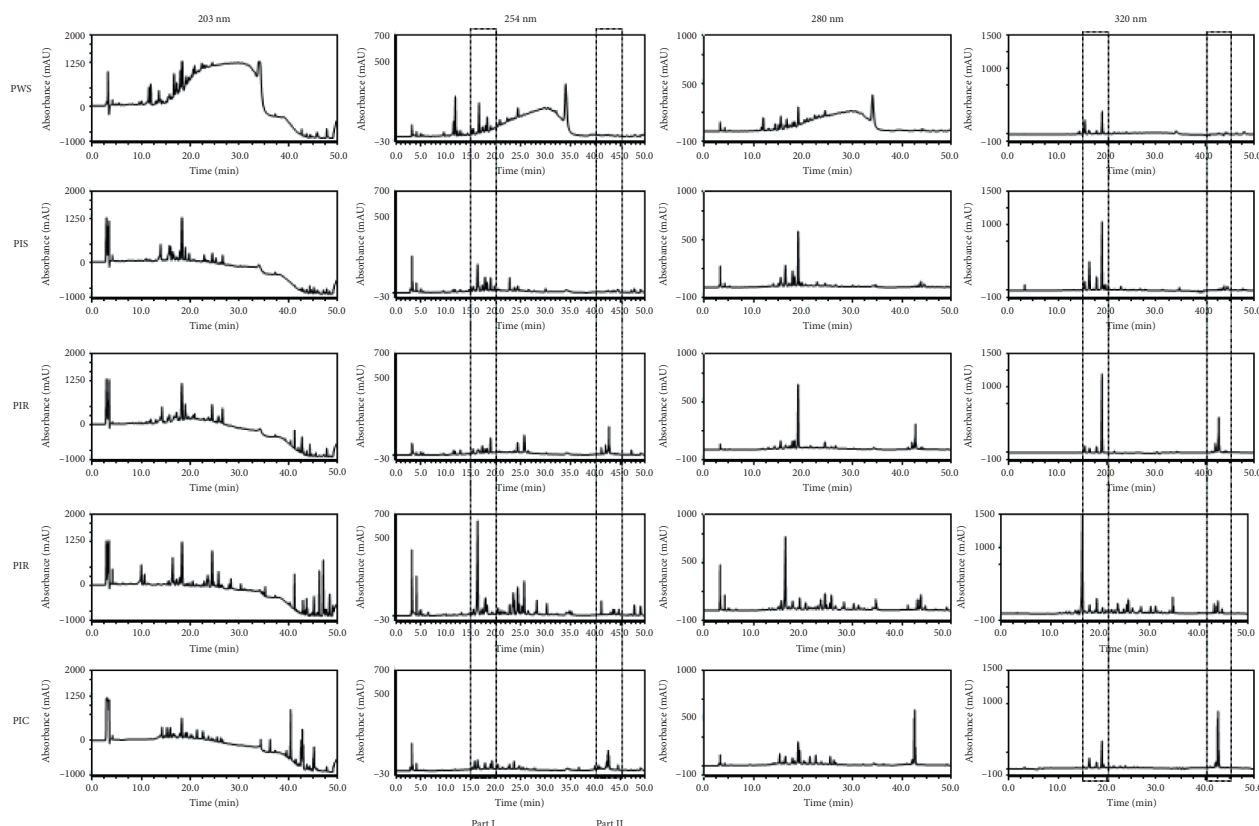


FIGURE 2: Finger-printing analysis of the extracts derived from *P. africana* by the HPLC-DAD method. PWS, mature *P. africana* stem bark; PIS, stem bark of juvenile cloned *P. africana*; PIR, root of juvenile cloned *P. africana*; PIL, leaves of juvenile cloned *P. africana*; PIC, callus generated from leaf explant of *P. africana*. Part I: retention part, 15–20 min; Part II: retention part, 40–45 min.

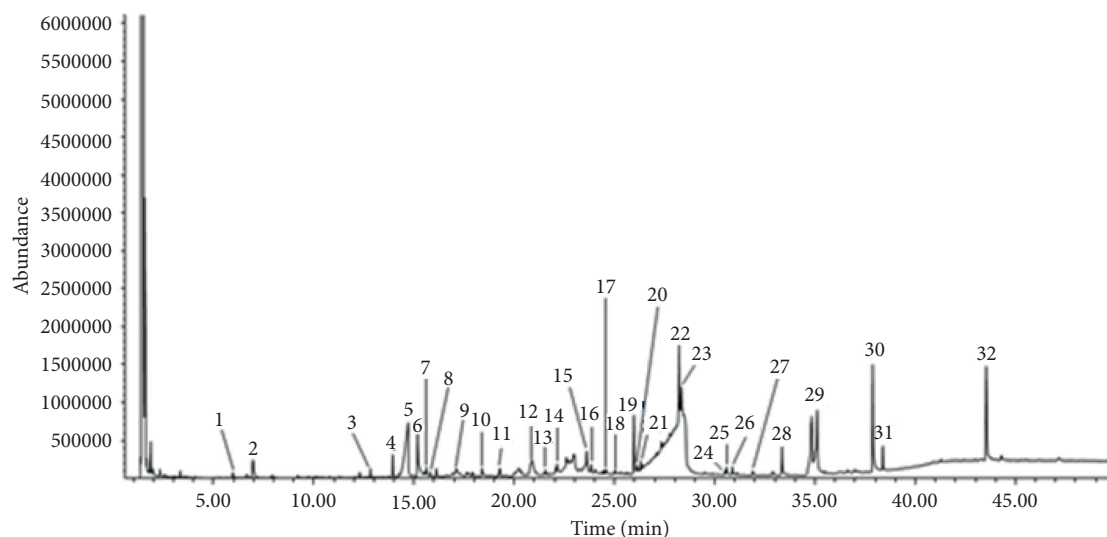


FIGURE 3: GC/MS chromatogram of the methanol extract of sample PWS.

the largest proportion of all compounds detected in a callus extract, compared with the PWS extract. In contrast, five components, including 3,4-altrosan (12), benzenepropanol, 4-hydroxy-3-methoxy- (15), benzaldehyde, 4-hydroxy-3, 5-dimethoxy- (16), 4-(hydroxymethyl)-2,6-dimethoxyphenol (17), and 6-hydroxy-5-trifluoromethylcyclohexa-1,3-diene (19), occurred only in PWS extracts. Vanillic acid (14) and

(R)- $\alpha$ -( $\beta$ -D-glucopyranosyloxy) benzene-acetonitrile (29) were detected in PWS and PIS extracts.

**3.3. Fourier Transform Near-Infrared Analysis of *P. africana*.** FT-NIR analyses of PWS, PIC, PIR, PIL, and PIS samples showed six prominent FT-NIR peaks within the region

TABLE 1: Phytochemical components detected in the methanol extract of *P. africana* experimental materials by GC/MS analysis.  $t_R$ : retention time (min); %: percent of total.

No.	Identified compound	PWS		PIS		PIR		PIL		PC	
		$t_R^1$	%2	$t_R$	%	$t_R$	%	$t_R$	%	$t_R$	%
1	3-Furanmethanol	5.96	0.39	—	—	—	—	5.97	0.16	5.97	0.79
2	Dihydroxyacetone	7.01	2.22	6.96	0.72	—	—	7.01	0.62	7.10	1.31
3	Benzoic acid, methyl ester	12.83	0.46	—	—	—	—	8.11	0.35	—	—
4	4H-Pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl-	13.95	1.13	13.95	0.63	13.94	0.66	9.19	0.06	14.00	2.87
5	Benzoic acid	14.68	14.02	14.60	3.10	14.55	1.83	12.83	0.15	14.48	0.71
6	Catechol	15.17	4.74	—	—	15.17	0.32	13.97	0.80	—	—
7	4-Vinylphenol	15.61	0.77	15.62	0.65	15.63	0.80	14.99	6.79	—	—
8	5-Hydroxymethyl-2-furaldehyde	15.81	0.31	15.81	0.81	15.81	0.11	15.20	0.80	16.03	24.79
9	Isosorbide	17.10	0.98	—	—	—	—	15.62	1.66	—	—
10	Phenol, 2,6-dimethoxy-	18.39	0.41	—	—	18.39	0.04	15.83	0.32	—	—
11	4-Hydroxy-3-methoxybenzaldehyde	19.30	0.41	25.03	0.14	—	—	—	—	—	—
12	3,4-Altrosan	20.84	3.30	—	—	—	—	—	—	—	—
13	Mandelamide	21.54	0.40	—	—	—	—	21.64	1.41	—	—
14	Vanillic acid	22.13	0.93	—	—	22.12	0.78	—	—	—	—
15	Benzenepropanol, 4-hydroxy-3-methoxy-	23.61	2.14	—	—	—	—	—	—	—	—
16	Benzaldehyde, 4-hydroxy-3,5-dimethoxy-	23.83	0.75	—	—	—	—	—	—	—	—
17	4-(Hydroxymethyl)-2,6-dimethoxyphenol	24.57	0.17	—	—	—	—	—	—	—	—
18	(E)-4-(3-Hydroxyprop-1-en-1-yl)-2-methoxyphenol	25.03	0.18	25.03	0.14	25.03	0.10	25.05	0.38	—	—
19	6-Hydroxy-5-trifluoromethylcyclohexa-1,3-diene	25.98	3.65	—	—	—	—	—	—	—	—
20	Benzoic acid, 4-hydroxy-3,5-dimethoxy-	26.13	0.29	26.12	0.08	26.20	0.13	—	—	—	—
21	Isopropyl myristate	26.31	0.40	26.31	0.15	—	—	—	—	—	—
22	Sorbitol	27.95	0.05	27.00	0.09	29.62	5.75	29.82	2.88	—	—
23	n-Hexadecanoic acid	28.21	4.95	28.22	2.34	28.22	3.72	28.24	1.52	28.23	3.18
24	9,12-Octadecadienoic acid (Z, Z)-	30.51	0.20	30.52	0.79	30.52	0.64	30.57	0.88	30.52	0.21
25	Oleic acid	30.58	0.76	30.60	0.99	—	—	—	—	30.60	1.72
26	Octadecanoic acid	30.87	0.47	30.87	0.66	—	—	30.89	0.58	30.88	0.69
27	Benzyl, beta-d-glucoside	31.90	0.32	31.90	0.17	—	—	32.05	0.28	31.97	0.16
28	9-Octadecenamide, (Z)-	33.35	1.95	33.35	0.80	33.35	1.05	33.36	0.33	33.35	0.59
29	(R)-alpha-(beta-D-glucopyranosyloxy)benzene-acetonitrile	35.10	6.60	—	—	35.10	1.91	—	—	—	—
30	13-Docosenamide, (Z)-	37.88	6.49	37.88	6.76	37.88	4.53	37.88	0.93	37.87	1.07
31	Squalene	38.38	1.09	—	—	—	—	38.40	5.34	—	—
32	Beta-sitosterol	43.55	8.37	43.57	16.77	43.56	7.75	43.56	4.76	43.55	4.02

between 8,500 and 4,000  $\text{cm}^{-1}$ , which included peaks at 8,273, 6,867, 6,344, 5,875–5,688, 5,172, and 4,938–4,500  $\text{cm}^{-1}$  (Figure 4(a)). The vertical scale of the dendrogram (Figure 4(b)) indicates the numerical distance between PWS, PIC, PIR, PIL, and PIS; as can be seen, all samples showed high heterogeneity at a distance of approximately 0.45. However, PIS, PIL, and PWS showed higher similarity and clustered with a spectral distance (heterogeneity) of 0.18, and further separation was observed in which PIL and PWS showed a closest spectral distance (heterogeneity) of approximately 0.12. Similarly, PIC and PIR clustered with a spectral distance (heterogeneity) of approximately 0.24.

**3.4. In Vitro Anticancer Effects of *P. africana* Extracts on PC-3 Cancer Cells.** A preliminary test failed to show any remarkable concentration-dependent antiprstate cancer effects from PIS, PIL, or PIC on PC-3 cell lines, whereby they were excluded from the main experiment. In contrast, PWS and PIR did show dose-dependent antiprstate cancer effects on PC-3 cells after exposure for 48 h. Therefore, we determined cancer cell viability using the CCK-8 assay and obtained  $\text{IC}_{50}$  values of 52.30 and 82.40  $\mu\text{g/mL}$  for PWS and PIR, respectively (Figure 5).

**3.5. Annexin-V and PI Staining.** To confirm that PWS and PIR induced apoptosis in PC-3 cells, we examined apoptosis levels after incubation with PWS and PIR extracts for 48 h using FACS, followed by annexin-V and PI staining. PWS and PIR induced apoptosis in PC-3 cells in a dose-dependent manner. Specifically, treatment with PWS produced a higher proportion of apoptotic cells than the PIR treatment (Figure 6(a)). The proportion of apoptotic cells correlated positively with extract concentration; furthermore, PWS at 90  $\mu\text{g/mL}$  resulted in 37.3% apoptotic cells, compared with 13.3% caused by PIR treatment (Figure 6(b)). A similar trend was observed for trypan blue staining, which showed more dead cells under the PWS treatment than under the PIR treatment (Figure 6(c)).

**3.6. 4',6-Diamidino-2-Phenylindole (DAPI) Staining.** The proportion of DAPI-stained apoptotic PC-3 cells following treatment with DMSO, PWS, PIR, and doxorubicin was 10.5%, 27%, 28%, and 27.5%, respectively (Figure 7). Furthermore, DAPI (4',6-diamidino-2-phenylindole) staining showed significant ( $p < 0.001$ ) induction of cell death after treatment with PWS, PIR, or doxorubicin (positive control), compared with

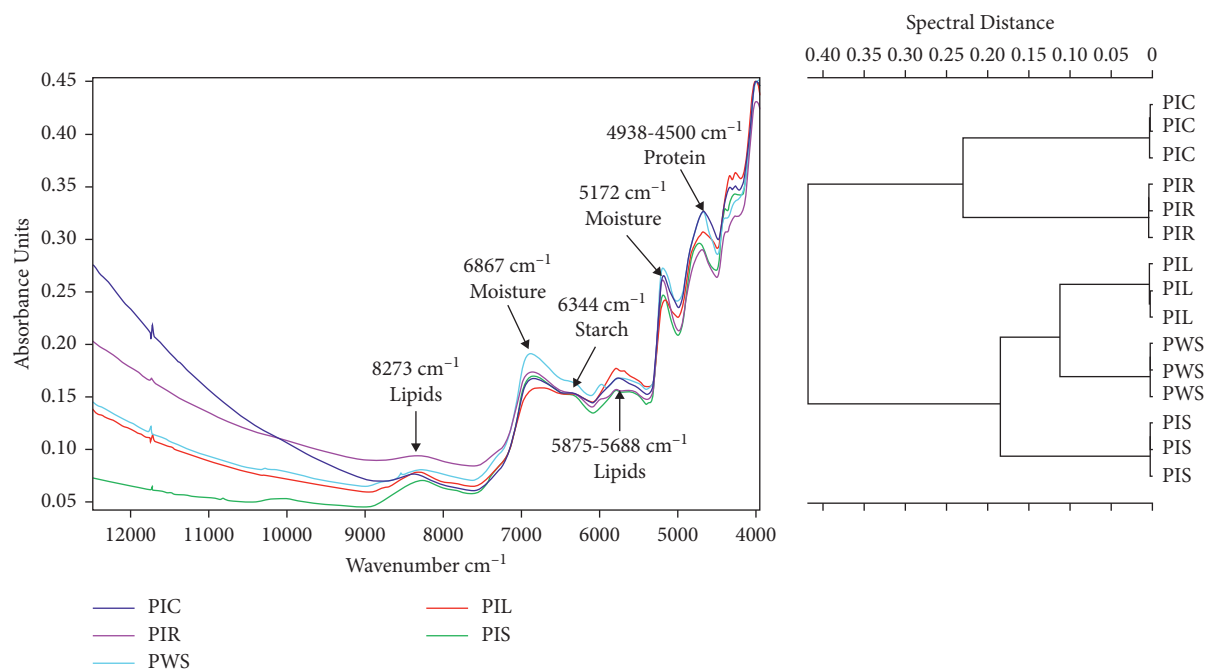


FIGURE 4: Multivariate statistical analysis of different samples obtained from *in vitro* regenerated and wild *Prunus africana* plants. (a) TANGO FT-NIR spectroscopy analysis results (wave number frequency range = 12,000–4,000  $\text{cm}^{-1}$ ). (b). FT-NIR chemical characterization based on Ward's algorithm clustering dendrogram (data preprocessing-first derivative + vector normalization; standard (Euclidean distance); frequency range = 12,000–4,000  $\text{cm}^{-1}$ ). PIC, *P. africana* callus sample; PIR, root sample obtained from *in vitro* regenerated *P. africana* plant; PIL, leaf sample obtained from *in vitro* regenerated *P. africana* plant; PWS, stem sample obtained from mature wild *P. africana* plant; PIS, stem sample obtained from *in vitro* regenerated *P. africana* plant.

the negative control, with no significant difference observed among PWS, PIR, or doxorubicin-treated cells.

**3.7. Western Blot Analysis.** Caspase-3 activation was determined by western blotting of cleaved caspase-3. PWS treatment induced higher cleaved caspase-3 levels in PC-3 cells than PIR treatment, an indication that PWS induced substantial apoptosis in PC-3 cells compared with PIR (Figure 8).

## 4. Discussion

FT-NIR spectrometry has been used in numerous studies to characterize chemicals present in samples [23, 26]. The absorption band at 8,273  $\text{cm}^{-1}$  in the current study was due to the second C–H overtone produced by lipids; in turn, the peak at 6,867  $\text{cm}^{-1}$  was due to the first O–H overtone caused by moisture, while the peak at 6,344  $\text{cm}^{-1}$  was due to the first O–H overtone linked to starches; additionally, the peak at 5,875–5,688  $\text{cm}^{-1}$  was due to the first C–H overtone linked to lipids; in turn absorbance peaks between 4,938 and 4,500  $\text{cm}^{-1}$  resulted from the combination of N–H, O–H, and C–H stretching associated with proteins [26–29]. Therefore, the similarity in the peaks of these samples associated with specific functional groups offers an indication of the high degree of chemical homogeneity among PWS, PIS, PIR, PIL, and PIC samples. Ward's algorithm clustering has been commonly used to characterize samples [30]. The dendrogram constructed herein showed high heterogeneity among PWS, PIS, PIR, PIL, and PIC samples, presumably

due to higher similarity of the various near-infrared spectra generated by the respective sample. As shorter distances between samples indicate close chemical phylogenetic relationships, the similarity of these samples regarding anti-prostate cancer effects may be due to the similarity in chemical composition among different *P. africana* samples.

In recent years, plant-derived phytochemicals have been widely used as chemopreventive and chemotherapeutic agents for treating various cancers, including prostate cancer [31]. In this study, numerous phytochemicals present in *P. africana* extracts were identified (Table 1), and anti-prostate cancer effects of the *P. africana* samples examined may be associated with some of these compounds.  $\beta$ -Sitosterol is one of the phytochemicals contributing to the antiprostata cancer effects of *P. africana* [18] and has been observed to induce apoptosis in human prostate cancer cells in cases of prostate lymph-node carcinoma [32, 33].

Nuclear factor kappa-B (NF- $\kappa$ B) inhibition is crucial in the arrest of cancer cell growth [34], and it exerts anti-mutagenic effects [35]. Therefore, the presence of 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-one in *P. africana* extracts may be responsible for the antiproliferative and proapoptotic effects of the different extracts on PC-3 cancer cells due to its ability to inactivate NF- $\kappa$ B. Additionally, the presence of benzoic acid in *P. africana* extracts may also be responsible for its anticancer effects. Indeed, previous studies revealed that benzoic acid derivatives delayed prostate cancer-cell growth, thereby preventing the expression of oncogenes by inhibiting histone deacetylases [36].

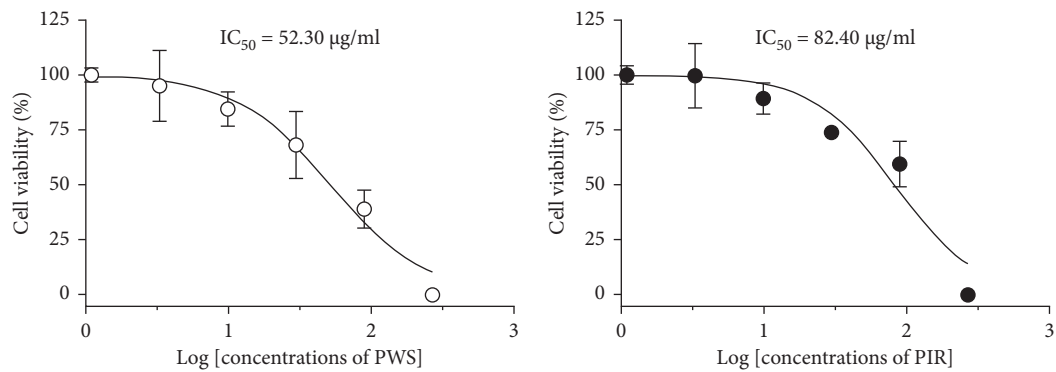


FIGURE 5: CCK-8 assay of PC-3 cells viability when exposed for 48 h at different concentrations of PWS and PIR samples. Results were expressed as percentage of cell viability and each point expressed as mean  $\pm$  SD ( $N=3$ ).  $IC_{50}$  values are calculated by using GraphPad Prism software.

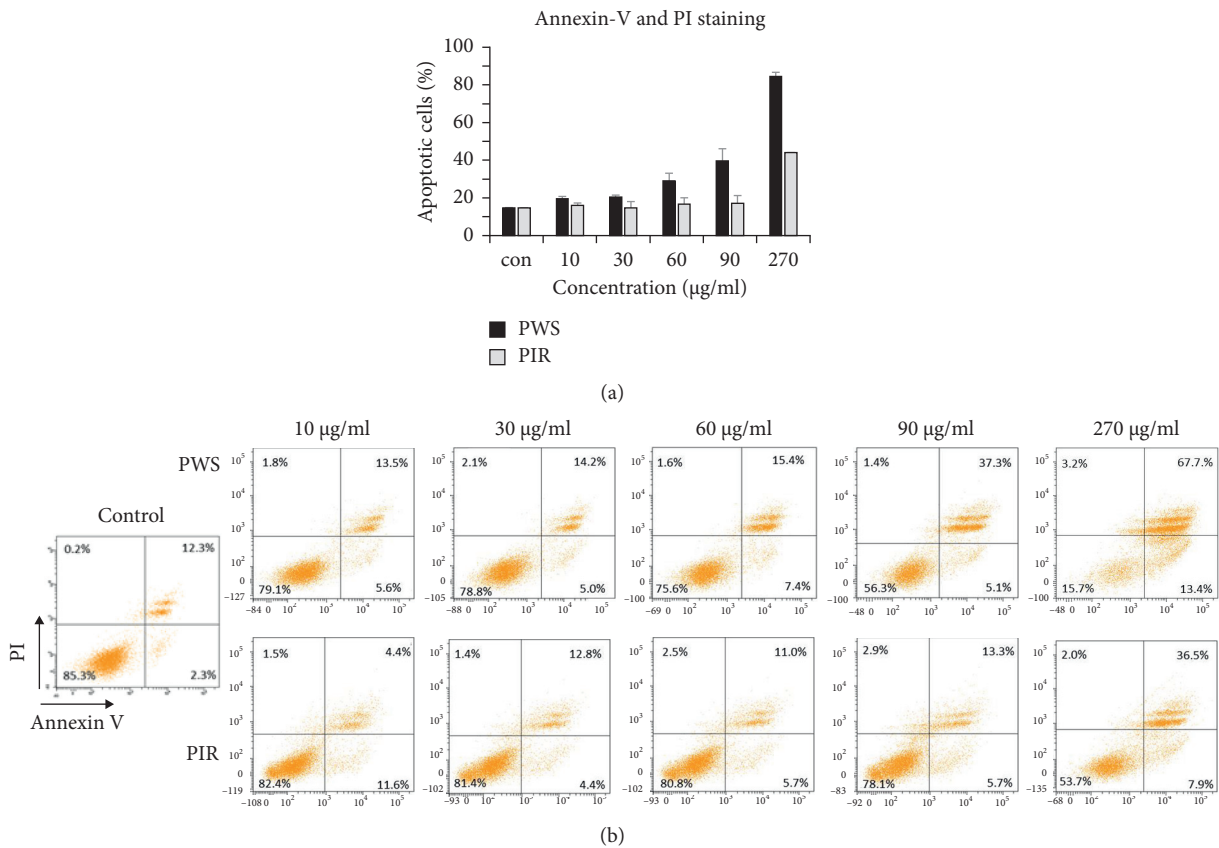


FIGURE 6: Continued.



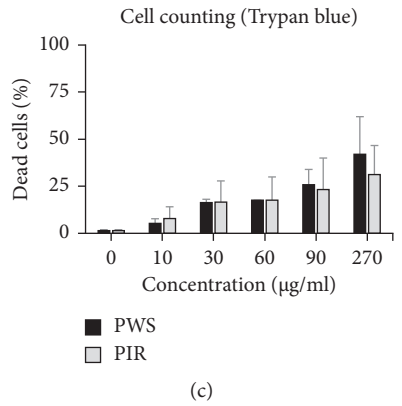


FIGURE 6: Apoptosis assay of PC-3 cells after 48 h treatment with PWS and PIR samples. (a) Apoptosis levels after annexin-V and PI staining of treated PC3-cells. (b) Apoptosis levels of treated PC-3 cells by flow cytometry (FACS) after annexin-V and PI staining (the upper left quadrant indicates necrotic cells (annexin V (-)/PI (+)), the upper right quadrant indicates late apoptotic cells (annexin V (+)/PI (+)), lower right quadrant indicates early apoptotic cells (annexin V (+)/PI (-)), and the lower left quadrant indicates healthy cells (annexin V (-)/PI (-)). (c) Dead cells of treated PC-3 cells when stained with trypan blue.

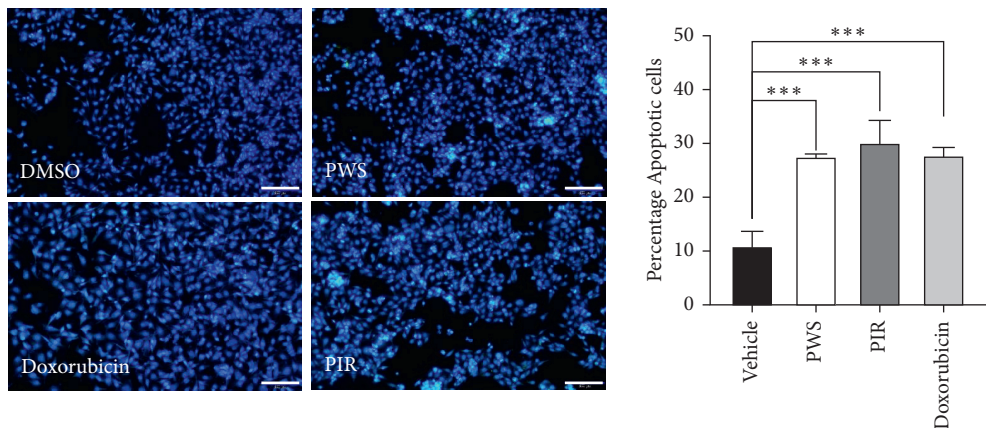


FIGURE 7: Changes in PC-3 cells nuclear condensation observed after DAPI staining when treated with PWS (52.30 µg/ml) or PIR (82.40 µg/ml), vehicle (0.1% DMSO), and doxorubicin (1.13 uM) as a positive control and incubated for 48 h. Representative image and percentage of apoptotic cells were shown. \*\*\* $p < 0.001$  compared with vehicle-treated controls.

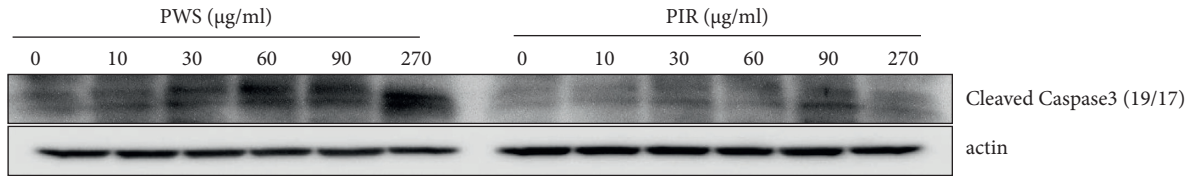


FIGURE 8: Western blot analysis of PC-3 after 48 h treatment with PWS and PIR samples.

Annexin-V and PI staining are important techniques for accurate assessment of cell death [37]. Hence, to determine whether the growth inhibitory effect of PWS and PIR on PC3 cells was associated with the induction of apoptosis, the cells were stained with Annexin V-FITC and propidium iodide. Annexin V is a calcium-dependent phospholipid-binding protein with a high binding affinity for phosphatidylserine-phospholipid, which is exposed at the outer layer of the cell membrane during the initial stages of apoptosis [38, 39]. Conjugation of a fluorophore to Annexin V (FITC) therefore

allows for detection of early apoptotic cells. Also, as apoptosis progresses, the cell membrane loses integrity and cells become necrotic. At this stage, propidium iodide—a fluorescent viability dye, which is impermeable to the cell membrane—diffuses freely into dying cells. Therefore, staining of cells with annexin V in conjunction with PI is usually done to establish the integrity of the cell membrane and distinguish living cells from both early and late apoptosis [40]. In the present study, annexin-V and PI staining showed significant induction of PC-3 cell death after

treatment with PWS and PIR extracts. As depicted in Figure 6, exposure of cells to PWS and PIR increased the proportion of apoptotic cells (both early and late apoptosis) in comparison with negative control cells, although PWS displayed higher apoptosis-inducing capacity compared with PIR. The extracts displayed different chemical profiles. Some of the major compounds identified in PWS were either absent or only found as minor constituents in PIR. This may partly account for the increased apoptosis-inducing effects of PWS since some of these bioactive compounds (e.g., squalene and vanillic acid) are known to induce apoptosis in cancer cells.

DAPI is a DNA-specific fluorochrome that binds strongly to adenine-thymine-rich regions of DNA and is widely used to analyze nuclear morphologic changes such as DNA fragmentation during apoptosis [41]. In the present study, the nuclear features of the cells were examined by DAPI staining. DAPI is known to only inefficiently pass through an intact cell membrane and hence preferentially stain dead cells [42] including dead PC-3 cells [43]. As depicted in Figure 7, data from this study showed that nuclei of the negative control cells were homogeneously stained with DAPI and displayed less blue fluorescence intensity due to the presence of more intact cell membrane compared with the higher staining intensity of the cells treated with PWS, PIR, and doxorubicin, which suggest a compromised apoptotic cell membrane. PC-3 cells treated with PWS, PIR, and doxorubicin (positive control) showed altered nuclear DNA staining, nuclear fragmentation, and condensation. In fact, the DAPI staining is an indication of PC-3 cell death via apoptosis [44].

In a previous *in vitro* anticancer activity study, *P. africana* stem bark methanolic and aqueous extracts had respective  $IC_{50}$  values of  $24.4 \pm 3.6$  and  $19.9 \pm 0.9 \mu\text{g/ml}$  against DU-145 prostate cancer cell lines [45]. In the same study, when these same extracts were tested against 22RV1 prostate cancer cell lines, the  $IC_{50}$  values were  $19.6 \pm 5.8$  and  $20.7 \pm 0.8 \mu\text{g/ml}$  for methanolic and aqueous extracts, respectively [45]. Compared with our findings, the  $IC_{50}$  values greatly differed. The differences in the  $IC_{50}$  values could be attributed to differences in the prostate cancer cell lines and extractants used. A study by Ghagane et al. [46] demonstrated that indeed the type of extracting solvent significantly influenced growth inhibition levels of PC-3 and DU-145 prostate cancer cell lines and thus the  $IC_{50}$  values. Another study by Yesil-Celiktas et al. [47] showed that different cancer cell lines were inhibited to varying degree by plant extracts.

Caspases are responsible for cell apoptosis, and specifically, caspase-3 activation plays a critical role in the execution of all apoptosis signaling pathways [48, 49]. Therefore, the detection of elevated levels of cleaved caspase-3 by western blotting following PWS and PIR treatment is a strong indication of apoptotic cell death in PC-3 cells via the intrinsic apoptosis pathway. In a previous *in vitro* study, the stem bark extract of *P. africana* was also observed to exhibit significant apoptosis in the PC-3 cell line and lymph node carcinoma of the prostate (LNCaP) [18].

## 5. Conclusion

PIR extracts exhibited a dose-dependent, *in vitro* anti-prostate cancer effect on PC-3 prostate cancer cells similar to that of the traditional PWS extract. Therefore, these extracts can be used as an alternative to stem bark collected from wild populations of *P. africana*, which may contribute to mitigating the threat of overexploitation of this endangered species. Furthermore, this study provides a sound theoretical basis for further research on the development of new prostate-cancer drugs from micropropagated *P. africana* plants.

## Data Availability

The data for this current study are available from the corresponding author upon reasonable request.

## Disclosure

Richard Komakech and Nam-Hui Yim are first coauthors.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this review paper.

## Authors' Contributions

Richard Komakech and Nam-Hui Yim contributed equally to this work as first coauthors.

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## Research Article

# The Application Effect of Traditional Chinese Medicine Nursing on General Anesthesia Combined with Epidural Anesthesia and Electric Resection for the Treatment of Bladder Cancer and Its Influence on Tumor Markers

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**Objective.** To explore the effects of traditional Chinese medicine nursing on general anesthesia combined with epidural anesthesia and electric resection to treat bladder cancer and its influence on tumor markers. **Methods.** A total of 160 patients with non-muscle-invasive bladder cancer who underwent general anesthesia combined with epidural anesthesia and resection were included in this study. The patients were divided into control group ( $n = 80$ ) and study group ( $n = 80$ ) according to the random number table method. The control group received hydroxycamptothecin bladder perfusion therapy, and the study group received traditional Chinese medicine nursing combined with hydroxycamptothecin bladder perfusion therapy. The clinical efficacy, three-year cumulative survival rate, and postoperative recurrence rate of the two groups of patients were detected. The levels of tumor markers including vascular endothelial growth factor (VEGF) and bladder tumor antigen (BTA) before and after treatment were also tested. The immune function, inflammatory factor levels, and quality of life of the two groups before and after treatment were evaluated. **Results.** The total effective rate of the study group (83.75%) was significantly higher than that of the control group (58.75%). After treatment, the serum VEGF and BTA levels, inflammatory factors interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels of the two groups of patients decreased, and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ ). After treatment, the levels of CD3+, CD4+, and CD4+/CD8+ in the two groups increased ( $P < 0.05$ ), and the increase in the study group was more significant than that in the control group ( $P < 0.05$ ). After treatment, the CD8+ levels of the two groups of patients decreased ( $P < 0.05$ ), and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ ). After treatment, the quality-of-life scores in both groups increased ( $P < 0.05$ ), and the increase in the study group was even more significant ( $P < 0.05$ ). **Conclusion.** Traditional Chinese medicine nursing has significant clinical effects on the treatment of bladder cancer with general anesthesia combined with epidural anesthesia and electric resection. It can more effectively prevent the risk of recurrence of bladder cancer after surgery, significantly improve the quality of life, improve immune system function, regulate the levels of VEGF and BTA, effectively reduce the level of serum inflammatory factors, inhibit tumor progression, and reduce tumor viability.

## 1. Introduction

Bladder cancer is one of the common clinical urinary system malignancies; its cause is long-term exposure to chronic infection, environment, foreign body stimulation, and other

factors, leading to inactivation of tumor suppressor genes and activation of oncogenes, which in turn induce bladder cancer [1]. The early clinical manifestations of bladder cancer are symptoms such as frequent urination, urgency, and hematuria, and they are nonspecific. A few patients only

have abdominal pain, and the rate of misdiagnosis and missed diagnosis is high [2]. Clinically, it can be classified into non-muscle-invasive bladder cancer (NMIBC), muscle-invasive bladder cancer, and metastatic bladder cancer [3]. NMIBC is one of the most common pathological types, accounting for more than 70% of bladder cancer, with high incidence, and its incidence has been increasing year by year in recent years and has become a critical disease endangering human health [4]. Early detection and scientific and effective intervention measures can effectively control the progression and deterioration of the disease and improve patients' quality of life.

Radical surgical resection is the main treatment for NMIBC, and most patients can be cured by transurethral resection of bladder tumor (TURBT) [5]. The application of anesthesia is an indispensable part of the operation, and the effects of different anesthesia methods are different, which directly relates to whether the operation can be carried out smoothly. General anesthesia combined with epidural anesthesia is widely used in clinical practice. Under the premise of ensuring the effect of anesthesia, this method has a small amount of anesthetic, which helps to reduce the perioperative stress response [6]. According to reports, the recurrence rate of bladder cancer is high, and about 1/3 of them have progressed, which seriously affects the effect of surgical treatment [7, 8]. Western medicine routinely uses chemotherapy drugs to prevent the recurrence of bladder cancer after surgery; although it can reduce the risk of tumor recurrence to a certain extent, the overall effect is still unsatisfactory. Long-term use of drugs has obvious side effects, and many patients give up because they cannot bear the perfusion therapy [9]. Studies have shown that traditional Chinese medicine (TCM) has obvious synergistic and detoxification effects on patients with bladder cancer postoperative perfusion. It can promote the recovery of body functions by enhancing the body's righteousness, which can regulate the body's immune function as a whole, prolong survival time, and improve the quality of life of patients [10]. We aimed to study the effects of traditional Chinese medicine nursing on patients after surgery and the impact on tumor markers.

## 2. Materials and Methods

**2.1. Clinical Information.** From March 2014 to October 2016, 160 patients with non-muscle-invasive bladder cancer who underwent general anesthesia combined with epidural anesthesia and resection at Yantai Yuhuangding Hospital, Yantai, Shandong, China, were selected and randomly divided into control group and study group, with 80 cases in each group. Control group comprised 67 males and 13 females, with age 43–71 years, average  $(52.65 \pm 7.32)$  years old; duration 0.4–2 years, average  $(0.93 \pm 0.36)$  years. Study group comprised 64 males and 16 females, with age 42–69 years, average  $(51.24 \pm 7.28)$  years; duration 0.5–2 years, average  $(0.98 \pm 0.41)$  years. There was no statistically significant difference in general information between the two groups ( $P > 0.05$ ).

**2.1.1. Inclusion Criteria.** All were in line with the “Guideline Manual for the Diagnosis and Treatment of Urological Diseases in China” [11] Western Medicine Diagnostic Standards and “Integrated Traditional Chinese and Western Medicine Urology” [12] Damp Toxins and Qi Deficiency Syndrome Differentiation Diagnosis Standards in Traditional Chinese Medicine; all were operated on pathologically confirmed, aware of this study, and signed informed consent; patients were without a history of radiotherapy, chemotherapy, and immunotherapy; expected survival time is more than 6 months.

**2.1.2. Exclusion Criteria.** Patients with autoimmune diseases, blood system diseases, systemic infectious diseases, or tumors in other parts; patients with stones or urinary tract infections; patients with severe mental diseases such as bipolar disorder, poor compliance, or other factors which makes it difficult to complete this research were excluded. This study was approved by the Ethics Committee of the Yantai Yuhuangding Hospital, Yantai, Shandong, China.

**2.2. Treatment Methods.** The control group was given bladder infusion of hydroxycamptothecin (Hubei Li Pharmaceutical Co., Ltd., National Medicine Standard H20033896, 2 mL: 5 mg). 40 mg was added to 40 mL of 0.9% medical sodium chloride injection and then injected into the bladder through a catheter, respectively, maintaining the left, right, supine, and prone positions for 30 minutes each, once a week for 8 times, and then changing to once a month. The study group added traditional Chinese medicine nursing treatment on this basis. The prescriptions were as follows: *Hedyotis diffusa* 30 g, honeysuckle 30 g, comfrey 30 g, agrimony 25 g, *rehmannia* 20 g, Wangbuliuxing 15 g, plantago 15 g, angelica 10 g, 6 g of *Prunella vulgaris*, 6 g of licorice flakes, 6 g of *Panax notoginseng* powder, and 6 g of cork. Take 1 dose per day, add 300 mL of water, decoct to 100 mL, and take it warmly in the morning and evening. The treatment time for both groups was 12 months.

## 2.3. Observation Indicators

- (1) Compare the clinical efficacy of the two groups [13]. The efficacy is divided into complete remission (CR), partial remission (PR), stable (SD), and disease progression (PD). Evaluation criteria are as follows: CR: all tumor lesions disappeared after treatment, or imaging examination showed that the lesion volume was reduced by more than 75%; PR: the lesion volume was reduced by 50% to 75%; SD: the lesion volume was reduced by 25% to 50%; PD: the size of the lesion decreased remained unchanged or expanded, and even new lesions were produced. Total effective rate is as follows:  $(CR + PR) / \text{total number of cases} \times 100\%$ .
- (2) Compare the levels of tumor markers before and after treatment in the two groups. Enzyme-linked immunosorbent assay was used to detect the levels of vascular endothelial growth factor (VEGF) in

patients. Radioimmunoassay was used to detect serum tumor markers including bladder tumor antigen (BTA) levels.

- (3) Compare the levels of inflammatory factors before and after treatment in the two groups. Enzyme-linked immunosorbent assay (ELISA) detects the levels of interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). The test kit is produced by Nanjing Jiancheng Institute of Biological Engineering and is operated strictly according to the kit instructions.
- (4) Compare the quality of life between the two groups before and after treatment. EORTC QOL-C30 scale was used to score [14]. Refer to the "Guidebook for Diagnosis and Treatment of Urological Diseases in China" to calculate the scores of physical function, cognitive function, role function, social function, and emotional function. Each item is worth 100 points. The higher the score, the better the quality of life.
- (5) Compare the immune function of the two groups before and after treatment. Flow cytometry was used to detect the levels of CD3+, CD4+, CD8+, and CD4+/CD8+.
- (6) Compare the long-term efficacy and recurrence rate of the two groups. Call monthly for return visits within 3 years after surgery, and calculate the cumulative survival rate for three years. Cystoscopy should be reviewed every 3 months within 1 year after surgery, and cystoscopy should be reviewed every 6 months in the second and third years. If suspicious lesions are found during cystoscopy, random mucosal biopsy or pathological biopsy of suspicious tissues will be performed to determine whether it is a recurrence of bladder cancer and to make statistics on the recurrence rate.

**2.4. Statistical Analysis.** The data was analyzed and processed by SPSS 19.0. Measurement data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) and subjected to  $t$  test; count data were expressed as  $n$  (%) and subjected to  $\chi^2$  test.  $P < 0.05$  indicated that the difference was statistically significant.

### 3. Results

**3.1. Comparison of Clinical Efficacy between the Two Groups of Patients after Treatment.** The total effective rate of treatment in the study group was 83.75%, and the total effective rate in the control group was 58.75%. The total effective rate of the study group was significantly higher than that of the control group ( $\chi^2 = 14.706$ ,  $P = 0.02$ ), as shown in Table 1.

**3.2. Comparison of Tumor Marker Levels before and after Treatment between the Two Groups.** Before treatment, there was no statistically significant difference in the levels of VEGF and BTA between the two groups of patients

( $P > 0.05$ ). After treatment, the levels of both indexes of the two groups of patients decreased, and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ ), as shown in Figure 1.

**3.3. Comparison of the Immune Function of the Two Groups of Patients before and after Treatment.** Before treatment, there was no significant difference in the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ between the two groups. After treatment, the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ in the study group were  $57.61 \pm 3.007$ ,  $43.19 \pm 2.695$ ,  $25.40 \pm 3.385$ , and  $1.577 \pm 1.104$ ; the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ in the control group were  $51.28 \pm 2.922$ ,  $37.34 \pm 2.697$ ,  $32.15 \pm 2.632$ , and  $1.233 \pm 0.111$ . The difference between the study group and the control group after treatment was statistically significant ( $P < 0.05$ , Figure 2).

**3.4. Comparison of the Patients' Quality of Life in Two Groups before and after Treatment.** Before treatment, there was no significant difference in the scores of physical function, role function, emotional function, cognitive function, and social function between the two groups of patients ( $P > 0.05$ ). After treatment, the scores of various indicators in the two groups increased compared with those before treatment ( $P < 0.05$ ), and the score of the study group increased significantly ( $P < 0.05$ , Table 2).

**3.5. Comparison of the Levels of Inflammatory Factors before and after Treatment between the Two Groups.** Before treatment, there was no significant difference in the levels of IL-6, CRP, and TNF- $\alpha$  between the two groups of patients ( $P > 0.05$ ). After treatment, the levels of three indicators of the two groups of patients decreased, and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ , Figure 3).

**3.6. Comparison of Long-Term Efficacy and Recurrence Rate between the Two Groups.** After three years of follow-up, the three-year cumulative survival rate of the study group was 71.25%, and the recurrence rate was 32.50%; the three-year cumulative survival rate of the control group was 56.25%, and the recurrence rate was 61.25%. The difference between the two groups was statistically significant ( $P < 0.05$ , Figure 4, Table 3).

### 4. Discussion

Bladder cancer is a common primary malignant tumor of the urinary system in clinical practice, and its incidence has ranked first among urogenital tumors in China.

The main clinical manifestations of the patient are urinary discomfort, pain, hematuria with frequent urination, and other symptoms. As the disease becomes more serious, it could block the patient's urine flow and cause certain difficulties in urination [15]. The main reason for the occurrence of this disease is the dual effect of internal genetic



TABLE 1: Comparison of clinical efficacy between the two groups of patients after treatment ( $n$  (%)).

Group	$n$	CR	PR	SD	PD	Total effective rate
Study group	80	25	42	9	4	67 (83.75)
Control group	80	11	36	21	12	47 (58.75)

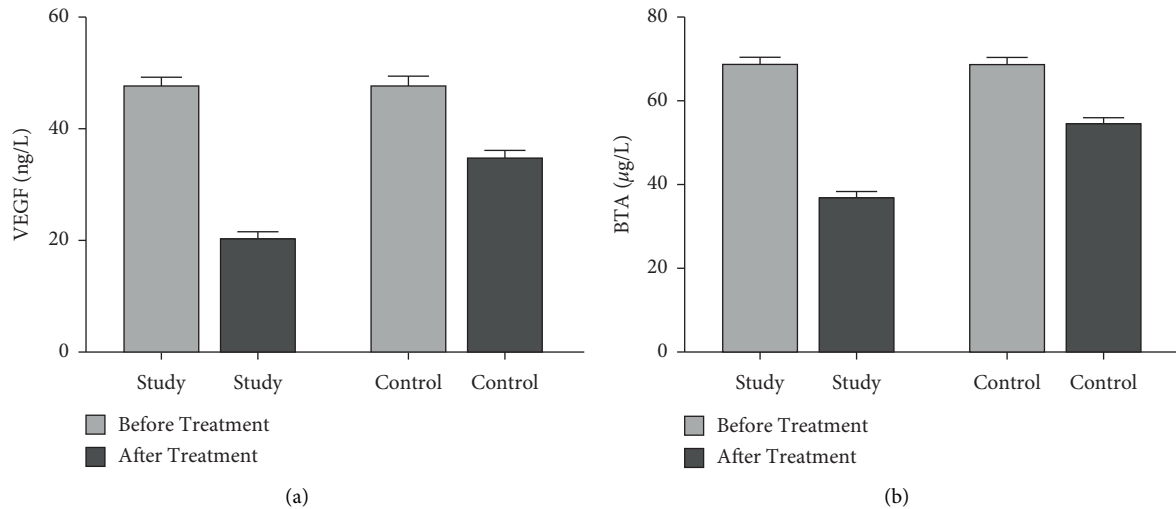


FIGURE 1: The levels of tumor markers in the two groups of patients before and after treatment. (a) The comparison of the VEGF levels of the two groups of patients before and after treatment. (b) The comparison of the BTA levels of the two groups of patients before and after the treatment.

factors and external environmental factors. Numerous studies have shown [4] that non-muscle-invasive bladder cancer accounts for more than 70% of initial bladder tumors and has the characteristics of strong infiltration, high malignancy, and easy recurrence. Surgery is currently the first choice for clinical treatment of this disease, and it effectively improves the patient's clinical symptoms and controls the progress of the disease. Because the bladder function can be kept normal, the postoperative recurrence rate is extremely high [16]. The tumor recurrence rate of 2 years after surgery is as high as 50%, and as much as 10% to 15% of patients with recurrent bladder cancer will experience varying degrees of deterioration. Some scholars pointed out [17] that early detection of bladder cancer and its recurrence is a key to successful cures and reducing mortality.

For the prevention of postoperative recurrence of patients with non-muscle-invasive bladder cancer, in Western medicine hydroxycamptothecin is mainly used as the primary chemotherapy drug for bladder perfusion therapy, which can reduce the recurrence rate caused by tumor cell dissemination after surgery, thereby effectively improving the therapeutic effects and improving the prognosis of patients [18]. The recurrence rate of bladder cancer with hydroxycamptothecin bladder perfusion is significantly lower than that of other chemotherapy drugs and its safety is higher [19]. It is currently one of the first-choice chemotherapy drugs for bladder perfusion in patients with bladder cancer. The toxic and side effects of hydroxycamptothecin are smaller than other chemotherapy drugs; however, because most patients are older at the time of diagnosis, their body is already in a declining

period, and the body's immune capacity is significantly reduced after surgery. Severe infection due to severe reduction of white blood cells caused by the myelosuppressive reaction after perfusion leads to poor prognosis of patients.

In recent years, the application of TCM in the adjuvant treatment of malignant tumors has made great progress. TCM is used to prevent and treat bladder tumors at all stages of tumor development and has obvious advantages in improving clinical symptoms, improving quality of life, and reducing toxic side effects [20]. According to TCM concepts, malignant tumors are caused by a lack of righteousness, internal invasion of evil toxins, blocking of qi and blood, stagnation of qi, blood stasis, and accumulation of toxins [21]. According to the TCM, the main pathogenesis of bladder cancer is damp heat or damp water gathering in the lower body [22]. The prescription used in this study consists of *Oldenlandia diffusa*, honeysuckle vine, comfrey, agrimony, *Rehmannia glutinosa*, wangbuliuxing, plantain, angelica, prunella, licorice, *Panax notoginseng* powder, and cork. Among these, *Oldenlandia diffusa* clears heat and detoxifies, relieves pain, and dissipates agglomeration, diuresis, and dehumidification; *Prunella vulgaris* clears fire and eyesight; licorice clears heat and detoxifies; honeysuckle clears heat and detoxifies, activates blood, and clears collaterals; *Lithospermum* cools and activates blood, clears heat, and detoxifies; *Panax notoginseng* powder stops bleeding, disperses blood stasis, and relieves pain; *Rehmannia glutinosa* nourishes and cools blood; Cheqianzi benefits water and heat and clears heat; *Phellodendron chinense* clears heat and dampness, purges fire, and detoxifies; angelica replenishes blood, promotes blood circulation, nourishes the intestines, and makes bowel

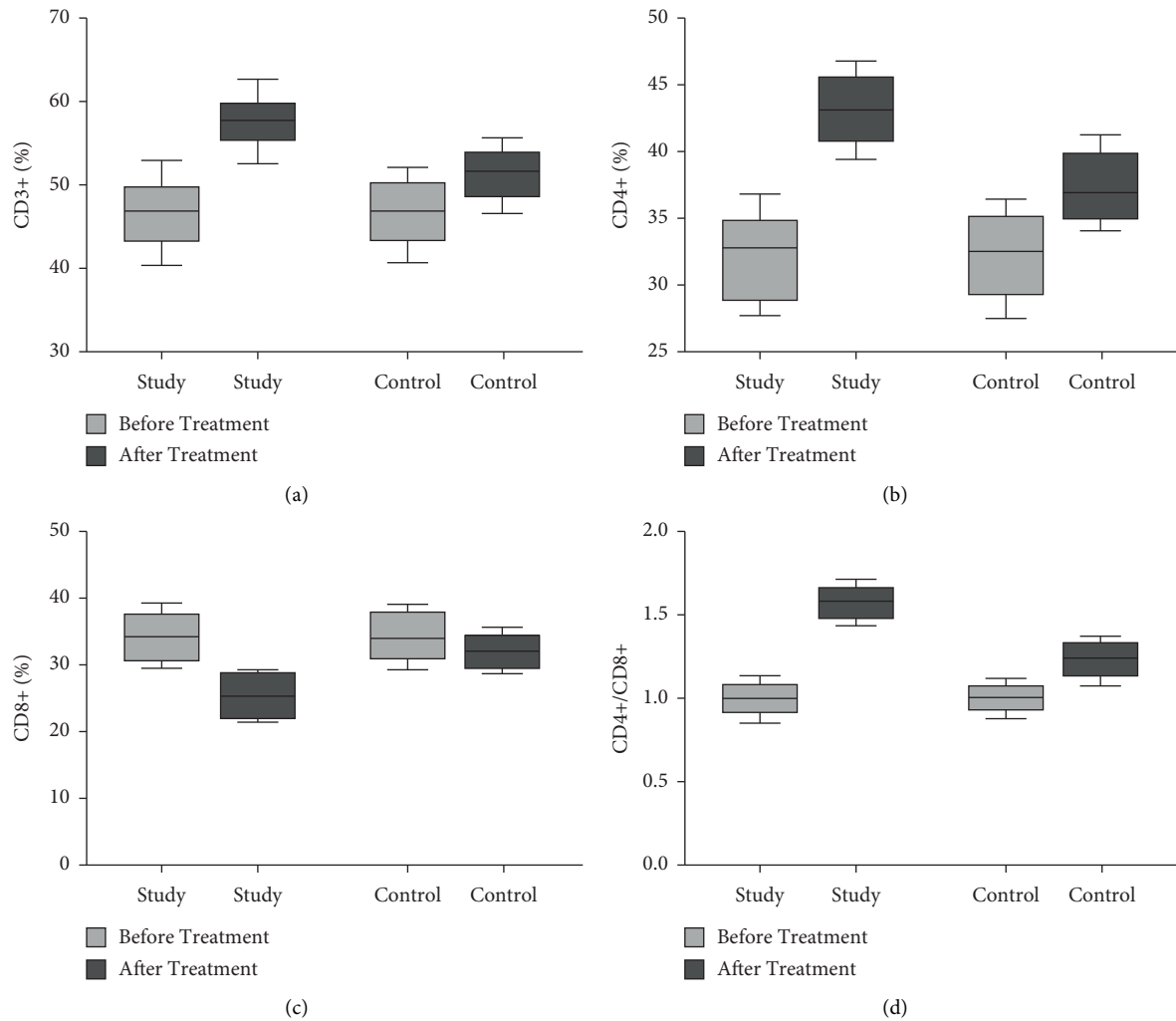


FIGURE 2: Comparison of the immune function of the two groups of patients before and after treatment. (a) The comparison of the CD3+ levels of the two groups of patients before and after treatment. (b) The comparison of the CD4+ levels of the two groups of patients before and after treatment. (c) The comparison of the CD8+ levels of the two groups of patients before and after treatment. (d) The comparison of CD4+/CD8+ levels before and after treatment in the two groups.

TABLE 2: Comparison of the quality of life of the two groups of patients before and after treatment ( $\bar{x} \pm s$ ).

Index	Study group ( $n = 80$ )	Control group ( $n = 80$ )	$t$	$P$
<i>Physical function</i>				
Before treatment	$54.32 \pm 4.36$	$55.25 \pm 4.47$	1.223	$>0.05$
After treatment	$75.63 \pm 5.42$	$62.37 \pm 5.11$	6.742	$<0.05$
<i>Role function</i>				
Before treatment	$51.25 \pm 5.63$	$51.77 \pm 5.71$	0.651	$>0.05$
After treatment	$78.46 \pm 6.52$	$64.71 \pm 6.27$	7.384	$<0.05$
<i>Affective function</i>				
Before treatment	$53.54 \pm 5.46$	$54.08 \pm 5.51$	0.877	$>0.05$
After treatment	$79.66 \pm 6.85$	$66.28 \pm 6.42$	11.393	$<0.05$
<i>Cognitive function</i>				
Before treatment	$56.34 \pm 5.47$	$55.89 \pm 5.26$	1.027	$>0.05$
After treatment	$72.34 \pm 6.67$	$63.71 \pm 6.27$	5.314	$<0.05$
<i>Social function</i>				
Before treatment	$51.43 \pm 4.15$	$51.22 \pm 4.23$	0.243	$>0.05$
After treatment	$78.96 \pm 6.53$	$63.38 \pm 5.22$	12.731	$<0.05$



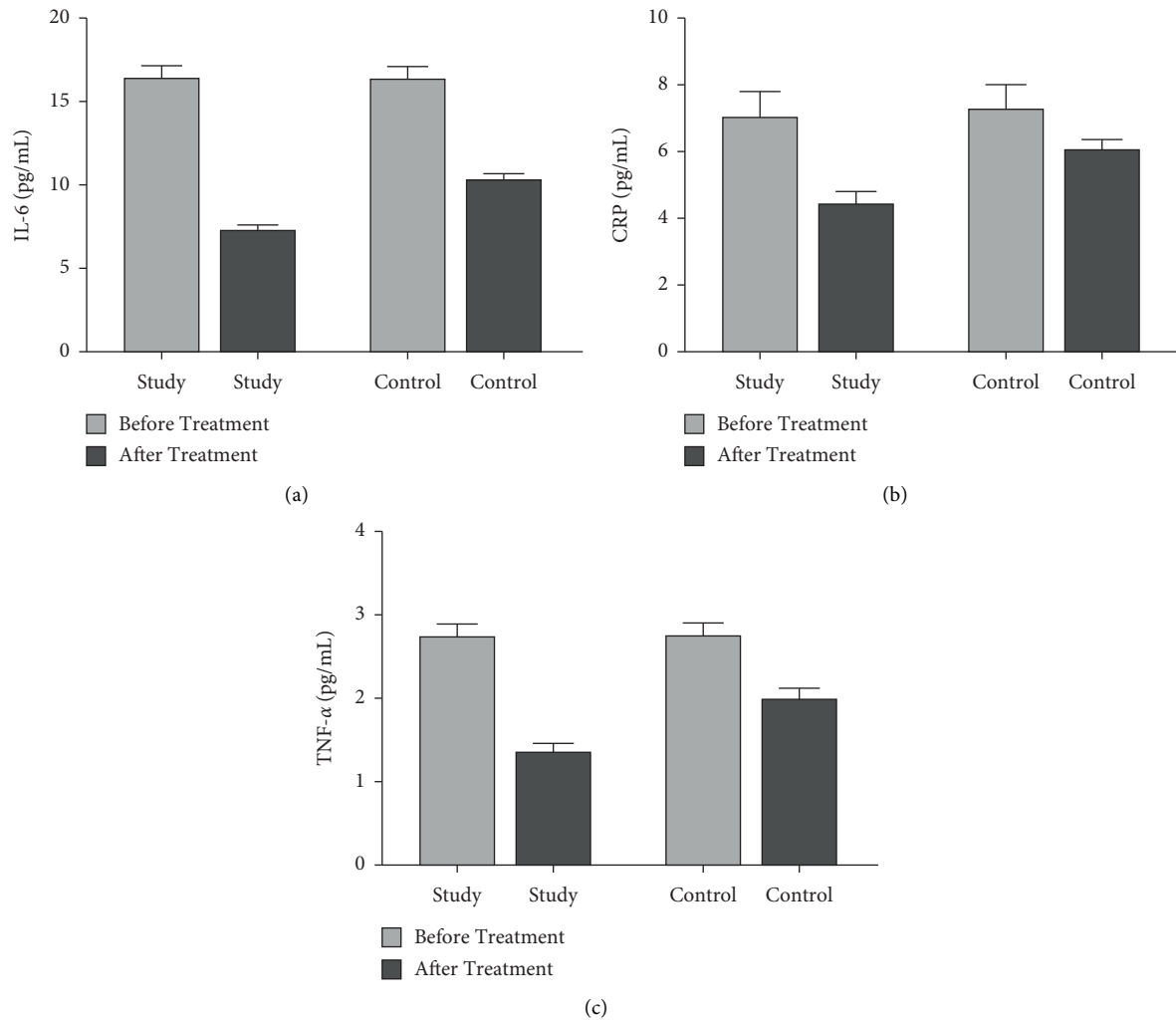


FIGURE 3: Comparison of the levels of inflammatory factors between the two groups of patients before and after treatment. (a) The comparison of IL-6 levels before and after treatment in the two groups of patients. (b) The comparison of CRP levels between the two groups of patients before and after treatment. (c) The comparison of TNF- $\alpha$  levels before and after treatment in the two groups.

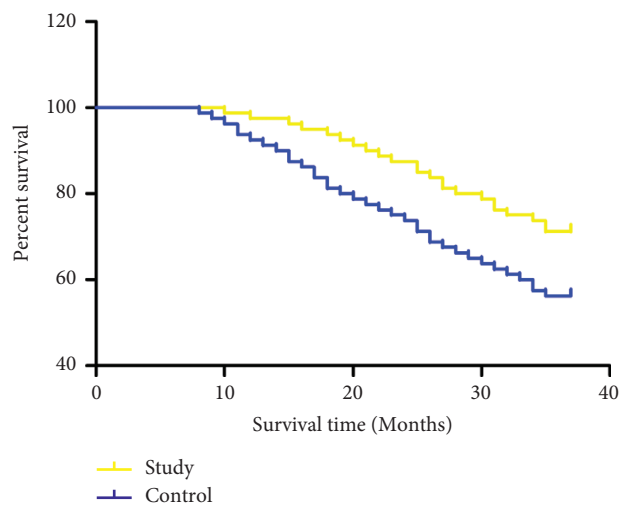


FIGURE 4: Comparison of the three-year cumulative survival rate of the two groups of patients.

TABLE 3: Comparison of the recurrence rate between the two groups of patients during the three-year follow-up ( $n$  (%)).

Group	$n$	Follow-up for 1 year	Follow-up for 2 years	Follow-up for 3 years
Study group	80	7 (8.75)	17 (21.25)	26 (32.50)
Control group	80	13 (16.25)	29 (36.25)	49 (61.25)

movement smooth; Wang buliuxing can promote blood circulation, detoxification and detumescence, diuresis, and gonorrhea; Agrimonia can stop bleeding and detoxify [23–27]. The combination of all medicines has the effects of clearing heat and detoxification, reducing swelling and blood stasis, stopping bleeding, and relieving pain.

VEGF is one of the essential cytokines that stimulate vascular endothelial cell proliferation and angiogenesis. Its increased expression level can promote endothelial cell differentiation and stimulate bladder tumor angiogenesis, which is closely related to the occurrence and development of bladder cancer and can be used to evaluate the malignancy of bladder tumors. It is an important reference index for prognosis [28]. Puntoni et al. [29] showed that VEGF is related to the clinicopathological characteristics of bladder cancer, which can reflect the development of bladder cancer patients to a certain extent, confirming that VEGF is closely related to the malignant development of bladder cancer patients, and it is expected to be used as a marker for prognostic evaluation. Zhu et al. [30] demonstrated that VEGF could promote tumor angiogenesis, regulate tumor cell proliferation, invasion, migration, and other malignant biological behaviors, and affect the prognosis and survival of patients with bladder cancer. Various studies have reported [31, 32] that, with the increase in the staging and grade of bladder tumors, the detection level of bladder tumor antigen (BTA) increases, the detection rate of multiple tumors is significantly higher than that of single tumors, and the initial tumor is significantly higher than that of single tumors, suggesting that BTA can be used as one of the important markers for the detection of bladder cancer. The results of this study revealed that the serum VEGF and BTA levels of patients after treatment were significantly lower than before treatment, and the serum marker levels of the study group were significantly lower than those of the control group. It is suggested that the TCM used in this study can effectively inhibit tumor progression and reduce tumor vitality. Long-term accumulation of toxins and glycation end products in patients with bladder cancer will increase the body's inflammatory factors, such as IL-6, CRP, TNF- $\alpha$ , and other acute reactive proteins. IL-6 can induce the synthesis of acute-phase protein and participate in the body's inflammatory response. TNF- $\alpha$  can easily provoke adhesion and infiltration of neutrophils and monocytes [33]. CRP is an inflammatory response marker protein, regulated by TNF- $\alpha$ , IL-6, and other mediators. The results of this study showed that the levels of inflammatory factors IL-6, CRP, and TNF- $\alpha$  in the patients after treatment were significantly lower than before treatment, and the levels of inflammatory factors in the study group were significantly lower than those in the control group, indicating that the use of traditional Chinese medicine in this study can significantly improve the inflammatory state to achieve the purpose of inhibiting tumor metastasis and recurrence. The results of this study showed that the clinical efficacy of the study group was significantly higher

than that of the control group; after treatment, the levels of CD3+, CD4+, CD8+, and CD4+/CD8+ in the two groups were significantly improved compared with those before treatment, and the difference between the study group and the control group was statistically significant ( $P < 0.05$ ). After treatment, the quality of life of the two groups was significantly improved compared to that of before treatment, and the difference between the two groups was statistically significant ( $P < 0.05$ ). After treatment, the three-year cumulative survival rate of the study group was significantly higher than that of the control group. The recurrence rate in the study group was significantly lower than that in the control group. It is suggested that traditional Chinese medicine nursing combined with bladder perfusion with hydroxycamptothecin for patients with non-muscle-invasive bladder cancer can effectively reduce the risk of postoperative recurrence, improve the quality of life, improve immune system function, enhance body immunity, and improve long-term survival. However, there is still a gap for improvements in this study. Small sample size may lead to a large probability of error in data deviation, so we hope to increase the sample size in future research to reduce the deviation of results. Moreover, the causes for the decrease of adverse drug reactions shall be further explored to get better outcomes. These are the directions of our follow-up and improvement, so as to find a better remedy for this condition.

In summary, the clinical effects of Chinese medicine adjuvant treatment of bladder cancer patients after general anesthesia combined with epidural anesthesia and resection are significant. The levels of tumor markers and inflammatory factors are significantly reduced, the recurrence rate of patients after surgery is reduced, and the prognosis of patients is relatively ideal.

## Data Availability

The datasets during the current study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they do not have any commercial or associative interest representing a conflict of interest in connection with the work submitted.

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## Research Article

# The Clinical Efficacy of Chemotherapy Combined with Traditional Chinese Medicine in the Treatment of Cervical Cancer and Its Influence on Cellular Immunity, Serum CEA, and TNF- $\alpha$

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**Background.** This study aims to investigate the clinical efficacy of chemotherapy combined with traditional Chinese medicine in patients with cervical cancer and its effect on cellular immunoglobulin, serum sugar chain antigen 125 (CA125), carcinoembryonic antigen (CEA), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). **Methods.** Conventional chemotherapy was performed in control and observation groups. Meantime, the observation group received traditional Chinese medicine. Finally, the clinical efficacy, immunoglobulin, serum tumor markers, and serum TNF- $\alpha$  of the two groups were compared. **Results.** Compared with the control group, total effective rate in the observation group was increased. After treatment, serum CD8+, TNF- $\alpha$ , CA125, and CEA levels were reduced in the two groups, and the observation group was higher. In the two groups, CD3+ and CD4+ levels were enhanced after treatment, and the observation group was also higher. Compared with the control group, the immunoglobulin IgG, IgA, and IgM levels increased in the observation group. The incidence of adverse reactions in the observation group was reduced compared to the control group. **Conclusion.** Chemotherapy combined with traditional Chinese can help improve the clinical efficacy and immunity in patients with cervical cancer. Moreover, the safety and feasibility of the treatment method are relatively high.

## 1. Introduction

Cervical cancer (CC) is a common type of gynecological malignant tumor, and its development is a slow and continuous process from quantitative change to qualitative change [1–3]. There can be no symptoms in the early stage of CC. As the disease progresses, patients may experience symptoms such as contact bleeding and abnormal vaginal discharge [4, 5]. CC occupies the second place among the deaths of female malignant tumors in China, and its prevalence ranks first among female genital malignant tumors. According to the statistics of global cancer data in 2018, there are more than 560,000 newly diagnosed cases worldwide each year, and the death toll exceeds 310,000 [6]. The causes and pathogenic mechanisms of cervical cancer

are very complicated. However, with the development technology, the cause of cervical cancer has gradually become clear. It has been confirmed that persistent HPV virus is the main cause of cervical cancer [7–11].

Recently, the diagnosis rate of CC is rising. However, the patient is already in the advanced stage at the time of diagnosis because of the stealthiest of CC incidence. Surgical treatment alone is less effective and has a lower survival rate for advanced patients. At present, the main treatment methods for CC include surgery, neoadjuvant chemotherapy [12–14], concurrent chemotherapy, radiotherapy, and short-term radiotherapy. Radiotherapy combined with systemic chemotherapy is often used for patients with advanced, recurrence, and metastasis CC. Chemotherapy includes adjuvant chemotherapy, consolidation chemotherapy,

induction chemotherapy, intensive chemotherapy, maintenance chemotherapy, and neoadjuvant chemotherapy. Clinically, it has been found that patients with CC have different treatment effects due to the differences in the sensitivity of chemotherapy. Although increased dose of chemotherapy can improve the efficacy to a certain extent, it increases the occurrence of adverse reactions and side effects in patients. The increase of adverse reactions will affect the effect of chemotherapy, increase the suffering of patients, and affect the life quality of patients.

Traditional Chinese medicine [15–17] can not only enhance the antitumor effect of chemotherapy drugs but also improve the immunity of cancer patients. The antitumor effect of Chinese medicine mainly include inhibition of tumor cell proliferation, promotion of cell apoptosis, and differentiation and improvement of body immunity [18–21]. Combined treatment can obviously prevent recurrence and metastasis, reduce the damage of radiotherapy and chemotherapy to the digestive tract and hematopoietic system, and strengthen the effect of radiotherapy and chemotherapy [22–26]. Therefore, we explored the clinical efficacy of chemotherapy combined with traditional Chinese medicine in patients with CC and its influence on cellular immunity, serum TNF- $\alpha$ , CA125, and CEA.

## 2. Materials and Methods

**2.1. Clinical Patients.** 78 patients with CC in Zhangqiu District People's Hospital from January 2018 to January 2019 participated in this research. This study was approved by the Ethics Committee of Zhangqiu District People's Hospital (2018-H15) and was performed based on the Declaration of Helsinki. In general information, no significant difference was found between the two groups ( $P > 0.05$ , Table 1).

### 2.1.1. Inclusion Criteria

- (1) Western medicine diagnosis: symptoms and pathological examination results are in line with the "International Federation of Obstetrics and Gynecology Guidelines for the Diagnosis and Treatment of Cervical Cancer in 2015" [27]
- (2) The CC was diagnosed by cytological examination and pathological biopsy
- (3) Traditional Chinese medicine (TCM) diagnosis: all patients meet the "Guiding Principles for Clinical Research of New Chinese Medicines" [28]
- (4) Chemotherapy for the first time
- (5) Expected survival time is  $\geq 6$  months
- (6) Patients have complete clinical data
- (7) Patients provided written informed consent

### 2.1.2. Exclusion Criteria

- (1) Patients with other malignancies
- (2) Liver, kidney, or other vital organ dysfunctions
- (3) Mental or blood system diseases

TABLE 1: Comparison of general clinical data between the two groups of patients ( $n$ ).

Features	Observation ( $n = 39$ )	Control ( $n = 39$ )
Age	$54.36 \pm 10.03$	$52.91 \pm 9.67$
Course of disease (years)	$2.6 \pm 0.7$	$2.4 \pm 0.8$
The pathologic types		
Squamous cell carcinoma	30 (76.9%)	32 (82.0%)
Adenocarcinoma	6 (15.4%)	5 (12.8%)
Gland scale cancer	3 (7.7%)	2 (2.2%)
Stage		
II A	7 (18.0%)	6 (15.4%)
II B	11 (28.2%)	12 (30.8%)
III A	10 (25.6%)	10 (25.6%)
III B	11 (28.2%)	11 (28.2%)

- (4) Patients are allergic to the drugs in our research
- (5) Treatment program was intolerant or refused to cooperate with this study

**2.2. Treatment Methods.** The control group received conventional chemotherapy. Before chemotherapy, the patient was treated with water chemotherapy for 3 days (liquid volume  $\geq 3500$  ml). Then, cisplatin (DDP) was continuously administered for the first 5 days of chemotherapy ( $40 \text{ mg/m}^2$ ). Bleomycin (BLM) was given in the first 3 days ( $15 \text{ mg/m}^2$ ). The observation group received simultaneous chemotherapy and traditional Chinese medicine. It has been taken since the first day of chemotherapy. Chinese medicine mainly focuses on clearing away heat and detoxification, invigorating the spleen and kidney, and nourishing blood. The prescriptions are as follows: *Codonopsis* 15 g, *Astragalus* 30 g, *Atractylodes* 15 g, *Poria* 15 g, *Angelica* 15 g, *Rehmannia* 15 g, *Lycium barbarum* 15 g, *Psoralen* 10 g, *Sichuan Dipsacus* 10 g, *Oldenlandia diffusa* 30 g, *Smilax glabra* 15 g, August stick 20 g, and Sunburn Licorice 6 g. Patients with nausea and vomiting were added *Evodia* 9 g. Patients with bloating and loss of appetite were added 15 g of fried malt, 15 g of fried grain sprouts, 9 g of tangerine peel, 10 g of roasted chicken inner gold, and 6 g of *Citrus aurantium*. Patients with insomnia were added 15 g Shouwu vine, 10 g Baiziren, and 3 g *Polygala*. Patients with cold stomach were add 3 g cloves and 6 g dried ginger. Patients with obvious fatigue were added 20 g of *Astragalus*.

**2.2.1. Observation Indicators.** The clinical efficacy of patients includes complete remission (CR, complete regression of the lesion for more than one month), partial remission (PR, reduction of the lesion by  $>50\%$  for more than one month), stable disease (SD), and disease progression (PD) [29].

$$\text{Total effective rate} = \frac{(\text{CR} + \text{PR})}{\text{total}} \times 100\%. \quad (1)$$

**2.2.2. Enzyme-Linked Immunosorbent Assay (ELISA).** 5 ml of fasting venous blood was taken and centrifuged at 3000 r/min for 10 min. The supernatant was aspirated into

the EP tube with a pipette. The i4000SR automatic immunoassay analyzer (Abbott, USA) was used to measure CA125, CEA, and TNF- $\alpha$  levels with special kits.

**2.3. Cellular Immunoglobulin.** The fluorescence molecular labeling method and flow cytometer were applied to detect immunoglobulin IgG, IgA, and IgM levels in peripheral blood.

**2.4. T Lymphocyte Subgroup Detection.** The flow cytometer (CyFlow® Cube8, Partec, Germany) and fluorescent molecular labeling method were used to detect the peripheral blood T lymphocyte subsets CD3+, CD4+, and CD8+. We calculated the CD4/CD8 ratio.

**2.5. Statistical Analysis.** All experiments were repeated 3 times. SPSS 22.0 software was used to analyze experimental data. Data are expressed as mean  $\pm$  SD. The count data are expressed in  $n$  (%). The  $\chi^2$  test was used for comparison. The difference is defined at  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Clinical Efficacy.** The clinical symptoms of the two groups were relieved after treatment. A short-term effect was observed 1 month after treatment. The observation group included 11 CR patients (28.2%), 24 PR patients (61.5%), 3 SD patients (7.7%), and 1 PD patient (2.6%). The clinical efficacy rate was 89.7% (35/39). In the control group, there were 9 CR (23.1%), 25 PR (64.1%), 4SD (10.2%), and 1 PD (2.6%). The clinical efficacy rate was 87.2% (34/39). No significant difference was found in short-term clinical efficacy between the two groups ( $P > 0.05$ , Table 2).

**3.2. Comparison of Serum Tumor Marker before and after Treatment.** After treatment, the serum TNF- $\alpha$ , CEA, and CA125 levels in the two groups decreased. The levels of CA125, CEA, and TNF- $\alpha$  in the observation group were reduced compared to the control group ( $P < 0.05$ , Figure 1). The possible reason is that traditional Chinese medicine may promote the production of immunosuppressive cytokines in CC, thereby suppressing the local cervical immune response. The results suggest that traditional Chinese medicine has anti-inflammatory and analgesic effects by inhibiting the production of CA125, CEA, and TNF- $\alpha$ .

**3.3. Comparison of T Lymphocyte Subsets.** After treatment, CD4+ and CD4+/CD8+ in the cervical tissues of the two groups were increased. Meanwhile, the CD8+ level in the two groups was reduced ( $P < 0.05$ , Table 3). Compared to the control group, the increased level of CD4+ and CD4+/CD8+ and decreased level of CD8+ were detected in the observation group ( $P < 0.05$ , Table 3).

**3.4. Comparison of Serum Immunoglobulin Levels before and after Treatment.** After treatment, IgG, IgA, and IgM levels in the observation group were significantly higher than those in

TABLE 2: Comparison of short-term efficacy between the two groups of patients ( $n$  (%)).

Indicators	Observation	Control	$P$
CR	11 (28.2%)	9 (23.1%)	0.152
PR	24 (61.5%)	25 (64.1%)	
SD	3 (7.7%)	4 (10.2%)	
PD	1 (2.6%)	1 (2.6%)	
ORR	35/39 (89.7%)	34/39 (87.2%)	

the control group ( $P < 0.05$ , Table 4). The increase in the patient's immune globulin level can effectively reflect the increase in the patient's immune level, further confirming the effectiveness of the drug.

**3.5. Comparison of Adverse Reaction.** Before and after treatment, the patient's serological indicators were detected as indicators for monitoring serological side effects. Neutropenia was significantly reduced in the observation group compared with the control group ( $P < 0.05$ , Figure 2(a)). Thrombocytopenia, hemoglobin counts, and leucopenia decreased in both groups. However, there was no statistically difference between the two groups ( $P > 0.05$ , Figure 2(a)). The incidence of nausea, vomit, and myelosuppression in the observation group was lower than that in the control group ( $P < 0.05$ , Figure 2(b)). The results indicate that this treatment has high safety and is well tolerated.

**3.6. Comparison of Life Quality Scores.** The life quality score in the observation group after treatment was higher than before treatment ( $P < 0.05$ , Figure 3). Similarly, high life quality score of patients was also found in the control group after treatment ( $P < 0.05$ , Figure 3). Compared to the control group, the observation group had a higher life quality score after treatment ( $P < 0.05$ , Figure 3). The life quality score survey shows that chemotherapy and traditional Chinese medicine can improve the life quality of patients.

### 4. Discussion

World Society of Epidemiology and Statistics has proposed that CC is a malignant tumor that seriously affects women [1] in worldwide. Its risk severity is second only to breast cancer, and its growth momentum is higher than breast cancer [2]. CC has grown rapidly in worldwide in recent years, and China occupies a huge proportion. Due to the decline in environmental levels and diet quality, the high incidence of cancer is becoming one of the major problems that increasingly plague mankind [3]. Meanwhile, the incidence of CC gradually tends to be younger. The mortality rate of young patients suffering from CC has a significant upward trend. Since there are no obvious abnormal symptoms in CC at early stage, patients often need to receive chemotherapy after surgery to more completely eliminate cancer cells. However, chemotherapy often brings certain adverse reactions, such as bone marrow suppression, vomiting, and nausea. With the extension of chemotherapy

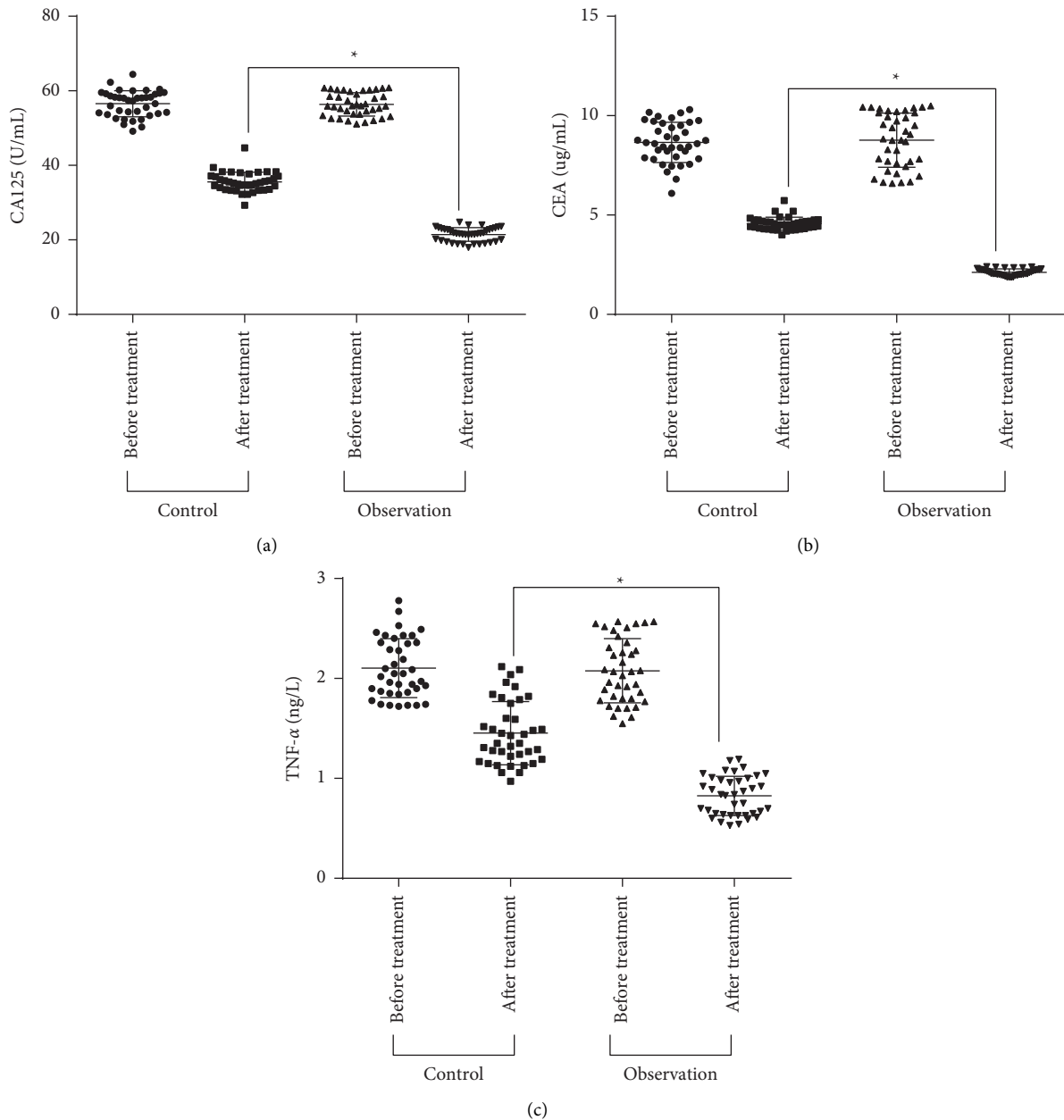


FIGURE 1: Comparison of serum tumor marker levels before and after treatment in the two groups. (a–c) CA125, CEA, and TNF- $\alpha$  levels were compared between two groups of patients ( $n = 39$ ). \* $P < 0.05$ .

TABLE 3: Comparison of immune function between the two groups.

Group	Time	CD4 <sup>+</sup>	CD8 <sup>+</sup>	CD4 <sup>+</sup> /CD8 <sup>+</sup>
Observation	Before treatment	27.35 $\pm$ 5.43	29.03 $\pm$ 6.10	0.99 $\pm$ 0.31
	After treatment	30.21 $\pm$ 5.03* <sup>#</sup>	25.76 $\pm$ 4.71* <sup>#</sup>	1.21 $\pm$ 0.30* <sup>#</sup>
Control	Before treatment	27.78 $\pm$ 5.21	29.51 $\pm$ 6.32	0.98 $\pm$ 0.31
	After treatment	28.98 $\pm$ 4.86*	27.63 $\pm$ 5.77	1.05 $\pm$ 0.29

Before and after treatment, \* $P < 0.05$ ; compared with the control group, <sup>#</sup> $P < 0.05$ .

time, the patient's body tolerance decreases, which can easily lead to the occurrence of various adverse reactions.

Recently, the use of integrated traditional Chinese and Western medicine in patients has become a popular method

for many scholars. TCM syndrome differentiation and evidence-based medicine helps improve the treatment effect and life quality of CC patients [30]. TCM has antivirus and strengthening the body's immunity effects and can avoid the



TABLE 4: Comparison of serum immunoglobulin levels between the two groups (g/L).

Group	Time	IgG	IgA	IgM
Control	Before treatment	11.03 ± 1.99	1.65 ± 1.16	1.39 ± 0.72
	After treatment	14.37 ± 2.17	2.07 ± 0.97	1.64 ± 0.73
Observation	Before treatment	11.23 ± 2.11	1.70 ± 1.21	1.42 ± 0.75
	After treatment	17.03 ± 2.74*	2.67 ± 0.78*	1.93 ± 0.83*

Compared with the control group after treatment, \* $P < 0.05$ .

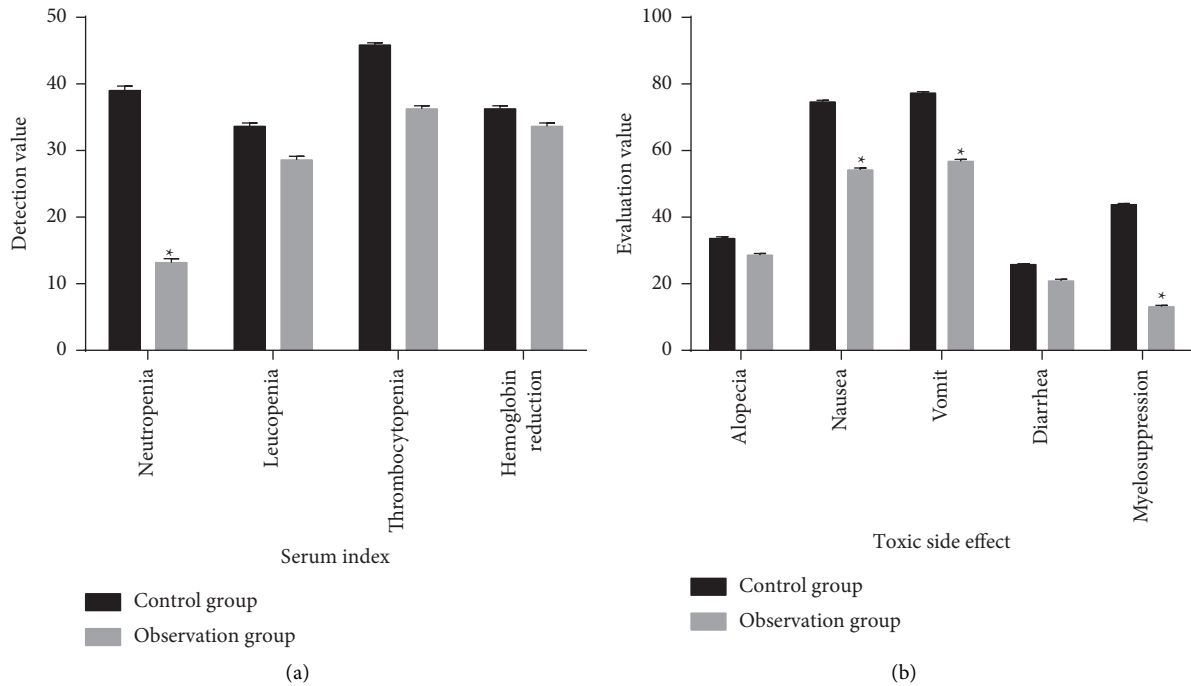


FIGURE 2: Comparison of adverse reactions between the two groups. (a) Comparison of serum toxicity and side effects between the two groups (% ,  $n = 39$ ). (b) The occurrence of clinical toxic and side effects compared between the two groups of patients (% ,  $n = 39$ ). \* $P < 0.05$ .

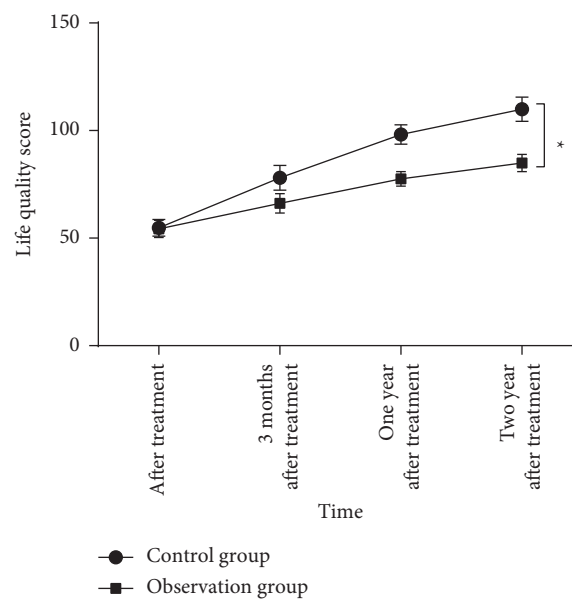


FIGURE 3: Comparison of life quality scores between the two groups ( $n = 39$ ). \* $P < 0.05$ .

trauma caused by physical and surgical treatment. Moreover, the prognosis of TCM is better. The systemic side effects of TCM are less [31]. Chemotherapy mainly uses poison to fight poison. Long-term treatment can cause fiery heat toxins to invade the patient's body. Therefore, qi and blood drugs should be used to improve the symptoms of such patients. In this study, *Astragalus*, *Atractylodes*, *Lycium barbarum*, and other traditional Chinese medicines can nourish the kidney and invigorate the spleen and kidney. Soil Fuling can clear away heat and detoxify. Psoralen can dispel blood stasis and masses.

In this study, the results showed that the clinical efficacy of traditional Chinese medicine combined with chemotherapy was better than chemotherapy alone. In addition, traditional Chinese medicine can improve the immune function and reduce the incidence of adverse reactions. Compared with chemotherapy alone, traditional Chinese medicine significantly reduced the serum tumor markers CA125, CEA, and TNF- $\alpha$  levels, immune index CD8+ levels, and adverse reactions. Traditional Chinese medicine also increased the degree of clinical symptom relief, immune index CD4+, CD4+/CD8+ levels, serum immunoglobulin IgG, IgA, and IgM levels, and life quality scores. The results show that traditional Chinese medicine can improve the tolerance and clinical efficacy of CC patients and reduce the toxic and side effects of chemotherapy. However, this study still has certain shortcomings. On the one hand, the research time is relatively short, and the patient's long-term tumor recurrence and quality of life are unknown. On the other hand, the number of selected cases is small, and the pathological type is single.

## 5. Conclusion

In summary, traditional Chinese medicine can help improve the clinical efficacy of chemotherapy and the serum tumor markers and immunoglobulin levels of CC patients. More importantly, this treatment method is feasible and safe, which is worthy of promotion.

## Data Availability

The datasets used during the present study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Diagnosis Value of Colposcope Combined with Serum Squamous Cell Carcinoma Antigen, Carbohydrate Antigen 125, and Carcinoembryonic Antigen for Moderate to Advanced Cervical Cancer Patients Treated with Modified Fuzheng Peiyuan Decoction

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**Objective.** To explore the diagnosis value of colposcope combined with serum squamous cell carcinoma antigen (SCC-Ag), carbohydrate antigen 125 (CA125), and carcinoembryonic antigen (CEA) for moderate to advanced cervical cancer patients treated with modified Fuzheng Peiyuan decoction. **Methods.** The clinical data of 43 moderate to advanced cervical cancer patients treated in Suzhou Hospital of Traditional Chinese Medicine from July 2018 to July 2019 were selected for the retrospective analysis, and 43 healthy women undergoing physical examination in our medical center in the same period were selected as the control group. The cervical cancer patients accepted the modified Fuzheng Peiyuan decoction treatment, the detection of SCC-Ag, CA125, and CEA and colposcope examination were performed to all research subjects, and the changes in indicators such as KPS scores and lesion perfusion parameters in cervical cancer patients before and after treatment were monitored, so as to analysis the clinical diagnosis value of combined diagnosis in treated patients. **Results.** After treatment, the mean KPS scores were greatly higher and various blood perfusion parameters of lesions and serum SCC-Ag, CA125, and CEA levels were remarkably lower than before ( $P$  value  $<0.001$  for all); the area under the curve of combined test was significantly larger than that of single test, and the sensitivity and specificity of the combined test were the highest; and after medication, the total incidence rate of toxic and side effects was 11.63%. **Conclusion.** Fuzheng Peiyuan decoction has significant effect in treating moderate to advanced cervical cancer, and colposcope combined with serum test presents more accurate and credible diagnosis results and has great significance for future treatment, which shall be promoted and applied.

## 1. Introduction

Cervical cancer is the most common malignant disease in women. There were 527,000 new cervical cancer cases in 2018; and every year in China, about 30,000 patients die of the disease and the maximum number of new cases can reach 12,000 [1, 2]. Currently, the methods for early screening and diagnosis of cervical cancer are still immature, resulting in a large proportion of patients already in middle or advanced stage at the time of presentation, thereby

missing the optimal timing of surgical resection. In the late stage of cervical cancer, because the tumor invades adjacent tissues or organs, patients will suffer from urgent micturition, frequent micturition, and sensation of anal bulge [3], as well as complications such as ureteral obstruction and damage to renal function, seriously harming life and health. Cisplatin is a common chemotherapeutic agent used in the current treatment of moderate to advanced ovarian cancer [4], which can effectively kill tumor cells, but at the same time cause certain adverse reactions including

myelosuppression and immune function impairment that are intolerable for patients [5]. Traditional Chinese medicine (TCM) has accumulated a large amount of experience in the treatment of gynecologic tumor diseases, and modern pharmacological studies have confirmed [6] the enriched astraglan component in Fuzheng Peiyuan decoction can enhance immunity and inhibit the pathogenic activity of virus, which has been demonstrated in the treatment of nonsmall cell lung cancer [7]. Colposcopy is a medical device used in the clinic to view the changes in the vagina, vulvar tissue, and cervical epithelium, which can assist in the localization and improve the positive rate of biopsies [8]. However, it also has some limitations, for instance, in elderly patients with stenosis of the vagina, colposcopy cannot achieve a good result in examining cervical adhesion, and only the 1–2 layers of epithelium on the surface can be viewed, but not the deep infiltrating carcinomas [9]. Therefore, an examination method with high diagnostic efficacy that can precisely grasp the lesion condition of such patients is necessary to provide them with highly effective treatment regimens. Serum marker detection is widely used in clinical practice in recent years for the diagnosis of cervical cancer and assists tumor screening, diagnosis, and efficacy evaluation. Based on this, the clinical diagnosis value of colposcope combined with serum SCC-Ag, CA125, and CEA for patients with moderate to advanced cervical cancer treated with modified Fuzheng Peiyuan decoction was explored herein.

## 2. Data and Methods

**2.1. General Information.** The clinical data of 43 moderate to advanced cervical cancer patients treated in Suzhou Hospital of Traditional Chinese Medicine from July 2018 to July 2019 were selected for the retrospective analysis, and 43 healthy women undergoing physical examination in our medical center at the same period were selected as the control group.

### 2.2. Inclusion and Exclusion Criteria

**2.2.1. Inclusion Criteria.** ① The patients met the diagnosis standards of cervical cancer in three-step diagnostic technique for cervical lesions [10] and were diagnosed after histopathological inspections, and the clinical manifestations included frequent micturition, urgent micturition, anal swelling, and contact bleeding; ② according to the international clinical staging criteria passed by the International Society of Obstetrics and Gynecology, the clinical stage was III–IV [11], and the patients did not receive chemoradiotherapy intervention before recruitment; and ③ the study met the World Medical Association Declaration of Helsinki [12] and was approved by the ethics committee of the Suzhou Hospital of Traditional Chinese Medicine.

**2.2.2. Exclusion Criteria.** ① The patients had immune or coagulation dysfunction; ② the patients took anticancer TCM preparation, immunomodulator, etc., four weeks before recruitment; and ③ the patients were allergic to the decoction applied in the study.

**2.3. Treatment and Test Methods.** Fuzheng Peiyuan decoction treatment was performed to patients with moderate to advanced cervical cancer, and the decoction contained 15 g of solomonseal rhizome, 15 g of ganoderma powder, 15 g of wild Chinese wolfberry fruit, 15 g of danshen root, 15 g of Chinese angelica, 12 g of epimedium herb, 12 g of medicinal cyathula root, 20 g of dodder seed, 20 g of prepared rehmannia root, and 30 g of Mongolian milkvetch root. The herbs were decocted with water to 300 ml as one dose and taken in two split times daily for 2 months.

The research objects of the two groups received colposcope and serum indicator examinations.

**2.3.1. Colposcope Examination.** The colposcope examination was performed to patients at a later date after the end of menstruation. Twenty-four hours before examination, vaginal administration, vaginal douche, and sexual life were prohibited. During examination, the patients took the bladder lithotomy position and relaxed, the vaginal speculum was put after routine vulva disinfection, 3% acetic acid solution was used to apply to the cervix uteri, the colposcope (model: HD902; manufacturer: Wuhan Yimei Medical Equipment Co., Ltd.) after adjusting the focal length of the probe, the cervix uteri image was enlarged on the display screen for observation, when the best image was obtained, normal saline was used to flush and clean the secretions, and after staining by the compound iodine solution, the condition of cervix uteri was observed under colposcope.

**2.3.2. Serum Indicator Measurement.** Before and after treatment, 5 ml of fasting venous blood was drawn from the patients before and after treatment, the serum was separated after procoagulant processing, the content of SCC-Ag in serum was measured by chemiluminescent microparticle immunoassay, and the content of CA125 and CEA was measured by enzyme-linked immunosorbent assay (ELISA). The measurement was operated according to the specification on the kits, which were purchased from Shanghai Enzyme-Linked Biotechnology Co., Ltd.

### 2.4. Observation Indicators

**2.4.1. Physical Strength.** The physical strength of patients before and after treatment was evaluated with the Karnofsky scores (KPS) [13], and on a scale of 0–100 points, higher scores indicated better physical strength.

**2.4.2. Lesion Perfusion Parameters.** The quantitative perfusion parameters, including the maximum intensity (IMAX), rise time (RT), time-to-peak (TTP), and mean transit time (mTT) at the cervical lesions in patients before and after treatment were measured by the US guided examination with DW-TB color Doppler ultrasonic diagnostic apparatus (manufacturer: Shanghai Mingyuan Industry Company Ltd.).

**2.4.3. Serum Indicators.** On the next day that the cervical cancer patients were admitted to the hospital and the day that the healthy individuals received physical examination, 5 ml of their fasting venous blood was drawn in the morning to separate the serum after centrifugation and then measure the contents of SCC-Ag, CA125, and CEA in the serum samples by ELISA method in strict accordance with the operation steps in the instructions of kits (manufacturer: Yilaisa Biotechnology Co., Ltd. (Jiangsu, China)).

**2.5. Statistical Methods.** In this study, the statistical analysis and processing of experimental data were conducted with SPSS 23.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), the enumeration data were examined by *t*-test and expressed by mean  $\pm$  SD, differences were considered statistically significant at  $P < 0.05$ , and with Mann-Whitney *U* test, the clinical diagnosis value was analyzed by the area under the receiver operating characteristic curve (ROC curve).

### 3. Results

**3.1. Comparison of KPS Scores before and after Treatment.** After treatment, the patients' mean KPS scores were greatly higher than before ( $P < 0.001$ ). See Figure 1.

**3.2. Comparison of Blood Perfusion Parameters of Lesion before and after Treatment.** After treatment, various blood perfusion parameters of lesion were significantly lower than before ( $P < 0.001$ ). See Table 1.

**3.3. Comparison of Changes in Serum SCC-Ag, CA125, and CEA Levels before and after Treatment.** After treatment, the serum SCC-Ag, CA125, and CEA levels were significantly lower than before ( $P < 0.001$ ). See Table 2.

**3.4. Analysis on Clinical Diagnosis Value of Combined Test for Patients after Treatment.** Analysis on clinical diagnosis value of combined test for patients after treatment is shown in Figure 2.

**3.5. Comparison of Area, Standard Error, Progressive Significance, and 95% Confidence Interval of Various Indicators.** The results of combined test were higher than various single test. See Table 3.

**3.6. Comparison of Positive Rate, Sensitivity, and Specificity of Various Indicators.** The sensitivity and specificity of combined test were the highest. See Table 4.

**3.7. Toxic and Side Effects.** By observing the occurrence of toxic and side effects in 43 patients during treatment, it was found that the total incidence rate was 11.63% (5/43), including 2 cases with gastrointestinal reaction, 1 case with

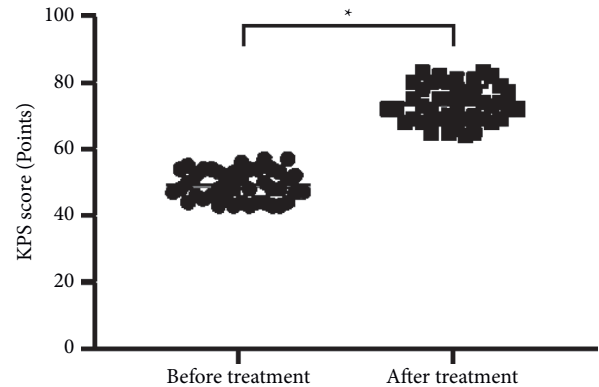


FIGURE 1: Comparison of KPS scores before and after treatment (mean  $\pm$  SD). Note: the horizontal axis denotes before and after treatment, and the vertical axis denotes the KPS score (points); before and after treatment, the patients' mean KPS scores were  $(49.07 \pm 4.35)$  and  $(73.42 \pm 5.47)$ , respectively; and \* indicates significant difference in the mean KPS scores before and after treatment ( $t = 22.847$ ,  $P < 0.001$ ).

TABLE 1: Comparison of blood perfusion parameters of lesion before and after treatment (mean  $\pm$  SD).

Time	IMAX	RT (s)	TTP (s)	mTT (s)
Before treatment	$25.17 \pm 6.18$	$20.16 \pm 3.17$	$34.27 \pm 8.52$	$43.18 \pm 4.92$
After treatment	$14.57 \pm 3.08$	$13.27 \pm 2.76$	$25.15 \pm 7.58$	$29.71 \pm 5.24$
<i>t</i>	9.949	10.624	5.183	12.145
<i>P</i> value	<0.001	<0.001	<0.001	<0.001

TABLE 2: Comparison of changes in serum SCC-Ag, CA125, and CEA levels before and after treatment (mean  $\pm$  SD).

Time	SCC-Ag (ng/ml)	CA125 (U/ml)	CEA (ng/ml)
Before treatment	$10.26 \pm 0.85$	$48.19 \pm 6.58$	$14.28 \pm 2.16$
After treatment	$6.82 \pm 0.72$	$40.52 \pm 6.18$	$9.74 \pm 2.07$
<i>t</i>	20.250	5.572	9.951
<i>P</i> value	<0.001	<0.001	<0.001

liver and kidney dysfunction, and 2 cases with platelet reduction. The patients with toxic and side effects were recovered after administration withdrawal.

### 4. Discussion

Cervical cancer is a common female reproductive disease with nontypical symptoms such as vaginal bleeding [14] and bloody leukorrhea that are also manifested in other gynecological inflammatory diseases, and combined with poor health awareness and fear of disease, most patients are diagnosed when they are in middle to late stages of the disease [15]. Malignant tumors can metastasize to the lymph and abdomen, and even distant sites such as the lung, pleura, and liver, seriously endangering women's life and health [16, 17]. Cisplatin, as a common drug for the treatment of cervical cancer, exerts the therapeutic effect by inhibiting the mitosis

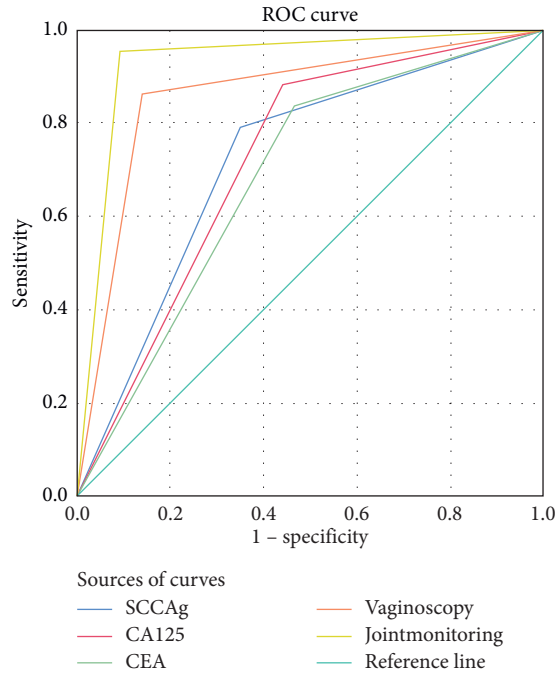


FIGURE 2: Analysis on clinical diagnosis value of combined test for patients after treatment.

TABLE 3: Comparison of area, standard error, progressive significance, and 95% confidence interval of various indicators.

Test result variable	Area	Standard error <sup>a</sup>	Progressive significance <sup>b</sup>	95% confidence interval	
				Lower limit	Upper limit
SCC-Ag	0.721	0.056	0.000	0.611	0.831
CA125	0.721	0.056	0.000	0.611	0.831
CEA	0.686	0.058	0.003	0.572	0.800
Colposcope	0.860	0.043	0.000	0.775	0.946
Combined test	0.930	0.032	0.000	0.868	0.993

<sup>a</sup>Nonparametric hypothesis; <sup>b</sup>null hypothesis, real area = 0.5.

TABLE 4: Comparison of positive rate, sensitivity, and specificity of various indicators.

Indicator	SCC-Ag	CA125	CEA	Colposcope	Combined test
Positive (cases)	34	38	36	37	41
Positive rate (%)	39.53	44.19	41.86	43.02	47.67
Sensitivity (%)	74.14	69.35	68.25	87.76	91.49
Specificity (%)	82.69	89.58	86.00	87.76	95.56

of tumor cells, but long-term use increases the drug resistance of tumor cells, which can produce severe toxic and side effects and then result in unbearable effects for patients [14, 18]. TCM has accumulated a lot of experience in the treatment of cervical cancer, and modified Fuzheng Peiyuan decoction is a TCM preparation for strengthening vital qi, which mainly contains Mongolian milkvetch root, dodder seed, and prepared rehmannia root. Among them, Mongolian milkvetch root has the effects including diuresis and elimination of toxicant, and invigorating qi for consolidating body resistance, dodder seed can strengthen and nourish liver and kidney, strengthen kidney to stop emission, and

arrest polyuria, and prepared rehmannia root works well in nourishing yin and blood as well as benefiting blood and vessels. The formula is able to invigorate spleen, kidney, qi, and yin, which can play a role in inhibiting cancer cell proliferation and improving the condition [19].

With the intensive study of serum biochemical indicators, it has been found that SCC-Ag exists in the cytoplasm of squamous cell carcinoma of the uterus, cervix, lung, etc., and is used in the auxiliary diagnosis for these cancers. The SCC-Ag content in the serum of patients with advanced cervical cancer is higher than that in patients of the early stage, indicating that it is increasing with the malignant progression of cervical lesions and the advancement of specific stage [20]. CA125 and CEA are two common serum tumor markers, the content of which is significantly elevated in many cancers, such as epithelial ovarian cancer, carcinoma of fallopian tube, and lung cancer, and related reports have indicated [21, 22] that high levels of CA125 and CEA have important reference values in the diagnosis and prognosis of cervical cancer. The results of this study showed that patients exhibited significant decreases in all serum markers after treatment with the modified Fuzheng Peiyuan decoction, indicating that



this TCM formula could reduce serum tumor marker levels in patients with advanced cervical cancer and was important for improving outcomes.

As a noninvasive diagnostic modality, colposcopy can observe color, vascular structure, and morphological structure of the abnormal parts of the cervix in patients in many ways, but not the lesions in the cervical canal, resulting in poor diagnostic results. Colposcopy combined with serum detection can significantly improve the pathological diagnosis rate of cervical cancer, because serum detection is convenient and can directly reflect the number, spread, and apoptosis of cancer cells [23]. Colposcopy is an imaging means currently used to screen for precancerous cervical lesions, which can amplify the image of the cervix and vagina mucosa, enable more precise visualization of tiny lesions, vascular tissue, and suspicious areas on the surface of the cervix that are not visible to the naked eye, and localize the biopsy to improve test accuracy. Therefore, combining colposcopy with serum detection can eliminate problems such as unnecessary treatment for false positive patients and ensure safety, reliability, and strong operability, which is suitable for clinical diagnosis and efficacy determination [24]. In this study, the efficacy of Fuzheng Peiyuan decoction in the treatment of moderate to advanced cervical cancer was evaluated by the combined test, and by plotting the ROC curve, it was found that combined test had an area under the curve larger than each single test, and high sensitivity, and specificity, and therefore it might serve as an effective diagnostic modality to objectively evaluate the treatment effect of cervical cancer patients. This study has some deficiencies. The selected patients were all treated in our hospital, so the source of cases lacked diversification; in addition, follow-up visits for the long-term efficacy of patients were not carried out. To sum up, the initial conclusion obtained in this study shall be perfected by more researches in the future.

In conclusion, Fuzheng Peiyuan decoction has significant effect in treating moderate to advanced cervical cancer, and colposcope combined with serum test presents more accurate and credible diagnosis results and has great significance for future treatment, which shall be promoted and applied.

## Data Availability

Data that support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

## Acknowledgments

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## Research Article

# Ginkgolic Acid (GA) Inhibits the Growth of OCa by Inhibiting lncRNA MALAT1/JAK2 Axis

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**Objective.** We aimed to observe the impact of ginkgolic acid (GA) on the proliferation and metastasis ability of ovarian cancer (OCa) cells and to further explore whether GA affects the malignant progress of OCa via regulating the lncRNA MALAT1/JAK2 axis. **Methods.** OCa cells SKOV3 and CAOV3 were administered with 1 ng/ml GA, 5 ng/ml GA, 10 ng/ml GA, 20 ng/ml GA, and DMSO as control, respectively. The cell proliferation and migration ability of the abovementioned cells in each group were measured by CCK-8 test and Transwell experiments. The expression levels of lncRNA MALAT1 and JAK2 protein were examined by qRT-PCR and western blot, respectively. Subsequently, in OCa cells treated with GA, lncRNA MALAT1 overexpression vector was transfected to continue to detect the proliferation activity and migration ability of each treatment group. Finally, the regulation of GA on activity of lncRNA MALAT1/JAK2 axis in OCa cells was further explored in nude mice. **Results.** Our data showed that the proliferation inhibition rate of cells at each ginkgolic acid concentration was higher than that of the control group ( $P < 0.05$ ), suggesting that GA has an inhibitory influence on the proliferation of OCa cells, in a dose-dependent way. GA was able to inhibit the proliferation rate and migration ability of OCa cells. Administration of ginkgolic acid downregulated the levels of lncRNA MALAT1 and JAK2 protein. Overexpression of lncRNA MALAT1 partially reversed the inhibited OCa proliferative capacity caused by GA treatment. Consistent with the results observed *in vitro*, we also found that the OCa tumor weight and volume of nude mice injected with lncRNA MALAT1 overexpression vector were enhanced and JAK2 protein level increased remarkably in comparison to the ginkgolic acid group. **Conclusions.** In summary, GA may exert its inhibitory effect on the proliferative and migratory capacities of OCa cells through suppressing the activity of lncRNA MALAT1/JAK2 axis.

## 1. Introduction

Gynecological malignancy as the main cause of tumor occurrence and death in women globally mainly includes ovarian tumor, uterine tumor, fallopian tube tumor, vulvar tumor, and vaginal tumor, among which ovarian and uterus tumor are the most common [1, 2]. The incidence of OCa ranks second in female reproductive system malignancies, among which epithelial OCa is the most common histological type, accounting for about 90% of the total number of cases, and its mortality ranks first in gynecological tumors [3, 4]. The latest statistics from the National Cancer Institute show that the mortality rate of ovarian cancer has not changed significantly, and the 5-year survival rate is only 45.6%. Due to the lack of effective screening methods, 70–80% of patients have been in the advanced stage (stage

III/IV) at the time of diagnosis, with a 5-year survival rate of only 20–30% [5, 6]. At present, tumor reduction surgery combined with platinum-based chemotherapy is the classic treatment for epithelial ovarian cancer. It has been clinically implemented for decades and is recognized as the most effective treatment for ovarian cancer worldwide; however, this classic approach has little effect on patients with platinum-resistant and recurrent ovarian cancer [7, 8]. Although the increase and improvement of treatment methods in recent years have enabled 80% of patients to achieve clinical remission, more than 60% of patients will eventually develop tumor recurrence, metastasis, and drug resistance, and the treatment effect of recurrent and drug-resistant OCa still remains to be solved [9, 10]. Early detection, diagnosis, and treatment of OCa are key factors affecting the prognosis of OCa. Thus, it is necessary to further explore the mechanism

of the occurrence and development of OCa and drug resistance to improve OCa patients' prognosis [11].

Ginkgolic acid (GA) is a derivative of 6-alkyl or 6-enyl salicylic acid. The number of side chain carbon atoms on the six bits can range from 13 to 19, and the number of side chain double bonds can range from 0 to 2. It can be seen that GA is a mixture composed of homologues of side chains of different lengths [12, 13]. Studies have shown that GA has a good antitumor effect and can inhibit the growth of a variety of tumor cells *in vitro*; while *in vivo*, it can also reduce the volume of mouse sarcoma and prolong the survival of mice [14, 15]. However, it is not clear whether ginkgolic acid can inhibit the malignant progression of OCa and how it regulates the progression of tumor cells [16, 17]. LncRNA plays a crucial role in carcinogenesis, invasion, and metabolism of many tissues [17, 18]. Therefore, this study mainly discussed the proliferation, metastasis, and molecular expression of ginkgolic acid in human OCa cells to further investigate the effect of ginkgolic acid on malignant progression of OCa and its underlying mechanism.

## 2. Methods

**2.1. Cell Lines and Reagents.** Human-derived OCa cells (SKOV3 and CAOV3) provided by the American Type Culture Collection (ATCC) (Manassas, VA, USA) company were cultured in Dulbecco's modified eagle medium (DMEM) supplemented with 10% fetal bovine serum (FBS) (Gibco, Rockville, MD, USA) in an incubator with 5% CO<sub>2</sub> at 37°C.

**2.2. Transfection.** Transfection was performed with pcDNA3.1-NC and pcDNA3.1-MALAT1 according to the manufacturer's instructions when cell density reached 30–50%. 48 hr later, cells were collected for cell function experiments.

**2.3. Cell Counting Kit-8 (CCK-8) Assay.** Cells of each group were seeded in a 96-well plate at a density of 2500 cells/well. CCK-8 assay (Dojindo, Kumamoto, Japan) was conducted based on instructions.

**2.4. Transwell Assay.** Each treated OCa cells SKOV3 and CAOV3 were resuspended in serum-free medium and counted. SKOV3 cells (4 × 10<sup>4</sup> cells) or CAOV3 cells (2 × 10<sup>4</sup> cells) were suspended in 200 µl serum-free MEM medium. The cells were then seeded into the upper chamber, and 500 µl of DMEM medium with 10% serum was added to the bottom chamber. After culturing in a cell incubator for 24 hours, the cells in the upper chamber were removed with a cotton swab; the lower cells were fixed with 4% paraformaldehyde for 30 minutes and then stained with crystal violet for 30 minutes. The cell membrane was washed with phosphate buffered saline (PBS), and the cells were photographed and counted under a 200-fold upright microscope.

**2.5. QPCR.** After corresponding treatment of OCa cells SKOV3 and CAOV3, 1 ml of TRIzol was used to lyse the cells to extract total RNA. QPCR detection was implemented based on the instructions of SYBR® Premix Ex Taq™ Kit

(TaKaRa, Tokyo, Japan), with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and U6 as internal parameters. Primers used in the qPCR reaction were as follows: lncRNA MALAT1: forward: 5'-GCTCTGTGGTGTGGGATTGA-3', reverse: 5'-GTGGCAAAATGGCGGACTTT-3'; GAPDH: forward: 5'-CCTGGCACCCAGCACAAAT-3', reverse: 5'-GCTGATCCACATCTGCTGGAA-3'.

**2.6. Western Blot.** Western blot analysis was performed according to standard procedures. The primary antibodies against JAK2 (Dilution: 1/500; CatNOs: ab108596) and GAPDH (dilution: 1:500; CatNOs: ab37168), and the secondary antibodies (dilution: 1/2000; CatNOs: ab6721) were all purchased from Abcam (Cambridge, MA, USA).

**2.7. In Vivo Xenograft Model.** *In vivo* nude mice tumorigenesis experiments were approved by The Animal Ethics and Use Committee. Fifteen 8-week-old male nude mice were purchased from the animal center and randomly divided into 3 groups (5 in each group). The OCa cells treated with GA were transfected with the MALAT1 overexpression vector and injected into the axilla of the mice subcutaneously. The tumor size was monitored every 5 days; then, the mice were sacrificed after 30 days. The volume of all samples is calculated using the following formula: tumor volume = (width × length)/2.

**2.8. Statistical Analysis.** Continuous variables were analyzed using Student's *t*-test, and categorical variables were analyzed using  $\chi^2$  test or Fisher's exact probability method. Data were processed by Statistical Product and Service Solutions (SPSS) 22.0 program (IBM, Armonk, NY, USA) and were expressed as  $X \pm SD$ .  $P < 0.05$  was considered statistically significant.

## 3. Results

**3.1. GA Inhibits OCa Cell Proliferation and Migration.** The proliferation inhibition rate of OCa cells in each treatment concentration of GA treatment group was higher than that of the control group ( $P < 0.05$ ), and the inhibitory effect was enhanced as the concentration of GA increases (Figure 1(a)). Meanwhile, Figure 1(b) shows that the OD value of OCa cells treated with GA observed in CCK-8 test decreased in comparison to the DMSO (0.1%) control group, suggesting an attenuated proliferative ability induced by GA (Figure 1(b)). Consistent to the changes in cell proliferation, the migration capacity of OCa cells was also attenuated by treatment of GA (Figure 1(c)).

**3.2. Ginkgolic Acid Regulates lncRNA MALAT1 Expression-JAK2 Axis of OCa Cells.** To test the mechanism by which GA inhibits the malignant progression of OCa, we examined the expression of lncRNA MALAT1 and JAK2 protein in OCa cells after GA treatment. As a result, we found a reduction in both the mRNA expression of lncRNA MALAT1 (Figure 2(a)) and the protein level of JAK2 (Figure 2(b)).

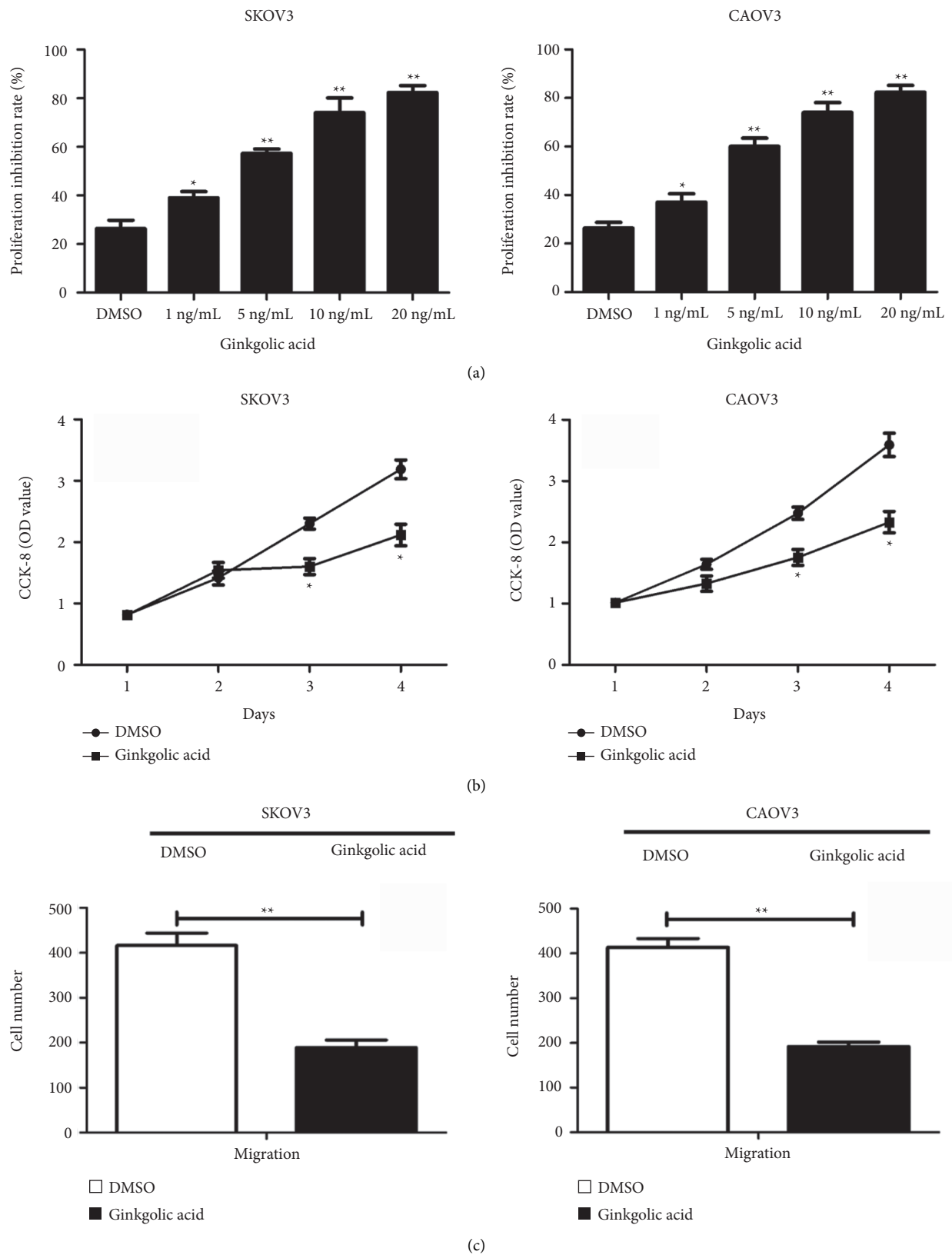


FIGURE 1: Ginkgolic acid inhibits the proliferation and migration of ovarian cancer cells. (a) Ginkgolic acid inhibited cell proliferation in a dose-dependent manner (1 ng/ml, 5 ng/ml, 10 ng/ml, and 20 ng/ml) in ovarian cancer cell lines SKOV3 and CAOV3; (b) ginkgolic acid inhibited cell proliferation in a time-dependent manner (1 d, 2 d, 3 d, and 4 d) in ovarian cancer cell lines SKOV3 and CAOV3; (c) Transwell test was used to detect the effect of ginkgolic acid treatment on cell migration in ovarian cancer cell lines SKOV3 and CAOV3. Data are presented as average  $\pm$  SD, \* $P < 0.05$ , \*\* $P < 0.01$ .

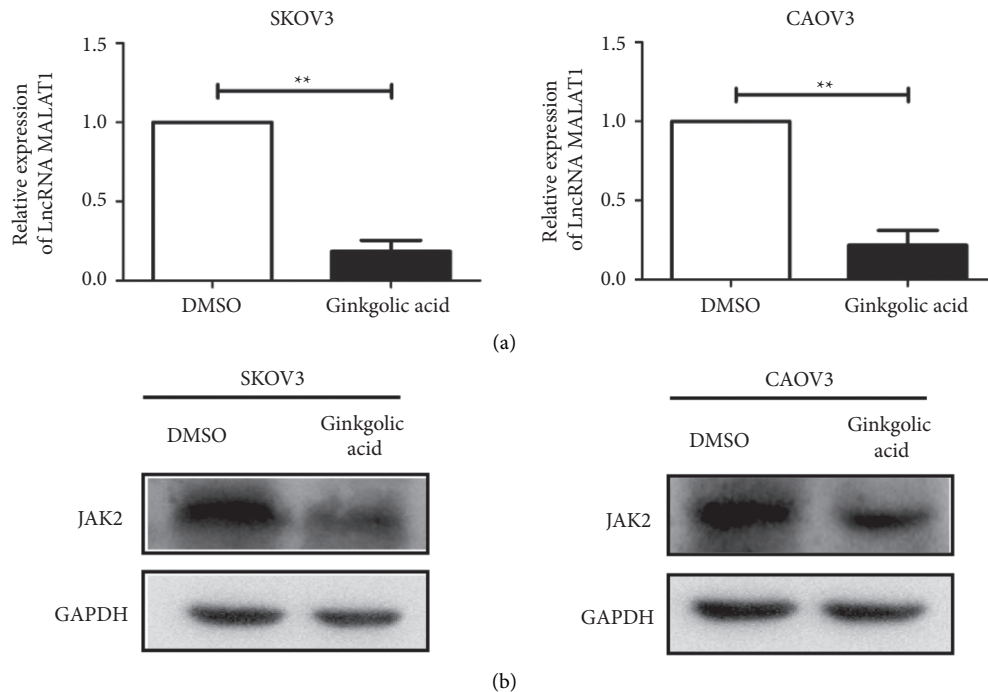


FIGURE 2: Ginkgolic acid regulates the lncRNA MALAT1-JAK2 axis. (a) qRT-PCR experiment was used to detect the expression level of lncRNA MALAT1 in ovarian cancer cell lines SKOV3 and CAOV3 after ginkgolic acid treatment; (b) western blot test was used to detect the expression level of JAK2 in ovarian cancer cell lines SKOV3 and CAOV3 after ginkgolic acid treatment. Data are presented as average  $\pm$  SD, \*\* $P < 0.01$ .

**3.3. lncRNA MALAT1 Promotes the Migration as Well as Proliferation of OCa Cells Treated with GA.** To further explore the role of lncRNA MALAT1 in the function of OCa cells, we constructed lncRNA MALAT1 overexpression model and verified the transfection efficiency by qPCR experiment (Figure 3(a)). It was found that knocking down lncRNA MALAT1 enhanced the inhibitory impact of GA on OCa cells proliferation (Figure 3(b)), while overexpression of lncRNA MALAT1 partially counteracted that (Figure 3(c)), measured by CCK-8 test. At the same time, Transwell experiments also showed that the number of transferring cells in Transwell increased remarkably after overexpression of lncRNA MALAT1, suggesting an enhanced metastasis (Figure 3(d)). We also observed an increased protein level of JAK2 induced by lncRNA MALAT1 upregulation, revealed by western blot assay (Figure 3(e)).

**3.4. Ginkgolic Acid Inhibits Tumorigenic Ability of Nude Mice with OCa.** OCa SKOV3 cells were inoculated into each nude mouse and injected in the left armpit; all of the mice were then treated with GA. As expected, compared with the blank control group, the tumor volume and weight of nude mice treated with GA were remarkably reduced, but could be enhanced partially by transfection of pcDNA3.1-MALAT1 (Figures 4(a) and 4(b)). Subsequently, total RNA and protein of nude mice tumor tissues were extracted, and qPCR and western blot experiments were carried out to measure the level of lncRNA MALAT1 and JAK2 protein. Figures 4(c) and 4(d) show that the expressions of JAK2 protein and

lncRNA MALAT1 were both remarkably reduced in nude mice treated with GA, however, could be partially reversed after lncRNA MALAT1 overexpression vector was injected in. Taken together, the above observations of *in vivo* experiments demonstrate that GA may suppress the tumorigenic ability of OCa cells in nude mice by downregulating the lncRNA MALAT1/JAK2 axis.

## 4. Discussion

Ovarian cancer is the most fatal gynecological malignancy and the second leading cause of cancer death in women [1–3]. The current standard treatment for advanced ovarian cancer includes surgery combined with radiotherapy and chemotherapy [4–7]. Despite the continuous development of new therapies (such as targeted therapy and immunotherapy) and the improvement of the 5-year survival rate [7, 8], the inherent or acquired multidrug resistance remains a major challenge [8–10]. Currently, no biomarkers for predicting chemotherapy-induced reactions have been used in clinical practice [9–11].

Ginkgolic acid has obvious growth inhibition effect on a variety of tumor cell lines *in vitro* [12, 13]. Some studies reported that ginkgolic acid compound was extracted from the outer seed skin of *Ginkgo biloba*, which had inhibitory effects on the growth of HCT-15 colorectal cancer cell line [12, 13], MCF-7 breast cancer cell line, A-549 lung cancer cell line, HT-1197 bladder cancer cell line, and SKOV3 uterine cancer cell line, but had little cytotoxicity to normal intestinal cells [12–15]. The present data revealed that the

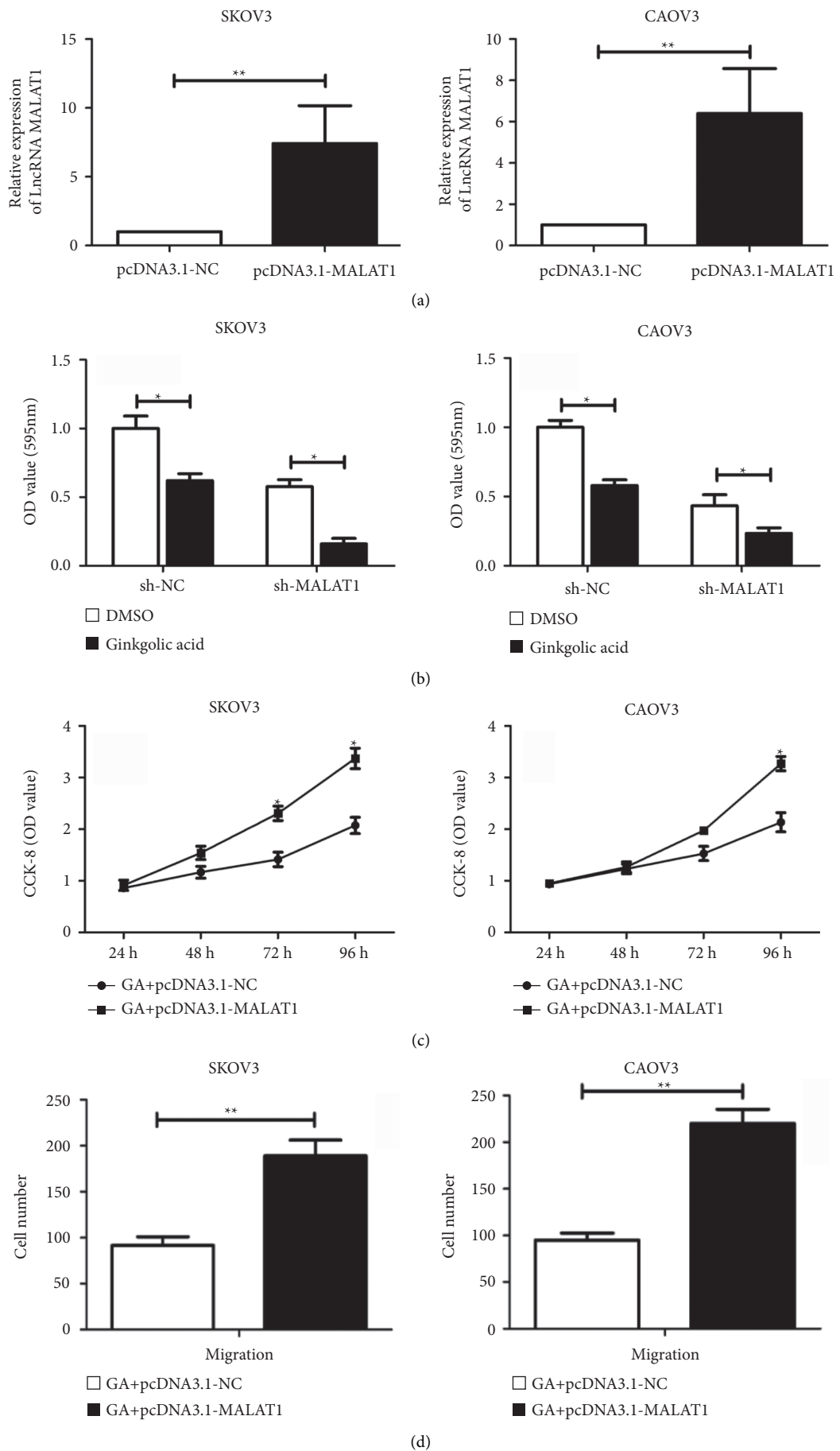


FIGURE 3: Continued.



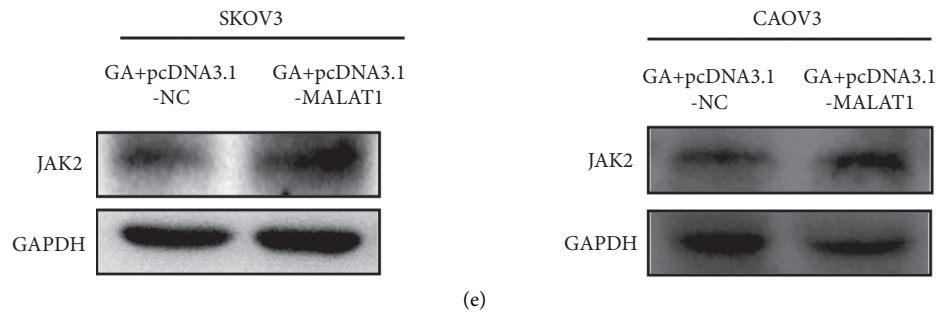


FIGURE 3: LncRNA MALAT1 promotes the proliferation and migration of ovarian cancer cells. (a) The qRT-PCR experiment detected the transfection efficiency of ovarian cancer cell lines SKOV3 and CAOV3 after transfecting lncRNA MALAT1 overexpression vector; (b) knocking down lncRNA MALAT1 enhanced the inhibitory impact of GA on OCa cells proliferation; (c) overexpression of lncRNA MALAT1 enhanced cell viability; (d) overexpression of lncRNA MALAT1 enhanced cell migration; (e) western blot test was used to detect the expression level of JAK2 after transfection of lncRNA MALAT1 overexpression vector in ovarian cancer cell lines SKOV3 and CAOV3 after ginkgolic acid treatment. Data are presented as average  $\pm$  SD, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

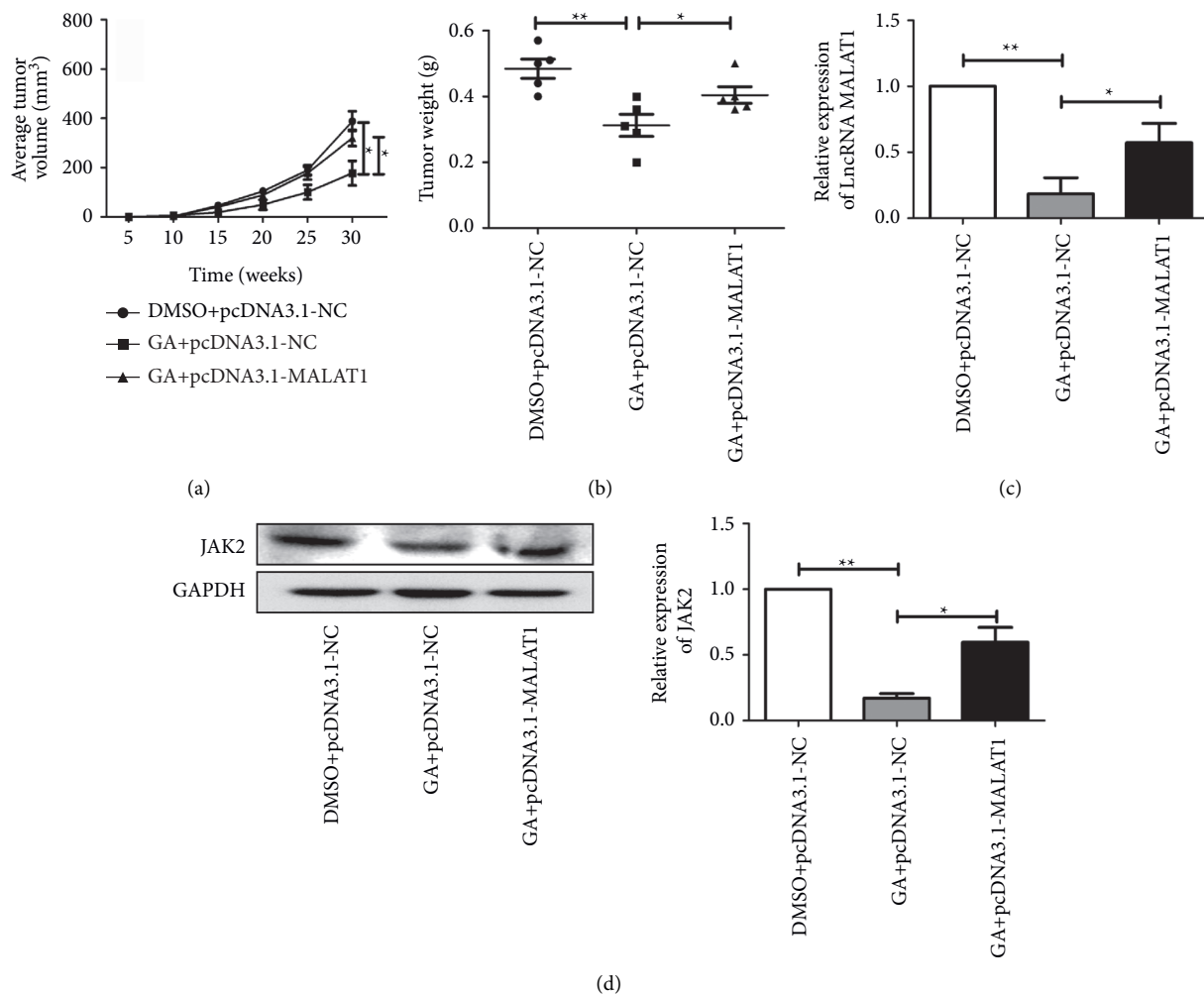


FIGURE 4: Ginkgolic acid inhibits the tumorigenic ability. (a). Ginkgolic acid inhibited the tumor volume, while pcDNA3.1-MALAT1 enhanced the tumor volume; (b) ginkgolic acid inhibited the tumor weight, while pcDNA3.1-MALAT1 enhanced the tumor weight; (c) the expression of lncRNA MALAT1 was remarkably reduced by ginkgolic acid; (d) the protein expression of JAK2 was significantly inhibited by ginkgolic acid, however, was partially reversed after lncRNA MALAT1 overexpression. Data are presented as average  $\pm$  SD, \*  $P < 0.05$ , \*\*  $P < 0.01$ .

proliferation inhibition rate of OCa cells treated with ginkgolic acid at each concentration was higher than that of the control group, and the metastasis and proliferative ability of OCa cells were remarkably reduced by ginkgolic acid treatment.

At present, studies have found that lncRNA, as an important part of gene regulation network, has important significance in biological behaviors such as cell proliferation, differentiation, apoptosis, invasion, and metastasis [16, 17]. Therefore, to find out whether the abnormal expression of lncRNA in OCa is related to the antitumor properties of ginkgolic acid and to analyze its function will help to improve the diagnosis and treatment level of OCa and improve the quality of life of patients. We found that the mRNA expression level of lncRNA MALAT1 and the protein expression of JAK2 were both remarkably downregulated after treatment of ginkgolic acid. To further explore the regulation of ginkgolic acid on lncRNA MALAT1 expression-JAK2 axis in OCa cells, we have constructed a MALAT1 overexpression model by lentivirus. As a result, we demonstrated that overexpression of lncRNA MALAT1 could promote the proliferative capacity and migration of OCa treated with ginkgolic acid and enhanced the protein levels of JAK2 in the abovementioned cells. Additionally, tumor formation in nude mice also demonstrated that ginkgolic acid inhibits tumor formation in nude mice by downregulating the lncRNA MALAT1/JAK2 axis.

## 5. Conclusions

In summary, these evidences suggest that ginkgolic acid inhibits the proliferation and migration of OCa cells through the downregulation of lncRNA MALAT1 expression/JAK2 axis. However, further molecular mechanism should still be explored in our future study. With the deepening of research, further understanding of ginkgolic acid inhibition of lncRNA MALAT1/JAK2 axis on the biological function of OCa cells and its role in the process of tumor development will be more conducive to the diagnosis, treatment, and prognosis assessment of OCa.

## Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Authors' Contributions

Zhiyi Fei and Yi Yu contributed equally to this work.

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## Research Article

# Clinical Efficacy of Fuzheng Guben Anticancer Decoction Combined with Taxol in Treating Ovarian Carcinoma and Its Effect on Complication Incidence

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**Objective.** To investigate the clinical value of Fuzheng Guben anticancer decoction combined with taxol in treating ovarian carcinoma (OC). **Methods.** The medical records of 80 OC patients treated in the First People's Hospital of Fuyang Hangzhou (January 2018–January 2021) were retrospectively analyzed, and the patients were split into the control group and the experimental group according to the treatment regimen, with 40 cases each. Those in the control group accepted the taxol chemotherapy, and on this basis, those in the experimental group took the Fuzheng Guben anticancer decoction, so as to compare its clinical efficacy and complication incidence. **Results.** No statistical between-group differences in patients' general information were observed ( $P > 0.05$ ); compared with the control group, the disease objective remission rate of the experimental group was greatly higher ( $P < 0.05$ ); before and after treatment, the changes in  $CD8^+$  were not significant, indicating no statistically significant between-group differences ( $P > 0.05$ ), and after treatment,  $CD3^+$ ,  $CD4^+$ , and  $CD4^+/CD8^+$  were obviously higher than before and were obviously higher in the experimental group than in the control group ( $P < 0.05$ ); after treatment, the CA125, CA199, and CEA levels were obviously lower than before and were significantly lower in the experimental group than in the control group ( $P < 0.05$ ); the mean survival of the experimental group was significantly higher than that of the control group ( $19.80 \pm 5.84$  vs.  $14.075 \pm 5.12$  months,  $P < 0.05$ ); and between the two groups, the incidence rate of adverse reactions of the experimental group was remarkably lower ( $P < 0.05$ ). **Conclusion.** On the basis of taxol chemotherapy, jointly applying Fuzheng Guben anticancer decoction can significantly improve the clinical efficacy of OC, help to improve patients' immune function, lower the complication incidence rate, and prolong the mean survival.

## 1. Introduction

Ovarian carcinoma (OC) is a malignant neoplastic disease that occurs in the ovaries of women, with an incidence second only to cervical cancer and endometrial carcinoma, which seriously threatens the life, health, and safety of women [1–4]. Clinically, the methods of treating OC mainly include surgical resection and chemoradiotherapy, and with the gradual and deep research of traditional Chinese medicine (TCM) in tumor treatment at the current stage, TCM is also applied for treating OC patients. Taxol can effectively inhibit tumor growth and control the condition,

but chemotherapy will reduce the immunity, which, combined with the untoward drug effects, has a large effect on patients [5–8]. With the continuous development of TCM technology, Chinese herbs have been gradually used in treating OC as an adjuvant therapy to regulate body immunity and relieve the adverse reactions from taxol chemotherapy, thus having an important role in improving the clinical efficacy of OC [9–12]. Fuzheng Guben anticancer decoction has the efficacy of regulating qi flowing to invigorate blood, resolving hard mass for detumescence, invigorating qi for strengthening vital qi, and nourishing blood for consolidating body resistance, which is a good choice for

the treatment of OC. At present, there are few studies on combining Fuzheng Guben anticancer decoction with taxol in treating OC patients. Based on this, the clinical efficacy of Fuzheng Guben anticancer decoction combined with taxol in treating OC and its effect on complication incidence were deeply analyzed in this study.

## 2. Study Methods

**2.1. Patient Grouping.** The medical records of 80 OC patients treated in the First People's Hospital of Fuyang Hangzhou from January 2018 to January 2021 were retrospectively analyzed, and the patients were divided into the control group and the experimental group according to whether they took the Fuzheng Guben anticancer decoction, with 40 cases each. Those only treated with taxol chemotherapy were included in the control group, and those who received the combined treatment of taxol chemotherapy and Fuzheng Guben anticancer decoction were included in the experimental group. The study was approved by the ethics committee of the First People's Hospital of Fuyang Hangzhou.

**2.2. Inclusion Criteria.** The inclusion criteria were as follows: ① the patients were diagnosed with OC after laboratory index inspection, imaging data, and pathological examination; ② the patients had complete data and high treatment compliance; ③ the patients met the indications of single taxol chemotherapy; and ④ the patients and their family members signed informed consent of the study.

**2.3. Exclusion Criteria.** The exclusion criteria were as follows: ① the patients had severe organ failure; ② the patients had cognition disorders; ③ the patients were allergic to the drugs applied herein; ④ the estimated survival of the patients was less than 6 months; and ⑤ the patients lost to follow-up during the study.

**2.4. Methods.** Single taxol chemotherapy was adopted to patients in the control group as follows. Before chemotherapy, the pretreatment with dexamethasone, diphenhydramine, and H2 receptor antagonist was performed; in the first 3 days of chemotherapy, 120–150 mg/m<sup>2</sup> of taxol (specification: 60 mg; manufacturing: Beijing Union Pharmaceutical Factory Co., Ltd.; NMPA approval no. H20083786) was administered via an intravenous drip, and at the 4<sup>th</sup> day, 90 mg/m<sup>2</sup> of taxol was administered via abdominal cavity perfusion for 2–3 times daily. Four weeks were regarded as one course, and the patients were treated for 3 consecutive courses totally [13]. On this basis, the patients in the experimental group took the Fuzheng Guben anticancer decoction. The formula was 20 g of Chinese angelica, 20 g of debark peony root, 30 g of American ginseng, 30 g of Mongolian milk vetch root, 15 g of dried tangerine peel, 15 g of *Pinellia* tuber, 15 g of *Fritillaria*, 6 g of liquorice root, and 6 g of Chinese date. The herbs were decocted according to the general decocting method, and the patients daily took one dose in two split times (in the

morning and the evening) when it was still warm. The follow-up time of all patients was not less than 12 months.

**2.5. Observation Indicators.** The patients' general information including their age, BMI, course of the disease, TNM stage, and pathological type was counted. The clinical treatment effect of patients in both groups was evaluated referring to the Response Evaluation Criteria in Solid Tumors (RECIST) [14] as follows. It was considered as complete response (CR) if the patients' lesion disappeared completely or for 4 weeks; partial response (PR) if the lesion was shrunk to over 30% for over 4 weeks; stable disease (SD) if the lesion was shrunk to less than 30% or increased by less than 20%; and progressive disease (PD) if the lesion was increased by more than 20% or there were new lesions. The objective remission rate (ORR) = (CR + PR)/total number × 100%.

The immune function indicators (CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, and CD4<sup>+</sup>/CD8<sup>+</sup>) were measured by the flow cytometry assay; and by drawing patients' upper limb venous blood, their levels of tumor markers including CA125, CA199, and CEA were measured by the enzyme-linked immunosorbent assay (ELISA), with the kits purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd. Through follow-up visits, the patients' mean survival was recorded, and their adverse reactions were analyzed.

**2.6. Statistical Processing.** The data differences were calculated with SPSS 22.0, picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), the enumeration data and measurement data were expressed by ( $n$  (%)) and ( $\bar{x} \pm s$ ) and examined by  $\chi^2$  test and  $t$ -test, respectively, and  $P < 0.05$  indicated a statistical difference.

## 3. Results

**3.1. General Information.** After comparing the patients' general information including age, BMI, course of the disease, TNM stage, and pathological type, the result was  $P > 0.05$ , which indicated no great between-group difference and met the study criteria of the controlled experiment. See Table 1.

**3.2. Clinical Efficacy.** Between the two groups, the ORR of the experimental group was greatly higher ( $P < 0.05$ ). See Figure 1.

**3.3. Immune Function.** Before and after treatment, the variation in CD8<sup>+</sup> of all patients was not significant, indicating no statistical meaning in the between-group difference ( $P > 0.05$ ). After treatment, the patients' other immune function indicators were obviously higher than before ( $P < 0.05$ ) and were significantly higher in the experimental group than in the control group ( $P < 0.05$ ). See Table 2.

**3.4. Levels of Tumor Markers.** After treatment, the CA125, CA199, and CEA levels were obviously lower than before ( $P < 0.05$ ) and were significantly lower in the experimental group than in the control group ( $P < 0.05$ ). See Table 3.

TABLE 1: General information ( $n = 40$ ).

Observation indicator	Control	Experimental	$\chi^2/t$	$P$
Age (years)	$51.17 \pm 8.58$	$51.30 \pm 8.79$	0.067	0.947
BMI ( $\text{kg}/\text{m}^2$ )	$23.24 \pm 2.11$	$23.15 \pm 2.08$	0.192	0.848
Course of the disease (years)	$2.27 \pm 0.30$	$2.31 \pm 0.32$	0.577	0.566
TNM stage				
IIIa	18 (45%)	21 (52.5%)	0.450	0.502
IIIb	14 (35%)	13 (32.5%)	0.056	0.813
IV	8 (20%)	6 (15%)	0.346	0.556
Pathological type				
Serous cystadenocarcinoma	12 (30%)	13 (32.5%)	0.058	0.809
Mucinous cystadenocarcinoma	10 (25%)	8 (20%)	0.287	0.592
Granular cell carcinoma	7 (17.5%)	8 (20%)	0.082	0.775
Embryonal carcinoma	7 (17.5%)	6 (15%)	0.092	0.762
Undifferentiated carcinoma	4 (10%)	5 (12.5%)	0.125	0.723

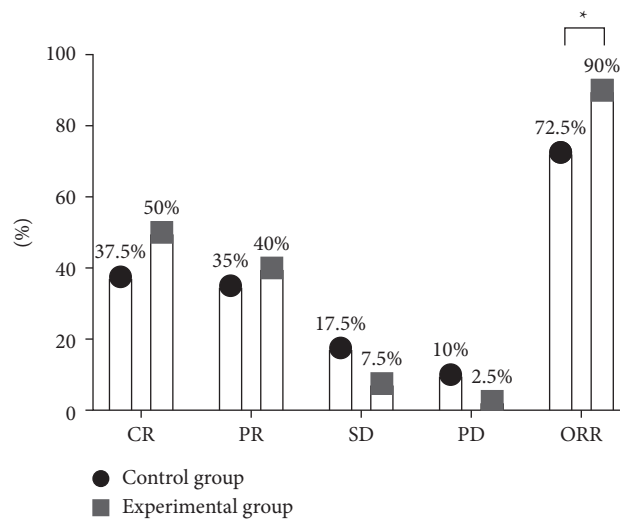


FIGURE 1: Between-group comparison of clinical efficacy. Note: the horizontal axis showed the evaluation dimensions, and the vertical axis showed the percentage. In the control group, there were 15 CR cases, 14 PR cases, 7 SD cases, and 4 PD cases, so the number of ORR cases was 29. In the experimental group, there were 20 CR cases, 16 PR cases, 3 SD cases, and 1 PD case, so the number of ORR cases was 36; \* indicated a significant between-group difference in ORR ( $\chi^2 = 4.021$ ,  $P = 0.045$ ).

TABLE 2: Between-group comparison of T-cell subset levels ( $\bar{x} \pm s$ ).

T-cell subset		Control	Experimental	$t/P$
CD3 <sup>+</sup> (%)	Before treatment	$46.55 \pm 5.54$	$46.76 \pm 5.60$	4.359/<0.001
	After treatment	$52.03 \pm 5.84^*$	$57.81 \pm 6.02^*$	
CD4 <sup>+</sup> (%)	Before treatment	$32.74 \pm 4.82$	$32.86 \pm 4.85$	4.407/<0.001
	After treatment	$37.13 \pm 4.30^*$	$41.60 \pm 4.76^*$	
CD8 <sup>+</sup> (%)	Before treatment	$32.60 \pm 3.29$	$32.44 \pm 3.18$	0.056/0.956
	After treatment	$33.82 \pm 3.19$	$33.86 \pm 3.21$	
CD4 <sup>+</sup> /CD8 <sup>+</sup>	Before treatment	$1.03 \pm 0.03$	$1.04 \pm 0.04$	13.416/<0.001
	After treatment	$1.10 \pm 0.05^*$	$1.25 \pm 0.05^*$	

\*indicated  $P < 0.05$  in the comparison of patients in the same group before and after treatment.

**3.5. Long-Term Efficacy.** The mean survival of the experimental group was significantly higher than that of the control group ( $19.80 \pm 5.84$  vs.  $14.075 \pm 5.12$  months,  $t = 4.544$ ,  $P < 0.001$ ). See Figure 2 for the survival curves.

**3.6. Adverse Reactions.** Between the two groups, the incidence rate of adverse reactions in patients was significantly lower in the experimental group ( $P < 0.05$ ). See Table 4.

TABLE 3: Between-group comparison of levels of tumor markers ( $\bar{x} \pm s$ ).

Test indicator		Control	Experimental	<i>t/P</i>
CA125 (U/ml)	Before treatment	90.86 $\pm$ 14.55	90.57 $\pm$ 14.33	9.829/<0.001
	After treatment	55.83 $\pm$ 10.62*	33.02 $\pm$ 10.13*	
CA199 (IU/L)	Before treatment	50.86 $\pm$ 6.64	51.02 $\pm$ 6.71	9.568/<0.001
	After treatment	30.91 $\pm$ 4.17*	21.75 $\pm$ 4.39*	
CEA (ng/ml)	Before treatment	27.25 $\pm$ 4.88	27.17 $\pm$ 4.79	6.155/<0.001
	After treatment	20.35 $\pm$ 3.22*	16.02 $\pm$ 3.07*	

\*indicated  $P < 0.05$  in the comparison of patients in the same group before and after treatment.

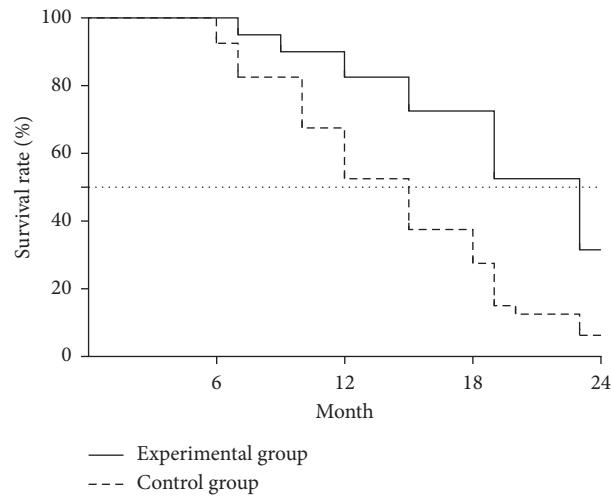


FIGURE 2: Survival curves.

TABLE 4: Adverse reaction incidence (*n* (%)).

Adverse reaction	Control	Experimental	$\chi^2$	<i>P</i>
Neurotoxicity	2 (5)	0 (0)	15.221	<0.001
Reduction of the white blood cell count	3 (7.5)	1 (2.5)		
Nausea and vomiting	6 (15)	3 (7.5)		
Anemia	4 (10)	0 (0)		
Joint and muscle pain	5 (12.5)	1 (2.5)		
Thrombocytopenia	4 (10)	2 (5)		
Total incidence rate	24 (60)	7 (17.5)		

#### 4. Discussion

With the development of China's society and economy, people's standard of living has been increasing and so has the life, work, and other stresses in women, and combined with objective factors such as environmental pollution, the number of new OC cases is rising year by year, and more and more young women also suffer from the disease, which has a fatality rate ranking the first among malignant tumors of the female reproductive system [15–18]. Currently, chemotherapy is the main means for the treatment of cancer, mainly improving patient symptoms and prolonging the survival through Western medicine [19–22]. Taxol is a natural anticancer drug extracted from Chinese yew. It exerts antitumor effects by interfering with the microtubule network essential for cell function in mitosis and interphase and can inhibit cell-cycle microvascular protein depolymerization, cell division, and consequently cell metabolism;

in addition, it is metabolized through the liver, has little renal toxicity, and is significantly less toxic than platinum-based chemotherapy. In the study conducted by Guoqiang et al. [23] and Jiwon et al. [24], taxol has better antitumor effect in diseases such as breast cancer, lung cancer, and ovarian cancer. From the perspective of TCM, OC belongs to the category of “abdominal mass,” which is mostly caused by weakness of the body, insufficient essence and blood of the liver and kidney, internal binding of phlegm turbidity and stasis toxin, etc., and chemotherapy can cause loss of yin, yang, blood, and qi, blood flow blockage, and weak organs in patients and even symptoms such as incoordination between the spleen and stomach and qi-blood loss in some cases. TCM believes that treating OC shall comply with the principle of strengthening body resistance and restoring vital energy, which shall focus on both warming the kidney and promoting blood circulation. In this study, the Fuzheng Guben anticancer decoction contained Chinese angelica



(nourishing yin for regulating menstruation and promoting blood circulation for relieving pain), debark peony root (tonifying blood for consolidating body resistance), American ginseng and Mongolian milk vetch root (nourishing the spleen for invigorating qi and warming the kidney for reinforcing yang), dried tangerine peel (regulating qi flowing for invigorating the spleen and regulating the spleen-stomach for dispelling dampness), *Pinellia tuber* (relieving oppression for resolving hard mass), *Fritillaria* (resolving masses for detumescence), liquorice root (clearing heat and removing toxicity, invigorating the spleen-stomach, and replenishing qi), and Chinese date (regulating the spleen-stomach and nourishing qi, tonifying blood, and invigorating the spleen). Combining all the herbs could exert the efficacy of replenishing qi, tonifying blood, invigorating the spleen and stomach, and warming the kidney for reinforcing yang. This formula is quite valued in the field of TCM against cancer, and a large number of animal experimental studies have been done on its anticancer effects in the international medical community. It was reported that, in a set of induced bladder cancer experiments, rats fed with Fuzheng Guben anticancer decoction were in a better state than the others, and this formula also showed a marked effect on liver cancer metastasis in experimental mice, presenting less side effects, the function of enhancing the immune function of patients, and an anticancer role.

In this study, the ORR was greatly higher in the experimental group than in the control group ( $P < 0.05$ ), which was consistent with the study report of Yiming and Huijun [25], implying that applying Fuzheng Guben anticancer decoction on the basis of taxol chemotherapy could effectively improve the efficacy of OC and was good for controlling the condition. Before and after treatment, the variation in CD8<sup>+</sup> of all patients was not significant, with no statistically meaningful between-group difference ( $P > 0.05$ ); after treatment, the patients' other immune function indicators were obviously higher than before and were significantly higher in the experimental group than in the control group ( $P < 0.05$ ). OC patients are often accompanied by immune dysfunction, which in turn is one of the important factors leading to disease progression, and among the immune function indicators, CD4<sup>+</sup> in T lymphocytes can assist other immune cells to exert antitumor effects. This result suggested that the combined regimen could greatly strengthen the immunity and promote the recovery of OC patients, and the reasons were as follows: Fuzheng Guben anticancer decoction could alleviate the damage of taxol chemotherapy on patients' immunity, reduce the body damage, and protect patients' immune function; modern pharmacology indicated that astragaloside and saponin from Mongolian milk vetch root could promote the body to synthesize proteins, improve immunity, and enhance cell antitumor activity; in addition, American ginseng was rich in polysaccharide, which could induce tumor cell apoptosis. After treatment, the patients' CA125, CA199, and CEA levels were obviously lower than before and were significantly lower in the experimental group than in the control group ( $P < 0.05$ ), demonstrating that Fuzheng Guben anticancer decoction could effectively reduce the

high expression of tumor markers in pathological tissue and serum of OC patients. According to the analysis on long-term efficacy, compared with the control group, the experimental group achieved significantly higher mean survival ( $19.80 \pm 5.84$  vs.  $14.075 \pm 5.12$  months,  $P < 0.05$ ) and lower incidence rate of adverse reactions ( $P < 0.05$ ), implying that Fuzheng Guben anticancer decoction could consolidate body resistance, cultivate the primordial spirit, and effectively reduce the adverse reactions caused by taxol.

In conclusion, jointly applying Fuzheng Guben anticancer decoction on the basis of taxol chemotherapy significantly improves the clinical efficacy, promotes immune function, reduces the incidence of complications, and prolongs the mean survival. However, because the sample size of this study was small, the conclusions obtained herein still need to be confirmed by a large-sample randomized double-blind trial; the study only intervened some patients who met the indication of single taxol chemotherapy, so it has certain limitations, and the effect of combining the TCM formula with other chemotherapeutic agents still needs to be explored.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Research Article

# Effects of Traditional Chinese Medicine for Vaginal Lavage Combined with Psychological Intervention in Postoperative Patients with Cervical Cancer

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**Purpose.** To explore the effects of traditional Chinese medicine for vaginal lavage combined with psychological intervention on the immune function and clinical efficacy in patients with cervical cancer. **Methods.** Patients with cervical cancer treated in our hospital from January 2020 to May 2021 were included in this study. All patients were treated with traditional Chinese medicine for vaginal lavage combined with psychological nursing intervention. The treatment outcomes of the patients were observed, and the quality-of-life scores and depression of the patients before and after treatment were compared. Changes in T-lymphocyte subset-related indicators, changes in blood routine-related indicators, and changes in the detection level of tumor markers were compared with anxiety scores. **Results.** After treatment, depression and anxiety were significantly reduced and the patient's quality of life significantly improved. After treatment, the patient's CD3<sup>+</sup>, CD4<sup>+</sup>, and CD4<sup>+</sup>/CD8<sup>+</sup> proportions were dramatically higher than before treatment ( $P < 0.05$ ), there was no significant difference in CD8<sup>+</sup> proportion before and after treatment ( $P > 0.05$ ), and the white blood cell (WBC), hemoglobin (Hb), platelet (PLT) of patients, and the level of tumor marker (CA125) after treatment were immensely lower than before treatment ( $P < 0.05$ ). **Conclusions.** Treating patients with cervical cancer with traditional Chinese medicine for vaginal lavage combined with psychological nursing can effectively improve the patient's immune function, effectively reduce the level of tumor marker CA125, increase the level of T-lymphocyte subsets, and improve the bone marrow hematopoietic function.

## 1. Introduction

Cancer is a leading condition that threatens human health and life, and its incidence and mortality are rapidly increasing. There are 4.29 million new cancer cases every year, accounting for 20% of the world's share, and 2.81 million deaths. The prevention and treatment of cancer are urgent needs [1]. Gynecological malignant tumors also have the characteristics of high morbidity and high mortality in the world, and their tendency in youth has become more evident in recent years, which seriously threatens the life and health of women. The incidence of cervical cancer ranks second

among gynecological malignancies in the world [2, 3]. According to the World Health Organization data, there are 530,000 new cases each year, and about 250,000 women die from cervical cancer. In China, there are about 140,000 new cases of cervical cancer and about 37,000 deaths each year, which is a high incidence area for cancer [4–7].

Currently, chemotherapy is commonly used in cervical cancer treatment. Chemotherapy before surgery can not only reduce the choice of surgery but also increase the resection rate of surgery, thereby controlling tumor development and prolonging the survival of patients. However, chemotherapy has a relatively large number of adverse

reactions in patients. It kills cancer cells in the patient's body and also has a more significant impact on normal cells. It is evident that it reduces the immune function of the patient's body [8]; the patient has symptoms such as decreased white blood cells, anemia, and loss of appetite [9]. In recent years, Chinese medicine has been widely used in the treatment of malignant tumors. After analyzing the pathogenesis of cervical cancer, oral Chinese medicine decoction for patients with cervical cancer can not only effectively improve the bone marrow suppression but also enhance the immune function of the patients. The adverse reactions caused by Chinese medicine are relatively lesser.

Previous medical research shows that the body's anti-tumor immune response mechanism is complex and delicate. The occurrence and development of tumors are closely related to the body's immune state. The body's immune system can eliminate tumor cells in the body that are sensitive to immune responses. Tumor cells escape the recognition, surveillance, and attack of the body's immune system and then continue to divide and proliferate through various mechanisms, which is also the main reason for the formation, development, and metastasis of tumors in the body. Cellular immunity mediated by T lymphocytes is the main aspect of tumor immunity. Abnormal numbers and functions can allow tumor cells to escape host immune surveillance [10]. Therefore, the detection of T-cell subsets has extremely high application value in the evaluation of clinical efficacy and prognosis of tumors, and its functional status directly reflects the body's ability to resist the invasion of cancer cells [11, 12]. Generally, the constant ratio of CD4<sup>+</sup>/CD8<sup>+</sup> maintains the balance of cellular immunity. If the balance between the CD4<sup>+</sup> and CD8<sup>+</sup> is broken, the immunity will be suppressed and the mutated tumor cells will not be recognized [13].

Due to factors such as lack of female characteristics caused by diseases and treatments, it is difficult for more gynecological malignant tumor patients to accept the status quo in a short time and thus psychological problems mainly manifested by depression and anxiety symptoms. Faced with the threat of disease, patients with malignant tumors are under physical, emotional, and social pressures during diagnosis and treatment, resulting in severe mental health problems. Some patients in a state of depression are associated with malignant tumors, and physical pain and mental illness increase the pain of patients. Pieces of evidence show that the incidence of depression in patients with gynecological malignancies is 12%–23% [14–16]. The presence of depression and anxiety will complicate the treatment of tumors and reduce the patient's compliance with treatment, thereby affecting the outcomes of therapy. With the transformation of the “biopsychosocial medical model,” the important influence of psychological factors such as depression and anxiety on the treatment of malignant tumors has attracted more and more attention from experts and scholars.

Psychological intervention treatment is standardized nursing methods including evidence-based medicine, holistic nursing, health education, and continuous quality improvement. Timeliness and sequentiality are its

distinguishing characteristics. The premise of path implementation is first to set up a clinical care pathway team and then to formulate a corresponding care pathway plan, so that patients can obtain the best-quality service, reduce the occurrence of complications, promote patient recovery and shorten the length of hospitalization, and reduce the waste of medical resources [17, 18].

The World Health Organization launched a global initiative: to expand prevention, screening, and treatment interventions and treat the elimination of cervical cancer as a public health issue in the 21st century. There are no Western medicines and vaccines with proven efficacy for the current postoperative treatment of cervical cancer, usually given local application of interferon treatment. In order to improve the symptoms of the disease, hinder the progress of the disease, and improve the quality of life of the patients, our hospital now adopts traditional Chinese medicine for vaginal lavage combined with psychological intervention to treat patients with high-risk HPV infection of the cervix.

## 2. Materials and Methods

**2.1. Research Objects.** All cases were diagnosed and treated at the Department of Oncology and Gynecology of Zhangqiu Maternity and Child Care Hospital, Jinan, Shandong, China. The patients (96 cases) who were diagnosed for the first time and underwent postoperative treatment of cervical cancer from January 1, 2020, to May 31, 2021, were included in the study group. There was complete clinical data, including 51 married cases, 45 unmarried cases, age range from 23 to 58 years old, with an average age of (38.11 ± 12.33) years, 86 cases of nonmenopause, and 10 cases of menopause. This study was approved by the ethics committee of the Zhangqiu Maternity and Child Care Hospital, and all patients provided written informed consent.

### 2.1.1. Inclusion Criteria

- (1) Patients with a history of sexual life
- (2) There was no history of cervical conization and hysterectomy
- (3) There was no vaginal medication within 2 weeks before treatment and no intercourse within 3 days
- (4) Individuals diagnosed with cervical cancer through various clinical examinations and have undergone surgical treatment
- (5) Have no history of mental illness or mental illness that affects informed consent, have certain communication and language skills, and exclude critically ill patients with severe illnesses
- (6) No other malignant tumors and severe comorbidities
- (7) Those who have surveyed questionnaires and have complete medical information

### 2.1.2. Exclusion Criteria

- (1) Age <20 years old or > 65 years old

- (2) Those with asexual life history
- (3) Those who do not meet the diagnostic criteria
- (4) Patients with cervical intraepithelial lesions and cervical cancer
- (5) Patients with severe heart, liver, kidney, blood, or endocrine system and other primary diseases, mental diseases, and immune diseases
- (6) Breastfeeding women and pregnant women
- (7) Incomplete medical information

## 2.2. Research Methods

**2.2.1. Treatment Methods.** Every night, 200 mL decoction of traditional Chinese medicine (20 g of *Sophora flavescens*, 20 g of *Cnidium monnieri*, 20 g of *Smilacis glabrae* rhizoma, 20 g of densefruit pittany root bark, 20 g of *Kochiae fructus*, 20 g of *herba hedyotidis*, and 20 g of *scutellariae barbatae* herba) was administered for vaginal lavage, followed by vaginal application of recombinant human interferon  $\alpha$ -2b vaginal effervescent tablets (Beijing Kaiin Technology Co., Ltd., S20120019). All patients were treated once a day for 10 consecutive days as a course of treatment. The next course of treatment was performed after 3 days of clean menstruation in the next month. The menopausal patients were treated for 10 consecutive days each month for a total of 3 courses of treatment. During treatment, if the patient has sex, condoms must be used. There were no noticeable adverse reactions in patients during the medication.

**(1) Psychological Intervention.** In the treatment visits, targeted psychological counseling and professional psychological interventions were provided to patients, and patients were patiently listened regarding their main complaints. Nurses use standardized reception language for patients, check the relevant information of the patients, ask the patients' inner feelings, and help the patients as much as possible to relieve the inner tension and anxiety.

The self-rating anxiety scale (SAS) and the self-rating depression scale (SDS) were applied to correctly assess the patients' mental state and guide them to talk. At the same time, the nurses patiently answer to alleviate patients' anxiety, fear, low self-esteem, and other psychologies. Effective communication was conducted with the patient's family members to understand and care more about the patient, reduce the patient's negative emotions, and increase confidence in recovery. After the operation, the patients were asked about their feelings, they were regularly asked about their feelings, and music sedation and analgesia intervention were given to reduce the patient's psychological stress after surgery.

### 2.2.2. Detection Indicators

**(1) Zung Self-Rating Depression Scale (SDS).** The scale adopts a 4-level scoring system to assess the frequency of symptoms. The criteria are as follows: "1" no or very little time, "2" a little time, "3" a lot of time, and "4" most of the time or all of the time. Result analysis: the scores for each of the 20 items are

added together to obtain the total crude score. The normal upper limit of the reference value for the total raw scores is 41, and the standard score is the integer portion of the total raw scores multiplied by 1.25. The higher the score, the more severe the symptoms in this area. The standard score is as follows: mild depression: 53–62, moderate depression: 63–72, and major depression: >72. The cutoff value is 53 points.

**(2) Zung Self-Rating Anxiety Scale (SAS).** The main statistical index of SAS is the total score. The score of each of the 20 items is added up to get the crude score. The higher the standard score is, the more serious the symptoms are. According to the Chinese norm SAS standard score, the total anxiety score below 50 is normal. Those with 50–59 scores were mild, those with 60–69 scores were moderate, and those with 70 or above scores were severe.

**(3) Changes of T-Lymphocyte Subset-Related Indicators ( $CD3^+$ ,  $CD4^+$ ,  $CD8^+$ , and  $CD4^+/CD8^+$ ) and blood routine-related indicators.** Before and after treatment, 5 mL of the patient's fasting venous blood was taken and placed on the automatic blood separator of our hospital for centrifugation, at 3,000 rpm, centrifuged for 10 min. The supernatant was taken and stored at  $-20^\circ\text{C}$  for examination. Before and after treatment, the counts of white blood cell (WBC), hemoglobin (Hb), platelet (PLT) in patients were detected.

**(4) Coagulation Function.** Before and 5 days after treatment, 6 mL elbow venous blood of patients in the morning was taken and centrifuged at 3,500 rpm for 10 min. Then, the supernatant was taken, and the coagulation function and the changes in fibrinogen (FIB) and D-dimer (D-D) were detected by a fully automatic biochemical analyzer (American Beckman AU5800).

The normal reference value of plasma FIB was 1.8–3.5 g/L, and the measured value (>3.5 g/L) was an outlier. The normal reference value of plasma D-D was 0–0.55  $\mu\text{g/mL}$ , and the measured value (>0.55  $\mu\text{g/mL}$ ) was an outlier, which was clinically proven effective when the FIB D-D value decreased.

**(5) Tumor Marker (CA125) Examination.** A total of 3 mL venous blood was collected on an empty stomach in all patients within 2 weeks before the operation, the serum was separated after centrifugation, and the level of serum CA125 was measured by the chemiluminescence method with Roche E70 automatic immunoanalyzer.

**2.3. Statistical Methods.** The detection data of all patients were expressed as mean  $\pm$  SD using SPSS 22.0 statistical analysis software. One-way ANOVA test or chi-square test was used to compare the differences between different groups. *T*-test was used to test the data between the same groups.  $P < 0.05$  was considered statistically significant.

## 3. Result

**3.1. Clinical Characteristics of Patients.** In this study, 96 cases of postoperative cervical cancer were selected, including 51 married patients and 45 unmarried patients, aged from 23 to



59 years old, with an average age of  $(38.11 \pm 12.33)$  years old, 86 premenopausal patients, and 10 postmenopausal patients. According to the International Federation of Gynecology and Obstetrics (FIGO) classification in 2009, there were 43 patients with stage I-II cervical cancer, aged between 23 and 56 years, with an average age of  $37.38 \pm 6.82$  years, and 53 patients with stage III-IV cervical cancer, aged between 25 and 59 years, with an average age of  $40.5 \pm 7.15$  years, as shown in Table 1.

**3.2. Postoperative Depression and Anxiety in Patients with Cervical Cancer.** The mean standard score of SDS in 96 patients with cervical cancer after the operation was  $47.2 \pm 10.3$ . According to SDS standard score, there were 17 patients with depression, accounting for 17.7%, and 79 patients without depression, accounting for 82.3%. According to the standard of depression degree, 11 people were mildly depressed, accounting for 11.4%, 4 people were moderately depressed, accounting for 4.2%, and 2 people were severely depressed, accounting for 2.1%, as shown in Figure 1(a). The mean standard score of SAS in 96 patients with cervical cancer after the operation was  $41.7 \pm 9.2$ . According to the SAS standard score, there were 21 patients (21.9%) with anxiety, 75 patients (78.1%) without anxiety, 15 patients (15.6%) with mild anxiety, 5 patients (5.2%) with moderate anxiety, and 1 patient (1.1%) with severe anxiety, as shown in Figure 1(b).

**3.3. The Comparison of SAS, SDS, and KPS.** Before and after treatment, the scores of SAS, SDS, and KPS were compared, as shown in Figure 2. Before psychological care, the scores of SAS, SDS, and KPS were all poor in patients with cervical cancer, and the intragroup difference was not statistically significant ( $P > 0.05$ ). After psychological nursing, the patients' SAS, SDS, and KPS scores were improved, and there was a significant difference in patients with cervical cancer before and after the treatment ( $P < 0.05$ ), indicating that Chinese medicine for vaginal lavage combined with psychological intervention can effectively improve the quality of life of patients with cervical cancer. Psychological intervention refers to basic nursing for patients with cervical cancer, while paying more attention to the condition of the patient, which is conducive to the rehabilitation of the patient, can effectively improve the patient's unhealthy mentality and improve the quality of life of the patient, which is a high-quality nursing guarantee.

**3.4. Comparison of T-Lymphocyte Subsets.** Although postoperative radiotherapy and chemotherapy for cervical cancer can prolong disease-free survival and reduce mortality, most patients have noticeable adverse reactions and suppressed immune function. Immunological studies have shown that the occurrence, development, and prognosis of tumors directly impact the immune function of the body, especially T-cell-mediated cellular immunity. T cells mainly include  $CD4^+$  and  $CD8^+$  subgroups. Traditionally,  $CD4^+$  T cell is considered as the helper T cell, and  $CD8^+$  T cell is

TABLE 1: Clinical characteristics of patients.

Clinical characteristics	Proportion of patients
Age	<35 12 (12.5%)
	35–60 84 (87.5%)
Marital status	Married 51 (53.1%)
	Unmarried 45 (46.9%)
FIGO stage	I-II 43 (44.8%)
	III-IV 53 (55.2%)

regarded as a suppressor T cell. Therefore, the proportion of  $CD4^+$ ,  $CD8^+$ , and  $CD4^+/CD8^+$  cells can directly reflect the cellular immune function of patients with cervical cancer. The proportion of  $CD4^+$  was  $38.82 \pm 4.55$  before treatment and  $52.98 \pm 4.28$  after treatment, and the proportion of  $CD8^+$  and  $CD4^+/CD8^+$  was  $34.01 \pm 6.42$  and  $1.14 \pm 0.15$  before treatment and  $32.24 \pm 5.73$  and  $1.56 \pm 0.16$  after treatment, respectively, as shown in Table 2. The results showed that the level of  $CD3^+$ ,  $CD4^+$ , and  $CD4^+/CD8^+$  significantly increased. In contrast, the level of  $CD8^+$  dramatically decreased after treatment compared with that before treatment ( $P < 0.05$ ), suggesting that traditional Chinese medicine for vaginal lavage can effectively enhance the immune function of postoperative patients with cervical cancer.

**3.5. The Comparison of Blood Routine Indexes of 96 Patients before and after Treatment.** The counts of WBC, Hb, and PLT in patients with cervical cancer before postoperative treatment were  $7.18 \pm 1.10 \times 10^9/L$ ,  $120.55 \pm 10.02$ , and  $214.37 \pm 10.14 \times 10^9/L$ . After vaginal lavage combined with psychological intervention, WBC, Hb, and PLT counts were  $5.34 \pm 1.05 \times 10^9/L$ ,  $100.18 \pm 7.70 g/L$ , and  $159.90 \pm 9.39 \times 10^9/L$ , respectively, as shown in Table 3. The levels of WBC, Hb, and PLT were enormously lower after treatment than that before treatment ( $P < 0.05$ ), suggesting that the vaginal lavage of traditional Chinese medicine can effectively improve the hematopoietic function of bone marrow in patients with cervical cancer.

**3.6. The Changes of FIB and D-D before and after Chinese Medicine Treatment.** It has been reported that abnormal coagulation mechanisms and fibrinolytic system caused by malignant tumors are the most important reasons leading to blood hypercoagulability and coagulation dysfunction. The coagulation function of patients with cervical cancer is increased, which is manifested in the increase of D-D and FIB. For the high coagulation value of FIB and D-D after the operation of cervical cancer, vaginal perfusion of traditional Chinese medicine can play an effective role in reducing FIB and D-D ( $P < 0.05$ ), as shown in Figure 3.

**3.7. The Comparison of Serum Tumor Marker (CA153) before and after Treatment.** Tumor markers are substances synthesized and released by tumor cells or released by the host to reflect the existence and growth of tumors in the process of tumor genesis and development. They are related to the severity of the disease and tumor size or stage, can monitor



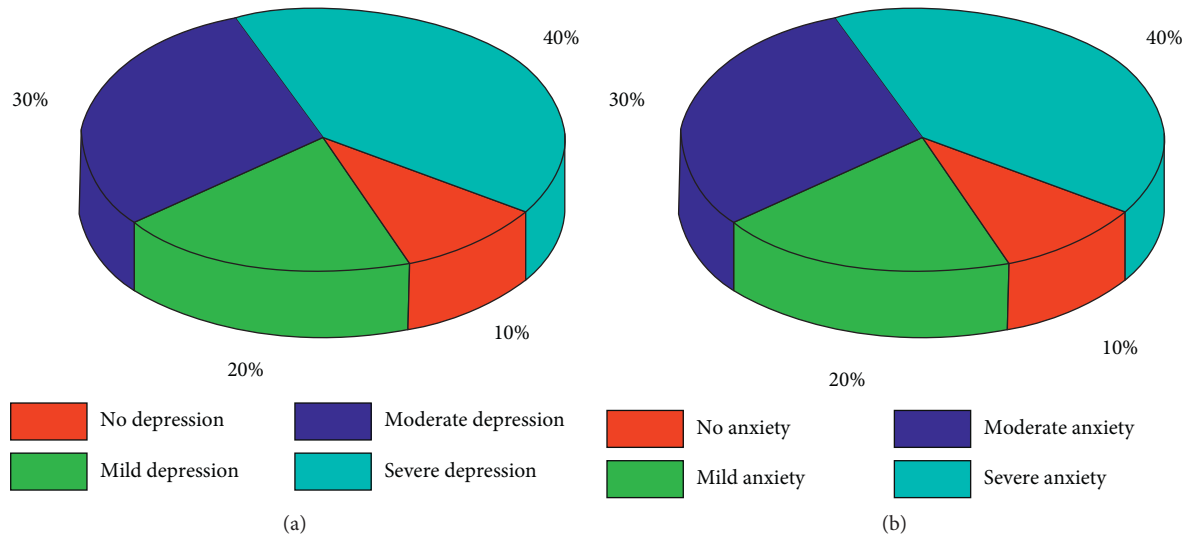


FIGURE 1: Postoperative depression and anxiety in patients with cervical cancer. (a) The score of SDS. (b) The score of SAS.

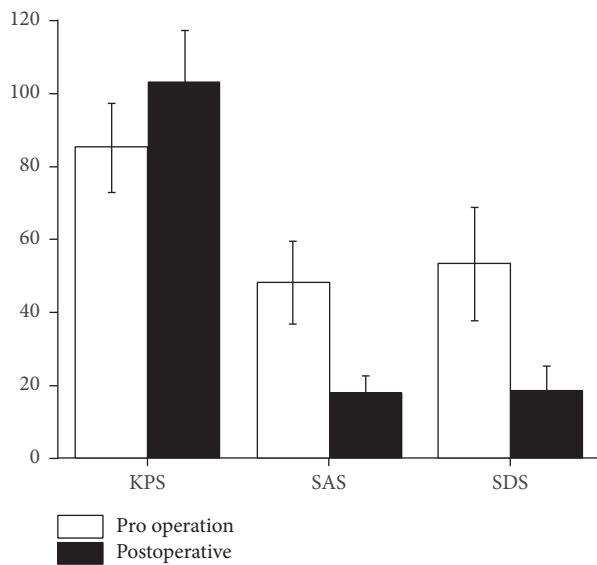


FIGURE 2: Comparison of psychological and quality-of-life scores before and after treatment.

TABLE 2: The comparison of T-lymphocyte subsets before and after treatment.

Time	CD3 <sup>+</sup>	CD4 <sup>+</sup>	CD8 <sup>+</sup>	CD4 <sup>+</sup> /CD8 <sup>+</sup>
Before treatment	54.85 ± 5.62	38.82 ± 4.55	34.01 ± 6.42	1.14 ± 0.15
After treatment	63.71 ± 6.54	52.98 ± 4.28	32.24 ± 5.73	1.56 ± 0.16
P	<0.001	<0.01	>0.05	>0.05

the therapeutic effect of tumor, and can monitor the recurrence and prognosis of tumor. CA125 is the best indicator for detecting cervical cancer recurrence, and it has

TABLE 3: The comparison of blood routine indexes of 96 patients before and after treatment.

Time	WBC (10 <sup>9</sup> /L)	Hb (g/L)	PLT (10 <sup>9</sup> /L)
Before treatment	7.18 ± 1.10	120.55 ± 10.02	214.37 ± 10.14
After treatment	5.34 ± 1.05	100.18 ± 7.70	159.90 ± 9.39
P	<0.05	<0.05	<0.001

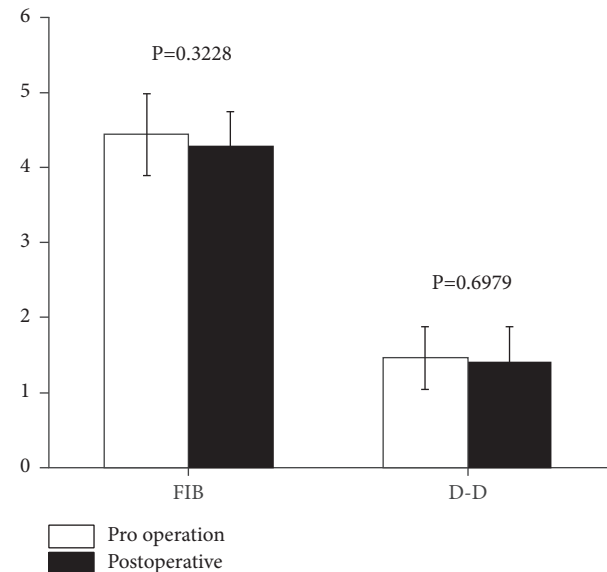


FIGURE 3: The comparison of FIB and D-D before and after Chinese medicine treatment.

certain clinical significance for the follow-up of cervical cancer.

The comparison of serum tumor marker (CA153) before and after treatment is shown in Figure 4. By t-test, the level

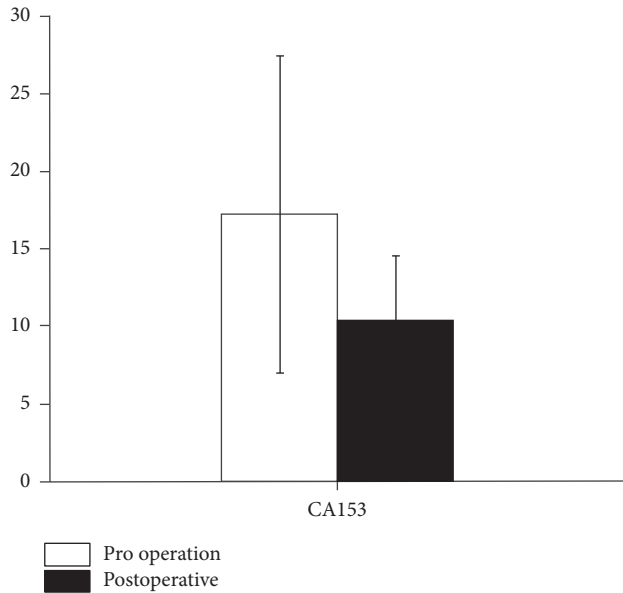


FIGURE 4: The comparison of serum tumor marker (CA153) before and after treatment.

of CA153 in patients with cervical cancer before treatment decreased from  $17.23 \pm 10.23$  to  $10.34 \pm 4.23$ . There was an apparent difference in CA153 level before and after treatment ( $P > 0.05$ ), suggesting that traditional Chinese medicine for vaginal lavage combined with psychological intervention can reduce serum tumor indexes.

#### 4. Discussion

Cervical cancer is the fourth most common cancer in women. It is a serious condition that threatens women's life and physical and mental health. At present, surgical treatment is one of the effective treatments for cervical cancer. However, comprehensive treatment principles such as radiation therapy, chemotherapy, endocrine therapy, biological therapy, and traditional Chinese medicine should be considered after surgery. Surgery or radiotherapy and chemotherapy are a heavy blow to the human body, and many complications often occur. In traditional Chinese medicine theory, surgical treatment consumes the healthy qi and damages the body fluid [19–21], so the therapeutic principle is to strengthen the body resistance to eliminate pathogenic factors.

This study is based on the application of interferon plus vaginal lavage with traditional Chinese medicine treatment. Chinese medicine has the function of clearing heat toxins, eliminating dampness and arresting leukorrhea, and killing ascarid [22, 23]. Pharmacological studies show that matrine in *Sophora flavescens* can effectively sterilize without damaging normal vaginal flora [24]. The dione, dictamnine, and obacunone in *Cortex Dictamni* have more potent antibacterial, anti-inflammatory, antianaphylaxis, anticancer, and insecticidal pharmacological activities [25–27]. *Cnidium cnidii*, *fructus kochiae*, and *rhizome smilacis glabrae* have anti-inflammatory, antiviral, and antitumor effects [28–30], and the therapeutic effects are mainly achieved by

promoting the apoptosis of corresponding cells. Spreading hedyotis herb contains flavonoids, iridoids, terpenoids, and anthraquinones, which can inhibit the growth of tumor cells and induce their apoptosis [31]. *Scutellaria barbata* D. Don contains diterpenes and its lactone, flavonoid, polysaccharides, etc., which have the pharmacological effects of promoting cellular immune function, anticancer, antivirus, antioxidation, and antiaging [32].

The results of this study showed that the percentage of  $CD4^+$  and  $CD3^+$  cells and the ratio of  $CD4^+/CD8^+$  in patients treated with vaginal Chinese medicine infusion were significantly increased compared with those before treatment ( $P < 0.05$ ). Better therapeutic outcomes have been achieved, and no adverse reactions were observed during the whole treatment process. This study adopts that the vaginal Chinese medicine perfusion can significantly improve the cellular immunity function of the organism, effectively hamper the levels of tumor marker CA125, reduce the side effects of chemotherapy, improve the bone marrow hematopoietic function, and can prevent cervical cancer recurrence and metastasis. However, there is still a gap to improve this potential concept. The insufficient sample size may lead to a large probability of error in data deviation, so we hope to increase the sample size in future research to reduce the deviation of results. In addition, the reasons for the decrease in adverse drug reactions shall be further explored to establish the efficacy of drugs better. These are the directions of our follow-up and improvement to find a better treatment for this disease.

Psychological intervention is the basic nursing of patients to pay more attention to the patient's state, conducive to the rehabilitation of patients with cervical cancer after surgical treatment. It could improve the patient's unhealthy mentality. Vaginal traditional Chinese medicine perfusion can directly act on the affected part of the body, and the clinical application is simple. Combined with psychological intervention, it is more effective to improve patients' quality of life, strengthen the treatment efficacy, and improve patient's compliance.

#### 5. Conclusions

In conclusion, the patient's quality of life was significantly improved, depression and anxiety were reduced, the patient's  $CD3^+$ ,  $CD4^+$ , and  $CD4^+/CD8^+$  indicators after treatment were higher than before treatment, and the patient's WBC, Hb, and PLT counts after treatment were lower than before treatment. The treatment of patients with cervical cancer with traditional Chinese medicine for vaginal lavage combined with a psychological nursing intervention program can effectively improve the patient's immune function, lower the level of tumor marker CA125, increase the level of T-lymphocyte subsets, and improve bone marrow hematopoietic function.

#### Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

## Authors' Contributions

Rufen Ma and Ruixiang Yu contributed equally.

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## Research Article

# The Diagnostic Value of Serum Ang, VEGF, and CRP Combined with the Chinese Medicine Antitumor Formula in the Treatment of Advanced Renal Carcinoma

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**Objective.** To explore the diagnostic value of serum angiopoietin (Ang), vascular endothelial growth factor (VEGF), and C-reactive protein (CRP) combined with the Chinese medicine antitumor formula in the treatment of advanced renal carcinoma. **Methods.** Retrospective analysis was performed for the data of 60 patients with advanced renal cancer admitted at Yantaishan Hospital from February 2019 to February 2020. All patients were treated with Chinese medicine antitumor formula. The serum Ang, VEGF, and CRP levels in venous blood samples were detected before and after treatment. Sensitivity, specificity, and AUC of combined serum Ang, VEGF, and CRP were analyzed utilizing the receiver operating characteristic curve (ROC) (95% CI). **Results.** There were 52 cases of clear-cell carcinoma (86.7%), 7 cases of papillary carcinoma (11.7%), and 1 case of chromophobe renal cell carcinoma (1.7%). The average tumor diameter was  $(9.67 \pm 0.65)$  cm, and the KPS score was  $(74.68 \pm 1.52)$ . About 75% of the patients had metastasis. After treatment, the level of serum Ang, VEGF, and CRP was immensely lower compared to that before treatment ( $P < 0.001$ ). The sensitivity, specificity, and AUC (95%CI) of the combined detection of Ang, VEGF, and CRP before treatment were 86.7%, 90.0%, and 0.883 (0.817–0.950), while the sensitivity, specificity, and AUC (95%CI) of the combined detection of Ang, VEGF, and CRP were 83.3%, 86.7%, and 0.850 (0.776–0.9524), respectively. **Conclusion.** The combined detection of serum Ang, VEGF, and CRP has high diagnostic value for patients with advanced renal cancer treated with Chinese medicine antitumor formula.

## 1. Introduction

Renal cancer is a malignant tumor that occurs in the urinary tubule epithelium of the renal parenchyma. The incidence rate of the disease in 2011 was 3.8%. According to the data of the Ministry of Health of China, its incidence has been increasing year by year in the past ten years and now ranks top ten among the highest incidence of male malignant tumors in China [1, 2]. Since the early symptoms of kidney cancer are not specific, most patients are being found in the

middle and late stages of the disease when they are diagnosed [3]. Patients with advanced metastatic renal cancer lack sensitivity to conventional treatments such as radiotherapy and chemotherapy [4]. Their average life expectancy is less than 1 year, and the five-year survival rate is less than 10% [5–7], and patients usually have a poor prognosis. Prolonging the survival time of patients with advanced renal cell carcinoma is the focus of clinical research. However, no optimum remedies for renal cancer have been found at present, and some studies have shown that traditional



Chinese medicine (TCM) has unique advantages in the treatment of malignant urinary tumors [8–10]. Since renal cancer is an immune-related malignant tumor, the application of TCM treatment based on the concept of holistic treatment and syndrome differentiation is beneficial to improve the body tolerance of patients and control the progression of renal cancer. The findings of the previous study show that the Chinese medicine antitumor formula has a substantial targeted effect on advanced cancer [11]. The prescription contains yangtao actinidia root, Fructus Akebiae, Herba Solani Lyrati, and Catechu, which can effectively reduce the level of inflammatory factors in patients, enhance their immunity, inhibit the expression of VEGF and its receptors, reduce the density of microvessels in tumor tissues, play a role in blocking the process of the cancer cell cycle, and prolong the survival period of patients with advanced cancer. However, few studies have used the Chinese medicine antitumor formula to treat renal cancer, and the drug's actual effect on patients with advanced renal cancer is still unclear. Therefore, when applying the Chinese medicine antitumor formula, attention should be paid to monitoring the patient's disease progression to ensure the patient gets the highest therapeutic benefit.

At present, there is a lack of ideal markers for diagnosing advanced renal cancer in clinical practice. For renal cancer patients treated with the Chinese medicine antitumor formula, an index with high consistency with the mechanism of action should be selected. VEGF is an important indicator that reflects the ability of blood vessel proliferation, and CRP is closely related to the level of inflammation in patients [12–14]. In addition to VEGF, Ang is also closely associated with angiogenesis, and Ang-1 and Ang-2 in this protein family belong to angiogenesis regulators. Numerous studies have confirmed that their expression levels are closely related to tumor stages and patient prognosis [15, 16]. Therefore, Ang, VEGF, and CRP were selected as the serological indicators to explore the value of their combined detection for patients with advanced renal cancer after treating with the Chinese medicine antitumor formula.

## 2. Methods

**2.1. Study Design.** This retrospective study was conducted at Yantaishan Hospital, Yantai, Shandong, China, from February 2019 to February 2020 to explore the diagnostic value of serum Ang, VEGF, and CRP combined detection in the treatment of advanced renal carcinoma after being treated with the Chinese medicine antitumor formula. A total of 60 patients with advanced renal cancer were included in this study. This study was double-blind, and neither the subjects nor the researchers knew about the grouping of the tests. The study designer was accountable for arranging and controlling all the tests.

**2.2. Object Recruitment.** A retrospective analysis was performed on the data of patients admitted at Yantaishan Hospital, Yantai, Shandong, China, from February 2019 to February 2020, and patients were selected according to the

following criteria: (1) Patients diagnosed with renal cancer by imaging and pathological examination, with stage III or IV according to Robson stage [17, 18]. (2) The patients treated in our hospital for the whole period without death cases, transfer to other hospitals, or cease of treatment. (3) The expected survival time was more than 3 months. (4) Patients with complete clinical data. (5) Patients over 18 years of age. (6) Patients with BMS, assessed without neurological abnormalities, and did not need to receive corticosteroid therapy. Patients were excluded according to the following criteria: (1) Unable to communicate with them due to hearing impairment, language barrier, unconsciousness, or mental illness. (2) Withdrawal from treatment, death, changes of treatment regimen, or loss of follow-up. (3) The presence of other serious diseases, such as liver, kidney, or cardiopulmonary dysfunction. (4) Abnormal hematopoietic function. (5) Severe infection exists.

**2.3. Moral Considerations.** This study was in accordance with the principles of the Declaration of Helsinki [19] and approved by the ethics committee of the Yantaishan Hospital, Yantai, China, and all the patients provided written informed consent for participation in the study.

**2.4. Exit Test Criteria.** If the following conditions occurred and the study group judged that it was unsuitable for continuing the study, the medical record form would be kept without data analysis: (1) Adverse events or serious adverse events occurred. (2) Deterioration of the condition during the test. (3) The subject has some serious coincidences or complications. (4) During the clinical trial, the object is unwilling to continue the clinical trial.

**2.5. Methods.** Sociodemographic data and clinical manifestation data were collected, and serological tests were performed before and after treatment with the Chinese medicine antitumor formula.

**2.5.1. Recipe Composition.** Radix Pseudostellariae, Dahurian Patrinia Herb, Red rattan, yangtao actinidia root, Sealwort, Turtle shell, Turtle plate, and Bittersweet Herb, 15 g respectively, Atractylodes, *Magnolia officinalis*, Catechu, Celandine, and amomum, 10 g respectively, *Poria cocos* and Fructus Akebiae, 12 g respectively, Coix seed and *Oldenlandia diffusa*, 30 g respectively, Pulsatilla, 20 g, and liquorice, 3 g, were used. The Chinese medicine antitumor formula was decocted to 200 ml in warm water every day and divided into two doses for 14 days.

Before and after treatment, venous blood was collected from the patients for Ang, VEGF, and CRP detection. A total of 5 ml of venous blood was collected from the patients on an empty stomach in the morning, stood at room temperature for 30 min in anticoagulant tubes, and centrifuged at 3000 r/min for 10 min. The levels of Ang-1, Ang-2, VEGF, and CRP were determined by enzyme-linked immunosorbent assay (Beijing Kewei Clinical Diagnostic Reagent Co., LTD., S20060028).



**2.6. Observation Criteria.** (1) General Information: a general information extraction table was established, including the number of inpatients, name, sex, age, body weight, tumor stage, clinical classification, mean tumor diameter, main clinical symptoms, metastasis, and KPS score. (2) Changes of serum Ang, VEGF, and CRP before and after treatment. (3) Diagnostic value of serum Ang, VEGF, and CRP in patients treated with the Chinese medicine antitumor formula: sensitivity, specificity, and AUC of combined serum Ang, VEGF, and CRP were analyzed by ROC (95% CI).

**2.7. Statistical Analysis.** Data processing software was SPSS20.0, and the image rendering software was GraphPad Prism 7 (San Diego, USA). ROC was calculated by SPSS Statistics, and AUC (95% CI) was compared. The research included counting data and measurement data, utilizing the  $\chi^2$  tests and *t*-test to analyze.  $P < 0.05$  means the difference is statistically significant.

### 3. Results

**3.1. Analysis of General Patient Data.** There were 38 male and 22 female patients aged from 28 to 84 years, with an average age of  $58.14 \pm 3.68$  years and an average bodyweight of  $58.65 \pm 1.65$  kg. The tumor stages of all patients were stage III or IV, including 24 cases (40.0%) of stage III and 36 cases (60.0%) of stage IV. There were 52 cases of clear-cell carcinoma (86.7%), 7 cases of papillary carcinoma (11.7%), and 1 case of chromophobe carcinoma (1.7%). The main clinical symptoms of the patient were hematuria, abdominal mass, pain, an average tumor diameter of  $(9.67 \pm 0.65)$  cm, and a KPS score of  $74.68 \pm 1.52$ . Lung metastasis was found in 18 (30.0%) cases, bone metastasis in 15 (25.0%) cases, liver metastasis in 10 (16.7%) cases, and brain metastasis in 2 (3.3%) cases (Table 1).

**3.2. Analysis of Changes in Serum Ang, VEGF, and CRP before and after Treatment.** The levels of Ang-1 and Ang-2 after treatment were enormously lower than before treatment ( $0.96 \pm 0.07$  vs.  $1.30 \pm 0.15$ ,  $P < 0.001$  and  $3.24 \pm 0.65$  vs.  $5.86 \pm 0.89$ ,  $P < 0.001$ , respectively), but the levels of Ang-1 and Ang-2 before and after treatment were still significantly higher than those in the control group ( $1.30 \pm 0.15$  vs.  $0.96 \pm 0.07$  vs.  $0.32 \pm 0.04$ ,  $P < 0.001$  and  $5.86 \pm 0.89$  vs.  $3.24 \pm 0.65$  vs.  $1.12 \pm 0.12$ ,  $P < 0.001$ ). The level of VEGF was tremendously lower after treatment than before ( $292.68 \pm 45.62$  vs.  $475.68 \pm 50.25$ ,  $P < 0.001$ ), but the levels of VEGF before and after treatment were still immensely higher than those in the control group ( $475.68 \pm 50.25$  vs.  $292.68 \pm 45.62$  vs.  $128.65 \pm 35.44$ ,  $P < 0.001$ ). The level of CRP was remarkably lower after treatment than before ( $9.65 \pm 0.87$  vs.  $22.54 \pm 1.22$ ,  $P < 0.001$ ), but the level of CRP of patients before and after treatment was still obviously higher than that of the control group ( $22.54 \pm 1.22$  vs.  $9.65 \pm 0.87$  vs.  $3.16 \pm 0.45$ ,  $P < 0.001$ ), as shown in Figure 1.

TABLE 1: The demographic characteristics of patients.

Demographic characteristics (n)	Observation group (n = 60)
Male	38
Female	22
Age ( $\bar{x} \pm SD$ )	28–84 ( $58.14 \pm 3.68$ )
Body weight ( $\bar{x} \pm SD$ )	$58.65 \pm 1.65$
<i>Tumor stages</i>	
Stage III	24 (40.0%)
Stage IV	36 (60.0%)
Clear-cell carcinoma	52 (86.7%)
Papillary carcinoma	7 (11.7%)
Chromophobe carcinoma	1 (1.7%)
Tumor diameter	$(9.67 \pm 0.65)$
KPS score	$74.68 \pm 1.52$
<i>Tumor metastasis</i>	
Lung metastasis	18 (30.0%)
Bone metastasis	15 (25.0%)
Liver metastasis	10 (16.7%)
Brain metastasis	2 (3.3%)

**3.3. A Diagnostic Value Analysis of Serum Ang, VEGF, and CRP in Patients Treated with the Chinese Medicine Antitumor Formula.** The sensitivity, specificity, and AUC (95%CI) of the combined detection of Ang, VEGF, and CRP before treatment were 86.7%, 90.0%, and 0.883 (0.817–0.950). The sensitivity, specificity, and AUC (95%CI) of the combined detection of Ang, VEGF, and CRP were 83.3%, 86.7%, and 0.850 (0.776–0.9524) after the treatment with the Chinese medicine antitumor formula, as shown in Figures 2 and 3.

### 4. Discussion

Renal cancer is a common malignant tumor of the urinary system, and its morbidity and mortality rank 14th and 16th, respectively, among malignant tumors globally [20]. The number of new patients with renal cancer is more than 400,000, and the number of deaths is more than 140,000 annually [21]. According to the data of the China Cancer Prevention and Control Research Office, the incidence of renal cancer in China is close to the average world level and is increasing year by year, with an average annual increase of about 6.0% [22, 23], indicating that it is a severe threat for Chinese residents. As the pathogenesis of renal cancer has not been clearly defined, the clinical treatment outcomes of renal cancer are not satisfactory, and immunotherapy in the past has significant side effects, and the remission rate is not high, accompanied by no significant improvement in the survival of patients [24, 25]. For patients with advanced renal cancer, chemotherapy and radiotherapy are the conventional treatment methods. However, patients with advanced renal cancer are usually accompanied by metastasis. Chemotherapy and radiotherapy cannot improve the 5-year survival rate, resulting in a poor prognosis. Research in recent years found that traditional Chinese medicine can effectively improve the immune status of patients and improve the overall curative effect, and the practice also confirmed that cancer patients prefer the combination of traditional Chinese and Western medicine treatment,

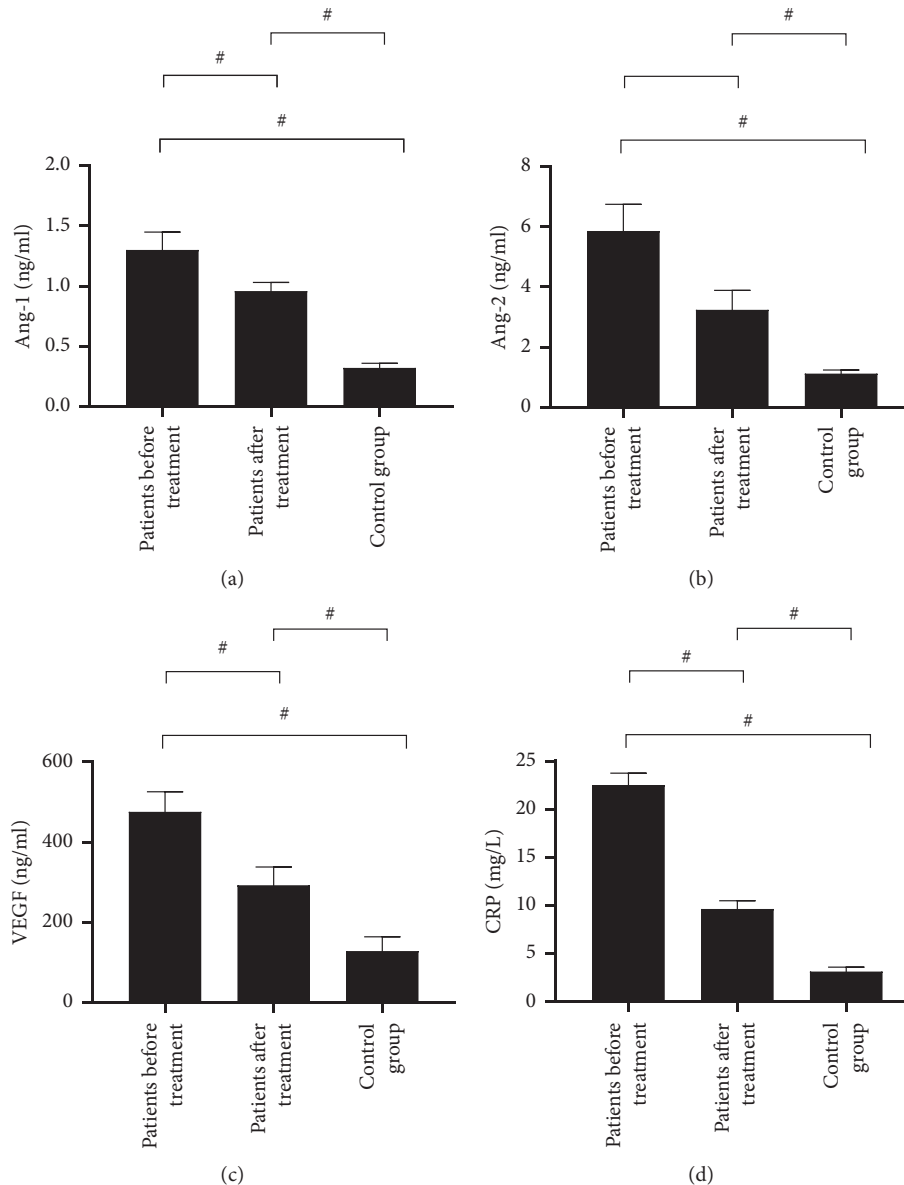


FIGURE 1: Analysis of changes in serum Ang, VEGF, and CRP before and after treatment ( $x \pm S$ ) vs. the control group,  $\#P < 0.01$ .

indicating that there is a broad space for the application of traditional Chinese medicine treatment [26]. The Chinese medicine antitumor formula evaluated in this study includes the root of *Kudaphora japonicus*, *Radix Pseudostellariae*, Bittersweet Herb, *Atractylodes*, *Celandine*, *Poria cocos*, *Fructus Akebiae*, and *Oldenlandia diffusa*, which can effectively enhance the immune function of patients, make T lymphocytes kill mutant cells in time, induce cell autophagy, and inhibit the progression of cancer. Some scholars evaluated the Chinese medicine antitumor formula in colon cancer patients and found that the medicine could prolong the survival period of patients. Moreover, relevant reports showed that the inhibitory rate of *Oldenlandia diffusa* in the prescription was over 80% [27], so the Chinese medicine antitumor formula may be beneficial to alleviate the disease progression of patients with advanced renal cancer.

There are few studies that evaluated the treatment of advanced renal cancer with a Chinese medicine antitumor formula, so its actual effect is not authenticated. In this study, the reason why serum Ang, VEGF, and CRP were utilized as an indicator of its efficacy in this study is that the Chinese medicine antitumor formula can control cell proliferation by inhibiting vascular hyperplasia, while both Ang and VEGF are closely related to vascular hyperplasia. The VEGF gene is highly expressed in lung cancer, liver cancer, and other tumors, while Ang is closely related to the occurrence and development of tumors. Ashing Kimlin Tam et al. reported that the Yangtao Actinidia Root could regulate the proliferation and apoptosis of breast cancer cells through the VEGF signaling pathway [28]. Zhang et al. found that compound preparation Yangtao Actinidia Root could inhibit the growth of transplanted tumor in CT26 mice and control the expression level of VEGF [29]. In

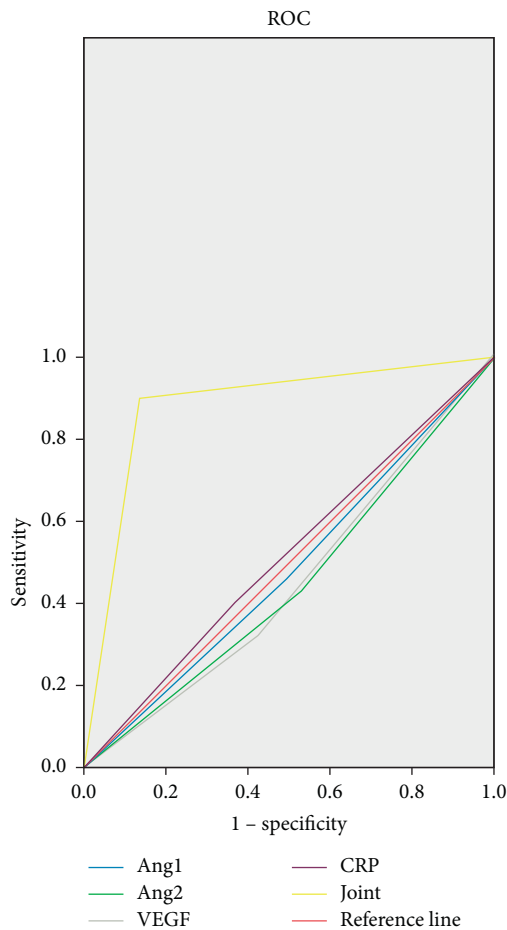


FIGURE 2: The diagnostic value of serum Ang, VEGF, and CRP before treatment. *Note.* The horizontal axis is 1-specificity, and the vertical axis is sensitivity. The blue line is the test result of Ang-1, the green line is the test result of Ang-2, the gray line is the test result of VEGF, the purple line is the test result of CRP, the yellow line is the test result of combined detection, and the red line is the reference line.

this study, there were significant differences in serum Ang and VEGF levels after treatment compared with before treatment, indicating that the renal cancer cells in the patient were controlled and the proliferation rate decreased significantly. In addition, CRP can also be considered to assess the prognosis of cancer patients. This indicator is not only an inflammatory indicator but also an immune indicator, which can activate complement, enhance cell phagocytosis, and maintain the normal function of the immune system. However, when patients' body is in stress conditions or diseases, CRP tends to rise; therefore, it is essential to maintain a rational CRP level. In this study, the CRP level of patients was improved after treatment, suggesting that the Chinese medicine antitumor formula has certain effects on the treatment of advanced renal cancer, and Ang, VEGF, and CRP can be considered as vital indicators to assess the disease progression in patients.

Among the patients included in this study, there were 52 cases (86.7%) of clear-cell carcinoma, 7 cases (11.7%) of papillary carcinoma, and 1 case (1.7%) of chromophobe cell carcinoma, with an average tumor diameter of ( $9.67 \pm 0.65$ ) cm.

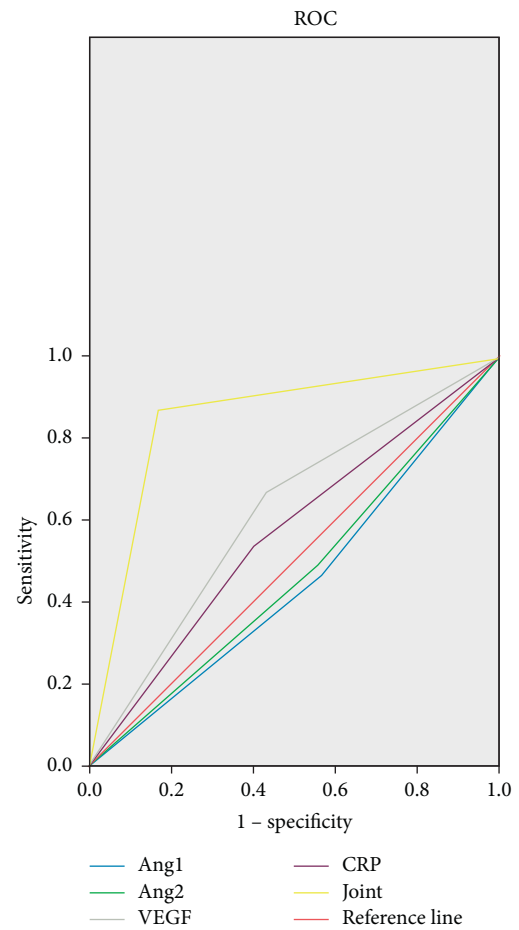


FIGURE 3: The diagnostic value of serum Ang, VEGF, and CRP after treatment. *Note.* The horizontal axis is 1-specificity, and the vertical axis is sensitivity. The blue line is the test result of Ang-1, the green line is the test result of Ang-2, the gray line is the test result of VEGF, the purple line is the test result of CRP, the yellow line is the test result of combined detection, and the red line is the reference line.

The sensitivity, specificity, and AUC (95% CI) of the combined detection of Ang, VEGF, and CRP before treatment were 86.7%, 90.0%, and 0.883 (0.817–0.950), while after treatment, the sensitivity, specificity, and AUC (95% CI) of the combined detection of Ang, VEGF, and CRP were 83.3%, 86.7%, and 0.850 (0.776–0.9524), suggesting that the combined detection of Ang, VEGF, and CRP has not only high diagnostic value for patients with advanced renal cancer before treatment but also good diagnostic value for patients after Chinese medicine antitumor formula treatment, which is conducive to the clinical judgment of the disease state of patients.

In conclusion, the combined detection of serum Ang, VEGF, and CRP has a potential diagnostic value for the Chinese medicine antitumor formula in treating patients with advanced renal cancer.

### Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Research Article

# Functions of Traditional Chinese Medicine Combined with Recombinant Human Interferon $\alpha 2b$ in Cervical Intraepithelial Neoplasias Patients

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Cervical cancer is a common malignant neoplasm in women, and its incidence is increasing year by year. This study explored the effects of traditional Chinese medicine combined with recombinant human interferon  $\alpha 2b$  in cervical cancer patients. 178 cervical intraepithelial neoplasias (CIN) combined with high-risk HPV-positive patients from June 2017 to August 2020 were divided into the study group ( $n = 89$  cases) and the control group ( $n = 89$  cases) by the random number table method. Patients in the control group were treated with recombinant human interferon  $\alpha 2b$ , and the study group was treated with traditional Chinese medicine (TCM) on the basis of the control group. After treatment, the recurrence rate in the study group was significantly decreased while the human papillomavirus (HPV) negative conversion rate was significantly increased. 3 months after treatment, the TCM symptom scores in the study group were lower than in the control group. Moreover, serum levels of inflammatory factors decreased in both groups, and the decrease was more significant in the study group. After treatment, the ultrasound parameters were significantly decreased in the study group than in the control group. In conclusion, traditional Chinese medicine combined with recombinant human interferon  $\alpha 2b$  in cervical cancer patients could effectively improve the negative conversion rate of HPV infection, the level of inflammatory factors, reduce the degree of cervical erosion, and enhance the immunity of patients with high safety and significantly improve the quality of life.

## 1. Introduction

Cervical cancer is the most common female malignant tumor disease nowadays, and in recent years, with the change in people's lifestyles, the incidence of this disease has been increasing year by year, which seriously affects the quality of life of female patients [1]. Human papillomavirus (HPV) is a cyclic double-stranded small DNA virus that is epitheliophilic and invades the cervical basal metaplasia epithelial cells and squamous epithelial transformation zone [2]. Cervical columnar intraepithelial neoplasia trauma provides a good environment for HPV to proliferate, and therefore, cervical columnar intraepithelial neoplasia is susceptible to HPV infection [3]. When cervical columnar intraepithelial neoplasia is combined with persistent HPV

infection, especially with high-risk human papillomavirus (HR-HPV), it is highly susceptible to carcinogenesis [4]. The results of a related study [5] showed that the development of CIN in patients was mainly caused by high-risk HPV infection and was also an important cause of cervical cancer. Therefore, enhancing the effective treatment of cervical HPV infection is important to reduce pain and improve the quality of life of patients.

Recombinant human interferon  $\alpha 2b$  is a commonly used antiviral drug that can effectively inhibit the replication of genetic material of the virus and enhance the immune system of patients, which can achieve better and shorter-term efficacy. However, the relapse rate is high after discontinuation of the drug, and long-term use of the drug may also affect the tolerance and compliance of patients [6]. In



Chinese medicine, cervical HPV infection is classified as “leukorrhea” and “multicolored vaginal discharge,” which should be treated by invigorating the spleen, removing dampness, and invigorating the spleen-stomach and replenishing qi [7].

In this study, the Buqi Qushi Jiedu decoction used was a self-prepared decoction, which could effectively remove pathogens from the body, improve the overall state of the body, and mobilize specific and nonspecific immune functions. Therefore, in this study, recombinant human interferon  $\alpha 2b$  and Buqi Qushi Jiedu decoction were combined to treat patients with cervical intraepithelial neoplasia.

## 2. Materials and Methods

**2.1. Clinical Data.** A total of 178 patients with CIN admitted at the People's Hospital of Rizhao, Rizhao, Shandong, China, from June 2017 to August 2020 were selected as the study objects.

Inclusion criteria were as follows: Western medicine diagnosis conformed to the diagnostic criteria of CIN established by the American Society for Colposcopy and Cervical Pathology (ASCCP) [8]; Chinese medicine diagnosis conformed to the diagnostic criteria of spleen deficiency and dampness excess in the Guidelines for Clinical Research on New Chinese Medicines [9]; pathological examination confirmed the diagnosis of patients with CIN grade I–II; HPV-DNA gene chip test for high-risk HPV; and those without hematologic disorders. Patients voluntarily participated in this study and signed the informed consent form.

Exclusion criteria were as follows: patients who had undergone physical or surgical treatment of the cervix within the last 3 months; patients with severe cardiac, hepatic, and renal insufficiency; patients with acute or subacute inflammation of the reproductive organs, such as vaginitis and pelvic inflammatory disease; and patients with allergy to drugs used in this study.

They were divided into study and control groups using the random number table method, with 89 cases in each group. The age of the study group was 21 to 38 years old, with a mean age of  $28.73 \pm 3.63$  years; 32 were married and 57 were unmarried; and the duration of the disease was 0.5 to 2 years, with a mean duration of  $0.91 \pm 0.27$  years. The average age of the control group was 20 to 36 years, with a mean age of  $28.41 \pm 3.42$  years; 35 cases were married and 54 cases were unmarried; the disease duration was 0.8 to 2 years, with a mean disease duration of  $1.03 \pm 0.34$  years. There was no statistically significant difference between the general data of the two groups ( $P > 0.05$ ). The study was approved by the ethics committee of the People's Hospital of Rizhao, Rizhao, Shandong, China.

### 2.2. Therapeutic Method

- (1) The control group was given a single recombinant human interferon treatment as follows: the patient was given recombinant human interferon on day 3

after the end of menstruation, the patient cleaned the vulva with a 0.5% potassium permanganate solution at bedtime, and a recombinant human interferon  $\alpha 2a$  suppository (State Drug Quantifier S20020103, Anhui Anke Biological Engineering, 100,000 IU/capsule) was disposed of in the posterior vaginal vault every other day. 1 capsule/time, 2~3 times a week for 3 months.

- (2) On the basis of the control group, the study group was given Buqi Qushi Jiedu decoction for treatment. The formula was as follows: milkvetch root 15 g, sargentgloryvine stem 15 g, Chinese thorowax root 10 g, coix seed 15 g, amur cork-tree 10 g, flying squirrel's droppings 10 g, barbated skullcup herb 15 g, liquorice root 6 g, Chinese angelica 10 g, Indian bread 10 g, light-yellow sophora root 12 g. Decocted with water, 200 mL of the solution was taken in 1 dose/d, divided into two doses in the morning and evening. Patients stopped taking the medicine during menstruation, and the treatment was continued for 3 months. Patients in both groups were instructed to strictly prohibit raw, cold, spicy, and greasy food during treatment, to eat a light diet, to strictly prohibit alcohol and carbonated beverages, to prohibit smoking, to develop good habits of early to bed and early to rise, to maintain an optimistic attitude to participate in treatment, and to refrain from sexual intercourse during treatment to avoid infections. If discomfort occurs, the patient should promptly inform the medical staff for effective treatment. Patients should strictly follow the doctor's instructions during the treatment, and it is strictly forbidden to change the dosage or stop the medication without permission. To minimize errors, patients should not use other medications during treatment. Figure 1 shows the flow diagram of the therapeutic approach used in this study.

**2.3. Observation Indicators and Criteria.** HPV negative conversion and HPV recurrence during follow-up were compared between the two groups. Cervical HPV exfoliated cells were collected, smears were performed, and then pap staining. An HPV negative conversion rate was detected according to HPV-DNA hybridization. HPV was detected by the PCR fluorescence method; the number of cases with negative conversion/total number of cases  $\times 100\%$  = HPV conversion rate [10]. Patients with negative HPV were followed up for 6 months to observe the HPV-positive condition, and the recurrence rate was calculated.

To compare the TCM symptom scores of the two groups, the symptom scores were evaluated according to the Guidelines for New Chinese Medicines [9] for the 2 groups before and 3 months after treatment for urinary frequency and urgency, leucorrhea and mucus, menstrual irregularity, pelvic heaviness, and dysmenorrhea, and each item was evaluated using a score of 0 to 3. The lower the score, the better the treatment outcomes.



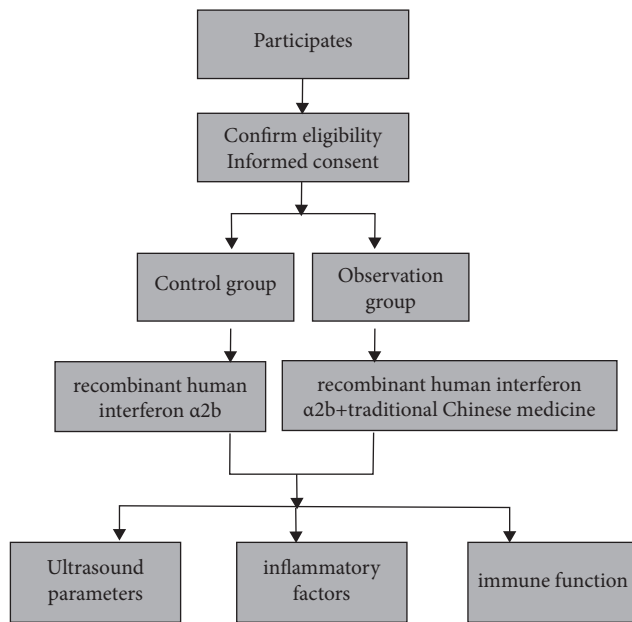


FIGURE 1: Flow diagram of therapeutic approach.

The incidence of adverse reactions during treatment was compared between the two groups of patients. The lower the incidence of adverse reactions, the higher the safety of clinical treatment.

The levels of inflammatory factors before and after treatment were compared between the two groups. 3 mL of fasting venous blood was collected on day 1, 30 days, 60 days, and 90 days of treatment in both groups, and the levels of TNF- $\alpha$  and IL-2, 6, and 10 were measured by using an enzyme-linked immunosorbent assay.

The changes of immune function indexes in the 2 groups before and after treatment were detected. T cell lymphocyte subsets of CD3+, CD4+, and CD8+ were detected by flow cytometry.

Ultrasound parameters were compared between the two groups before and after treatment. TechnosDU8 (Prima Brands, Italy) with SonoVue (Bracco, Italy) contrast agent was used, and the probe frequency was 2.0–9.0 MHz. The uterus and the appendages of all patients were examined by two-dimensional ultrasound to determine the scanning surface and fix it. Then, switch to the contrast imaging mode and start the timer (3 min) at the same time as the contrast agent injection to observe the changes of blood perfusion and echo intensity. For the regions of interest in the scanning results, the relevant parameters were recorded: development starting time (T1), filling time (T2), peak time (T3), max intensity, area under the curve (area), rising slope (SLOPE1), fast descending slope (SLOPE2), and slow descending slope (SLOPE3).

Ultrasound parameters before and after treatment were compared between the two groups of patients. The ultrasound imaging machine used was TechnosDU8 (Esaote, Italy), the contrast agent was SonoVue (Bracco, Italy), and the probe frequency was 2.0–9.0 MHz. The uterus and its adnexa of all patients were first scanned with 2D ultrasound, and the scanning surface was determined and fixed. Then,

the imaging mode was switched to contrast imaging mode, and a timer (3 min) was started while the contrast agent was injected to observe the blood perfusion and echo intensity changes. For the area of interest in the scan results, the relevant parameters were recorded: start of contrast time (T1), filling time (T2), time to peak (T3), maximum intensity (max intensity), area under the curve (area), rising slope (slope1), fast falling slope (slope2), and slow falling slope (slope3).

The pain level and quality of life were compared between the two groups of patients before and after treatment. Pain level was measured by VAS score [11]; the VAS score was used to evaluate the pain level of the lower abdomen before and after treatment in both groups, with a total score of 0 to 10, and higher scores represented higher pain levels. Quality of life was evaluated by the quality-of-life scale [12] (SF-36 scale): the quality of life was evaluated by the SF-36 scale before and after treatment in both groups, and the total score of this scale was 0 to 100, and the higher the score, the better the quality of life of the patients.

**2.4. Statistical Analysis.** SPSS 20.0 software was used for statistical analysis, and the counting data were expressed as percentages. The  $\chi^2$  test was used, and the measurement data were expressed as  $\bar{x} \pm s$ . The  $t$ -test was used, and  $P < 0.05$  was considered a statistically significant difference.

### 3. Results

**3.1. Comparison of HPV Conversion Rate and Recurrence Rate after Treatment between the Two Groups.** There were 81 cases of HPV conversion in the study group, with a negative conversion rate of 91.01%, and 62 cases of HPV conversion in the control group, with a conversion rate of 69.66%. There were 8 cases of HPV recurrence in the study group, with a recurrence rate of 9.88%; 16 cases of HPV recurrence in the control group, with a recurrence rate of 25.81%. The difference between the data of both groups was statistically significant ( $P < 0.05$ , Figure 2 and 3).

**3.2. Comparison of TCM Symptom Scores between the Two Groups.** The TCM symptom scores of both groups 3 months after treatment were lower than those before treatment ( $P < 0.05$ ); the scores of urinary frequency and urgency, leucorrhea and mucus, irregular menstruation, pelvic heaviness, and dysmenorrhea were lower than those of the control group 3 months after treatment in the study group ( $P < 0.05$ , Table 1).

**3.3. Comparison of the Levels of Inflammatory Factors before and after Treatment between the Two Groups.** On the first day of treatment, there was no statistically significant difference in the levels of serum IL-2, IL-6, IL-10, and TNF- $\alpha$  between the two groups ( $P > 0.05$ ), and the levels of IL-2, IL-6, IL-10, and TNF- $\alpha$  in both groups showed a decreasing trend with the extension of treatment time. After 90 days of treatment, the decrease of each index was more significant in the study group compared to the control group ( $P < 0.05$ , Figure 4).

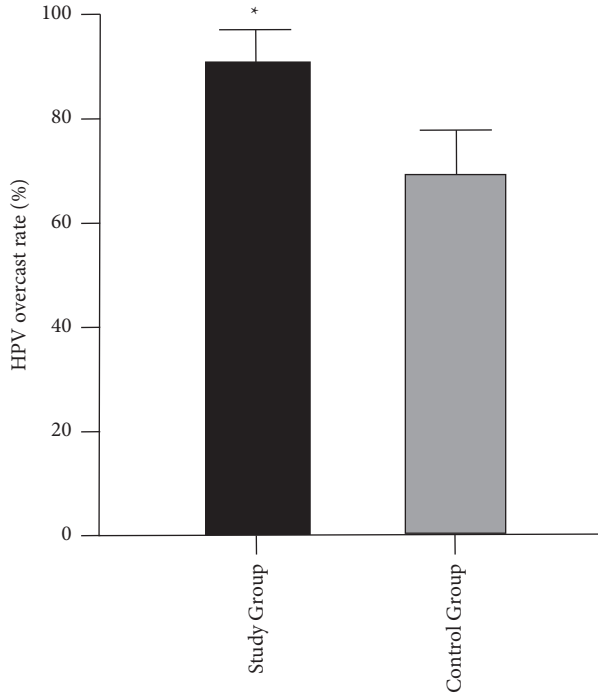


FIGURE 2: HPV conversion rate after treatment in both groups (\* $P < 0.05$ ).

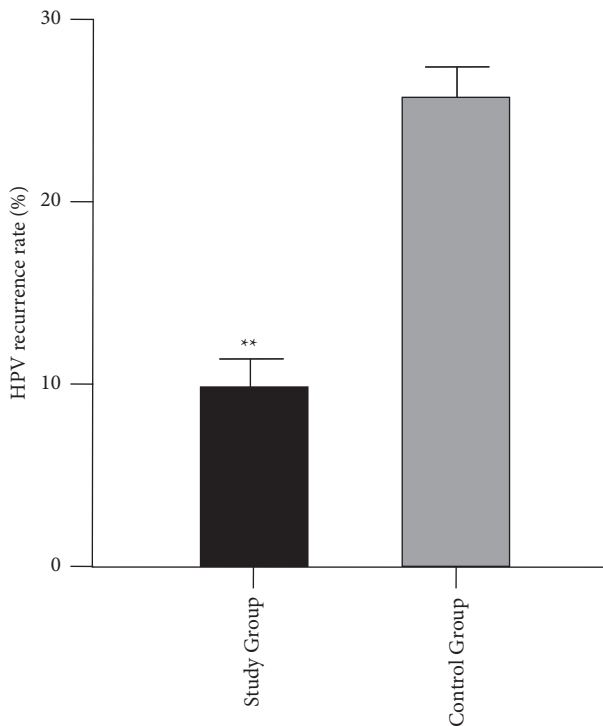


FIGURE 3: HPV recurrence rate after follow-up in both groups (\*\* $P < 0.01$ ).

**3.4. Comparison of Ultrasound Parameters of Cervical Lesions before and after Treatment.** The differences in max intensity, area, and slope1 between the two groups before treatment were not statistically significant; after

TABLE 1: Comparison of TCM symptom scores between the two groups ( $\bar{x} \pm s$ ).

Symptoms	Study group	Control group	<i>t</i>	<i>P</i> value
<i>Urinary frequency and urgency</i>				
Before treatment	2.51 ± 0.32	2.53 ± 0.34	0.227	>0.05
3 months after treatment	0.65 ± 0.14	1.76 ± 0.22	4.652	<0.05
<i>Leukorrhea and mucus</i>				
Before treatment	2.57 ± 0.26	2.54 ± 0.31	0.346	>0.05
3 months after treatment	0.71 ± 0.18	1.63 ± 0.27	10.371	<0.05
<i>Menstrual irregularities</i>				
Before treatment	2.43 ± 0.48	2.45 ± 0.52	0.732	>0.05
3 months after treatment	0.96 ± 0.11	1.72 ± 0.34	7.611	<0.05
<i>Pelvic heaviness</i>				
Before treatment	2.46 ± 0.34	2.44 ± 0.35	0.546	>0.05
3 months after treatment	0.83 ± 0.16	1.68 ± 0.23	6.230	<0.05
<i>Dysmenorrhea</i>				
Before treatment	2.37 ± 0.58	2.34 ± 0.56	0.934	>0.05
3 months after treatment	0.74 ± 0.17	1.65 ± 0.29	12.456	<0.05

treatment, max intensity, area, and slope1 decreased, and the differences were statistically significant before and after treatment (\* $P < 0.05$ ), and the decrease was more significant in the study group than in the control group ( $\Delta P < 0.05$ ) (Table 2).

**3.5. Comparison of Immune Function between the Two Groups before and after Treatment.** Before treatment, there was no statistically significant difference in the levels of each index of immune function between the two groups ( $P > 0.05$ ). After treatment, the levels of CD3+, CD4+, and CD4+/CD8+ in the study group were significantly increased than those in the control group, while the CD8+ level in the study group was significantly decreased than that in the control group ( $P < 0.05$ , Figure 5).

**3.6. Comparison of Pain Level and Quality of Life between the Two Groups before and after Treatment.** Before treatment, there was no statistically significant difference in VAS scores and SF-36 scores between the two groups ( $P > 0.05$ ). After treatment, VAS scores decreased in both groups, and the decrease was more significant in the study group than in the control group ( $P < 0.05$ ). After treatment, SF-36 scores increased in both groups, and the increase was more significant in the study group than in the control group ( $P < 0.05$ , Table 3).

**3.7. Comparison of the Incidence of Adverse Reactions after Treatment between the Two Groups.** There was no statistically significant difference in the incidence of adverse reactions between the two groups ( $P > 0.05$ , Table 4).

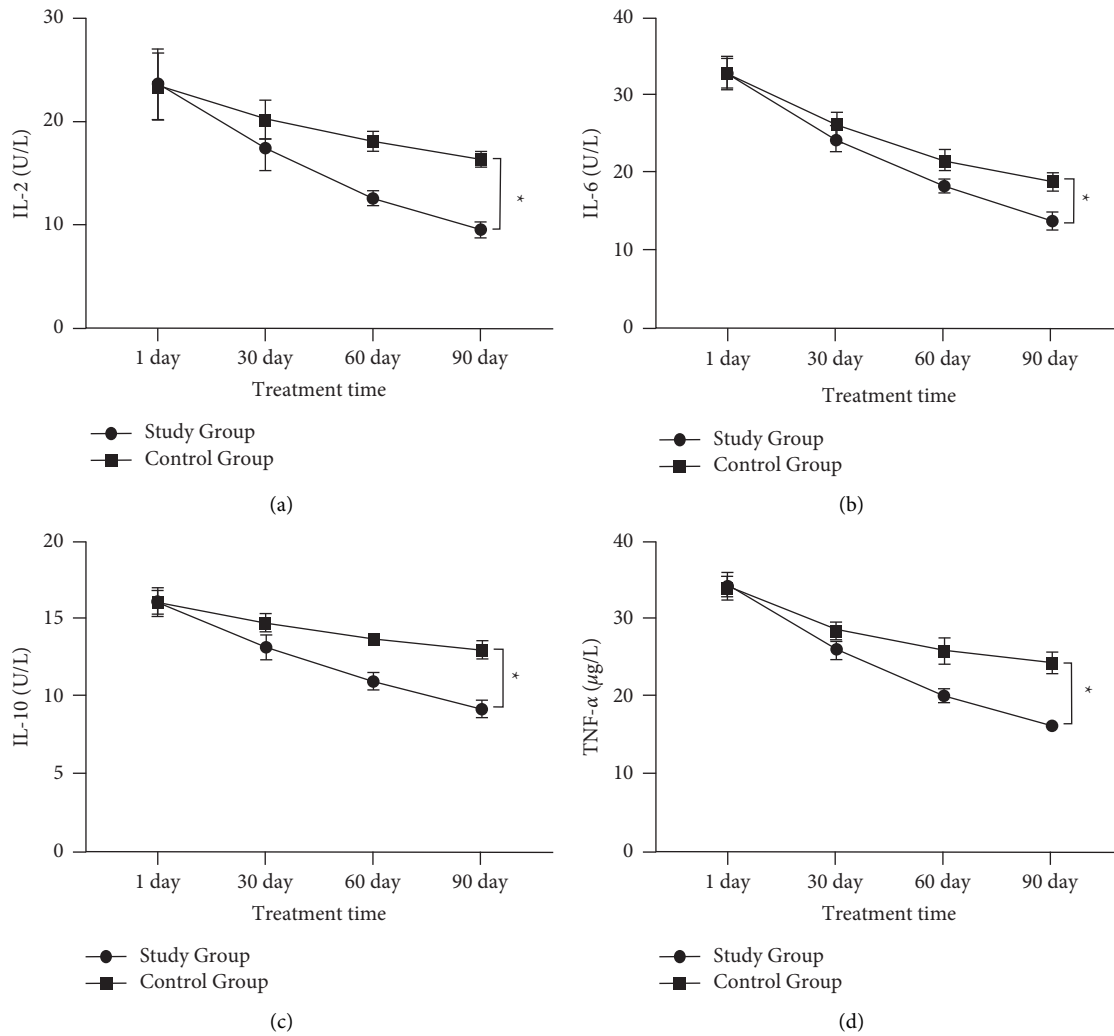


FIGURE 4: Comparison of inflammatory factor levels before and after treatment in two groups. (a) The comparison of IL-2 levels before and after treatment in two groups; (b) the comparison of IL-6 levels before and after treatment in two groups; (c) the comparison of IL-10 levels before and after treatment in two groups; (d) the comparison of TNF- $\alpha$  levels before and after treatment in two groups. \* $P < 0.05$ .

TABLE 2: Comparison of ultrasound parameters of cervical lesions before and after treatment.

Index	Study group (n = 89)		Control group (n = 89)	
	Before treatment	After treatment	Before treatment	After treatment
T1(s)	13.673	10.357	13.224	12.253
T2(s)	15.894	16.861	15.978	16.249
T3(s)	33.146	27.462	33.317	30.175
Max intensity(dB)	213.678	116.894* $\Delta$	215.266	131.246*
Area	18237.662	13798.519* $\Delta$	18368.143	16037.030*
Slope1	9.774	5.792* $\Delta$	9.681	7.234*
Slope2	-2.253	-2.015	-2.287	-2.071
Slope3	-0.414	-0.322	-0.426	-0.353

\* $P < 0.05$ ; before treatment vs. after treatment.  $\Delta P < 0.05$ ; study group vs. control group.

#### 4. Discussion

HPV is a double-stranded cyclic DNA virus divided into high- and low-risk types according to the risk of tumorigenesis. HPV infection in humans often develops into CIN, and high-risk HPV is closely associated with the

development of cervical cancer [13]. According to the tissue origin, CIN is classified into three grades: I, II, and III, and the degree of involvement of cervical epithelial cells deepens successively [14]. During the progressive development of CIN, regular HPV examination, early detection, and treatment are of great significance to reduce the incidence and

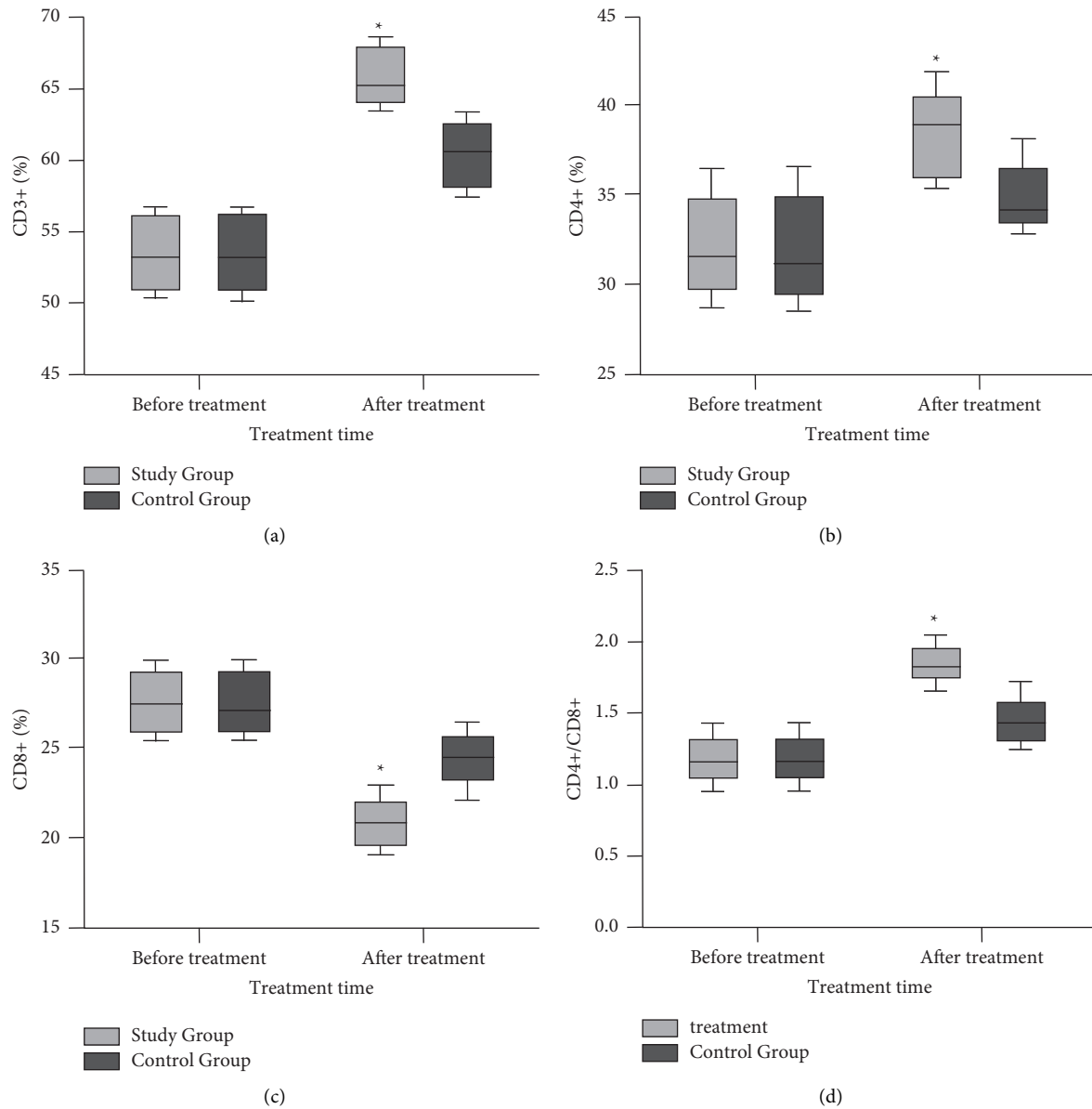


FIGURE 5: Comparison of immune function before and after treatment between the two groups. (a) The comparison of CD3+ levels before and after treatment between the two groups; (b) the comparison of CD4+ levels before and after treatment between the two groups; (c) the comparison of CD8+ levels before and after treatment between the two groups; (d) the comparison of CD4+/CD8+ levels before and after treatment between the two groups. \* $P < 0.05$ .

TABLE 3: Comparison of pain levels and quality of life before and after treatment between two groups of patients.

Index		Study group	Control group	<i>t</i>	<i>P</i> value
VAS score	Before treatment	$6.23 \pm 1.67$	$6.17 \pm 1.53$	0.217	$>0.05$
	After treatment	$1.96 \pm 0.52$	$3.68 \pm 0.93$	6.431	$<0.05$
SF-36 score	Before treatment	$44.23 \pm 6.74$	$43.67 \pm 6.52$	0.933	$>0.05$
	After treatment	$78.63 \pm 9.56$	$61.71 \pm 8.67$	7.249	$<0.05$

mortality of CIN and even cervical cancer [15]. The number of female patients with HPV infection is currently increasing, and effective treatment usually includes surgery and medications. However, due to the generally low age of the patients, they may be nervous during the surgery as it

may cause trauma to the cervix's surface, which affects the quality of life of the patients and is especially unfavorable for unmarried and infertile women [16].

Recombinant human interferon, which is a protein in nature, can bind to interferon receptors on the surface of

TABLE 4: Comparison of the incidence of adverse reactions after treatment in the two groups (*n* (%)).

Group	<i>n</i>	Increased secretion	Vaginal itching	Vulvar pain	Nausea and vomiting	Liver and kidney abnormalities
Study group	89	4(4.5)	1(1.1)	2(2.2)	2(2.2)	1(1.1)
Control group	89	7(7.9)	2(2.2)	4(4.5)	5(5.6)	3(3.4)
$\chi^2$						0.230
<i>P</i> value						0.994

affected tissues and exert antiviral effects, which can interfere with viral replication, thereby inhibiting viral synthesis, enhancing the phagocytosis of macrophages to strengthen the immune function of patients, regulate progesterone levels in the body, and improve the internal environment of the patient's vagina [17].

Recombinant human interferon  $\alpha 2b$  is a new interferon agent that is mostly used clinically to treat HPV infection [18]. Recombinant human interferon can be placed in the patient's vagina, and local administration will not cause damage to the patient's organism, and the application is simple and convenient, which is easily accepted by patients.  $\alpha 2b$  can improve the killing capacity of the body's lymphocytes, enhance the phagocytosis of macrophages, reduce cervical secretions during patient treatment, improve vaginal cleanliness, enhance the body's immunity, reduce clinical adverse effects, and improve the ability to fight against viruses [19]. According to Sen et al. [20, 21],  $\alpha 2b$  can exert an induction effect on antiviral proteins, enhance phagocytosis of macrophages, stimulate lymphocytes, inhibit viral protein synthesis, and thus inhibit HPV replication and transcription, which is important for the removal of HPV virus.

In Chinese medicine, HPV is categorized as "morbid vaginal discharge" or "parti-colored vaginal discharge" according to the patient's clinical manifestations. According to recent research, cervical HPV infection is mainly due to the channel imbalance and the conception channel irregularity of the leukorrhea and the invasion of dampness, which causes damage to the cells surrounding the cervix, resulting in changes in the odor, color, and state of vaginal secretions and eventually leading to the development of the disease [22, 23]. In clinical practice, the main treatments are clearing heat, removing toxicity, invigorating the spleen, and eliminating dampness. In this study, the scores of urinary frequency and urgency, leucorrhea and mucus, irregular menstruation, pelvic heaviness, and dysmenorrhea in the study group were lower than those in the control group after treatment ( $P < 0.05$ ), indicating that Buqi Qushi Jiedu decoction combined with recombinant human interferon  $\alpha 2b$  can effectively improve the symptom score of patients with cervical HPV infection and facilitate their recovery. In this formula, the combination of milkvetch root, light-yellow sophora root, Indian bread, and liquorice root can achieve the effects of invigorating the spleen and eliminating dampness; the combination of sargentgloryvine stem, Chinese thorowax root, and amur cork-tree can achieve the effect of clearing heat and removing toxicity; the combination of barbated skullcup herb, flying squirrel's droppings, and Chinese angelica has the effect of promoting blood circulation for removing blood stasis; and Coix seed has

anti-inflammatory and antitumor functions and can enhance the immune functions of the body. The rational combination of the abovementioned drugs has the ability to clear heat and remove toxicity, invigorate the spleen and stomach, and replenish qi [24–26].

In this study, serum TNF- $\alpha$ , IL-2, 6, and 10 were lower in the study group than in the control group after treatment ( $P < 0.05$ ), suggesting that Buqi Qushi Jiedu decoction could significantly improve the levels of inflammatory factors in patients with cervical HPV infection and control disease development. Studies [27–29] have shown that the main way for human immune cells to exert their biological activity is through their own secreted cytokines, and inflammatory factors such as IL-2, IL-6, IL-10, and TNF- $\alpha$  have essential roles. IL-2 plays an active role in antitumor and anti-pathogen immunity. IL-6 can regulate the growth and differentiation of various cells, regulate immune response, acute phase response, and hematopoietic function, and plays an essential role in the anti-infection immune response of the body. IL-10 has an active role in enhancing the infection sensitivity of immune cells. TNF- $\alpha$  is a proinflammatory cytokine expressed in the development of tissue inflammation response. We also observed that the CD3+ and CD4+ levels and CD4+/CD8+ ratios were significantly higher and CD8+ levels were significantly lower in both groups after treatment, and the changes in these indexes were more significant in the study group ( $P < 0.05$ ), and the HPV negative conversion rate was significantly higher in the study group than in the control group, and the recurrence rate was significantly lower than in the control group. The combination of Buqi Qushi Jiedu decoction with recombinant human interferon  $\alpha 2b$  suppository had a positive effect on HPV clearance and improvement of immune function in patients, which could effectively prevent and control the occurrence of cervical inflammatory reactions, improve the HPV conversion rate and histological efficacy of cervical lesions, and reduce the long-term recurrence rate of patients with CIN combined with HR-HPV.

In this study, the combination of Buqi Qushi Jiedu decoction with recombinant human interferon  $\alpha 2b$  did not increase the incidence of adverse effects and helped improve patients' treatment tolerance and compliance. Ultrasonography can show blood perfusion at the capillary level and can monitor the tissue microvascular environment [30]. The results of this study showed that the maximum intensity, area, and slope1 of both groups gradually decreased as the condition improved, and the decrease was more significant in the study group ( $P < 0.05$ ). The max intensity indicates the amount of contrast medium when the local vessels are filled with the most contrast medium, reflecting the maximum blood volume; slope1 represents the local perfusion rate,

which becomes slower as the condition continues to improve [31, 32]. Therefore, among the parameters of ultrasonography, max intensity, area, and slope1 have high clinical significance and can provide a clinical basis for early screening of CIN combined with HR-HPV. The follow-up time of this study was limited, and the long-term effective rate of combination therapy could be analyzed by increasing the sample size and extending the follow-up time.

In conclusion, the combination of Buqi Qushi Jiedu decoction with recombinant human interferon  $\alpha 2b$  could make the qi and blood flow smooth in patients with CIN combined with HR-HPV, and the clinical effects were favorable. It could significantly improve the HPV conversion rate, reduce the distant recurrence rate, and lower the TCM symptom score. It could reduce the level of inflammatory factors and improve the immunity of the body with high safety.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Breviscapine Participates in the Progression of Prostate Cancer by Inhibiting ZFP91 Expression through Upregulation of MicroRNA-129-5p

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**Objective.** To investigate the effect of breviscapine (BVP) on the development of prostate cancer and its molecular mechanism. **Materials and Methods.** After treatment with breviscapine and microRNA-129-5p, MTT (3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide) and cell counting kit-8 (CCK-8) tests were performed to examine the proliferation rate of cells, while Transwell was used to analyze cell migration ability; at the same time, quantitative real-time polymerase chain reaction (qRT-PCR) was applied to detect the expression of microRNA-129-5p and ZFP91 in prostate cancer cells. In addition, the binding of microRNA-129-5p and ZFP91 was confirmed by dual-luciferase reporting assay; meanwhile, cell reverse experiment verified that breviscapine can regulate ZFP91 via upregulating microRNA-129-5p. **Results.** The results of MTT, CCK-8, and Transwell experiments demonstrated that breviscapine inhibited the proliferation as well as the migration capacities of PC cells; meanwhile, it upregulated the level of microRNA-129-5p in PC cells while downregulated that of ZFP91. Furthermore, dual-luciferase reporter gene assay verified that ZFP91 was a potential target of microRNA-129-5p. Finally, cell reverse experiment confirmed that breviscapine downregulated ZFP91 expression by upregulating microRNA-129-5p, while downregulation of microRNA-129-5p partially reversed the inhibitory effect of breviscapine on cell proliferation ability. **Conclusions.** Breviscapine may inhibit the expression of ZFP91 through upregulating microRNA-129-5p and thus participating in the progression of PC.

## 1. Introduction

Natural existing compounds are regarded as the most promising drugs for the prevention and treatment of cancer. They have various model effects and limited toxicity and can regulate cell proliferation and cell cycle arrest [1–3]. Breviscapine (BVP) is isolated from Chinese herbs and has been shown to exert comprehensive biological and pharmacological effects. The main active components of BVP are baicalein, 4, 5, 6-tetrahydroxy flavone-7-glucoside acid [4]. BVP is often applied for long-term treatment of paralysis in Chinese folk medicine [4]. Therefore, BVP plays an effective role in the treatment of cerebrovascular diseases caused by cerebral infarction, chronic arachnoiditis, and its sequelae [5]. In addition, studies have found that BVP can be used to

induce apoptosis and inhibit cell proliferation, thus preventing the progress of various tumors [6]. However, there have been rare studies about the effect of BVP in the development of PC.

MicroRNAs (miRNAs) are a group of endogenous non-coding RNAs with about 22 nucleotides in length. miRNA can regulate various biological processes such as cell proliferation, differentiation, and apoptosis [7]. Abnormal miRNA expression has been found in various human tumor tissues including prostate cancer tissues [8–10]. In addition, abnormal expression of some miRNAs has been proved to be closely related to the drug resistance and metastasis of prostate cancer [11–13]. These miRNAs can be used as biomarkers for predicting the progress of prostate cancer. For example, the level of microRNA-141 in serum of patients

with PC is remarkably higher than that of the normal control group, which is easy to be detected and has the potential of tumor markers of PC [14]. Besides, microRNA-18a level is markedly increased in patients with prostate cancer, which is closely correlated with the progress of PC [15]. The above studies suggest that miRNAs can serve as biomarkers for the diagnosis of prostate cancer. A previous study demonstrated that BVP exerted anti-tumor and anti-metastasis roles in prostate cancer by inhibiting PAQR4-mediated PI3K/Akt pathway [16]. However, so far, there is no study on the mechanism of BVP combined with miRNAs in regulating the progression of prostate cancer.

Here, we found that breviscapine can lead to the increase of microRNA-129-5p expression in PC cells. MicroRNA-129-5p could inhibit the proliferation of PC cells. Meanwhile, we found that microRNA-129-5p can directly bind to ZFP91 and inhibit its expression. We hypothesized that breviscapine, as a promoter of microRNA-129-5p expression, may provide new directions for the drug treatment of PC.

## 2. Materials and Methods

**2.1. Cell Culture.** Two PC cell lines, LNCap and PC3, were obtained from the American Type Culture Collection (ATCC) (Manassas, VA, USA) and cultured with Roswell Park Memorial Institute 1640 (RPMI 1640) (HyClone, South Logan, UT, USA) supplemented with 10% fetal bovine serum (FBS) (Gibco, Rockville, MD, USA), 100  $\mu$ g/mL penicillin, and 100 U/mL streptomycin in a 37°C, 5% CO<sub>2</sub> incubator.

**2.2. Cell Transfection.** LNCap and PC3 cells were plated in 6-well plates. MicroRNA-129-5p mimics (10 pmol) or microRNA-129-5p inhibitor (15 pmol) and miRNA-NC were transfected into cells to achieve microRNA-129-5p overexpression and knockdown using Lipofectamine 2000 (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's standard protocol.

**2.3. MTT (3-(4,5-Dimethylthiazol-2-yl)-2, 5-Diphenyl Tetrazolium Bromide) Assay.** Transfected cells were plated in 96-well plates (1.0  $\times$  10<sup>3</sup> per well) and were then treated with breviscapine (20, 40, and 80  $\mu$ g/mL) overnight. Then, 0.5 mg/ml MTT (Sigma-Aldrich, St. Louis, MO, USA) was added to each well. After 4 hours, the medium in each well was replaced with 100  $\mu$ L of formazan solubilization solution. The plate was gently mixed for 10 minutes so that the formazan crystals could be fully dissolved. Lastly, the optical density (OD) value of each well was detected in the microplate reader (BioTek Instruments, Winooski, VT, USA) at 450 nm absorption wavelength.

**2.4. Cell Counting Kit-8 (CCK-8) Assay.** Cells were digested, and cell density was adjusted to 3000 cells in 200  $\mu$ L of medium per well in a 96-well plate. After 24 hours of culture, the corresponding siRNA or inhibitor/mimics or NC was

transfected into cells. After the treatment (24, 48, and 72 h, respectively), 10  $\mu$ L of CCK-8 reagent (Dojindo, Kumamoto, Japan) was added. After 20 minutes, the OD value of each well was detected by a microplate reader at 450 nm.

**2.5. Transwell Assay.** Transfected prostate cancer cells (density of 1  $\times$  10<sup>5</sup> cells/mL) were resuspended in serum-free medium and added to Transwell's upper chamber plate. The lower chamber of Transwell was added with RPMI 1640 containing 10% FBS. The staining and quantity of the migrated cells were determined by randomly selecting the average of five visual field counts under an optical microscope.

**2.6. Quantitative Real-Time Polymerase Chain Reaction (qRT-PCR).** Total RNA was extracted with TRIzol reagent (Invitrogen, Carlsbad, CA, USA). Complementary deoxyribose nucleic acid (cDNA) was synthesized using a reverse transcription kit (Thermo Fisher Scientific, Waltham, MA, USA). MicroRNA-129-5p expression was examined by real-time quantitative PCR detection, with U6 used as an internal control. The 2<sup>- $\Delta\Delta$ Ct</sup> method was applied to reflect the difference in expression between the target group and the control group. The primer sequences are as follows: microRNA-129-5p (f), 5'-CGGCGGTTTTTTCGGTCTGGGCT-3', microRNA-129-5p (r), 5'-AGCCCAGACCGCAAAAACCGCCG-3'; U6 (f) 5'-CTCGCTTCGCGCA-GAACA-3', U6 (r), 5'-ACGCTTCACGAATTTGCGT-3'; GAPDH (f) 5'-GAAGAGAGAGACCTCAGCTG-3', glyceraldehyde-3-phosphate dehydrogenase (GAPDH) (r) 5'-ACTGTGAGGAGGGAGATTCACT-3'; ZFP91 (f) 5'-TGAGACCTACAAACCCCACTT-3', ZFP91 (r) 5'-CCTTTTGGGTAAACGTGGACTTT-3'.

**2.7. Dual-Luciferase Reporter Gene Assay.** The binding relationship of microRNA-129-5p to ZFP91 was evaluated by a dual-luciferase reporter experiment. To achieve this, the sequence of ZFP91 (including the binding site of microRNA-129-5p (ZFP91-WT) and the ZFP91 mutant (ZFP91-MUT) containing mismatched microRNA-129-5p binding sequences) was cloned into pmirGLO vector (Promega, Madison, WI, USA). Then, microRNA-129-5p mimics were co-transfected into LNCap and PC3 cells with ZFP91-MUT or ZFP91-WT containing Lipofectamine 2000. Then, the fluorescence intensity was measured. The relative expression of the reporter gene was calculated according to the reporter gene fluorescence intensity/internal reference fluorescence intensity.

**2.8. Statistical Analysis.** All statistical analyses were performed using Statistical Product and Service Solutions (SPSS) software version 22.0 (IBM, Armonk, NY, USA). Significant differences between data were calculated using a paired two-tailed Student's *t*-test or chi-square test. All measurement data are expressed as mean  $\pm$  SD (standard deviation). *P* < 0.05 was considered statistically different.

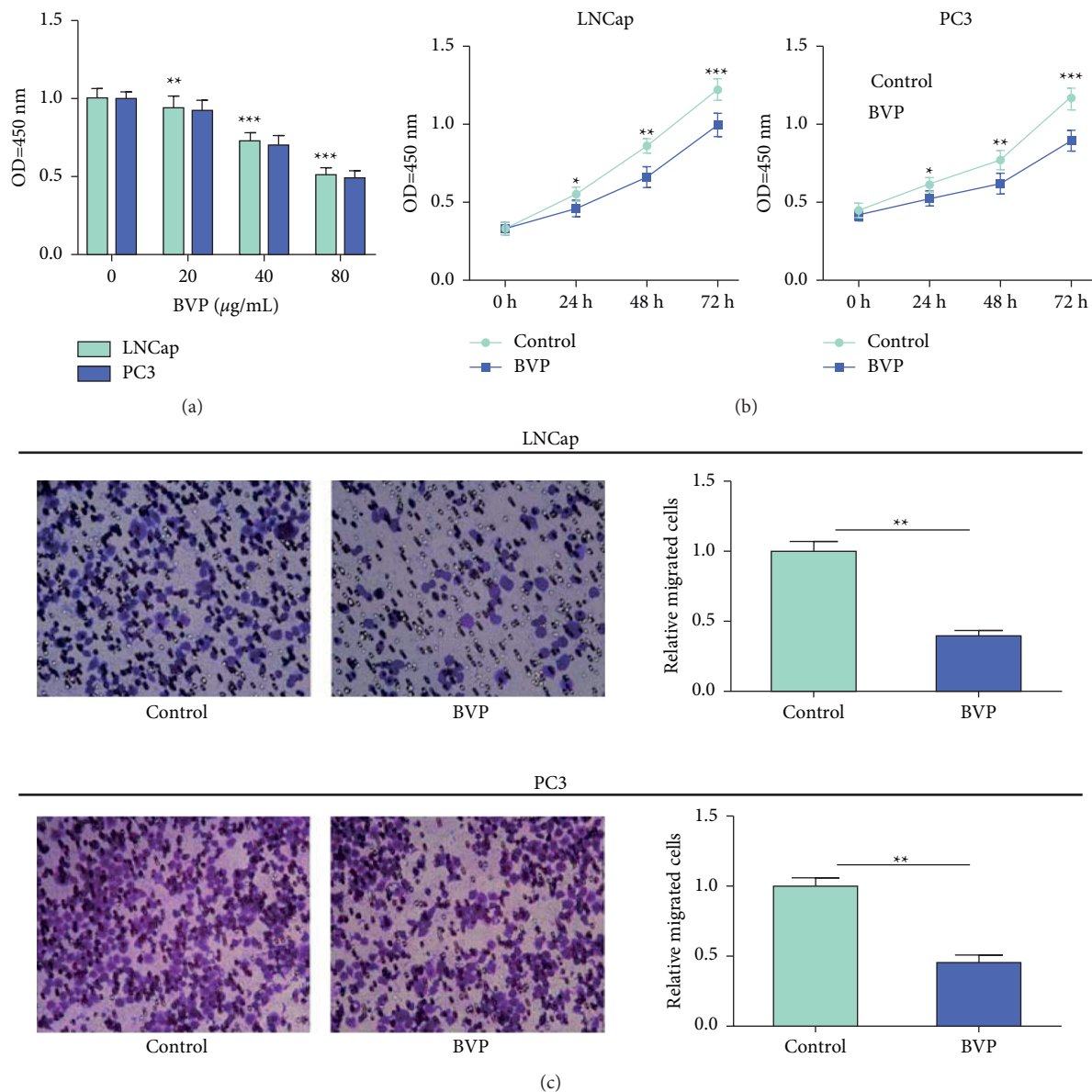


FIGURE 1: Breviscapine inhibits proliferation and migration of prostate cancer cells. (a) After treatment with 20, 40, and 80 µg/ml breviscapine for 24 h, the cell proliferation ability of LNCap and PC3 cells was significantly inhibited in a concentration-dependent manner. (b) The proliferation ability of cells was significantly inhibited after treatment of LNCap and PC3 cells with 40 µg/mL breviscapine. (c) Treatment with 40 µg/mL breviscapine significantly inhibited the migration ability of LNCap and PC3 cells (\* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$ ).

### 3. Results

**3.1. Breviscapine Inhibits Proliferation and Migration of Prostate Cancer Cells.** In this experiment, in order to detect whether breviscapine has an effect on PC cell proliferation, cells were administered with different concentrations of breviscapine, and MTT assay was performed 24 hours later. The results of MTT assay showed that breviscapine markedly inhibited the proliferation of PC cell lines *in vitro* with dose dependence (Figure 1(a)). At the same time, we carried out the subsequent CCK-8 and Transwell experiments, which showed that breviscapine markedly inhibited the proliferative and migrant ability of LNCap and PC3 cells

(Figures 1(b) and 1(c)). These results demonstrated that breviscapine inhibits the proliferative and migrant ability of PC cells.

**3.2. Breviscapine Promotes Expression of MicroRNA-129-5p.** MicroRNA-129-5p expression was detected by qRT-PCR under different concentrations of breviscapine (0, 20, 40, and 80 µg/mL). We found that the level of miR-129-5p was remarkably elevated by breviscapine in a dose-dependent way (Figure 2(a)). At the same time, in order to detect whether microRNA-129-5p was involved in the progression of prostate cancer cells, we overexpressed miR-129-5p and

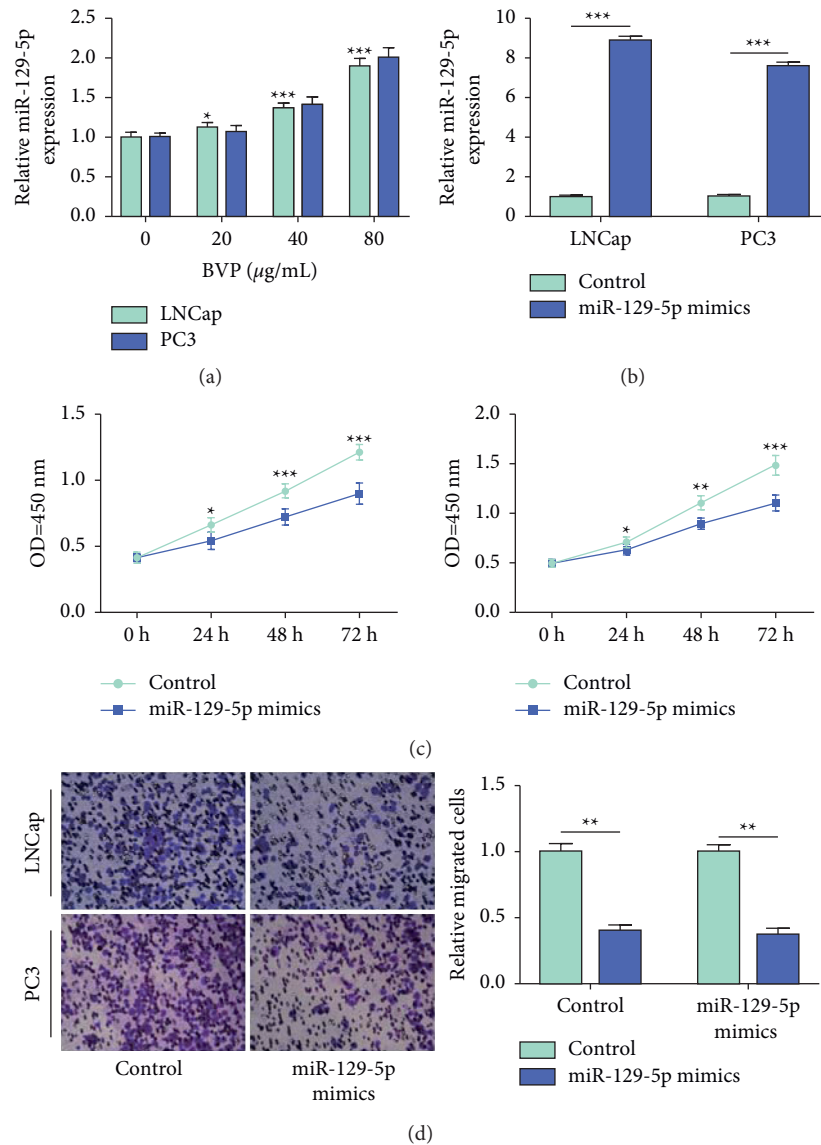


FIGURE 2: Breviscapine promotes the expression of miR-129-5p. (a) After treatment of LNCap and PC3 cells with 20, 40, and 80  $\mu\text{g/mL}$  breviscapine, the expression of miR-129-5p was significantly increased in a concentration-dependent manner. (b) After transfection of miR-129-5p mimics in LNCap and PC3 cells, the expression of miR-129-5p was significantly increased. (c, d) After upregulating the expression of miR-129-5p in LNCap and PC3 cells, the cell proliferation and migration ability was significantly inhibited ( $*P < 0.05$ ,  $**P < 0.01$ , and  $***P < 0.001$ ).

its negative control into LNCap and PC3 cells, and its expression was significantly upregulated (Figure 2(b)). The CCK-8 results suggested that the proliferation of LNCap and PC3 cells was significantly reduced after microRNA-129-5p overexpression (Figure 2(c)). At the same time, Transwell experiments showed that the migrant ability of LNCap and PC3 cells was remarkably decreased after microRNA-129-5p overexpression (Figure 2(d)). This indicated that microRNA-129-5p may play a tumor suppressing role in PC.

**3.3. ZFP91 Is a Potential Target of MicroRNA-129-5p.** By database prediction, we identified ZFP91 as a possible target for microRNA-129-5p (Figure 3(a)). To further clarify that

this sequence was the target sequence of microRNA-129-5p on ZFP91 mRNA, we constructed the ZFP91 mRNA 3'UTR into the luciferase reporter system and named it ZFP91-WT, and the mutation binding site was also built into the luciferase reporting system and was named ZFP91-MUT. MicroRNA-129-5p mimics were co-transfected with an empty control vector (empty vector) and ZFP91-WT or ZFP91-MUT. The results showed that in LNCap and PC3 cells, the fluorescence expression of the ZFP91-WT + miR-129-5p group was markedly lower than that of the ZFP91-WT + NC group, while the fluorescence intensity of the ZFP91-MUT + miR-129-5p group was correlated with ZFP91-MUT (Figures 3(a)–3(c)). This result indicated that microRNA-129-5p can bind to ZFP91. After transfection of

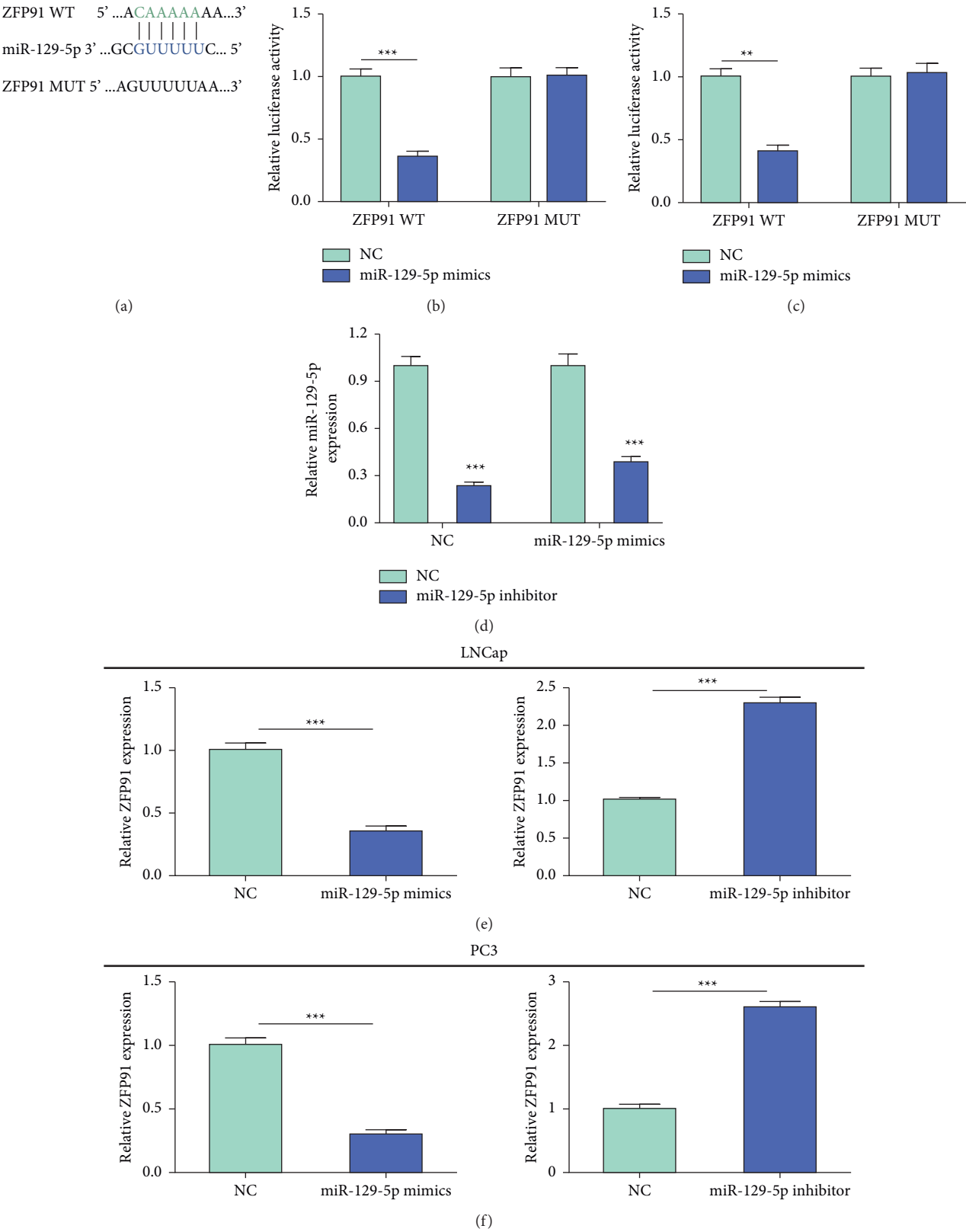


FIGURE 3: ZFP91 is a potential target gene for miR-129-5p. (a) Bioinformatics analysis revealed that miR-129-5p has a potential binding site with ZFP91. (b, c) The results of the dual-luciferase reporter gene assay confirmed the binding relationship between the two. (d) After transfection of miR-129-5p inhibitor in LNCap and PC3 cells, miR-129-5p expression was significantly reduced. (e, f) The mRNA level of ZFP91 was significantly decreased after upregulating the expression of miR-129-5p in LNCap and PC3 cells; the mRNA level of ZFP91 was significantly increased after downregulating the expression of miR-129-5p (\* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$ ).



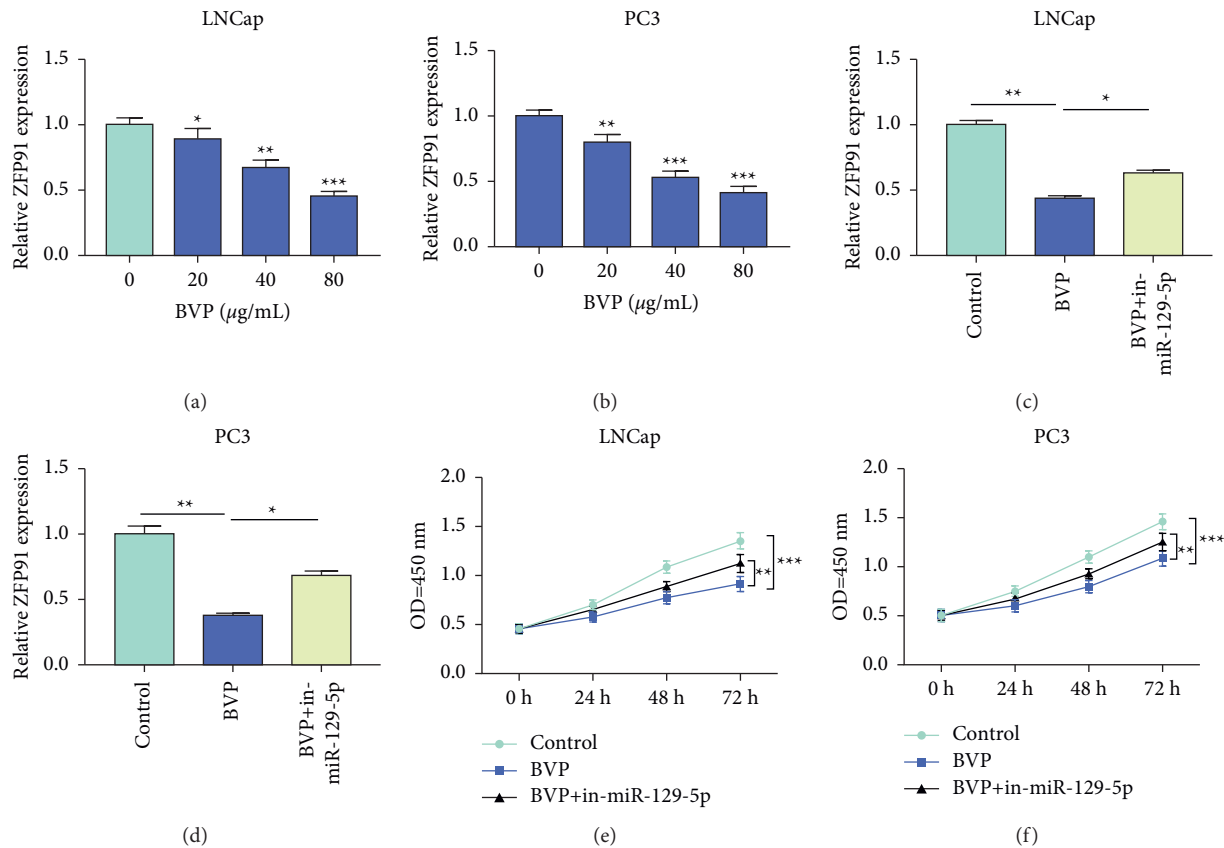


FIGURE 4: Breviscapine inhibits the expression of ZFP91 by upregulating miR-129-5p. (a, b) After treatment of LNCap and PC3 cells with 20, 40, and 80 µg/ml breviscapine, the expression of ZFP91 was significantly decreased in a concentration-dependent manner. (c, d) Simultaneous inhibition of miR-129-5p expression in LNCap and PC3 cells treated with breviscapine at a concentration of 40 µg/mL partially reversed the inhibitory effect of breviscapine on ZFP91 expression. (e, f) Simultaneously downregulating the expression of miR-129-5p partially reversed the inhibitory effect of breviscapine on the proliferation of LNCap and PC3 cells (\* $P < 0.05$ , \*\* $P < 0.01$ , and \*\*\* $P < 0.001$ ).

the microRNA-129-5p inhibitor in LNCap and PC3 cells, microRNA-129-5p expression was markedly reduced (Figure 3(d)). To investigate the regulation of ZFP91 expression by microRNA-129-5p at the cellular level, we transfected microRNA-129-5p inhibitor/mimics and negative control (NC) into LNCap and PC3 cells, respectively, and detected the expression of ZFP91 by qRT-PCR. The results suggested that ZFP91 expression was markedly decreased after transfection with microRNA-129-5p mimics, while ZFP91 expression was markedly increased after microRNA-129-5p inhibition (Figures 3(e) and 3(f)). The above results indicated that ZFP91 was a potential target gene of microRNA-129-5p.

**3.4. Breviscapine Inhibits ZFP91 by Upregulating MicroRNA-129-5p.** To investigate whether breviscapine could also affect the expression of ZFP91, we examined the expression of ZFP91 after treatment with breviscapine. We found that the expression of ZFP91 was markedly reduced in a concentration-dependent manner, which indicated that breviscapine can inhibit the expression of ZFP91 (Figures 4(a) and 4(b)). Similarly, downregulation of microRNA-129-5p expression in PC cells treated with 80 µg of breviscapine

partially reversed the inhibitory effect of breviscapine on ZFP91 expression (Figures 4(c) and 4(d)). Further CCK-8 experiments showed that simultaneous downregulation of microRNA-129-5p partially reversed the inhibition of breviscapine on cell proliferation (Figures 4(e) and 4(f)). In combination with the above experiments, breviscapine may exert anti-cancer effects by upregulating the expression of microRNA-129-5p and inhibiting ZFP91.

## 4. Discussion

Prostate cancer (PC) remains the most common cancer in men worldwide and the second leading cause of cancer-related deaths in the US. In the past decade, the mortality rate of PC has markedly decreased due to the improvement of prostate cancer screening [17]. Serum prostate-specific antigen (PSA) has been used to monitor the progression or recurrence of prostate cancer after treatment. However, patients with prostatitis, benign prostatic hyperplasia, and urinary tract infection can also exhibit elevated serum PSA [18]. Therefore, we should search for biomarkers with higher cancer specificity or a combination of several biomarkers. Understanding the molecular mechanism of prostate cancer

and finding more effective treatment strategies for PC is of great importance.

Breviscapine, as a new derivative of traditional Chinese medicine, was proved to inhibit the proliferative and migrant ability of PC cells in this study. In order to further explore the mechanism of its action, we further studied and found that its mechanism may be related to microRNA-129-5p and ZFP91. MicroRNA-129-5p has been recognized as a tumor suppressor for glioblastoma, breast cancer, colorectal cancer, and so on [19–21]. MicroRNA-129-5p is one of the most significantly downregulated miRNAs in PC cells and participates in cell metabolism and proliferation regulation by inhibiting key proteins in the carnitine cycle [22]. In this study, our experiment showed that microRNA-129-5p, as an anti-cancer gene for prostate cancer, was upregulated under the action of breviscapine and inhibited the proliferation and migration of tumor cells.

Several oncogenes, including PAK5 and RET, have been identified as target genes for microRNA-129-5p [23, 24]. However, the regulation between microRNA-129-5p and ZFP91 has not been studied. It has been reported that ZFP91 plays an oncogene role in various tumors, including gastric cancer, pancreatic cancer, and colon cancer [25–27]. More importantly, ZFP91 has also been shown to be an oncogene for prostate cancer [28]. Here, we proved that ZFP91 was negatively regulated by the tumor suppressor microRNA-129-5p in PC cells through dual-luciferase reporter gene experiment, PCR, and functional experiments. Combined with previous studies, we determined that breviscapine played a role by promoting the expression of microRNA-129-5p and negatively regulating the prostate cancer oncogene ZFP91. This study still has some limitations. For example, we did not verify the above conclusions in animal models. In the future, we will perfect some animal experiments to verify some of the regulatory effects and mechanisms of BVP on the occurrence and development of prostate cancer in vivo.

## 5. Conclusions

In conclusion, our study showed that breviscapine can inhibit the process of prostate cancer. Breviscapine inhibited the proliferative and migrant ability of PC cells by upregulating the level of tumor suppressor microRNA-129-5p, thereby inhibiting the expression of its downstream target gene ZFP91. The discovery of breviscapine/microRNA-129-5p/ZFP91 axis not only provides a new target for the treatment of PC but also provides a new perspective for a deeper understanding of the pathogenesis of PC.

## Data Availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Combination of Traditional Chinese Medicine with Western Medicine on Endometrial Carcinoma and Its Influence on Ultrasound, MRI, Tumor Markers HE4 and CA125

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**Objective.** To study the clinical efficacy of integrated traditional Chinese medicine (TCM) and Western medicine (WM) in treating endometrial cancer and the influence on ultrasound, magnetic resonance imaging (MRI), tumor markers, human epididymis protein 4 (HE4) and carbohydrate antigen 125 (CA125). **Method.** A total of 152 cases of patients with endometrial carcinoma were randomly divided into two groups: the TCM + WM group and the WM group. The WM group was treated with megestrol acetate tablets, and the TCM + WM group was treated with Radix Astragali injection on the basis of the control group. The levels of inflammatory factors, HE4 and CA125 in serum, were detected using enzyme-linked immunosorbent assay (ELISA) or radioimmunoassay. The characteristics of ultrasound images and MRI images were observed and recorded. Toxicity, side effects, and the 3-year cumulative survival rate after treatment were assessed. **Results.** After treatment, the levels of interleukin-4 (IL-4), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and high-sensitivity C-reactive protein (hs-CRP) in both groups decreased, and the decrease in the TCM + WM group was more obvious than that in the WM group. There were statistically significant differences between the two groups in lesion shape, boundary, blood flow signal, lesion diameter, resistance index (RI), echo, intima thickness, and muscle layer infiltration from transvaginal ultrasound images after treatment. The diameter, echo, boundary, shape, composition, and enhancement degree of lesions between the two groups have a significant difference. Moreover, the levels of serum HE4 and CA125 in both groups decreased after treatment, and the decrease in the TCM + WM group was more obvious than that in the WM group. There were statistically significant differences between the two groups in the occurrence of myelosuppression, abnormal liver function, decreased platelet number, gastrointestinal reactions, leukopenia, and cardiotoxicity. After three years of follow-up, the cumulative survival rate of the TCM + WM group was 76.32%, and the cumulative survival rate of the WM group was 57.89%. **Conclusion.** Radix Astragali injection combined with megestrol acetate tablets has obvious therapeutic effects against endometrial cancer. Through vaginal ultrasonography and MRI, it can significantly improve the size, shape, and blood flow signals of patients' lesions, reduce the level of serum inflammatory factors and tumor markers HE4 and CA125, reduce the incidence of toxic and side reactions, improve the patient's immunity, improve the patient's condition significantly, and prolong the survival time of patients.

## 1. Introduction

Endometrial cancer is a malignant tumor of the female reproductive system, which occurs more frequently during the perimenopausal and postmenopausal periods of women,

and the main symptoms are vaginal bleeding and menstrual disorders [1]. At present, the disease has a high morbidity and mortality rate and is showing a continuous growth trend worldwide, and the incidence is increasing at a young age, which seriously threatens the physical and mental health of

most female patients [2]. Radiotherapy and chemotherapy are currently important adjuvant treatments for endometrial cancer, which mainly consist of cytotoxic drugs to directly target the growth and reproduction of cancer cells, thereby inhibiting and killing cancer cells [3]. Megestrol acetate can act on proliferative cancer cells, binding estrogen receptors, blocking their binding with estrogen, and inhibiting endometrial cancer cell proliferation and metastasis [4]. Although this treatment method can eliminate cancer cells in the patient's body, it has a cytotoxic effect on normal cells in the proliferation stage, causing adverse clinical symptoms such as leukopenia and myelosuppression in the patient's body, reducing the patient's tolerance to treatment, and having high toxic side effects [5]. TCM has certain advantages in enhancing efficacy and reducing the toxic effects of chemotherapy and has been widely used in the adjuvant treatment of chemotherapy for endometrial cancer in recent years [6, 7]. Studies have shown that the combination of TCM injection and chemotherapy can reduce the side effects of chemotherapy, and patients who use Western medicine for antitumor therapy can still use TCM injection to stabilize and strengthen the therapeutic effects [8]. Radix Astragali injection is one of the TCM injections in the National Medical Insurance Catalog. It can be combined with chemotherapy to improve the patients' immunity and improve the quality of life of patients [9]. In recent years, as an immune enhancer, Radix Astragali injection has been used in the clinical treatment of various diseases (such as ovarian and breast cancer) and has achieved good therapeutic outcomes and antitumor effects [10, 11]. However, its therapeutic outcomes in endometrial cancer are rarely reported. Studies have found that serum levels of CA125 and HE4 are closely related to the onset and development of endometrial cancer [12, 13]. This study explores the efficacy of integrated TCM and WM in endometrial cancer.

## 2. Materials and Methods

**2.1. The General Information.** A total of 152 endometrial cancer patients admitted to Zhangqiu Maternity and Child Care Hospital, Jinan, Shandong, China, from December 2015 to January 2018 were selected, all of whom were diagnosed by pathological biopsy. The inclusion criteria were as follows: (1) meet the diagnostic criteria for endometrial cancer [14]; (2) clinical survival >3 months; (3) the lesion tissue can be clinically detected, with symptoms such as irregular vaginal bleeding and lower abdominal pain; and (4) no symptoms of allergy to the study drug. The exclusion criteria were as follows: (1) the presence of mental and cognitive disorders; (2) complicated with serious dysfunction of the heart, lung, and kidney; (3) patients who received radiotherapy, chemotherapy, or traditional Chinese medicine 3 months before enrollment; (4) complicated with other malignant tumors, accompanied by breast lumps and other adverse symptoms; and (5) uterine fibroids and fallopian tube cancer during lactation or pregnancy. All patients were randomly divided into the Western medicine (WM) group and the integrated traditional Chinese and Western medicine (TCM + WM) group, with 76 cases in each group. The

age of the WM group was 37–68 years old, with an average of  $51.4 \pm 8.1$  years old; the course of disease was 3–12 months, with an average of  $8.22 \pm 2.74$  months; and cancer types were as follows: 8 cases of clear cell carcinoma, 26 cases of adenosquamous carcinoma, and 42 cases of adenocarcinoma. The age of the TCM + WM group was 38–70 years, with an average of  $49.6 \pm 8.6$  years; the course of disease was 4–13 months, with an average of  $(8.48 \pm 2.84)$  months; cancer types were as follows: 10 cases of clear cell carcinoma, 27 cases of adenosquamous carcinoma, and 39 cases of glandular cancer. There was no statistically significant difference between the two groups' general information ( $P > 0.05$ ), and they were comparable. This study was reviewed and approved by the Medical Ethics Committee of Zhangqiu Maternity and Child Care Hospital, and the patients and their families had informed consent and signed an informed consent form. This study was conducted in accordance with the Declaration of Helsinki.

**2.2. Treatment Method.** After admission, the two groups of patients underwent routine examinations under the supervision of medical staff and were treated according to their actual conditions. Both groups were given 80 mg paclitaxel (Haikou Qili Pharmaceutical Co., Ltd., drug approval number: H20063169) and 40 mg cisplatin (Qilu Pharmaceutical Co., Ltd., drug approval number: H37021358) for basic treatment, a total of 4 chemotherapy treatments. At the same time, patients in the WM group were given oral megestrol acetate tablets (Shanghai Xinyi Tianping Pharmaceutical Co., Ltd., drug approval number: H20053712) for treatment, 2 times/d, 80 mg/time for 12 weeks. On the basis of the WM group, the patients of the TCM + WM group were treated with Huangqi injection (Drug approval number, Heilongjiang Zhenbaodao Pharmaceutical Co., Ltd., 2 ml/branch), intramuscular injection, 3 ml/time, 1 time/d, 21 days as a cycle, 3 consecutive chemotherapy cycles.

**2.3. Ultrasonography.** All patients were examined by using GE E8 color Doppler ultrasonography with a probe frequency of 3.5–8 MHz. The bladder was kept full before scanning, and the bladder lithotomy position was taken. Transvaginal ultrasonography was performed routinely to carefully observe the endometrial morphology, intrauterine lesion morphology, size, internal echo, and muscle layer infiltration depth. Color Doppler flow imaging (CDFI) mode was used to observe the blood flow of the lesion in multiple sections and measure the blood RI value.

**2.4. MRI Examination.** All patients were examined using a GE 1.5T superconducting MRI scanner with an 8-channel phased array coil. Before the examination, the patient kept his bladder properly filled and laid in a supine position with a routine plain scan. The scan sequences included transection, coronal planes, sagittal plane autogyro wave T2W1 and T2W1 fat suppression sequence, and transection autogyro wave T1W1 sequence. After plain scanning, enhanced

scanning was performed. The contrast agent gadolinium spray meglumine (0.1 mmol/kg) was injected intravenously to analyze tumor morphology, size, echo, and signal intensity under different sequence scanning.

**2.5. Observation Index.** (1) The serum inflammatory factors and tumor marker levels were compared between the two groups before and after treatment. 5 ml of fasting venous blood of the two groups in the morning was collected before and after treatment, and centrifuged in a test tube for 5 min to obtain the supernatant. The contents of TNF- $\alpha$ , hs-CRP, IL-4, and HE4 in serum were determined by enzyme-linked immunosorbent assay (ELISA), and the content of tumor marker CA125 in serum was determined by radioimmunoassay. Reagents were provided by Roche Reagent Co., Ltd. of Germany. (2) Transvaginal color ultrasound image features and MRI image features of patients in the two groups were observed. The shape, diameter, boundary, echo, blood flow signal, and enhancement degree of the lesion were recorded. (3) The incidence of toxic and side effects was compared between the two groups, including myelosuppression, abnormal liver and kidney function, decreased platelet number, gastrointestinal reactions, leukopenia, and cardiotoxicity. (4) Three-year cumulative survival rates were compared between the two groups. Through monthly telephone follow-up, the patient's condition and survival were inquired and recorded, and the three-year cumulative survival rate was calculated.

**2.6. Statistical Analysis.** SPSS 23.0 software was used for data analysis. Counting data were expressed as examples or percentages, measurement data were expressed as  $\bar{x} \pm s$ , and  $\chi^2$  test was used.  $P < 0.05$  means the difference is statistically significant.

### 3. Results

**3.1. Comparison of the Levels of Inflammatory Factors before and after Treatment between the Two Groups.** There were no significant differences in serum IL-4, TNF- $\alpha$ , and hs-CRP levels between the two groups before treatment (Figure 1). After treatment, the levels of serum IL-4, TNF- $\alpha$ , and hs-CRP in two groups decreased compared with before treatment, and the decrease in the TCM + WM group was more obvious than in the WM group (Figure 1).

**3.2. Comparison of the Characteristics of Transvaginal Color Doppler Ultrasound Images before and after Treatment between the Two Groups.** Before treatment, there was no statistically significant difference in the characteristics of transvaginal color Doppler ultrasound images between the two groups ( $P > 0.05$ ) (Table 1). After treatment, the two groups of patients had statistically significant differences in lesion shape, boundary, blood flow signal, lesion diameter, RI, echo, intimal thickness, and muscle infiltration ( $P < 0.05$ ) (Table 2).

**3.3. Comparison of MRI Image Characteristics between the Two Groups before and after Treatment.** Before treatment, there was no statistically significant difference in MRI features between the two groups ( $P > 0.05$ ) (Tables 3). After treatment, there were statistically significant differences in lesion diameter, echo, boundary, shape, composition, and enhancement degree between the two groups ( $P < 0.05$ ) (Table 4).

**3.4. Comparison of Serum CA125 and HE4 Expression Levels between the Two Groups before and after Treatment.** There was no significant difference in serum (CA125 and HE4) expression levels between the two groups before treatment ( $P > 0.05$ ) (Figure 2). After treatment, the expression levels of serum CA125 and HE4 in both groups decreased compared with before treatment ( $P < 0.01$ ), and the decrease of the expression levels of serum in the TCM + WM group was more obvious than those in the WM group; the difference was statistically significant ( $P < 0.01$ ) (Figure 2).

**3.5. Comparison of Toxicities and Side Effects between the Two Groups.** After treatment, there were 2 cases of myelosuppression, 3 cases of abnormal liver function, 2 cases of decreased platelet number, 1 case of gastrointestinal reaction, 2 cases of leukopenia, and 3 cases of cardiotoxicity in the TCM + WM group (Table 5). In the WM group, there were 7 cases of myelosuppression, 9 cases of abnormal liver function, 9 cases of decreased platelet number, 10 cases of gastrointestinal reaction, 11 cases of leukopenia, and 8 cases of cardiotoxicity (Table 5). The difference was statistically significant ( $P < 0.05$ ) (Table 5).

**3.6. Comparison of 3-Year Cumulative Survival Rates between the Two Groups.** After three years of follow-up, 18 patients in the TCM + WM group died, and the cumulative survival rate was 76.32%, while 32 patients in the WM group died, and the cumulative survival rate was 57.89%. The difference was statistically significant ( $P < 0.05$ ) (Figure 3).

### 4. Discussion

Endometrial cancer is a malignant tumor disease that occurs in the epithelium of the endometrium. Its main clinical manifestations include vaginal bleeding, vaginal discharge, and lower abdominal pain, and lymph node metastasis and distant organ metastasis can also occur in the late stage of the disease [1]. Endometrial cancer has many pathogenic factors, and its incidence is closely related to lifestyle, but its specific etiology is still unclear. At present, surgical treatment is the primary treatment for endometrial cancer, but some patients who have surgical contraindications or refuse surgery for other reasons need to be treated with drugs to control the progression of the disease. Thus, finding more effective therapies for endometrial cancer has great significance.

At present, progesterone drugs are frequently used in the treatment of endometrial cancer. Megestrol is one of the



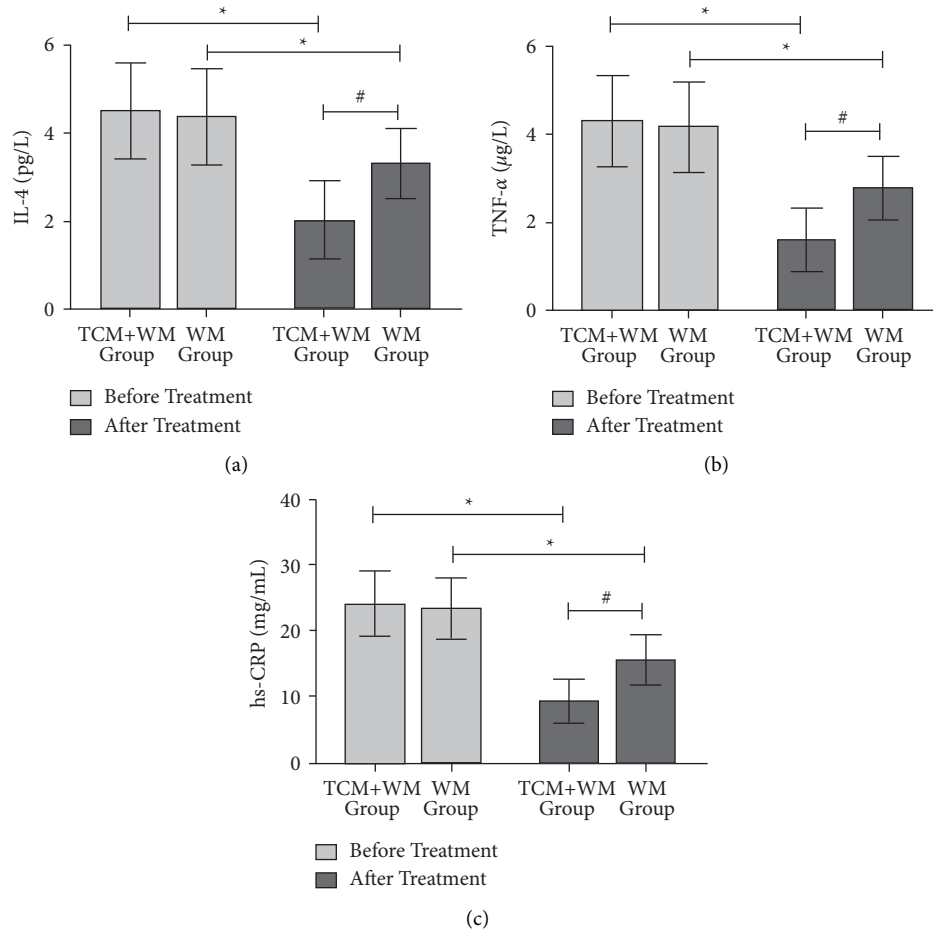


FIGURE 1: Comparison of inflammatory factors levels between the two groups before and after treatment (\* compare with before treatment,  $P < 0.05$ ; # compare with the control group,  $P < 0.05$ ). (a) The comparison of IL-4 levels between the two groups before and after treatment. (b) The comparison of TNF- $\alpha$  levels between the two groups before and after treatment. (c) The comparison of hs-CRP levels between the two groups before and after treatment.

TABLE 1: Comparison of the characteristics of transvaginal ultrasound images between the two groups of patients before treatment ( $n$ ).

Image characteristics	TCM + WM ( $n = 76$ )	WM ( $n = 76$ )	$\chi^2$	$P$
Shape			0.110	0.740
Irregularity	47	45		
Agglomerate	29	31		
Boundary			0.365	0.546
Sharpness	14	17		
Obscure	62	59		
Blood flow signal			0.380	0.827
No	4	5		
Abundant	51	53		
Not abundant	21	18		
Lesion diameter			0.292	0.589
$\geq 2$ cm	53	56		
$< 2$ cm	23	20		
RI			0.468	0.494
$\leq 0.4$	48	52		
$> 0.4$	28	24		
Echo			0.249	0.618
Low	45	48		

TABLE 1: Continued.

Image characteristics	TCM + WM ( <i>n</i> = 76)	WM ( <i>n</i> = 76)	$\chi^2$	<i>P</i>
Uneven	31	28		
Intimal thickness			0.128	0.721
$\geq 1.5$ cm	55	53		
$< 1.5$ cm	21	23		
Muscle infiltration			0.272	0.873
None	5	6		
Shallow	32	34		
Deep	39	36		

TABLE 2: Comparison of characteristics of transvaginal ultrasound images between the two groups after treatment (*n*).

Image characteristics	TCM + WM ( <i>n</i> = 76)	WM ( <i>n</i> = 76)	$\chi^2$	<i>P</i>
Shape			10.125	0.006
No	32	14		
Irregularity	27	39		
Agglomerate	17	23		
Boundary			6.779	0.009
Sharpness	49	33		
Obscure	27	43		
Blood flow signal			6.657	0.036
No	37	22		
Abundant	28	42		
Not abundant	11	12		
Lesion diameter			12.440	0.002
No	32	14		
$\geq 2$ cm	28	48		
$< 2$ cm	16	14		
RI			13.633	$< 0.001$
$\leq 0.4$	12	32		
$> 0.4$	64	44		
Echo			16.067	$< 0.001$
Low	16	39		
Uneven	26	20		
High	34	17		
Intimal thickness			6.410	0.011
$\geq 1.5$ cm	20	35		
$< 1.5$ cm	56	41		
Muscle infiltration			7.916	0.019
None	39	22		
Shallow	18	26		
Deep	19	28		

commonly used drugs; it can effectively regulate hormones secreted by pituitary stimulation, inhibit the action of the female hormone secretion, at the same time also can block the body's hormone receptors from binding to estrogen, thus inhibiting the proliferation and diffusion of tumor cells, but also can promote the body cell differentiation, improve the clinical symptoms and prolong survival time [15, 16]. However, this treatment method has serious side effects and drug resistance problems [17]. As the quintessence of Chinese medicine, TCM plays a vital role in treating various diseases and has certain advantages in enhancing the efficacy and reducing the toxicity of chemotherapy. The combination of TCM and WM can reduce the side effects of radiotherapy and chemotherapy and improve patients' quality of life. According to TCM approaches, endometrial cancer is a

systemic disease although its lesion site is in the uterus, which is a syndrome of asthenia in origin and excess in superficiality caused by the dysfunction of zang-fu organs and poor blood flow [9]. The main purpose of treatment is to promote blood circulation, remove blood stasis, clear heat, and detoxify. Radix Astragali injection is an effective extract of Astragalus. Modern pharmacological investigations have confirmed that it has immunomodulatory, anti-infective, antioxidant, antiviral, antitumor, and hypoglycemic effects and can regulate blood pressure bidirectionally and protect various organs such as the lung, spleen, liver, and kidney [9].

IL-4 is mainly produced by activated T cells. It can not only participate in inflammatory reactions but also increase the number of platelets, make the patient's blood coagulation function abnormal, cause blood flow to slow

TABLE 3: Comparison of MRI image features between the two groups before treatment ( $n$ ).

Image characteristics	TCM + WM ( $n = 76$ )	WM ( $n = 76$ )	$\chi^2$	$P$
Lesion diameter			0.032	0.857
$\geq 2$ cm	55	54		
$< 2$ cm	21	22		
Echo			0.256	0.613
Low	47	50		
Uneven	29	26		
Boundary			0.158	0.691
Sharpness	17	15		
Obscure	59	61		
Shape			0.452	0.501
Irregularity	50	46		
Agglomerate	26	30		
Composition			0.106	0.744
Solid	35	33		
Cystic	41	43		
Enhancement degree			0.778	0.678
No	2	3		
Slightly	18	14		
Obviously	56	59		

TABLE 4: Comparison of MRI image features between the two groups after treatment ( $n$ ).

Image characteristics	TCM + WM ( $n = 76$ )	WM ( $n = 76$ )	$\chi^2$	$P$
Lesion diameter			6.147	0.046
No	30	16		
$\geq 2$ cm	33	42		
$< 2$ cm	13	18		
Echo			6.531	0.038
Low	27	36		
Uneven	15	21		
High	34	19		
Boundary			8.622	0.003
Sharpness	51	33		
Obscure	25	43		
Shape			8.927	0.012
No	30	16		
Irregularity	24	41		
Agglomerate	22	19		
Composition			7.097	0.029
No	30	16		
Solid	17	28		
Cystic	29	32		
Enhancement degree			7.647	0.022
No	33	20		
Slightly	12	8		
Obviously	31	48		

down, increase the accumulation of tumor cells in circulation, and cause the damage of the basement membrane to transfer to other tissues and organs [18]. TNF- $\alpha$  is produced by macrophages and can act on vascular endothelial cells, causing damage to endothelial cells and vascular inflammation, resulting in changes in vascular

function and the development and metastasis of tumor cells [19]. Hs-CRP, an inflammatory response protein produced by the liver, is a marker of inflammation in the acute stage and can cause vascular endothelial damage and tumor angiogenesis [20]. The results of this study showed that the levels of IL-4, TNF- $\alpha$ , and Hs-CRP in both groups decreased after treatment, and the decrease was more evident in the TCM + WM group than in the WM group. These results indicated that the combination of TCM and WM in the treatment of endometrial cancer could inhibit the release of inflammatory factors, significantly improve the inflammatory environment in vivo, and thus inhibit tumor cell growth, which plays an essential role in adjuvant therapy.

CA125 is an important tumor marker, widely used in the early diagnosis and clinical prognosis evaluation of malignant tumors [21–23]. Studies have reported that the high level of CA125 is related to the occurrence and development of endometrial cancer [24]. HE4, as a newly discovered tumor marker for endometrial cancer, is a secretory glycoprotein with high sensitivity and specificity [25]. Studies have documented that serum HE4 and CA125 levels can reliably predict the poor prognosis of patients with endometrial cancer [26]. Li et al. pointed out that serum HE4 levels can be used as an indicator for early diagnosis of endometrial cancer [27]. Other studies have shown that the combined detection of HE4 and CA125 can effectively improve the diagnostic accuracy and sensitivity of endometrial cancer [12]. Here, integrated TCM and WM can significantly reduce serum HE4 and CA125 levels, thus decreasing tumor activity and inhibiting tumor proliferation and growth in patients with endometrial cancer. It is further indicated that the combination of TCM and WM in the treatment of endometrial cancer can reduce the toxicities and side effects, balance the platelets and white blood cell numbers in the patient, and protect the bone marrow at the

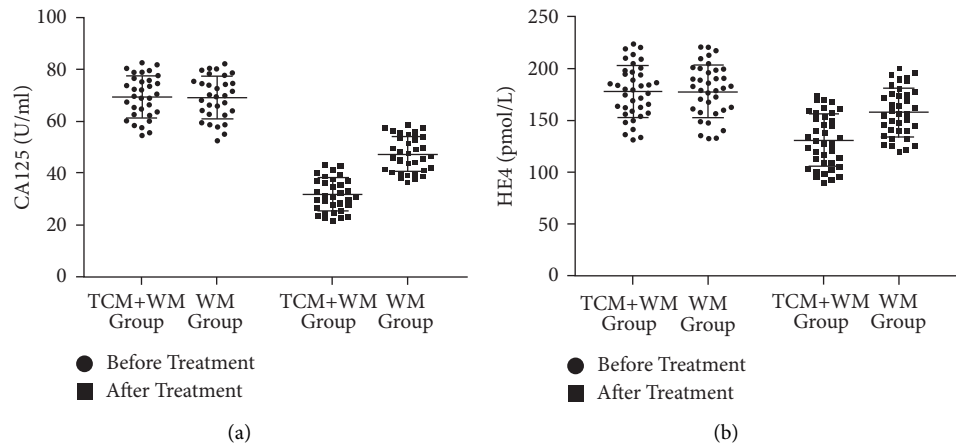


FIGURE 2: Comparison of serum (CA125 and HE4) expression levels between the two groups before and after treatment. (a) The comparison of serum CA125 expression levels between the two groups before and after treatment. (b) The comparison of HE4 expression levels between the two groups before and after treatment.

TABLE 5: Comparison of the occurrence of toxicities and side effects between the two groups.

Group	Myelosuppression	Abnormal renal and liver function	Decreased platelet number	Gastrointestinal reactions	Leukopenia	Cardiotoxicity
TCM + WM	2 (2.63)	3 (3.95)	2 (2.63)	1 (1.32)	2 (2.63)	3 (3.95)
WM	7 (9.21)	9 (11.84)	9 (11.84)	10 (13.16)	11 (14.47)	8 (10.53)

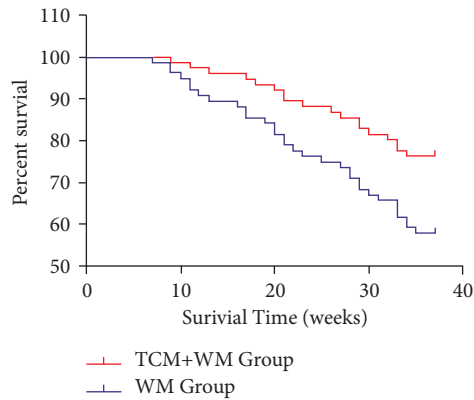


FIGURE 3: Comparison of 3-year cumulative survival rates between the two groups.

same time, which is of high safety, and can also induce the cancer cell apoptosis and prolong the life cycle. Transvaginal ultrasound can not only display two-dimensional ultrasound images but also further observe the nature of blood flow, speed, and other information, so as to sensitively and accurately reflect the pathological changes of the endometrium [28, 29]. MRI has high tissue resolution and can accurately assess the degree and extent of lesion invasion in patients with endometrial cancer [30, 31]. The two detection methods are not invasive and are more acceptable to patients. The results of the two detection methods can further confirm that the treatment of endometrial cancer with integrated TCM and WM has good clinical efficacy, effectively clearing the focus and improving patients' clinical symptoms and immunity.

## 5. Conclusion

Radix Astragali injection combined with megestrol treatment of endometrial cancer has certain clinical curative effects. It can enhance immunity, effectively control the development condition, improve the quality of life, reduce the inflammatory response and CA125 and HE4 levels, inhibit tumor cell growth, reduce the size of the lesion area, and prolong survival time.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Wenshentiaojing Decoction on Hormone Level and Follicular Number in Patients with Menstrual Disorder of Polycystic Ovary Syndrome

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**Objective.** To explore the curative effect of Wenshentiaojing Decoction on the treatment of menstrual disorder caused by PCOS. **Methods.** Patients with menstrual disorders caused by PCOS admitted to our department from January 2020 to January 2021 were selected as the research objects and were divided into a control group and observation group according to the random number table method. The control group was treated with Western medicine, and the observation group was treated with Wenshentiaojing Decoction on the basis of Western medicine. The clinical efficacy of the two groups was compared. Before and after treatment, sex hormones (LH, FSH, LH/FSH, and testosterone (T)), ovarian volume, endometrial thickness, cervical mucus score, follicular number, menstrual conditions (menstrual duration, menstrual cycle, and menstrual volume), and other indicators in both groups were recorded. **Results.** After treatment, the total effective rate of the observation group (91.1% (41/45)) was higher than that of the control group (77.8% (35/45)), and the difference was statistically significant ( $P < 0.05$ ). After treatment, the LH, LH/FSH, and T levels in the observation group were lower than those in the control group, while the FSH level was higher than that in the control group ( $P < 0.05$ ). After treatment, the ovarian volume, endometrial thickness, cervical mucus score, and follicle number in the observation group were higher than those in the control group ( $P < 0.05$ ). After treatment, the menstrual duration and menstrual volume in the observation group were longer than those in the conventional group, and the menstrual cycle was shorter than that in the conventional group ( $P < 0.05$ ). **Conclusion.** For patients with menstrual disorders caused by PCOS, the treatment effect of Wenshentiaojing Decoction assisted with Western medicine is better, which can effectively improve the level of sex hormones, cervical mucus, and menstrual conditions, increase the ovarian volume, endometrial thickness, and follicle number, and improve the treatment effect, with fewer adverse reactions, which is worthy of further promotion and application.

## 1. Introduction

Polycystic ovary syndrome (PCOS) is a relatively common endocrine disease in gynecology [1, 2], mostly affecting women of reproductive age, with an incidence of about 6%–21% [3]. It is characterized by chronic anovulation, excess androgen secretion, and insulin resistance (IR). Its etiology is still unknown [4–8]. PCOS is also associated with insulin resistance in surrounding tissues, hyperinsulinemia, and

abnormal degree of obesity and is one of the most common causes of menstrual irregularities in adolescent women giving birth. The menstrual cycle mainly depends on the hormone regulation of the “hypothalamic-pituitary-ovarian axis” [9–11], which is manifested as periodic endometrial exudation, and the mechanism of PCOS is the above-mentioned functional abnormalities and metabolic changes [12–14]. With the change of living habits and diet structure, as well as the increase of life pressure, patients are easily



affected by anxiety and other factors, resulting in a significant increase in the incidence of PCOS menstrual irregularities, which may cause reproductive disorders in patients, seriously affect their physical and mental health and quality of life, and even affect their family harmony [15, 16].

At present, the western medicine treatment of PCOS is mainly aimed at establishing a normal menstrual cycle with ovulation, restoring patients' fertility and eliminating clinical manifestations such as hirsute. It takes estrogen, progesterone symptomatic treatment. Treatment methods include the use of drugs to regulate the menstrual cycle, reduce androgen levels, improve insulin resistance, and induce ovulation, which has achieved a certain effect. However, clinical needs have not been fully met. For example, long-term hormone therapy may cause nausea, vomiting, breast tenderness, and other adverse reactions in some patients, affecting their confidence in treatment, and long-term application of hormone drugs may lead to a series of adverse reactions or drug dependence [17]. Therefore, it is particularly important to select an adjuvant therapy with high safety, strong selectivity, and fewer adverse reactions.

TCM treatment is based on the overall regulation and has the characteristics of precise curative effect and safety [18–20]. Chinese medicine thinks if kidney gas is insufficient, kidney essence cannot turn unripe Qi and blood, blunt ren is not filled, blood vessel is not surplus, it and leads to menstruation maladjustment and infertility. Wenshentiaojing Decoction from “Ye Tianshi female department secret recipe for diagnosis and treatment,” is a classic formula for treating infertility, amenorrhea, irregular menstruation, and other symptoms of women. It has been widely used in ancient and modern gynecological clinical cases, with remarkable effect. In modern clinical application, according to the actual symptoms of patients, the types or dosage of medicinal materials are added or reduced, and most pills are changed into decoction, so that the therapeutic effect is remarkable. Deficiency of kidney Yang can not only stimulate the biochemical and growth of kidney Yin but also make Qi and blood run powerless, stasis and flush ren cell veins, and even lack of motive force for ovulation, so kidney deficiency is the root cause of ovulation disorder [21, 22]. Kidney deficiency can further lead to the imbalance of Qi, blood, and Yin and Yang. This fully discusses the role of the kidney in female development and reproduction [23–25]. The Wenshentiaojing decoction is a good prescription for treating infertility, amenorrhea, and irregular menstruation, which is widely used in gynecology clinic with remarkable effect. In modern clinical application according to the actual symptoms of patients, the content of each component is adjusted and pills are replaced with soup. The effect is more obvious.

This study explored the clinical efficacy of Wenshentiaojing Decoction in the adjuvant treatment of PCOS menstrual disorders and its effect on clinical symptoms and hormone levels and aimed to understand the specific situation of reducing hormone side effects of Chinese medicine decoction in the treatment of PCOS in detail and evaluate its clinical application effect and to explore the advantages of its therapeutic methods and provide reference for further promoting the application of the clinical pathway.

## 2. Materials and Methods

### 2.1. Selection of General Information and Medical Records

**2.1.1. Subjects.** Patients with polycystic ovary syndrome complicated with menstrual disorders admitted to our department from January 2020 to January 2021 were selected as the research objects. All patients were confirmed by clinical symptoms, biochemical indicators and vaginal ultrasound examination, etc. According to the random number table method, they were divided into a control group and observation group.

### 2.1.2. Diagnostic Criteria

- (1) Western diagnostic criteria: the standards recommended by the Rotterdam Expert Meeting of The European Society of Human Reproduction and Embryology and the American Society of Reproductive Medicine were adopted: ① continuous anovulation or sporadic ovulation; ② clinical manifestations of hyperandrogen and/or hyperandrogenemia. Ultrasound showed polycystic ovary. In addition, other hyperandrogen diseases such as congenital adrenal hyperplasia, Cushing's syndrome, and androgen-secreting tumors were excluded.
- (2) According to the diagnostic criteria of irregular menstruation in Guiding Principles for Clinical Research of New Chinese Medicine Drugs issued by the Ministry of Health of China, including premenstruation, late menstruation, irregular menstrual succession, prolonged menstruation, menorrhagia, less monthly passage, etc.
- (3) According to the diagnostic criteria of amenorrhea in The Guidelines for Clinical Research on New Chinese Medicine Drugs issued by the Ministry of Health of China, the former refers to primary amenorrhea, while the latter refers to secondary amenorrhea.

### 2.1.3. Inclusion Criteria

- (1) Meet the diagnostic criteria of Western medicine
- (2) Consistent with the diagnosis of menstrual disorders or amenorrhea in traditional Chinese medicine
- (3) Female patients aged 18–45 years
- (4) Understand the effects of drugs and possible side effects, strong compliance, and active cooperation
- (5) The person who agrees and signs the informed consent

### 2.1.4. Exclusion Criteria

- (1) Congenital adrenal hyperplasia, Cushing's syndrome, androgen-secreting tumors, and other causes of high androgen

- (2) Menstrual disorders caused by serious organic diseases
- (3) Complicated with serious cardiovascular and cerebrovascular diseases, liver and kidney injury, pulmonary diseases, blood diseases, or complicated with mental disorders
- (4) Pregnant or breast-feeding or postmenopausal women
- (5) Patients with poor compliance cannot be guaranteed to refrain from using other therapies during treatment

### 2.1.5. Peeling Standards

- (1) Patients with severe adverse reactions
- (2) Voluntarily quit the research

## 2.2. Treatment Methods

### 2.2.1. General Treatment

- (1) Resting, avoiding heavy physical activity, preventing various infections and stress states, and eating a high-protein, high-calorie diet
- (2) Psychological treatment: the included subjects were given psychological counseling to eliminate the interference of psychological factors, ensure a good attitude, and actively cooperate with the treatment
- (3) Others: doing appropriate physical exercise, but paying attention to avoid overwork

### 2.2.2. Drug Therapy

- (1) Control group: clomiphene was treated. The control group began to take clomiphene for 5 consecutive days from the 5th day of menstruation, once a day, 50 mg each time. One course of treatment was 1 month, and the treatment lasted for 3 courses.
- (2) Treatment group: on the basis of the treatment of the control group, to warm the kidney, Tiaojing decoction Chinese medicine treatment is used.

The decoction is based on the addition and reduction of Yougui pill, which is combined with kidney tonifying and regulating menstruation drugs according to different menstrual cycles. Main drug composition: aconite, cinnamon, antler gum, cooked *Rehmannia officinalis*, *Cornus officinalis*, wolfberry fruit, Chinese yam, Dodder seed, *Eucommia ulmoides*, Angelica, etc.

- (1) Postfollicular stage: the kidney should be warmed to help Yang, nourishing qi and blood mainly. You GUI pills are added and subtracted, and donkey-hide gelatin, *Ligustrum lucidi*, Chuanduan, Dangshen, *Atractylodes atractylodes*, etc. are added.
- (2) Intermenstrual ovulation period: kidney Yijing and huoxue qi should be warmed. You GUI pills are

added and subtracted, and Chuanduan, *Achyranthes bidentata*, *Salvia miltiorrhiza*, Chuanxiong, Xiangfu, etc. are added.

- (3) Premenstrual luteal phase: kidney should be tonified, and it should help Yang, qi, and blood circulation. Yougui pills are added and subtracted, and cistanche, *Euphorbia officinalis*, Chuanduan, Xiangfu, Chuanxiong, *Salvia miltiorrhiza*, etc. are added.
- (4) Menstruation period: it is advisable to warm the kidney and nourish blood, invigorate blood, and regulate menstruation. Right GUI pills are added and subtracted, and Dangshen, *Atractylodes macrocephala*, Xiangfu, Chuanxiong, *Achyranthes bidentata*, etc. are added.

Usage: one dose daily, decocted in water, divided in the morning and evening, treatment for 3 months. Medicine is taken when the fasting iodine content is too high in raw, cold, fish, mutton, and spicy products.

### 2.3. Observation Indicators

- (1) TCM syndrome integral scale: the TCM syndrome integral scale was formulated according to the relevant standards in The Guiding Principles for Clinical Research of Chinese Medicine New Drugs, and the TCM symptoms were quantitatively scored, and the changes of TCM syndrome integral of patients in the two groups before and after treatment were compared.
- (2) Test indicators: serum indicators (CRP, IGF-1, and TNF- $\alpha$ ) and sex hormones (FSH, LH, and E2, T) were measured: the changes of indicators in both groups were observed before and after treatment. T lymphocytes were detected by flow cytometry: CD3+, CD4+, CD8+, and Body Mass Index (BMI).
- (3) Ovarian volume, endometrial thickness, cervical mucus score, and number of follicles.
- (4) Menstrual conditions.

**2.4. Clinical Efficacy Standards.** According to the efficacy evaluation criteria and nimodipine scoring method in The Guidelines for Clinical Research of New Chinese Medicine, the improvement of clinical symptoms of the patients was determined by the following criteria:

- (1) Significant effect: clinical symptoms and signs basically disappeared, menstruation basically returned to normal, B ultrasound and biochemical indicators were normal, and 70% $\leq$  overall improvement rate <90%
- (2) The clinical symptoms and signs were improved compared with before treatment, menstruation basically returned to normal, B ultrasound and biochemical indicators were improved, and 30% $\leq$  overall improvement rate <70%

- (3) Invalid: there were no significant changes or exacerbations in clinical symptoms, signs, and menstruation, and the overall improvement rate was less than 30%
- (4) The levels of sex hormones after treatment were compared between the two groups, and the observation indexes included FSH, LH, T, E2, and LH/FSH values

**2.5. Statistical Analysis Methods.** Statistical software SPSS22.0 was used for statistical analysis. Measurement data were described by mean  $\pm$  standard deviation ( $\bar{X} \pm S$ ). An independent-sample *T* test was used for intergroup comparison, and a paired-sample *T* test was used for intragroup comparison. A C2 test was used for counting data.  $P < 0.05$  was considered as a significant difference.

### 3. Results

**3.1. General Data Analysis.** The control group was 20–38 years old, with an average age of ( $28.5 \pm 2.3$ ) years. The course of disease ranged from 5 months to 8 years, with an average course of ( $4.7 \pm 1.2$ ) years. There were 30 married cases and 15 unmarried cases. There were 27 cases with fertility history and 18 cases without fertility history. The observation group was 20–39 years old, with an average age of ( $28.2 \pm 2.4$ ) years. The course of disease ranged from 6 months to 8 years, with an average course of ( $4.5 \pm 1.1$ ) years. 32 cases were married, and 13 cases were unmarried. There were 29 cases with fertility history and 16 cases without. There was no significant difference in general data between the two groups ( $P > 0.05$ ), as shown in Table 1.

#### 3.2. Therapeutic Efficacy Evaluation

**3.2.1. Comparison of Therapeutic Effects.** Comparison of curative effect between 2 groups. The curative effect of the observation group was significantly better than that of the control group ( $\chi^2 = 2.159$ ,  $P = 0.016 < 0.05$ ), as shown in Figure 1.

**3.2.2. TCM Syndrome Integral.** There was no significant difference in the scores of menstrual volume syndrome, menstrual cycle syndrome, and overall TCM syndrome between the two groups before treatment ( $P > 0.05$ ). After treatment, the scores of menstrual volume syndrome, menstrual cycle syndrome, and overall TCM syndrome in both groups were significantly lower than those before treatment ( $P < 0.05$ ). Compared with the control group, the scores of menstrual volume syndrome, menstrual cycle syndrome, and overall TCM syndrome in the observation group were lower after treatment ( $P < 0.05$ ), as shown in Table 2.

**3.2.3. Body Mass Index (BMI).** Before treatment, there was no significant difference in BMI between the two groups ( $P > 0.05$ ), indicating comparability. After treatment, the

BMI of both groups decreased, and the treatment group was lower than the control group, with statistical significance ( $P < 0.05$ ), as shown in Figure 2.

**3.3. Comparison of Serum Indicators.** After treatment, the levels of serum CRP, IGF-1, and TNF- $\alpha$  in 2 groups were lower than those before ( $P < 0.05$ ). Compared with the control group, the observation group improved better. After treatment, serum CRP, IGF-1, and TNF- $\alpha$  levels in the observation group were lower than those in the control group ( $P < 0.05$ ), as shown in Figure 3.

**3.4. Comparison of Sex Hormone Levels.** Sex hormone status is a direct indicator of hypothalamic-pituitary-gonadal axis function, and abnormal sex hormone is also the key to the occurrence and development of menstrual disorders. Among them, E2 is mainly related to ovarian function, LH and FSH can synergistically regulate luteal formation and SECRETION of P, and P can induce endometrium from proliferation to secretion. Therefore, insufficient secretion of E2, LH, and FSH is an important reason for the occurrence of menstrual disorders in PCOS patients.

Before treatment, there were no significant differences in E2, FSH, and LH between 2 groups ( $P > 0.05$ ). After treatment, hormone levels in the two groups were significantly improved ( $P < 0.05$ ), but the levels of LH, LH/FSH, and T in the observation group were significantly lower than those in the control group ( $P < 0.05$ ), and the levels of FSH, P, and E2 were significantly higher than those in the control group ( $P < 0.05$ ), see Table 3 for details.

**3.5. Comparison of Cellular Immune Indexes.** Comparison of cellular immunity and humoral immunity between the 2 groups before treatment, there was no difference in the levels of cellular immunity and humoral immunity between the 2 groups ( $P > 0.05$ ); after treatment, the indexes of cellular immunity and humoral immunity in the observation group were improved ( $P < 0.05$ ). Compared with the control group, the levels of CD3+ and CD8+ in the observation group decreased after treatment ( $P < 0.05$ ), while the levels of CD4+ and CD4+/CD8+ increased ( $P < 0.05$ ), as shown in Figure 4. The possible reason is that the chemical components of Chinese yam mainly contain diosgenin, saponin, mucilage, glycoprotein, vitamin C, etc. Pharmacological studies show that Chinese yam polysaccharide can enhance immune function and have an antiaging effect.

**3.6. Ovarian Volume, Endometrial Thickness, Cervical Mucus Score, and Number of Follicles.** In clinical practice, abnormal levels of FSH and LH in PCOS lead to abnormal follicular development, resulting in long-term anovulation, menstrual disorders, infertility, and increased incidence of endometrial cancer. Therefore, it is of great significance to observe ovarian volume and follicle number of PCOS patients.

Before treatment, there were no significant differences in ovarian volume, endometrial thickness, cervical mucus score, and follicle number between the two groups

TABLE 1: Comparison of general data between the two groups ( $\bar{x} \pm S$ ).

Project	Observation group ( $n = 45$ )	Control group ( $n = 45$ )	$T$	$P$
Age	20 ~ 49	20 ~ 38		
Average age	$28.8 \pm 2.4$	$28.5 \pm 2.3$	0.625	0.295
Course of disease	6 months–8 years	5 months–8 years		
Mean duration/year	$4.5 \pm 1.1$	$4.7 \pm 1.2$	0.332	0.416
Married	32	30		
Childbearing history	29	27		

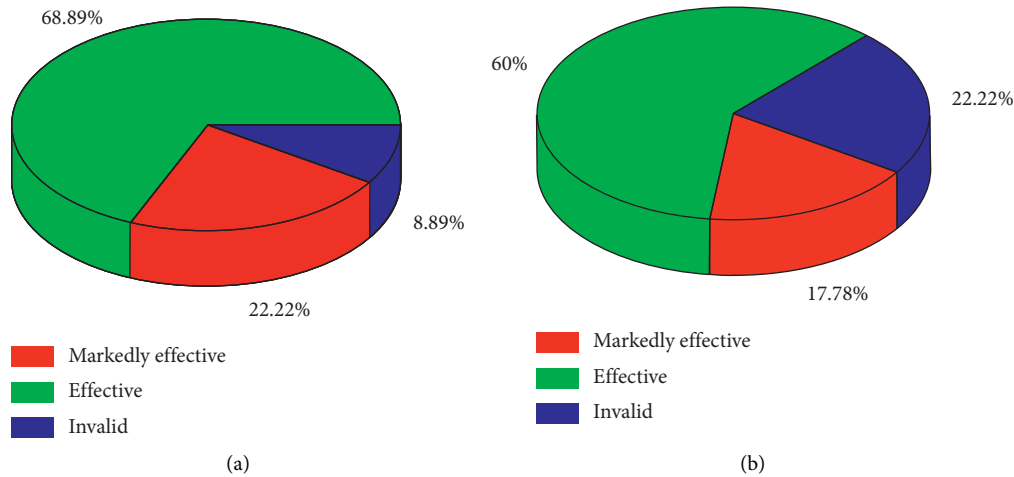


FIGURE 1: Comparison of efficacy between the two groups after treatment. (a) Observation group treatment efficacy; (b) control group treatment efficacy.

TABLE 2: Comparison of TCM syndrome score difference between the two groups before and after treatment ( $\bar{X} \pm S$ ).

Project	Observation group ( $n = 45$ )		Control group ( $n = 45$ )	
	Before treatment	After treatment	Before treatment	After treatment
Menstrual cycle	$3.21 \pm 2.31$	$1.58 \pm 1.43^{* \#}$	$3.56 \pm 2.19$	$2.01 \pm 1.56^{*}$
Menstrual blood volume	$3.37 \pm 0.58$	$1.68 \pm 1.62^{* \#}$	$3.22 \pm 1.78$	$2.17 \pm 1.36^{*}$
Dysmenorrhea	$1.94 \pm 1.70$	$1.42 \pm 1.36^{*}$	$1.89 \pm 1.58$	$1.73 \pm 1.44$
Inhibited sexual desire	$1.84 \pm 1.88$	$1.03 \pm 1.05^{* \#}$	$2.01 \pm 1.65$	$1.56 \pm 1.25$
Doldrums	$1.42 \pm 1.28$	$0.84 \pm 1.00^{* \#}$	$2.28 \pm 1.25$	$1.55 \pm 1.09$
Languid	$2.68 \pm 1.92$	$1.31 \pm 1.28^{* \#}$	$2.67 \pm 0.90$	$1.84 \pm 1.03^{*}$
Soreness and weakness of the waist and knees	$2.65 \pm 1.98$	$1.32 \pm 1.30^{* \#}$	$2.83 \pm 1.52$	$2.52 \pm 1.01$
Hypomnesia	$1.73 \pm 1.29$	$1.15 \pm 1.11^{* \#}$	$1.61 \pm 1.25$	$2.00 \pm 0.69$

Note. Compared with before treatment,  $^{*}P < 0.05$ . Compared with the control group after treatment,  $^{\#}P < 0.05$ .

( $P > 0.05$ ). After treatment, ovarian volume, endometrial thickness, cervical mucus score, and follicle number in the experimental group were higher than those in the conventional group ( $P < 0.05$ ), as shown in Figure 5. It indicates that warming kidney meridian decoction can effectively improve the number of follicles in patients. The possible reason is that *Rehmannia glutinosa* has the effect of nourishing Yin and blood, nourishing essence, and filling pulp. Wolfberry and dodder seed can nourish Yin in the kidney. *Angelica* can regulate menstruation and relieve pain and invigorate blood circulation. Modern pharmacological studies show that dodder has an estrogen-like effect and can stimulate follicular development and luteal formation. Chinese herbs such as *Angelica* for promoting blood

circulation can improve microcirculation and help to improve ovarian blood supply. The combination of these drugs can improve tissue microcirculation, dilate blood vessels, improve blood oxygen supply around the lesion, and induce ovulation.

**3.7. Menstruation.** Before treatment, there were no significant differences in menstrual duration, menstrual cycle, and menstrual volume between the two groups ( $P > 0.05$ ). After treatment, menstrual duration and menstrual volume in the experimental group were longer than those in the conventional group, and menstrual cycle was shorter than that in the conventional group ( $P < 0.05$ ), as shown in Figure 6.

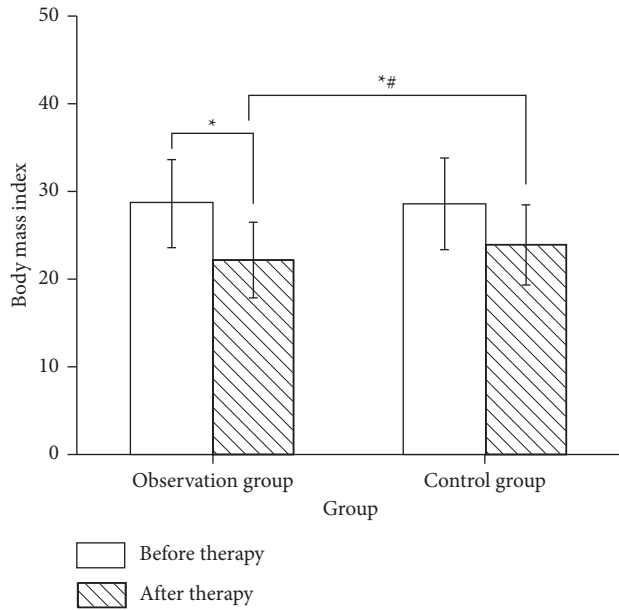


FIGURE 2: Comparison of efficacy between the two groups after treatment. Note. Compared with before treatment, \* $P < 0.05$ . Compared with the control group after treatment, \* $P < 0.05$ .

The results showed that, after TCM-assisted treatment, the menstrual situation of the patients improved continuously, and it had statistical significance. The possible reason was that *Rehmannia glutinosa* in the prescription could rapidly increase the number of red blood cells and promote the body's hematopoietic function and blood circulation. *Angelica* can nourish blood and regulate menstruation, inhibit platelet aggregation, and inhibit the proliferation of vascular smooth muscle cells in hyperplastic intima.

#### 4. Discussion

The incidence of polycystic ovary syndrome is increasing year by year, and the early clinical manifestations are often hidden. With the further development of the disease, severe menstrual disorders, loss of sexual desire, and even infertility and abortion occur. It is mainly manifested by excessive LH secretion, and the disorder of gonadotropin level secreted by the pituitary gland is very likely to lead to follicular dysplasia and hyperandrogenemia [26]. Generally, patients' condition will improve after Western medicine treatment, but some patients have poor compliance, tolerance, and side effects, and long-term alternative treatment also increases the risk of angina, myocardial infarction, osteoporosis, and fracture.

The main pathogenesis of polycystic ovary syndrome leading to menstrual disorders is the deficiency of kidney Yang and imbalance of the lung and ren, and the treatment should take warming the kidney and regulating meridian decoction as its core. According to the different menstrual cycles in our hospital, you GUI pill can be used to treat menstrual disorders, which can adjust the related indicators such as sex hormones and improve the clinical symptoms. This study evaluated the clinical efficacy of Wenshentiaojing

Decoction in the treatment of menstrual disorders and explored new ideas of TCM treatment of the disease.

In this study, patients in the control group were treated with Western medicine, using clomiphene, which can improve the ovulation cycle of patients, interfere with estrogen negative feedback, and competitively inhibit estrogen receptors in the hypothalamus, which is a first-line ovulation inducing drug. Clomiphene is an estrogen-inhibiting drug, and long-term use can reduce endometrial susceptibility, seriously affect cervical mucus and endometrial thickness, increase the risk of abortion in women of childbearing age, and reduce the pregnancy rate [27]. Polycystic ovary syndrome in traditional Chinese medicine belongs to menstrual diseases, infertility and other categories, kidney deficiency, and blood stasis, and the existence of the disease is closely related.

In the treatment of menstrual disorders caused by PCOS, traditional Chinese medicine not only invigorates the liver and kidney to regulate menstruation but also promotes blood circulation and facilitates menstruation. According to syndrome differentiation, it also stimulates the function of the gonad axis in vivo, restores the positive and negative feedback function of the gonad axis, and causes the hypothalamus and pituitary gland to release FSH and LH rapidly. FSH and LH receptors on follicular granulosa cells and endometrial cells are stimulated by FSH and LH, and a large amount of estrogen (E2 and E1) is synthesized under the action of aromatase, so that all FSH and LH accumulated in the pituitary storage pool are released rapidly, forming the PEAK of FSH and LH and promoting the rapid development and maturation of follicles. In this study, the patients with menstrual disorders caused by PCOS were treated with Wenshentiaojing Decoction assisted with Western medicine, and it was found that the observation group was superior to the control group in terms of improving TCM symptoms, inflammatory factors, and sex hormones, and the total effective rate of the observation group was higher than that of the control group after treatment. LH, FSH, LH/FSH, T, ovarian volume, endometrial thickness, cervical mucus score, follicle number, and menstruation were all superior to the control group. *Achyranthes bidens*, *Salvia miltiorrhiza*, safflower, and peach kernel promote blood circulation and remove blood stasis. Duzhong and dodder strengthen the waist, knee, liver, and kidney. Antler gum, cinnamon, and aconite warm and tonify kidney Yang. Chinese yam, wolfberry fruit, cornus officinalis, and ripe *Rehmannia* root nourish the liver and spleen, nourish Yin, and nourish the kidney. Modern pharmacological studies show that *Rehmannia glutinosa* can rapidly increase the number of red blood cells and promote the body hematopoietic function and blood circulation. *Angelica* can inhibit platelet aggregation and proliferation of vascular smooth muscle cells in hyperplastic intima.

The results of this study showed that, in the observation group, TCM-assisted treatment of menstrual disorders caused by PCOS could improve the menstrual duration, menstrual cycle, and menstrual volume, without significantly increasing adverse reactions, indicating high safety. On the basis of clomiphene, the combination of warming the

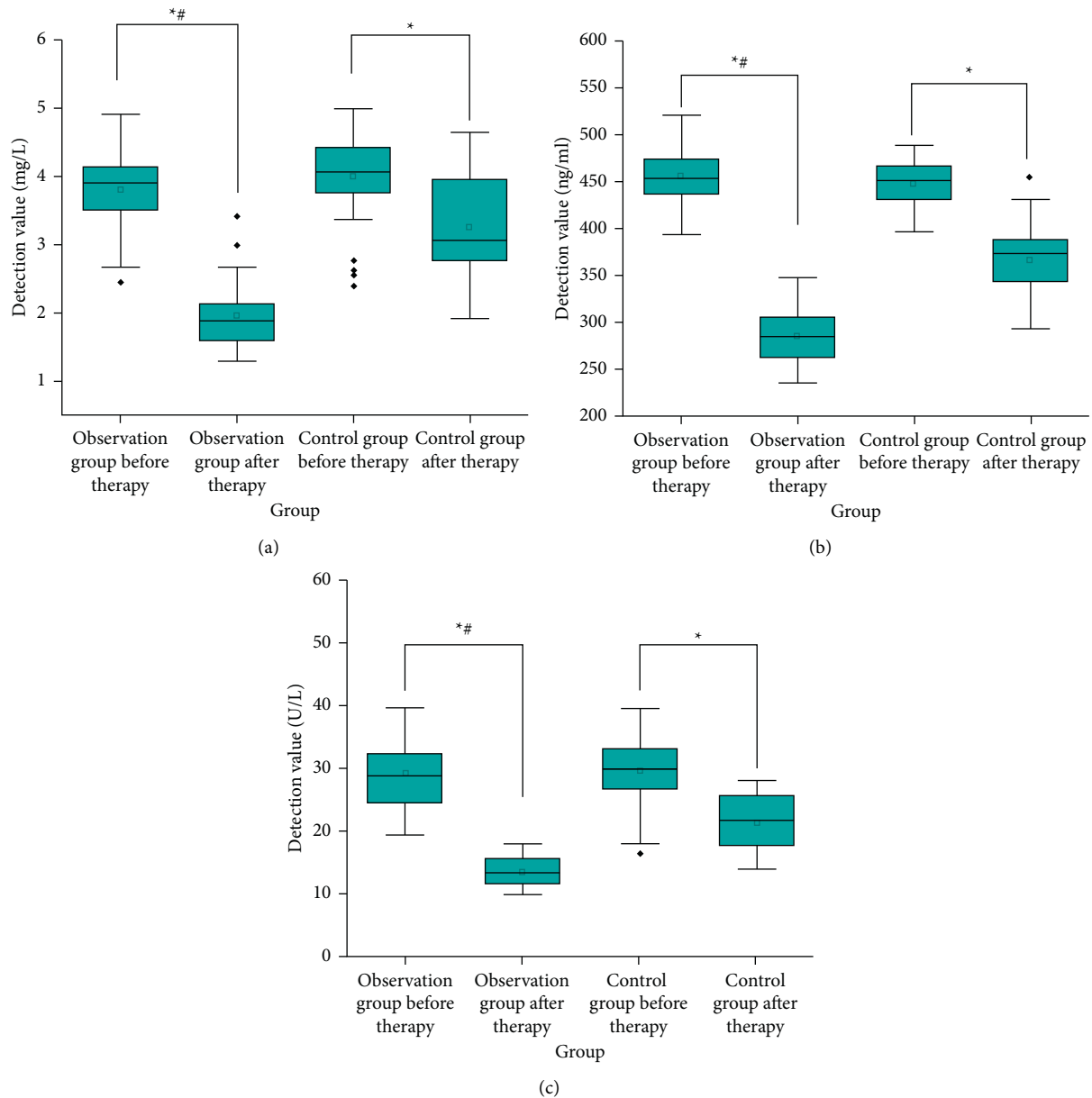


FIGURE 3: Comparison of serum CRP, IGF-1, and TNF- $\alpha$  levels between the two groups ( $\bar{x} \pm S$ ). Note. Compared with before treatment, \* $P < 0.05$ . Compared with the control group after treatment, # $P < 0.05$ .

TABLE 3: Comparison of hormone levels between the two groups before and after treatment.

Project	Observation group ( $n = 45$ )		Control group ( $n = 45$ )	
	Before treatment	After treatment	Before treatment	After treatment
LH (mIU/L)	$15.22 \pm 6.22$	$6.28 \pm 1.95^{* \#}$	$15.36 \pm 6.59$	$9.51 \pm 1.62^{*}$
FSH (mIU/L)	$5.31 \pm 2.39$	$6.50 \pm 1.66^{* \#}$	$5.40 \pm 2.86$	$5.98 \pm 1.62^{*}$
LH/FSH	$3.28 \pm 0.93$	$0.94 \pm 0.33^{* \#}$	$3.26 \pm 0.79$	$1.52 \pm 0.61^{*}$
T (ng/dl)	$91.56 \pm 16.99$	$48.52 \pm 12.54^{* \#}$	$92.05 \pm 17.61$	$68.57 \pm 18.22^{*}$
E2 (pmol/L)	$66.82 \pm 15.33$	$157.63 \pm 22.68^{* \#}$	$66.92 \pm 17.45$	$99.57 \pm 18.94^{*}$

Note. Compared with before treatment, \* $P < 0.05$ . Compared with the control group after treatment, # $P < 0.05$ .

kidney and regulating meridian decoction, removing blood stasis, preserving the power of tonic, nourishing kidney Yang, activating blood, and tonifying kidney can further improve insulin resistance, anti-inflammatory property,

improve pelvic blood microcirculation, and regulate the function of the hypothalamic-pituitary-ovarian axis.

Above all, polycystic ovary syndrome to menstrual disorder was treated by warming the kidney and regulating



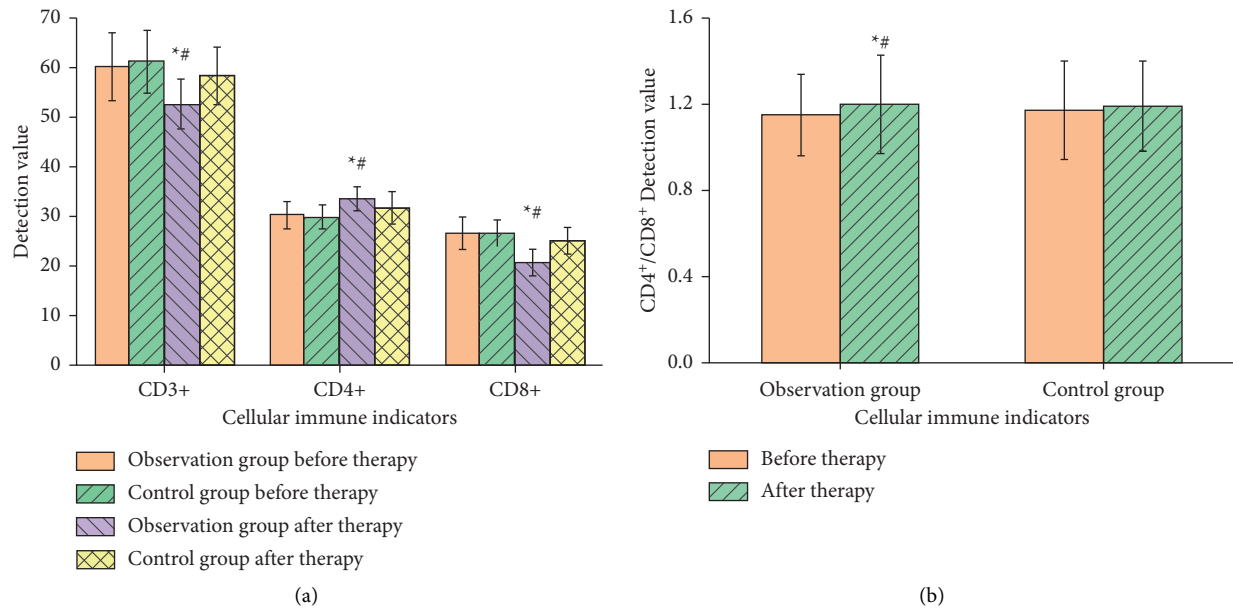


FIGURE 4: Comparison of cellular immune indexes between the two groups before and after treatment. *Note.* Compared with before treatment,  $*P < 0.05$ ; compared with the control group after treatment,  $^{\#}P < 0.05$ .

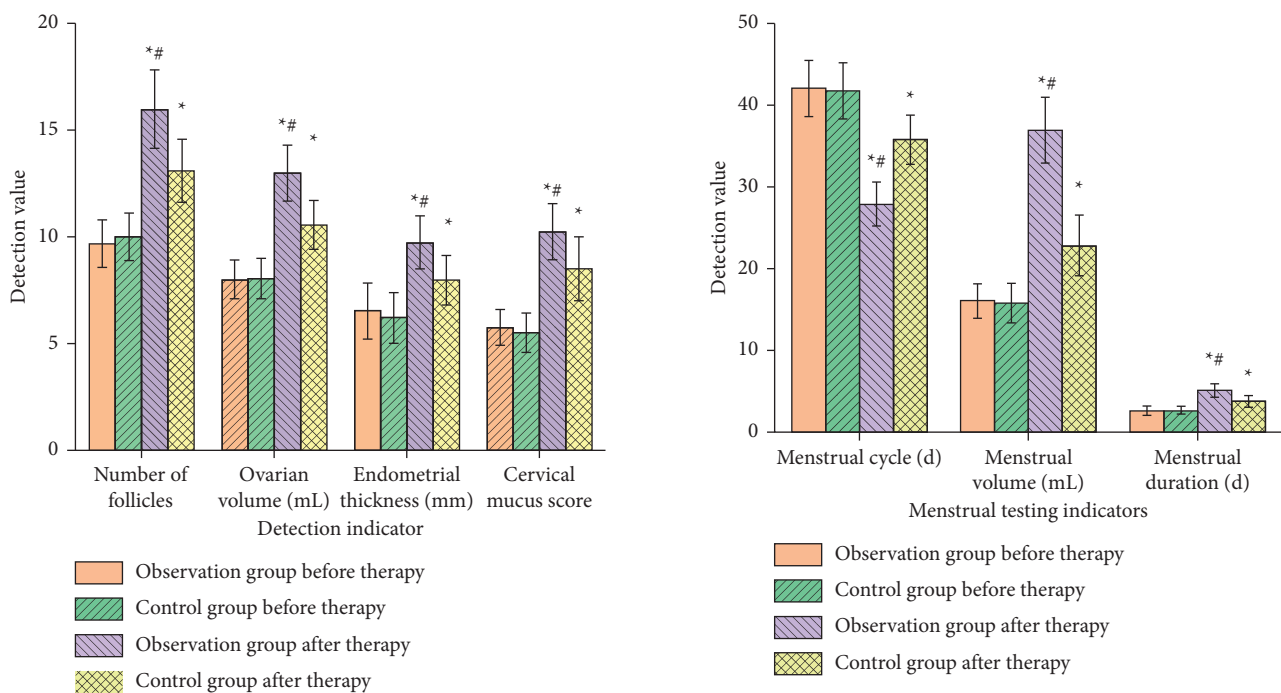


FIGURE 5: Comparison of physiological conditions between the two groups. *Note.* Compared with before treatment,  $*P < 0.05$ . Compared with the control group after treatment,  $^{\#}P < 0.05$ .

FIGURE 6: Comparison of menstrual conditions between the two groups. *Note.* Compared with before treatment,  $*P < 0.05$ . Compared with the control group after treatment,  $^{\#}P < 0.05$ .

the menstrual function soup auxiliary treatment, patients can effectively adjust the serum sex hormone levels, and related reproductive sex gland secretion function is obviously improved, which can effectively improve the patients with cervical mucus and menstruation, restore ovarian volume, improve endometrial thickness, increase the

number of follicles, and has less adverse reactions, worthy of clinical application.

### Data Availability

All figures and tables are included in this article.

## Conflicts of Interest

The authors declare that there are no conflicts of interest.

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## Research Article

# Alkannin Inhibits the Development of Ovarian Cancer by Affecting miR-4461

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**Background.** Previous studies have shown that alkannin has anticancer, anti-inflammatory, and antibacterial effects. However, the effect of alkannin in the development of ovarian cancer (OC) remains unknown. Therefore, this study aims to elucidate the function of alkannin in OC progression. **Methods.** RT-qPCR and western blot analysis were used to measure mRNA and protein expression. Cell viability and metastasis were detected by the CCK-8 assay, flow cytometry analysis, and transwell assay. **Results.** Alkannin had no cytotoxicity toward normal ovarian cells, but alkannin can inhibit cell proliferation and induce apoptosis in OC cells. In addition, alkannin inhibited cell migration and invasion and blocked EMT in OC. Besides, upregulation of miR-4461 was found in OC tissues and cells, which was regulated by alkannin. More importantly, miR-4461 can inverse the effects of alkannin on cell viability and metastasis in OC cells. **Conclusion.** Alkannin restrains cell viability, metastasis, and EMT in OC by downregulating miR-4461 expression.

## 1. Introduction

Ovarian cancer (OC) is one of the common malignant tumors of female reproductive organs, and its incidence is second only to cervical cancer and uterine body cancer [1]. OC is the most common epithelial cancer, followed by malignant germ cell tumors. Among them, the mortality rate of epithelial OC ranks first among all kinds of gynecological tumors [2], which can pose a serious threat to women's lives. OC is mostly asymptomatic in the early stage, and gastrointestinal symptoms such as lower abdominal discomfort, bloating, and loss of appetite may appear at the advanced stage [3]. The main treatment methods for OC include surgical resection, drug therapy, and radiation therapy. The overall prognosis of OC patients is poor, and OC is generally difficult to cure [4, 5]. The 5-year survival rate of early patients is higher. However, advanced patients are prone to recurrence and metastasis.

Some patients will experience adverse reactions after radiotherapy [6]. Therefore, it is necessary to find effective drugs with low side effects to treat OC.

Alkannin is a crystalline powder found in the roots of *Lithospermum erythrorhizon* Sieb. et Zucc. and *Arnebia euchroma* (Royle) Johnston [7]. Alkannin is often used to treat acute icteric or nonicteric hepatitis, chronic hepatitis, and flat warts [8]. In addition, alkannin is also effective for liver cirrhosis (ascites) and common warts [9]. Besides, alkannin has been reported to regulate tumorigenesis. For example, alkannin inhibited the growth and invasion of C6 glioma cells through the IQGAP/mTOR signaling pathway [10]. Alkannin restrained the growth, migration, and invasion of oral squamous carcinoma cells by regulating the microRNA-9/RECK axis [11]. However, the function of alkannin in the progression of OC has not been reported.

Many studies have shown that traditional Chinese medicine can regulate the development of human cancer by

mediating miRNAs [12, 13]. For example, apigenin suppressed the proliferation, invasion, and epithelial-mesenchymal transition (EMT) of cervical carcinoma cells by regulating the miR-152/BRD4 axis [14]. Curcumin inhibited prostate cancer progression by regulating the miR-30a-5p/PCLAF axis [15]. In addition, alkannin has been found to inhibit the growth of pancreatic cancer cells by downregulating miR-199a [16]. Here, the interaction between alkannin and miR-4461 was investigated in OC. miR-4461 has been reported to inhibit the tumorigenesis of renal cell carcinoma by targeting PPP1R3C [17]. However, miR-4461 was regarded as a potential onco-miRNA in OC by targeting PTEN [18]. These results indicate that miR-4461 is tissue specific.

In this study, the effects of alkannin on the viability and metastasis of OC cells were observed. And the regulatory mechanism of alkannin and miR-4461 was preliminarily discussed. This research lays an experimental and theoretical basis for the clinical treatment of OC.

## 2. Materials and Methods

**2.1. Clinical Tissues.** Forty-eight OC patients from Weifang People's Hospital participated in the study. Before the start of the experiment, we obtained informed consent of all OC patients. Except for surgery, OC patients did not receive any treatment. This study has been approved by the Ethics Committee of Weifang People's Hospital.

**2.2. Cell Culture.** Ovarian epithelial cells (HOSEpiC) or OC cell line SKOV3 were purchased from ATCC (Manassas, VA, USA). The growth conditions are 5% CO<sub>2</sub>, 37°C, and culture medium (90% RPMI-1640 + 10% FBS).

**2.3. Alkannin Treatment.** Alkannin (purity>95.0%, Sigma, St. Louis, MO, USA) was dissolved in methanol and diluted in the RPMI-1640 medium to concentrations of 0, 1, 5, 10, 15, and 20  $\mu$ M. HOSEpiC and SKOV3 cells were incubated with different doses of alkannin for 12 h. SKOV3 cells were treated with 10  $\mu$ M alkannin for 0, 2, 4, 6, 8, 10, 12, 14, and 16 h to detect the effects of alkannin treatment time.

**2.4. Cell Transfection.** miR-4461 mimics and inhibitor were synthesized by RiboBio (Guangzhou, China). They were transfected into alkannin-treated SKOV3 cells using Lipofectamine 2000 (Invitrogen, Carlsbad, USA), respectively.

**2.5. RT-qPCR.** Total RNA extraction was performed using TRIzol reagent (Invitrogen). The cDNA solution was synthesized using the miScript II RT Kit (Qiagen, Valencia, CA, USA). RT-qPCR was performed on an ABI 7500 Fast Real-Time PCR system using miScript SYBR Green PCR Kit (Qiagen). miR-4461 was normalized to the U6 internal reference. The primer sequences used were as follows: miR-4461, forward: 5'-GAG TGTCGGGGCAGCTCAGT-3' and reverse: 5'-GCAGGGTCCGAGGTATTC-3'; U6, forward: 5'-GCTTCGGCAGCACATATACTAAAAT-3' and reverse:

5'-CGCTTCACGAATTTGCGTGTCAT-3'. Their expressions were quantified using the  $2^{-\Delta\Delta ct}$  method.

**2.6. CCK-8 Assay.** SKOV3 cells were added in a 96-well plate and incubated for 12 h. Then, the culture was added with different concentrations of alkannin and incubated for 0, 2, 4, 6, 8, 10, 12, 14, and 16 h. Next, 10  $\mu$ L of CCK-8 solution was added to incubate these cells for 1 h. Finally, the wavelength of 450 nm in each well was measured on a Microplate Reader (ELx800, BioTek Instruments, Winooski, VT).

**2.7. Flow Cytometry Analysis.** The apoptosis of SKOV3 cells was detected after treatment with alkannin (10  $\mu$ M) for 24 h. Following the instructions of Annexin V-Phycoerythrin (PE) Kit (Beyotime Biotechnology, Shanghai, China), SKOV3 cells were washed with PBS. After discarding the supernatant, the cells were resuspended in 100  $\mu$ L of binding buffer. 4  $\mu$ L Annexin V-FITC and 5  $\mu$ L PI staining solution were added to each tube. After 15 minutes of incubation in the dark, the apoptosis rate was detected by flow cytometry.

**2.8. Transwell Assay.** The membrane on the bottom of the transwell was coated with Matrigel. The cells were adjusted to a density of  $5 \times 10^5$  cells/mL with serum-free medium. 200  $\mu$ L of cell suspension was added to the upper chamber of the transwell. 500  $\mu$ L of the culture medium containing 20% FBS was added to the lower chamber. The cells were cultured for another 12 h, and the transwell chamber was taken out and washed twice with PBS. The upper chamber cells were wiped with cotton swabs, fixed with methanol for 15 min, and stained with 0.1% crystal violet at room temperature for 30 min. The number of invaded cells was counted under the microscope. Matrigel is not used in the migration experiment, and the rest of the steps are the same as the invasion experiment.

**2.9. Western Blot Analysis.** RIPA lysis buffer was used to obtain protein samples. Next, 10% SDS-PAGE was used to separate 25  $\mu$ g of protein. Protein samples were transferred to the PVDF membrane. Blocked with 5% skimmed milk, the protein samples were incubated with vimentin, E-cadherin, N-cadherin, and GAPDH primary antibodies (Abcam, Cambridge, MA, USA) at 4°C overnight. Then, protein samples were incubated with HRP-conjugated secondary antibody (Abcam, USA) for 1 h. Finally, ECL (ECL, Pierce) was used to measure protein expression. Quantity One 4.52 analysis software was used to measure the gray value of the band. Relative expression of target protein (IOD) = gray value of the target protein/gray value of internal reference GAPDH.

**2.10. Statistical Analysis.** All experiments were repeated three times. Data are expressed as mean  $\pm$  SD and analyzed by SPSS 18.0 or GraphPad Prism 6. One-way ANOVA with Bonferroni post hoc test was used to analyze differences between groups.  $P < 0.05$  is considered as a statistically significant difference.

### 3. Results

**3.1. Alkannin Inhibits Cell Proliferation and Induces Apoptosis in OC.** In order to explore the effect of alkannin on the viability of OC cells, CCK-8 assay was performed. The results showed that alkannin at concentrations of 5 ( $P < 0.05$ ), 10 ( $P < 0.01$ ), 15 ( $P < 0.01$ ), and 20  $\mu\text{M}$  ( $P < 0.01$ ) suppressed cell proliferation in SKOV3 cells (Figure 1(a)). Because the 50% inhibitory effect of alkannin on cell viability appears at about 10  $\mu\text{M}$ , therefore, 10  $\mu\text{M}$  alkannin was used for the following experiments. Next, we found that the decline in SKOV3 viability caused by alkannin appeared in a time-dependent pattern. The best-fit value for the variable slope is approximately 12 h (Figure 1(b)). Hence, SKOV3 cells were treated with 10  $\mu\text{M}$  alkannin for 12 h in the following experiments. In addition, the viability of ovarian epithelial cells HOSEpiC after treatment with 0, 1, 5, 10, 15, and 20  $\mu\text{M}$  alkannin was detected. We found that the cell viability of HOSEpiC cells did not change significantly ( $P > 0.05$ , Figure 1(c)). The result indicates that alkannin is not cytotoxic to normal ovarian cells. Moreover, flow cytometry analysis showed that alkannin significantly induced apoptosis ( $P < 0.01$ , Figure 1(d)). All these results demonstrate that alkannin can inhibit cell proliferation and induce apoptosis in OC.

**3.2. Alkannin Inhibits the Migration and Invasion of OC Cells.** To further explore the function of alkannin in OC, transwell assay was performed to measure cell migration and invasion. We found that alkannin inhibited cell migration in SKOV3 cells ( $P < 0.01$ , Figure 2(a)). Moreover, the inhibitory effect of alkannin on cell invasion was also found in SKOV3 cells ( $P < 0.01$ , Figure 2(b)). In addition, the effect of alkannin on EMT was also investigated in SKOV3 cells. Western blot analysis showed that alkannin enhanced the expression level of E-cadherin and inhibited N-cadherin and vimentin expressions in SKOV3 cells ( $P < 0.01$ , Figure 2(c)). The above results indicate that alkannin inhibits cell metastasis and blocks EMT in OC.

**3.3. miR-4461 Expression Is Upregulated in OC Tissues and Cells.** In order to confirm whether miR-4461 is involved in the progression of OC, the expression of miR-4461 in OC tissues and cells was evaluated. RT-qPCR showed that miR-4461 expression in OC tissues was higher than that in normal tissues ( $P < 0.01$ , Figure 3(a)). Compared with ovarian epithelial cells HOSEpiC, miR-4461 in SKOV3 cells was upregulated ( $P < 0.01$ , Figure 3(b)). In addition, we found that miR-4461 expression in SKOV3 cells treated with alkannin was significantly reduced ( $P < 0.01$ , Figure 3(c)). These findings confirm the abnormal expression of miR-4461 in OC tissues and cells, indicating that miR-4461 may play an important role in the pathogenesis of OC.

**3.4. Alkannin Restrains the Progression of OC by Decreasing miR-4461 Expression.** Finally, miR-4461 mimics and inhibitor were transfected into SKOV3 cells treated with alkannin. RT-

qPCR showed that miR-4461 mimics increased its expression, while the miR-4461 inhibitor decreased its expression in SKOV3 cells treated with alkannin ( $P < 0.01$ , Figure 4(a)). Functionally, CCK-8 assay showed that miR-4461 overexpression promoted cell proliferation in alkannin-stimulated SKOV3 cells. However, downregulation of miR-4461 showed the opposite effect ( $P < 0.01$ , Figure 4(b)). At the same time, miR-4461 overexpression inhibited alkannin-stimulated SKOV3 cell apoptosis, while miR-4461 downregulation aggravated cell apoptosis ( $P < 0.01$ , Figure 4(c)). Besides, cell migration and invasion were both augmented by miR-4461 overexpression and inhibited by miR-4461 downregulation in alkannin-stimulated SKOV3 cells ( $P < 0.01$ , Figures 4(d) and 4(e)). The above results corroborate that alkannin inhibits the progression of OC by reducing miR-4461 expression (Figure 5).

### 4. Discussion

Commonly used drugs for OC are some chemotherapy drugs; the main drugs are cisplatin, carboplatin, paclitaxel, cyclophosphamide, and etoposide [19]. However, while chemotherapeutic drugs inhibit the proliferation of tumor cells, they also have a great killing effect on normal cells [20], which seriously affects their clinical application and efficacy. Therefore, the development of effective treatments for OC with fewer side effects is of great significance to women's health. After chemotherapy, the patient's body is in a state of qi and blood deficiency and is vulnerable to virus invasion [21]. TCM treatment starts from the whole and can improve the body's environment, improve immunity and disease resistance, and prevent tumor recurrence and metastasis [22]. In recent years, plant extracts have received widespread attention in cancer treatment due to their small side effects.

A large number of literature studies reported that plant extracts have a positive effect on inhibiting the viability of cancer cells. For instance, farrerol induced cancer cell death through ERK activation in SKOV3 cells [23]. Scutellarein induced apoptosis and inhibited the proliferation, migration, and invasion of OC cells by blocking EZH2/FOXO1 signaling [24]. Liu et al. reported that alkannin inhibited the viability, adhesion, invasion, and migration of human gastric cancer cell line MGC-803 through the toll-like receptor 2/ nuclear factor- $\kappa$ B pathway [25]. Alkannin can also cause cell-cycle arrest and induce apoptosis by regulating the EGFR-NF signaling pathway in human epidermoid carcinoma A431 cells [26]. Similar to the above results, we also found that alkannin can inhibit cell proliferation and induce apoptosis in OC.

The metastasis of cancer cells plays an important role in the development of cancer. Many plant extracts have been found to suppress the metastasis of cancer cells. In this study, alkannin was found to inhibit cell migration, invasion, and EMT in OC. Similar to our results, Jang et al. proposed that alkannin prevents the migration and invasion of human breast cancer cells by inhibiting the activation of matrix metalloproteinase-9 [27]. The inhibitory effect of alkannin on cell metastasis has also been found in colorectal cancer [28]. More importantly, alkannin induced apoptosis and

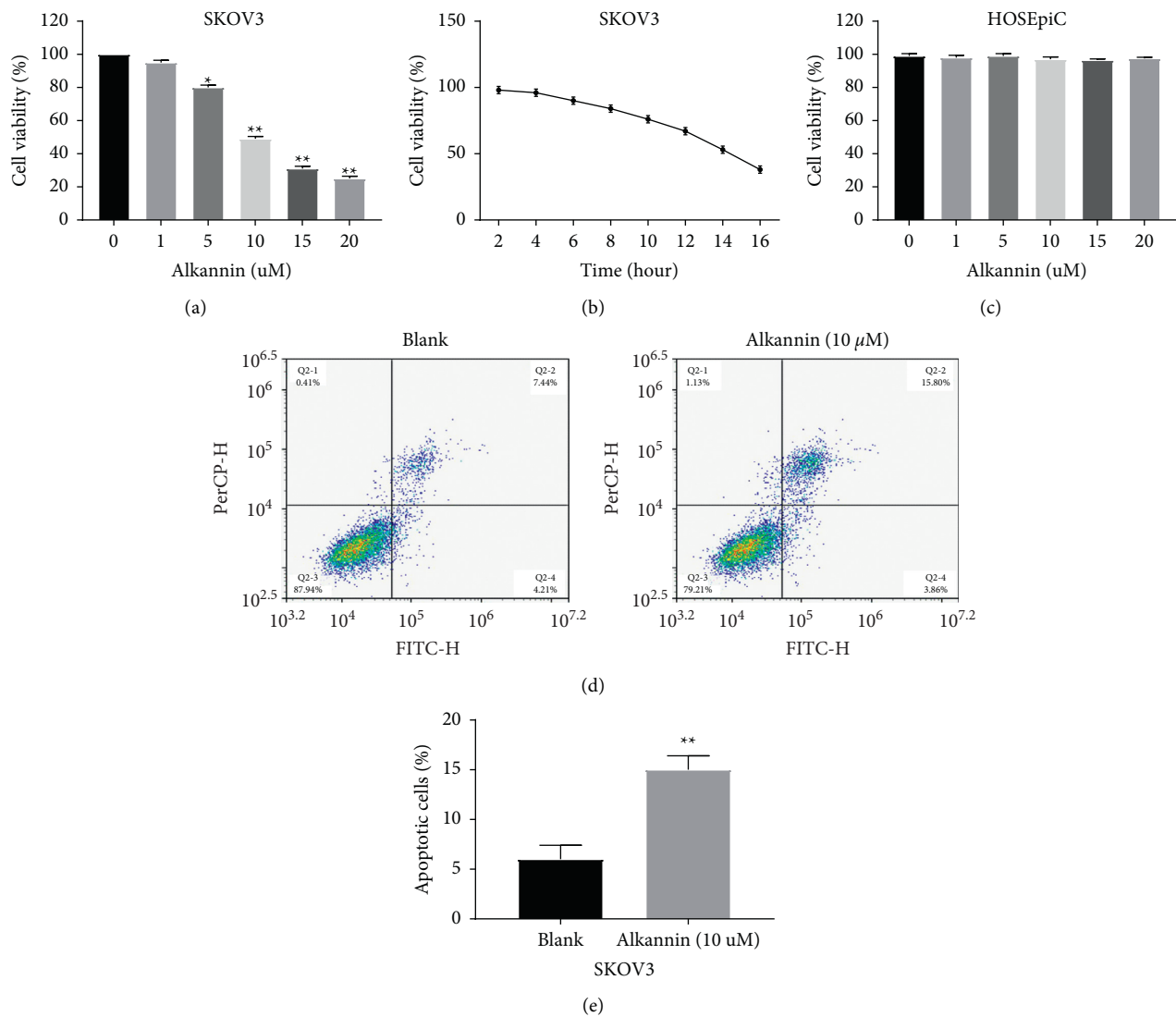


FIGURE 1: Alkannin inhibits cell proliferation and induces apoptosis in OC. (a) The viability of SKOV3 cells treated by alkannin at concentrations of 0, 1, 5, 10, 15, and 20  $\mu$ M for 12 h was detected. (b) SKOV3 cells were treated by 10  $\mu$ M alkannin for 0, 2, 4, 6, 8, 10, 12, 14, and 16 h. (c) The viability of ovarian epithelial cells HOSEpiC treated by alkannin at concentrations of 0, 1, 5, 10, 15, and 20  $\mu$ M for 12 h was detected. (d) Cell apoptosis was detected in SKOV3 cells treated by alkannin (10  $\mu$ M) for 12 h. \* $P < 0.05$  and \*\* $P < 0.01$ .

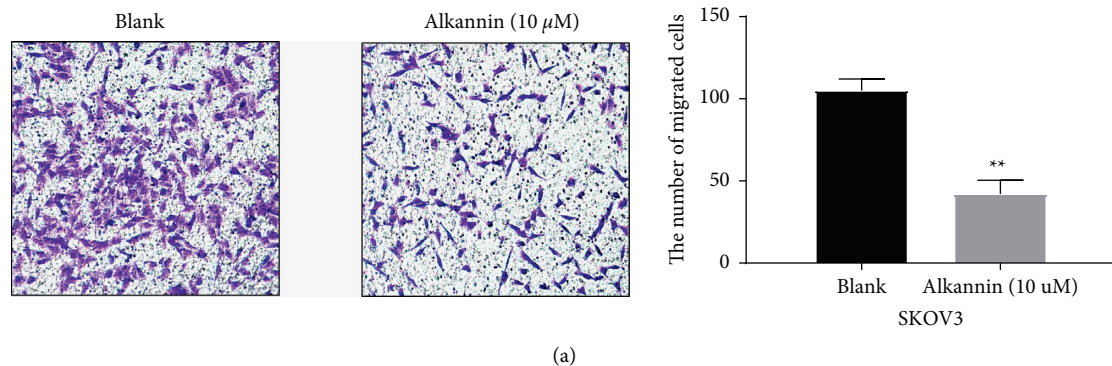


FIGURE 2: Continued.



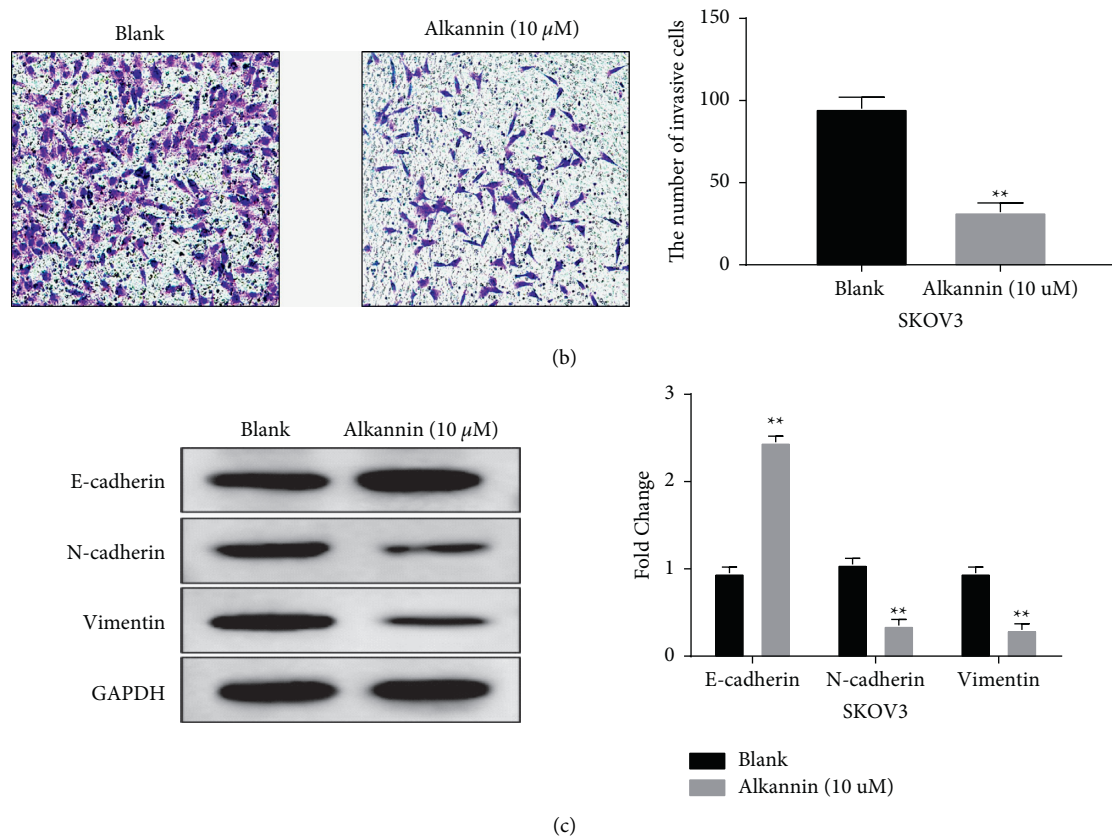


FIGURE 2: Alkannin inhibits the migration and invasion of OC cells. (a, b) Cell migration and invasion were detected in SKOV3 cells treated by alkannin (10 μM) for 12 h (magnification, 200x). (c) The expression of E-cadherin, N-cadherin, and vimentin was measured in SKOV3 cells treated by alkannin (10 μM) for 12 h \*\* $P < 0.01$ .

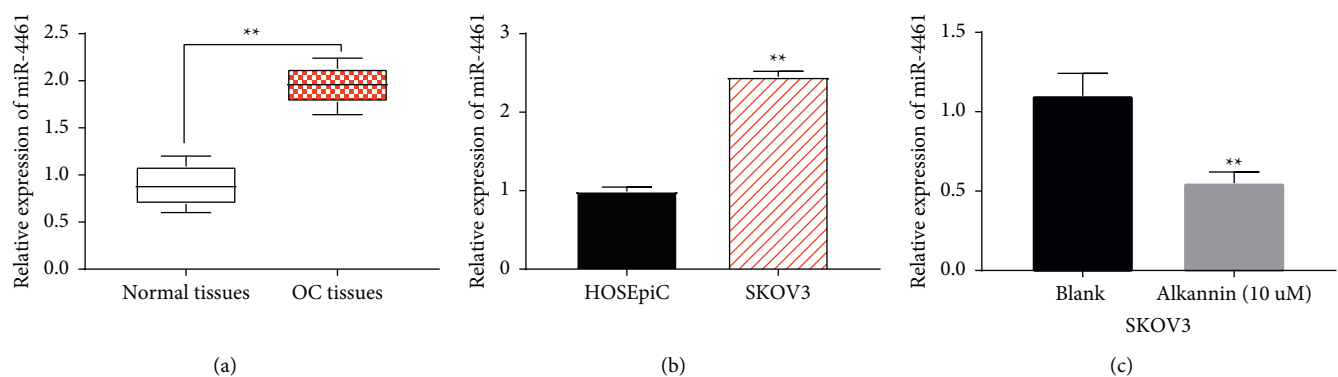


FIGURE 3: miR-4461 expression is upregulated in OC tissues and cells. (a) The expression level of miR-4461 was determined by RT-qPCR in OC tissues and normal tissues ( $n = 48$ ). (b) miR-4461 expression was detected in HOSEpiC and SKOV3 cells. (c) miR-4461 expression was assessed in SKOV3 cells treated by alkannin (10 μM) for 12 h \*\* $P < 0.01$ .

inhibited the migration of OC cells by inhibiting the phosphorylation of Src and FAK [29], which is consistent with our results. Different from the above studies, we found that alkannin plays an antitumor effect in OC by down-regulating miR-4461 [18]. Moreover, miR-4461 can promote

cell growth and metastasis in OC. This also confirmed the inhibitory effect of alkannin in the tumorigenesis of OC. However, our conclusion has not been verified by animal experiments. *In vivo* experiment will be conducted in the future.

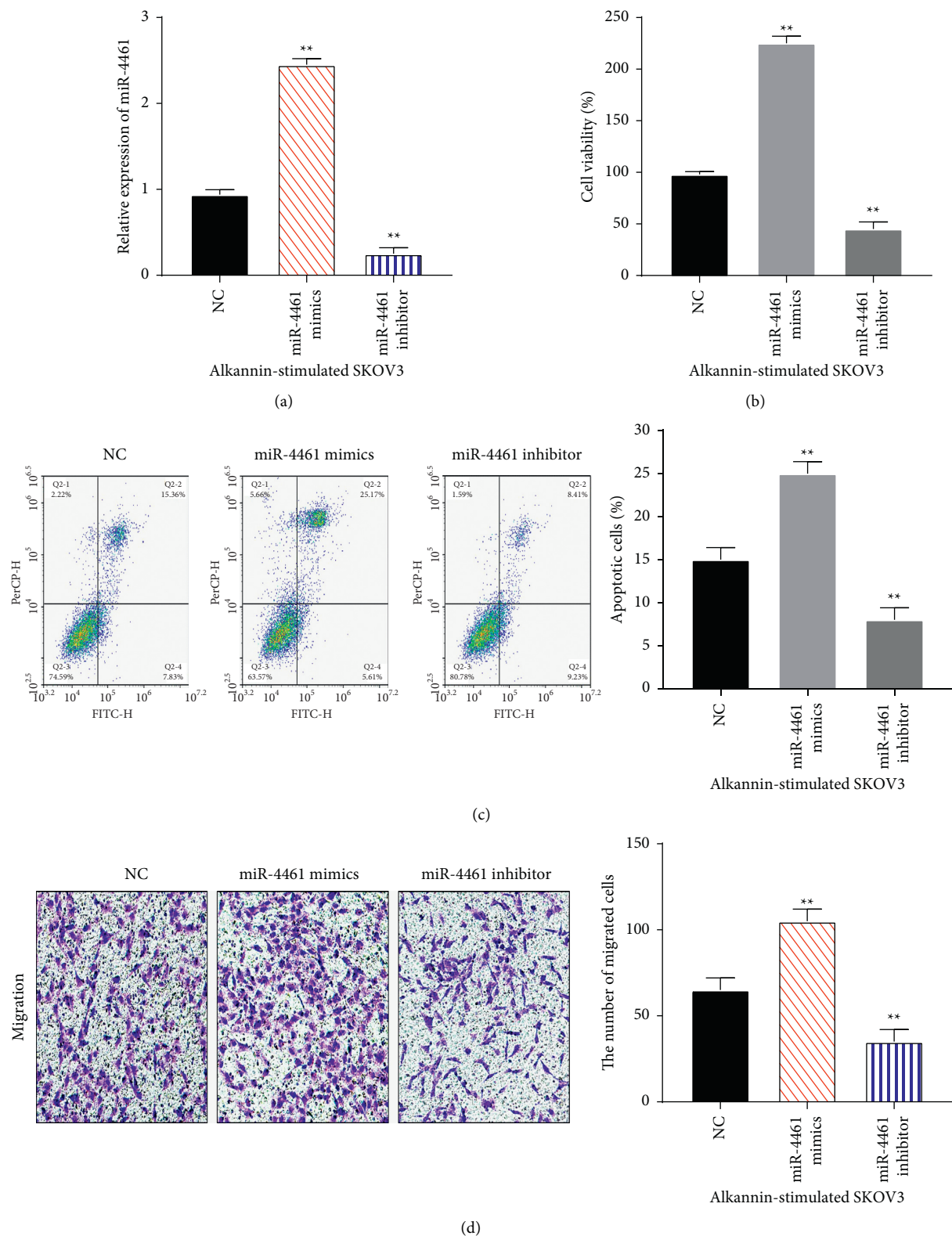


FIGURE 4: Continued.

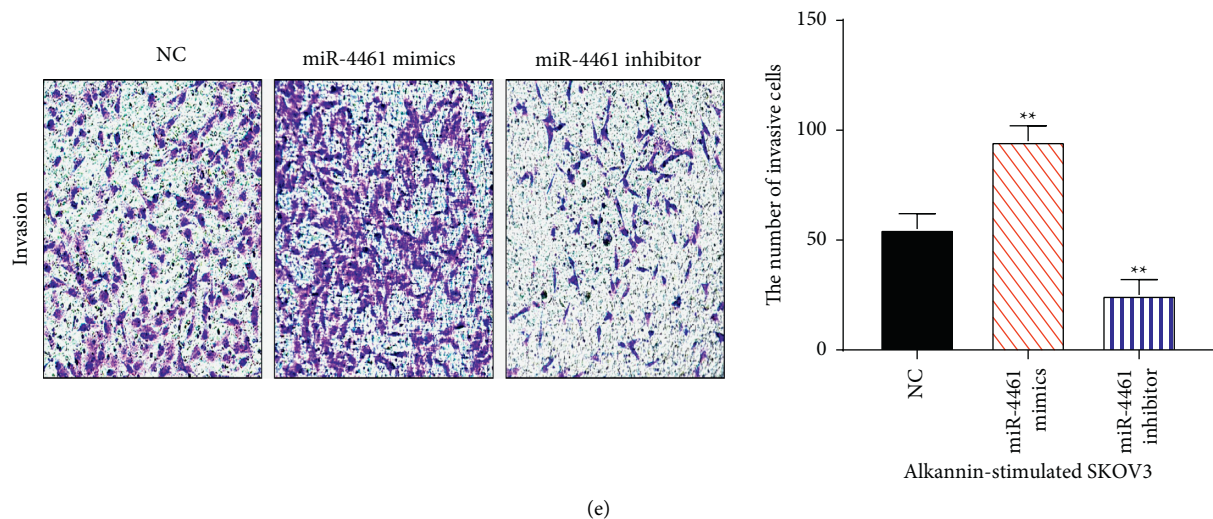


FIGURE 4: Alkannin restrains the progression of OC by decreasing miR-4461 expression. (a) miR-4461 expression was detected in alkannin-stimulated SKOV3 cells with miR-4461 mimics or inhibitor. (b, c) Cell proliferation and apoptosis were assessed in alkannin-stimulated SKOV3 cells with miR-4461 mimics or inhibitor. (d, e) Cell migration and invasion were detected in alkannin-stimulated SKOV3 cells with miR-4461 mimics or inhibitor (magnification, 200x). \*\* $P < 0.01$ .

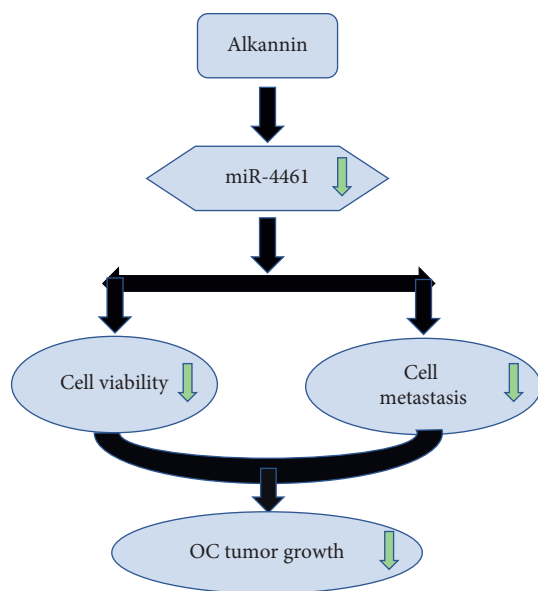


FIGURE 5: Alkannin inhibits cell viability and metastasis in OC by decreasing miR-4461 expression.

## 5. Conclusion

In summary, this study shows that alkannin inhibits cell viability, metastasis, and EMT in OC by inhibiting miR-4461 expression. And alkannin can also prevent EMT in the progression of OC. However, the specific regulatory mechanism of alkannin in OC is still largely unknown. Therefore, more thorough experiments are still needed to corroborate this problem.

## Data Availability

The datasets used during the present study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effects of Psychological Intervention on Perioperative Quality of Life and Serum PSA and FPSA Levels of Patients with Prostate Cancer Treated with Integrated Traditional Chinese and Western Medicine

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**Objective.** To observe the effects of psychological intervention on the perioperative quality of life and serum prostate-specific antigen (PSA) and free PSA (FPSA) levels in patients with prostate cancer treated with integrated traditional Chinese and Western medicine. **Method.** A total of 208 prostate cancer patients were selected and randomly divided into a study group with 104 cases and a control group with 104 cases. The control group received a plan of basic nursing combined with integrated traditional Chinese and Western medicine, and the study group received psychological intervention on the basis of the control group. Negative emotion, pain degree, quality of life, maximum urine flow rate, residual urine volume, International Prostate Symptom Score (IPSS), and incidence of adverse reactions were compared between the two groups before and after the treatment. The levels of PSA and FPSA and the long-term efficacy of the two groups of patients before and after treatment were compared. **Results.** After nursing, Hamilton Anxiety Scale (HAMA) score, Hamilton Depression Scale (HAMD) score, pain degree, maximum urine flow rate, residual urine volume, IPSS score, emotional function, social function, role function, and physical function scores of patients in two groups were decreased, and the decrease was more significant in the study group. After treatment, serum PSA and FPSA levels in the study group were obviously lower than those in the control group. The two-year cumulative survival rate of the study group was higher than that of the control group. There was no significant difference in the cognitive function score and incidence of adverse reactions between the two groups. **Conclusion.** Psychological intervention combined with traditional Chinese and Western medicine in the treatment of prostate cancer can effectively improve the patient's psychological state, reduce the degree of pain in patients, improve the therapeutic effect and the quality of life of patients, and significantly reduce serum PSA and FPSA levels, which could lead to a prolonged life.

## 1. Introduction

Prostate cancer is a common multiple malignant tumor in men. Its clinical manifestations include dysuria, slow urine

flow, incontinence, fine urinary line, hematuria, impotence, and other symptoms, and it is highly invasive and prone to metastasis [1]. In recent years, the incidence of prostate cancer in China has shown the characteristics of increasing



incidence, rapid disease progression, higher mortality, and younger, posing a severe threat to the life and health of patients [1]. Prostate cancer can be caused by many factors, such as family genetics and bad eating habits and living habits [2]. At the time of clinical diagnosis, many patients were already in the advanced stage when the disease was diagnosed because there were no clinical symptoms at the early stage, missing the best opportunity for radical surgery [3]. In addition, with the development of the disease, the tumor gradually increased, bringing some challenges to the treatment of prostate cancer [3]. Transurethral green laser vaporization of the prostate has a good effect on prostate cancer treatment, effectively relieving urethral obstruction and alleviating patients' clinical symptoms [4]. However, Lai et al. suggested that this surgical treatment still cannot completely remove the tumor tissue, and the remaining tissue can continue to grow under the stimulation of various factors, causing the urinary tract to be compressed again [5]. And patients in the perioperative period usually have anxiety, fear, and other emotions, affecting the smooth operation and postoperative recovery [6]. Thus, effective psychological nursing is crucial. Traditional Chinese medicine (TCM) is an important means of treating diseases in China. It contains rich practical experience and medical technology of ancient medical scientists, and TCM has made great progress in the treatment of prostate cancer in modern medicine [7]. Prostate cancer belongs to the category of "uroschesis," "stranguria," and "hematuria" in TCM, and its treatment should detoxicate and abscise mass, activate blood to remove blood stasis, and strengthen body resistance to consolidate constitution [8]. Studies have shown that the combination of traditional Chinese and Western medicine has a better therapeutic effect on the treatment of prostate cancer [9]. In this study, psychological intervention combined with integrated traditional Chinese and Western medicine was used to treat prostate cancer, aiming to observe its influence on perioperative quality of life and serum indicators of prostate cancer patients. The report is as follows.

## 2. Materials and Methods

**2.1. Normal Information.** A total of 208 prostate cancer patients admitted at Weifang People's Hospital, Weifang, China, from July 2016 to July 2018 were selected and randomly divided into a study group and a control group with 104 cases each, all of which were confirmed by pathological diagnosis. The age range in the study group was 53–77 years, with an average of  $66.53 \pm 8.06$  years, and the course of illness was 7–28 months, with an average of  $11.83 \pm 4.76$  months. Clinical staging: 23 cases in stage I, 48 cases in stage II, and 33 cases in stage III. There were 10 cases of squamous cell carcinoma and 94 cases of adenocarcinoma. Distant metastasis occurred in 71 cases, and no distant metastasis occurred in 33 cases. The age range in the control group was 55–76 years, the average age was  $65.24 \pm 8.83$  years, the course of the disease was 6 to 30 months, and the average course of the disease was  $11.28 \pm 4.35$  months. Clinical staging: 26 cases in stage I, 47 cases in stage II, and 31 cases in

stage III. There were 7 cases of squamous cell carcinoma and 97 cases of adenocarcinoma. Remote metastasis occurred in 69 cases, and no distant metastasis occurred in 35 cases. There was no statistically significant difference in clinical data between the two groups of patients in terms of age, course of the disease, clinical stage, and remote metastasis, and they were comparable. This study was approved by the ethics committee of Weifang People's Hospital, Weifang, China. This study was conducted under the Declaration of Helsinki.

**2.2. Inclusion and Exclusion Criteria.** Inclusion criteria were as follows: (1) all meet the relevant diagnostic criteria of prostate cancer in the "Guidelines for the Diagnosis and Treatment of Urological Diseases in China" [10] and are confirmed by B-assisted prostate biopsy; (2) age <80 years; (3) IPSS scores are >8 points; (4) patients signed an informed consent form. Exclusion criteria were as follows: (1) patients with severe heart, lung, liver, and other organ dysfunction and neurological diseases; (2) patients with other malignant tumors; (3) patients with lymphatic system, bone marrow system, and autoimmune diseases; (4) patients allergic to the drugs used in this study.

**2.3. Treatment Method.** Patients in the control group were given basic nursing combined with integrated traditional Chinese and Western medicine treatment, and patients in the study group were treated with psychological intervention on the basis of the control group.

**2.4. Basic Nursing.** Dietary taboos information was provided and explained to patients and their family members. Clean and tidy ward conditions were provided for patients, and patients were guided to use drugs rationally.

**2.5. Integrated Traditional Chinese and Western Medicine Treatment Methods.** After the patient is admitted at the hospital, detailed understanding of his personal data, time of illness, emotional state, and family relationship should be known in detail to evaluate patients' ability of daily living and psychological state. For patients with paranoia, depression, fear, anxiety, and resistance, psychological quantitative assessment should be carried out in time, and the details should be recorded. Western medicine treatment: patients were given flutamide tablets orally, 3 times per day, 250 mg per time. TCM treatment: the main ingredients of TCM decoction include *Polygonum* 10 g, *Astragalus* 30 g, *Hedyotis diffusa* herba 15 g, *Curcuma* 10 g, *Scutellaria baicalensis* 35 g, whole scorpion 12 g, *Polygonatum* 16 g, *Achyranthes bidentata* 16 g, *Polygonum cuspidatum* 15 g, Rhizoma *Atractylodis Macrocephalae* 11 g, and *Poria cocos* 10 g. The aforementioned TCM was decocted to 200 ml, 1 dose/d (in the morning and evening, respectively), and the course of treatment was 3 months.



**2.6. Psychological Intervention Treatment Methods.** (1) Pre-operative nursing: the nurse actively communicates with the patient and explains the disease situation, treatment methods, the operation principle, anesthesia methods, and precautions to the patient and family members, so as to eliminate the patient's worries, reduce the patient's nervousness, and enable the patient to receive treatment in a good state of mind. In the evening, one day before the operation, the patient was told to eat easy-to-digest food for dinner, fast for 12 hours, and water restriction for 4 hours before the operation, allowing the patient to rest as soon as possible to ensure sleep. For some patients with poor sleep, appropriate sedative and hypnotic drugs can be used. (2) Postoperative nursing: the nurse guides the family members or the caregiver to provide a nutritious and reasonable diet and assists the patient with moderate exercise. The nurse patiently urges the patient to strictly follow the doctor's advice and take medicine on time. When providing nursing services to patients, they should be active, enthusiastic, sincere, and patient and enhance patients' compliance with treatment. A quiet, comfortable, and safe treatment environment was provided to patients. Family members, relatives, and friends of patients should be educated on hygiene and psychology, are required to understand prostate cancer and the patient's condition, not irritate or demand the patient, and provide financial support to make the patient feel the warmth of the family. Regular lectures are held to explain some successful cases of treatment and articles that inspire the soul to enhance the confidence and determination of patients to overcome the disease. (3) Continuing nursing: after the patient is discharged from the hospital, a monthly follow-up visit should be conducted to understand the patient's medication and recovery status. If there are adverse reactions and poor medication compliance, correct guidance should be given to help the patient build confidence in treatment. The evaluation, care, treatment, follow-up, and other information of each patient were organized and archived.

**2.7. Observation Index.** (1) The negative emotional state of the two groups of patients before and after nursing was compared. The evaluation is based on the HAMA and HAMD scales [11], with a total score of 0 to 56 points. The lower the score, the milder the patient's anxiety and depression. (2) The pain degree and quality of life of the two groups of patients before and after nursing were compared. The visual analogue scoring (VAS) method was used to evaluate the pain degree of the two groups [12]. The score ranged from 1 to 10 points. The higher the score, the more obvious the pain degree. The European QLQ-C30 functional scale was used to evaluate the recovery of the two groups of patients from the five dimensions of emotional function, cognitive function, social function, role function, and physical function [13]. Each item was scored 100 points. The higher the score, the better the corresponding functional recovery. (3) The PSA and FPSA indexes of the two groups before and after treatment were compared. In the morning, 5 mL of venous blood from the

patient's elbow was collected on an empty stomach, centrifuged at 3500 r/min for 15 minutes, and the upper serum was taken and stored in a low-temperature refrigerator at  $-60^{\circ}\text{C}$  for testing. Enzyme-linked immunoassay (ELISA) was used to detect the serum PSA and FPSA contents of patients. The kit was purchased from the American Biotech Reagent Co., Ltd. The operation steps were strictly in accordance with the instructions. (4) The maximum urine flow rate, residual urine volume, and prostate symptom scores (International Prostate Symptom Score, IPSS) were compared between the two groups [14]. The maximum urine flow rate and residual urine volume of the two groups were counted before and after nursing, and the IPSS was used for evaluation. The score was proportional to the severity of prostate symptoms: 0–7 points: mild; 8–19 points: moderate; 20–35 points: severe. (5) The long-term efficacy of the two groups of patients was compared. Follow-up for two years, once a month, and the two-year cumulative survival rate of the two groups were recorded and calculated. (6) The incidence of adverse reactions (including gastrointestinal reactions, liver damage, breast development, infections, and bladder spasm) between the two groups was compared.

**2.8. Statistical Analysis.** SPSS 22.0 software performs statistical analysis on the data. Measurement data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), and comparison between groups was performed by paired sample *t*-test. The enumeration data were expressed in terms of the number of cases and the rate (%), and the  $\chi^2$  test was used for comparison between groups. The difference is statistically significant with  $p < 0.05$ .

### 3. Results

**3.1. Comparison of Negative Emotions between Two Groups of Patients before and after Nursing.** After one day of nursing, there was no significant difference in the HAMA score and HAMD score between the two groups. After 30 days, 60 days, and 90 days of nursing, the HAMA score and HAMD score of the two groups decreased, and the scores of patients in the study group decreased more significantly than the control group ( $p < 0.05$ ) (Figure 1).

**3.2. Comparison of Pain Degree and Quality of Life between Two Groups before and after Nursing.** Before nursing, there was no significant difference in pain degree and the scores of the quality of life between the two groups. After 30 days, 60 days, and 90 days of nursing, the pain degree of the two groups decreased, and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ ) (Table 1). After nursing, there was no statistically significant difference in cognitive function scores between the two groups, and there was a decline in emotional function, social function, role function, and physical function scores, and the decline in the study group was even more significant ( $P < 0.05$ ) (Table 2).

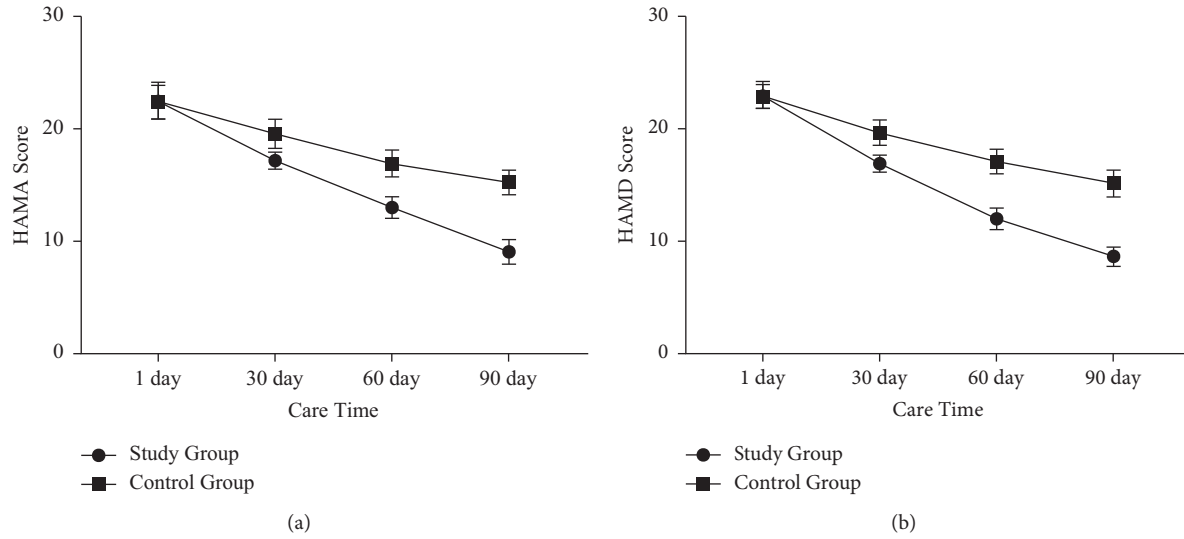


FIGURE 1: Comparison of negative emotions between the two groups of patients before and after nursing. (a) The comparison of HAMA scores between the two groups of patients before and after nursing. (b) The comparison of HAMD scores between the two groups of patients before and after nursing.

TABLE 1: Comparison of pain degree between the two groups of patients before and after nursing ( $\bar{x} \pm s$ ).

Group	Cases	Before nursing	Nursing for 30 days	Nursing for 60 days	Nursing for 90 days
Study	104	8.03 ± 1.14	5.74 ± 0.86	3.26 ± 0.69	1.85 ± 0.56
Control	104	8.17 ± 1.08	6.78 ± 0.94	5.52 ± 0.88	4.81 ± 0.93
<i>t</i>		0.026	4.957	7.660	12.381
<i>P</i>		0.743	0.001	<0.001	<0.001

TABLE 2: Comparison of the quality of life of the two groups of patients before and after care ( $\bar{x} \pm s$ ).

Project	Time	Study	Control	<i>t</i>	<i>P</i>
Emotional function	Before nursing	52.37 ± 7.65	53.14 ± 7.87	0.324	>0.05
	After nursing	78.54 ± 8.53* <sup>△</sup>	61.94 ± 7.15*	10.374	<0.05
Cognitive function	Before nursing	63.54 ± 6.63	65.42 ± 6.26	0.463	>0.05
	After nursing	66.87 ± 6.91	67.25 ± 7.12	0.527	>0.05
Social function	Before nursing	55.68 ± 5.62	54.34 ± 5.73	0.297	>0.05
	After nursing	78.56 ± 7.88* <sup>△</sup>	66.48 ± 6.54*	7.872	<0.05
Role function	Before nursing	53.43 ± 6.71	54.29 ± 6.82	0.782	>0.05
	After nursing	73.62 ± 7.53* <sup>△</sup>	62.85 ± 6.31*	4.965	<0.05
Physical function	Before nursing	51.03 ± 5.58	51.27 ± 5.63	0.164	>0.05
	After nursing	68.65 ± 6.34* <sup>△</sup>	59.56 ± 6.17*	7.313	<0.05

Compared with the same group before treatment, \* $P < 0.05$ ; compared with the control group,  $\Delta P < 0.05$ .

**3.3. Serum PSA and FPSA Levels Were Compared between the Two Groups.** After 1 day of treatment, there was no significant difference in serum PSA and FPSA levels between two groups (Figures 2 and 3). With the increase of treatment time, the levels of the two indexes decreased (Figures 2 and 3). After 90 days of treatment, serum PSA and FPSA levels in the study group were obviously decreased versus the control group (Figures 2 and 3).

**3.4. Comparison of Maximum Urine Flow Rate, Residual Urine Volume, and IPSS Score between Two Groups before and after Nursing.** Before nursing, there were no significant

differences in maximum urine flow rate, residual urine volume, and IPSS score between two groups (Table 3). After nursing, each index was decreased, and the decrease in the study group was more obvious than the control group (Table 3).

**3.5. Comparison of the Incidence of Adverse Reactions between the Two Groups.** In the study group, 23 patients had gastrointestinal reactions, 21 had liver damage, 17 had breast development, 6 had an infection, and 2 had bladder spasm (Table 4). In the control group, there were 27 cases of

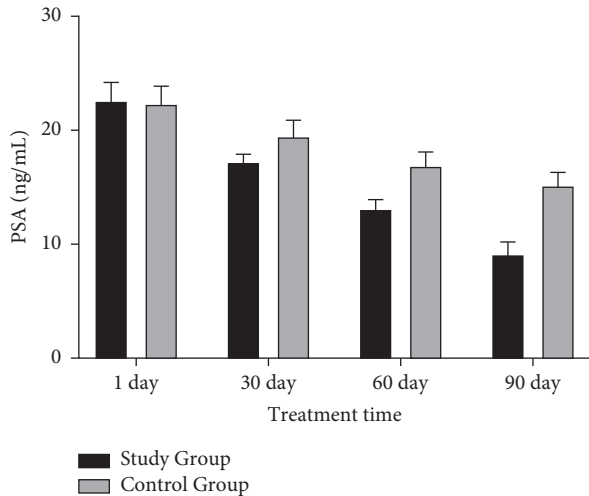


FIGURE 2: Comparison of PSA levels between the two groups before and after treatment.

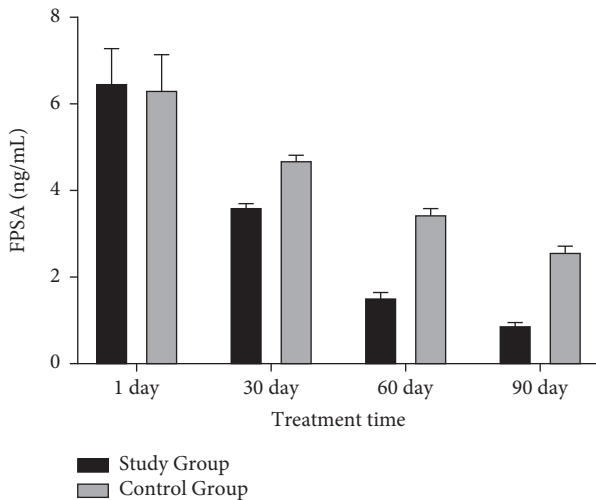


FIGURE 3: Comparison of FPSA levels between the two groups before and after treatment.

TABLE 3: Comparison of maximum urine flow rate, residual urine volume, and IPSS score between the two groups before and after nursing ( $\bar{x} \pm s$ ).

Indexes	Study	Control	<i>t</i>	<i>P</i>
<i>Maximum urine flow rate (ml/s)</i>				
Before nursing	9.54 ± 3.67	9.71 ± 3.59	0.234	>0.05
After nursing	20.13 ± 3.34	13.46 ± 3.28	10.315	<0.05
<i>Residual urine volume (ml)</i>				
Before nursing	47.63 ± 7.89	48.15 ± 7.93	0.762	>0.05
After nursing	13.87 ± 3.36	27.61 ± 4.74	12.370	<0.05
<i>IPSS score</i>				
Before nursing	22.64 ± 2.98	22.37 ± 2.65	0.523	>0.05
After nursing	5.16 ± 0.45	9.68 ± 1.06	7.662	<0.05

gastrointestinal reactions, 24 cases of liver damage, 23 cases of breast development, 10 cases of infection, and 7 cases of bladder spasm (Table 4). There was no statistically significant difference in the incidence of adverse reactions between the

two groups of patients in gastrointestinal reactions, liver damage, breast development, infection, and bladder spasm (Table 4).

**3.6. Comparison of the Long-Term Efficacy of the Two Groups.** The two-year cumulative survival rate in the study group (84.62%) was higher than that in the control group (63.46%) (Figure 4).

## 4. Discussion

The clinical pathogenesis of prostate cancer is unclear and related to many factors [15]. Prostate cancer patients usually have anxiety, fear, depression, and other negative emotions, as well as the reduction of the androgen level after surgical treatment, affecting sexual function, which will not only cause inferiority but also affect the recovery of the body. Hence, the quality of psychological care has higher requirements [16, 17]. This study showed that, after nursing, the HAMA and HAMD scores of the study group were significantly lower than those of the control group, suggesting that psychological care can improve patients' negative emotions. In this study, the mental state of patients was evaluated before nursing, which avoided the blindness of nursing and improved the pertinence and applicability of nursing measures. Here, the pain degree of patients in the two groups was obviously reduced, and the quality of life was notably improved, and the improvement of the study group was more significant, indicating that the actual situation of patients should be fully understood in psychological nursing to prevent their mood deterioration. Some patients have psychological resistance to treatment, worry about physical disability after surgery, and inferiority mentality, so patients' wrong understanding should be corrected to enhance their confidence in life during psychological nursing. Their psychological state should be closely monitored in nursing [18]. Compared with general nursing, psychological intervention in this study improves the purpose of nursing, avoids the waste or shortage of nursing resources, and fully meets the needs of patients.

In recent years, clinicians have gradually begun to pay attention to the use of Chinese medicine as the adjuvant treatment in prostate cancer. According to TCM approaches, prostate cancer is mainly caused by the weakness of the human body to protect the body surface, as well as external evil, wind, cold, wet, heat, and other internal invasions caused by deficiency [19]. Treatment should follow the principles of supporting righteous qi and regulating the body's disease resistance, fighting poison with poison to dissipate agglomeration, promoting blood circulation, and dissipating blood stasis [20]. In this study, *Polyporus* eliminated dampness and diuresis, facilitated urination, and dissolved dampness for subsiding swelling; *Astragalus* can not only replenish qi of the whole body but also good tonify qi of the muscle surface; *Hedyotis diffusa* herba can clear heat and remove toxicity, diuresis, and dehumidification; *Curcuma* promotes blood circulation for removing blood stasis; *Scutellaria baicalensis* can clear away heat and detoxify and

TABLE 4: Comparison of the incidence of complications between the two groups (*n*).

Group	Cases	Gastrointestinal reactions	Liver damage	Breast development	Infection	Bladder spasm
Study	104	23	21	17	6	2
Control	104	27	24	23	10	7
$\chi^2$		0.421	0.255	1.114	1.083	2.903
<i>P</i>		0.516	0.613	0.291	0.298	0.088

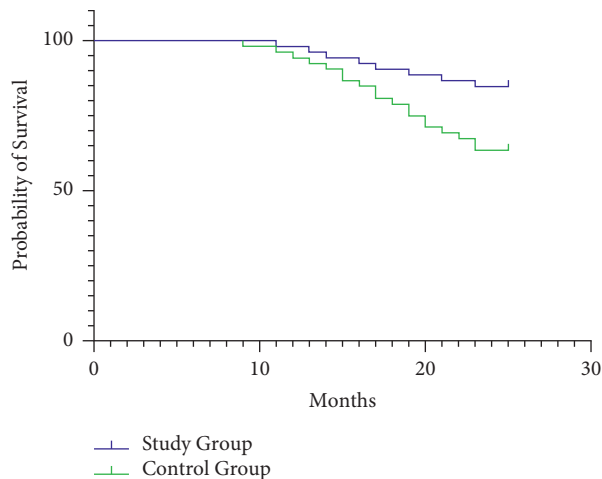


FIGURE 4: Comparison of two-year cumulative survival rates between the two groups.

treat diseases caused by dampness and heat accumulation in the body; whole scorpion can treat convulsions; also, it has analgesic effects; *Polygonatum* can supplement qi and nourish yin, strengthen the spleen, moisten the lung, and reinforce the kidney; *Achyranthes bidentata* promotes blood circulation for removing blood stasis, reinforces the liver and kidney, strengthens muscles and bones, and induces diuresis for treating stranguria; *Polygonum cuspidatum* removes dampness, clears heat and detoxification, dispels stasis, stanches pain, and resolves phlegm for relieving cough; Rhizoma Atractylodis Macrocephalae could invigorate qi, strengthen the spleen, remove moisture from the body and stop sweating; *Poria cocos* eliminates dampness and diuresis, tonifies the spleen, harmonizes the stomach, and makes peace of mind [21–26]. The combination of multiple drugs can improve the immune function of the patient's body, thereby alleviating the patient's clinical symptoms. After treatment, the serum PSA and FPSA levels of the two groups were decreased significantly compared to before treatment. Serum PSA is a specific marker of prostate cancer. It is a serine protease produced in prostate epithelial cells, and its normal function is to help hydrolyze and liquefy semen clots [27]. PSA is associated with male fertility, and the serum PSA level of prostate disease will increase [28]. It shows that the combination of traditional Chinese and Western medicine combined with psychological intervention has significant therapeutic effects in patients with prostate cancer, significantly improving the patients' serum PSA and FPSA levels and improving the body's immunity. After nursing, the maximum urine flow rate, residual urine volume, and IPSS score of the two groups of patients decreased, and the

decrease in the study group was more predominant than that of the control group. It further shows that the combination of psychological intervention and integrated traditional Chinese and Western medicine in this study has good effects on prostate cancer, and it is worthy of clinical application. There was no significant difference in the occurrence of adverse reactions between the two groups after treatment, indicating that the safety of the two treatment methods was basically the same.

## 5. Conclusion

In summary, the combination of psychological intervention and integrated traditional Chinese and Western medicine in the treatment of prostate cancer can significantly improve the therapeutic effects, regulate the body's immune function, improve the quality of life of patients, and reduce the side effects of Western medicine.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Efficacy of Restricting Dietary Protein Intake Combined with Buyang Huanwu Decoction in Treating Diabetic Nephropathy and Its Effect on Patients' Inflammatory Factor Levels

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**Objective.** To study the efficacy of restricting dietary protein intake combined with Buyang Huanwu decoction in treating diabetic nephropathy (DN) and its effect on patients' inflammatory factor levels. **Methods.** The medical data of 150 DN patients treated in Wuhan No.1 Hospital (June 2018–May 2021) were retrospectively analyzed. All patients received regular therapy, those who received the intervention of restricting dietary protein intake were included in the control group ( $n = 75$ ), and on this basis, those treated with Buyang Huanwu decoction were included in the experimental group ( $n = 75$ ), so as to scientifically evaluate their efficacy and inflammatory factor levels after treatment. **Results.** The patients' general information was not statistically different between the two groups ( $P > 0.05$ ); after treatment, the experimental group gained remarkably higher marked effective rate and total effective rate of treatment than the control group ( $P < 0.05$ ); the inflammatory factor levels of all patients were obviously better than before ( $P < 0.05$ ), and the levels of TNF- $\alpha$ , IL-2, IL-8, IL-4, and IL-10 were obviously lower in the experimental group than in the control group ( $P < 0.05$ ); the levels of fasting blood glucose, 2 h postprandial blood glucose, and glycosylated hemoglobin of all patients were remarkably lower than before ( $P < 0.05$ ), but with no significant between-group difference ( $P > 0.05$ ); the renal function indexes of all patients were better than before, and between the two groups, the levels of 24 h microalbuminuria, 24 h urine protein excretion, and serum creatinine were obviously lower and the glomerular filtration rate was significantly higher in the experimental group ( $P$  all  $< 0.05$ ), and the patients' traditional Chinese medicine (TCM) symptom scores were remarkably lower in the experimental group ( $P < 0.05$ ). **Conclusion.** Jointly applying Buyang Huanwu decoction on the basis of restricting dietary protein intake can effectively promote the clinical efficacy of DN, which is conducive to adjusting the inflammatory factor levels, promoting the patients' renal function, and alleviating the clinical symptoms.

## 1. Introduction

Diabetic nephropathy (DN), a microvascular complication of diabetes, is a chronic kidney disease caused by diabetes and an important trigger of renal failure [1, 2]. Its pathogenesis is not fully defined yet, but it is generally believed that blood glucose, blood pressure, and the course of the disease are all key factors leading to structural and functional damage to the kidney. DN is treated clinically by glycemic and blood pressure control and urinary protein reduction, including lifestyle interventions, correcting lipid metabolism disorders, and treating renal dysfunction [3–5]. Among them, lifestyle interventions aim to achieve glucose lowering

and standard protein intake maintenance by controlling the patients' diet. The intervention of dietary protein intake restriction excludes the disadvantages of traditional patterns, reduces the patients' urinary protein excretion, and alleviates renal function impairment through restricting the dietary protein intake in their diet. In recent years, traditional Chinese medicine (TCM) therapy has shown great advantages in the clinical treatment of kidney diseases. Based on the TCM theory and combined with the pathogenesis features of DN, the author concluded that spleen-kidney deficiency and the syndrome of dampness-heat and blood stasis are the main pathogenic features of DN, while Buyang Huanwu decoction, which comes from *Yilin Gaicuo*, is a



representative formula for invigorating qi and blood, which is mostly used to treat disease syndromes from qi deficiency and blood stasis, with efficacy that has been shown in clinical practice. Currently, there are few related studies on dietary protein restriction intervention and Buyang Huanwu decoction in curing DN, and the effectiveness of their combination remains controversial. Based on this, the study retrospectively analyzed 150 DN patients treated in our hospital to explore the efficacy of restricting dietary protein intake combined with Buyang Huanwu decoction for the treatment of DN.

## 2. Study Plan

**2.1. Patient Screening and Grouping.** The medical records of 150 DN patients treated in *Wuhan No.1 Hospital* (June 2018–May 2021) were retrospectively analyzed. All patients received the regular therapy, those who received the intervention of restricting dietary protein intake were included in the control group ( $n = 75$ ), and on this basis, those treated with Buyang Huanwu decoction were included in the experimental group ( $n = 75$ ). The study was approved by the ethics committee of *Wuhan No.1 Hospital*.

**2.2. Inclusion Criteria.** (1) The patients met the clinical diagnosis criteria for DN [6] as well as the dialectical diagnostic criteria for TCM syndromes [7]; (2) the patients were 30–75 years old; (3) the patients had normal cognitive function and communication function, and their medical records were complete; and (4) the patients and their family members signed the informed consent for the review of their relevant clinical data in this study.

**2.3. Exclusion Criteria.** (1) Patients treated with other therapies that affected observation during the same period; (2) patients with complicated severe urinary diseases, cardiovascular and cerebrovascular diseases or malignancies, etc.; (3) patients with type I diabetes mellitus; (4) patients who had to receive a low-protein diet, angiotensin-converting enzyme inhibitor (ACEI), or angiotensin II receptor antagonists; and (5) patients with unstable blood pressure.

**2.4. Methods.** After admission, all patients received routine treatment measures including diet control, exercise therapy, oral hypoglycemic agents, and subcutaneous injection of insulin for lowering the blood glucose, blood pressure reduction, lipid modification, and improvement of renal microcirculation [8].

Based on regular therapy, those in the control group accepted restricting dietary protein intake intervention. According to the food substitution method for diabetes mellitus, the dietician specified the balanced diet for the patients to rigorously follow, which contained 0.8 g/kg of protein with not less than half of high-quality protein, 104.6–125 kJ·kg<sup>-1</sup>·d<sup>-1</sup> of calories, 25–30% of fat-supplied heat, and 50–60% of carbohydrate supply, cellulose, and inorganic salt, with the proportion of polyunsaturated fatty

acid: monounsaturated fatty acid: saturated fatty acid = 1 : 1 : 1 [9, 10]. Additionally, those in the experimental group took the Buyang Huanwu decoction, and the formula was 60 g of Mongolian milkvetch root, 9 g of peony root, 9 g of Chinese angelica, 9 g of peach seed, 9 g of earthworm, 9 g of safflower, and 6 g of Sichuan lovage rhizome. All herbs were decocted with water, and the patients took one dose daily. The treatment cycle of all patients was 3 months.

**2.5. Observation Indicators.** Before treatment, the patients' general information including age, course of DN, course of diabetes, BMI, gender, complications, and human serum albumin (HSA) were recorded. The treatment effect of patients was evaluated by the *Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine* (2014) [11] and *Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine for Chronic Glomerulonephritis* [12]; i.e., compared to before treatment, 24 h urinary albumin excretion rate decreased by 50% and above was considered as marked effective, decreased by 20% and above but less than 50% as effective, and decreased by less than 20% or even increased as ineffective; and the total effective rate of treatment = (marked effective + effective)/total × 100%.

Patients' venous blood was extracted and placed under room temperature for 30 min and then centrifuged for 10 min under 3,000 r/min to take the supernatant for standby application, and the patients' tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-2 (IL-2), IL-4, IL-8, and IL-10 were measured by enzyme linked immunosorbent assay (ELISA). Patients' fasting blood glucose and 2 h postprandial blood glucose before and after treatment were measured by the glucose oxidase method with the automatic biochemical analyzer; the glycosylated hemoglobin level was measured by cation exchange-high-performance liquid chromatography (HPLC) with the VARIAC Type II Glycosylated Hemoglobin Analyzer. The patients' 24 h microalbuminuria and 24 h urine protein excretion levels were measured by radiometric analysis, the serum creatinine was measured by the sarcosine oxidase method, and the glomerular filtration rate was detected.

The scores of TCM clinical symptoms were evaluated with the *Guidelines for Clinical Research of New Drugs of Traditional Chinese Medicine* [13], mainly including fatigue, short breath and no desire to speak, lumbago, chest pain, back pain, pain worsening at night, limb numbness, dark-colored tongue, wiry pulse, ecchymosis, and astringent pulse. On a scale of 0–3 points, each clinical symptom was classified as none, occasional, often, and continuous.

**2.6. Statistical Processing.** The differences in study data were calculated with SPSS22.0, the pictures were drawn with GraphPad Prism 7 (GraphPad Software, San Diego, USA), the items included were enumeration data and measurement data, which were expressed by  $[n (\%)]$  and  $(\bar{x} \pm s)$  and examined by the  $\chi^2$  test and  $t$  test, respectively, and differences were considered statistically significant at  $P < 0.05$ .

### 3. Results

**3.1. General Information.** The patients' general information was not statistically different between the two groups ( $P > 0.05$ ), which met the study criterion of controlled experiment, see Table 1.

**3.2. Clinical Efficacy.** Between the two groups, the marked effective rate and total effective rate of treatment were greatly higher in the experimental group ( $P < 0.05$ ), presenting statistical significance, see Figure 1.

**3.3. Levels of Inflammatory Factors.** After treatment, the levels of inflammatory factors in patients of both groups were obviously better than before ( $P < 0.05$ ), and the levels of TNF- $\alpha$ , IL-2, IL-8, IL-4, and IL-10 were obviously lower in the experimental group than in the control group ( $P < 0.05$ ), see Table 2.

**3.4. Blood Glucose Levels.** After treatment, the levels of fasting blood glucose, 2 h postprandial blood glucose, and glycosylated hemoglobin in patients of both groups were significantly lower than before ( $P < 0.05$ ), but with no significant between-group differences ( $P > 0.05$ ), see Table 3.

**3.5. Renal Function.** After treatment, various renal function indicators of patients in both groups were better than before, and the patients in the experimental group obtained obviously lower levels of 24 h microalbuminuria, 24 h urine protein excretion, and serum creatinine and significantly higher glomerular filtration rate ( $P$  all  $< 0.05$ ) than the control group, see Table 4.

**3.6. Scores of TCM Clinical Symptoms.** Compared with the control group after treatment, the scores of TCM clinical symptoms in patients of the experimental group were obviously lower ( $P < 0.05$ ), with statistical significance, see Figure 2.

### 4. Discussion

Recently, relevant studies have shown that the occurrence of type II diabetes and its common complications is closely related to the inflammatory response, and tumor necrosis factor- $\alpha$  and interleukin factors are clinically common inflammatory response markers that can effectively predict the incidence of type II diabetes [14–16]. The study by Ma et al. [17] showed that the decreased glomerular filtration rate and increased serum creatinine level were usually accompanied by an obvious increase in the levels of inflammatory factors, and thus, the acute inflammatory response in type II diabetic patients was strongly linked to the emergence and progression of DN. Besides, the chronic inflammatory response intensity also parallels the degree of renal damage in diabetes; with higher urinary protein levels, the inflammatory response in patients is more severe. It follows that the increased levels of inflammatory factors in serum of DN

TABLE 1: Between-group comparison of patients' general information ( $n = 75$ ).

Indicator	Control	Experimental	$X^2/t$	$P$
Age (years)	$61.58 \pm 7.24$	$61.93 \pm 7.38$	0.293	0.770
Course of DN (years)	$1.36 \pm 0.44$	$1.35 \pm 0.51$	0.129	0.898
Course of diabetes (years)	$8.84 \pm 3.15$	$8.96 \pm 3.22$	0.231	0.818
BMI ( $\text{kg}/\text{m}^2$ )	$22.28 \pm 1.23$	$22.56 \pm 1.27$	1.372	0.172
Gender			0.118	0.731
Male	50 (66.67)	48 (64)		
Female	25 (33.33)	27 (36)		
Complication				
Hypertension	36 (48)	33 (44)	0.242	0.623
Hyperlipidemia	25 (33.33)	27 (36)	0.118	0.731
Educational level			0.242	0.623
Junior high school and below	39 (52)	42 (56)		
Above junior school	36 (48)	33 (44)		
Serum albumin ( $\text{g}/\text{L}$ )	$52.85 \pm 6.22$	$53.57 \pm 7.36$	0.647	0.519

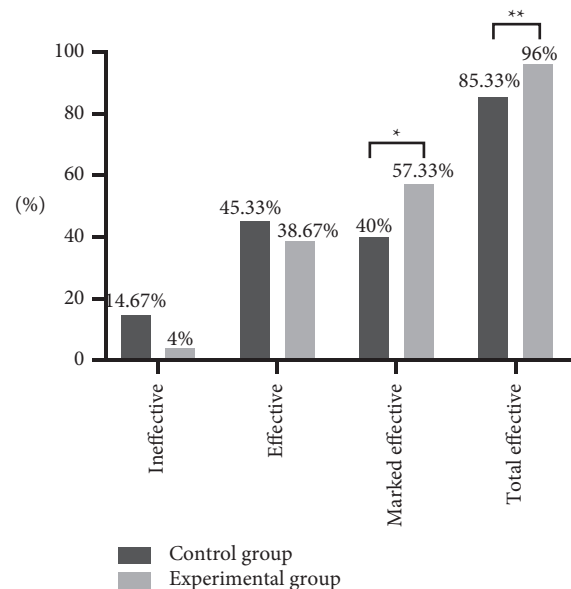


FIGURE 1: Between-group comparison of clinical efficacy (%). Note: the horizontal axis indicated the evaluation dimensions, and the vertical axis indicated the percentage (%); the numbers of ineffective cases, effective cases, and marked effective cases in the control group were 11, 34, and 30, respectively, and the number of total effective cases was 64; the numbers of ineffective cases, effective cases, and marked effective cases in the experimental group were 3, 29, and 43, respectively, and the number of total effective cases was 72; \* indicates a significant between-group difference in the marked effective rate of treatment ( $X^2 = 4.510$ ,  $P = 0.034$ ), and \*\* indicates a significant between-group difference in the total effective rate of treatment ( $X^2 = 5.042$ ,  $P = 0.025$ ).

patients are the important factor for the development of diabetic microangiopathy, and thus, anti-inflammatory therapy will also be a novel strategy for preventing, monitoring, and treating type II diabetes and its complications [18, 19]. Based on relevant TCM studies, it seems that the occurrence of DN may be due to the deficiencies of qi and yin caused by the disease with the symptom of frequent

TABLE 2: Between-group comparison of levels of inflammatory factors (ng/L,  $\bar{x} \pm s$ ).

Indicator		Control ( $n = 75$ )	Experimental ( $n = 75$ )	$t/P$
TNF- $\alpha$	Before	31.75 $\pm$ 6.83	32.06 $\pm$ 6.79	0.279/0.781
	After	24.34 $\pm$ 5.12*	15.23 $\pm$ 3.11*	13.170/<0.001
IL-2	Before	24.87 $\pm$ 4.76	25.31 $\pm$ 5.42	0.528/0.598
	After	19.02 $\pm$ 3.46*	12.14 $\pm$ 2.05*	14.815/<0.001
IL-4	Before	44.27 $\pm$ 5.86	43.85 $\pm$ 5.24	0.463/0.644
	After	31.58 $\pm$ 5.02*	21.23 $\pm$ 3.41*	14.770/<0.001
IL-8	Before	46.92 $\pm$ 8.35	47.27 $\pm$ 8.26	0.258/0.797
	After	33.85 $\pm$ 6.11*	18.45 $\pm$ 4.27*	17.892/<0.001
IL-10	Before	50.26 $\pm$ 5.24	50.34 $\pm$ 3.01	0.115/0.909
	After	35.67 $\pm$ 6.51*	25.83 $\pm$ 6.39*	9.342/<0.001

Note: \*significant differences in the levels of inflammatory factors before and after treatment in the same group ( $P < 0.05$ ).

TABLE 3: Between-group comparison of patients' blood glucose levels ( $\bar{x} \pm s$ ).

Indicator		Control group	Experimental group	$t/P$
Fasting blood glucose (mmol/L)	Before treatment	8.74 $\pm$ 1.46	8.85 $\pm$ 1.52	0.452/0.652
	After treatment	6.46 $\pm$ 0.79*	6.33 $\pm$ 0.75*	1.034/0.303
2 h postprandial blood glucose (mmol/L)	Before treatment	11.65 $\pm$ 2.07	12.04 $\pm$ 2.12	1.140/0.256
	After treatment	7.15 $\pm$ 1.02*	7.22 $\pm$ 1.01*	0.422/0.673
Glycosylated hemoglobin (%)	Before treatment	7.20 $\pm$ 0.88	7.17 $\pm$ 0.86	0.211/0.833
	After treatment	5.17 $\pm$ 0.58*	5.25 $\pm$ 0.62*	0.816/0.416

Note: \*significant differences in the levels of blood glucose indicators before and after treatment in the same group ( $P < 0.05$ ).

TABLE 4: Between-group comparison of patients' renal function indicators ( $\bar{x} \pm s$ ).

Observation indicator		Control group	Experimental group	$t/P$
24 h microalbuminuria (mg/24 h)	Before treatment	237.45 $\pm$ 26.14	238.85 $\pm$ 26.44	0.326/0.745
	After treatment	116.08 $\pm$ 14.63*	101.67 $\pm$ 15.24*	5.907/<0.001
24 h urine protein excretion (g/24 h)	Before treatment	0.38 $\pm$ 0.08	0.39 $\pm$ 0.09	0.719/0.473
	After treatment	0.24 $\pm$ 0.05*	0.15 $\pm$ 0.04*	12.173/<0.001
Serum creatinine ( $\mu$ mol/L)	Before treatment	93.47 $\pm$ 8.26	93.24 $\pm$ 8.30	0.170/0.865
	After treatment	75.86 $\pm$ 6.64*	62.33 $\pm$ 6.15*	12.947/<0.001
Glomerular filtration rate (ml/min)	Before treatment	86.54 $\pm$ 7.34	86.81 $\pm$ 7.50	0.223/0.824
	After treatment	103.16 $\pm$ 8.48*	113.75 $\pm$ 9.26*	7.304/<0.001

Note: \*significant differences in the indicators before and after treatment of the same group ( $P < 0.05$ ).

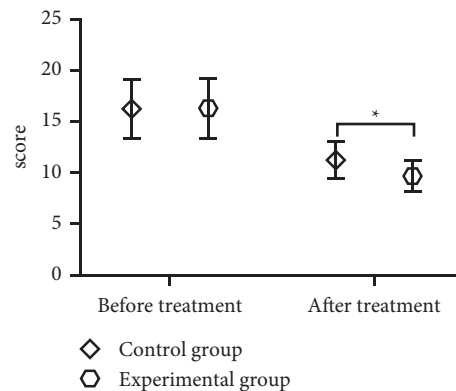


FIGURE 2: Between-group comparison of patients' scores of TCM clinical symptoms ( $\bar{x} \pm s$ ). Note: the horizontal axis indicates before and after treatment, and the vertical axis indicates the scores; before and after treatment, the scores of TCM clinical symptoms of the control group were (16.24  $\pm$  2.85) and (11.24  $\pm$  1.83), and those of the experimental group were (16.30  $\pm$  2.92) and (9.67  $\pm$  1.51), respectively; and \* indicates the significant between-group difference in the scores of TCM clinical symptoms after treatment ( $t = 5.701$ ,  $P < 0.001$ ).

drinking and urination, in which the deficiency of yin is the primary aspect and the dryness-heat is the secondary aspect. Over time, the deficiency of yin involves qi and causes qi-yin

deficiency, and the dryness-heat will be recessed gradually. Qi deficiency causes weak blood circulation, while yin deficiency causes obscure bloodstream, and either one of the

results in unsmooth blood flow, stasis, and blocking the meridians, forming the syndrome of blood stasis due to qi deficiency. The occurrence and development of DN show a dynamic evolution process, and finally, spleen-kidney deficiency is mingled with damp-heat and blood stasis [20–22]. Therefore, invigorating the spleen and kidney and promoting blood circulation to remove blood stasis are the root for treatment, and Buyang Huanwu decoction, a classic TCM formula for qi invigoration and blood activation, is exactly a perfect choice for symptomatic treatment of syndromes caused by qi deficiency and blood stasis. A great amount of Mongolian milkvetch root in the formula can invigorate the primordial qi and then promote the circulation of blood. The study by Yin et al. [23] showed that Mongolian milkvetch root could reduce the urine protein excretion of DN patients, which might be related to the fact that the herb is associated with the regulating effect of renal cortex IV collagen and transforming growth factor- $\beta$  in diabetes patients. In addition, peony root, Sichuan lovage rhizome, Chinese angelica, peach seed, and safflower are effective in promoting blood circulation to remove blood stasis, and combined with the results of modern pharmacological experiment, the first three also have the effect of dilating blood vessels and improving microcirculation. Also, earthworm in the formula has the moving and fleeing nature, so it can exert its effect of promoting blood circulation for removing obstruction in collaterals. Hence, the decoction mainly reduces proteinuria, improves the renal function, and then, treats DN by invigorating qi, promoting blood circulation and dredging channels.

In the author's opinion, medical nutrition intervention is also an essential part in the treatment of DN patients, the key point of which is to promote glomerular vasodilation through suitable protein intake and to increase the synthesis of prostaglandin E2 and prostaglandin F1 $\alpha$ . In addition, the study by Couteur et al. [24] reported that suitable protein intake could increase glucagon secretion, which could control patients' blood glucose to a certain extent and improve clinical symptoms. Therefore, in this study, all enrolled patients accepted the intervention of restricting dietary protein intake and those in the experimental group received Buyang Huanwu decoction therapy additionally, and by comparing various clinical indicators, the results showed that the experimental group gained greatly higher marked effective rate and total effective rate of treatment than the control group ( $P < 0.05$ ); after treatment, the levels of inflammatory factors in all patients were better than before ( $P < 0.05$ ), and the levels of TNF- $\alpha$ , IL-2, IL-8, IL-4, and IL-10 were obviously lower in the experimental group than in the control group ( $P < 0.05$ ); after treatment, the levels of fasting blood glucose, 2 h postprandial blood glucose, and glycosylated hemoglobin were significantly lower than before ( $P < 0.05$ ), but with no significant between-group differences ( $P > 0.05$ ), which was consistent with the report by Liu et al. [25]; various renal function indicators of all patients were better than before, and the experimental group obtained obviously lower levels of 24 h microalbuminuria, 24 h urine protein excretion, and serum creatinine and significantly higher glomerular filtration rate ( $P$

all  $< 0.05$ ) compared with the control group after treatment, the scores of TCM clinical symptoms were significantly lower in the experimental group ( $P < 0.05$ ). It can be concluded from these results that implementing the restriction on dietary protein intake showed high efficacy in controlling inflammatory responses, reducing urine protein amount, and improving kidney function, and the combined application of Buyang Huanwu decoction could further improve the efficacy in DN patients, especially on the regulation of inflammatory factor levels. Besides, either treatment did not generate adverse reaction on patients' blood glucose control.

In conclusion, the combined application of Buyang Huanwu decoction and restricting dietary protein intake can effectively improve the clinical efficacy of DN, which is beneficial for adjusting the levels of inflammatory factors, improving the renal function of patients, and alleviating clinical symptoms. However, restricting dietary protein intake in this study was limited by the implementation cost and practice, and the clinical application program still needs further exploration on nutrition recipe, patient cooperation, supervision, and habit formation to ensure the effect of the program.

## Data Availability

Data to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

## Authors' Contributions

Dan Chen and Dan Huang contributed equally to this article.

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## Research Article

# Clinical Effects of Jiawei Danggui Beimu Kushen Pills in the Treatment of Prostate Cancer and Their Influence on the Expression of Serum Prostate Specific Antigen

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**Objective.** To observe the clinical effects of Jiawei Danggui Beimu Kushen pills in treating prostate cancer and their influence on the expression of serum prostate specific antigen. **Methods.** A total of 234 prostate cancer patients were selected and randomly divided into observation group and control group, with 117 cases in each group. The control group was given oral bicalutamide tablets, while the observation group was treated with Jiawei Danggui Beimu Kushen pills on the basis of the control group. The treatment efficacy, IPSS score, TCM syndrome score, VAS score, quality-of-life score, and immune function of the two groups were compared before and after treatment. The serum PSA and f-PSA levels of patients before treatment and after 30 days, 90 days, and 180 days of treatment in the two groups were compared. The five-year cumulative survival rate and the incidence of adverse reactions were compared between the two groups. **Results.** After treatment, the total effective rate of the observation group was 88.03% (103/117), which was higher than that of the control group 69.23% (81/117); the difference was statistically significant ( $P < 0.05$ ). After treatment, the IPSS score, TCM syndrome score, and VAS score of the two groups were reduced, and those in the observation group were lower than those in the control group; the difference was statistically significant ( $P < 0.05$ ). After treatment, the quality-of-life scores of the two groups increased, and the observation group was higher than the control group; the difference was statistically significant ( $P < 0.05$ ). Before treatment, there was no significant difference in serum PSA levels and f-PSA levels when comparing between the two groups of patients ( $P > 0.05$ ). With the increase of treatment time, the two index levels of the two groups were gradually decreased. After 180 days of treatment, the two index levels of the two groups of patients were significantly lower than those before treatment, and the two index levels of the observation group were significantly lower than those of the control group; the difference was statistically significant ( $P < 0.05$ ). After treatment, the levels of IgM and IgA in the two groups were decreased, and the level of IgG was increased. The difference between the two groups in the levels of each index before and after treatment was statistically significant ( $P < 0.05$ ), and the difference between the two groups in the levels of each index after treatment was also statistically significant ( $P < 0.05$ ). The five-year cumulative survival rate of the observation group was 69.23%, and the five-year cumulative survival rate of the control group was 46.15% ( $P < 0.05$ ). There was no statistically significant difference between the two groups in the incidence of dizziness, fatigue, and gastrointestinal reactions ( $P > 0.05$ ), but the difference in the incidence of dysuria as well as dysuria and hematuria was statistically significant ( $P < 0.05$ ). **Conclusion.** Jiawei Danggui Beimu Kushen pills are effective in treating prostate cancer, which can effectively reduce the patients' IPSS score and TCM syndrome scores, relieve the pain, and improve the quality of life of patients. They also have a potential role in regulating serum PSA levels, clearing tumor lesions, reducing postoperative complications, and improving related symptoms.

## 1. Introduction

Prostate cancer (PCa) is an epithelial malignant tumor that occurs in the prostate. The clinical manifestations of prostate cancer are symptoms such as slow urinary flow, dysuria,

increased nocturia, incomplete urination, urinary incontinence, and hematuria and dysuria [1]. With the intensification of the aging society, the changes in people's living habits, dietary structure, and the improvement of the level of diagnosis and treatment, the incidence of prostate cancer has



been on the rise in recent years, and it has the characteristics of high mortality rate, poor prognosis, and gradual younger age. Prostate cancer has become the main cause threatening the life and health of Chinese older adults [2]. PCa mostly has a relatively insidious onset, relatively slow growth, and no obvious clinical symptoms in the early stage and is at the late clinical stage when diagnosed. With the progress of PCa, symptoms of metastasis and compression may appear, bringing about certain difficulties to the treatment of PCa [3]. Presently, prostate cancer is mainly treated with anti-androgen therapy, and Bicalutamide is currently the commonly used drug for the clinical treatment of PCa. Although Bicalutamide can have a better curative effect, it will make patients become hormone-dependent, cannot cure prostate cancer, and is prone to adverse reactions [4]. Traditional Chinese medicine practice includes rich practical experience and medical technology of ancient medical scientists. TCM treatment of prostate cancer has made great progress. In TCM, prostate cancer belongs to the categories of TCM “dysuria,” “Lin syndrome,” and “blood urine.” Treatment of prostate cancer should be through attacking toxins, promoting blood circulation and removing blood stasis, strengthening the body, and consolidating the foundation [5]. Danggui Beimu Kushen pill is one of the more promising prescriptions, which has good anti-inflammatory effects and can reduce patients’ dependence on hormone therapy and improve the therapeutic efficacy of prostate cancer [6]. This study analyzed the clinical efficacy of Jiawei Danggui Beimu Kushen pills in adjuvant treatment of prostate cancer and detected their effect on the expression of serum prostate specific antigen in patients.

## 2. Materials and Methods

### 2.1. General Information

**2.1.1. Inclusion Criteria.** The relevant diagnostic criteria of PCa in the “Guidelines for Diagnosis and Treatment of Urology” should be met [7]. The patient was pathologically confirmed by a puncture biopsy of the rectum and prostate. This study was approved by the ethics committee of the the People’s Hospital of Guangrao, Dongying, Shandong, China, and the patients signed informed consent.

**2.1.2. Exclusion Criteria.** Exclusion criteria were as follows: patients with organ dysfunction, mental illness, and immunosuppression; patients with major diseases such as hematopoietic, endocrine system or heart, liver, and kidney dysfunction; patients who are allergic to the drugs used and their ingredients; patients with other malignant tumors; patients with incomplete clinical data or lack of accuracy; and patients with a poor compliance or severe adverse reactions during treatment.

**2.1.3. Case Selection and Grouping.** 234 PCa patients at the People’s Hospital of Guangrao, Dongying, Shandong, China, from January 2008 to January 2015 were selected and divided into control group (117 cases) and observation group (117

cases) according to different treatment plans. Patients in the control group were 49–76 years old, with an average age of  $62.37 \pm 5.48$  years. The patient’s course of illness was 1–7 years, with an average of  $4.23 \pm 1.54$  years. The body mass index of patients was  $22.00\text{--}26.00 \text{ kg/m}^2$ , with an average of  $23.86 \pm 0.64 \text{ kg/m}^2$ . There were 103 cases in T3 stage and 14 cases in T4 stage. The patients in the observation group were 50–78 years old, with an average age of  $62.32 \pm 5.18$  years. The course of illness of patients was 1–8 years, with an average of  $4.86 \pm 1.63$  years. The body mass index of patients was  $22.00\text{--}25.00 \text{ kg/m}^2$ , with an average of  $23.57 \pm 0.68 \text{ kg/m}^2$ . The clinical stage of the patients was 106 cases in T3 stage and 11 cases in T4 stage. There was no statistically significant difference between the two groups of patients in general information ( $P > 0.05$ ).

**2.2. Treatment Methods.** The control group was given Bicalutamide tablets (AstraZeneca Pharmaceutical Co., Ltd., registration number H20130043, specification: 150 mg/tablet), 150 mg/time, once daily. The observation group was given Jiawei Danggui Beimu Kushen pills on the basis of the control group. Jiawei Danggui Beimu Kushen pills are composed of Chinese medicines such as *Angelica* 10 g, *Sophora flavescens* 10 g, *Fritillaria thunbergii* 20 g, *Polygonum cuspidatum* 20 g, *Patrinia vulgaris* 10 g, Combined Spicebush Root 15 g, and *Panax pseudo-ginseng* powder 3 g. The medicine was boiled and concentrated, and one dose was given daily. Patients in both groups were treated for 6 months.

### 2.3. Observation Indicators and Evaluation Criteria for Curative Effects

- (1) The treatment effects of the two groups were compared, and the criteria for determining the efficacy were formulated according to the “Guidelines for Diagnosis and Treatment of Urology” [7]. Ineffectiveness means that there is no significant change or further aggravation of the relevant clinical symptoms after treatment, the PSA level is slightly lower than that before treatment, and the increase is  $<25\%$  before treatment, or the PSA level is higher than that before treatment, and the IPSS score is lower than that before treatment by  $<30\%$ . Efficient means that the clinical symptoms have improved, the PSA level has decreased by 50%, and the IPSS score has decreased by 30% to 60%. Significantly efficient means that the clinical symptoms are significantly improved, the PSA level returns to the normal range, and the IPSS score drops  $>60\%$ . The total effective rate is (markedly effective + effective)/total number of cases  $\times 100\%$ .
- (2) The serum prostate specific antigen (PSA) levels and free prostate specific antigen (f-PSA) levels before treatment and after 30 days, 90 days, and 180 days of treatment in the two groups were compared. 5 mL of fasting venous blood was drawn from the patient in the morning and centrifuged for 5 minutes, and then

the supernatant was removed and refrigerated for testing. Chemiluminescence immunoassay was used to determine the serum PSA and f-PSA levels of patients.

- (3) The IPSS score, TCM syndrome score, and VAS score were compared before and after treatment between the two groups. The clinical symptoms were assessed using the International Prostate Symptom Score (IPSS) [8], with a total score of 35 points. The higher the score, the more severe the clinical symptoms. For TCM syndrome score, refer to “Guidelines for Clinical Evaluation of Prostate Cancer in Traditional Chinese Medicine” [9]. The scoring content includes dysuria, frequent urination, incessant dripping, constipation, soreness of waist and knees, multiple pains, and five upset heat. According to the degree of severity, it is recorded as 0–3 points, and the sum of the scores of each content is the TCM syndrome points. According to the visual analogue scale (VAS) [10], the pain is evaluated, and the total score is 10 points. The higher the score, the more severe the pain.
- (4) The quality of life of the two groups before and after treatment is compared. The EORTC QOL-C30 self-rating scale [11] is used for evaluation, including five items: social function, cognitive function, emotional function, physical function, and role function. The total score is 100 points; the higher the score, the better the patient’s quality of life.
- (5) The immune functions of the two groups of patients are compared. An automatic biochemical analyzer is used to detect immune function indicators. The detection approach is an immunoturbidimetric method, and the detection indicators are IgM, IgA, and IgG.
- (6) The five-year cumulative survival rates of the two groups are compared. There is a regular call for follow-up, the patient’s survival is recorded, and the cumulative survival rate is calculated.
- (7) The incidences of adverse reactions between the two groups are compared. Adverse reactions include dizziness, fatigue, gastrointestinal reactions, dysuria, and hematuria and dysuria.

**2.4. Statistical Processing.** SPSS 22.0 statistical software was used for analysis. The *t*-test is performed to analyze the measurement data, which is expressed as mean  $\pm$  standard deviation (SD). The  $\chi^2$  test is performed to analyze the count data, which is expressed as a rate (%).  $P < 0.05$  is considered statistically significant. All experiments in this article were repeated three times.

### 3. Results

**3.1. Comparison of Clinical Efficacy between the Two Groups of Patients after Treatment.** The clinical efficacy of the observation group after treatment was 88.03%, which was

significantly higher than that of the control group (69.23%), and the difference was statistically significant ( $X^2 = 12.428$ ,  $P = 0.002$ ) (Table 1).

**3.2. Comparison of Serum PSA Levels and f-PSA Levels before Treatment and after 30 Days, 90 Days, and 180 Days of Treatment between the Two Groups.** Before treatment, there was no significant difference in serum PSA level and f-PSA level between the two groups of patients ( $P > 0.05$ ). With the increase of treatment time, the two index levels of the two groups of patients gradually decreased. After 180 days of treatment, the two index levels of the two groups of patients were significantly lower than those before treatment, and the index levels of the observation group were significantly lower than those of the control group; the difference was statistically significant ( $P < 0.05$ ) (Figure 1).

**3.3. Comparison of IPSS Scores, TCM Syndrome Scores, and VAS Scores between the Two Groups of Patients before and after Treatment.** Before treatment, there was no significant difference in IPSS score, TCM syndrome score, and VAS score between the two groups of patients ( $P > 0.05$ ). After treatment, the three scores of the two groups of patients decreased. The difference between the groups before and after treatment was statistically significant ( $*P < 0.05$ ), and the difference between the groups after treatment was statistically significant ( $*P < 0.05$ ), as shown in Table 2.

**3.4. Comparison of the Quality-of-Life Scores between the Two Groups of Patients before and after Treatment.** Before treatment, there was no statistically significant difference in the quality-of-life scores between the two groups of patients ( $P > 0.05$ ). (Table 3).

**3.5. Comparison of the Immune Function of the Two Groups of Patients before and after Treatment.** Before treatment, there was no significant difference in IgM, IgA, and IgG levels between the two groups of patients ( $P > 0.05$ ). After treatment, the levels of IgM and IgA in the two groups decreased, and IgG levels increased. The difference in the level of each index between the two groups before and after treatment was statistically significant ( $P < 0.05$ ), and the difference in the level of each index between the two groups after treatment was statistically significant ( $P < 0.05$ ) (Figure 2).

**3.6. Comparison of the Five-Year Cumulative Survival Rates in the Two Groups of Patients.** The five-year cumulative survival rate of the observation group was 69.23%, and the five-year cumulative survival rate of the control group was 46.15%. The difference between the two groups was statistically significant ( $P < 0.05$ ) (Figure 3).

**3.7. Comparison of the Incidence of Adverse Reactions between the Two Groups of Patients after Treatment.** In the observation group, there were 3 cases of dizziness, 1 case of

TABLE 1: Comparison of clinical efficacy between the two groups of patients after treatment.

Groups	Number	Significantly efficient	Efficient	Ineffectiveness	Total effective rate
Observation group	117	42	61	14	103 (88.03)
Control group	117	31	50	36	81 (69.23)
$\chi^2$					12.428
$P$					0.002

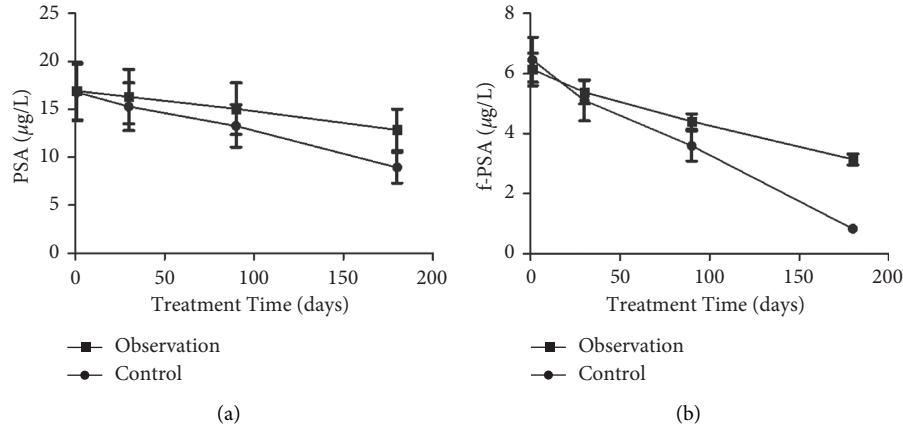


FIGURE 1: Comparison of serum PSA levels and f-PSA levels before treatment and after 30 days, 90 days, and 180 days of treatment between the two groups. (a) Comparison of serum PSA levels before treatment and after 30 days, 90 days, and 180 days of treatment between the two groups. (b) Comparison of serum f-PSA levels before treatment and after 30 days, 90 days, and 180 days of treatment between the two groups.

TABLE 2: Comparison of IPSS score, TCM syndrome score, and VAS score before and after treatment between the two groups.

Groups	Number		IPSS score	TCM syndrome score	VAS score
Observation group	117	Before treatment	19.36 $\pm$ 5.64	12.62 $\pm$ 3.46	7.56 $\pm$ 1.73
		After treatment	9.69 $\pm$ 3.37**	8.04 $\pm$ 2.11**	2.34 $\pm$ 0.96**
		$t$	13.664	11.248	14.625
		$P$	<0.05	<0.05	<0.05
Control group	117	Before treatment	19.78 $\pm$ 5.83	12.31 $\pm$ 3.28	7.47 $\pm$ 1.52
		After treatment	15.43 $\pm$ 4.91*	4.69 $\pm$ 1.73*	4.81 $\pm$ 1.15*
		$t$	7.223	6.451	5.230
		$P$	<0.05	<0.05	<0.05

TABLE 3: Comparison of the quality-of-life scores of the two groups of patients before and after treatment.

Index		Observation group (117)	Control group (117)	$t$	$P$
Social function	Before treatment	52.66 $\pm$ 7.56	53.17 $\pm$ 7.84	0.982	>0.05
	After treatment	81.63 $\pm$ 6.45**	68.43 $\pm$ 6.87*	8.231	<0.05
Affective function	Before treatment	51.41 $\pm$ 8.52	51.77 $\pm$ 8.35	0.530	>0.05
	After treatment	77.16 $\pm$ 5.43**	62.84 $\pm$ 6.72*	7.412	<0.05
Cognitive function	Before treatment	56.53 $\pm$ 6.85	56.79 $\pm$ 6.42	0.678	>0.05
	After treatment	78.27 $\pm$ 5.46**	66.71 $\pm$ 5.97*	10.236	<0.05
Physical function	Before treatment	53.63 $\pm$ 8.87	53.29 $\pm$ 8.66	0.374	>0.05
	After treatment	78.57 $\pm$ 6.41**	65.92 $\pm$ 6.25*	9.623	<0.05
Role function	Before treatment	55.47 $\pm$ 6.78	55.86 $\pm$ 6.93	0.417	>0.05
	After treatment	79.41 $\pm$ 7.79**	64.36 $\pm$ 7.02*	11.642	<0.05

fatigue, 4 cases of gastrointestinal reactions, 2 cases of dysuria, 2 cases of hematuria, 1 case of odynuria. In the control group, there were 5 cases of dizziness, 3 cases of fatigue, 5 cases of gastrointestinal reactions, 11 cases of dysuria, 13 cases of hematuria, and 9 cases of odynuria.

There was no significant difference in the incidence of dizziness, fatigue, and gastrointestinal reactions between the two groups ( $P > 0.05$ ). The differences in the incidence of dysuria as well as dysuria and hematuria between the two groups were statistically significant ( $P < 0.05$ ) (Table 4).

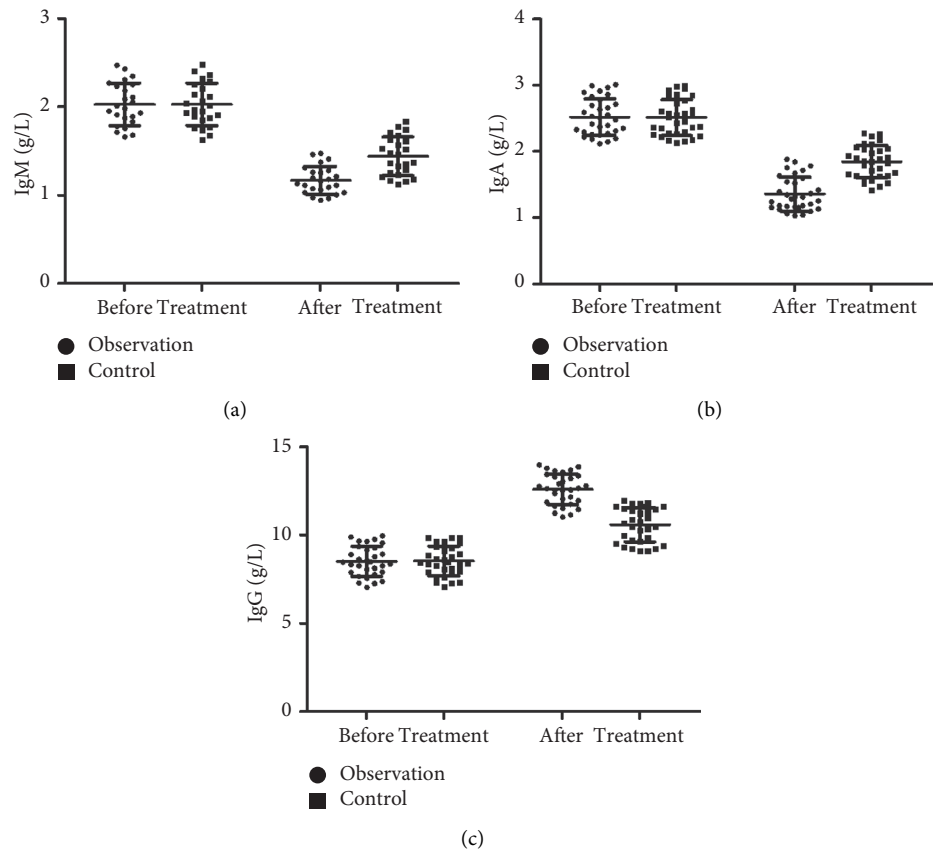


FIGURE 2: Comparison of the immune function of the two groups of patients before and after treatment. (a) Comparison of IgM levels between the two groups of patients before and after treatment. (b) Comparison of IgA levels between the two groups of patients before and after treatment. (c) Comparison of IgG levels between the two groups of patients before and after treatment.

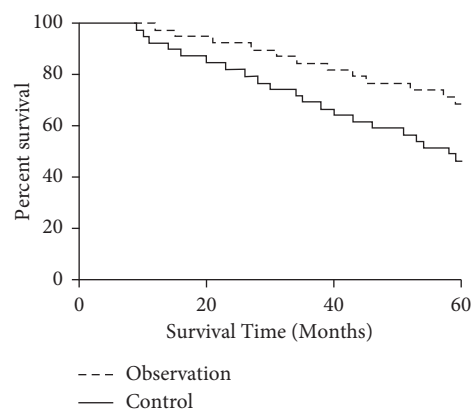


FIGURE 3: Comparison of the five-year cumulative survival rates of the two groups of patients.

TABLE 4: Comparison of the incidence of adverse reactions between the two groups of patients after treatment.

Groups	Number	Dizziness	Fatigue	Gastrointestinal reaction	Dysuria	Hematuria	Painful urination
Observation group	117	3	1	4	2	2	1
Control group	117	5	3	5	11	13	9

#### 4. Discussion

Prostate cancer, a urological disease, is a common and more frequent disease in modern times, which specifically refers to the presence of malignant epithelial tumors in the prostate. At present, the specific cause of PCa is not clear in clinical practice, but studies have shown that it may be related to the patient's age, region, race, genetics, environment, diet, and other factors, and it is more common in middle-aged and older adults [12, 13]. PCa has no specific symptoms in the early stage, and it is mostly in the middle and late stages when it is discovered. With the gradual enlargement of the prostate body, it can compress the urethra, causing symptoms such as dysuria and thin urine lines, and even endanger the vascular and nerve bundles and bladder, leading to impotence and hematuria, which seriously endanger the physical and mental health of patients [14]. Therefore, it is particularly necessary to find a scientific and effective treatment plan to intervene in time. The treatment of clinical PCa includes various treatment approaches such as surgery and drugs [15, 16], but surgery will cause certain wounds to patients and also affect the psychological state of patients, and some patients do not receive surgical treatment. Studies have found that [17] the growth of cancer cells in PCa patients has a certain dependence on male hormones. Bicalutamide is a class of antiandrogen drugs, which are nonsteroidal antihormonal drugs and are often used in the treatment of prostate cancer. When Bicalutamide enters the human body, it has a certain competitive effect on androgen receptor binding, reducing the production of androgens, inhibiting the proliferation and growth of tumor cells to a certain extent, and improving clinical symptoms. Bicalutamide is usually taken once a day, but it will produce androgen-dependency after taking it for a long time, which will have a certain impact on the therapeutic efficacy [18]. Regarding the various adverse reactions due to Western medicine treatment, clinicians began to seek the treatment of prostate cancer from the concepts of Chinese medicine, in order to reduce the severity and incidence of adverse reactions and improve the therapeutic effects against prostate cancer. Jiawei Danggui Beimu Kushen pills are one of the more promising prescriptions in the study of ancient Chinese medicine prescriptions for chronic prostatitis. In the prescription, *Angelica* has the effects of promoting blood circulation and removing blood stasis, moistening the intestines, and laxative. *Fritillaria thunbergii* clears away heat and reduces phlegm, relieves cough and detoxification, and has the effect of moisturizing the lungs. *Sophora flavescens* clears away heat and dampness and expels wind. Combined with *Fritillaria thunbergii*, *Sophora flavescens* can clear the lungs and dispel bladder stasis and heat. On this basis, the addition of *Polygonum cuspidatum* and *Patrinia vulgaris* is to remove the damp and heat of the lower body, and Combined Spicebush Root can relieve qi and pain, Panax pseudo-ginseng powder promotes blood circulation and removes blood stasis and relieves pain [19–22]. The combination of various medicines can make the damp heat dispel, the blood pulse cleared, and the blood stasis scattered, as well as smooth urination.

Serum PSA is the preferred specific marker for pre-adenocarcinoma. Serum PSA is produced in prostate epithelial cells, and its normal function is to help hydrolyze and liquefy semen clots. Serum PSA is closely related to male fertility, and the expression level is 0 in the state of no tumor. Studies have shown that PSA will be released into the blood in large quantities after PCa patients' prostate epithelium is damaged. PSA is expressed at a high level in the serum of prostate cancer patients and is positively correlated with the progression of the disease [23–25]. The results of this study showed that, before treatment, the serum PSA levels and f-PSA levels of the two groups were highly expressed. After treatment, the two index levels of the two groups decreased significantly, and in the observation group they were more significantly lower than the control group ( $P < 0.05$ ). The results indicated that the use of Jiawei Danggui Beimu Kushen pills could significantly reduce the serum PSA level of PCa patients, inhibit tumor vitality, and improve the clinical symptoms of patients. The results of this study show that the therapeutic efficacy, IPSS score, TCM syndrome score, VAS score, and quality-of-life score in observation group are better than those of the control group. The results show that Jiawei Danggui Beimu Kushen pills have better therapeutic effects in the treatment of PCa, which can reduce the pain intensity and improve the quality of life of patients. The results of this study showed that the serum IgM and IgA levels of the observation group were lower than those of the control group, and the IgG level was higher than that of the control group, suggesting that the use of Jiawei Danggui Beimu Kushen pills to treat PCa can improve the patient's resistance and enhance the patient's immune function. The results of this study showed that the five-year cumulative survival rate of the observation group was predominantly higher than that of the control group, and the incidence of adverse reactions was lower than that of the control group, indicating that the use of Jiawei Danggui Beimu Kushen pills to treat PCa can reduce the toxic and side effects in patients using Western medicine and improve the survival time of patients, which is of great significance for the prognosis of patients.

To sum up, Jiawei Danggui Beimu Kushen pills have potential curative effects in prostate cancer treatment, significantly improving clinical symptoms, enhancing immunity, regulating PSA levels, and inhibiting tumor vitality. They can improve the quality of life of patients, prolong the survival time of patients, and reduce the incidence of adverse reactions.

#### Data Availability

The data used to support the findings of this study are included within the article.

#### Conflicts of Interest

All authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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## Research Article

# Study of the Therapeutic Effects of Chinese Herbal Decoction Combined with Glucocorticoid in Treating Primary Nephrotic Syndrome in Children

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**Background.** To investigate the clinical effects of Chinese medicine decoction combined with glucocorticoid in treating children with primary nephrotic syndrome. **Methods.** A total of 70 children with pediatric nephritis nephrotic syndrome treated at Weifang People's Hospital from January 2019 to December 2019 were randomly allocated to the therapy group and the control group, each with 35 cases. The control group was treated with conventional Western medicine, and the therapy group received Western medicine and Chinese medicine. After 12 weeks of treatment, the therapeutic effect of the two groups was compared. **Results.** After receiving the treatment, the levels of urine protein (UPro), triglyceride, and cholesterol were significantly decreased in the two groups ( $p < 0.05$ ), and these levels in the therapy group were much lower than those of the control group ( $p < 0.05$ ). However, the level of albumin (ALB) was predominantly increased in the two groups after treatment ( $p < 0.05$ ), and this level in the therapy group was much higher than that of the control group ( $p < 0.05$ ). Moreover, the immune indicators, coagulation function, and recurrence rate were noticeably improved after treatment ( $p < 0.05$ ), and the therapy group was better than the control group ( $p < 0.05$ ). Furthermore, the comparison of renal function indexes, liver function indexes, and blood routine between the two groups showed no statistical significance in the incidence of adverse reactions between the two groups ( $p > 0.05$ ). **Conclusions.** For the treatment of refractory nephrotic syndrome in children, based on conventional shock therapy, the addition of traditional Chinese medicine (Liuwei Dihuang pill decoction) remedy can significantly improve the disease symptoms in children and improve the efficacy, and the incidence of adverse reactions is low.

## 1. Introduction

Primary nephrotic syndrome (PNS) is a syndrome of glomerular diseases caused by a variety of etiologies, with increased levels of proteinuria ( $>3.5$  g/24 h), hypoalbuminemia (serum albumin  $<30$  g/L), and hyperlipidemia and varying degrees of edema being the main manifestations of the clinical syndrome [1, 2]. The course of childhood nephrotic syndrome is protracted and difficult to heal, and it can enter adulthood at the longest. Due to incomplete

physiological development and poor immunity, children with this condition are highly susceptible to infection during the treatment process, which can lead to severe kidney disease [3–5], which seriously threatens the patient's life and safety and causes economic and psychological problems to the patient. As a result, the quality of life is greatly affected. Therefore, effective treatment of this condition to delay its progress has become an urgent need.

Current medical treatment of pediatric nephrotic syndrome includes glucocorticoids [6, 7], immunosuppressants,

and immunomodulators, among which glucocorticoids are the drugs of choice for nephrotic syndrome. Although it can effectively reduce protein exudation by controlling the occurrence of the body's inflammatory reaction, its immunosuppressive effects could cause infection, osteoporosis, gastrointestinal reactions, lipid metabolism disorders and liver enzyme abnormalities, and other adverse reactions [8]. Most pediatric patients with primary nephrotic syndrome are relieved after initial hormone therapy, and about 85% of the children relapse after the initial treatment remission, of which 25%–43% have frequent recurrences [9, 10]. Several clinical studies have reported [11] that 80% to 90% of children with primary nephrotic syndrome are sensitive to glucocorticoids and can be relieved by hormone therapy, while the rest are hormone-resistant. In addition, 50% of hormone-sensitive children will have hormone dependence or recurrent illnesses. If the symptoms are not relieved timely, serious complications may occur or even can lead to end-stage renal disease [10].

Because this disease has the characteristics of recurrence and relapse easily, coupled with poor patient compliance, it becomes challenging to achieve the desired outcomes. The use of traditional Chinese medicine (TCM) can not only reduce the side effects of hormones, increase the sensitivity of hormones, and inhibit the recurrence of the disease, but also improve the overall physical condition of the patient and improve the prognosis of the patient [9, 12, 13]. TCM occupies an indispensable and important position in the treatment of this disease. It is clinically proven that TCM treatment of nephrotic syndrome can turn urine protein into negative, reduce the use of hormones and side effects, and improve the quality of life of children with nephropathy. Therefore, through clinical investigation in children with recurrent nephrotic syndrome based on TCM syndrome differentiation, analysis of their prescription medication rules, analysis of appropriate prescriptions, and selection of therapeutic drugs, the experience is summarized for TCM syndrome differentiation and treatment of nephrotic syndrome so as to better guide the clinical application of TCM approaches.

Recently, there have been few reports on the clinical application and effect evaluation of TCM for primary nephrotic syndrome. This article was aimed to explore further the clinical effects of TCM decoction combined with glucocorticoids in the treatment of primary nephrotic syndrome, understand in detail the specific situation of Chinese medicine decoction in the treatment of primary nephrotic syndrome in reducing the side effects of hormones, evaluate its clinical application effect, discuss the advantages of its treatment methods, and provide a potential reference for further improving and promoting its clinical application.

## 2. Materials and Methods

### 2.1. General Information and Medical Records

**2.1.1. Research Objects.** A total of 70 children with pediatric nephritis nephrotic syndrome treated at the pediatric outpatient clinic or inpatient department of the Weifang

People's Hospital, Weifang, Shandong, China, from January to December 2019 were selected. Among them, 48 were inpatient medical records and 22 were outpatient medical records, all diagnosed with nephrotic syndrome. Among them, 52 were male children and 18 were female children, with a male-to-female ratio of 2.9:1. The age distribution was 41 cases from 2 to 5 years old, 17 cases from 6 to 9 years old, 9 cases from 10 to 13 years old, and 3 cases from 14 to 18 years old; the youngest age was 2 years old, the oldest age was 17 years old, and the average age was 6.14 years old. At the time of treatment, the shortest course of illness was 3 days and the longest was 8 years.

### 2.1.2. Diagnostic Criteria

**Western Medicine Diagnostic Criteria.** According to the diagnostic criteria of pediatric primary nephrotic syndrome formulated by the Nephrology Group of the Pediatric Branch of the Chinese Medical Association in 2000 at the Zhuhai Conference [14] and the "Hormone Sensitivity/Relapse" formulated by the Nephrology Group of the Pediatric Branch of the Chinese Medical Association in 2016 relying on the diagnostic criteria of the Evidence-Based Guidelines for Diagnosis and Treatment of Nephrotic Syndrome, the diagnostic criteria are as follows: (1) massive proteinuria: 3 qualitative urine protein in one week (+++) ~ (++++), or random or morning urine protein/creatinine (mg/mg)  $\geq 2.0$ ; 24 h urine protein quantitative  $\geq 50$  mg/kg. (2) Hypoalbuminemia: plasma albumin is less than 25 g/L. (3) Hyperlipidemia: plasma cholesterol is higher than 5.7 mmol/L. (4) Different degrees of edema. (5) Exclude secondary nephrotic syndrome and congenital nephrotic syndromes, such as diabetic nephropathy and lupus nephritis. (6) Frequent recurrence of primary nephrotic syndrome: primary nephrotic syndrome during the disease, there are more than 2 recurrences within half a year, and more than 4 recurrences within 1 year (nephrotic syndrome recurrence: consecutive 3 days, morning urine protein changes from negative to 3+ or 4+, or morning urine uPCR (urine protein/creatinine)  $\geq 2$  g/g, or 24 h urine protein quantitative  $\geq 50$  mg/kg). The diagnosis can be made on those who have the above (1), (2), (5), and (6) criteria. **Diagnostic Criteria of Chinese Medicine.** This standard refers to the "Guiding Principles for Clinical Research of New Chinese Medicines (Trial)" issued by the National Medical Products Administration in 2002 and "Diagnosis, Syndrome Differentiation and Efficacy Evaluation of Primary Nephrotic Syndrome" issued by the Nephropathy Branch of the Chinese Society of Chinese Medicine in 2006.

**2.1.3. Inclusion Criteria.** Inclusion criteria were defined as follows: (1) meet the diagnostic criteria of Western medicine; (2) meet the diagnostic criteria of Chinese medicine; (3) children aged 1–18 years old; (4) oral hormones or additional immunosuppressive therapy, and the prescribed treatment course of hormones is stopped after half a year; (5) accepting treatment voluntarily and having a guardian sign the "Informed Consent"; (6) no children with serious

diseases such as cardiovascular, liver, and hematopoietic system; and (7) regular follow-up visits and telephone follow-ups.

**2.1.4. Exclusion Criteria.** Exclusion criteria were defined as follows: (1) congenital and secondary nephrotic syndrome; (2) patients with severe diseases such as cardiovascular, liver, hematopoietic system, etc; (3) those who have participated in clinical research of other drugs within the last 1 month; (4) those who are allergic to Chinese medicine; (5) children who are <2 years old and >18 years old; (6) patients with mental illness; and (7) those who fail to use the prescribed drugs and cannot determine the efficacy.

**2.1.5. Case Dropout or Termination Criteria.** Case dropout or termination criteria were defined as follows: (1) those who did not meet the inclusion criteria and were mistakenly included; (2) those who meet the inclusion criteria but fail to take the prescribed medication after inclusion; (3) those with severe adverse reactions, serious adverse events, complications or special physiological changes, who are not suitable to continue the trial, or quit by themselves during the trial; (4) cases in which the patients who have not ended the treatment for various reasons automatically withdraw from the trial, are lost to follow-up or die, and the data is incomplete, which affects the investigation; and (5) if the condition deteriorates during the course of the disease, and the clinical trial should be terminated according to the clinician's judgment, the clinical trial of the case should be terminated immediately. During the trial process, it was discovered that the trial protocol had major mistakes and the effectiveness of the treatment plan could not be evaluated for various reasons.

**2.1.6. Grouping.** Seventy patients who met the criteria for inclusion and exclusion were randomly divided into two groups, namely, the control group: hormone therapy alone, and the therapy group: TCM combined with hormone therapy, with 35 cases in each group. This study was approved by the ethics committee of the Weifang People's Hospital, Weifang, Shandong, China (approval no. 2019-01004), and all patients in the study sought the consent of their guardians and signed the "Informed Consent."

**2.2. Treatment Methods.** The control group was treated with prednisone (2 mg/kg/d) orally for 8 weeks. 2–4 weeks after complete remission, they were treated with prednisone every other day after breakfast for 4 weeks, and the maximum amount should not be greater than 60 mg/d. After that, the maximum amount was reduced 2.5–5 mg every 2 to 4 weeks for 9 months of treatment. If recurrence occurs, the immunosuppressant cyclophosphamide should be added on this basis. The general dose is 2.0–2.5 mg/kg/d in 3 divided doses. The course of treatment is 8–12 weeks. The total amount should not exceed 200 mg/kg. (2) The therapy group was treated with Liuwei Dihuang Wan on the basis of the control group. Weight  $\leq 25$  kg: *Astragalus* 10 g, *Atractylodes*

*macrocephala* 10 g, Chinese yam 12 g, Habitat 8 g, Paeonolium bark 8 g, Poria 10 g, Dogwood 10 g, *Alisma orientalis* 8 g, Dog ridge 10 g, *Cuscuta* 10 g, *Salvia miltiorrhiza* 8 g. Weight >25 kg: *Astragalus* 15 g, *Atractylodes macrocephala* 12 g, Chinese yam 15 g, Habitat 10 g, Dan bark 8 g, Poria 12 g, Dogwood 10 g, *Alisma orientalis* 8 g, Dog ridge 10 g, *Cuscuta* 15 g, *Salvia* 10 g. Children older than 12 years, 80–100/time, 2 times a day; children 7–12 years old, 50–80 ml/time, 2 times a day; and children 2–7 years old, 30–50 ml/time, daily 2 times.

## 2.3. Clinical Observation

### 2.3.1. Safety Observation Indicators

The general condition of the patients: heart rate, blood pressure, pulse, etc

The blood routine, electrocardiogram, liver enzyme alanine aminotransferase (ALT), and aspartate aminotransferase (AST) tests were checked before and after the test

### 2.3.2. Curative Effects Observation Index

- (1) 24-hour urine protein quantification: the 24-hour urine output was collected and the urine albumin was determined, which was tested by the laboratory of our hospital every two weeks.
- (2) ALB, triglycerides (TG), total serum cholesterol (TC), coagulation function-related indicators, creatinine, and urea nitrogen were tested by the laboratory of our hospital every four weeks.
- (3) Urine routine was tested once a week by the laboratory of our hospital.

### 2.3.3. Efficacy Evaluation Criteria

- (1) Short-term curative effect: the urine protein of the children was observed after 8 weeks of treatment. (i) Complete remission: blood biochemistry and urine examination were completely normal, urine protein turned negative, and edema disappeared. (ii) Partial remission: urine protein was ++ or less, and edema disappeared. (iii) No remission: urine protein was +++ or more, and the edema remained unchanged from before treatment.
- (2) Long-term curative effect: (i) cure: the child was completely relieved, and the treatment was stopped for not less than 3 years. (ii) Improvement: except for the occasional small amount of proteinuria, other indicators were normal for more than 3 years. (iii) Invalid: urine protein was still +++ (or higher) or death [15].

### 2.3.4. Safety Evaluation Standards

- (1) Safety assessment: Level 1: safe, without any adverse reactions; Level 2: relatively safe, if there were adverse reactions, do not need to do any treatment to

continue the administration; Level 3: there are safety issues and moderate adverse reactions, and the drug could be continued after treatment; and Level 4: the test was discontinued due to adverse reactions.

- (2) Evaluation of the degree of adverse reactions: Mild: the symptoms of adverse reactions were mild, usually without treatment; Moderate: the symptoms of adverse reactions were obvious, important organs and tissues were damaged to a certain extent, and it was easy to recover; Severe: vital organs are damaged, and life is endangered.

**2.3.5. Observation Time and Follow-Up.** (1) Continuous treatment for 12 weeks, and records of TCM symptoms and laboratory-related examination results were used as the basis for the short-term efficacy evaluation of the examination. After 12 weeks of treatment, those who still do not work should use other treatments or avoid delaying the disease. (2) Investigation and follow-up for half a year after the end of treatment, to record the recurrence of children with NS. (3) Recurrence rate was calculated using the following equation:

$$\text{recurrence rate} = \frac{\text{number of relapsed cases}}{\text{number of remission cases}} \times 100\%. \quad (1)$$

**2.4. Statistical Methods.** Independent repetitions of experiments were 3 times. The detection index data were expressed as  $\bar{x} \pm s$  and analyzed by SPSS22.0 software (IBM, NY, USA). Differences between different groups were compared by analysis of variance or chi-square test, and the data between the two groups was tested by *t*-test.  $p < 0.05$  was considered as statistically significant.

### 3. Results

**3.1. General Conditions before Treatment.** The basic conditions between the two groups were compared and results showed that the two groups had no statistical difference in gender distribution, age distribution, and length of disease distribution before treatment, and they were comparable (Figures 1(a)–1(c)).

**3.2. Comparison of the Levels of 24 h UPro in the Two Groups (g/24 h).** As shown in Table 1, there was no significant difference between the therapy group and the control group in the 24 h UPro before treatment ( $p > 0.05$ ). However, the therapy group and the control group have higher UPro after treatment compared with before treatment ( $^{**}p < 0.05$ ). Moreover, the therapy group had a better curative effect in reducing 24 h UPro than the control group after treatment ( $^{*}p < 0.05$ ).

**3.3. Comparison of the ALB Level between the Two Groups (g/L).** Results from Table 2 revealed that the ALB level in the therapy group and the control group was  $20.54 \pm 1.72$  and

$20.43 \pm 1.41$ , and there was no significant difference between the therapy group and the control group before treatment ( $p > 0.05$ ). After treatment, the ALB level in the therapy group ( $37.92 \pm 3.62$ ) and the control group ( $31.08 \pm 1.95$ ) increased significantly ( $^{**}p < 0.05$ ), indicating that the treatment was effective. The level of ALB in the therapy group was higher than that of the control group, suggesting that the combination of western medicine and TCM in the therapy group has a better effect on the improvement of hypoalbuminemia ( $^{*}p < 0.05$ ).

**3.4. Comparison of the Levels of Triglyceride and Cholesterol between the Two Groups.** The triglyceride level of the therapy group and the control group before treatment was  $7.31 \pm 1.95$  and  $7.45 \pm 2.07$ , and the cholesterol level was  $3.21 \pm 0.57$  and  $3.17 \pm 0.63$ , respectively. There was no significant difference between the control group and the therapy group in the two indexes of blood lipid ( $p > 0.05$ ), and they were comparable. The levels of triglycerides and cholesterol in the therapy group and the control group after treatment were lower than those before treatment ( $^{*}p < 0.05$ ), indicating that the treatments of both groups were effective, and the triglyceride and cholesterol levels in the therapy group decreased more as compared to the control group ( $^{*}p < 0.05$ ), indicating that the therapy group was better than the control group in improving the patient's blood lipid status (Table 3).

**3.5. Comparison of the Coagulation Function between the Two Groups.** There was no difference in coagulation between the therapy group and the control group before treatment ( $p > 0.05$ ), which was comparable. After treatment, the fibrinogen and D-dimer in both groups were significantly improved ( $^{*}p < 0.05$ ), and the effect of the combined Chinese and Western medicine therapy group was significantly better than that of the control group. However, there was no significant difference between the two groups in prothrombin time and activated partial thrombin time (Table 4).

**3.6. Comparison of the Renal Function between the Two Groups.** The children's renal function was evaluated by the creatinine and urea nitrogen levels. Results showed that the creatinine and urea nitrogen levels of the control group and therapy group were not significantly different ( $p > 0.05$ ), which was comparable. After treatment, the creatinine and urea nitrogen levels of the patients in the therapy group and the control group were decreased, but not significantly ( $^{*}p > 0.05$ ), indicating that the renal function of the two groups had no notable changes after treatment. There was no significant difference in renal function between the two groups after treatment ( $^{*}p > 0.05$ ), which further indicated that there was no renal toxicity after TCM combined with hormone therapy, and this treatment method was safe and could be used in clinical treatment (Table 5).

**3.7. Comparison of the Related Immune Indexes between the Two Groups.** There was no significant difference in T lymphocyte population and humoral immunity levels

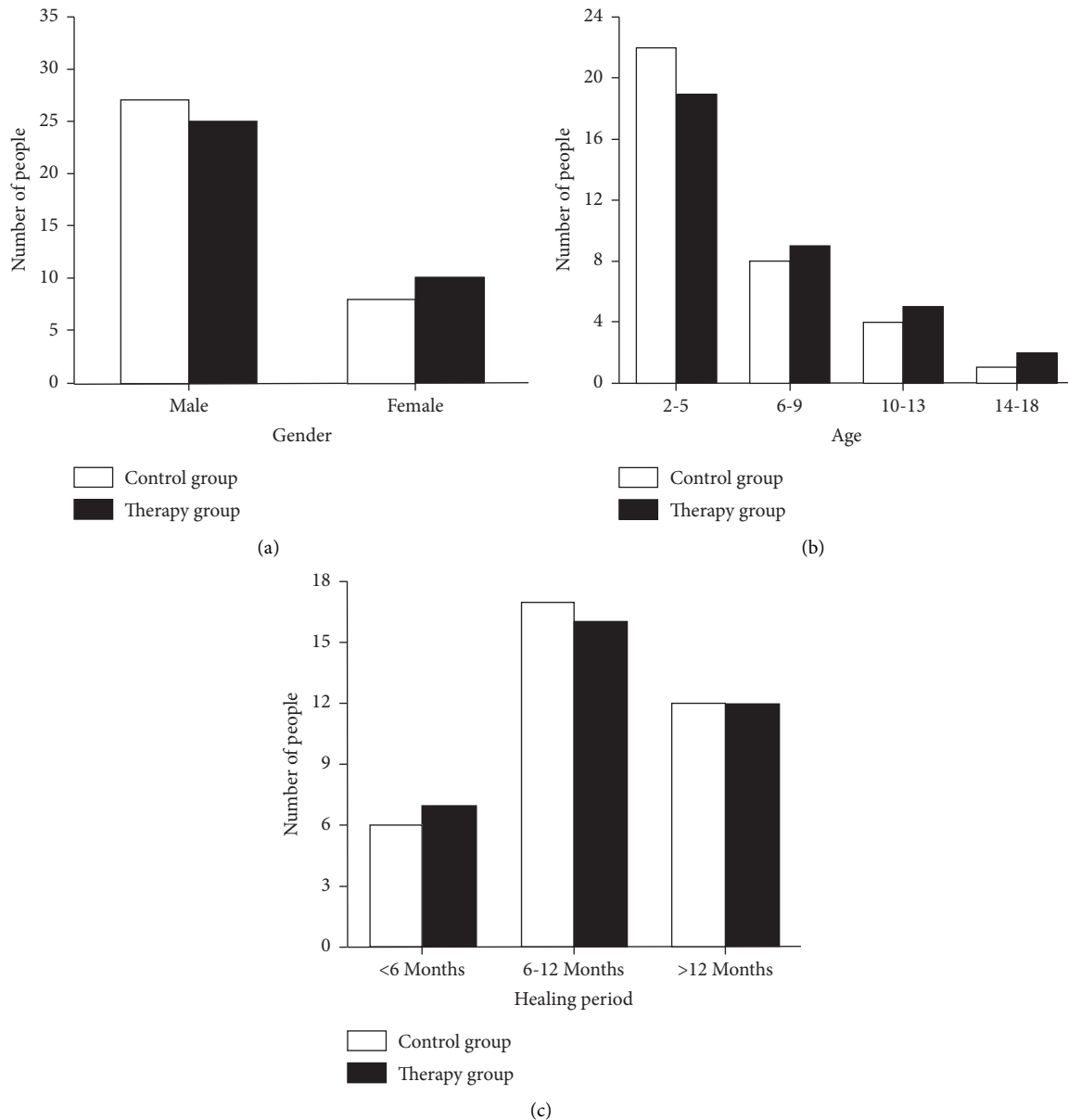


FIGURE 1: General conditions before treatment. (a) The gender distribution in the control group and therapy group. (b) The age distribution in the control group and therapy group. (c) The length of disease distribution in the control group and therapy group.

TABLE 1: Comparison of 24 h UPro level between the two groups (g/24 h).

Group	Before treatment	After treatment
Therapy group	$4.51 \pm 1.73$	$0.76 \pm 0.42^{*}$
Control group	$4.63 \pm 1.77$	$1.74 \pm 0.69_{\#}$

$_{\#}p < 0.05$  vs. after treatment;  $^{*}p < 0.05$  vs. therapy group.

between the two groups of children before treatment. The cellular immunity and humoral immunity levels of the therapy group were significantly higher than those of the control group ( $p < 0.05$ ) (Figures 2 and 3). Moreover, the infection rate of the therapy group was significantly reduced. At the same time, the indicators of immunoglobulin and T cell subgroups increased significantly after the application

TABLE 2: Comparison of the ALB level between the two groups (g/L).

Group	Before treatment	After treatment
Therapy group	$20.54 \pm 1.72$	$37.92 \pm 3.62^{*}$
Control group	$20.43 \pm 1.41$	$31.08 \pm 1.95_{\#}$

$_{\#}p < 0.05$  vs. after treatment;  $^{*}p < 0.05$  vs. therapy group.

of TCM, suggesting that PNS immunodeficiency has been effectively improved, thereby reducing the side effects of hormones and immunosuppressants.

### 3.8. Comparison of Curative Effect between the Two Groups.

The children were followed up for six months. Among them, 3 cases were lost to follow-up in the control group, 2 cases

TABLE 3: Comparison of the levels of triglyceride and cholesterol between the two groups (mmol/L).

Blood lipids	Group	Before treatment	After treatment
Triglycerides	Therapy group	7.31 ± 1.95	4.85 ± 1.37 <sup>#*</sup>
	Control group	7.45 ± 2.07	5.73 ± 1.84 <sup>#</sup>
Cholesterol	Therapy group	3.21 ± 0.57	1.82 ± 0.53 <sup>#*</sup>
	Control group	3.17 ± 0.63	2.31 ± 0.71 <sup>#</sup>

<sup>#</sup>*p* < 0.05 vs. after treatment; \**p* < 0.05 vs. therapy group.

TABLE 4: Comparison of the coagulation function between the two groups.

Coagulation function	Group	Before treatment	After treatment
Prothrombin time (s)	Therapy group	11.4 ± 1.6	12.7 ± 2.0
	Control group	11.9 ± 1.8	12.0 ± 1.5
Activated partial prothrombin time (s)	Therapy group	31.0 ± 2.7	33.6 ± 2.4
	Control group	31.8 ± 3.8	36.1 ± 4.3 <sup>#</sup>
Fibrinogen (g/L)	Therapy group	5.09 ± 1.1	2.13 ± 0.8 <sup>#*</sup>
	Control group	5.15 ± 1.3	2.72 ± 0.8 <sup>#</sup>
D-dimer (ug/ml)	Therapy group	1.42 ± 0.4	0.44 ± 0.2 <sup>#*</sup>
	Control group	1.37 ± 0.4	0.71 ± 0.3 <sup>#</sup>

<sup>#</sup>*p* < 0.05 vs. after treatment; \**p* < 0.05 vs. therapy group.

TABLE 5: Comparison of the renal function between the two groups.

Kidney function	Group	Before treatment	After treatment
Creatinine (μmol/L)	Therapy group	104.33 ± 24.34	95.92 ± 20.53 <sup>#*</sup>
	Control group	106.79 ± 29.78	102.03 ± 22.93 <sup>#</sup>
Urea nitrogen (mmol/L)	Therapy group	7.23 ± 2.97	6.46 ± 3.14 <sup>#*</sup>
	Control group	7.17 ± 3.15	6.45 ± 3.36

<sup>#</sup>*p* < 0.05 vs. after treatment; \**p* < 0.05 vs. therapy group.

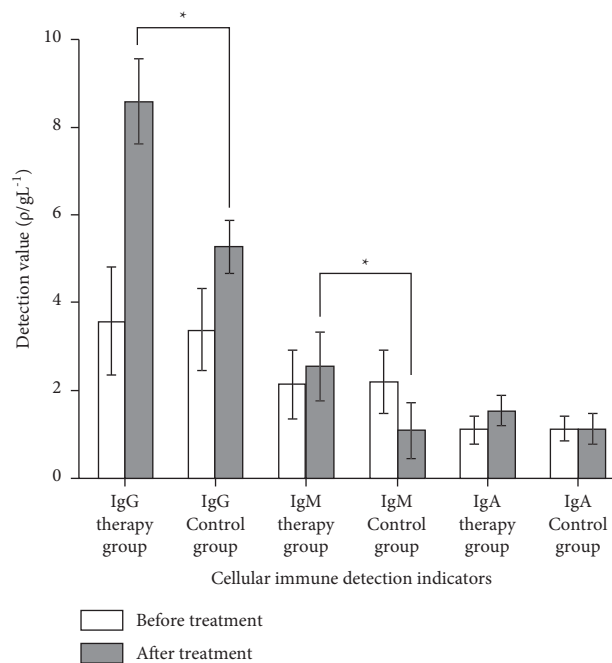


FIGURE 2: Comparison of cellular immunoassay between the two groups before and after treatment.

were missed to follow-up in the therapy group, and the missed cases were dropped from investigation. The curative effects of the two groups are shown in Tables 6 and 7, where

the total effective rate of the therapy group was higher than that of the control group (*p* < 0.05), suggesting that in the therapy group better outcomes were achieved.



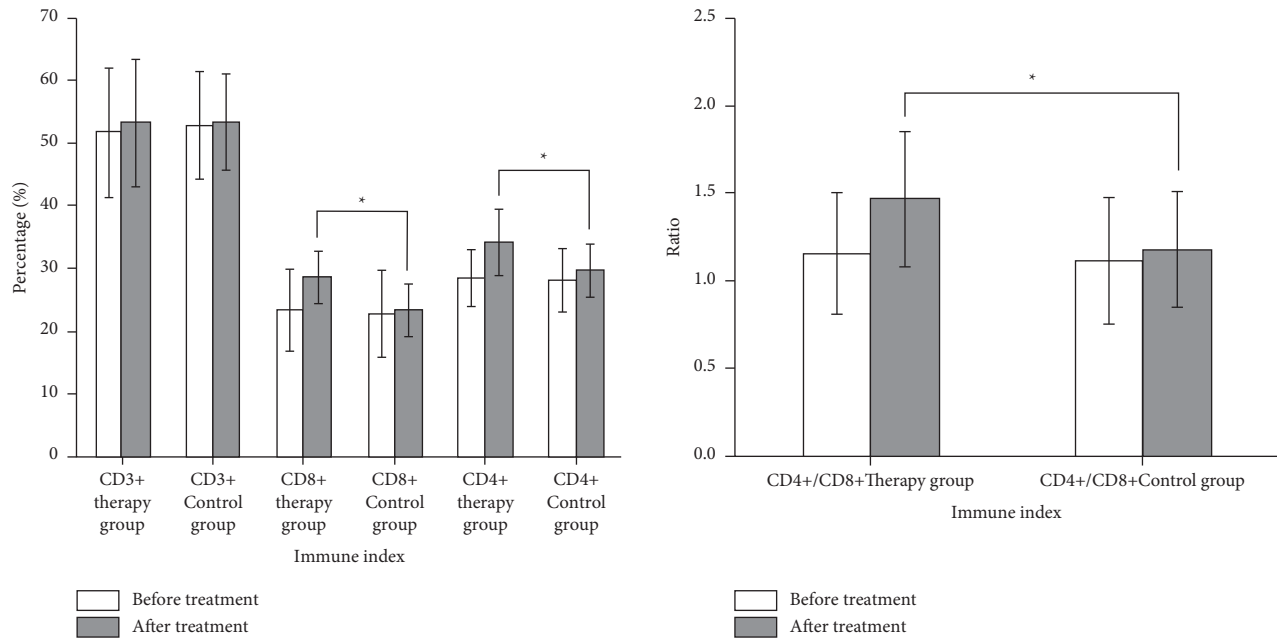


FIGURE 3: Comparison of humoral immune indexes before and after treatment between the two groups.

TABLE 6: Comparison of recent treatment courses between the two groups ( $n$  (%)).

Group	$n$	Complete response	Some relief	No relief	Total effective rate (%)
Therapy group	32	11 (34.4%)	13 (40.6%)	8 (25.0%)	75.0
Control group	33	17 (51.5%)	14 (42.4%)	2 (6.1%)	93.9

TABLE 7: Comparison of recent treatment courses between the two groups ( $n$  (%)).

Group	$n$	Cure	Get better	Invalid	Death	Total effective rate (%)
Therapy group	32	7 (21.9%)	16 (50.0%)	8 (25.0%)	1 (3.1%)	71.9
Control group	33	18 (54.5%)	14 (42.4%)	1 (3.0%)	0 (0.0%)	97.0

**3.9. Security Comparison.** As shown in Figure 4, there is no significant difference in liver function between the therapy group and the control group before treatment ( $p > 0.05$ ), which is comparable. The two important indexes of liver function in the therapy group and the control group have no significant changes ( $p > 0.05$ ). Moreover, there was no statistically significant difference between the two groups before and after treatment ( $p > 0.05$ ).

Furthermore, results from Figure 5 showed that there is no difference between the therapy group and the control group in blood routine before treatment ( $p > 0.05$ ), which is comparable. There was no significant difference in the two important liver function indexes before and after treatment in the therapy group and the control group ( $p > 0.05$ ). Moreover, there was no statistical difference between the two groups after treatment ( $p > 0.05$ ), indicating that the therapy group and the control group had no difference in blood routine effects before and after treatment. These results suggested that neither the therapy group nor the control

group had any obvious adverse reactions during the experiment. Although in some children mild digestive system reactions were observed after taking this drug, they could be relieved by themselves or corresponding interventions, without affecting the trial process.

**3.10. Comparison of Recurrence Rate between the Two Groups.** After the patients were treated, the children with effective cases in the two groups were followed up for 6 months. Results showed that there were 33 effective cases in the Chinese medicine decoction combined with the hormone therapy group, 7 relapses, and the recurrence rate in the therapy group is 21.1%. In the hormone therapy group alone, there were 32 effective cases, 17 relapsed, and the recurrence rate was 53.1%, suggesting that the recurrence rate of the Chinese medicine decoction combined with the hormone therapy group was significantly lower than that of the control group, and the difference was statistically significant

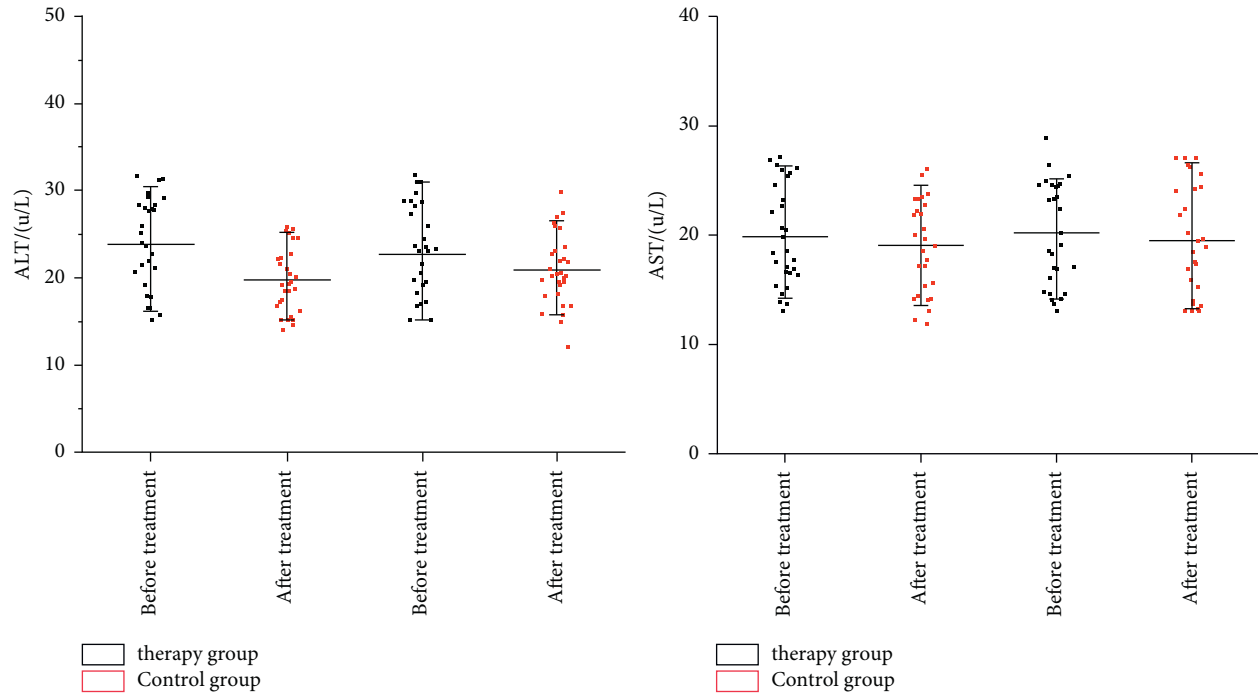


FIGURE 4: Comparison of changes in liver function between the two groups ( $\mu/L$ ).

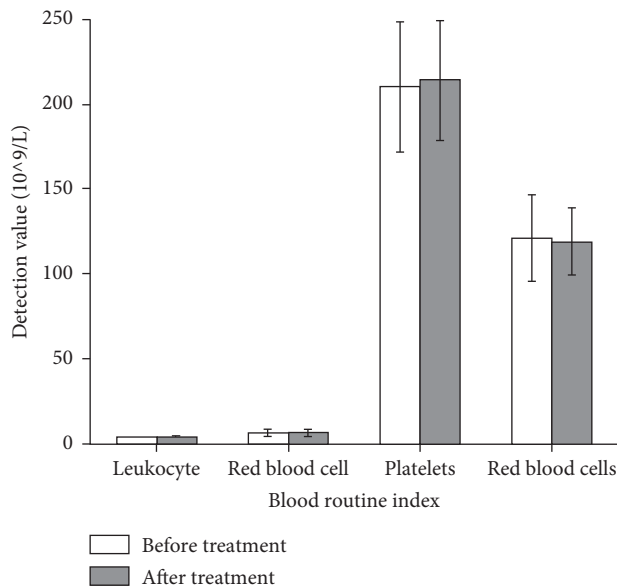


FIGURE 5: Comparison of blood routine between the two groups.

( $p < 0.05$ ) (Table 8). These results indicate that the Chinese medicine decoction combined with hormone treatment has a good effect in PNS.

#### 4. Discussion

Previous studies revealed that many hormonal Western medicines used to treat primary nephrotic syndrome could cause adverse reactions such as osteoporosis, digestive system infections, lipid metabolism disorders, atrophy of the

TABLE 8: Comparison of the recurrence rate between the two groups.

Group	Case	0	1	2	$\geq 3$ times	Recurrence rate (%)
Therapy group	33	26	4	3	0	21.1
Control group	32	15	7	6	4	53.1

adrenal cortex, and hypofunction [16]. However, the side effects of the drug can be reduced by adding TCM that strengthens the spleen and qi and nourishes the Yin and kidney. The main mechanism of TCM is to allow corticosteroids (GC) to combine with GCR to exert pharmacological effects. Clinical trials have shown that TCMs such as *Astragalus* can increase the number of GCR and increase the effective combination of GC and GCR. This kind of TCM can alleviate the disease of Yang hyperactivity and Yin deficiency, reduce the adverse reaction of hormone drugs on the immune mechanism in children, improve the immune function of the body, and play a good role in reducing recurrence, consolidating curative effect, preventing cold, and playing a positive role in the treatment of diseases.

*Astragalus* is a tonic TCM with the functions of invigorating qi and promoting yang, promoting hydration, reducing swelling, and strengthening the surface and antiperspirant. Its active ingredients are mainly *Astragalus* polysaccharides, flavonoids [17], and saponins [18], which have various pharmacological effects such as regulating immune function, antitumor, regulating body metabolism, and antiaging. The pharmacological effects of astragalus aqueous extract in adriamycin nephropathy improved the state of high coagulation and high viscosity of blood and the coagulation time, (1) avoiding the formation of thrombi; (2)

increasing the number of CD3+ lymphocytes in vivo, increasing the ratio of CD4+/CD8+, and improving the immune function; (3) improving urinary albumin and increasing plasma albumin level; (4) reducing total cholesterol and triglyceride levels, improving endogenous creatinine clearance rate, urea nitrogen, and other renal function indexes; (5) relieving edema. *Astragalus* plays a role in the intervention of nephropathy, such as supplementing qi and strengthening surface, supplementing qi of spleen and lung, supplementing kidney and supplementing qi, and benefiting water in reducing swelling. In addition, in clinical use of *Astragalus* and Western medicine intervention, nephrotic syndrome can reduce the adverse effects of chemical drug intervention.

In this study, glucocorticoids combined with TCM were used for the comprehensive treatment of primary nephrotic syndrome in children, and results showed that the urinary protein quantification, triglycerides, cholesterol levels, and children's recurrence rate were significantly lower than those of the control group, and the levels of total protein and albumin, immune indexes, and blood coagulation function were significantly higher than those of the control group. The comparison of the renal function indexes, liver function indexes, and blood routine concluded that there is no noticeable difference in the incidence of adverse reactions between the two groups.

## 5. Conclusion

In summary, the use of hormones and TCMs to treat children with primary nephrotic syndrome can effectively reduce the adverse reactions caused by hormone therapy, improve therapeutic outcomes, and reduce the recurrence rate. Moreover, it could improve the sensitivity of children to hormones and further shortens the hormone-induced remission time, and it has a better synergistic effect in the use of hormones in the treatment of primary nephrotic syndrome in pediatric patients.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author upon reasonable request.

## Disclosure

The funding body had no role in the design of the study, collection, analysis, interpretation of data, or writing of the manuscript.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Diagnostic Value of Serum Markers Combined with TVCDS in Ovarian Cancer Patients Treated with Bushen Yiqi Quyu Prescription

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**Background.** To compare the diagnostic value of serum markers human epididymal protein 4 (HE4) and cyclooxygenase-1 (COX-1) combined with transvaginal color Doppler sonography (TVCDS) in ovarian cancer (OC) treated with Bushen Yiqi Quyu prescription. **Methods.** A total of 232 OC patients treated at the hospital from January 2018 to October 2020 were randomly divided into an observation group ( $n = 116$ ) and control group ( $n = 116$ ). The control group was treated with essential Western medication, and the observation group was treated with essential Western medication and Bushen Yiqi Quyu prescription. The clinical efficacy of the two groups was compared. The levels of HE4 and COX-1 were compared between the two groups before and after treatment. The ultrasonic features of TVCDS were compared between the two groups before and after treatment. The ROC curve was drawn to compare the sensitivity, specificity, and accuracy of single and combined detection of HE4, COX-1, and TVCDS in the observation group. **Results.** The total effective rate of the observation group was significantly higher than that of the control group. After treatment, HE4 and COX-1 levels in both groups were considerably lower than those before treatment, and in the observation group, they decreased significantly than in the control group. HE4 and COX-1 were positively correlated with the clinical stage of OC. The higher the clinical stage, the higher the levels of HE4 and COX-1. After treatment, there was no significant difference in tumor location and the boundary between the two groups. There were statistically significant differences in tumor echo, nature, morphology, calcification, internal blood flow, and lymph node metastasis, and the difference in the observation group was more evident than in control group. The sensitivity, specificity, accuracy, positive detection rate, and negative detection rate of combined detection were higher than those of single detection. **Conclusions.** Bushen Yiqi Quyu prescription has certain curative effects in the treatment of OC patients, which can significantly reduce the level of tumor markers and improve the symptoms of OC patients. The combined detection of HE4, COX-1, and TVCDS has high sensitivity, specificity, and accuracy, which can effectively detect OC and reduce missed diagnosis and misdiagnosis.

## 1. Introduction

Ovarian cancer (OC) is one of the common malignant tumors of the female reproductive system, and its incidence varies in the world. In China, the incidence of OC is high and on the rise, second only to endometrial cancer and cervical cancer [1]. Clinically, epithelial ovarian cancer has a high mortality rate, ranking first among female reproductive system malignant tumors [2]. The incidence of OC is

insidious, and most clinically diagnosed patients are in the middle and late stages. The 5-year survival rate is only about 30%, posing a serious threat to patients' life [3]. Therefore, early screening can timely detect the disease and provide an effective treatment plan to patients. It has been reported that if patients can be diagnosed at stage I-II, the 5-year survival rate increases from 30% to more than 70% [4]. Therefore, finding an accurate and effective diagnostic method is the key to early diagnosis and treatment of OC.

HE4 is a new marker for OC. Studies have found that HE4 is highly expressed in OC cells, predominantly serous and ovarian endometrioid tumors, and currently plays an essential role in the early diagnosis, prognosis, and disease monitoring of OC [5]. COX-1 is a new ovarian tumor-associated antigen, which exists in some OC and cervical cancer cell lines. COX-1 is not expressed in healthy tissues, but is closely related to OC tissues [6]. At present, transvaginal color Doppler sonography (TVCDs) is a commonly used imaging examination method in diagnosing OC. It has the advantages of simple operation, being economical and noninvasive, and displaying the blood supply characteristics of tumors through CDFI, which is widely used in the screening and diagnosis of gynecological diseases [7].

The treatment of OC is mainly surgery, supplemented by radiotherapy and chemotherapy. However, long-term use of chemotherapy drugs can damage normal cells and cause a series of adverse reactions, seriously affecting the normal life of patients [8]. Studies in recent years have shown [9] that TCM has achieved remarkable results in adjuvant chemotherapy for tumor treatment, which can not only improve the efficacy but also alleviate the adverse reactions caused by chemotherapy and enhance the immune function of the body. In TCM, OC could be classified as “accumulation,” “abdominal mass,” and “female abdominal mass” [10]. The occurrence of OC is caused by the weakness of the body resulting in low vitality [11]. Wu et al. [12] claimed that the pathogenesis of OC was due to the deficiency of vital qi and poor blood flow, and treatment should focus on replenishing qi and removing blood stasis, with Shi Quan Da Bu decoction as the prescription. Wang Y et al. [13] reported that the etiology and pathogenesis of OC were the imbalance of Yin and Yang in the body, the obstruction of blood flow, and the accumulation of blood stasis. The treatment should be combined with the combination of strengthening and removing pathogenic factors. Bushen Yiqi Quyu prescription can not only reduce the adverse reactions of radiotherapy and chemotherapy but also enhance the immune function of the body, to improve the therapeutic effects against tumor.

The purpose of this study was to observe the diagnostic value of HE4 and COX-1 combined with TVCDs in OC patients treated with Bushen Yiqi Quyu prescription.

## 2. Materials and Methods

**2.1. General Information.** A total of 232 OC patients treated at the Tengzhou Central People's Hospital, Tengzhou, Shandong, China, from January 2018 to October 2020 were randomly divided into an observation group ( $n = 116$ ) and control group ( $n = 116$ ). Inclusion criteria: (1) diagnosed by histopathology; (2) met the Western medicine diagnostic criteria [14] and TCM syndrome differentiation criteria [15]; (3) have not undergone other gynecological operations; and (4) the expected survival time is more than 6 months. Exclusion criteria: (1) patients allergic to medication used in this study; (2) complicated with other gynecological diseases and benign and malignant tumors; (3) have mental or communication disorders, unable to communicate; and (4) incomplete case data. The informed consent of all patients

was obtained and approved by the ethics committee of the Tengzhou Central People's Hospital, Tengzhou, Shandong, China. There was no significant difference in general data between the two groups (Table 1).

**2.2. The Treatment.** The control group was treated with prescribed Western medicine (including surgery and radiotherapy and chemotherapy in routine), and the observation group was given Bushen Yiqi Quyu prescription on the basis of the treatment in the control group. The ingredients of Bushen Yiqi Quyu prescription are 30 g *Scutellariae Barbatae* Herba, 30 g *Fallopia multiflora*, 30 g *Dioscoreae Rhizoma*, 30 *Rehmanniae Radix* Praeparata, 20 g *Scutellaria baicalensis*, 20 g *Codonopsis Radix*, 15 g *Ligustri Lucidi Fructus*, 15 g *Chuanxiong Rhizoma*, 15 g *Corni Fructus*, 15 g *Solanum nigrum*, 15 g *Curcumae Rhizoma*, 15 g *Poria*, 15 g *Herba Hedyotidis*, and 6 g *Glycyrrhizae Radix et Rhizoma* Praeparata cum Melle. This prescription was decocted with water and taken warm on an empty stomach in the morning and evening, 200 mL/time, once per 1 d. The treatment period was 21 d, and the treatment period was 3.

**2.3. Observed Indicators.** Clinical efficacy [16]: complete remission (CR), all lesions disappeared, and no new lesions were observed for more than 1 month; partial remission (PR), the lesions were 1/2 smaller than before chemotherapy, and there was no lesion enlargement; stable disease (SD), the lesion was without shrinkage or enlargement; and progression disease (PD), the lesions increased by 1/4 compared with before treatment, or new lesions were seen. Total effective rate was calculated using the following equation:

$$\text{Total effective rate} = \left[ \frac{(\text{CR} + \text{PR})}{\text{total number of cases}} \right] \times 100\%. \quad (1)$$

**2.4. Determination of Serum Marker Levels.** 5 ml fasting venous blood was collected from the two groups in the morning and made to stand at room temperature for 30 min. The serum was separated by centrifugation and stored in a refrigerator at  $-20^{\circ}\text{C}$ . HE4 level was detected by enzyme-linked immunosorbent assay (ELISA) (Kananga, Sweden). The cox-1 level was measured by electrochemiluminescence (Roche). All were operated in strict accordance with the manual requirements, and all quality control met the criteria. The criteria were COX-1  $> 12 \text{ U/mL}$  was positive and HE4  $> 150 \text{ pmol/L}$  was positive.

**2.5. TVCDs.** The PHILIPS iU22 color Doppler ultrasound diagnostic instrument with a probe frequency of 7.5 MHz was used for TVCDs. The patient emptied the bladder and probed the uterus and adnexa area with an intracavitary probe through the vagina. The size and internal structure of the adnexa tumor were carefully scanned to observe the size, location, boundary, shape, and internal echo of the tumors.



TABLE 1: Comparison of general clinical data between the two groups.

	Observation group ( $n = 116$ )	Control group ( $n = 116$ )	$\chi^2$	$P$
Age (years)			0.075	0.784
>50	74	76		
≤50	42	40		
Weight (kg)			0.163	0.687
>62	69	72		
≤62	47	44		
The course of OC (years)			0.309	0.578
>2	37	41		
≤2	79	75		
Symptom			0.086	0.769
Obvious abdominal pain	83	85		
No obvious symptoms	33	31		
Clinical stage			0.177	0.981
I	27	29		
II	35	34		
III	43	41		
IV	11	12		
Pathological type			0.395	0.941
Serous cystadenocarcinoma	78	75		
Endometrial carcinoma	7	6		
Mucinous cystadenocarcinoma	19	22		
Others	12	13		

**2.6. Statistical Analysis.** SPSS 22.0 software was used for statistical analysis. Measurement data were expressed by mean  $\pm$  standard deviation, and comparison between groups was performed by the  $t$ -test. Count data were expressed by  $[N(\%)]$ , and comparison between groups was performed by the  $\chi^2$  test. An ROC curve was drawn to calculate sensitivity and specificity.  $p < 0.05$  was considered statistically significant.

### 3. Results

**3.1. Comparison of Clinical Efficacy between the Two Groups.** The total effective rate of the observation group was 83.62%, significantly higher than that of the control group 62.93% (Table 2). The results show that Bushen Yiqi Quyu prescription can improve the curative effects.

**3.1.1. Comparison of Serum Tumor Marker Levels between the Two Groups before and after Treatment.** Before treatment, there was no significant difference in serum HE4 and COX-1 levels between two groups. After treatment, HE4 and COX-1 of the observation group were  $(106.01 \pm 46.58)$  pmol/L and  $(11.05 \pm 3.11)$  U/mL, respectively. The levels of HE4 and COX-1 in the control group were  $(156.32 \pm 47.17)$  pmol/mL and  $(26.03 \pm 4.68)$  U/mL, respectively. After treatment, the levels of HE4 and COX-1 were significantly lower than before treatment. After treatment, the levels of HE4 and COX-1 in the observation group were lower than those in the control group (Figure 1).

**3.1.2. Comparison of Serum Tumor Markers in Patients with Different Stages of OC.** The results showed that the levels of HE4 and COX-1 were positively correlated with the clinical

stage of OC. The higher the clinical stage, the higher the levels of HE4 and COX-1 (Table 3).

**3.1.3. Comparison of the Ultrasonic Features in OC Patients before and after Treatment between the Two Groups.** Before treatment, there was no significant difference in ultrasound indexes between the two groups. After treatment, there were statistically significant differences in echo, nature, morphology, calcification, internal blood flow, and lymph node metastasis between the two groups, and the difference in the observation group was more obvious than in the control group (Table 4).

**3.1.4. Comparison of the Diagnostic Value of HE4, COX-1, and TVCDS in Single and Combined Detection of OC.** The sensitivity, specificity, accuracy, positive rate, and negative rate of COX-1 in the diagnosis of OC were 65.38%, 81.58%, 70.69%, 87.93%, and 55.17%, respectively. The sensitivity, specificity, accuracy, positive rate, and negative rate of HE4 in the diagnosis of OC were 73.08%, 84.21%, 76.72%, 90.48%, and 60.38%, respectively. The sensitivity, specificity, accuracy, positive rate, and negative rate of TVCDS in the diagnosis of OC were 67.95%, 86.84%, 74.14%, 91.38%, and 59.90%, respectively. The sensitivity, specificity, accuracy, positive rate, and negative rate of combined detection were 92.31%, 92.11%, 92.24%, 96.00%, and 85.37%, respectively. The results showed that the combined detection was higher than the single detection, and the difference in sensitivity, accuracy, and negative detection rate was statistically significant (Figure 2 and Table 5).

### 4. Discussion

OC is one of the common malignant tumors of the female reproductive system and has the highest mortality rate

TABLE 2: Comparison of clinical efficacy between the two groups.

Group	<i>n</i>	CR	PR	SD	PD	Total effective rate
Observation group	116	38 (32.76)	59 (50.86)	13 (11.21)	6 (5.17)	97 (83.62)
Control group	116	21 (18.10)	52 (44.83)	27 (23.28)	16 (13.79)	73 (62.93)
$X^2$						14.785
<i>P</i>						0.002

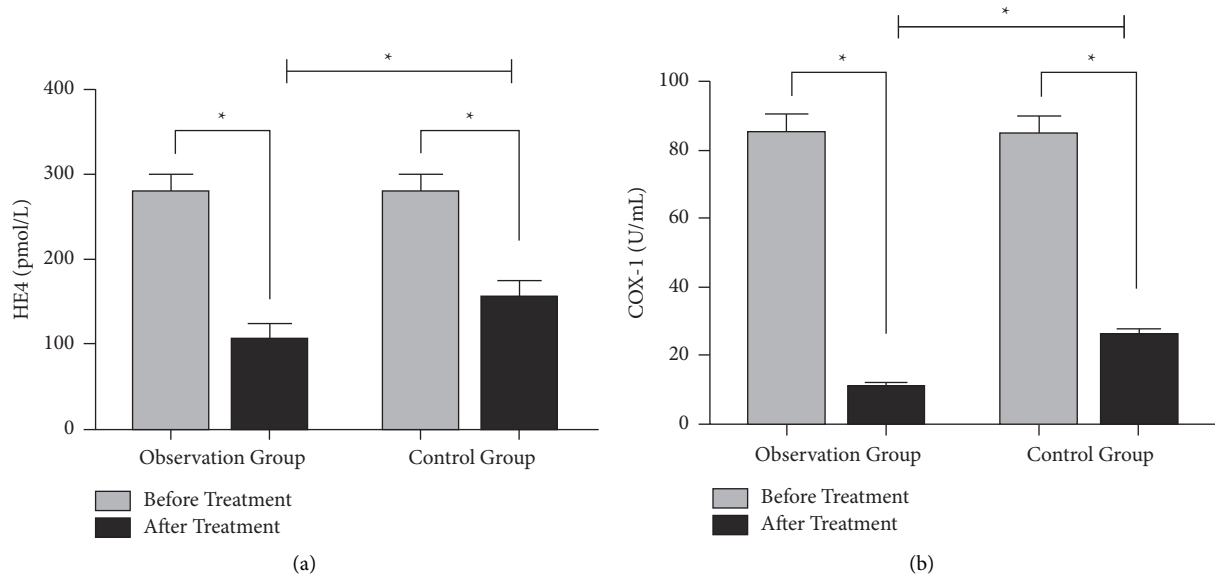
FIGURE 1: Comparison of serum tumor marker levels between the two groups before and after treatment. (a) comparison of HE4 between the two groups before and after treatment. (b) The comparison of COX-1 between the two groups before and after treatment. \* $p < 0.05$ .

TABLE 3: Comparison of serum tumor markers in patients with different stages of OC.

Clinical stage	<i>n</i>	HE4 (pmol/L)	COX-1 (U/mL)
I	56	193.52 ± 41.64	46.32 ± 8.65
II	69	227.83 ± 43.12	65.94 ± 9.28
III	84	278.96 ± 38.57	91.76 ± 11.37
IV	23	353.67 ± 32.86	136.54 ± 13.71
<i>t</i>		8.623	7.540
<i>P</i>		<0.05	<0.05

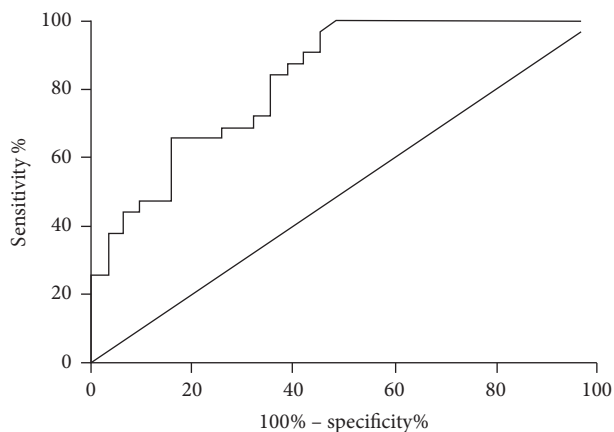
among gynecological tumors. As the early clinical symptoms are not apparent, it is easy to cause missed diagnosis and misdiagnosis, so most OC patients are found with the advanced stage at the time of diagnosis commonly [17]. OC is difficult to treat, with surgery and chemotherapy as the main treatment, but the prognosis is poor and the recurrence rate is high [18]. Chemotherapy has therapeutic effects, but it usually causes severe side effects. According to Chinese traditional medicine, the kidney is the innate book and the spleen is the root of acquired. The spleen and kidney can be treated together to nourish the viscera and restore vital qi [19]. If vital qi is deficient, kidney qi will become further weak and the body will produce Yin and Yang imbalance to aggravate the disease. Health professionals have different opinions about treating OC. Francisco Fernandez et al. [20] believed that invigorating the spleen and tonifying the

kidney could improve the fatigue symptoms of OC patients. Tao et al. reported [21] that the treatment of OC should be based on disease differentiation, constitution differentiation, and combination of disease differentiation and syndrome differentiation.

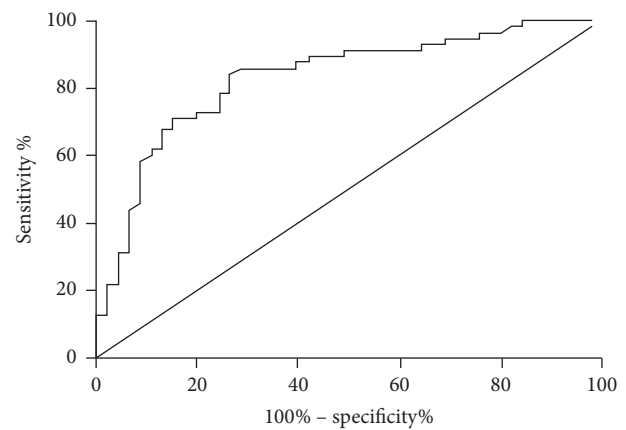
According to our findings, the total effective rate in the observation group was significantly higher than that in the control group. HE4 and COX-1 levels in the observation group were predominantly higher than those in the control group after therapy. After treatment, there were significant differences between the two groups in tumor echo, nature, morphology, calcification, internal blood flow, and lymph node metastasis. This is because *Rehmanniae Radix*, *Præparata*, *Corni Fructus*, and *Dioscoreae Rhizoma* have a nourishing role. *Corni Fructus* can tonify the liver and kidney and cure frequent urination, backache,

TABLE 4: Comparison of ultrasonographic features of TVCDS in OC patients before and after treatment between the two groups.

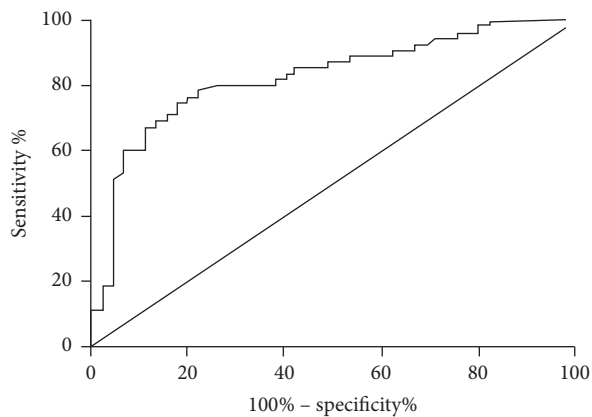
Ultrasonographic features		Observation group		Control group		$X^2$	$p$
		Before treatment ( $n = 116$ )	After treatment ( $n = 78$ )	Before treatment ( $n = 116$ )	After treatment ( $n = 95$ )		
Location	Above the middle	74	52	69	57	1.347	>0.05
	Below	42	26	47	38		
Echo	Hypoechoic	87	31	85	52	33.288	<0.05
	High or equal echo	29	47	31	43		
Boundary	Clarity	79	55	82	74	2.642	>0.05
	Obscure	37	23	34	21		
Characters	Solid	47	16	44	27	40.247	<0.05
	Cyst-solid	42	13	43	29		
Shape	Cystic	27	49	29	39	5.443	<0.05
	Round or oval	49	23	53	37		
Calcification	Irregular	67	55	63	58	54.532	<0.05
	No	12	25	15	23		
Internal blood flow	Tiny	38	43	40	46	25.605	<0.05
	Bulky	66	10	61	26		
Lymph node metastasis	Not rich	41	53	44	51	39.780	<0.05
	Rich	75	25	72	44		
	No	51	66	53	60		
	Yes	65	12	63	35		



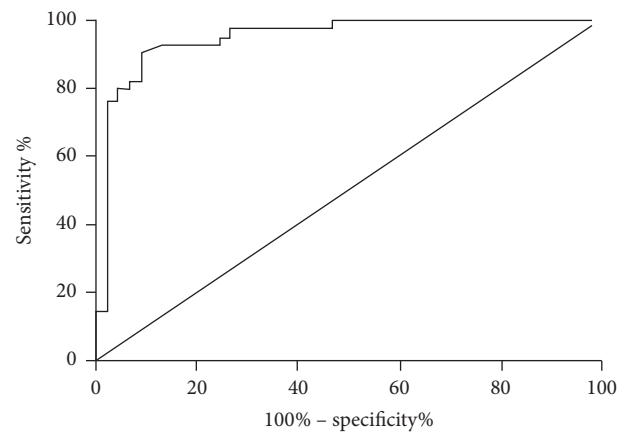
(a)



(b)



(c)



(d)

FIGURE 2: ROC curves of HE4, COX-1, and TVCDS for single and combined detection of OC. (A) ROC curve of COX-1 for the diagnosis of OC. (B) ROC curve of HE4 in the diagnosis of OC. (C) ROC curve of TVCDS in the diagnosis of OC. (D) ROC curve of the combined diagnosis of OC.

TABLE 5: Diagnostic value of HE4, COX-1, and TVCDS in the single and combined detection of OC.

	Sensitivity	Specificity	Accuracy	Positive rate	Negative rate
HE4	73.08 (57/78)	84.21 (32/38)	76.72 (89/116)	90.48 (57/63)	60.38 (32/53)
COX-1	65.38 (51/78)	81.58 (31/38)	70.69 (82/116)	87.93 (51/58)	55.17 (32/58)
TVCDS	67.95 (53/78)	86.84 (33/38)	74.14 (86/116)	91.38 (53/58)	56.90 (33/58)
Combined detection	92.31 (72/78)	92.11 (35/38)	92.24 (107/116)	96.00 (72/75)	85.37 (35/41)

dysmenorrhea, and vaginal bleeding. Dioscoreae Rhizoma can nourish the spleen and strengthen the kidney. Rehmanniae Radix Praeparata can nourish Yin and blood. Ligustri Lucidi Fructus can nourish kidney Yin. Codonopsis Radix can tonify qi and enhance immunity. Chuanxiong Rhizoma can promote qi, activate blood, and dispel wind for dispelling pain. Solanum nigrum can remove heat and eliminate toxicity and dissipate blood stasis for detumescence. Curcumae Rhizoma can remove blood stasis and relieve pain and protect the liver and kidney. Poria can nourish the heart to tranquilize, reinforce Qi, and strengthen the spleen. Scutellariae Barbatæ Herba can clear heat and remove toxicity and boost blood circulation for removing blood stasis and detumescence for relieving pain. *Fallopia multiflora* has the effect of reinforcing the kidney for supplementing essence and detoxification. Herba Hedyotis and *Scutellaria baicalensis* can clear heat and remove toxicity and promote urination. Glycyrrhizae Radix et Rhizoma Praeparata cum Melle has the effect of benefiting qi for nourishing yin and activating Yang [22–24]. Choi et al. [25] found that *Scutellaria baicalensis* can effectively inhibit the proliferation and induce apoptosis of OC cells. Ruan et al. [26] found that *Poria cocos* extract can inhibit the occurrence and development of OC by interfering with mitochondrial function, galactose, and fatty acid metabolism. All these remedies can improve the clinical symptoms of OC patients and promote their recovery by boosting blood circulation and removing blood stasis, resolving static blood for relieving pain, diuresis, tonifying the kidney and spleen, tonifying qi, and moistening the lung.

Early screening of OC is of great significance. Serum markers play an important role in diagnostic oncology. In recent years, many potential markers have been identified and used individually or in combination to improve specificity and sensitivity, especially in the early stages of disease [27]. TVCDS is also commonly used in the diagnosis of gynecological carcinomas. It is characterized by the ability to precisely display the blood flow signals in the lesions and can directly observe the patient's ovarian morphology, size, and abnormal surrounding tissues, so as to accurately evaluate the patient's tumor. It is noninvasive, easy to operate, and economical and can be used as an important auxiliary approach for the clinical examination of OC [28, 29]. The results showed that serum HE4 and COX-1 levels increased gradually with the increase of clinical stage, indicating that the two serum markers can assist the early diagnosis of OC. In this study, the sensitivity, specificity, and accuracy of HE4 and COX-1 combined with TVCDS were significantly higher than those of either assay alone. Combined detection can further improve the diagnosis rate and reduce the rate of missed diagnosis and misdiagnosis. However, the sample

size of this study is small, and the results may be biased to some extent. It is necessary to increase the sample size for further research in the future.

## 5. Conclusions

In conclusion, Bushen Yiqi Quyu prescription in this study has good therapeutic effects in treating OC, which can significantly reduce the serum indexes of patients and improve the tumor deterioration. The application of TVCDS combined with HE4 and COX-1 in the treatment of OC is optimum and significantly higher than each single detection, which has potential of clinical application for the early diagnosis of OC.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Research Article

# Curcumin Protects against Renal Ischemia/Reperfusion Injury by Regulating Oxidative Stress and Inflammatory Response

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**Objective.** The aim of this study was to explore the pharmacological effects of curcumin on oxidative stress and inflammatory response of renal dysfunction induced by renal ischemia/reperfusion (RIRI). **Methods.** Fifty male SD rats (Sprague Dawley) were randomly divided into the sham group, RIRI group, and curcumin group (low, medium, and high). The RIRI model was established by clipping the left renal artery for 45 min and then reperfusion for 24 h and resection of the contralateral kidney. In the curcumin group, curcumin was intraperitoneally injected once a day for 3 consecutive days using different dosage regimens. The RIRI group was intraperitoneally administered with normal saline. Renal injury was evaluated by measuring the concentration of creatinine (Cr) and urea nitrogen (BUN) in serum. Oxidative stress was assessed by assessing the level of malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione (GSH), and iron reduction/antioxidant capacity (FRAP) in tissues. In addition, the protective effect of RIRI was investigated by measuring Paller scores, the level of serum inflammatory factors and caspase-3, and the number of apoptotic cells. **Results.** Ischemia/reperfusion resulted in increased levels of Cr and BUN in serum and MDA in tissues and decreased levels of SOD, CAT, GPx, GSH, and FRAP. Curcumin pretreatment strikingly increased the level of SOD, CAT, GPx, GSH, IL-10, IFN- $\gamma$ , and FRAP and significantly decreased MDA, Cr, BUN, IL-8, TNF- $\alpha$ , IL-6, and myeloperoxidase (MPO) expressions in tissues. **Conclusion.** Curcumin can relieve the degree of renal injury and improve renal function in ischemia-reperfusion, which may be related to the fact that curcumin can increase SOD content in serum and reduce MDA and FRAP levels in the rat model.

## 1. Introduction

Renal ischemia-reperfusion injury (RIRI) is a common clinical pathological phenomenon, which is commonly seen in vascular surgery and kidney transplantation, and is one of the common causes of acute renal failure [1, 2]. RIRI refers to that after the restoration of blood and oxygen supply to the renal organ after ischemia, the damage of the renal organ is aggravated or even irreversible, usually caused by an inflammatory cascade reaction, including reactive oxygen species (ROS), reactive nitrogen species (RNS), and

cytokine, chemokine, and leukocyte activation [3, 4]. RIRI is a very complex pathological process, which mainly causes kidney damage through mitochondrial damage, inflammation, apoptosis, and oxidative stress. As an endocrine organ, the kidney is also a hyperperfusion organ, which is particularly sensitive to ischemia and reperfusion. When renal ischemia-reperfusion occurs, a large number of reactive oxygen species will be produced in the late stage of ischemia-reperfusion, which puts the kidney in a state of high oxidative stress and triggers a series of harmful cellular reactions, leading to inflammatory responses, cell apoptosis,



and acute renal failure and even damage to other organs [5, 6].

Curcumin is a pigment extracted from turmeric, which is mainly distributed in tropical and subtropical areas such as India, China, and Southeast Asia. It is widely used as food pigment and has good safety in human body. Curcumin can reduce renal injury caused by renal ischemia-reperfusion by reducing oxidative stress response, upregulating APPL1 expression, inhibiting the Akt phosphorylation pathway, inhibiting activation of the INOS/NO/CGMP/PKG signaling pathway, inhibiting inflammatory cell infiltration, upregulating HO-1, inhibiting NF- $\kappa$ B activity, and reducing the production of vasoactive substances [7, 8]. Curcumin has anti-inflammatory, antioxidant, antifibrosis, anticoagulation, and antitumor activities [9–12]. For instance, Nguyen-Ngo C et al. reported that curcumin markedly inhibited TNF-induced chemokines (CCL2-4, CXCL1, CXCL5, and CXCL8) expression, proinflammatory cytokines (IL-1 $\alpha$ , IL-1 $\beta$ , and IL-6), and upregulated anti-inflammatory cytokines (IL-4 and IL-13) mRNA expression in visceral adipose tissue, human placenta, and subcutaneous adipose tissue [13]. Therefore, curcumin can be used as a new treatment method for renal ischemia-reperfusion (I/R). The purpose of this study was to investigate the protective effect of curcumin in antioxidant stress and inflammation in rats with IRI.

## 2. Materials and Methods

**2.1. Animals.** SPF male SD rats, weighing  $240 \pm 20$  g, were provided by the Experimental Animal Center of the Nanjing University of Chinese Medicine. All experiments in this study were authorized by the Institutional Animal Care and Use Committee. SD rats were raised under standard SPF conditions, kept under controlled temperature conditions ( $22\text{--}24^\circ\text{C}$ ), dark/light cycle for 12 hours, and allowed to eat and drink freely.

**2.2. Drugs and Reagents.** Curcumin (specification: 100 g/box, lot no.: 20181209) was purchased from Bio Basic, Canada. Superoxide dismutase (SOD) and malondialdehyde (MDA) detection kits were purchased from Sigma-Aldrich (St. Louis, MO, USA).

**2.3. Establishment of Animal Models of Ischemia and Reperfusion.** After ether anesthesia [14, 15], the body temperature was maintained at  $37^\circ\text{C}$ , and abdominal incision through midline was performed with electrocautery to fully explore bilateral renal arteries and veins. At the same time, the renal arteries and veins were clamped bilaterally for 45 minutes. Once the ischemia time was reached, the clamps were released immediately [16]. At the end of the ischemia, the surgical area was sutured, and the rats were injected with curcumin or normal saline (NS) through a tail vein and free to get food and water. All tools used in this procedure are sterilized by autoclave or Deconex.

Throughout the procedure, a rectal probe was applied to measure the animal's temperature. A heating lamp and a

heating plate were performed to keep the animal's body temperature within the range of  $37 \pm 1^\circ\text{C}$  [17].

**2.4. Grouping and Administration.** The rats were randomly divided into 5 groups (10 in each group): sham group (Sham), renal ischemia-reperfusion injury group (RIRI), RIRI-curcumin high-dose group (60 mg/kg), RIRI-curcumin medium-dose group (30 mg/kg), and RIRI-curcumin low-dose group (15 mg/kg). The sham group and RIRI group were given the same amount of normal saline in the tail vein, and in the curcumin group, curcumin was injected into the tail vein according to the dose, for a total of 5 days [18].

**2.5. Renal Function Assessment.** After 24 h of reperfusion, rats were anesthetized with 3% pentobarbital sodium (50 mg/kg) to obtain 2–5 mL of inferior venous blood. Then, the inferior venous blood was centrifuged at  $2\text{--}8^\circ\text{C}$  for 10 min at 3000 rpm. Then, the upper serum was collected and stored in a refrigerator at  $-80^\circ\text{C}$  for later experimental detection. The serum of rats was measured by an automatic analyzer (Technicon, RA-1000, USA) to evaluate renal function.

**2.6. Renal Histomorphological Changes and Scoring.** The renal tissues were fixed with 40 g/L neutral paraformaldehyde solution for 24 h, embedded in paraffin, stained with hematoxylin-eosin (H&E), and observed under a microscope: 10 fields were randomly selected, 10 renal tubules were scored in each field, and the cortical medulla was divided in half. Renal tubules were scored according to Paller criteria: 100 renal tubules were scored with a total score of 1000 points. The higher the score was, the more serious the degree of renal tubule injury was.

**2.7. Detection of Oxidative Stress Indicators.** An appropriate amount of renal tissue was taken to prepare a 0.9% renal tissue homogenate using a tissue homogenizer and then centrifuged at 3000 rpm at  $4^\circ\text{C}$  for 15 min to obtain the supernatant. MDA content was detected by the thiobarbituric acid method, and the content of SOD was detected by xanthine oxidase according to the instructions of the kit strictly. A total of  $50\ \mu\text{L}$  tissue homogenate supernatant and FRAP concentration detection reagent were added to each test tube. FRAP levels were determined by measuring light absorption at 593 nm. The levels of SOD, CAT, GPX, and GSH in serum were measured using ELISA kits as per manufacturer's instructions. All reagents were purchased from Sigma-Aldrich.

**2.8. Detection of TNF- $\alpha$ , IL-6, and IL-8 Levels.** Total RNA was isolated from the entire kidney tissue using TRIzol (Japan, Takara) as per the manufacturer's instructions. Total RNA was then reversed using Advantage<sup>®</sup> RT-for-PCR Kit (Takara, Japan). Real-time PCR amplification was achieved using an ABI 7500 system (Massachusetts Thermoelectric, USA). Primers used for reverse transcription polymerase

chain reaction (Invitrogen, Carlsbad, CA) are given in Table 1. Reverse transcription was performed at 95°C for 30 s and circulated at 95°C for 40 s, then at 60°C for 34 s, and then at 95°C for 15 s.

**2.9. Determination of TNF- $\alpha$ , IL-6, IL-10, IFN- $\gamma$ , and MPO Levels in Serum.** The levels of TNF- $\alpha$ , IL-6, IL-10, IFN- $\gamma$  and MPO were detected by ELISA kit in strict accordance with kit operation instructions. All reagents were purchased from Sigma-Aldrich.

**2.10. Statistical Analysis.** Data were shown as mean  $\pm$  SD. Comparisons between groups of all measured parameters were performed using the one-way ANOVA test and *t*-test. All data were analyzed using SPSS 18 statistical software.  $P < 0.05$  was considered statistically significant.

### 3. Results

**3.1. Effect of Curcumin on Renal Dysfunction.** The level of Cr and BUN was strikingly increased in the RIRI group compared with sham operation ( $P < 0.01$ ) (Figure 1(a)). In this study, significant differences in serum Cr concentrations were observed in the groups treated with different doses of curcumin during a 24-hour reperfusion period compared with the Sham group, and curcumin significantly reduced the concentration of serum Cr (Figure 1(a)). In summary, the level of serum Cr in the RIRI group was higher than those in the sham group ( $P < 0.01$ ), while the concentration of serum Cr in the high-dose curcumin group was dramatically lower than that in the RIRI group ( $P < 0.05$ ).

As shown in Figure 1(b), the concentration of serum BUN was  $19.2 \pm 1.91$  mg/dL in the sham group and  $58.24 \pm 5.46$  mg/dL in the RIRI group ( $P < 0.01$ ). Compared with the RIRI group, curcumin at three different doses resulted in a notably lower concentration of serum BUN ( $P < 0.01$ ); in addition, the high-dose curcumin group led to a lower concentration of serum BUN compared with medium and low doses ( $P < 0.05$ ). The above results showed that curcumin pretreatment could reduce renal ischemia-reperfusion injury in rats, and the higher the concentration of curcumin, the more obvious the antiinjury effect.

**3.1.1. Renal Histopathological Observation and Score.** Severe congestion and edema were observed in the renal cortex and medulla pallor in the ischemia-reperfusion group. The medulla of the curcumin group showed mild congestion and edema, while no abnormality was observed in the sham group. Under the light microscope, the renal tubules in the ischemia-reperfusion group were notably dilated, the epithelial cells were swollen, vacuolated, and granular degeneration, the capillaries in the glomerulus were dilated, red blood cells were exudated, and interstitial edema and inflammatory cell infiltration were observed. Compared with the RIRI group, the lesion of the curcumin group was prominently reduced, and the renal tissue structure of the sham group was normal. Paller scores were prominently

higher in the RIRI group than in the sham group ( $P < 0.01$ ). Paller scores of the curcumin group were prominently decreased compared with the RIRI group ( $P < 0.01$ ), as given in Table 2.

**3.2. Assessment of Oxidative Stress.** Oxidative stress was assessed by measuring MDA, SOD, CAT, GPX, and GSH, which are the end products of lipid peroxidation caused by reactive oxygen species. Figure 2(a) shows that the level of MDA in the sham group was  $56.96 \pm 4.62$  nmol/kg. Compared with the RIRI group, the MDA level in the sham group was prominently increased by 78% ( $P < 0.01$ ). Compared with the RIRI group, curcumin markedly reduced the level of MDA in renal tissues ( $P < 0.05$ ), but still higher than that of the sham operation group ( $P < 0.01$ ), indicating that the expression level of MDA in the curcumin group was negatively correlated with the dose of curcumin; the higher the intervention concentration of curcumin, the lower the level of MDA. The levels of SOD, CAT, GPx, and GSH in the RIRI group were  $186.34 \pm 8.04$  U/g,  $194.31 \pm 11.47$  U/g,  $41.94 \pm 3.59$  U/g, and  $24.97 \pm 4.74$  nmol/g, respectively, and markedly lower than that in the sham group ( $734.98 \pm 12.97$  U/g,  $1021.73 \pm 20.03$  U/g,  $342.94 \pm 12.05$  U/g, and  $83.43 \pm 6.03$  nmol/g, respectively) ( $P < 0.05$ ). The expression levels of SOD, CAT, GPx, and GSH in the curcumin group were markedly higher than those in the RIRI group in dose-dependent manner ( $P < 0.05$ ), indicating that the higher the intervention concentration of curcumin was, the higher the expression level was, as shown in Figure 2. The experimental results revealed that the ischemia-reperfusion injury can produce oxidative stress in rat kidneys, and the antioxidant activity of curcumin could prevent a series of oxidative reactions. Our results also suggested that RIRI caused a significant reduction of FRAP in renal tissue compared to the sham group ( $P < 0.01$ ). Although three different doses of curcumin increased FRAP levels, this change was only significant in the high-dose curcumin group compared with the RIRI group ( $P < 0.05$ ).

**3.3. Effect of Curcumin on TNF- $\alpha$ , IL-6, and IL-8 mRNA Level.** As given in Table 3, TNF- $\alpha$ , IL-6, and IL-8 mRNA levels in the RIRI group were markedly higher than those in the sham group ( $P < 0.05$ ). However, curcumin pretreatment dramatically reduced the levels of TNF- $\alpha$  and IL-8 than the RIRI group ( $P < 0.05$ ).

**3.4. Effects of Curcumin on Anti-Inflammatory Effects.** The contents of TNF- $\alpha$ , IL-6, IL-10, IFN- $\gamma$ , and MPO in serum of the RIRI group were dramatically higher than those of the sham group ( $P < 0.05$ ). The expression level of IL-10 in serum of the curcumin group was dramatically higher in a dose-dependent manner than that of the RIRI group ( $P < 0.05$ ); the higher the intervention concentration of curcumin, the higher the expression level of IL-10. The expression levels of TNF- $\alpha$ , IFN- $\gamma$ , IL-6, and MPO in the curcumin group were memorably lower than those in the RIRI group ( $P < 0.05$ ), indicating that curcumin

TABLE 1: Real-time quantitative PCR primer.

Gene	Sense strand sequence	Antisense strand sequence
TNF- $\alpha$	AACACGAGTGACAAGCCCGTAG	GTATCACCAGTTGGTTCTCTTTGA
IL-6	AGGTTCCATGTGCAAGTGTCT	GACAGCCCTGGTCAAAGGTT
IL-8	CTGCAAGAGACTTCCATCCAG	AGTGGTATAGACAGGTCTGTTGG
$\beta$ -Actin	AGAGGGAAATCGTGCGTGAC	CAATAGTGATGACCTGGCCGT

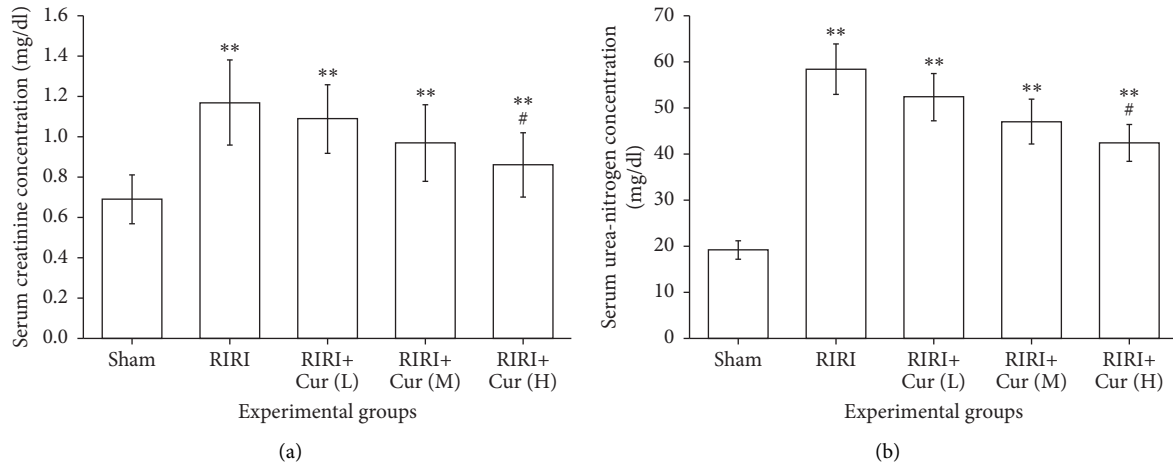


FIGURE 1: (a) The concentration of serum Cr in rats in the RIRI group, sham group, curcumin group L, M, and H, and renal ischemia-reperfusion group. (b) The concentration of serum BUN in rats in the RIRI group, sham group, curcumin group L, M, and H, and renal ischemia-reperfusion group (\*\* $P < 0.01$ , vs. the sham group. # $P < 0.05$ , vs. the RIRI group). L, low; M, medium; H, high.

TABLE 2: Comparison of Paller scores in rats.

Group	<i>n</i>	Paller score
Sham group	10	103.29 $\pm$ 16.38
RIRI group	10	509.23 $\pm$ 30.07
Low-dose curcumin group	10	430.97 $\pm$ 25.13
Medium-dose curcumin group	10	397.58 $\pm$ 20.75
High-dose curcumin group	10	351.34 $\pm$ 17.59

pretreatment decreased the secretion of TNF- $\alpha$ , IFN- $\gamma$ , IL-6, and MPO (Figure 3), and the expression levels of TNF- $\alpha$ , IFN- $\gamma$ , IL-6, and MPO in the curcumin group were negatively correlated with the dose of curcumin; the higher the intervention concentration of curcumin was, the lower the expression level was, as shown in Figure 3. The results indicated that ischemia-reperfusion injury could lead to inflammatory injury of renal tissue, and the anti-inflammatory effect of curcumin could prevent this pathological process.

**3.5. Effects of Curcumin against Apoptosis.** The apoptosis number of the RIRI group was  $18.87 \pm 1.94$ , which was memorably higher than that of the sham group ( $7.72 \pm 2.15$ ) ( $P < 0.05$ ). The number of apoptotic cells in the curcumin group was memorably lower than that in the RIRI group ( $P < 0.05$ ), suggesting that the apoptosis number of cells in the curcumin group was negatively correlated with the dose of curcumin; the higher the intervention concentration of curcumin, the fewer apoptotic cells. The expression level of caspase-3 in the RIRI group was  $61.96 \pm 8.69$  ng/g, which was memorably higher than that in the sham group

( $15.27 \pm 2.48$  ng/g) ( $P < 0.05$ ). The expression level of caspase-3 in the curcumin group was observably lower than that in the RIRI group ( $P < 0.05$ ), indicating that the expression level of caspase-3 in the curcumin group was negatively correlated with the dose of curcumin; the higher the intervention concentration of curcumin, the lower the expression level, as shown in Figure 4. The results showed that curcumin alleviated renal ischemia-reperfusion injury via exerting the antiapoptosis effect.

## 4. Discussion

Ischemia-reperfusion injury leads to the deterioration of the function of the transplanted kidney after the restoration of blood supply [19]. RIRI is the main cause of acute kidney injury after partial nephrectomy and kidney transplantation [20], which is closely related to morbidity and mortality [21]. Therefore, effective preventive and therapeutic measures are necessary to reduce renal ischemia-reperfusion injury. Inflammation is an important pathophysiological mechanism of RIRI. RIRI can induce inflammatory cell aggregation, release inflammatory factors (such as TNF- $\alpha$ , IL-6 and IL-8), and increase adhesion molecules, which together stimulate inflammatory cascade, leading to organ damage [22]. After renal ischemia, renal cell ischemic necrosis occurs, and then, restored perfusion can cause secondary damage to the kidney [23]. When renal function injury reaches a certain degree, it can exacerbate the level of BUN and Cr [5].

Current studies on the prevention and treatment of RIRI mainly focus on antioxidants and antiapoptotic drugs

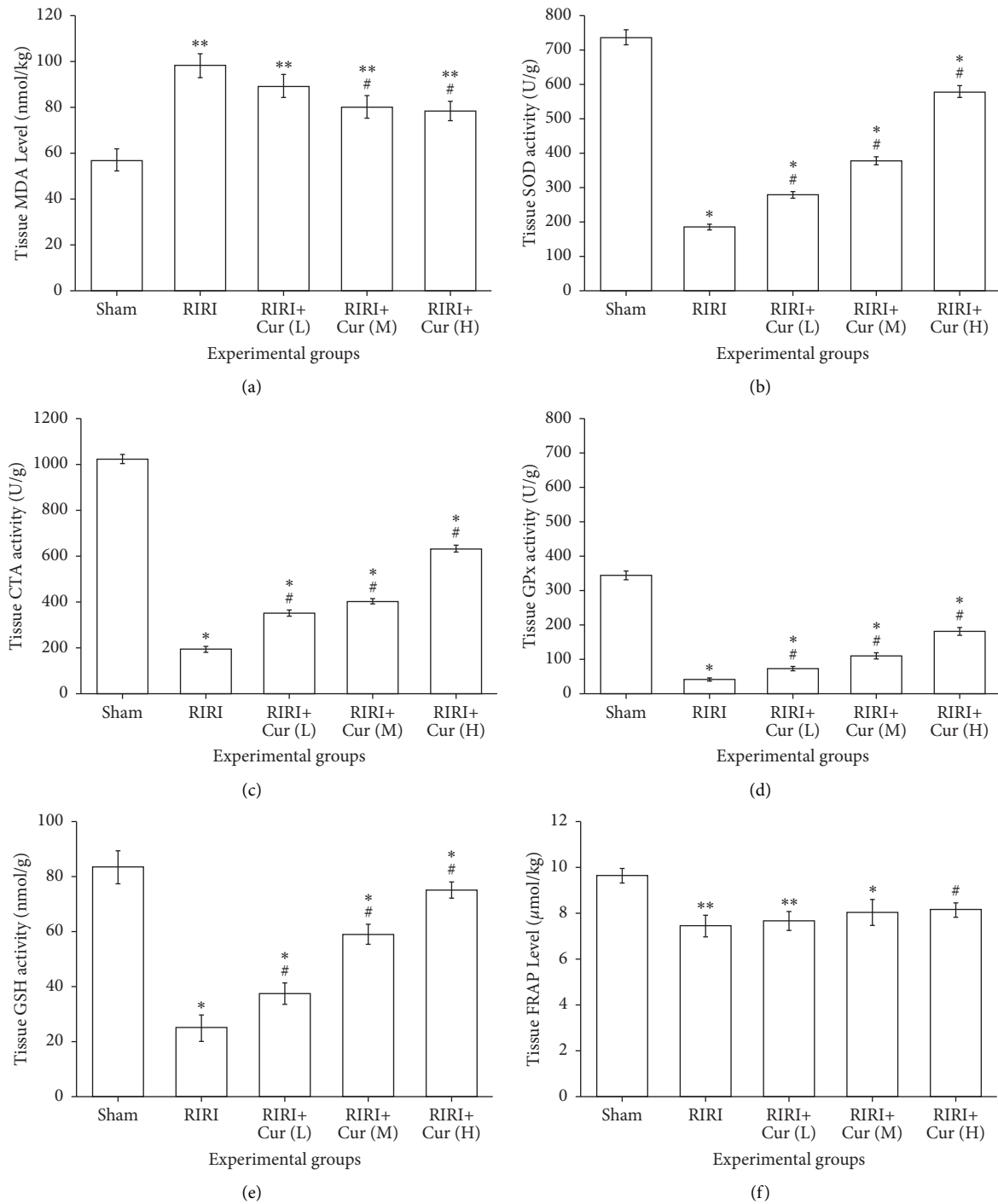


FIGURE 2: Protective effect of curcumin on ischemia-reperfusion injury in rats. The levels of MDA (a), SOD (b), CAT (c), GPX (d), GSH (e), and FRAP (f) in renal tissues are detected. \* $P < 0.05$ , vs. the sham group. # $P < 0.05$ , vs. the RIRI group.

TABLE 3: Effects of curcumin pretreatment on TNF- $\alpha$ , IL-6, and IL-8 mRNA levels in the kidney after renal ischemia-reperfusion injury.

Group	TNF- $\alpha$ (mRNA)	IL-6 (mRNA)	IL-8 (mRNA)
Sham group	$1.07 \pm 0.19^{**}$	$1.14 \pm 0.21^{**}$	$0.96 \pm 0.118^{**}$
RIRI group	$12.36 \pm 1.85$	$5.09 \pm 0.37$	$7.63 \pm 0.82$
Low-dose curcumin group	$6.53 \pm 0.99^*$	$2.07 \pm 0.52^*$	$3.77 \pm 0.46^*$
Medium-dose curcumin group	$5.87 \pm 0.43^*$	$1.76 \pm 0.47^*$	$2.49 \pm 0.38^*$
High-dose curcumin group	$4.74 \pm 0.34^*$	$1.48 \pm 0.39^*$	$2.01 \pm 0.17^*$

\* $P < 0.05$ , \*\* $P < 0.01$ , vs. the RIRI group.

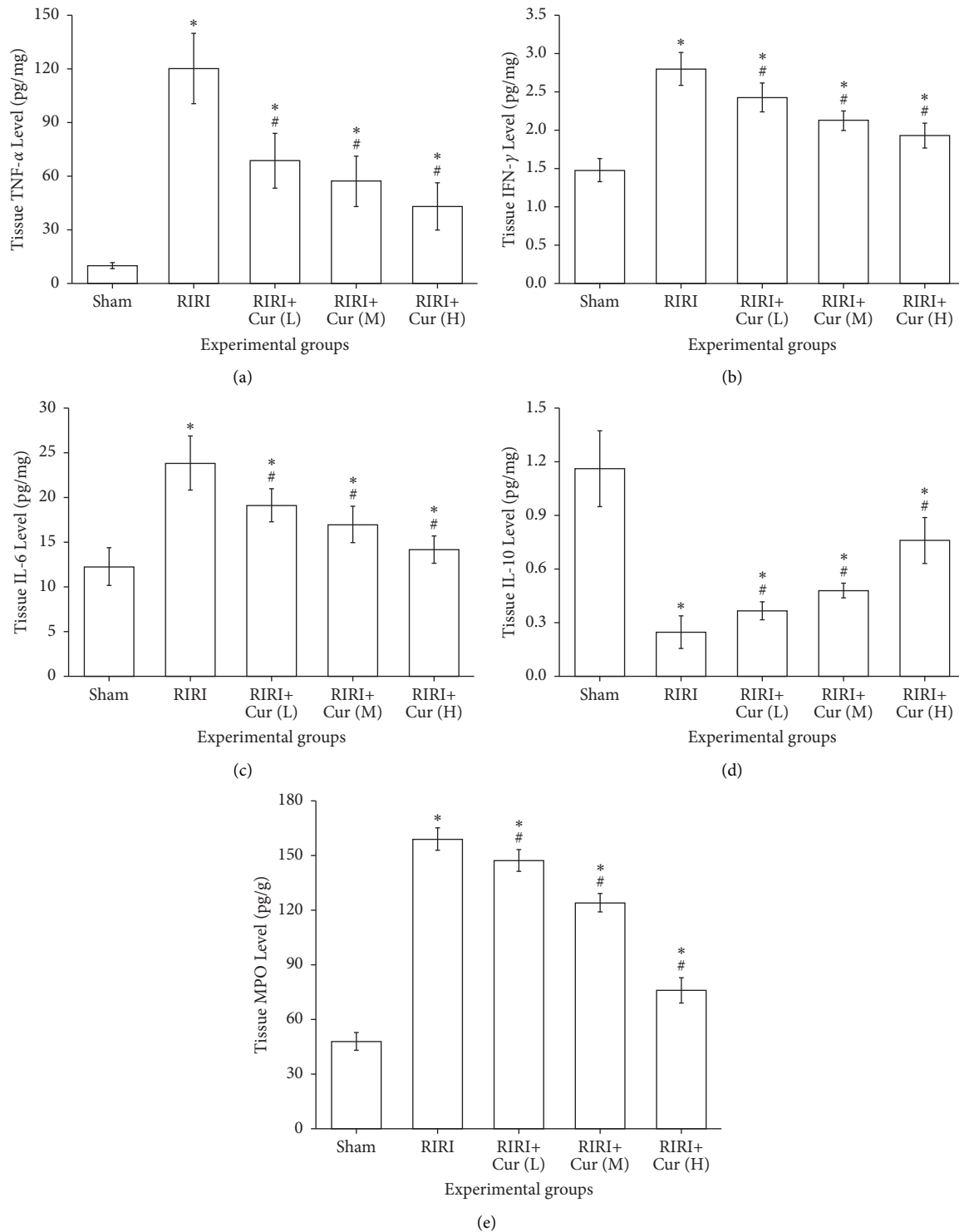


FIGURE 3: Effect of curcumin pretreatment on expression of TNF- $\alpha$ , IFN- $\gamma$ , IL-6, IL-10, and MPO in the kidney after renal ischemia-reperfusion injury.

[24]. Curcumin is an extract from the rhizome of turmeric, which is an orange knot powder and is widely used as pigment, food additive, and condiment [25]. Previous studies have shown that curcumin has antioxidant [26], anti-inflammatory [27], immunomodulatory [28], and antimicrobial effects [29]. At the same time, curcumin has

little toxic and side effects in rodents and humans, and no obvious adverse reactions have been observed even at high doses [30]. Therefore, curcumin has broad medicinal prospects.

The results of this study showed that serum Cr and UBN were highly elevated in the RIRI group, possibly due to a

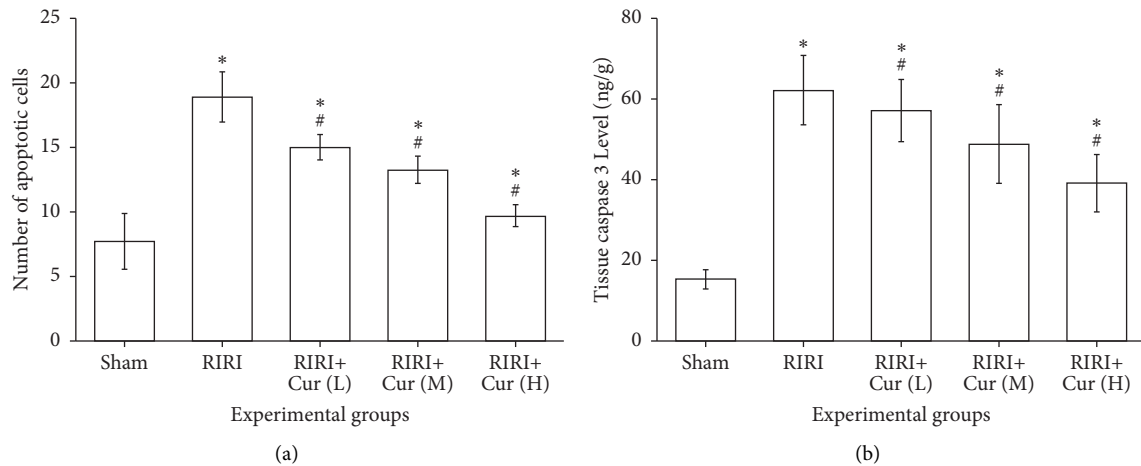


FIGURE 4: Effect of curcumin pretreatment on apoptosis of ischemia-reperfusion injury rats vs. the sham group,  $^{\#}P < 0.05$ , and vs. the RIRI group,  $*P < 0.05$ .

sharp decrease in glomerular filtration rate (GFR) and significant damage to renal tubule function in the RIRI group, and the application of curcumin resulted in partial recovery of renal function and reduced oxidative stress induced by RIRI. The content of BUN and Cr in the RIRI group was higher than those in the sham group, indicating that renal function was obviously damaged. After curcumin treatment, serum BUN and Cr decreased signally, indicating that curcumin has a protective effect on renal function, which is consistent with the findings reported in the literature [6].

When RIRI occurs, the mitochondria of kidney cells are also damaged, leading to decreased activities of SOD and GSH and being unable to effectively remove oxygen free radicals in the body, resulting in the disorder of the body's redox system and aggravating body damage. Curcumin has antioxidant effects and can regulate the activities of GSR, CAT, and SOD in free radicals, thus playing an antiinjury role. Endothelial cell dysfunction during RIRI can produce many inflammatory mediators and release a variety of inflammatory transmitters and adhesion molecules, leading chemotactic neutrophils and inflammatory cells to adhere to vascular endothelial or enter cells. At the same time, neutrophils and other inflammatory cells themselves can release chemotactic substances, which act on the kidney and cause renal ischemia-reperfusion, further aggravating kidney injury. In our study, ischemia/reperfusion resulted in an increased level of MDA and a reduced level of FRAP in the renal tissues of the RIRI group, which was consistent with the previous studies [31]. The content of SOD in the RIRI group was lower than that in the sham group, while the content of MDA was higher than that in the sham group, indicating that after renal ischemia and reperfusion, the body showed obvious lipid peroxidation reaction and weakened antioxidant capacity. Compared with the RIRI group, the content of SOD significantly increased and the content of MDA decreased in the curcumin group, indicating that curcumin treatment can reduce the content of oxygen free radical and inhibit biofilm lipid peroxidation

caused by oxygen free radical accumulation, thus enhancing the antioxidant capacity of the kidney and protecting renal ischemia-reperfusion injury [32].

The limitation of this study is that there is no further study on the downstream signaling pathway in which curcumin plays a role. In future studies, we will apply fluorescently labeled curcumin to explore the way in which it acts on cells, such as cell surface receptors or endocytosis.

In summary, curcumin plays a protective role in renal function by preventing cell damage and inhibiting cellular oxidative stress, inflammatory response, and apoptosis, but the specific protective and repair mechanism needs further exploration.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Ampelopsin Inhibits Cell Viability and Metastasis in Renal Cell Carcinoma by Negatively Regulating the PI3K/AKT Signaling Pathway

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**Background.** Previous studies have shown that Ampelopsin has an inhibitory effect on human tumors. However, the effect of Ampelopsin on renal cell carcinoma (RCC) is rarely reported. Therefore, this study aims to explain the role of Ampelopsin in RCC. **Methods.** Different concentrations of Ampelopsin (0, 10, 25, 50, and 100  $\mu$ M) were used to treat 786-O cells. Cell viability was detected by MTT assay, colony formation assay, and flow cytometry assay. Transwell assay and Wound healing assay were used to detect cell migration and invasion. Western blot analysis was applied to detect protein expression. **Results.** Ampelopsin inhibited cell proliferation and induced apoptosis in RCC. And Ampelopsin can inhibit cell migration and invasion in RCC. All these results changed in a dose-dependent manner. Ampelopsin (100  $\mu$ M) had the strongest inhibitory effect on cell viability and metastasis. In addition, Ampelopsin negatively regulated the PI3K/AKT signaling pathway in RCC cells. Moreover, Ampelopsin was only cytotoxic to RCC cells. **Conclusion.** Ampelopsin inhibits cell viability and metastasis in RCC by negatively regulating the PI3K/AKT signaling pathway.

## 1. Introduction

Renal cell carcinoma (RCC) accounts for about 90% of renal malignancies, and the ratio of male to female is about 2 : 1. The age of onset was more than 40 years old, with a median age of 65 years [1]. RCC is usually a solid tumor; 10%–25% is cystic or mainly cystic cancer. The occurrence of RCC is related to smoking, occupation, obesity, genetics, and diabetes. Smoking is a high-risk factor for RCC [2]. For early localized RCC, surgical resection is the best treatment option. However, about 30% of patients with localized RCC will have local recurrence or distant metastasis after surgery [3].

Metastatic RCC has a poor prognosis and is not sensitive to radiotherapy and chemotherapy. The 5-year survival rate of metastatic RCC is less than 10% [4]. Moreover, there are no obvious symptoms in the early stage of RCC, and about 30% of patients are already metastatic RCC at the time of diagnosis [5]. Therefore, it is very important to find effective drugs for the treatment of metastatic RCC.

Ampelopsin is the main active ingredient of *Ampelopsis grossedentata*. *Ampelopsis grossedentata* has the effects of clearing away heat, detoxifying, and improving immunity [6]. Ampelopsin is mostly used in the adjuvant treatment of upper respiratory tract infection, fever, anti-inflammatory

analgesia, swelling, and diuresis [7, 8]. Many studies have shown that Ampelopsin has the effect of inhibiting human tumors. For example, Ampelopsin induced apoptosis in human lung adenocarcinoma cells [9]. Ampelopsin inhibited the growth of breast cancer cell through the mitochondrial apoptosis pathway [10]. Ampelopsin reduced the migration and invasion of ovarian cancer cells by inhibiting epithelial-to-mesenchymal transition (EMT) [11]. However, the function of Ampelopsin in RCC is still unknown.

The PI3K/AKT signaling pathway plays an important role in a variety of biological processes such as cell metabolism, cell cycle, cell proliferation, and apoptosis [12]. Many traditional Chinese medicines play a role in human diseases by regulating the PI3K/AKT signaling pathway. For example, Ampelopsin inhibited the migration and invasion of human glioblastoma cells by regulating the PI3K/AKT signaling pathway [13]. The Chinese herbal formula tao hong si wu decoction protected cerebral ischemia-reperfusion injury through the PI3K/AKT signaling pathway [14]. In addition, it was also found that PI3K/AKT was involved in the pathogenesis of RCC. For example, HOXA6 inhibited cell proliferation and induced apoptosis by suppressing the PI3K/AKT signaling pathway in RCC [15]. Bufalin suppressed the proliferation and metastasis of RCC cells by inhibiting the PI3K/AKT/mTOR signaling pathway [16]. However, the interaction between Ampelopsin and PI3K/AKT signaling pathway has not been reported in RCC.

Therefore, the purpose of this study is to explore the role of Ampelopsin in RCC and explain the regulatory mechanism of Ampelopsin/PI3K/AKT signaling pathway in RCC.

## 2. Materials and Methods

**2.1. Cell Culture.** Normal kidney cells HK-2 and human RCC cells 786-O were purchased from Shanghai Institute of Biological Sciences (Shanghai, China). HK-2 cells were seeded in a 1:1 mixture of DMEM and Ham's F12 medium containing 10% fetal bovine serum (FBS, Life Technologies). 786-O cells were maintained in DMEM medium containing 10% FBS. They were cultured in a humidified incubator with 5% CO<sub>2</sub> at 37°C.

**2.2. Ampelopsin Treatment.** Ampelopsin stock solution (0.1 M in dimethyl sulfoxide, HPLC ≥ 98%, Guilin Natural Ingredient, Inc., Guangxi, China) was added to the medium to reach the indicated concentrations (10, 25, 50, and 100 μM). Then, different concentrations of Ampelopsin were incubated with the cells at 24 h and 48 h. A dimethyl sulfoxide solution without Ampelopsin was used as a blank control.

**2.3. Determination of Cell Viability.** To determine the cytotoxicity of Ampelopsin, MTT assay was performed to assess cell viability. 786-O and HK-2 cells ( $1 \times 10^4$  cells/well) were seeded in 24-well plates with different concentrations of Ampelopsin and incubated at 37°C for 24 h or 48 h. After the exposure period, the cells were incubated with MTT

(5 mg/mL) for 4 h. The 96-well plates were placed in the microplate reader to measure the absorbance at 540 nm.

**2.4. Detection of Cell Proliferation.** Human RCC cells 786-O were pretreated with different concentrations of Ampelopsin for 24 h. Next, they were seeded in 24-well plates (300 cells/well) and cultured in complete medium for 7 days. Then, the colonies were fixed with 10% formaldehyde for 10 min and stained with 1.0% crystal violet for 5 min. The number of colonies was counted.

**2.5. Detection of Cell Apoptosis.** The Annexin V/PI double staining method was used to detect the apoptosis rate. The RCC cell line 786-O ( $3 \times 10^5$  cells/mL) was seeded in a 12-well plate. After 7 h, cells in each group were washed 3 times with PBS. Annexin V and PI solution (5 μL, light-proof operation) were added and mixed. The cells were incubated for 20 minutes (surrounding avoidance). And apoptosis rate of each group was detected and analyzed by the flow cytometer.

**2.6. Cell Migration.** The RCC cell line 786-O ( $5 \times 10^5$  cells/mL) was seeded into a 6-well plate and cultured in a 37°C, 5% CO<sub>2</sub> incubator for 24 h. When the cell adhesion density reaches 80%–90%, a pipette was used to suck the cell liquid vertically and scrape it evenly. The cells were washed once with PBS to remove cell debris, and medium was added. After culturing in a 37°C, 5% CO<sub>2</sub> incubator for 24 h, the cells were observed and photographed under an inverted microscope. Photoshop 7.0 software was used to analyze the migration distance of cells. And cell migration rate was calculated. Cell migration rate (%) = (0 h scratch spacing – 24 h scratch spacing) / 0 h scratch spacing × 100%.

**2.7. Cell Invasion.** Transwell chamber was placed at the bottom of the 24-well plate. 786-O cell suspension ( $1 \times 10^6$  cells/mL) was added to the upper chamber. 600 μL of medium was added to the lower chamber. The cells were cultured in a 37°C, 5% CO<sub>2</sub> incubator for 24 h. After the culture is completed, the remaining cells on the inner surface of the upper membrane are wiped with a cotton swab. The invaded cells were fixed with 4% paraformaldehyde for 15 min and then stained with 0.1% crystal violet solution for 5 min. The invaded cells were observed and photographed under an inverted optical microscope.

**2.8. Western Blot Assay.** 786-O cells were lysed with RIPA lysis buffer (BeyoTime Biotech) on ice to extract total protein. The BCA method was used for protein quantification. 40 μg of total protein was separated by 12% SDS-PAGE and transferred to PVDF membranes (Millipore, USA). The membranes were then blocked with 5% skimmed milk and incubated with Bax, Bcl-2, E-cadherin, N-cadherin, vimentin, PI3K, p-PI3K, AKT, p-AKT, and GAPDH primary antibodies at 4°C overnight. Then, the secondary antibody was added and incubated at room temperature for

40 min. Chemiluminescence (ECL) was used for development. Quantity One 4.52 analysis software was used to measure the gray value of the band. Relative expression of target protein (IOD) = gray value of target protein/gray value of internal reference GAPDH.

**2.9. Statistical Analysis.** All experiments were repeated 3 times. SPSS 20.0 software was used for statistical analysis. The data are shown as mean  $\pm$  SD. The statistically significant values were compared by Student's *t*-test or one-way ANOVA followed by Tukey's post hoc test.  $P < 0.05$  is considered to indicate a statistically significant result.

### 3. Results

**3.1. The Cytotoxicity of Ampelopsin to Normal Human Renal Cells and RCC Cells.** Normal kidney cells HK-2 and human RCC cells 786-O were treated with Ampelopsin at different concentrations (0, 10, 25, 50, and 100  $\mu$ M) for 24 or 48 h. MTT assay showed that after 24 h of Ampelopsin treatment, no significant cytotoxicity was observed in normal kidney cells HK-2 (Figure 1(a)). We also found that 10, 25, and 50  $\mu$ M Ampelopsin treatments were not cytotoxic to HK-2 cells at 48 h. However, 100  $\mu$ M Ampelopsin had little effect on the survival of HK-2 cells for 48 h ( $P < 0.05$ ; see Figure 1(b)). In addition, Ampelopsin (10, 25, 50, and 100  $\mu$ M) inhibited the proliferation of 786-O cells in a dose-dependent manner for 24 h and 48 h ( $P < 0.05$ ; see Figures 1(c) and 1(d)). These results indicate that Ampelopsin is only cytotoxic to RCC cells.

**3.2. Ampelopsin Inhibits Cell Viability in RCC.** In order to further explore the effect of Ampelopsin on the viability of RCC cells, colony cell formation assay and flow cytometry analysis were performed. We found that Ampelopsin from 25 to 100  $\mu$ M suppressed the proliferation of 786-O cells in a dose-dependent manner ( $P < 0.05$ ; see Figure 2(a)). In addition, it was found that Ampelopsin (25 to 100  $\mu$ M) induced a greater number of apoptotic cells in 786-O cells ( $P < 0.05$ ; see Figure 2(b)). To further explore the underlying molecular mechanism, Western blot analysis was used to investigate the effect of Ampelopsin on Bax/Bcl-2 in 786-O cells. The results showed that Ampelopsin (25 to 100  $\mu$ M) significantly reduced Bcl-2 and increased Bax levels in 786-O cells ( $P < 0.05$ ; see Figure 2(c)). The above results demonstrate that Ampelopsin inhibits cell proliferation and induces apoptosis in RCC.

**3.3. Ampelopsin Inhibits Cell Metastasis in RCC.** Next, the effect of Ampelopsin on cell metastasis was investigated in 786-O cells. Wound healing assay showed that the migration distance of 786-O cells treated with Ampelopsin (25 to 100  $\mu$ M) was significantly shortened ( $P < 0.05$ ; see Figure 3(a)), indicating that Ampelopsin can inhibit cell migration in RCC cells. Transwell assay showed that Ampelopsin (25 to 100  $\mu$ M) significantly inhibited the invasion of 786-O cells ( $P < 0.05$ ; see Figure 3(b)). In addition,

the effect of Ampelopsin on EMT was investigated in 786-O cells. We found that Ampelopsin (25 to 100  $\mu$ M) reduced the expression of N-cadherin and vimentin and enhanced E-cadherin expression in 786-O cells ( $P < 0.05$ ; see Figure 3(c)). In summary, Ampelopsin can inhibit cell metastasis in RCC.

**3.4. Ampelopsin Negatively Regulates the PI3K/AKT Signaling Pathway in RCC Cells.** In order to further clarify the possible underlying mechanism of Ampelopsin in RCC, the effect of Ampelopsin on the PI3K/AKT pathway was examined by Western blot analysis. The results showed a dose-dependent inhibition of p-PI3K and p-AKT in Ampelopsin-treated 786-O cells ( $P < 0.05$ ; see Figure 4). However, the protein expression of PI3K and AKT in each drug group was not statistically different from that in the 0  $\mu$ M group ( $P > 0.05$ ; see Figure 4). Collectively, Ampelopsin negatively regulates the PI3K/AKT signaling pathway in RCC cells.

### 4. Discussion

RCC is resistant to almost all cellular drugs, and a small number of patients can be treated with high-dose interleukin-2 (IL-2), interferon, and other cytokines. In addition, RCC is not sensitive to radiotherapy and chemotherapy. Although the chemotherapy of RCC has been greatly improved, the prognosis of patients is still very poor. Many studies have shown that chemotherapy drugs isolated from natural plants can be effective killers of cancer cells. For example, Apigenin induced apoptosis by simultaneously suppressing Bcl-xl and Mcl-1 in colon cancer [17]. Curcumin inhibited cell proliferation and motility by suppression of TROP2 in bladder cancer [18]. In addition, the traditional Chinese medicine Bu-Shen-Jian-Pi-Fang has been reported to attenuate the glycolysis and immune escape of clear cell RCC [19]. Nevertheless, effective drugs are still needed to improve the prognosis of RCC patients.

Ampelopsin is a naturally occurring flavonoid compound found in grapes, fruits, vegetables, and herbs [20]. Ampelopsin has attracted the attention of researchers because of its biological activities such as antifatigue, anti-inflammatory, antitumor, liver protection, and regulation of lipid metabolism [21, 22]. More importantly, Ampelopsin is almost nontoxic to animal models [23]. In this study, we also found that Ampelopsin had no significant cytotoxicity to normal human kidney cells. In addition, it was found that Ampelopsin can inhibit cell viability and metastasis in RCC cells. Similar to our results, Ampelopsin has been reported to inhibit cell proliferation and induce apoptosis in leukemia by downregulating the AKT signaling pathway [24]. Ampelopsin reduced the migration and invasion of ovarian cancer cells by inhibiting EMT [11]. These results demonstrate that Ampelopsin has an antitumor effect in RCC.

In the current study, Ampelopsin suppressed cell metastasis in RCC by inhibiting EMT. EMT is related to the acquisition of invasion and migration characteristics and provides tumor cells with the ability to invade adjacent tissues [25]. Here, the expression of E-cadherin in 786-O cells was

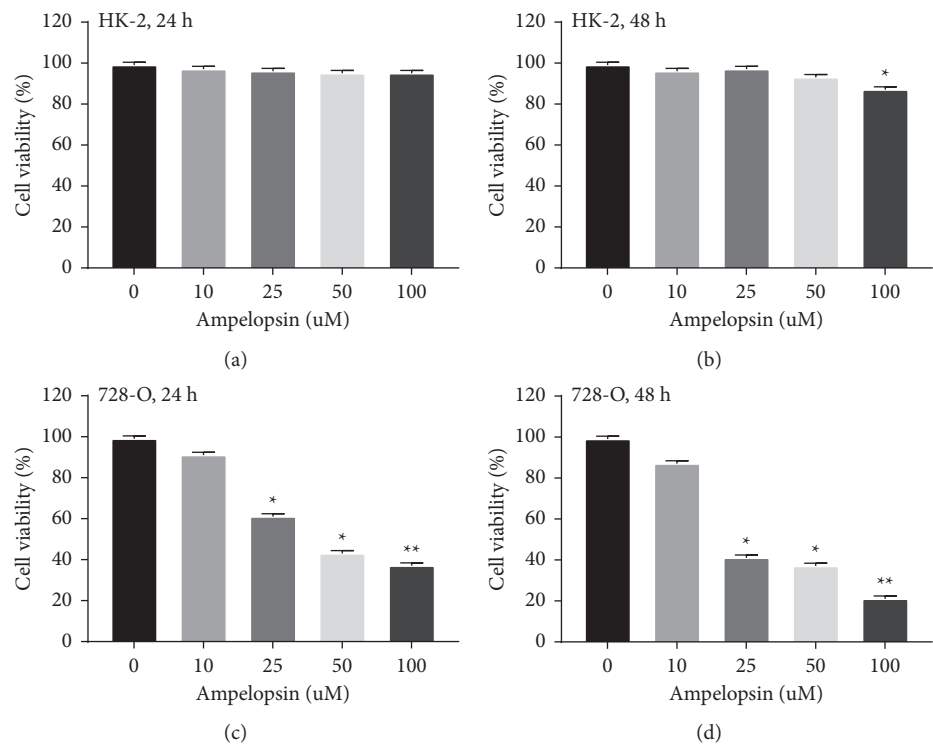


FIGURE 1: The cytotoxicity of Ampelopsin to normal human renal cells and RCC cells. (a- b) Normal kidney cell line HK-2 was treated with Ampelopsin (0, 10, 25, 50, and 100 uM) for 24 h and 48 h, and then the cell proliferation was detected by MTT analysis. (c-d) Human RCC cells 786-O were treated with Ampelopsin (0, 10, 25, 50, and 100 uM) for 24 h and 48 h, followed by MTT analysis to assess cell proliferation. \* $P < 0.05$ ; \*\* $P < 0.01$ .

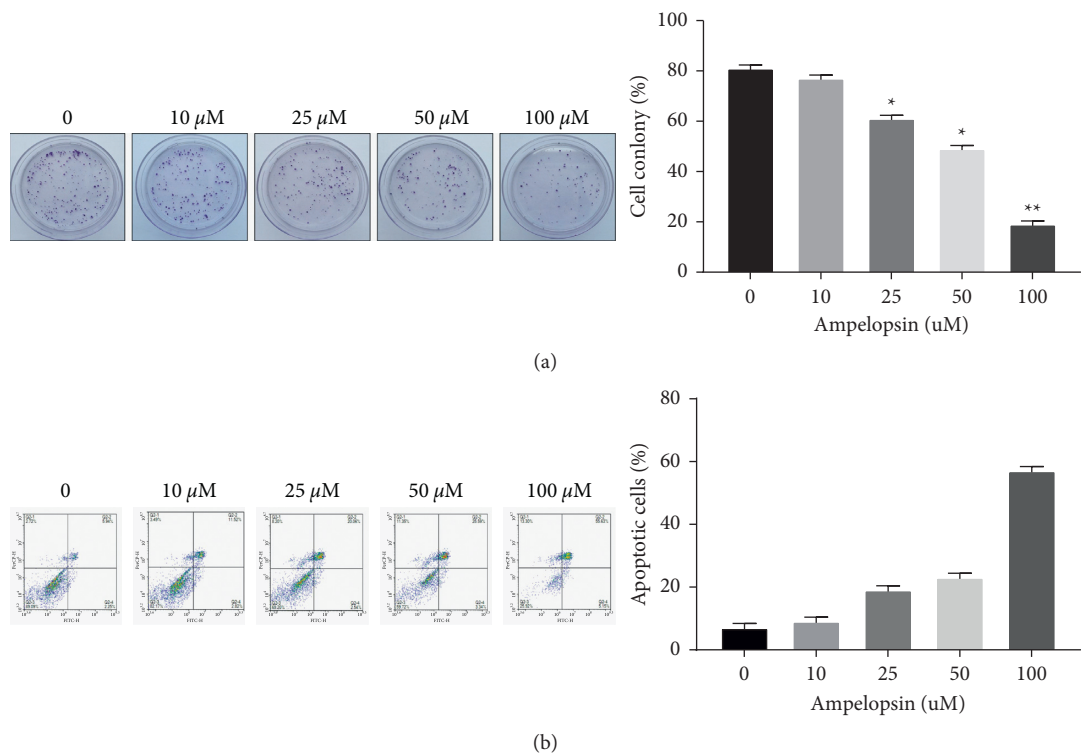


FIGURE 2: Continued.



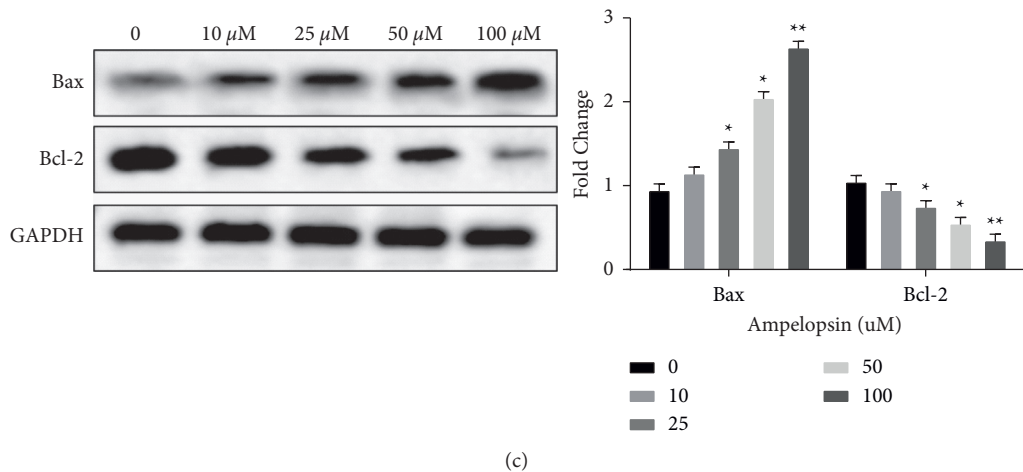


FIGURE 2: Ampelopsin inhibits cell viability in RCC. (a) The colony formation results of 786-O after treatments of Ampelopsin (0, 10, 25, 50, and 100  $\mu$ M) for 24 h were exhibited. (b) Cell apoptosis was detected in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100  $\mu$ M). (c) The protein expression of Bax and Bcl-2 was measured in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100  $\mu$ M). \* $P < 0.05$ ; \*\* $P < 0.01$ .

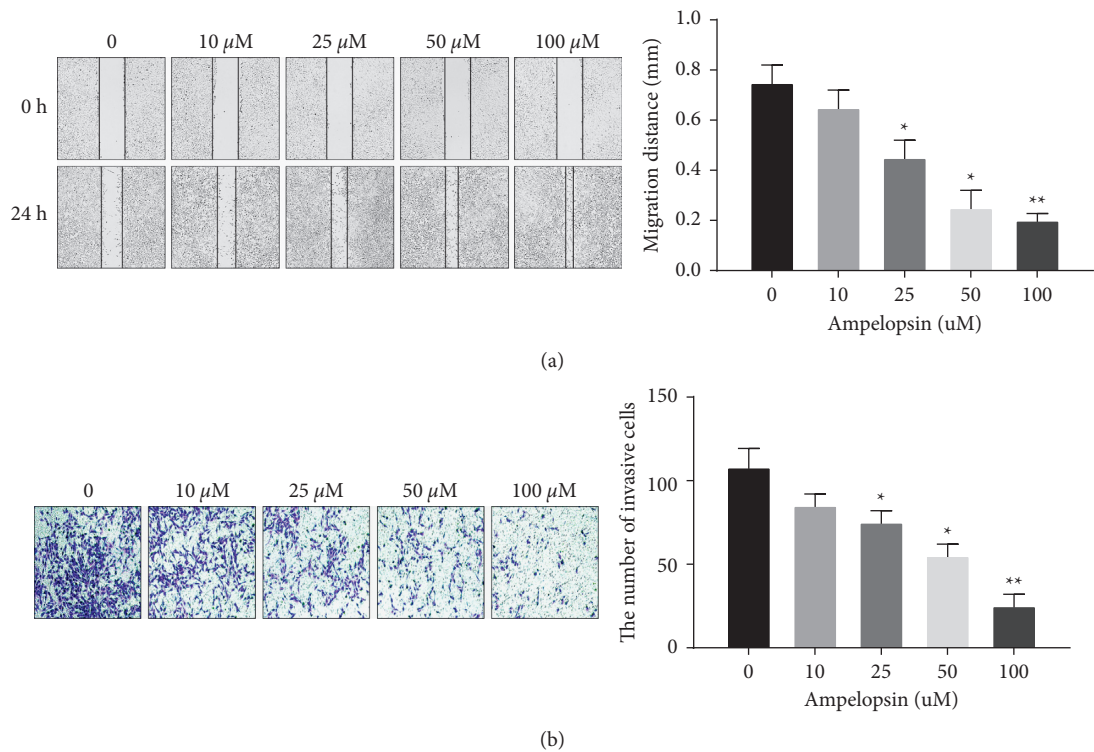


FIGURE 3: Continued.

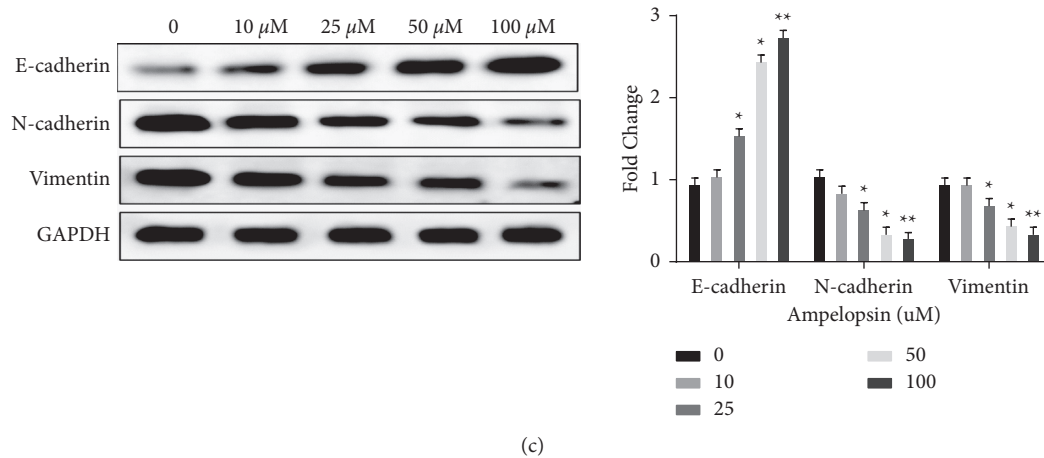


FIGURE 3: Ampelopsin inhibits cell metastasis in RCC. (a) Cell migration was detected by Wound healing assay in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100 μM). (b) Cell invasion was detected by Transwell assay in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100 μM). (c) The protein expression of E-cadherin, N-cadherin, and vimentin was measured in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100 μM). \* $P < 0.05$ ; \*\* $P < 0.01$ .

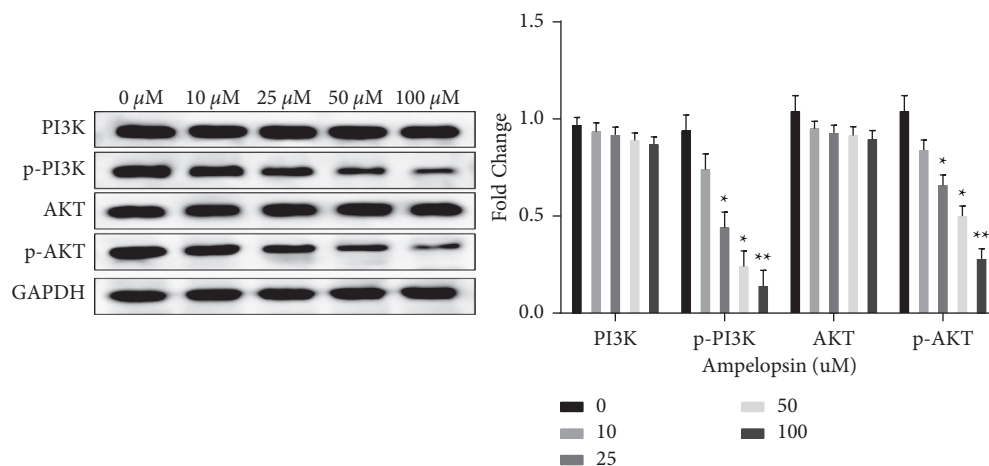


FIGURE 4: Ampelopsin negatively regulates the PI3K/AKT signaling pathway in RCC cells. The protein expression of PI3K, p-PI3K, AKT, and p-AKT was measured in 786-O cells treated with different concentrations of Ampelopsin (0, 10, 25, 50, and 100 μM). \* $P < 0.05$ ; \*\* $P < 0.01$ .

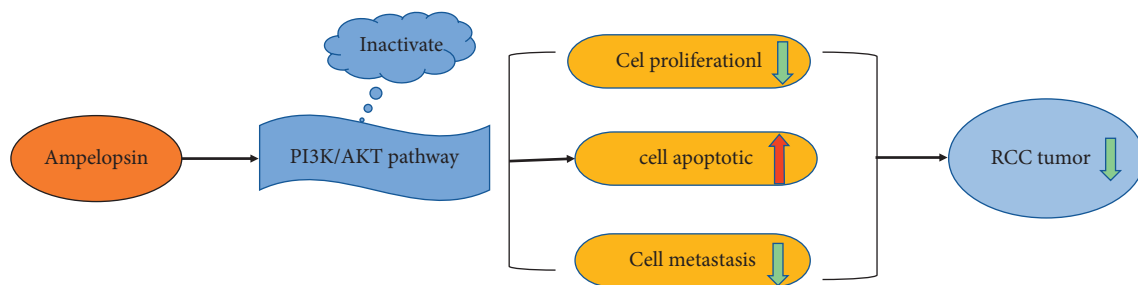


FIGURE 5: Ampelopsin inhibits cell viability and metastasis in RCC by negatively regulating the PI3K/AKT signaling pathway.

increased in a dose-dependent manner by Ampelopsin, while N-cadherin and vimentin were decreased. This indicates that EMT is inhibited by Ampelopsin. Therefore, we infer that

Ampelopsin at least partly reduces the metastasis of RCC cells to prevent the development of RCC. In addition, we found that Ampelopsin negatively regulated the PI3K/AKT signaling

pathway in RCC cells. Qi et al. reported that Ampelopsin reduced endotoxin inflammation by inhibiting the activation of PI3K/AKT/NF- $\kappa$ B signaling pathway [26]. The above result suggests that Ampelopsin may inhibit the progression of RCC by blocking EMT and PI3K/AKT pathways (Figure 5). However, our conclusion has not been verified by *in vivo* experiment. Thus, animal experiment will be performed in the future to further confirm our results.

## 5. Conclusion

In summary, Ampelopsin can inhibit cell viability and metastasis in RCC in a dose-dependent manner. Ampelopsin may play an antitumor effect in RCC by negatively regulating the PI3K/AKT signaling pathway. In addition, Ampelopsin has low cytotoxicity to normal human kidney cells. Therefore, Ampelopsin can be considered as a promising strategy to prevent the development of human RCC.

## Data Availability

The datasets used during the present study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effects of Buzhong Yiqi Decoction Combined with THP Bladder Perfusion on Postoperative Efficacy in Patients with Bladder Cancer

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**Background.** As a traditional Chinese medicine tonic, Buzhong Yiqi decoction has the effects of invigorating Qi and lifting Yang. In this study, the effects of Buzhong Yiqi Shenge decoction combined with THP bladder perfusion on postoperative efficacy in bladder cancer were investigated. **Methods.** A total of 70 cases of bladder cancer patients were divided into the experimental group and control group according to the random number table method, with 35 cases in each group. The control group was treated with THP bladder perfusion. The experimental group was treated with Buzhong Yiqi Shenge decoction on the basis of the control group. The number of urine white blood cells, VEGF level, the incidence of adverse reactions, and KPS score were compared between the two groups before and after treatment. **Results.** After 3 and 6 months of therapy, the KPS score of the experimental group increased significantly compared with the control group. However, after 12 months of treatment, there was no difference in KPS scores between the two groups. Moreover, there was no significant variation in serum VEGF between two groups after 3 months of treatment. However, Buzhong Yiqi decoction notably reduced the level of VEGF after 6 months and 12 months. After 3 months, the urine white blood cell count was lower in the experimental group than in the control group. After 6 and 12 months, there was no difference in urine white blood cell count between the two groups. Furthermore, a total of 14 patients in two groups had recurrence after one year. Our results showed that there was no significant difference in postoperative recurrence rate between the experimental group and the control group. The occurrence rates of frequent and urgent urination, nausea/loss, and abnormal urine routine of appetite in the experimental group were significantly lower than those in the control group. But there was no difference in the occurrence rate of low heat, hematuria between the experimental group and the control group. **Conclusion.** Buzhong Yiqi decoction combined with THP bladder perfusion has no advantage in the short-term recurrence rate of bladder cancer patients. However, Buzhong Yiqi decoction can alleviate the symptoms of adverse reactions and improve the quality of life of patients.

## 1. Introduction

Bladder cancer is a malignant tumor arising from bladder epithelium and stroma. Bladder cancer is a common tumor of the urinary system, and its morbidity and mortality rank at the forefront of malignant tumors [1]. According to clinical characteristics, bladder cancer can be divided into

three types: nonmuscular invasive bladder cancer, muscular invasive bladder cancer, and metastatic bladder cancer [2]. Nonmuscular invasive bladder cancer is an early stage of bladder cancer, and transurethral resection of bladder tumor (TURBT) is the best therapeutic option [3]. However, patients are prone to recurrence after TURBT surgery, and the recurrence rate is as high as 70% [4]. Therefore, bladder

perfusion of chemotherapy drugs is usually performed after TURBT surgery to prevent recurrence [5, 6]. The commonly used perfusion drugs are hydroxycamptothecin, theprubicin (THP), mitomycin, epirubicin, and BCG [7, 8]. However, a series of serious complications such as bladder contracture and chemical cystitis can be produced by routine perfusion therapy.

The etiology of bladder cancer is not well understood clinically so far, which may be associated with the internal and external factors. Intrinsic factors may have some genetic origin, while extrinsic factors may be related to the patient's eating habits, smoking, infectious diseases, and chemicals [9, 10]. Regarding pathogenesis and clinical signs, according to modern Chinese medicine approaches, generally the pathogenesis is a deficiency of Qi in the kidney and accumulation of dampness heat in the bladder [11]. Clinical observation data show that TCM has protective effects on the patients' circulatory system and digestive system [12]. Adding TCM to the chemotherapy can reduce the side effects of surgery and get better therapeutic effects [13–15]. Gong et al. reported that Qici Sanling decoction repressed cell growth by downregulating the Wnt/ $\beta$ -catenin pathway in bladder cancer [16]. Tanshinone IIA suppressed EMT by inhibiting STAT3-CCL2 in bladder cancer [17]. Therefore, the clinical treatment of TCM combined with Western medicine is a new way to improve the treatment of bladder cancer.

In this study, Buzhong Yiqi Shenge decoction combined with THP bladder instillation was used to treat nonmuscular invasive bladder cancer, and the postoperative recurrence rate and adverse reactions were observed. Our study could provide a potential clinical basis for the treatment of bladder cancer with integrated TCM and Western medicine.

## 2. Materials and Methods

**2.1. General Information.** Seventy patients with nonmuscular invasive bladder cancer who were treated at Chengyang People's Hospital, Qingdao, Shandong, China, between February 2019 and November 2020, were selected as the study subjects. There were 51 males and 19 females. The patients were 35–79 years old, with an average age of  $58.9 \pm 11.3$  years. All patients were newly diagnosed with bladder cancer by biopsy and postoperative pathology. The diagnostic criteria were according to the Chinese Guidelines for the Diagnosis and Treatment of Urological Diseases in 2014. These patients were randomly divided into the control group and experimental group. The control group was treated with THP bladder perfusion. The experimental group received Buzhong Yiqi Shenge decoction on the basis of the control group. There was no statistical significance in age, gender, pathological grade, and clinical stage between the two groups (Table 1). All patients have signed the informed consent, and this study was approved by the Ethics Committee of the Chengyang People's Hospital, Qingdao, Shandong, China.

Inclusion criteria: underwent TURBT surgery, diagnosed as nonmuscular invasive bladder cancer, the

functions of the heart, lung, liver, and kidney were basically normal, and voluntarily participated in clinical studies and signed the informed consent.

Exclusion criteria: with serious heart, liver, kidney, and other systemic diseases, allergic to the drug used in this study, pregnant or lactating women, and the observation period was less than 1 year.

**2.2. Clinical Treatment.** In the control group, TURBT surgery was performed, first with THP bladder perfusion within 24 hours after TURBT surgery. 30 mg THP (Shenzhen Main Luck Pharmaceuticals Inc., SFDA approval number: H10930105) was fully dissolved in 40 ml 5% glucose injection and injected into the bladder through a urethral catheter under aseptic condition. Perfusion was performed once a week for a total of 8 times and then once a month for a total of 10 times. THP bladder perfusion treatment lasted for one year.

The experimental group was treated with Buzhong Yiqi decoction on the basis of THP bladder perfusion in the control group. The prescription of Buzhong Yiqi decoction was as follows: 25 g Astragali Radix, 10 g Radix Ginseng, 10 g Radix Angelicae Gigantis, 6 g Radix Glycyrrhizae, 10 g Rhizoma Atractylodis, 10 g Rhizoma Cimicifugae, 10 g Pericarpium Aurantii Nobilis, and 10 g Radix Bupleuri. Usage: decocted in water, one dose a day, twice in the morning and evening on an empty stomach, until 1 year after surgery.

## 3. Observed Indicators

**3.1. KPS Score.** KPS score was based on the patient health status score in progress of clinical oncology. After 3, 6, and 12 months of treatment, patients in both groups were evaluated for KPS scores.

**3.2. Serum VEGF Detection.** After 3, 6, and 12 months, 5 ml of fasting peripheral venous blood was collected from the patients in the two groups. Serum was collected after centrifugation at 3000 r/min for 10 min. Serum VEGF levels were determined by the enzyme-linked immunosorbent assay (ELISA).

**3.3. Routine Urine Cytology.** Cytological examination of urine or bladder irrigated specimens is one of the main methods for diagnosing bladder cancer. The number of white blood cells in urine was counted by a urine microscopy.

**3.4. The Recurrence Rates.** Cystoscopy was performed once every after 6 months. If suspicious lesions were found, a pathological biopsy could be performed to determine whether the bladder cancer has recurred. Recurrence cases were recorded at 6 and 12 months after THP bladder perfusion.

TABLE 1: Comparison of general clinical data between two groups.

Clinical parameters	Experimental group ( <i>n</i> = 35)	Control group ( <i>n</i> = 35)	$\chi^2$	<i>P</i> value
Age (years)				
≤58	10	12	0.265	0.607
>58	25	23		
Gender				
Female	26	25	0.072	0.788
Male	9	10		
TNM stage				
Ta	26	23	0.612	0.434
T1	9	12		
Tumor grade				
G1	18	17	0.566	0.754
G2	14	13		
G3	3	5		

**3.5. Statistical Analysis.** SPSS20.0 software was used for data analysis. The chi-square test was used for counting data analysis between the two groups, and the *t*-test was used for measurement data analysis. *P* < 0.05 was considered statistically significant.

## 4. Results

**4.1. Comparison of KPS Scores between Two Groups.** Sixty-five of the 70 patients completed the study. In the control group, 2 cases were lost during follow-up, and 1 case could not be reexamined on time. In the experimental group, 2 patients could not take Buzhong Yiqi decoction as prescribed. As given in Table 2, there was no difference in KPS scores between the two groups before treatment. After 3 and 6 months of treatment, the KPS score of the experimental group increased significantly compared with the control group. However, after 12 months of treatment, there was no difference in KPS scores between the two groups.

**4.2. Comparison of Serum VEGF Level between Two Groups.** Before treatment, there was no significant difference in serum VEGF between the two groups, and the same results were observed after 3 months of treatment. After 6 and 12 months of treatment, serum VEGF levels in the experimental group were significantly lower than those in the control group (Table 3). Therefore, Buzhong Yiqi decoction notably reduced the level of VEGF after 6 months and 12 months.

**4.3. Comparison of Urine White Blood Cells between Two Groups.** The urine white blood cell count of the two groups is given in Table 4. After 3 months, the urine white blood cell count was lower in the experimental group than in the control group. After 6 and 12 months, there was no difference in urine white blood cell count between the two groups (Table 4).

**4.4. Comparison of Recurrence Rate between Two Groups.** As given in Table 5, a total of 14 patients in two groups recurred after one year. In the control group, 6 patients of postoperative recurrence after half a year were found, with a recurrence rate of 18.75%. 8 patients with postoperative

recurrence after one year were found in the control group, with a recurrence rate of 25.00%. In the experimental group, 4 patients had recurrence after half a year, with a recurrence rate of 12.12%, and 6 patients had recurrence after one year, with a recurrence rate of 18.18%. The results showed that there was no significant difference in postoperative recurrence rate between the experimental group and the control group. Therefore, Buzhong Yiqi decoction did not affect the recurrence of short-term bladder cancer patients.

**4.5. Comparison of Adverse Reactions between Two Groups.** Adverse reactions were observed in both groups during treatment. The occurrence rates of frequent and urgent urination, nausea/loss, and abnormal urine routine of appetite in the experimental group were significantly lower than those in the control group (Table 6). But there was no difference in the occurrence rate of low heat, hematuria between the experimental group and the control group (Table 6). Our results showed that Buzhong Yiqi decoction could effectively reduce the incidence of adverse reactions.

## 5. Discussion

Bladder perfusion is the main method to prevent postoperative recurrence of bladder cancer, which can prevent tumor invasion and effectively reduce recurrence [18]. Long-term bladder perfusion will inevitably lead to different degrees of adverse reactions in the body [19]. According to traditional medicine approaches, bladder cancer is mainly caused by deficiency of Qi in the kidney and accumulation of dampness, heat, and toxin in the bladder. TCM helps the body to recover vital Qi by strengthening the body and eliminating pathogenic factors, so as to improve the clinical symptoms, reduce toxic and side effects, and improve the quality of life of patients. For example, compound Fufang Fufangteng mixture can alleviate bladder irritation and gross hematuria caused by THP bladder perfusion and improve symptoms [20]. Liu et al. found that Xiaozheng decoction combined with hydroxycamptothecin can effectively reduce the incidence of adverse reactions and prevent postoperative recurrence of bladder cancer [21]. Furthermore, Zhibai Dihuang decoction combined cysteine injection therapy can

TABLE 2: Comparison of KPS scores between two groups.

	Before treatment	3 months after treatment	6 months after treatment	12 months after treatment
Control group	73.65 ± 4.61	78.15 ± 10.31	82.47 ± 6.26	88.61 ± 11.32
Experimental group	72.21 ± 6.34	83.54 ± 6.37	90.92 ± 9.38	92.23 ± 7.26
<i>t</i>	2.153	2.578	1.354	2.047
<i>P</i>	0.655	0.028	0.034	0.421

TABLE 3: Comparison of the serum VEGF level between two groups (pg/ml).

	Before treatment	3 months after treatment	6 months after treatment	12 months after treatment
Control group	379.1 ± 105.9	366.9 ± 120.1	353.7 ± 125.6	331.4 ± 135.2
Experimental group	381.4 ± 90.7	353.7 ± 110.4	329.5 ± 121.4	290.3 ± 142.8
<i>t</i>	0.914	2.563	1.685	2.264
<i>P</i>	0.745	0.306	0.042	0.027

TABLE 4: Comparison of urine white blood cells between two groups (cells/ $\mu$ L).

	Before treatment	3 months after treatment	6 months after treatment	12 months after treatment
Control group	59.24 ± 6.41	25.26 ± 4.27	19.14 ± 2.41	9.37 ± 3.74
Experimental group	58.62 ± 8.36	20.14 ± 2.09	18.46 ± 3.12	9.10 ± 2.46
<i>t</i>	3.64	2.72	1.38	2.67
<i>P</i>	>0.05	0.037	>0.05	>0.05

TABLE 5: Comparison of recurrence rate between two groups.

	<i>n</i>	6 months after treatment		12 months after treatment	
		<i>n</i>	Recurrence rate (%)	<i>n</i>	Recurrence rate (%)
Control group	32	6	18.75	8	25.00
Experimental group	33	4	12.12	6	18.18
$\chi^2$			0.548		0.447
<i>P</i>			0.459		0.504

TABLE 6: Comparison of adverse reactions between two groups.

	<i>n</i>	Frequent and urgent urination	Nausea/loss of appetite	Low heat	Hematuria	Abnormal in urine routine
Control group	32	25 (78.13%)	16 (50.00%)	8 (25.00%)	11 (34.38%)	15 (46.88%)
Experimental group	33	12 (36.36%)	8 (24.24%)	5 (15.15%)	6 (18.18%)	7 (21.21%)
$\chi^2$		4.093	4.628	0.985	2.206	4.779
<i>P</i>		0.043	0.031	0.321	0.137	0.029

prevent the toxic side effects and improve the amount of bioactive mass of bladder cancer with a syndrome of fire hyperactivity due to yin deficiency type [22]. Therefore, the combination of Chinese and Western medicine can improve clinical efficacy.

Our study showed that the adverse reactions in the treatment of the two groups were mainly manifested as nausea, loss of appetite, hematuria, frequent and urgent urination, abnormal urine routine, and low fever. Buzhong Yiqi decoction combined with THP bladder perfusion can reduce the incidence of nausea, loss of appetite, frequent and urgent urination, and abnormal urine routine and improve patients' quality of life. VEGF is highly specific and can induce the proliferation of vascular endothelial cells and promote the angiogenesis of tumor cells, which has a certain relationship with tumor recurrence. Therefore, detection of the VEGF level can be used to determine the status of tumor

metastasis and treatment outcomes. In this study, it was found that Buzhong Yiqi decoction combined with THP bladder perfusion could reduce the serum VEGF level in postoperative patients with bladder cancer, which was beneficial to reduce tumor recurrence and metastasis. Moreover, the urine white blood cell count in the experimental group was significantly lower than that in the control group only after 3 months. The results showed that Buzhong Yiqi decoction could relieve short-term postoperative inflammatory reactions.

Buzhong Yiqi decoction is from the spleen and stomach theory written by Li Gao, a famous medical scientist in the Jin and Yuan Dynasties. The prescription has achieved good therapeutic outcomes in the internal medicine, surgery, gynecology, pediatrics, and other clinical departments. The therapeutic formula consists of eight herbs: Radix Astragali, Radix Ginseng, Radix Angelicae Gigantis, Radix

Glycyrrhizae, Rhizoma Atractylodis, Rhizoma Cimicifugae, Pericarpium Aurantii Nobilis, and Radix Bupleuri. These herbs interact with each other to play the role of supplementing the middle and replenishing Qi, lifting Yang and lifting depression, warming, and removing heat. Modern studies have shown that Buzhong Yiqi decoction can regulate spleen and gastrointestinal function [23], immune function [24], antipyretic [7], and antitumor [25] and protect the myocardium [26].

## 6. Conclusion

In conclusion, Buzhong Yiqi decoction combined with THP bladder perfusion in the treatment of bladder cancer plays an essential role in reducing adverse reactions during chemotherapy. Buzhong Yiqi decoction combined with THP bladder perfusion in the treatment of bladder cancer has the potential for therapeutic application.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Lentian Combined with (125)I Brachytherapy for Recurrent Ovarian Cancer

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**Objective.** To investigate the clinical value of lentian combined with (125)I brachytherapy in the treatment of recurrent ovarian cancer. **Methods.** A total of 160 patients with recurrent ovarian cancer admitted at Jiaozhou Central Hospital from June 2009 to October 2015 were enrolled in this study and randomly divided into observation group (80 cases) and control group (80 cases). The control group received chemotherapy. Observation group (80 cases) was treated with lentian combined with (125)I brachytherapy on the basis of control group, and the efficacy, adverse reactions, and Karnofsky Performance Scale (KPS) and quality of life scale (QOL) scores of the two groups were analyzed and compared. **Results.** After treatment, the levels of CA125, CA199, and CA724 in the 2 groups were markedly lower than those before treatment, and the observation group was lower than the control group ( $P < 0.05$ ). After treatment, the proportion of CD4<sup>+</sup>/CD8<sup>+</sup> cells and helper T cells and NK cells in the control group remarkably depleted, while the proportion of CD4<sup>+</sup>/CD8<sup>+</sup> cells, NK cells, and B cells in the observation group increased significantly compared to that before treatment, and the level of IgA, IgG, and IgM in the control group decreased, while that in the observation group showed no conspicuous difference compared with that before chemotherapy ( $P > 0.05$ ). The effective rate of observation group (85%) was higher than that of control group (75%) ( $P < 0.05$ ). The overall survival of patients in the control group was ( $16.2 \pm 2.04$ ) months and that of the observation group was ( $24.8 \pm 1.8$ ) months. KPS and QOL scores in both groups were enormously higher than those before treatment, and the observation group was higher than the control group ( $P < 0.05$ ). The incidence of hemoglobin reduction, leukopenia, aglobulia, granulocytopenia, nausea and vomiting, hepatorenal toxicity, and neurovirulence in the observation group was significantly lower than that in the control group. **Conclusion.** Lentian combined with (125)I brachytherapy is effective in treating recurrent ovarian cancer, with mild adverse reactions and good tolerance.

## 1. Introduction

Ovarian cancer (OC) accounts for 5% of cancer deaths in women [1]. Recurrent ovarian cancer refers to the signs of tumor recurrence in patients who have reached complete remission after optimal cytoreduction and adjuvant platinum-based chemotherapy and have to suspend the drug for half a year [2]. After relapse, first-line chemotherapy drugs such as topotecan and doxorubicin alone have no effect on prognosis, which triggers many adverse reactions, and most patients with relapse have a poor quality of life. Therefore,

additional and alternative therapeutic strategies to improve outcomes are necessary.

In the last decade, percutaneous image-guided (125)I implantation has been regarded as a useful and minimally invasive treatment for various malignancies owing to its curative effects, such as head and neck tumors and pancreatic, lung, and hepatic cancer [3–6]. At the same time, its successful application in OC is still limited. Meanwhile, (125)I particle implantation can also cause a series of adverse reactions, such as pneumothorax, pulmonary hemorrhage, and sputum blood. New drugs are urgently needed to

alleviate its side effects. *Lentinus edodes* (Shiitake) is the world's second-largest cultivated medicinal, edible fungus and has a long history in the oriental folklore of treating tumors [7]. Lentinan is the active ingredient extracted from the natural product *Lentinus edodes* mycelium, mainly composed of B1-3, B1-6 dextran [8]. Previous studies suggest that lentinan exerts its antitumor effects by activating the host's immune response instead of directly attacking cancer cells [9]. The antitumor activity of lentinan was believed to be mediated through a thymus-dependent immune mechanism.

In this study, the clinical study of lentinan combined with (125)I brachytherapy in patients with recurrent ovarian cancer was conducted to explore the application value of this therapeutic approach in such patients.

## 2. Methods

**2.1. Patients.** A total of 160 patients with recurrent ovarian cancer after surgery from June 2009 to October 2015 at the Jiaozhou Central Hospital, Qingdao, Shandong, China, were enrolled in this study. Biopsy pathology showed 70 cases of poorly differentiated serous papillary cystadenocarcinoma, 60 cases of moderately differentiated serous papillary cystadenocarcinoma, 14 cases of highly differentiated serous papillary cystadenocarcinoma, and 16 cases of poorly differentiated mucinous papillary cystadenocarcinoma, all of which were confirmed as recurrent oocyte carcinoma by imaging and histopathological examination. All patients underwent surgical treatment in the early stage, and the preoperative TNM staging was stage III-IV. The tumor was confirmed to be recurrent by ultrasound biopsy after surgery, and the time between the first operation and the current recurrence was  $24.2 \pm 2.3$  months. Karnofsky Performance Scale (KPS) was  $>60$ , and estimated survival time was  $>6$  months. According to the principle of randomness, 160 cases subjects were divided into 80 cases in the observation group and 80 cases in the control group. All patients signed informed consent before participation, and this study was approved by the Ethics Committee of the Jiaozhou Central Hospital, Qingdao, Shandong, China.

**2.2. Study Design.** The control group was intravenously injected with Taxol liposome ( $135 \text{ mg/m}^2$ ). Before chemotherapy, dexamethasone and diphenhydramine were routinely pretreated. Then arterial infusion chemotherapy was performed the next day. The catheter was introduced through femoral artery puncture by the Seldinger method; under the monitoring of DSA, the catheter was selected to the inferior mesenteric artery or internal iliac artery for angiography to observe the blood supply status of the tumor. Carboplatin ( $200 \text{ mg/m}^2$ ) was diluted and slowly injected into the tumor supplying artery through the catheter. Routine symptomatic treatment such as liver protection and antiemetic and gastric protection was given, repeated once every 21 days.

The observation group was treated with (125)I particle implantation and *Lentinus edodes* polysaccharide tablets.

The number of (125)I seeds and the planning target volume (PTV) were determined using a treatment planning system. PTV was defined as tumor target area expansion of 5–10 mm, and matched peripheral dose (MPD) was 110–160 Gy. During the operation, CT scanning was used to locate the puncture direction and puncture point. After disinfection and anesthesia, (125)I seeds were implanted percutaneously under the guidance of CT with an interval of 0.5 cm. A postoperative CT review was performed to understand the particle distribution. When lesions were present in both ovaries, the interval of particle implantation in the other lesion should be more than 3 days. *Lentinus edodes* polysaccharide tablets (Kaifeng Pharmaceutical Co., Ltd., Chinese drug approval number H41025015) were orally administered with 1 tablet per time and 2 times per day for 2 months. Within 3 days after (125)I seed implantation, the same chemotherapy treatment was performed as the control group.

**2.3. Testing Index.** Venous blood was collected before and after treatment to separate the serum. Then the level of IgG, IgM, and IgA in serum was determined by immunoturbidimetry. The kit was provided by Changchun Huili Biotechnology Co., Ltd.

Total 3 mL of fasting peripheral blood was collected from all patients before and after treatment. Flow cytometry was performed to evaluate the immune function of patients in both groups within 1 week after treatment. Total T cells ( $\text{CD3}^+$ ), helper T cells ( $\text{CD3}^+ \text{CD4}^+$ ), killer T cells ( $\text{CD3}^+ \text{CD8}^+$ ),  $\text{CD4}^+/\text{CD8}^+$ , and NK cells ( $\text{CD3}^- \text{CD56}^+$ ), CIK cells ( $\text{CD3}^+ \text{CD56}^+$ ), regulatory T cells ( $\text{CD4}^+ \text{CD25}^{\text{high}} \text{FOXP3}^+$ ),  $\text{CD14}^+$ , and  $\text{CD19}^+$  B cells were detected.

Laboratory tests including hemoglobin (HGB), white blood cells (WBC), platelets (PLT), neutrophils (NEU), red blood cells (RBC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine (CREA), urea nitrogen (BUN), and electrocardiograph also were recorded before and after treatment. Chemotherapy side effects were graded according to WHO acute and subacute toxicity criteria, which were divided into 0, I, II, III, and IV. Blood toxicity, gastrointestinal reaction, liver and kidney function, cardiotoxicity, and peripheral neurotoxicity were assessed and compared between the two groups.

**2.4. Evaluation Criteria for Short-Term Efficacy.** Efficacy was evaluated according to RECIST criteria. Complete remission (CR) means complete disappearance of all target lesions. Partial response (PR) means reduction of the sum of the maximum diameters of target lesions  $\geq 30\%$ . Stable disease (SD) is the sum of the maximum diameter of the target lesions decreases without reaching PR or increases without reaching PD. Disease progression (PD) is an increase of  $\geq 20\%$  in the sum of the maximum diameters of the target lesions or the appearance of new lesions. The efficiency (RR) was calculated by  $\text{CR} + \text{PR}$ , while disease control rate (DCR) was calculated by  $\text{CR} + \text{PR} + \text{SD}$ .

The patient's functional status was assessed with a KPS score, and the higher the score, the better the patients' functional status. Quality of life scale (QOL) (SF-36) was performed to evaluate patients' quality of life, and the higher the score, the better the quality of life.

All objects were followed up for 5–46 months, and the overall survival of patients in the two groups was statistically compared.

**2.5. Statistical Method.** SPSS 21.0 statistical software was performed for data analysis. The data were expressed by  $\bar{x} \pm s$ .  $\chi^2$  test or  $t$  test was applied for comparison between groups, Kaplan–Meier survival analysis and log-rank test univariate analysis were used to compare the difference in survival rates between the two groups.  $P < 0.05$  indicates that the difference is statistically significant.

### 3. Results

**3.1. Pathological Characteristics.** There were 160 patients with recurrent ovarian cancer, including 80 cases in the control group and 80 cases in the observation group. Table 1 shows that there were no significant differences in age, TNM stage, pathological type, differentiated status, and CA125 level at recurrence between the two groups, as shown in Table 1.

**3.2. Blood-Related Indexes.** The HGB, WBC, PLT, NEU, and RBC levels in two groups before treatment showed no statistically significant difference ( $P > 0.05$ ). After treatment, the level of HGB, WBC, NEU, and RBC in control group decreased enormously, and the level of WBC and NEU in observation group attenuated tremendously, while the level of HGB, WBC, NEU, and RBC in observation group was obviously higher than that of control group, as shown in Table 2.

**3.3. Immunologic Function.** In order to further analyze the effect of Lentinus edodes polysaccharide combined with (125)I particle and chemotherapy treatment on the immune status of patients, the proportion of each immune cell in peripheral blood of patients before and after treatment was compared, as shown in Table 3. After chemotherapy treatment, the proportion of helper T cells, CD4<sup>+</sup>/CD8<sup>+</sup> cells, and NK cells in the control group remarkably depleted, while after Lentinus edodes polysaccharide combined with (125)I particle and chemotherapy treatment, the proportion of CD4<sup>+</sup>/CD8<sup>+</sup> cells, NK cells, and B cells in the observation group aggrandized enormously compared to that before treatment.

The level of immunoglobulin (IgA, IgG, and IgM) in the control group decreased immensely after chemotherapy compared with before chemotherapy. In contrast, the level of IgA, IgG, and IgM in the observation group showed no apparent difference after treatment compared with before chemotherapy ( $P > 0.05$ ), as shown in Table 4.

**3.4. Tumor Markers.** There was no difference in the level of CA125, CA199, and CA724 between the two groups after treatment compared with before treatment ( $P > 0.05$ ). After treatment, the levels of CA125, CA199, and CA724 in both groups alleviated broadly, while the levels of CA125, CA199, and CA724 in the observation group diminished prominently than the control group ( $P < 0.05$ ), as shown in Table 5.

**3.5. Therapeutic Effect.** According to the evaluation of the therapeutic effect of solid tumor, the DCR of the two groups was 60/80 (75%) and 68/80 (85%), respectively, while the efficacy of Lentinus edodes polysaccharide combined with (125)I particle and chemotherapy treatment was superior to that of chemotherapy alone ( $P < 0.05$ ) (Table 6). A total of 160 subjects were followed up for 5–46 months (median time: 26 months). The overall survival of patients in the control group was ( $16.2 \pm 2.04$ ) months and that of the observation group was ( $24.8 \pm 1.8$ ) months (Figure 1). Log-rank test was applied to compare the survival of the two groups, and the observation group was significantly higher than the control group.

**3.6. KPS and QOL Score.** There was no significant difference in KPS score and QOL score between the two groups before treatment. The scores of KPS and QOL in both groups were significantly improved after treatment, and the observation group was significantly higher than the control group ( $P < 0.05$ ), as shown in Table 7.

**3.7. Incidence of Adverse Reactions.** The incidence of nausea and vomiting, neurotoxicity, and hepatorenal toxicity in the observation group was lower than that in the control group ( $P < 0.05$ ), as shown in Table 8.

### 4. Discussion

Ovarian cancer is a gynecological malignant tumor with high incidence, and most patients are accompanied by ascites, which is difficult to treat and results in a poor prognosis. At present, chemotherapy is still the preferred treatment for recurrent ovarian cancer, but it is difficult to achieve the desired outcomes by chemotherapy or radiotherapy because of the large tumor load in patients with recurrent ovarian cancer [10]. Therefore, looking for adjuvant treatment options has become the focus of clinical research.

(125)I radioactive particles can have a continuous effect on tumor cells, block cells in  $G_2/M$  phase, prolong cell cycle, and lead to the loss of proliferation ability of tumor cells [11, 12]. (125)I radioactive particles are implanted within the range of radiation therapy, and the dose of radiation dose decreases with the increase of distance. Therefore, (125)I particle implantation can produce a high dose at the site, while the radiation dose of surrounding normal tissues is low, with highly conformal radiation [13–15]. Zhao et al. found that (125)I seed implantation based on CT-guided 3D template-assisted technique can

TABLE 1: Comparison of pathological characteristics between the two groups.

	Control group	Observation group	P value
Age	49 ± 5.3	48 ± 4.6	0.945
TNM stage			0.564
III	44 (55%)	47 (59%)	
IV	36 (45%)	33 (41%)	
Pathological type			0.215
Serous papillary cystadenocarcinoma	69 (86%)	75 (94%)	
Mucinous papillary cystadenocarcinoma	11 (14%)	5 (6%)	
Differentiated			0.341
Poorly differentiated	46 (58%)	40 (50%)	
Moderately differentiated	28 (35%)	32 (40%)	
Highly differentiated	6 (7%)	8 (10%)	
CA125			0.645
≤35 U/ml	21 (26)	25 (31)	
>35 U/ml	59 (74)	55 (69)	

TABLE 2: Comparison of blood-related indexes between two groups ( $\bar{x} \pm s$ ).

	Control group		P value	Observation group		P value
	Before treatment	After treatment		Before treatment	After treatment	
WBC ( $\times 10^9/L$ )	7.02 ± 0.56	1.84 ± 0.24	<0.001	7.09 ± 0.48	4.05 ± 0.16**	0.032
NEU ( $\times 10^9/L$ )	5.02 ± 0.45	1.45 ± 0.26	0.015	4.97 ± 0.78	2.68 ± 0.45*	0.045
HGB (g/L)	115.84 ± 13.65	71.26 ± 10.23	0.002	116 ± 14.62	110.25 ± 12.15**	0.315
PLT ( $\times 10^9/L$ )	251.23 ± 32.15	227.16 ± 26.12	0.124	249.13 ± 14.26	239.45 ± 32.16	0.421
RBC ( $\times 10^{12}/L$ )	4.87 ± 0.15	1.38 ± 0.24	0.026	4.97 ± 0.12	3.15 ± 0.21*	0.051

Versus control group, \* $P < 0.05$ , \*\* $P < 0.01$ .

TABLE 3: Proportion of peripheral blood immune cells in the two groups before and after treatment (median (P25, P75)).

	Control group (%)		P value	Observation group (%)		P value
	Before treatment	After treatment		Before treatment	After treatment	
CD3 <sup>+</sup>	75.76 (47.78, 87.79)	75.18 (52.36, 82.31)	0.915	74.54 (51.23, 80.31)	73.61 (50.31, 81.24)	0.769
CD3 <sup>+</sup> CD4 <sup>+</sup>	48.89 (18.97, 65.12)	39.6 (19.02, 78.68)	0.034	45.36 (17.65, 71.62)	49.75 (13.64, 74.16)	0.054
CD3 <sup>+</sup> CD8 <sup>+</sup>	33.89 (17.84, 45.26)	35.62 (20.69, 49.74)	0.549	36.16 (21.36, 48.37)	34.15 (19.65, 47.59)	0.512
CD4 <sup>+</sup> CD8 <sup>+</sup>	1.65 (0.61, 2.89)	1.09 (0.48, 2.84)	0.048	1.69 (0.69, 2.79)	2.43 (0.64, 3.86)*	0.019
CD3 <sup>+</sup> CD56 <sup>+</sup>	9.65 (5.24, 41.26)	8.25 (5.81, 37.64)	0.031	9.26 (6.31, 42.36)	14.26 (5.96, 36.16)*	0.023
CD3 <sup>+</sup> CD56 <sup>+</sup>	3.68 (0.42, 10.29)	3.45 (0.59, 9.78)	0.794	3.78 (0.39, 11.29)	4.22 (0.57, 9.78)	0.145
CD 14 <sup>+</sup>	4.78 (0.23, 32.04)	5.21 (0.02, 24.17)	0.359	5.61 (0.29, 36.19)	6.26 (0.16, 30.26)	0.278
CD 19 <sup>+</sup>	8.41 (2.71, 17.41)	8.14 (5.78, 37.26)	0.571	7.89 (2.61, 26.45)	11.45 (5.14, 33.15)*	0.036
CD4 <sup>+</sup> CD25high <sup>+</sup> FOXP3 <sup>+</sup>	4.74 (0.04, 11.68)	3.36 (0.15, 12.27)	0.401	4.16 (0.12, 12.31)	5.48 (0.34, 16.45)	0.141

Versus control group, \* $P < 0.05$ , \*\* $P < 0.01$ .

TABLE 4: Comparison of immunoglobulin levels between the two groups ( $\bar{x} \pm s$ , g/L).

	Control group		P value	Observation group		P value
	Before treatment	After treatment		Before treatment	After treatment	
IgG	12.94 ± 1.02	10.84 ± 0.24	0.025	12.77 ± 0.93	12.65 ± 1.02*	0.082
IgM	1.76 ± 0.21	1.20 ± 0.12	0.004	1.75 ± 0.36	1.88 ± 0.36**	0.056
IgA	2.39 ± 0.23	1.87 ± 0.36	0.016	2.31 ± 1.01	2.44 ± 0.95*	0.054

Versus control group, \* $P < 0.05$ , \*\* $P < 0.01$ .

effectively alleviate the tumor and improve the survival rate in patients with refractory malignant tumors [16]. Despite the significant effect of (125)I seed implantation in the treatment of cancer, the adverse reactions caused by it cannot be ignored [17]. Zhang et al. reported that (125)I brachytherapy triggers a higher relative risk of

pneumothorax, pneumorrhagia, and bloody sputum compared with chemotherapy alone [18]. Martinez-Monge et al. reported that the complication rate of 125I radiotherapy with short-range and high dose rate was 20% [19]. Therefore, it is equally important to kill tumor cells and protect immune function in tumor treatment.

TABLE 5: Comparison of tumor markers in blood between the two groups before and after treatment ( $\bar{x} \pm s$ ).

Group	CA125 (U/ml)		<i>P</i> value	CA199 (IU/ml)		<i>P</i> value	CA724 (IU/ml)		<i>P</i> value
	Before treatment	After treatment		Before treatment	After treatment		Before treatment	After treatment	
Control group	48.32 $\pm$ 12.32	25.64 $\pm$ 6.15	0.012	81.23 $\pm$ 7.36	53.21 $\pm$ 3.64	0.004	34.68 $\pm$ 4.61	14.56 $\pm$ 4.8	0.006
Observation group	49.12 $\pm$ 11.13	18.45 $\pm$ 3.14	0.003	80.64 $\pm$ 6.45	41.54 $\pm$ 4.65	<0.001	35.48 $\pm$ 6.48	9.12 $\pm$ 4.71	<0.001
<i>P</i> value	0.821	0.027		0.754	0.018		0.634	0.035	

TABLE 6: Comparison of short-term efficacy between the two groups, *n* (%).

Group	<i>n</i>	CR	PR	SD	PD	RR	DCR
Control group	80	13 (16%)	45 (56%)	2 (3%)	20 (25%)	58 (73%)	60 (75%)
Observation group	80	16 (20%)	48 (60%)	4 (5%)	12 (15%)	64 (80%)	68 (85%)
$\chi^2$				4.312			
<i>P</i> value				0.026			

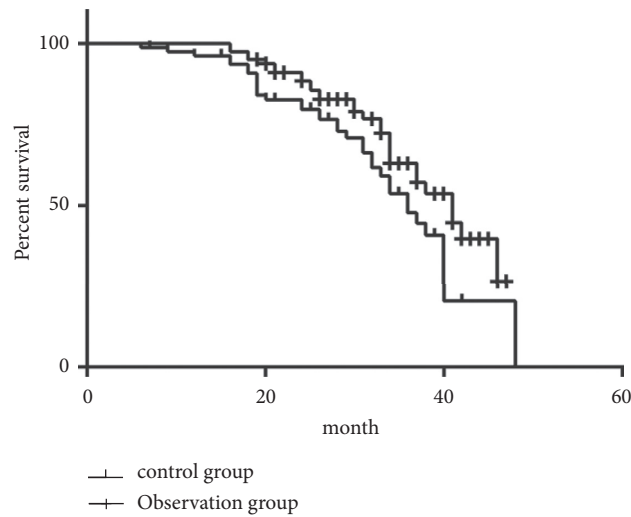


FIGURE 1: The overall survival of the two groups.

TABLE 7: Comparison of KPS and QOL scores between the two groups ( $\bar{x} \pm s$ ).

Group	KPS score		<i>P</i> value	QOL score		<i>P</i> value
	Before treatment	After treatment		Before treatment	After treatment	
Control group	71.43 $\pm$ 5.31	80.12 $\pm$ 6.32	0.034	24.61 $\pm$ 6.21	37.65 $\pm$ 5.87	0.041
Observation group	70.65 $\pm$ 5.87	93.12 $\pm$ 5.87	0.005	25.65 $\pm$ 6.48	50.21 $\pm$ 4.87	0.002
<i>P</i> value	0.742	0.025		0.674	0.035	

TABLE 8: Comparison of the incidence of adverse reactions between the two groups (*n*).

Adverse reactions	Control group				Observation group				<i>P</i> value	$\chi^2$
	I	II	III	IV	I	II	III	IV		
Nausea and vomiting	16	8	2	0	7	2	0	0	0.005	5.123
Renal injury	5	0	0	0	1	0	0	0	0.041	2.654
Liver injury	6	1	0	0	2	0	0	0	0.036	4.659
Neurovirulence	4	0	0	0	3	0	0	0	0.157	1.054

Lentinan has significant inhibitory effects on the transplanted tumor, allogeneic tumor, and primary tumor, preventing carcinogenic effects caused by chemical factors or viruses, inhibiting and preventing postoperative micro-metastasis of gastric cancer, lung cancer, liver cancer, rectal cancer, and breast cancer [20–24]. Kimura et al. used lentinan in combination with chemotherapy to treat recurrent gastric cancer and found that lentinan can reduce adverse reactions to chemotherapy and improve the immune and nutritional status of patients [25]. The mechanism of lentinan's action does not involve the direct attack on the pathogenic source, but to improve the balance of the host body by stimulating the maturation, differentiation and proliferation of immune cells, to restore and improve the responsiveness of host cells to lymphokines, hormones, and other physiologically active factors [26]. In this study, lentinan tablets combined with (125)I particle implantation were applied to observe the effects in antitumor and immune function.

In this study, we used lentinan combined with (125)I particle implantation to treat patients with recurrent ovarian cancer, and we found that the complete remission rate was 20% and partial remission rate was 60% after treatment, significantly higher than the control group, and the overall survival in the observation group was significantly higher than that in the control group, suggesting that (125)I particle implantation was effective in the treatment of recurrent ovarian cancer patients. After treatment, the proportion of CD4<sup>+</sup>/CD8<sup>+</sup> cells, helper T cells, and NK cells in the control group remarkably depleted, while the proportion of CD4<sup>+</sup>/CD8<sup>+</sup> cells, NK cells, and B cells in the observation group aggrandized enormously, and the level of IgA, IgG, and IgM in the control group decreased immensely, while that in the observation group did not change significantly, suggesting that lentinan can substantially improve the immunosuppression induced by radiotherapy and chemotherapy. The observation of toxicity in this study suggested that hematological toxicity in the control group mainly manifested as hemoglobin reduction, leukopenia, aglobulia, and granulocytopenia. At the same time, the above reactions were alleviated in the observation group after taking lentinan, indicating that lentinan can promote bone marrow hyperplasia. The main toxic reactions of the digestive system were nausea and vomiting; these reactions in this study mainly occurred 2–8 days after intravenous infusion, while these symptoms were relieved after lentinan treatment. Concurrently, the incidence of hepatorenal toxicity and neurovirulence could be alleviated by lentinan treatment.

In this comparative evaluation, we observed that the lentinan combined (125)I particles implantation treatment of recurrent ovarian cancer could improve the recent curative effect of recurrent ovarian cancer, strengthen the immune function of the patients, and reduce the treatment of gastrointestinal reaction and bone marrow suppression. It could lessen other side effects and improve the quality of life of patients, suggesting that lentinan combined (125)I brachytherapy may be an effective therapeutic approach for recurrent ovarian cancer.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Qin Jiang and Shuai Pang contributed equally to this work.

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## Research Article

# Efficacy and Prognostic Factors of Androgen Deprivation Therapy Combined with Radiation Therapy for Prostate Cancer

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**Objective.** To analyze the efficacy of androgen deprivation therapy (ADT) combined with radiation therapy (also known as radiotherapy) for prostate cancer. **Methods.** The clinical data of 94 prostate cancer patients treated in the Oncology Department of Xiangzhou People's Hospital from January 2017 to January 2018 were retrospectively analyzed, and the patients were divided into the combined group and the reference group according to their admission order, with 47 cases each. The patients in the reference group only received the radiotherapy, and on this basis, those in the combined group accepted ADT, so as to evaluate the efficacy of different treatment methods by comparing the patients' serum total prostate-specific antigen (T-PSA), vascular endothelial growth factor (VEGF), and other indicators and analyze the relevant factors affecting patients' prognosis by Cox single-factor and multi-factor regression models. **Results.** Compared with the reference group after treatment, the patients in the combined group obtained significantly lower T-PSA and VEGF levels ( $P < 0.001$ ), significantly higher objective remission rate and disease control rate ( $P < 0.05$ ), and remarkably longer modified progression-free survival (mPFS) and overall survival (OS) ( $P < 0.001$ ), and after the multi-factor research, it was found that the Gleason score of 8–10, positive lymphatic metastasis, and single radiotherapy were the factors affecting the clinical prognosis of prostate cancer. **Conclusion.** Combining ADT with radiotherapy ensures a better survival benefit for prostate cancer patients and has a fairly well efficacy. Further study will be conducive to establishing a better solution for such patients.

## 1. Introduction

Authoritative survey data show [1] that the incidence of prostate cancer reaches the 5<sup>th</sup> place among malignant tumors, becoming one of the important diseases endangering the male population. The tumor has an insidious onset and slow growth and will trigger dysuria, interruption of urinary stream, hematuria, and other symptoms once it causes swelling of the prostate, resulting in high deterioration, difficulty in treatment, and poor clinical prognosis and seriously affecting the physical and psychological functions of patients. It is generally believed that radical surgery is a more thorough treatment for prostate cancer but because the initial symptoms are not obvious, most diagnosed patients

are often inoperable because of the late pathological stage and older age [2–4]. With the continuous improvement of radiotherapy technology, precise and adaptable radiotherapy treatments are widely recommended in the clinic to benefit patients [5]. However, radiotherapy can damage the body's immune system and then lead to decreased immune function, and most patients also experience nausea and vomiting and other gastrointestinal reactions, affecting the treatment effect. Previous studies have found [6] that this neoplastic disease is an androgen-dependent malignancy and that cancer cells undergo apoptosis in the absence of androgen stimulation, and therefore the inhibition of disease progression can be achieved by reducing androgen levels. Some foreign scholars [7] found that surgical castration and

androgen deprivation can delay the progression of metastatic prostate cancer to some extent, thereby pioneering the hormonal therapy. Currently, there are many reports on androgen castration therapy and radiotherapy for prostate cancer, but few focus on the efficacy and prognostic factors of the combination of the two for prostate cancer patients. Based on this, a control study was carried out herein to explore the efficacy and prognostic factors of the combined therapy for prostate cancer patients, with the results reported as follows.

## 2. Case Data and Methods

**2.1. General Information.** The clinical data of 94 prostate cancer patients treated in the Oncology Department of Xiangzhou People's Hospital from January 2017 to January 2018 were retrospectively analyzed, and the patients were divided into the combined group and the reference group according to their admission order, with 47 cases each. This study was approved by the ethics committee of Xiangzhou People's Hospital.

### 2.2. Inclusion and Exclusion Criteria

**2.2.1. Inclusion Criteria.** ① The enrolled patients met the diagnosis criteria for prostate cancer in the 2018 version of Specification for Diagnosis and Treatment of Prostate Cancer [8], presented the clinical manifestations such as urgent micturition, frequent micturition, dysuria, and urinary incontinence, and were diagnosed after pathological examination; ② the patients' estimated survival was more than one year and their clinical data were complete; ③ the patients obtained over 70 points in the KPS score and not greater than 2 points in the U.S. Eastern Cooperative Oncology Group (ECOG) score [9], did not have radiotherapy contraindications, and could accept the entire treatment; ④ the patients accepted relevant immunotherapy and hormonal therapy; and ⑤ the patients or their statutory guardians understood the study process and signed the informed consent.

**2.2.2. Exclusion Criteria.** ① The Gleason score was less than 7 points; ② the patients suffered from other malignant tumors or immune dysfunction; ③ the patients presented severe cardiovascular and cerebrovascular diseases, viral hepatitis, or other chronic hepatic diseases; and ④ the patients presented abnormal mental state and could not go through the study.

**2.3. Methods.** The patients in the reference group only received the image-guided radiation therapy (IGRT) with the following steps. The CT scanning simulation was conducted after fixing the phantom, the patient's position, ISO-center, and reference points on skin were determined under the CT scan simulator, and the exposure range included the whole pelvis, local prostate, and pelvic lymph nodes [10]. The median radiation dose was 74 Gy, and four fields were radiated daily. For the whole pelvis, it was 2 Gy

each time, 5 times a week for 5 weeks (total 25 times). Then, the fields were shrunk to the local prostate with a supplementary dose of 24 Gy, and the dose of planning target volume (PTV) was 1.8–2.0 Gy each time and 5 times a week for 2–3 weeks. The treatment was discontinued in case of grade III or above adverse reactions. During treatment, drugs to relieve vomiting, protective agents for gastric mucosa, and granulocyte colony stimulating factor were applied according to the patients' symptoms. After radiation therapy, the patients received regular follow-up checks [11, 12].

On the basis of radiation therapy, the patients in the combined group received ADT with the following steps. 3.6 mg of goserelin acetate sustained-release implant (manufactured: AstraZeneca UK Limited; registration no. H20100314; specification: 3.6 mg × one dose) was administered subcutaneously in the anterior abdominal wall every 28 days. Meanwhile, for anti-androgen hormones, 150 mg of bicalutamide tablets (manufactured: AstraZeneca UK Limited; NMPA approval no. J20150050; specification: 50 mg × 28 s) was taken orally 30 min after meal once a day for 2–4 weeks. The patients' liver function and blood routine parameters were checked regularly. The treatment should be stopped in case of any liver dysfunction (jaundice, cholestasis, and elevation of aminotransferase).

### 2.4. Evaluation Indexes

**2.4.1. Serum Indicator Detection.** Fasting elbow venous blood (5 ml) was collected from the patients in both groups after treatment and centrifuged with the centrifugal machine (manufactured: Jinan OLABO Technology Co., Ltd.; model: TD-4X) under 3,000 r/min for 15 min to separate serum for test. T-PSA level values of patients before and after treatment were determined by electrochemiluminescence assay, and VEGF level values were determined by immunosorbent assay, with the kits provided by Beijing Aviva Systems Biology Co., Ltd. The operation procedures were performed according to the kit instructions.

**2.4.2. Efficacy Determination.** The clinical efficacy after treatment of patients in the two groups was evaluated by referring to the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [13] recommended by the World Health Organization (WHO), and the number of cases with complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD) was counted. The T-PSA level values in patients after treatment were regarded as the evaluation criterion for efficacy, i.e., referring to the percentage of the PSA difference after treatment divided by the T-PSA value before treatment, the reduction rate  $\geq 75\%$  indicated CR,  $75\% < \text{reduction rate} \leq 50\%$  indicated PR,  $49\% < \text{reduction rate} \leq 30\%$  indicated SD, and reduction rate  $< 29\%$  indicated PD; the disease control rate (DCR) = (CR + PR + SD) cases/total number × 100%, and the objective remission rate (ORR) = (CR + PR) cases/total number × 100%.

**2.4.3. Follow-Up Observation.** The researchers obtained clinical data and pathological characteristics by reviewing the patients' medical records in detail and by telephone follow-up with the patients or their legal guardians, and all patients were regularly reviewed for CT scans and tumor markers to record their overall survival (OS) and disease progression-free survival (PFS).

**2.5. Statistical Methods.** In this study, the data were analyzed by the statistic software SPSS 26.0, the measurement data were expressed by (mean  $\pm$  SD) and examined by *t*-test, the enumeration data were expressed by *n*(%) and examined by  $\chi^2$  test, the factors affecting patients' prognosis were analyzed by single-factor and multi-factor Cox proportional-hazards regression models, and differences were considered statistically significant at  $P < 0.05$ .

### 3. Results

**3.1. Between-Group Comparison of Baseline Data.** No significant differences in the mean age, BMI values, prostate volume, TNM pathological stage, and other general information between the two groups were observed ( $P > 0.05$ ) (see Table 1).

**3.2. Between-Group Comparison of Serum T-PSA and VEGF Level Values after Treatment.** After treatment, the serum T-PSA and VEGF levels were significantly lower in the combined group than in the reference group ( $P < 0.001$ ) (see Figure 1).

**3.3. Between-Group Comparison of Treatment Effect.** Compared with the reference group after treatment, the combined group obtained remarkably higher ORR and DCR ( $P < 0.05$ ) (see Table 2).

**3.4. Between-Group Comparison of mPFS and OS.** The mPFS and OS were significantly longer in the combined group than in the reference group ( $P < 0.001$ ) (see Figure 2).

**3.5. Single-Factor and Multi-Factor Retrospective Analyses on Clinical Prognosis of Patients.** It was found that single radiation therapy, Gleason score of 8–10, and positive lymphatic metastasis were the factors affecting patients' clinical prognosis (see Tables 3 and 4).

### 4. Discussion

Prostate cancer refers to the epithelial malignancy in the prostate [14, 15], which often occurs in people over 55 years old and is an important disease that endangers men's life and health. With the increasing worldwide aging population in recent years, its incidence is rising year by year, seriously affecting patients' physical health [16, 17]. Surgery is currently the main treatment for prostate cancer because the condition can be effectively controlled by tumor resection, but some patients are inoperable because of the late

pathological stage, older age, and more comorbidities when diagnosed [18]. Radiotherapy has the advantages of significant efficacy and wide indications, further increasing the radiation dose to the cancer target area and reducing radiation damage to the surrounding tissues, which has been demonstrated in elderly patients with advanced prostate cancer [19]. But radiotherapy will adversely affect normal cells in the body while killing cancer cells and then cause immune function damage and affect rehabilitation. In recent years, studies have revealed a strong association between androgen in the human body and a number of prostate diseases. Based on this theory, the androgen castration, a unique treatment that targets the prostate, was developed [20], which completely blocks androgen in patients by drug action and achieves the goal of controlling or reducing the proliferation and spread of tumor cells. As a non-steroid drug, the bicalutamide tablets used in this study have better peripheral selectivity and can bind to the androgen receptor without effective gene expression, thus inhibiting the stimulation of androgens and causing the atrophy of prostate tumors. It is demonstrated [21] that more than 85% of low-risk prostate cancer patients who accepted the androgen castration obtain a 5-year postoperative survival rate; however, some scholars believe that although castration surgery can effectively block testis-derived androgen, the progression of prostate cancer can be promoted by the adrenal gland-secreted androgen. Therefore, most scholars agree that the androgen deprivation therapy with oral drugs is more effective, tolerable, and convenient [22, 23].

In this study, single radiotherapy and combining ADT with radiotherapy were implemented to 94 prostate cancer patients in the two groups, respectively, and the results showed that compared with the reference group, the clinical effect and serum indicators of the combined group were better. T-PSA is a glycoprotein secreted by prostate glandular acinus and is present in the prostatic ductal system, where its blood epithelial barrier will be disrupted following carcinogenesis of the prostate ductal system, resulting in the rising serum content [24]. It was found in this study that the serum T-PSA of treated patients in the combined group was significantly lower than that of the reference group ( $P < 0.001$ ), indicating that the combined therapy could synergistically exert mutual promoting effects and further promote the apoptosis of cancer cells, thereby inhibiting the proliferation of cancer tissues and effectively reducing the content of serum markers, which have been proved in locally advanced prostate cancer [25]. It was also found that compared with the reference group, the mPFS and OS of the combined group were remarkably longer, denoting that the combined therapy worked better in prolonging patients' survival than the single method. The Cox proportional-hazards model is a semiparametric retrospective model, which simultaneously analyzes the effects of numerous factors on survival and is widely used in medical follow-up studies. In addition, Cox proportional-hazards regression models were also adopted to analyze the factors affecting the prognosis of prostate cancer patients, and it was concluded that the affecting factors were Gleason score of 8–10, positive lymphatic metastasis, and single radiotherapy. The Gleason

TABLE 1: Between-group comparison of baseline data ( $n = 47$ ).

Item	Combined group	Reference group	$X^2/t$	$P$
Mean age (mean $\pm$ SD, years)	63.37 $\pm$ 5.47	64.08 $\pm$ 5.39	0.634	0.528
BMI (mean $\pm$ SD, kg/m <sup>2</sup> )	21.13 $\pm$ 4.37	21.17 $\pm$ 4.41	0.046	0.964
Prostate volume (mean $\pm$ SD, cm <sup>3</sup> )	25.17 $\pm$ 3.28	25.13 $\pm$ 3.34	0.060	0.952
Disease duration (mean $\pm$ SD, month)	7.12 $\pm$ 2.14	7.15 $\pm$ 2.18	0.069	0.945
TNM pathological stage				
II	25 (53.19%)	28 (59.57%)	0.389	0.533
III	17 (36.17%)	16 (34.04%)	0.047	0.829
IV	5 (10.64%)	3 (6.38%)	0.593	0.441
Accompanied metastasis				
Bone metastasis	25 (53.19%)	22 (46.81%)	0.383	0.536
Lymph node metastasis	16 (34.04%)	12 (25.53%)	0.814	0.367
Viscera metastasis	6 (12.77%)	13 (27.66%)	3.232	0.072
Nationality ( $n(\%)$ )			0.712	0.399
Han	43 (91.49%)	45 (95.74%)		
Non-Han	4 (8.51%)	2 (4.26%)		
ECOG score				
0 points	23 (48.94%)	25 (53.19%)	0.170	0.680
1 point	16 (34.04%)	15 (31.91%)	0.048	0.826
2 points	8 (17.02%)	7 (14.89%)	0.079	0.778
Degree of differentiation				
Poor differentiation	14 (29.79%)	17 (36.17%)	0.433	0.510
Moderate differentiation	21 (44.68%)	20 (42.55%)	0.043	0.835
Well differentiation	12 (25.53%)	10 (21.28%)	0.237	0.626
Marital status ( $n(\%)$ )				
Single	2 (4.26%)	3 (6.38%)	0.211	0.646
Married	41 (87.23%)	38 (80.85%)	0.714	0.398
Divorced	4 (8.51%)	6 (12.77%)	0.448	0.503
Place of residence ( $n(\%)$ )			0.170	0.680
Urban area	24 (51.06%)	22 (46.81%)		
Rural area	23 (48.94%)	25 (53.19%)		
Educational degree [ $n(\%)$ ]				
Junior college and above	8 (17.02%)	10 (21.28%)	0.275	0.600
Senior high school	26 (55.32%)	23 (48.94%)	0.384	0.536
Junior high school and below	13 (27.66%)	14 (29.79%)	0.052	0.820

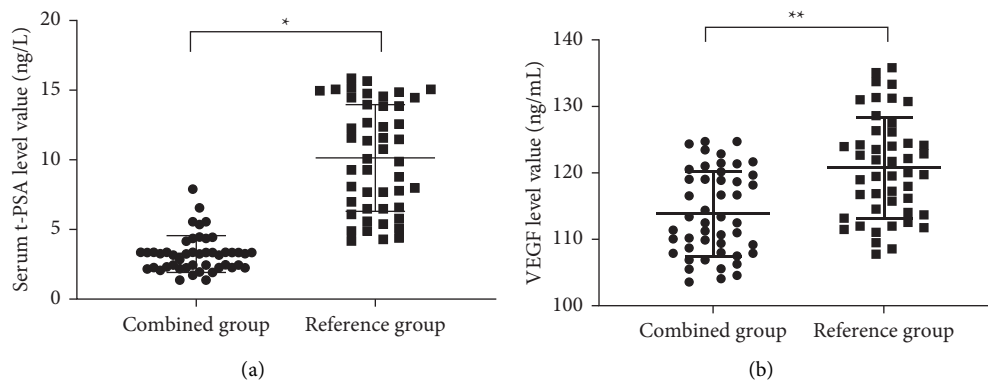


FIGURE 1: Between-group comparison of serum T-PSA and VEGF level values after treatment (mean  $\pm$  SD). (a) The between-group comparison of serum T-PSA level values after treatment. The horizontal axis denoted the combined group and the reference group, and the vertical axis denoted the value (ng/mL). After treatment, the mean serum T-PSA level values of the combined group and the reference group were (3.15  $\pm$  1.32) and (10.07  $\pm$  3.84), respectively, and \* indicated that the mean serum T-PSA level values after treatment between the two groups were significantly different ( $t = 11.683$ ,  $P < 0.001$ ). (b) The between-group comparison of serum VEGF level values after treatment. The horizontal axis denoted the combined group and the reference group, and the vertical axis denoted the value (ng/mL). After treatment, the mean serum VEGF level values of the combined group and the reference group were (113.90  $\pm$  6.41) and (120.84  $\pm$  7.61), respectively, and \*\* indicated that the mean serum VEGF level values after treatment between the two groups were significantly different ( $t = 4.782$ ,  $P < 0.001$ ).

TABLE 2: Between-group comparison of treatment effect ( $n(\%)$ ,  $n = 47$ ).

Group	CR	PR	SD	PD	ORR (CR + PR)	DCR (CR + PR + SD)
Combined	17 (36.17)	8 (17.02)	19 (40.43)	3 (6.38)	53.19% (25/47)	93.62% (44/47)
Reference	11 (23.40)	4 (8.51)	24 (51.06)	8 (17.02)	31.91% (15/47)	82.98% (39/47)
$X^2$					4.352	3.891
$P$					0.037	0.049

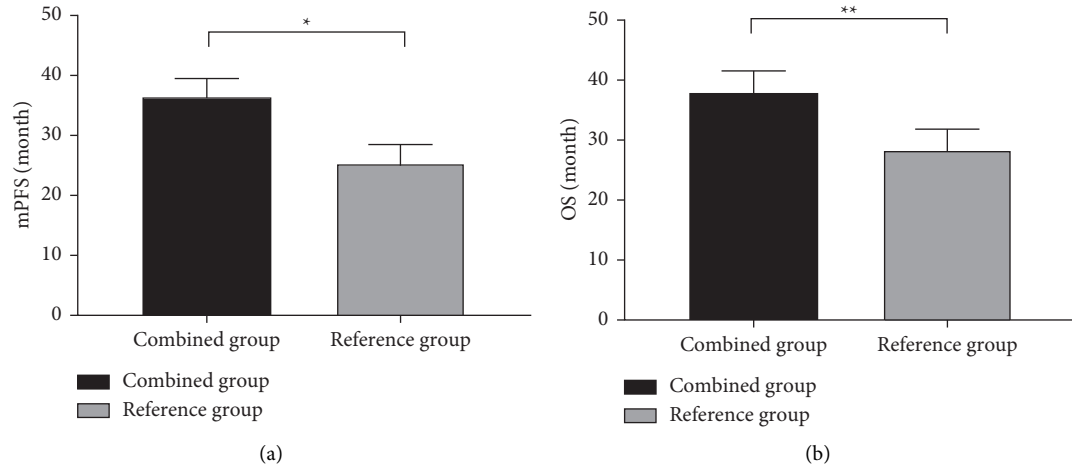


FIGURE 2: Between-group comparison of mPFS and OS (mean  $\pm$  SD). (a) The between-group comparison of mPFS. The horizontal axis denoted the combined group and the reference group, and the vertical axis denoted mPFS (month). The mPFS of the combined group and the reference group was  $(36.23 \pm 3.27)$  and  $(25.36 \pm 3.53)$ , respectively, and \* indicated significant difference in mPFS between the two groups ( $t = 15.487$ ,  $P < 0.001$ ). (b) The between-group comparison of OS. The horizontal axis denoted the combined group and the reference group, and the vertical axis denoted OS (month). The OS of the combined group and the reference group was  $(38.17 \pm 3.43)$  and  $(28.44 \pm 3.46)$ , respectively, and \*\* indicated significant difference in OS between the two groups ( $t = 13.692$ ,  $P < 0.001$ ).

TABLE 3: Single-factor retrospective analysis on clinical prognosis.

Factor	$B$	$S_b$	Wald $X^2$	$P$	OR	95% CI	
						Lower limit	Upper limit
Age	1.364	0.836	3.462	0.463	3.267	0.253	1.732
Pathological stage	2.047	3.276	2.373	0.624	2.165	0.437	1.537
Tumor size	1.564	0.436	2.361	0.253	5.472	0.734	1.345
Treatment method	1.932	2.357	0.836	0.006	4.274	1.323	3.267
Gleason score	2.367	0.924	1.263	0.026	3.274	1.367	2.276
KPS score	1.628	0.637	1.935	0.628	4.274	0.367	2.351
Lymphatic metastasis	0.895	1.924	4.365	0.007	3.574	1.527	2.354

TABLE 4: Multi-factor retrospective analysis on clinical prognosis.

Factor	$b$	$S_b$	Wald $X^2$	$P$	OR	95% CI	
						Lower limit	Upper limit
Age	1.364	0.836	3.462	0.463	3.267	0.253	1.732
Pathological stage	2.047	3.276	2.373	0.624	2.165	0.437	1.537
Tumor size	1.578	0.436	2.361	0.253	5.472	0.734	1.345
Treatment method	1.932	2.357	0.836	0.018	3.736	1.467	3.327
Gleason score	3.273	1.947	1.037	0.014	3.843	1.426	2.357
KPS score	1.738	0.737	2.374	0.628	4.348	0.367	2.351
Lymphatic metastasis	1.236	1.924	4.247	0.002	2.183	1.683	2.874

score is an important indicator for evaluating the degree of malignancy of prostate cancer, and  $\geq 8$  points indicate a high degree of malignancy and high possibility of bone metastasis or other tissue metastasis; a positive lymph node metastasis indicates that the tumor has undergone malignant transformation; and radiotherapy alone will adversely affect the patients' immune system. Therefore, corresponding clinical preventive measures should be carried out to lower the adverse factors that may affect patient treatment. This study conducted a preliminary efficacy exploration of ADT combined with radiotherapy for the treatment of prostate cancer, but due to the limitation of time and other factors, it still has the following deficiencies: ① no relevant studies on postoperative toxicity in patients were conducted; ② the source of cases was not exclusive, and the number of enrolled cases was small, which might affect the overall efficacy decision of patients; and ③ only the changes in serum T-PSA and VEGF levels in patients were analyzed, but to make the clinical study more scientific, other objective evaluation indexes such as follicle-stimulating hormone (FSH) should be included.

In conclusion, combining ADT with radiotherapy obtains significantly better efficacy than single radiotherapy in treating prostate cancer and is therefore recommended in the clinical treatment of prostate cancer.

## Data Availability

The data used to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Traditional Chinese Medicine Combined with Bladder Perfusion with Hydroxycamptothecin on Color Ultrasound and Clinical Efficacy in Patients with Bladder Cancer Surgery

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**Objective.** To observe the clinical effect of Xiaozheng Decoction combined with bladder perfusion with hydroxycamptothecin in the treatment of bladder cancer. **Methods.** A total of 92 bladder cancer patients admitted to our hospital from January to December 2018 were selected and divided into an observation group and a control group according to the random number table method, with 46 cases in each group. The observation group was given Xiaozheng Decoction combined with bladder perfusion with hydroxycamptothecin, and the control group was given hydroxycamptothecin. The levels of serum-related factors (intercellular adhesion molecule-1 (ICAM-1), E-cadherin, cell adhesion molecules (CAM), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF)), white blood cell (WBC) level, immune function indexes, short-term total response rate, and incidence of adverse reactions were compared between the two groups before and after treatment. **Results.** After 2 years of postoperative treatment, the levels of ICAM-1, E-cadherin, CAM-1, FGF, and VEGF (a, b, c) in both groups were improved compared with those before treatment and the observation group was better than the control group ( $p < 0.01$ ). The number of WBCs was significantly higher than in the control group after Traditional Chinese Medicine (TCM) treatment. The observation group was better than the control group in increasing CD3+ and CD4+ levels and decreasing CD8+ level ( $p < 0.05$ ), indicating that this prescription could improve the immune function of patients. The recurrence rate in the observation group was 6.52% after 2 years of treatment, lower than 17.39% in the control group. Color ultrasound parameters showed that there were no statistically significant differences in arrive time (AT) and time to peak (TTP) between patients with and without recurrence and peak intensity (PI) and washout time (WT) were higher in patients with recurrence than in patients without recurrence ( $p < 0.01$ ). The incidence of adverse reactions was significantly lower than that of the control group ( $p < 0.01$ ). **Conclusion.** The clinical effect of Xiaozheng Decoction combined with hydroxycamptothecin on the treatment of bladder cancer was clear and superior to that of hydroxycamptothecin, which could effectively improve the serological indicators of patients with a low incidence of adverse reactions and prolong the survival cycle of patients. Therefore, it is worthy of promotion and application.

## 1. Introduction

Bladder cancer is the most common tumor of the urinary system in China [1], and its morbidity and mortality have shown an increasing trend in recent years [2]. Currently,

transurethral bladder tumor resection (TUR-BT) is the main treatment method for nonmuscular invasive bladder cancer [3, 4]. The surgical technique is mature, and the trauma is small, but still 10%–67% of patients will relapse within 12 months. The recurrence rate is as high as 50%–70% [5–9].

Therefore, it is urgent to explore a safe and effective treatment to prevent postoperative recurrence of bladder cancer, which is an urgent topic in this field.

At present, bladder infusion of chemotherapy drugs is still the most commonly used method to prevent postoperative recurrence of TUR-BT [10–12]. There are many chemotherapeutic drugs in bladder infusion, including Bacillus Calmette–Guerin (BCG) vaccine, mitomycin, and hydroxycamptothecin [13, 14]. The recurrence rate of bladder cancer treated with BCG and mitomycin was 24.24% and 27.27%, respectively [9]. However, long-term chemotherapeutic drugs often cause chemical cystitis, bone marrow suppression, bladder contracture, and other complications [15]. Therefore, there is an urgent need for a safe and effective treatment to prevent postoperative recurrence of bladder cancer.

Any chemotherapy drugs will inevitably cause adverse reactions such as frequent urination, urgent urination, gross hematuria, low fever, and loss of appetite. Traditional Chinese Medicine (TCM) has the effect of reducing toxicity and increasing efficiency, reducing the toxic and side effects of chemotherapy drugs, improving the quality of life of patients, and playing an increasingly important role in the treatment of bladder cancer [16, 17]. TCM believes that the pathogenesis of postoperative recurrence of bladder cancer is always characterized by the deficiency of essential qi and the interaction of dampness and toxin [18, 19]. Therefore, it is suggested that supplementing qi, invigorating dampness, and detoxifying are the basic treatment methods for postoperative recurrence of bladder cancer. On this basis, Xiaozheng Decoction was used to treat postoperative recurrence of bladder cancer.

Color ultrasound examination can be used for early screening of patients with bladder cancer and follow-up observation of patients with bladder cancer. Color ultrasound examination of the urinary system has been widely used in clinical practice because of its advantages of safety, efficiency, noninvasiveness, and low cost. Color ultrasound examination of the bladder can be done by transabdominal ultrasound and transrectal ultrasound. Because of its simple and effective characteristics, it has become an important detection method for bladder cancer after surgery and can accurately determine the recurrence of postoperative tumor, which has an important reference value for the postoperative examination and diagnosis of bladder cancer.

This study was aimed to observe the clinical effect of Xiaozheng Decoction combined with bladder perfusion with hydroxycamptothecin in the treatment of bladder cancer, and results showed that the combination of hydroxycamptothecin and Xiaozheng Decoction could significantly reduce the incidence of side effects such as frequency of urination, urgency of urination, and nausea after bladder perfusion, and improve the quality of life of the patients.

## 2. Methods

### 2.1. Data and Methods

**2.1.1. Clinical Data.** A total of 92 patients with bladder cancer admitted to our hospital from January to December 2018 were selected, including 73 males and 19 females. The

average age was  $65.72 \pm 12.24$  years. All cases were confirmed by pathological examination as transitional epithelial carcinoma. According to the classification standards of bladder cancer diagnosis and treatment guidelines in the 2014 Edition of “Guidelines for the Diagnosis and Treatment of Urological Diseases,” postoperative pathological stages of tumor were 38 cases of PTa stage, 52 cases of PT1 stage, and 2 cases of PTis stage. Pathological grades of tumor were as follows: G1, 43 cases; G2, 47 cases; and G3, 2 cases. According to the random number table method, the patients were divided into observation group and control group, 46 cases in each group. The age of the observation group was  $42 \sim 79$  ( $65.24 \pm 2.13$ ) years, and that of the control group was  $39 \sim 78$  ( $65.45 \pm 2.41$ ) years. This study was reviewed and approved by the Medical Ethics Committee of Qingdao Hospital of Traditional Chinese Medicine, Qingdao Hiser Hospital (approval no. 2019-12-0406). The patients and their families were aware of the study content and signed informed consent.

**2.1.2. Inclusion and Exclusion Criteria.** (1) *Inclusion Criteria.* (1) Patients in this study were clearly diagnosed with bladder cancer. (2) All patients underwent TUR-BT. (3) Patients have normal heart, lung, liver, and kidney functions. (4) They participated voluntarily and signed informed consent forms.

(2) *Exclusion Criteria.* (1) Patients have severe cardiac and renal failure. (2) Patients have coagulation dysfunction. (3) Patients have serious cardiovascular and cerebrovascular complications, contraindications of chemotherapy, and radiotherapy. (4) Patients have primary malignancies other than bladder cancer and require concurrent use of other antitumor drugs, immunomodulators, and cytokines.

### 2.2. Treatment

**2.2.1. Control Group (Hydroxycamptothecin Bladder Infusion Group).** Hydroxycamptothecin injection (Shenzhen Wanle Pharmaceutical Co., Ltd., approval no. 20043063) was used as a recurrence prevention infusion drug. 40 mL of normal saline was added into 40 mg of hydroxycamptothecin and injected into the bladder by catheterization. The hydroxycamptothecin was placed in the left, right, supine, and prone positions for 30 minutes each and retained for 2 hours in total. The course of treatment is as follows: once a week, a total of 8 times, and once a month thereafter, up to 2 years after surgery.

**2.2.2. Observation Group (Chinese Medicine Xiaozheng Decoction Combined with the Bladder Perfusion Group).** On the basis of the bladder infusion of hydroxycamptothecin, Chinese Medicine Xiaozheng Decoction was added: Huijiaren 30 g, *Astragalus membranaceus* 20 g, Huang Jing 15 g, *Hedyotis wilsonii* 15 g, Zhu Ling 15 g, Zedoary 9 g, and Tabei 9 g. Chinese medicine decoction is 1 dose per day, and the course of treatment was 2 years after surgery.

**2.3. Ultrasound Examination.** Philip-iu22 color ultrasonic diagnostic instrument with probe frequency of 3.5 MHz was applied. Before the examination, the patient was properly filled with the bladder, and the supine position was routinely taken, or the side decubitus position or the knee bend decubitus chest position was taken if necessary, fully exposing the lower abdomen to the symphysis pubis. The probe was carried out through multisection and multiangle scanning in the bladder region, and the lesions were carefully observed. Two-dimensional ultrasound was used to observe tumor location, morphology, size, and tumor diameter (maximum diameter and minimum diameter). During the examination, the interference of the artifact in the bladder should be avoided as far as possible, and the same patient was examined by the same physician before and after chemotherapy. The examination results were compared and analyzed and then compared with the postoperative pathological results.

#### 2.4. Observation Indicators

**2.4.1. Serum-Related Factors.** The levels of serum-related factors (ICAM-1, E-cadherin, CAM, FGF, and VEGF) in the two groups were compared before and after treatment.

**2.4.2. Changes in Leukocyte Values.** The ratio of patients with decreased white blood cell (WBC) was observed, and the efficacy was evaluated. Grade I:  $3.0 \times 10^9/L \leq WBC < 4.0 \times 10^9/L$ ; Grade II:  $2.0 \times 10^9/L \leq WBC < 3.0 \times 10^9/L$ ; Grade III:  $1.0 \times 10^9/L \leq WBC < 2.0 \times 10^9/L$ ; Grade IV:  $WBC < 1.0 \times 10^9/L$  were used to evaluate the efficacy.

**2.4.3. VEGF Levels.** Serum VEGF levels were detected by enzyme-linked immunosorbent assay (ELISA) before and 12 months after treatment.

**2.4.4. Indicators of Immune Function.** The levels of CD3+, CD4+, CD8+, CD4+/CD8+, and NK were detected by flow cytometry before treatment and 12 months after treatment. Before and after treatment, 5 mL of fasting venous blood was taken from the patients and placed on the automatic blood centrifugation machine in our hospital for centrifugation. The speed of centrifugation was adjusted to 3000 r/min for 10 min. The supernatant was taken and placed in a refrigerator at  $-20^\circ\text{C}$  for examination. The relative indexes of T lymphocyte subsets in serum were detected by flow cytometry. T lymphocyte subsets (CD3+, CD4+, CD8+) and NK levels were detected by Beckman Coulter EpicsXL flow cytometry, and CD4+/CD8+ was calculated.

**2.4.5. Follow-Up Recurrence Rate.** The recurrence cases were recorded at 6, 12, 18, and 24 months after the operation, and the percentage was calculated. Reexamination was performed by color ultrasound.

**2.4.6. Incidence of Adverse Reactions.** A number of adverse reactions such as nausea and vomiting, frequent urination, urgent urination, abnormal urine routine, hematuria, and low fever were recorded during the treatment period, and the percentage was calculated.

**2.5. Statistical Methods.** Independent repetitions of experiments were 3 times. SPSS 20.0 software (IBM, NY, USA) was used for statistical analysis of the data. The measurement data were expressed as  $\bar{x} \pm s$ , and *t*-test was used for comparison between groups. Count data were expressed as frequency/rate (%), and  $\chi^2$  test was used for comparison between groups.  $p < 0.05$  was considered statistically significant.

### 3. Results

**3.1. Color Ultrasound Image of a Patient with Preoperative Bladder Cancer.** The staging of bladder tumors was based on the TNM staging method (6<sup>th</sup> edition, 2002) of the International Union against Cancer: Stage Ta: noninvasive, superficial tumor; T1: tumor invasion into subepithelial connective tissue; Stage T2a: tumor invasion of the superficial muscle layer; Stage T2b: tumor invasion of deep muscle layer; and >Stage T2: tumor invasion of the peribladder tissue. Imaging features of bladder tumor stage were determined by 3D-CEUS: Ta stage: the bladder wall at the base of the tumor was clear, and the angiography showed continuous and bright lines of the bladder wall; T1: the contrast agent perfusion was slightly stronger in the mucosa layer of the bladder wall than in the muscle layer. T2a stage:  $<1/2$  bladder wall and tumor contrast agent perfusion synchronous, consistent degree of enhancement; T2b stage:  $>1/2$  bladder wall and tumor contrast agent perfusion synchronous, consistent degree of enhancement; and >Stage T2: full bladder wall or surrounding tissue perfusion time, intensity, and characteristics of bladder tumor.

Among the 46 cases of bladder cancer in the control group, 27 tumors were located in the trigone, 18 cases were located in the lateral wall, and 1 case was located at the top. Among the 46 cases of bladder cancer in the observation group, 28 cases were located in the trigone region, 17 cases were located in the lateral wall, and 1 case was located at the top. The characteristics of two-dimensional ultrasonography of patients in both groups were improved after surgery.

**3.2. Short-Term Efficacy Evaluation.** According to the Guideline for the evaluation of TCM Clinical Efficacy in bladder cancer [20], TCM curative effect of bladder cancer was defined as clinical benefit, which was divided into obvious benefit, benefit, and no benefit. A significant benefit is as follows: effective or stable tumor evaluation + significant effect of symptom evaluation + effective or stable quality of life evaluation + effective or stable body weight evaluation. Benefits are as follows: stable tumor evaluation + effective symptom evaluation + effective or stable quality of life evaluation. No benefit is as follows: those who do not meet the above targets. All patients observed in this study were



post-TUR-BT patients, so tumor evaluation was not used as the criteria for clinical efficacy.

After 2 years of postoperative treatment, the total effective rate in the observation group was 91.30%, which was higher than 67.39% in the control group ( $p < 0.05$ ), as shown in Table 1.

**3.3. Comparison of Serum-Related Factor Levels.** Before treatment, there was no significant difference in the levels of ICAM-1, E-cadherin, CAM-1, FGF, VEGF (a, b, c) between the two groups ( $p < 0.05$ ). After 5 courses of treatment, the levels of ICAM-1, E-cadherin, CAM-1, FGF, and VEGF (a, b, c) in both groups were improved compared with before treatment, and the observation group was better than the control group ( $p < 0.01$ ), as shown in Table 2.

**3.4. Changes in White Blood Cell Values.** Table 3 shows 11 (23.91%) patients with leukocyte suppression in the observation group and 27 (58.70%) patients in the control group. The observation group has significantly better efficacy than the control group.

According to Figure 1, there was no significant difference between the two groups before treatment ( $p > 0.05$ ), and the internal comparison between the two groups after treatment was statistically significant ( $p < 0.05$ ). There were still significant differences between the two groups after treatment ( $p < 0.05$ ), indicating that the number of WBC in the observation group after treatment was significantly higher than that in the control group.

**3.5. Comparison of Immune Function Indexes between the Two Groups before and after Treatment.** The level of CD4+/CD8+ in the control group was significantly increased after treatment ( $p < 0.05$ ). CD3+ and CD4+ levels were higher ( $p < 0.05$ ) and CD8+ level were lower than those before treatment ( $p < 0.05$ ). CD3+, CD4+, and CD4+/CD8+ levels and NK level in the observation group were significantly increased after treatment ( $p < 0.05$ ). CD8+ level were significantly decreased ( $p < 0.05$ ). After treatment, the increase of CD4+/CD8+ level in the observation group was significantly better than that in the control group ( $p < 0.05$ ). After treatment, the observation group was superior to the control group in increasing the levels of CD3+, CD4+, and NK and decreasing CD8+ level ( $p < 0.05$ ), as shown in Figure 2, suggesting that this formula can improve the immune function of patients.

**3.6. Comparison of Serum VEGF Levels between the Two Groups before and after Treatment.** There was no significant difference in serum VEGF levels between the two groups before treatment ( $p > 0.05$ ). After three months of treatment, there was no significant difference in serum VEGF levels between the two groups ( $p > 0.05$ ). After six and twelve months of treatment, VEGF levels in both groups were significantly decreased, and VEGF levels in the observation group and control group were significantly decreased after treatment ( $p < 0.05$ ). Compared with the two groups after

treatment, the observation group was superior to the control group in reducing VEGF level ( $p < 0.05$ ), as shown in Table 4.

**3.7. Recurrence Rate.** All patients in this study were treated with perfusion and followed up for 24 months. Specific results: the recurrence rates of bladder tumors in the observation group were 23.91%, 17.39%, 10.86%, and 6.52% at 0.5, 1, 1.5, and 2 years, respectively, while those in the control group were 28.26%, 26.09%, 23.91%, and 17.39% at 0.5, 1, 1.5, and 2 years, respectively. The recurrence rate of bladder tumor in the observation group was 4.35%, 8.70%, 13.05%, and 10.87% lower than that in the control group, respectively. After statistical treatment, there was no significant difference in recurrence rate between the two groups at 0.5 years and 1 year ( $p > 0.05$ ). The recurrence rate in the observation group was significantly lower than that of the control group at 1.5 and 2 years ( $p < 0.05$ ). In conclusion, compared with the control group, the effect of the observation group on reducing the recurrence rate of bladder tumor was increasingly obvious over time, as shown in Figure 3.

**3.8. Comparison of Parameters of Contrast-Enhanced Ultrasound in Bladder Cancer Patients with and without Recurrence at Two Years.** In the observation group, 3 of the 46 patients were positive by ultrasonography, the maximum tumor size was  $0.9\text{ cm} \times 0.5\text{ cm}$ , and the minimum tumor size was  $0.6\text{ cm} \times 0.4\text{ cm}$ . The tumor was broad base, papillary, triangular, mound, or corrugated protruding into the bladder with regular or irregular protruding edges. There was no boundary or fuzzy boundary between the base edge and the bladder wall, and the internal echo was uneven low, equal, or slightly strong. The bladder wall in the tumor area had thickening, stiffness, or no hierarchical sonographic changes. The recurrence of bladder cancer was confirmed by surgical pathology.

In the observation group, preoperative ceUS showed rapid filling of contrast agent in arterial phase in the mass, with arrival time earlier than the bladder wall, prostate, or cervix, and the intensity of contrast agent filling was higher than the bladder wall, prostate, or cervix. In the delayed stage, the internal mass was gradually cleared of contrast media. There was no significant difference in AT and TTP between recurrent and nonrecurrent patients ( $p > 0.05$ ). PI and WT in recurrent patients were higher than those in nonrecurrent patients, and the differences were statistically significant ( $p < 0.05$ ), as shown in Table 5. In patients with recurrence, 66.7% (2/3) showed fast forward and slow regression in contrast enhancement mode, and 33.3% (1/3) showed fast forward and slow regression in pathological grading. Among the patients without recurrence, 86.0% (37/43) showed fast forward and fast regression in contrast enhancement mode, and 14.0% (6/43) showed fast forward and slow regression in pathological grading.

**3.9. Adverse Reactions.** In the control group, 31 cases had frequent urination, 28 cases had nausea or loss of appetite, and 22 cases had abnormal urine routine. In the observation

TABLE 1: Comparison of short-term efficacy evaluation between the two groups.

Group	Complete remission	Partial remission	Stable	Progress	Total effective rate (%)
Control group	3(6.52)	13(28.26)	15(32.61)	15(32.61)	67.39
Observation group	12(26.09)	17(36.96)	16(34.78)	4(8.70)	91.30

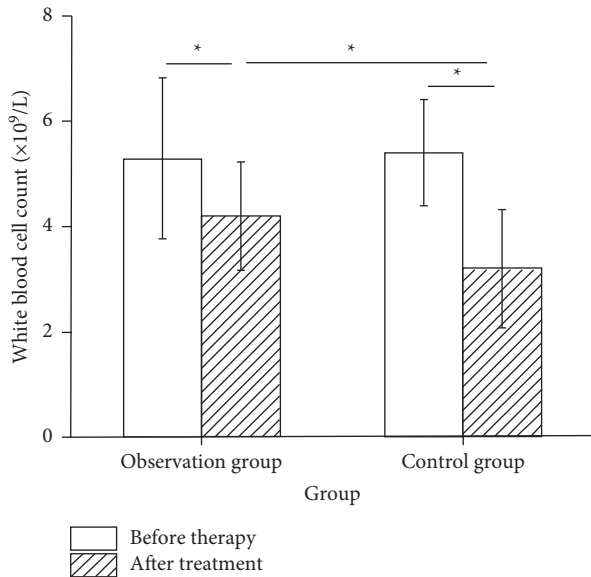
TABLE 2: Comparison of serum-related factors between the two groups before and after treatment.

Project	Observation group		Control group	
	Before treatment	After treatment	Before treatment	After treatment
ICAM-1 (ng/L)	75.98 ± 17.11	35.03 ± 6.22*	75.73 ± 17.88	47.14 ± 9.03*#
E-cadherin (ng/L)	76.90 ± 13.78	37.02 ± 5.34*	77.02 ± 14.01	64.22 ± 5.52*#
CAM (ng/L)	21.54 ± 3.85	71.30 ± 13.64*	21.67 ± 4.12	38.71 ± 8.09*#
FGF (pg/L)	26.14 ± 6.72	7.73 ± 2.75*	26.34 ± 7.00	13.66 ± 3.23*#
VEGF-a (μg/L)	196.32 ± 26.24	82.37 ± 5.07*	197.21 ± 27.33	162.87 ± 14.28*#
VEGF-b (μg/L)	126.45 ± 16.02	105.98 ± 12.73*	126.08 ± 16.21	65.63 ± 3.79*#
VEGF-c (μg/L)	151.35 ± 13.03	123.96 ± 7.33*	151.12 ± 13.22	71.99 ± 6.93*#

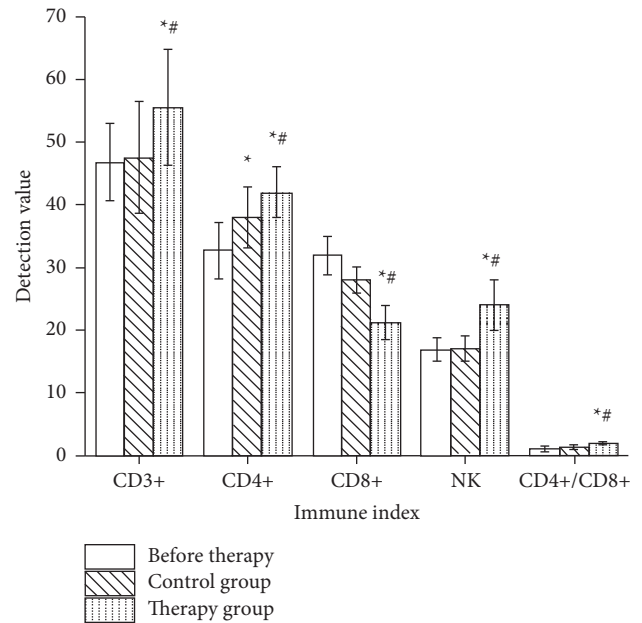
\* $p < 0.05$  versus after treatment; # $p < 0.05$  versus the control group.

TABLE 3: Comparison of white blood cell suppression grades between the two groups ( $n$  (%)).

Group	$n$	I	II	III	IV	Total
Observation group	46	8(17.39)	2(4.35)	1(2.17)	0(0.00)	11(23.91)
Control group	46	13(28.26)	8(17.39)	4(8.69)	2(4.35)	27(58.70)

FIGURE 1: Comparison of the number of WBC between the two groups of patients before and after treatment. \* $p < 0.05$ .

group, 12 cases of frequent urination, 11 cases of nausea or anorexia, and 11 cases of abnormal urine routine, Chinese medicine combined with hydroxycamptothecin can significantly reduce the incidence of frequent urination, urgent urination, nausea, and abnormal urine routine after bladder perfusion, and the difference was significant ( $p < 0.05$ ). Meanwhile, there were 20 cases of low fever in the control

FIGURE 2: Comparison of immune function indexes between the two groups before and after treatment. \* $p < 0.05$  versus after treatment; # $p < 0.05$  versus control group.

group, 12 cases of low fever in the observation group, 16 cases of hematuria in the control group, and 11 cases of hematuria in the observation group. There was no significant difference between the two groups ( $p > 0.05$ ). No other adverse reactions such as myelosuppression were found during the treatment (Figure 4).

#### 4. Discussion

Bladder cancer is one of the most common solid tumors in the genitourinary system and the second most common malignant tumor in the genitourinary system, with more than 400,000 new cases occurring every year [21]. At present, more than 2 million people in China suffer from bladder

TABLE 4: Comparison of serum VEGF levels between the two groups before and after treatment.

Group	Before treatment	Three months after treatment	Six months after treatment	Twelve months after treatment
Observation group	388.5 ± 98.4	346.3 ± 114.4	349.7 ± 110.8	308.2 ± 152.8
Control group	389.7 ± 99.7	378.9 ± 130.7	388.7 ± 102.6	356.3 ± 159.2
<i>t</i>	0.597	1.598	2.445	2.014
<i>p</i>	0.551	0.097	0.021*	0.049*

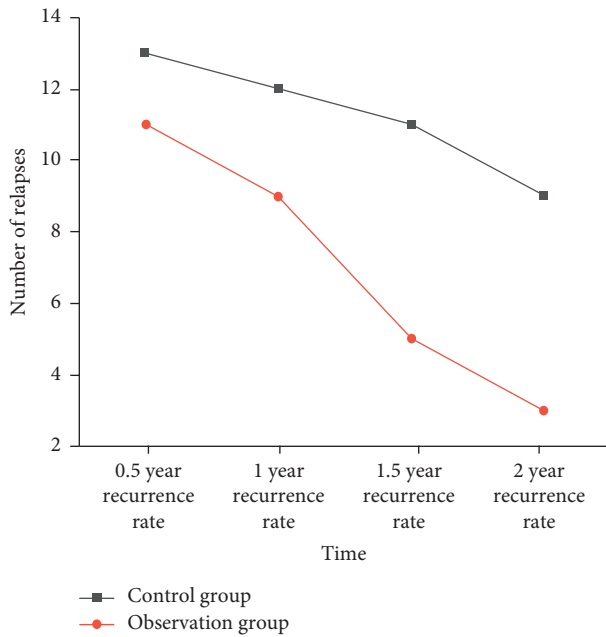


FIGURE 3: Comparison of efficacy in the recurrence rate of bladder tumor between the two groups.

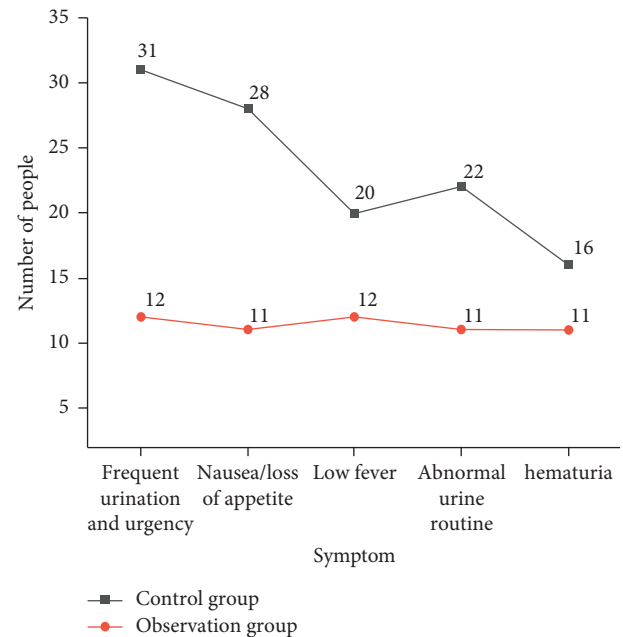


FIGURE 4: Comparison of adverse reactions between the two groups.

TABLE 5: Comparison of contrast ultrasonography parameters of recurrent and nonrecurrent bladder cancer patients in the observation group.

Group	Cases	AT (s)	TTP (s)	PI (dB)	WT (s)
Relapsed patients	3	21.6 ± 1.5	30.9 ± 2.4	22.0 ± 12.2	36.7 ± 10.3
Nonrelapsed patients	43	22.0 ± 1.7	29.1 ± 1.8	14.9 ± 8.9	21.9 ± 8.1

cancer [22]. There were 430,000 new cases of bladder cancer in 2012, making it the ninth most common cancer worldwide. In recent decades, there has been little success in reducing the incidence of bladder cancer for many reasons [23]. Bladder cancer has a high postoperative recurrence rate due to being multifocal, implantable, and urinary-derived [24]. 50%~70% of patients have recurrence after bladder-sparing surgical treatment, and 20%~30% of superficial bladder cancer develops into invasive or metastatic cancer after surgery, with poor long-term efficacy [25, 26]. All bladder cancer patients who underwent bladder preservation had a higher risk of recurrence. Therefore, postoperative local perfusion chemotherapy should be performed to kill the remaining tumor cells as much as possible, prevent tumor progression, reduce the probability of recurrence, and delay recurrence. At present, although there are many

chemotherapeutic drugs available for postoperative bladder infusion chemotherapy, about 30% of patients still have a recurrence.

Previous studies have found that hydroxycamptothecin is basically not absorbed by the bladder mucosa. It inhibits DNA replication, transcription, and mitosis by acting on DNA topoisomerase I and has an inhibitory effect on the development of tumors [27, 28]. The adverse reactions are relatively small, and the patient's recurrence rate is low, which is better than the preventive effect of mitomycin and BCG. In our hospital, hydroxycamptothecin has been used for adjuvant chemotherapy after bladder preservation in patients with bladder cancer, and good efficacy has been achieved for many years. However, because most patients are older at the onset of the disease, and the body constitution is in the decline stage, and the return of surgical treatment, the body's resistance is significantly reduced, and it can also be seen in the clinic that the patient has severely reduced white blood cells and decreased body immunity due to myelosuppressive reaction after perfusion, resulting in severe infections and a poor prognosis for the patient.

TCM can enhance the curative effect of chemotherapy drugs and the immune function of the body. This study explored the effect of hydroxycamptothecin bladder perfusion (control group) and Xiaozheng Decoction combined with hydroxycamptothecin bladder perfusion (observation



group) to prevent bladder cancer recurrence after surgery. The recurrence rates at 1.5 years and 2 years after surgery were lower than those in the control group ( $p < 0.05$ ), and with the passage of time, the recurrence rate of patients in the observation group gradually decreased.

Long-time bladder perfusion chemotherapy can cause different degrees of adverse reactions. This study showed that the adverse reactions in the treatment of the two groups were mainly manifested as anorexia, nausea and vomiting, hematuria, low fever, frequent urination and urgent urination, and abnormal urine routine. Pharmacological experiments showed that Xiaozheng Decoction can inhibit tumor formation, enhance immunity, and reduce adverse reactions caused by chemotherapy drugs. This present study indicated that Xiaozheng Decoction combined with hydroxycamptothecin bladder infusion can reduce the incidence of anorexia, nausea and vomiting, frequent and urgent urination, and abnormal urine routine and improve the quality of life of patients to a certain extent. VEGF is highly specific and can induce the proliferation of vascular endothelial cells and promote the angiogenesis of tumor cells, which plays an important role in the occurrence and development of bladder tumor and has a certain relationship with tumor recurrence [29, 30]. Therefore, the detection of VEGF level can be used to determine the status of tumor metastasis and treatment effect. In this present study, that the levels of VEGF in the two groups showed a downward trend after treatment. At 6 and 12 months after treatment, the VEGF levels in the observation group were lower than those in the control group ( $p < 0.05$ ). These results indicated that the combination of Chinese and Western drugs can reduce the level of VEGF in postoperative patients with bladder cancer, which is beneficial to reducing the recurrence and metastasis of tumor.

The application of chemotherapeutic drugs is often accompanied by serious gastrointestinal reactions, bone marrow suppression, nerve damage, and other toxic and side effects, and many patients often end treatment halfway because they cannot tolerate the toxic and side effects of chemotherapy [31]. The results of this study showed that the white blood cells count in the observation group was significantly higher than that of the control group after TCM treatment. In addition, the observation group was superior to the control group in increasing the levels of CD3+, CD4+, and NK and decreasing the level of CD8+ ( $p < 0.05$ ), indicating that this prescription could improve the immune function of patients. These results suggested that TCM combined with hydroxycamptothecin infusion in the treatment of bladder cancer had a significant protective effect on white blood cells, which was worthy of popularization and application.

## 5. Conclusion

In conclusion, Xiaozheng Decoction combined with hydroxycamptothecin bladder perfusion can significantly reduce the recurrence rate after TUR-BT; reduce the incidence of frequent urination, urgency, nausea, and abnormal urine routine after bladder perfusion; and improve the

quality of life of patients. Therefore, the combination of TCM and Western medicine treatment can improve the clinical efficacy and alleviate the suffering of patients, which is worthy of clinical promotion. However, the mechanism of Xiaozheng Decoction remains to be further studied.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

## Disclosure

The funding body had no role in the design of the study, collection, analysis, interpretation of data, or writing of the manuscript.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Clinical Effects of Integrated Traditional Chinese and Western Medicine in Treating Severe Preeclampsia and Its Influence on Maternal and Infant Outcomes after Cesarean Section under Combined Lumbar and Epidural Anesthesia

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**Objective.** This study is aimed to observe the clinical effects of integrated traditional Chinese and Western medicine in treating severe preeclampsia (SPE) and its effects on maternal and infant outcomes after cesarean section under combined lumbar and epidural anesthesia. **Method.** One hundred and sixty-six pregnant women with SPE were randomly divided into an experimental group and control group, with 83 cases in each group. The control group was given conventional treatments such as magnesium sulfate, and the experimental group received self-made traditional Chinese medicine decoction for oral administration. **Results.** The total clinical effective rate of treatment in the experimental group was significantly higher than that in the control group. After treatment, the systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and 24 h proteinuria (24 h PRO) levels of the experimental group were significantly lower than those of the control group. After cesarean section (c-section) under combined lumbar and epidural anesthesia, there were statistically significant differences in placental abruption, uterine weakness, fetal intrauterine distress, and neonatal asphyxia in the experimental group, while there were no significant differences in oligohydramnios. After treatment, the contents of inflammatory factors in both groups decreased, and the decrease was more prominent in the experimental group. After treatment, the levels of blood urea nitrogen (BUN), serum creatinine (Scr), and albumin (Alb) and  $\beta_2$  microglobulin ( $\beta_2$ -MG) of the two groups of patients decreased, and the levels of them in the experimental group decreased. After treatment, the levels of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in the two groups increased. However, the levels of malondialdehyde (MDA), lipid peroxide (LPO), and advanced oxidation protein products (AOPP) all reduced, and the increase or decrease in the experimental group was more prominent. **Conclusion.** The combination of traditional Chinese and Western medicine can reduce the blood pressure of a patient with SPE. After the combined spinal-epidural anesthesia and cesarean section, it can significantly improve the maternal and infant outcomes and renal function, reduce inflammatory factors levels and body oxidative stress, and increase the activities of antioxidant enzymes.

## 1. Introduction

Severe preeclampsia (SPE) is an idiopathic condition during pregnancy with persistently elevated hypertension and proteinuria (PRO) after 20 weeks of gestation period.

Compared with mild-to-moderate preeclampsia, SPE patients often have significantly higher blood pressure and can even have significant symptoms such as persistent headache or upper abdominal pain [1]. SPE is a particular type of pregnancy-induced hypertension, with early onset, rapid

progression, many complications, and poor perinatal prognosis, which can cause serious harm to maternal and infant health and even endanger their lives [2]. Numerous studies have shown that SPE can increase the long-term risk of cardiovascular and cerebrovascular diseases, kidney diseases, and diabetes for the mother and fetus [3]. Cesarean sections (c-sections), which can quickly separate the fetus from the adverse intrauterine environment and stop the vicious cycle between mother and fetus, are mainly used for the termination of pregnancy in patients with SPE [4]. Different anesthesia methods used in c-sections for women with SPE also have different effects on maternal hemodynamics [5]. Combination of lumbar and epidural block anesthesia is effective and widely used in normal c-sections, especially emergency c-sections [6]. However, patients in the early stage still need to rely on drug treatment. The spasmolytic and hypotensive methods are often used in clinics, while magnesium sulfate is a common spasmolytic drug, which can dilate smooth muscle and reduce blood vessel resistance and blood pressure in pregnant women [7]. However, there are individual differences in the effect of magnesium sulfate, which may lead to magnesium poisoning and poor safety [8]. According to the traditional Chinese medicine system, preeclampsia belongs to the category of “pregnancy vertigo” and “gestational vertigo” [9]. During pregnancy, the accumulation of Yin and blood, deficiency of essential qi, imbalance of Yin and Yang of liver and kidney, and disorder of qi and blood result in eclampsia [9]. Therefore, one hundred and sixty-six cases of SPE in our hospital were treated with TCM decoction with magnesium sulfate and other conventional treatment, and the outcomes were satisfactory.

## 2. Materials and Methods

**2.1. General Information.** A total of 166 pregnant women with SPE treated at Yantai Hospital, Yantai, Shandong, China, from April 2018 to September 2020, were selected, all of them met the relevant diagnostic criteria for SPE in China [10]. Inclusion criteria were as follows: (1) aged from 20 to 35 years; (2) all were first pregnancies; (3) single child; and (4) signed informed consent and voluntary participation in the study. Exclusion criteria were as follows: (1) patients with chronic kidney disease and history of chronic hypertension before pregnancy; (2) patients with severe heart, brain, liver, lung, kidney, and other important organ dysfunction, as well as coagulation dysfunction, blood system diseases; and (3) patients with other malignant tumors, hemorrhagic diseases, drug allergies, gestational diabetes, etc. Patients were randomly divided into an experimental group and control group, eighty-three cases in each group. The experimental group was 21–33 years old, with an average of  $27.2 \pm 3.4$  years old; gestational age ranged from 24 to 33 weeks, mean  $29.6 \pm 2.7$  weeks; and body mass index (BMI) was  $21.4 \sim 28.9 \text{ g/m}^2$ , with an average of  $25.3 \pm 2.7 \text{ g/m}^2$ . The control group was 23–32 years old, with an average of  $27.6 \pm 3.6$  years old; gestational age ranged from 25 to 33 weeks, with an average of  $29.3 \pm 2.8$  weeks; and BMI was  $21.7 \sim 29.4 \text{ g/m}^2$ , mean  $25.8 \pm 2.9 \text{ g/m}^2$ . There was no

significant difference between the two groups of general information ( $P > 0.05$ ), and they were comparable. This study was approved by the Ethics Committee of Yantai Hospital, Yantai, Shandong, China.

**2.2. Diagnostic Criteria.** Western medicine diagnostic criteria were as follows: patients meet the criteria of “Chinese Obstetrics and Gynecology” [11] for early-onset SPE: hypertension occurs for the first time after 20 weeks of pregnancy, that is, systolic blood pressure (SBP)  $\geq 160 \text{ mmHg}$  and/or diastolic blood pressure (DBP)  $\geq 110 \text{ mmHg}$ , accompanied by any of the following: (1) PRO  $\geq 50 \text{ g/24 h}$ , or random PRO was positive, or PRO/creatinine  $\geq 0.3$ ; (2) no PRO, but with heart, liver, lung, kidney and other important organs, or digestive system, blood system, nervous system and other abnormal changes, placenta-fetal involvement. TCM diagnostic criteria: patients meet the criteria for syndromes of Yin deficiency and liver vigor in “Chinese Medicine and Gynecology” [12]; dizziness, tinnitus, insomnia, blurred vision, anguish are the main symptoms, facial blushing, dry mouth and throat, feverishness in palms and soles are secondary symptoms, and red tongue, less moss, pulse a few strings.

**2.3. Treatment Method.** After admission, patients in both groups were given conventional treatment: 5 g 25% magnesium sulfate injection (Tianjin Pharmaceutical Jiaozuo Co., LTD., Approval No. H20043974) with 100 mL 10% glucose injection was administered intravenously within half an hour for spasmolysis. Then, 15 g 25% magnesium sulfate injection and 500 mL 5% glucose injection were given intravenously. At the same time, 2.5 g magnesium sulfate injection could be given intramuscularly according to the patient's blood pressure, but the total dosage of magnesium sulfate was less than 30 g, 3 times per day, 2.5 mg per time. On this basis, the experimental group was supplemented with our hospital's self-made Chinese medicine decoction. The prescriptions were *uncariae ramulus cum uncis* (15 g), *Salvia miltiorrhiza* (15 g), *Astragalus propinquus* (15 g), *puerariae lobatae radix* (15 g), *eucommiae cortex* (12 g), *leonuri herba* (12 g), *ginseng radix et rhizoma* (10 g), *paeoniae radix alba* (10 g), *poria* (10 g), *dioscoreae rhizoma* (10 g), 5 g of *angelicae sinensis radix*, and 3 g of *glycyrrhizae radix et rhizoma*. The above prescription was decocted to 200 mL, once a day, orally with warm water twice in the morning and evening. Treatment was terminated 1 day before termination of pregnancy in both groups.

**2.4. Observation Index.** (1) The clinical efficacy of the two group patients was compared [13]. Special effect: clinical symptoms disappeared completely or significantly improved, blood pressure decreased  $>20 \text{ mmHg}$  ( $1 \text{ mmHg} = 0.133 \text{ kPa}$ ), and PRO and edema symptoms disappeared. Valid: clinical symptoms improved, blood pressure decreased by 10–20 mmHg, and edema and PRO both improved significantly. Invalid: those who did not meet the above standards. The total effective rate of



treatment = (special effect + valid) number of cases/total number of cases  $\times 100\%$ . (2) Blood pressure (SBP, DBP), mean arterial pressure (MAP), and 24-h PRO levels were compared between the two groups after treatment. (3) Serum levels of interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), C-reactive protein (CRP), and homocysteine (Hcy) were compared between the two groups before and after treatment. IL-6 and TNF- $\alpha$  levels were determined by an enzyme-linked immunosorbent assay (ELISA) kit. Hcy levels were determined by the circulating enzyme method, and serum CRP levels were determined by immunoturbidimetry. (4) The stress indexes of the two groups were compared before and after treatment. The activity of superoxide dismutase (SOD) was determined by the xanthine oxidase method. The activity of glutathione peroxidase (GSH-Px) was determined by the dithio-dinitrobenzoic acid method. The levels of malondialdehyde (MDA) and lipid peroxide (LPO) were determined by the thiobarbituric acid method. And the level of advanced oxidation protein products (AOPP) was determined by the chloramine colorimetric method. (5) The renal function of the two groups was compared before and after treatment. Serum creatinine (SCr) and blood urea nitrogen (BUN) were detected by immunoturbidimetry, and albumin (Alb) and  $\beta 2$  microglobulin ( $\beta 2$ -MG) were detected by radioimmunoassay. (6) The incidence of adverse pregnancy outcomes was compared between the two groups. Before cesarean section under combined lumbar and epidural anesthesia, routine fasting was 8 h, and drugs such as hibernation mixture and magnesium preparation were given within 6 h before operation. The parturient was placed in a standard right decubitus position and routinely disinfected. Intervertebral needle insertion was selected between L3 and 4. 10 mg bupivacaine injection (Shanghai Harvest Pharmaceutical Co., LTD) was injected into the subarachnoid space. Placental abruption, uterine atonia, fetal distress, neonatal asphyxia, and oligohydramnios were recorded.

**2.5. Statistical Analysis.** SPSS 20.0 software was used for statistical analysis of the data obtained in this study. The measurement data were expressed as  $\bar{x} \pm s$  and the *T*-test was adopted. The count data were expressed in percentage, and the  $\chi^2$  test was used.  $P < 0.05$  was considered statistically significant.

### 3. Results

**3.1. Comparison of Clinical Efficacy between the Two Groups of Patients.** The total clinical effective rate of treatment in the experimental group was 90.36% and in the control group was 71.08% (Table 1). The difference between the two groups was statistically significant ( $\chi^2 = 13.267$ ,  $P = 0.001$ ) (Table 1).

**3.2. Comparison of Blood Pressure, MAP, and 24 h PRO Content between the Two Groups of Patients after Treatment.** After treatment, the SBP, DBP, MAP, and 24 h PRO levels of the experimental group were significantly lower than those of the control group (Figure 1).

**3.3. Comparison of Serum Inflammatory Factor Levels before and after Treatment between the Two Groups.** Before treatment, there was no significant difference in serum Hcy, CRP, IL-6, and TNF- $\alpha$  levels between the two groups of patients ( $P > 0.05$ ) (Figure 2). After treatment, the levels of inflammatory factors in the two groups of patients decreased, and the decrease in the experimental group was more significant ( $P < 0.05$ ) (Figure 2).

**3.4. Comparison of Stress Indicators between the Two Groups of Patients before and after Treatment.** Before treatment, there was no significant difference in the content of stress indicators between the two groups of patients ( $P > 0.05$ ) (Table 2). After treatment, the levels of SOD and GSH-Px in the two groups increased, and the increase in the experimental group was more significant ( $P < 0.05$ ) (Table 2). The levels of MDA, LPO, and AOPP in the two groups of patients decreased, and the decrease in the experimental group was more significant ( $P < 0.05$ ) (Table 2).

**3.5. Comparison of Renal Function Indexes between the Two Groups of Patients before and after Treatment.** Before treatment, there was no significant difference in renal function indexes between the two groups ( $P > 0.05$ ) (Figure 3). After treatment, the levels of BUN, Scr, Alb, and  $\beta 2$ -MG of the two groups of patients decreased, and the levels of various indicators in the experimental group decreased more significantly ( $P < 0.05$ ) (Figure 3).

**3.6. Comparison of Maternal and Infant Outcomes between the Two Groups.** The experimental group had statistically significant differences in placental abruption, uterine atonia, fetal distress, and neonatal asphyxia ( $P < 0.05$ ), and there was no statistically significant difference in the comparison of oligohydramnios ( $P > 0.05$ ) (Table 3).

## 4. Discussion

SPE is a common complication of pregnancy-induced hypertension, and its pathogenesis may be related to genetics, diet, immune regulation, and other factors, resulting in elevated blood pressure and inadequate placental perfusion [14]. If the treatment is not given timely, it can lead to abortion and even pose a threat to the life safety of pregnant women and fetuses [15]. Therefore, early detection and early treatment are very important to improve outcomes in mother and infant. Magnesium sulfate is the drug of choice for the treatment of SPE, which has the effect of relieving spasm of vascular smooth muscle, inhibiting central and motor nerves and the release of acetylcholine, reducing muscle contraction, dilating vascular smooth muscle, expanding spasm of peripheral blood vessels, and reducing blood pressure [16]. However, the clinical effect of single use is not good because severe placental ischemia and hypoxia will lead to maternal endothelial dysfunction [17]. Studies have found that giving a scientific dose of magnesium sulfate for preeclampsia maternity can reduce the incidence of

TABLE 1: Comparison of clinical efficacy between the two groups of patients ( $n$  (%)).

Group	Cases	Special effect	Valid	Invalid	Total effective rate
Experimental	83	36 (43.37)	39 (46.99)	8 (9.64)	75 (90.36)
Control	83	19 (22.89)	40 (48.19)	24 (28.92)	59 (71.08)
$\chi^2$					13.267
$P$					0.001

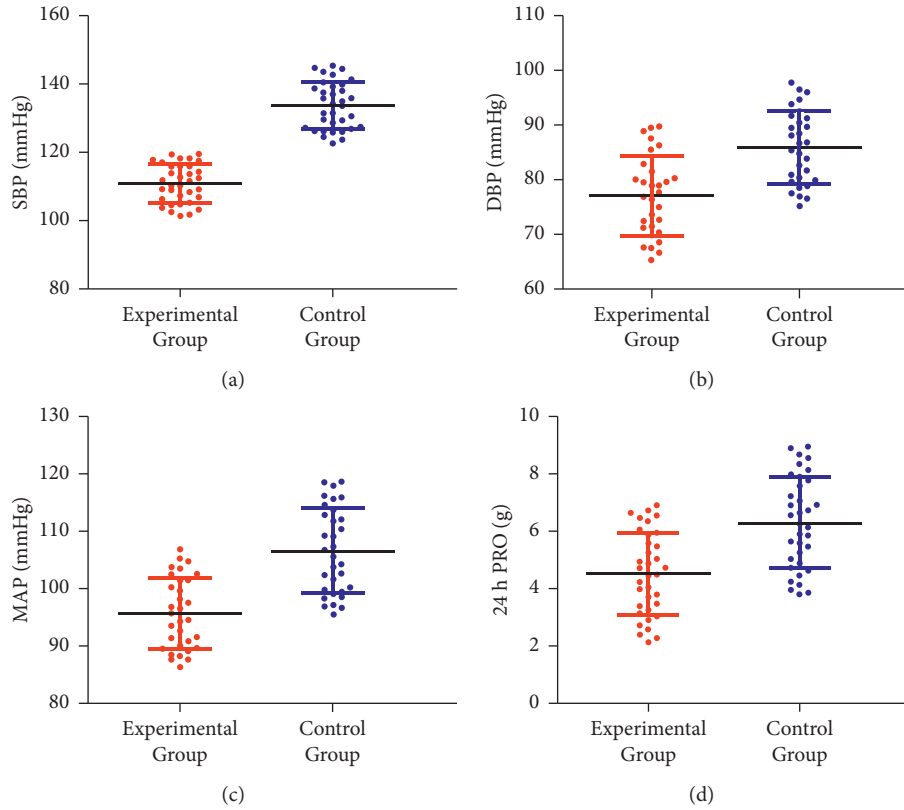


FIGURE 1: Comparison of blood pressure, MAP, and 24 h PRO content between the two groups of patients after treatment. (a) The comparison of SBP after treatment of the two groups of patients. (b) The comparison of DBP after treatment of the two groups of patients. (c) The comparison of the MAP between the two groups of patients after treatment. (d) The comparison of PRO content of the two groups of patients at 24 h after treatment.

cerebral palsy in children [18]. However, Ugwu et al. reported that long-term application of magnesium sulfate has the risk of magnesium ion poisoning, which is not conducive to maternal and child health [19]. Therefore, searching for safe and more effective prevention and treatment measures has become an urgent medical problem in obstetrics.

TCM experts believe that the key treatment principles for SPE are nourishing Yin and tonifying kidney, calming liver, and promoting blood circulation [20]. Glycyrrhizae radix et rhizoma mixed with various medicines, *Salvia miltiorrhiza* and *Astragalus propinquus*, can promote blood circulation and remove stasis, nourish blood and tranquilizing mind, and regulate the metabolism of water and salt in the body [21]. At the same time, studies have found that *Salvia miltiorrhiza* can also effectively remove oxygen free radicals in the body and reduce or block microcirculation disorders in the body, so as to significantly improve the renal function of pregnant women with SPE [22]. *Angelicae*

*sinensis* radix and *leonuri* herba can nourish qi and promote blood circulation; *ginseng* radix et rhizoma can improve the metabolic products in the blood of patients with hypertension and restore normal body function; *uncariae* ramulus cum uncis has the effect of calming the liver, extinguishing the wind, and reinforcing yang; *paeoniae* radix alba can soothe the liver and relieve pain and nourish blood for regulating menstruation; *dioscoreae* rhizoma can invigorate spleen-stomach and replenish qi, nourish the stomach and spleen, and strengthen yin and benefit kidney; *eucommiae* cortex can reinforce liver and kidney; *puerarin* is the main isoflavone compound of *puerariae lobata* radix, which has been widely used in clinical treatment of cardiovascular diseases; *poria* can invigorate spleen for eliminating dampness [23–26]. Recent pharmacological studies shown that *puerarin* can reduce the content of endothelin and play a role in reducing blood pressure. The combination of all drugs play the effect of tonifying liver and kidney,

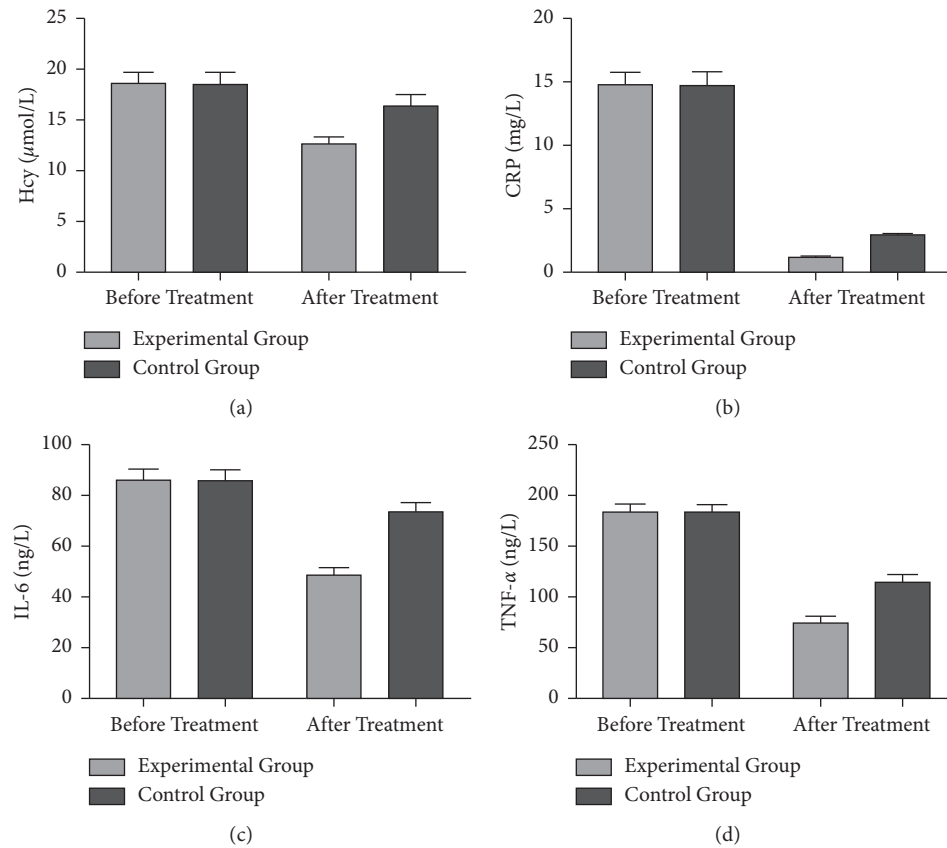


FIGURE 2: Comparison of serum inflammatory factor levels before and after treatment between the two groups. (a) The comparison of Hcy levels between the two groups of patients before and after treatment. (b) The comparison of CRP levels between the two groups of patients before and after treatment. (c) The comparison of IL-6 levels before and after treatment in the two groups of patients. (d) The comparison of TNF- $\alpha$  levels before and after treatment in the two groups.

TABLE 2: Comparison of stress indicators between the two groups of patients before and after treatment ( $\bar{x} \pm s$ ).

Indicators		Experimental	Control	<i>t</i>	<i>P</i>
SOD (U/mL)	Before treatment	83.66 $\pm$ 9.63	84.07 $\pm$ 9.73	0.264	>0.05
	After treatment	141.57 $\pm$ 6.34	113.28 $\pm$ 7.46	7.823	<0.05
GSH-Px (U/mL)	Before treatment	98.37 $\pm$ 10.84	98.72 $\pm$ 10.21	0.665	>0.05
	After treatment	133.56 $\pm$ 8.71	110.42 $\pm$ 9.02	10.234	<0.05
MDA (mmol/L)	Before treatment	9.23 $\pm$ 2.37	9.15 $\pm$ 2.64	0.456	>0.05
	After treatment	4.87 $\pm$ 1.13	7.23 $\pm$ 1.58	4.871	<0.05
LPO (nmol/L)	Before treatment	15.87 $\pm$ 3.72	15.96 $\pm$ 3.45	0.674	>0.05
	After treatment	7.34 $\pm$ 2.23	12.62 $\pm$ 2.73	6.257	<0.05
AOPP (μmol/L)	Before treatment	31.36 $\pm$ 5.24	31.93 $\pm$ 5.48	0.931	>0.05
	After treatment	18.37 $\pm$ 3.66	25.89 $\pm$ 3.91	12.554	<0.05

nourishing yin and helping yang, calming wind, and relieving spasm.

According to the results of this study, the total clinical effective rate of the experimental group was obviously higher than that of the control group, indicating that the treatment of SPE by integrated traditional Chinese and Western medicine is better than that by Western medicine alone. After treatment, the contents of SOD and GSH-Px in the experimental group were notably higher than those in the control group, while the levels of MDA, LPO, and AOPP in

the experimental group were dramatically lower than those in the control group, which may be related to the components of *Salvia miltiorrhiza* in the TCM decoction. It has the effect of promoting blood circulation and removing blood stasis, improving vascular endothelial function damage, enhancing antioxidant capacity of the body, and alleviating oxidative stress injury [27]. After treatment, blood pressure, MAP, and 24-h PRO content in the experimental group were markedly lower than those in the control group. In this study, puerariae lobamle radix and uncariae ramulus cum



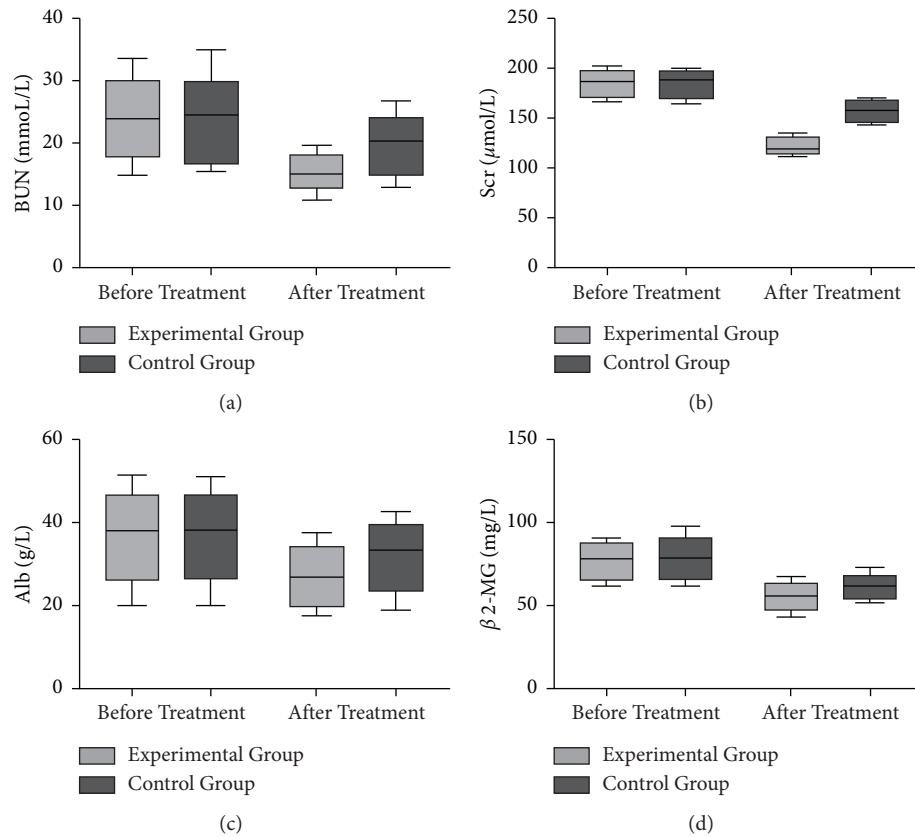


FIGURE 3: Comparison of renal function indexes of the two groups of patients before and after treatment. (a) The comparison of BUN levels between the two groups of patients before and after treatment. (b) The comparison of Scr levels between the two groups of patients before and after treatment. (c) The comparison of Alb levels between the two groups of patients before and after treatment. (d) The comparison of  $\beta$ 2-MG levels before and after treatment in the two groups.

TABLE 3: Comparison of maternal and infant outcomes between the two groups (n).

Group	Cases	Placental abruption	Oligohydramnios	Uterine asthenia	Fetal distress	Neonatal asphyxia
Experimental	83	6	4	5	4	2
Control	83	16	7	13	13	9
$\chi^2$		6.631	1.132	5.457	10.226	11.392
P		<0.05	>0.05	<0.05	<0.05	<0.05

uncis have antihypertensive effects and help control blood pressure. IL-6, TNF- $\alpha$ , and CRP can cause vascular endothelial dysfunction and participate in the occurrence of hypertension during pregnancy [28, 29]. Elevated levels of Hcy can aggravate vascular endothelial cell damage and promote eclampsia. After treatment, the level of inflammatory factors in the experimental group was obviously lower than that in the control group, and the renal function was significantly better than that in the control group, indicating that the TCM decoction used in this study has the potential of nourishing Yin and kidney, can reduce the level of inflammatory factors in the body, and improve the immune function of the human body. C-section is an important means of pregnancy termination for patients with SPE. Combination of lumbar and epidural block anesthesia has the advantages of small dosage, perfect block, and quick

effect, which can reach the anesthesia level required by operation in a short time, and has good analgesic effects and high safety profile [30]. In terms of maternal and infant outcomes, the experimental group was superior to the control group as a whole, suggesting that the addition of Chinese medicine decoction used in this study can significantly reduce the patients' blood pressure and the damage to the mother and fetus.

In summary, the combination of traditional Chinese and Western medicine has significant therapeutic effects in the treatment of SPE, which can decrease blood pressure, IL-6, TNF- $\alpha$ , CRP, and Hcy levels and oxidative stress and improve the body's immune function. Therefore, this therapeutic strategy can reduce the incidence of adverse pregnancy outcomes after c-section under combined lumbar and epidural anesthesia.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

## Conflicts of Interest

The authors declare that they have no competing interests.

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## Research Article

# Sinomenine Inhibits the Progression of Bladder Cancer Cells by Downregulating LncRNA-HEIH Expression

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**Background.** Sinomenine has been reported to effectively repress the progression of lung cancer and breast cancer. However, the effects of sinomenine in bladder cancer are not well understood. The purpose of this study was to evaluate the effects of sinomenine in bladder cancer. **Methods.** The mRNA expression of HEIH in bladder cancer cells was measured by RT-qPCR. T24 and SW780 cells were treated with sinomenine for 24 hours. Cell viability was detected by the MTT assay. Cell migration and invasion were detected by the transwell assay. Western blotting assay was performed to assess the protein expression of Bcl-2, Bax, and caspase-3. **Results.** Sinomenine significantly suppressed cell viability in T24 and SW780 cells. Moreover, cell migration and invasion were significantly inhibited by sinomenine. Sinomenine accelerated the expression of Bax and caspase-3 but decreased the expression of Bcl-2. HEIH was upregulated in bladder cancer cells compared with normal bladder epithelial cells. Besides this, we noticed that HEIH knockdown blocked cell proliferation, migration, and invasion but facilitated cell apoptosis in bladder cancer cells. Additionally, HEIH reversed the suppression of the progression induced by sinomenine. **Conclusion.** Sinomenine was observed to suppress cell progression of bladder cancer cells by inhibiting HEIH expression. Our findings suggested that the use of sinomenine might be an effective treatment for bladder cancer.

## 1. Introduction

Bladder cancer, the most common malignant tumor of the urinary system, is a malignant tumor that occurs in the bladder mucosa. Globally, there are approximately 570,000 new cases of bladder cancer and 210,000 deaths every year [1]. At present, the cause of bladder cancer is associated with many factors, such as smoking, diet, occupational exposure, long-term exposure to high-risk chemicals, and activation of related oncogenes [2]. The treatment of bladder cancer is mainly surgery and adjuvant chemotherapy. However, all available treatments have adverse effects, and the prognosis is often not ideal [3, 4]. Therefore, it is essential to search for effective remedies to reduce the mortality of bladder cancer.

Chinese medicinal herbs are medicine used in traditional Chinese medicine (TCM). In recent years, the benefits of Chinese medicinal herbs in cancer treatment have attracted

the attention of scholars. It has been reported that TCM treatment can effectively reduce postoperative complications, control the metastasis and diffusion of cancer cells, promote postoperative recovery, and enhance immunity [5, 6]. Kaempferol was reported to repress the proliferation of bladder cancer cells by blocking the expression of cyclin D1, CDK4, p-Akt, Bid, Bcl-XL, and McL-1 and promoting the expressions of p53, p21, p38, p-ATM, Bax, Bid, and p-BRCA1 [7]. Almeida et al. observed that resveratrol reduced cell proliferation and caused DNA damage in bladder cancer cells [8].

Sinomenine is a monomer alkaloid component extracted from *Caulis Sinomenii*, which belongs to isoquinoline alkaloid. Sinomenine has anti-inflammatory, antirheumatism, antitumor, sedation, antihypertensive, antiarrhythmia, immunosuppression, and other pharmacological effects [9–11]. Numerous experiments have shown that sinomenine can

inhibit the development of breast cancer, stomach cancer, lung cancer, and ovarian cancer [12–14]. Bai et al. reported that sinomenine restrained cell migration and proliferation by suppressing the expression of  $\alpha 7$  nicotinic acetylcholine, TTF-1, SP-1, and p-ERK/ERK in lung cancer [15]. Moreover, sinomenine suppressed cell invasion and growth by inhibiting the PI3K/Akt/mTOR pathway in breast cancer side population cells [16]. At the same time, the role of sinomenine on the development of bladder cancer is unclear.

Consequently, our study focused on the mechanism of sinomenine in the development and progression of bladder cancer cells. The function of sinomenine was investigated in the proliferation, invasion, migration, and apoptosis of bladder cancer cells, and findings confirmed that sinomenine has a role in bladder cancer by regulating HEIH.

## 2. Materials and Methods

**2.1. Cell Culture and Treatment.** Human bladder cancer cells (T24, 5637, HT-1197, SW780, and TCCSUP) and human normal bladder epithelial cells (SV-HUC-1) were obtained from Bena Culture Collection (Beijing, China). The cell cryopreservation tube was thawed in a water bath at 37°C. 5 ml Roswell Park Memorial Institute 1640 (RPMI-1640) medium containing 10% foetal bovine serum (FBS) was added to the tube and centrifuged at 1000 rpm for 5 min at room temperature. After the supernatant was discarded, 5 ml RPMI-1640 medium was added to prepare cell suspension. The cells were cultured in an incubator with 5% CO<sub>2</sub> and 37°C. Cell passage was carried out when the cell fusion rate reached 80%.

Sinomenine was purchased from Chengdu Herbpurify Co., Ltd. (Chengdu, China). Sinomenine powder was added to normal saline to configure different concentrations of sinomenine solution (0, 0.25, 0.5, 0.75, and 1 mM). T24 and SW780 cells were treated with sinomenine at different concentrations for 24 h. Also, cells stimulated with dimethyl sulphoxide (DMSO) at the same concentration were used as a control group.

**2.2. MTT Assay.** MTT assay was used to investigate cell viability in T24 and SW780 cells. 100  $\mu$ L cell suspension was inoculated on 96-well plates with 2000 cells in each well. Cells were cultured in a cell incubator with 5% CO<sub>2</sub> and 37°C. After culturing for 1, 2, 3, 4, and 5 days, cells were added with 20  $\mu$ L MTT solution and then cultured for another 4 hours. After added with 150  $\mu$ L DMSO, the 96-well was shaken on the oscillator for 10 min. The absorbance value at 490 nm was detected with a microplate reader.

**2.3. Transwell Assay.** Transwell assay was carried out to measure cell migration and invasion in bladder cancer cells. 100 cell suspension ( $1 \times 10^5$  cells/ml) was inoculated in a transwell chamber. Different from the migration experiment, matrigel glue was added to the upper chamber for the invasion experiment. After culturing for 48 h, the culture medium was discarded in the well and washed with PBS 3 times. Then, after wiping the upper cells, the chamber was

fixed with formaldehyde for 30 mins. Then, cells were stained with 0.1% crystal violet for 30–60 min. Cells were observed and counted in 5 fields randomly by using a microscope.

**2.4. RT-qPCR Assay.** The mRNA expression of HEIH was detected by the RT-qPCR assay. Total RNA was extracted from bladder cancer cells by the TRIzol method. RNA concentration was measured by Nanodrop. Reverse transcription experiments were performed by using PrimeScript RT Reagent Kit with gDNA Eraser. Then, SYBR Premix Ex Taq II was used for the RT-PCR experiment. GAPDH was used as an internal control for HEIH. The primer sequences were as follows: HEIH forward: 5'-ATGCGAGAAGCCATGAGACC-3', HEIH reverse: 5'-GGAACAGCTTGTGTGACCGA-3'; GAPDH forward: 5'-CTCTGCTCCTCCTGTTTCGAC-3', GAPDH reverse: 5'-GACTCCGACCTTCACCTTCC-3'. The relative expressions of HEIH were calculated by the  $2^{-\Delta\Delta CT}$  method.

**2.5. Western Blotting Assay.** The western blotting assay was performed to detect the protein expression of apoptosis-related proteins (Bax, Bcl-2, and caspase-3). Total protein was extracted from the treated cells and quantified by the BCA method. 10  $\mu$ g total protein was separated by 10% SDS-PAGE protein gel electrophoresis. After membrane transfer, the strips were sealed for 1 h at room temperature. After washing 3 times with TBST, the strips were incubated with the corresponding primary antibody overnight. Then, the strips were placed in the horseradish peroxidase-labeled secondary antibody and incubated. After washing with TBST 3 times, the strips were placed in an ECL kit. Protein expression level = absorbance value of target protein/absorbance value of GAPDH.

**2.6. Statistical Analysis.** GraphPad software was used for the statistical analysis of all data. Data were expressed as mean  $\pm$  SD. ANOVA and Student's *t*-test were used to analyze the comparison.  $p < 0.05$  represented a significant difference.

## 3. Results

**3.1. HEIH Acted as an Oncogene in Bladder Cancer Cells.** In our study, the expression of HEIH was detected by the RT-qPCR assay. Elevation of HEIH was found in T24, 5637, HT-1197, TCCSUP, and SW780 cells compared with normal bladder epithelial cells (SV-HUC-1) (Figure 1(a)). To investigate the function of HEIH in bladder cancer progression, we knocked down the expression of HEIH in T24 and SW780 cells. As shown in Figure 1(b), HEIH expression was downregulated in T24 and SW780 cells' transfection with si-HEIH. Next, the role of HEIH on cell viability, metastasis, and apoptosis in cells was investigated by MTT, transwell, and western blotting assays. Our results showed that HEIH knockdown repressed cell proliferation (Figures 1(c) and 1(d)). In addition, HEIH downregulation facilitated the expression of Bax and caspase-3, but declined the expression



of Bcl-2 (Figure 1(e)). The results showed that HEIH knockdown promoted cell apoptosis rate. Next, the inhibiting effect of HEIH silencing was discovered in cell migration and invasion (Figures 2(a) and 2(b)). Taken together, HEIH was observed to be an oncogene in bladder cancer cells.

### 3.2. Sinomenine Suppresses Cell Growth in Bladder Cancer Cells.

First, the effects of different doses of sinomenine (0, 0.25, 0.5, 0.75, and 1 mM) on bladder cancer cells were investigated. MTT assay was carried out to detect the cell viability of bladder cancer cells. After treatment with sinomenine for 24 h, cell viability was discovered to be significantly suppressed in a dose-dependent manner (Figures 3(a) and 3(b)). Most importantly, cell viability began to decline considerably at 0.5 mM sinomenine. Hence, 0.5 mM was selected as the appropriate concentration for the subsequent experiments. Next, the expression of cell apoptosis proteins was measured by the western blotting assay. We found that sinomenine accelerated the expression of Bax and caspase-3, but decreased the expression of Bcl-2 (Figure 3(c)). These results imparted that sinomenine restrained cell viability and induced cell apoptosis in bladder cancer cells.

### 3.3. Sinomenine Inhibited Cell Migration and Invasion in Bladder Cancer Cells.

Transwell assay was used to assess the effect of sinomenine on the cellular motility of bladder cancer cells. We found that cell migration capacity was notably reduced in T24 and SW780 cells treated with sinomenine (Figure 4(a)). Likewise, similar results were discovered in the cell invasion experiment. Sinomenine suppressed cell invasion capacity in T24 and SW780 cells (Figure 4(b)). All the observations declared that sinomenine could block cell migration and invasion in bladder cancer.

### 3.4. Sinomenine Acted the Antigrowth Effect in Bladder Cancer Cells by Inhibiting HEIH Expression.

Next, the expression of HEIH in bladder cancer cells stimulated with sinomenine was investigated. We noticed that HEIH was lower in bladder cancer cells after manipulation with sinomenine (Figure 5(a)). To investigate how sinomenine regulated HEIH in the progression of bladder cancer, T24 and SW780 cells transfected with pc-HEIH were treated with sinomenine. The data showed that HEIH reversed the suppression of cell proliferation induced by sinomenine (Figure 5(b)). As we expected, the sinomenine-induced decline in cell migration was restored by HEIH overexpression (Figure 5(c)). Similarly, the suppression of cell invasion induced by sinomenine was restored by HEIH overexpression (Figure 5(d)). Besides this, HEIH reduced cell apoptosis induced by sinomenine (Figure 5(e)). Therefore, sinomenine was confirmed to suppress the progression of bladder cancer by inhibiting HEIH expression.

## 4. Discussion

In China, TCM is used in almost every aspect of cancer treatment. Rational application of TCM in tumor treatment can potentiate the curative effects, effectively control tumor recurrence and metastasis, and prolong the survival time [17, 18]. The function of TCM in the procession of bladder cancer has been widely studied in recent years. For example, orientin repressed bladder cancer cell growth and facilitated cell apoptosis by downregulating NF-kappaB and Hedgehog pathway [19]. Curcumin inhibited bladder cancer cell growth through multiple signaling pathways [20, 21]. In our experiment, we investigated the role of sinomenine on bladder cancer cells. Sinomenine was discovered to suppress cell viability, migration, and invasion and facilitate cell apoptosis in T24 and SW780 cells. Besides this, our findings indicated that sinomenine possesses antitumor effects by suppressing HEIH expression in bladder cancer.

Sinomenine is an alkaloid monomer extracted from *Sinomenium acutum*. It has unique pharmacological properties and can be used in the treatment of inflammatory and autoimmune diseases [22]. Sinomenine has been widely reported in the treatment of rheumatoid arthritis and neuralgia [9, 23]. In addition, the antitumor effects of sinomenine have been found in various cancers. Shen et al. reported that sinomenine restrained migration and invasion of lung cancer cells by repressing miR-211 and MMPs [24]. Moreover, sinomenine enhanced renal carcinoma cell apoptosis by promoting autophagy and suppressing the PI3K/AKT/mTOR pathway [25]. Consistent with our results, sinomenine was proved to block cell proliferation, migration, and invasion but induce cell apoptosis in prostate cancer [26]. Furthermore, Yuan et al. documented that sinomenine blocked cell growth and evoked cell apoptosis in gastric cancer cells, which is comparable to our findings [27]. Additionally, sinomenine inhibited glioma cell growth and promoted G0/G1 cell cycle arrest by promoting p53 and downregulating SIRT1 expression [28]. In consistency with previous studies, we confirmed that sinomenine could effectively repress the progression of bladder cancer.

LncRNA-HEIH has been reported to be carcinogenic in various cancers. In this experiment, we found that HEIH was upregulated in bladder cancer cell lines (T24, 5637, HT-1197, TCCSUP, and SW780). Additionally, HEIH knockdown was confirmed to block cell growth and motility, but evoke cell apoptosis in bladder cancer cells. Consistent with our results, Gao's study has shown that HEIH was overexpressed in retinoblastoma, and HEIH knockdown remarkably suppressed the viability, migration, and invasion of retinoblastoma cells [29]. Moreover, in ovarian cancer, HEIH facilitated cell progression and blocked cell senescence by regulating miR-3619-5p and CTTNBP2 [30]. Furthermore, HEIH silencing was observed to downregulate Bcl-2, cyclin D1, vimentin, MMP-2, and MMP-8 and upregulate Bax, cleaved caspase-3, and p53 [31]. Similar to previous results, we found that HEIH knockdown reduced the expression of Bcl-2 but accelerated the expression of Bax



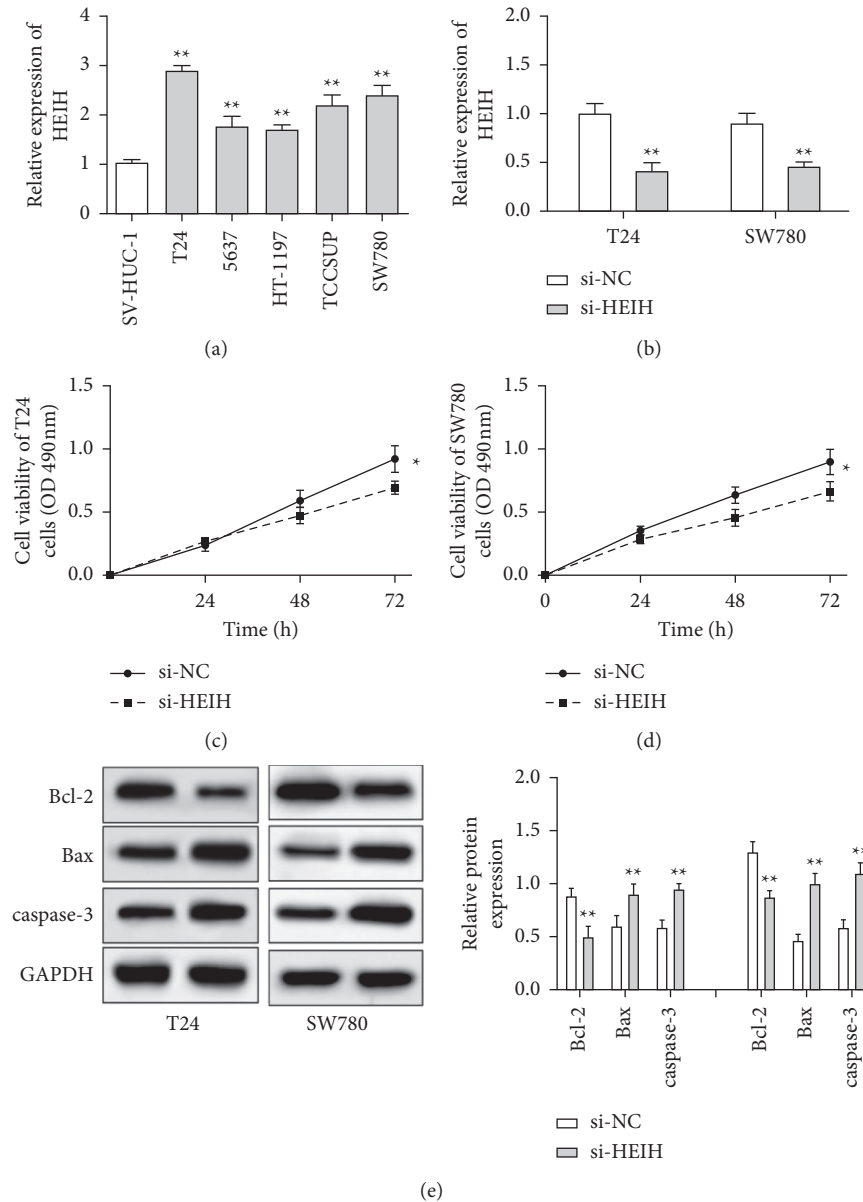


FIGURE 1: HEIH knockdown inhibited cell viability and accelerated cell apoptosis in bladder cancer cells. (a) HEIH was upregulated in T24, 5637, HT-1197, TCCSUP, and SW780 cells compared with normal bladder epithelial cells (SV-HUC-1). (b) The expression of HEIH was notably reduced in T24 and SW780 cells transfected with HEIH si-RNA. (c, d) HEIH knockdown suppressed cell viability in T24 and SW780 cells. (e) HEIH knockdown accelerated the expression of Bax and caspase-3 but reduced the expression of Bcl-2. \* $p < 0.05$ ; \*\* $p < 0.01$ .

and cleaved caspase-3. Moreover, we investigated the relationship between sinomenine and HEIH in bladder cancer progression. Our results indicated that HEIH reversed the suppression of cell progression induced by

sinomenine. However, the effect of sinomenine on bladder cancer was only in vitro, so more in vivo experiments should be carried out in the future to clarify its antitumor mechanism.

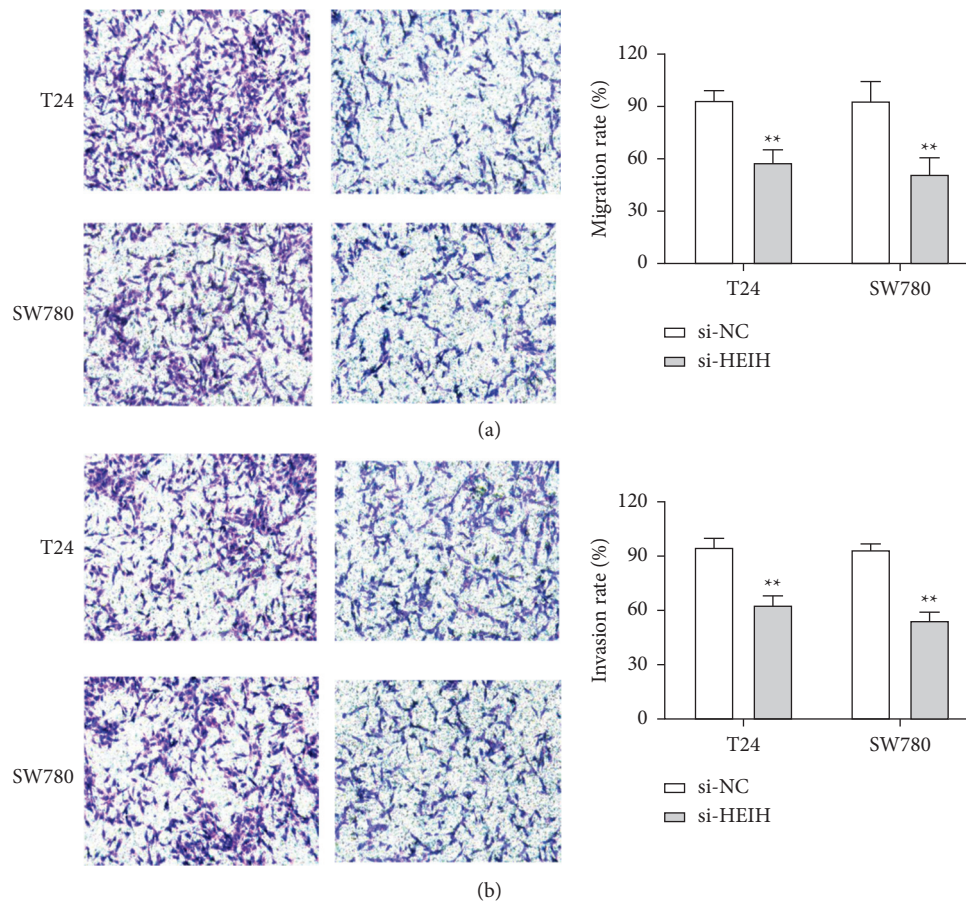


FIGURE 2: HEIH knockdown suppressed cell migration and invasion in bladder cancer cells. (a) HEIH knockdown significantly suppressed cell migration ability in T24 and SW780 cells. (b) HEIH knockdown significantly suppressed cell invasion ability in T24 and SW780 cells. \*\* $p < 0.01$ .

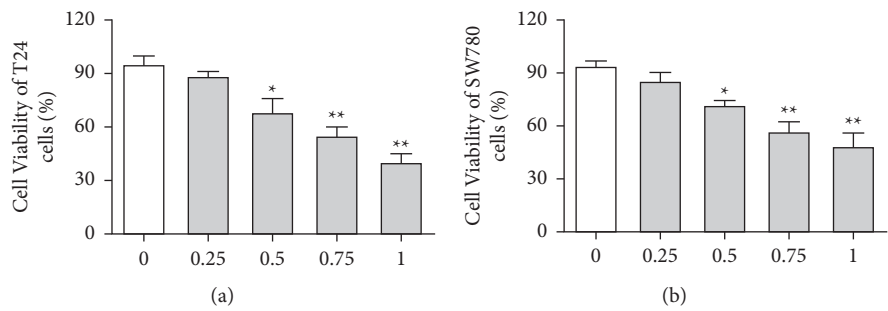


FIGURE 3: Continued.

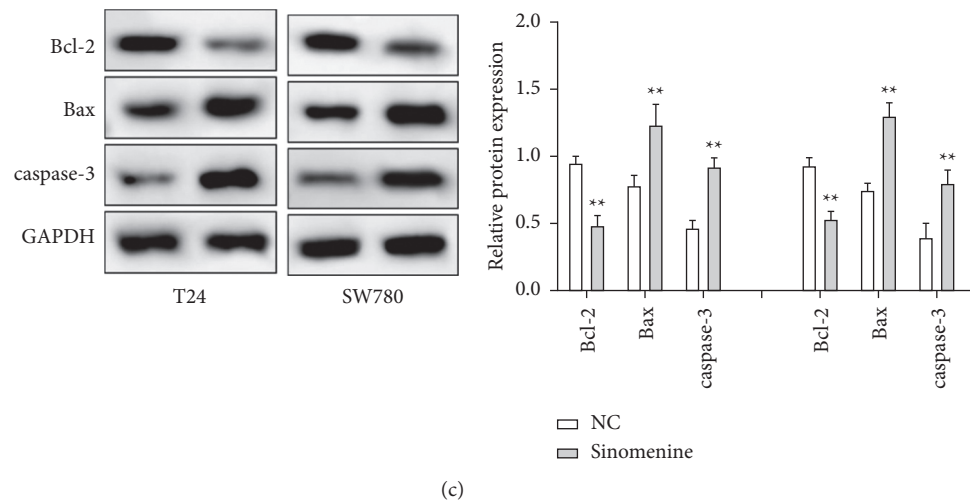


FIGURE 3: Sinomenine suppressed cell viability and induced cell apoptosis in bladder cancer cells. (a, b) Sinomenine (0, 0.25, 0.5, 0.75, and 1 mM) suppressed T24 and SW780 cell viability in a dose-dependent manner. (c) Sinomenine reduced the expression of Bcl-2 and increased the expression of Bax and caspase-3. \* $p < 0.05$ ; \*\* $p < 0.01$ .

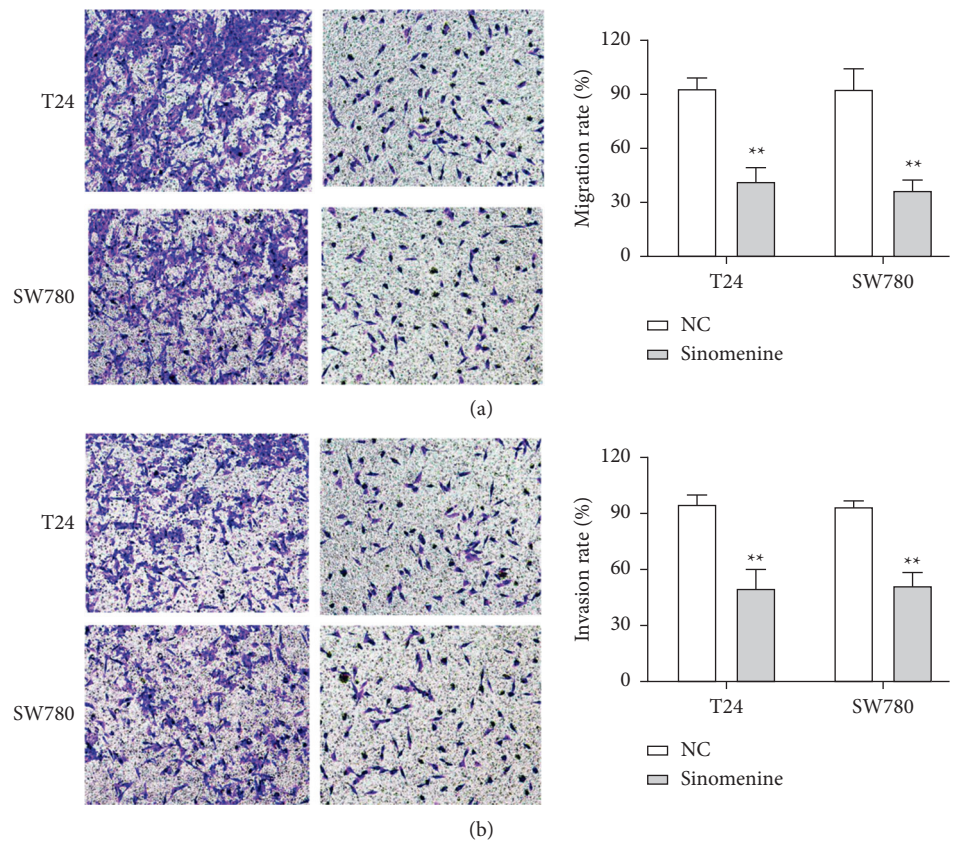


FIGURE 4: Sinomenine suppressed cell migration and invasion in bladder cancer cells. (a) Sinomenine significantly suppressed cell migration ability in T24 and SW780 cells. (b) Sinomenine notably inhibited cell invasion ability in T24 and SW780 cells. \*\* $p < 0.01$ .

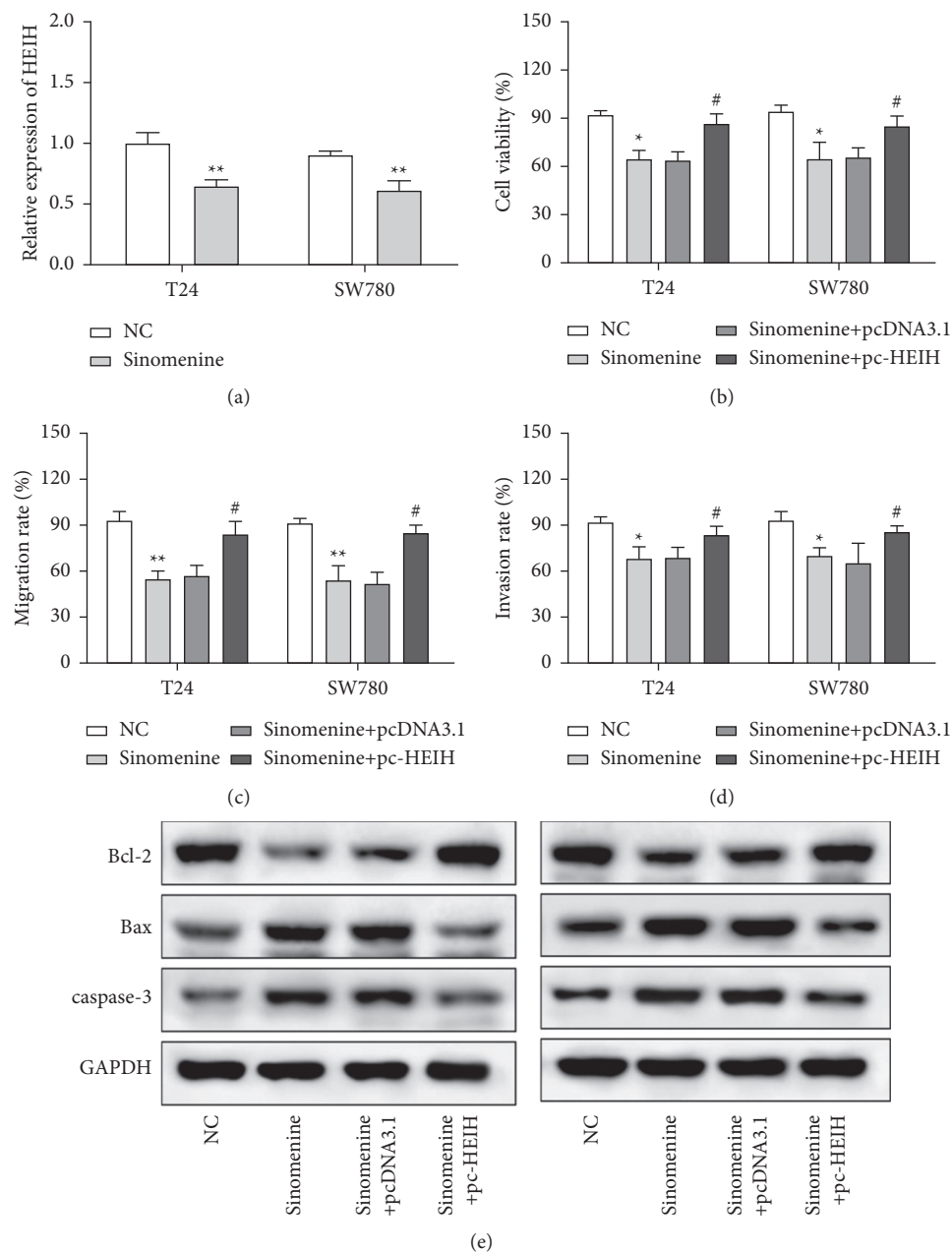


FIGURE 5: Sinomenine acted the antgrowth effect in bladder cancer cells by inhibiting HEIH expression. (a) Sinomenine suppressed the expression of HEIH. (b–e)  $*p < 0.05$  and  $**p < 0.01$  compared with the control group;  $#p < 0.05$  compared with the sinomenine + pcDNA3.1 group.

# 5. Conclusion

In conclusion, we reported that sinomenine blocked cell viability, migration, and invasion and induced cell apoptosis in bladder cancer cells by suppressing HEIH expression. Therefore, we confirmed the antitumor effect of sinomenine, providing a new idea and potential approach for treating bladder cancer.

# Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

# Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Correlation Analysis of Huayu Tongmai Decoction Intervention and Prognosis Indexes of Patients with Carotid Atherosclerosis

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**Background.** Carotid atherosclerosis (CAS) is a common disease which seriously threatens the health of senile patients. The studies have indicated that traditional Chinese medicine (TCM) may effectively improve the symptom of CAS, while the therapeutic effect of Huayu Tongmai decoction on CAS remains unclear. Thus, this study aimed to explore the correlation between traditional Chinese medicine Huayu Tongmai decoction intervention and prognosis indexes of patients with CAS. **Methods.** Ninety CAS patients admitted to Zibo TCM-Integrated Hospital from September 2018 to September 2020 were selected as the research object and randomly divided into the control group and the observation group according to the male-female ratio of 1 : 1. Patients in the control group accepted the atorvastatin intervention, and on this basis, patients in the observation group were further intervened with TCM Huayu Tongmai decoction. Before and after treatment, patients' levels of total cholesterol (TC), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) were measured by the enzyme photometric colorimetry; hypersensitive c-reactive protein (hs-CRP) levels were measured by the ELISA method; nitric oxide (NO) levels were measured by the nitrate reductase assay and endothelin-1 (ET-1) levels were measured by radioimmunoassay; and the right and left carotid internal diameter (CAD), intima-media thickness (IMT), and plaque volume were measured by carotid ultrasonography. **Results.** The TC, TG, and LDL-C levels significantly decreased in patients compared to those before intervention; compared with the control group, patients who accepted Huayu Tongmai decoction combined with atorvastatin saw more significant improvement in their blood lipid indexes ( $P < 0.01$ ); after intervention, patients' hs-CRP and ET-1 levels dropped significantly while the NO level rose remarkably, and between the two groups, the improvement in levels of hs-CRP, ET-1, and NO of patients in the observation group was significantly better ( $P < 0.01$ ); it was concluded from the imaging diagnosis results that compared with using atorvastatin alone, the combined intervention could better improve patients' CAD, IMT, and plaque volume. **Conclusion.** Huayu Tongmai decoction can effectively improve patients' blood lipid, reduce inflammatory response, enhance levels of relevant regulatory factors of CAS, and alleviate the symptoms.

## 1. Introduction

Atherosclerosis (AS) has a high incidence rate in the middle-aged and elderly people and is a direct cause of organ insufficiency as well as a major factor triggering coronary heart disease (CHD), cerebral ischemia, and peripheral vascular diseases in patients [1, 2]. Currently, the main therapeutic strategies for AS in clinic include surgical intervention and drug intervention. Surgical intervention is the major surgical

means to ameliorate the symptoms of AS in patients, with the characteristics such as instant effect and good treatment outcome [3]. But AS patients are mostly elderly, so the risk of surgical intervention is usually higher and the surgical conditions have some limitations on their physical fitness. In response to this, statins such as atorvastatin or simvastatin are often used clinically to delay the progression of AS in patients. In addition, statins can inhibit the progression of carotid atherosclerosis (CAS) by reducing blood lipid levels,

reducing body TG synthesis, and improving cholesterol levels in patients [4]. However, despite atorvastatin's ability to effectively reduce patients' blood lipids, some studies have confirmed that the drug may trigger adverse effects such as headache, edema, and diarrhea [5].

In recent years, the value of traditional Chinese medicine (TCM) in the treatment of CAS has received extensive attention. Studies have confirmed that active ingredients from some herbs in TCM have good therapeutic effects on AS [6]. TCM has proved that the Huayu Tongmai decoction, which contains tangshen, danshen root, golden thread, Sichuan lovage rhizome, hawthorn fruit, tall gastrodia tuber, coix seed, turmeric root tuber, and other herbs, has the effect of ameliorating inflammation and activating blood circulation to eliminate stasis, among which danshen root, golden thread, and Sichuan lovage rhizome have documented efficacy of improving blood lipid levels in patients. This study focused on the therapeutic effect of Huayu Tongmai decoction on CAS and aimed to provide a certain reference for the study of TCM on ameliorating CAS.

## 2. Study Methods

**2.1. General Information.** The study was approved by the ethics committee of *Zibo TCM-Integrated Hospital*, and all experiments were conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ninety CAS patients treated in *Zibo TCM-Integrated Hospital* from September 2018 to September 2020 were selected as the research object and randomly divided into the control group and the observation group according to the male-female ratio of 1:1 (Figure 1). As shown in Table 1, patients' age, gender, body mass index (BMI), drinking history, smoking history, and place of residence were not significantly different between the two groups. This study was a randomized controlled trial.

### 2.2. Inclusion and Exclusion Criteria

- (1) **Inclusion Criteria.** Patients' general clinical information were complete; patients were diagnosed with AS after imaging examination; patients met the diagnosis standards for CAS; patients did not use any drugs that affect their blood lipid or coagulation function in the recent 3 months before the study; and patients or their accompanying family members signed the informed consent.
- (2) **Exclusion Criteria.** Patients had liver and kidney failure; patients suffered from hematological diseases that would seriously affect the experiment results; patients had serious mental diseases; and patients could not accept clinical follow-up.

### 2.3. Methods

- (1) Patients in the control group accepted the conventional western medicine treatment, i.e., orally taking 100 mg of aspirin enteric-coated tablets (Beijing Shuguang Pharmaceutical Co., Ltd., Beijing, China) and 10 mg of atorvastatin (Beijing Jialin

Pharmaceutical Co., Ltd., Beijing, China) every day for 3 months.

- (2) On the basis of drug administration of the control group, patients in the observation group took the concentrate granules of Huayu Tongmai formula. The drug was mixed with 200 mL of boiling water and split into two doses, with one in the morning and one in the evening. The Huayu Tongmai formula (provided by Sanjiu Medical & Pharmaceutical Co. Ltd.) contained tangshen, danshen root, and coix seed (20 g each), Sichuan lovage rhizome, hawthorn fruit, tall gastrodia tuber, and turmeric root tuber (10 g each), and 6 g of golden thread. The patients received the intervention of Huayu Tongmai decoction for 3 months.

### 2.4. Observation Indexes

- (1) **Blood Lipid Measurement.** Before and after intervention, 3 mL of fasting venous blood was drawn from patients in the morning, put into the stimulative coagulation tube that contained separation gel, and placed under room temperature for 1 hour. Then, the venous blood was centrifuged under 3,000 r/min for 10 min to extract the supernatant, which was then placed in the freezer of  $-20^{\circ}\text{C}$  for reservation. The levels of triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) were measured by automatic biochemical analysis.
- (2) **Carotid Ultrasonography Diagnosis.** Under the probe frequency of 10.5 MHz, patients' right and left common carotid arteries were detected for the carotid internal diameter (CAD), intima-media thickness (IMT), and plaque volume with the U.S. ATL-5000 color doppler ultrasound machine.
- (3) **Hypersensitive C-Reactive Protein (hs-CRP) Level Detection.** 3 mL of fasting venous blood was drawn from patients in the morning, put into the stimulative coagulation tube that contained separation gel, and placed under room temperature for 1 hour. The venous blood was centrifuged under 3,000 r/min to extract the supernatant, which was then placed in the freezer of  $-20^{\circ}\text{C}$  for reservation. The levels of hs-CRP in the serum were measured with the ELISA kit (Shanghai Meilian Biological Co., Ltd., Shanghai, China).
- (4) **Vascular Endothelial Function Detection.** Before and after treatment, 3 mL of venous blood was drawn from the patients, put into the vacuum sampling tube and placed under room temperature for 30 minutes, and then it was centrifuged under 3,500 r/min for 10 minutes to extract the supernatant, which was then placed under  $-20^{\circ}\text{C}$  for reservation. The level of nitric oxide (NO) was measured by the nitrate reductase assay and the level of endothelin-1 (ET-1) was measured by the radioimmunoassay.

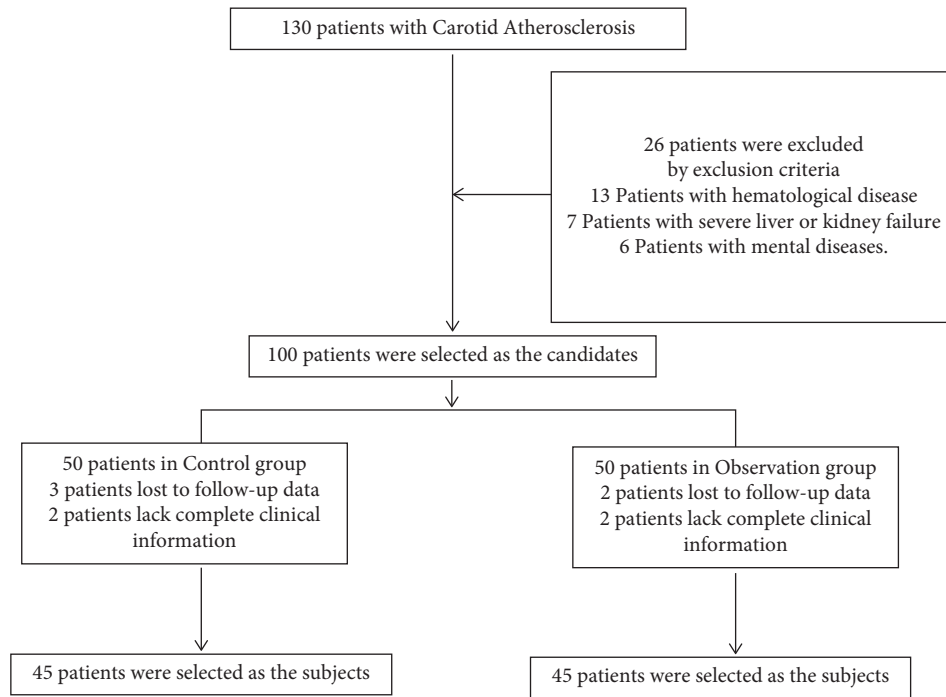


FIGURE 1: The patient flow of the study.

TABLE 1: Patients' general information.

Item	Control group	Observation group	<i>P</i>	<i>t</i>
Mean age	67.16 ± 7.73	67.07 ± 7.61		0.056
Male-female ratio			<i>P</i> > 0.05	
Male	23	21		
Female	22	24	<i>P</i> > 0.05	0.098
BMI (kg/m <sup>2</sup> )	23.23 ± 5.23	23.36 ± 5.09	<i>P</i> > 0.05	0.119
Smoking history				
Yes	15	16		
No	40	39	<i>P</i> > 0.05	0.445
Drinking history				
Yes	16	18		
No	39	37	<i>P</i> > 0.05	0.17
Place of residence				
Urban area	29	27		
Rural area	16	18	<i>P</i> > 0.05	0.189

**2.5. Statistical Processing.** The results of the experiment were analyzed by SPSS19.0, the between-group or within-group differences were examined with *t* test or analyzed by ANOVA and Tukey test and recorded as mean value ± standard deviation, and differences were considered statistically significant at *P* < 0.05.

### 3. Results

**3.1. Changes in Levels of TC, TG, and LDL-C in Patients of the Two Groups before and after Intervention.** The levels of TC, TG, and LDC-C in patients of the two groups before and

after drug intervention are shown in Table 2. The results indicated that after intervention, the levels of TC, TG, and LDC-C in patients of the two groups significantly decreased (*P* < 0.05), and these levels were significantly lower in the observation group than in the control group (*P* < 0.05).

**3.2. Changes in hs-CRP Levels of Patients in the Two Groups before and after Intervention.** The hs-CRP levels in patients of the two groups before and after drug intervention are shown in Figure 2. The results indicated that after intervention, the serum hs-CRP levels of both groups significantly decreased (*P* < 0.05), and compared with the control group, the observation group achieved significantly lower serum hs-CRP levels (*P* < 0.05) and more obvious improvement (*P* < 0.05).

**3.3. Changes in NO Levels of Patients in the Two Groups before and after Intervention.** The serum NO levels in patients of the two groups before and after drug intervention are shown in Figure 3. The results indicated that after intervention, the NO levels of both groups significantly increased (*P* < 0.05), and compared with the control group, the observation group achieved significantly higher serum NO levels (*P* < 0.05) and more obvious improvement (*P* < 0.05).

**3.4. Changes in ET-1 Levels of Patients in the Two Groups before and after Intervention.** The serum ET-1 levels in patients of the two groups before and after drug intervention are shown in Figure 4. The results indicated that after intervention, the ET-1 levels of both groups dropped significantly (*P* < 0.05), and compared with the control group, the

TABLE 2: Changes in levels of TC, TG, and LDL-C in patients of the two groups before and after intervention.

Group	Time	TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)
Control group ( $n = 45$ )	Before	$1.86 \pm 0.39$	$5.67 \pm 0.79$	$3.53 \pm 0.63$
	After	$1.53 \pm 0.21^a$	$4.13 \pm 0.63^a$	$2.69 \pm 0.32^a$
Observation group ( $n = 45$ )	Before	$1.85 \pm 0.32$	$5.69 \pm 0.71$	$3.51 \pm 0.53$
	After	$1.25 \pm 0.17^{ab}$	$3.81 \pm 0.57^{ab}$	$2.49 \pm 0.39^{ab}$

Note. a indicated significant within-group differences in patients' indexes before and after intervention ( $P < 0.05$ ), and b indicated significant between-group differences in patients' indexes before and after intervention ( $P < 0.05$ ).

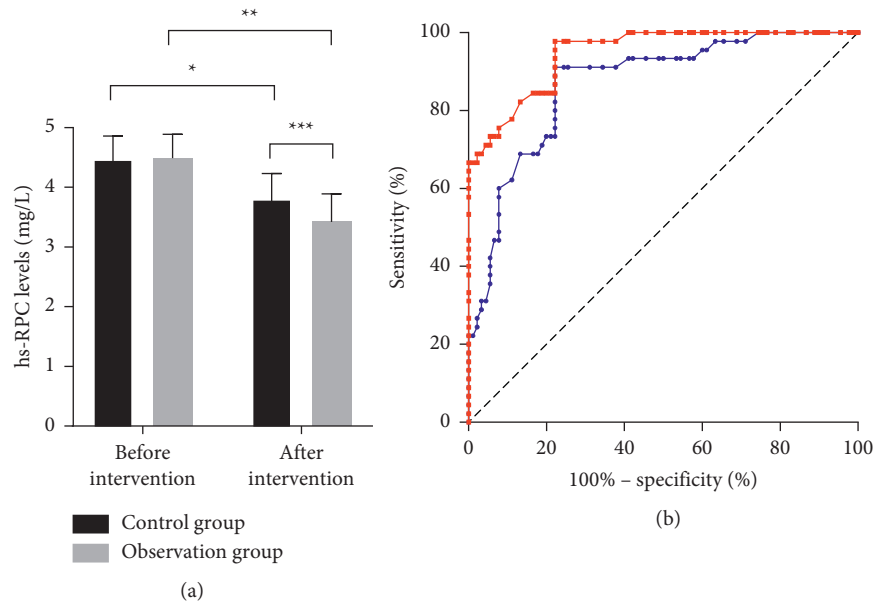


FIGURE 2: Changes in patients' hs-CRP levels before and after intervention. (a) Patients' hs-CRP levels before and after intervention. (b) ROC curves of changes in patients' hs-CRP levels after treatment (blue: control group; red: observation group). \* and \*\*, respectively, indicated the comparison within the control group and that within the observation group before and after intervention, and \*\*\* indicated the comparison between the control group and the observation group after intervention.

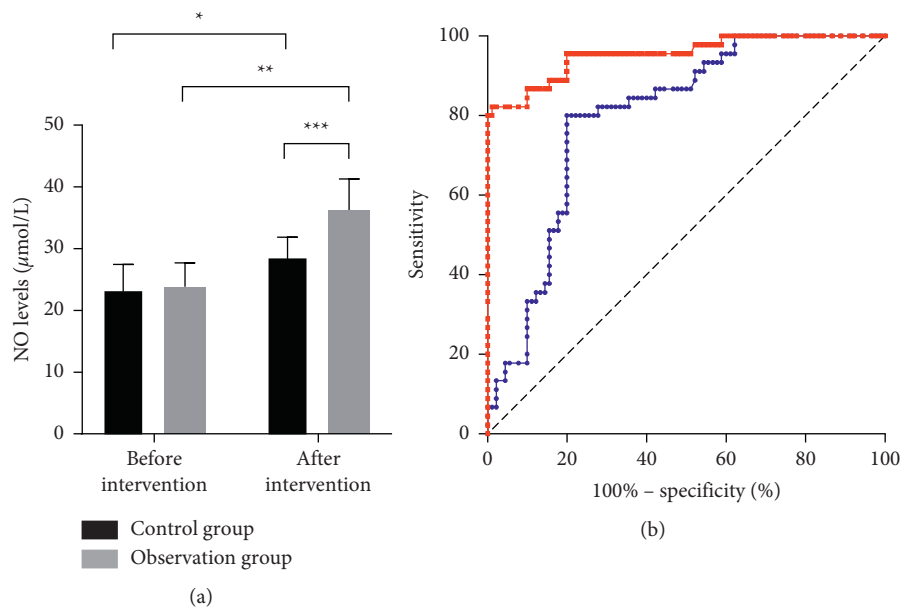


FIGURE 3: Changes in patients' NO levels before and after intervention. (a) Patients' NO levels before and after intervention. (b) ROC curves of changes in patients' NO levels after treatment (blue: control group; red: observation group). \* and \*\*, respectively, indicated the comparison within the control group and that within the observation group before and after intervention, and \*\*\* indicated the comparison between the control group and the observation group after intervention.

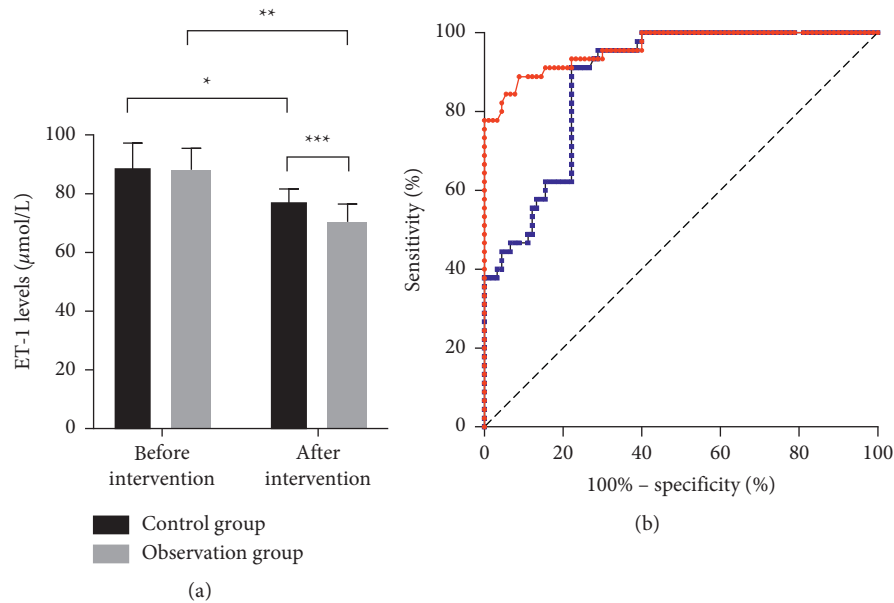


FIGURE 4: Changes in patients' ET-1 levels before and after intervention. (a) Patients' ET-1 levels before and after intervention. (b) ROC curves of changes in patients' ET-1 levels after treatment (blue: control group; red: observation group). \* and \*\*, respectively, indicated the comparison within the control group and that within the observation group before and after intervention, and \*\*\* indicated the comparison between the control group and the observation group after intervention.

observation group achieved significantly lower serum ET-1 levels ( $P < 0.05$ ) and more obvious improvement ( $P < 0.05$ ).

**3.5. Ultrasonic Diagnostic Examination.** The values of CAD, IMT, and plaque volume of the patients in the two groups before and after drug intervention are shown in Table 3. The results indicated that after intervention, the values of CAD, IMT, and plaque volume of both groups were improved significantly ( $P < 0.05$ ), and compared with the control group, the observation group achieved significantly lower values of CAD, IMT, and plaque volume ( $P < 0.05$ ) and more obvious improvement ( $P < 0.05$ ) (see Table 3).

#### 4. Discussion

CAS plaque is one of the leading causes of ischemic stroke in patients. Currently, the therapies for CAS mainly include endovascular treatment and drug intervention, of which the endovascular treatment is able to improve arterial blood flow in patients through arterial thrombolysis, endovascular thrombus removal, and implantation of stents [7, 8]. However, there are certain risks of intravascularly implanting stents because it may cause damage to patients' blood vessel wall and also trigger new branch artery occlusion and then worsen the condition. Therefore, drug intervention is often used clinically to control the condition of AS patients [9]. Statins such as atorvastatin serve as an important class of drugs to prevent AS and intervene in the course of CAS in clinic [10]. Recent studies have confirmed that some TCM strategies work well in the treatment of CAS [11]. Based on this, the study explored the effect of combining Huayu Tongmai decoction with atorvastatin in the

improvement of symptoms in CAS patients and confirmed that after intervention, the levels of TC, TG, and LDL-C in patients who accepted the combined therapy were significantly lower than those who received atorvastatin alone, indicating that Huayu Tongmai decoction could effectively improve the patients' blood lipid levels and then delay the progression of CAS. Huayu Tongmai decoction contained tangshen, danshen root, golden thread, Sichuan lovage rhizome, hawthorn fruit, tall gastrodia tuber, coix seed, and turmeric root tuber, of which danshen root and golden thread had the effect of improving the levels of TC, TG, and LDL-C in human body [12–14] because danshen root could regulate the OTUD7B/KLF4/NMHC IIA signal axes to improve the abnormal proliferation of vascular smooth muscle cells and vascular remodeling [15], which had been proved by Yang et al., and golden thread also had been shown to alleviate CAS symptoms in rats [16]. In addition, according to some studies, Sichuan lovage rhizome could stimulate the NO synthase expression of vascular endothelial cells in rats and then improve the NO levels and had significant anti-inflammation effect as well [17].

There is a close relationship between the formation and development of AS and the levels of inflammatory factors in the body of patients because high levels of inflammatory factors can induce endothelial cell damage. CRP may serve as a risk marker for CAS, which may promote endothelial cell inflammation and injury by mediating the upregulation of adhesion molecules and chemotactic factors, and studies have confirmed that CRP levels significantly increase in the lesions of AS patients [18]. The study herein proved that applying Huayu Tongmai decoction on the basis of atorvastatin intervention could further improve the hs-CRP levels in patients. In the research by Luo et al., it was found



TABLE 3: Results of common carotid artery ultrasonography before and after intervention.

Group	Time	CAD (mm)	IMT (mm)	Plaque volume (mm <sup>3</sup> )
Control group ( <i>n</i> = 45)	Before	5.79 ± 0.53	1.28 ± 0.23	89.51 ± 8.93
	After	4.96 ± 0.39 <sup>a</sup>	0.98 ± 0.19 <sup>a</sup>	46.27 ± 3.23 <sup>a</sup>
Observation group ( <i>n</i> = 45)	Before	5.83 ± 0.60	1.30 ± 0.21	89.51 ± 9.13
	After	4.70 ± 0.37 <sup>ab</sup>	0.91 ± 0.17 <sup>ab</sup>	43.39 ± 3.09 <sup>ab</sup>

Note. a indicated significant within-group differences in patients' indexes before and after intervention ( $P < 0.05$ ), and b indicated significant between-group differences in patients' indexes before and after intervention ( $P < 0.05$ ).

that danshen root could effectively lower the hs-CRP levels in CHD patients and then improve their systemic inflammatory levels [19]. Xue et al. also proved that golden thread could significantly lower the hs-CRP levels in rats to remarkably ameliorate the symptoms of carotid thrombosis [16]. Endothelial cells have certain regulatory effect on the contraction and relaxation of blood vessels, and normal endothelial cells can effectively inhibit the formation of arterial plaques by suppressing the adhesion and stacking of platelets. Vascular endothelial cells dysfunction is one of the main reasons for initiating AS, and platelets are able to aggregate at damaged endothelial cells, which leads to thrombosis [20, 21]. Studies have confirmed that NO can effectively inhibit the aggregation of inflammatory factors and platelets and suppress free radical induced endothelial cell injury through antagonism. In the study herein, compared with single atorvastatin intervention, patients who accepted the combined intervention of Huayu Tongmai decoction and atorvastatin saw obvious increase in their serum NO levels. Zhang et al. confirmed in their study that using danshen root and hawthorn fruit together could significantly lower the levels of TC, TG, and LDL-C in patients, greatly reduce the levels of IL-1 $\beta$  and IL-18 to improve the systematic inflammation, and inhibit endothelin expression by increasing the serum NO level to improve the CAS symptoms in patients [22]. ET-1 can regulate vasoconstriction, but overexpressed ET-1 is able to promote the progression of AS. Studies have shown that the expression abundance of ET-1 can reach about twice the normal level at sites of coronary atherosclerosis [23]. Our study demonstrated that Huayu Tongmai decoction could further reduce the ET-1 levels in patients' serum on the basis of atorvastatin. Wu et al. confirmed that Sichuan lovage rhizome could effectively reduce the ET-1 level and improve the blood supply volume to the brain in a migraine rat model [17]. In addition, the results of imaging diagnosis herein showed that patients who received the combined intervention obtained more significant improvements in CAD, IMT, and plaque volume than those who received single atorvastatin intervention, indicating that the adoption of Huayu Tongmai decoction on the basis of atorvastatin could effectively improve the symptoms of CAS in patients. Further investigation is required on the conclusion of the study due to the limited number of the patients selected. In addition, the mechanism of Huayu Tongmai decoction in treating AS should also be further studied in depth.

In conclusion, the study proves that Huayu Tongmai decoction can significantly improve the symptoms of CAS in patients, which is worthy of application in clinic. Moreover,

this study only focused on the therapeutic effect of Huayu Tongmai decoction on CAS, and thus the pharmacological mechanism of Huayu Tongmai decoction in progression of improving correlation analysis is necessary.

### Data Availability

The data used to support the findings of this study are available on reasonable request from the corresponding author.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Cinpezide Maleate on Serum Inflammatory Factors of ICU Patients with Severe Cerebral Hemorrhage after Surgery

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**Objective.** To explore the effect of cinpezide maleate on serum inflammatory factors of intensive care unit (ICU) patients with severe cerebral hemorrhage after surgery. **Methods.** 116 ICU patients with severe cerebral hemorrhage treated in Taian Maternal and Child Health Hospital from June 2018 to June 2020 were selected as the research objects and randomly divided into the control group and experimental group, with 58 patients in each group. The control group was given routine treatment, while the experimental group was additionally given an intravenous drip of cinpezide maleate to compare the clinical efficacy and serum inflammatory factors between the two groups. **Results.** The total effective rate in the experimental group was higher than that in the control group ( $P < 0.05$ ). After treatment, the Glasgow Coma Scale (GCS), National Institutes of Health Stroke Scale (NIHSS), and Fugl-Meyer scores in both groups were better than those before treatment, and the scores in the experimental group were better than those in the control group ( $P < 0.05$ ). The oxidative stress indexes such as total antioxidant capacity (T-Aoc), superoxide dismutase (SOD), and glutathione peroxidase (GSH-PX) in the experimental group were higher than those in the control group, while malondialdehyde (MDA) in the experimental group was lower than that in the control group ( $P < 0.05$ ). The high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels in the experimental group were lower than those in the control group ( $P < 0.05$ ). Compared with the control group, the cerebrovascular function in the experimental group was significantly improved ( $P < 0.05$ ), with statistically significant differences. **Conclusion.** Cinpezide maleate can effectively reduce the serum inflammatory factor levels of ICU patients with severe cerebral hemorrhage after surgery, alleviate the oxidative stress response in the body, and improve the cerebrovascular function and cerebral nerve function, which is worthy of clinical promotion.

## 1. Introduction

Cerebral hemorrhage (also known as spontaneous intracerebral hemorrhage) refers to nontraumatic primary intraparenchymal hemorrhage, accounting for about 20%–30% of acute cerebrovascular diseases [1–4]. According to clinical statistics, about 80% of patients have cerebral hemorrhage in the cerebral hemisphere, with the remaining 20% in the cerebellum and brainstem. Cerebral hemorrhage is a type of acute cerebrovascular disease with the highest mortality rate, mostly in elderly patients over 50 years old or in patients

with a history of hypertension. In clinical treatment, most patients receive medical treatment. In the acute phase, bleeding control and reducing intracranial pressure are the main measures, and supportive medical care is necessary after cerebral hemorrhage is stopped [5–8]. Cinpezide maleate is a calcium channel blocker to inhibit  $\text{Ca}^{2+}$  influx, relax the vascular smooth muscle, and dilate coronary arteries. In clinical studies, animal experiments have confirmed that this substance has a certain inhibitory effect on the inflammatory response in the process of focal cerebral ischemia-reperfusion injury in rats, protecting the brain

[9–12]. In recent years, the medical research about cinpezide maleate mostly focuses on its effect on hypertensive cerebral hemorrhage (HICH) and lacks studies on severe cerebral hemorrhage. To further clarify the clinical effect of cinpezide maleate on patients with severe cerebral hemorrhage, this paper explored the effect of cinpezide maleate on serum inflammatory factor levels of ICU patients with severe cerebral hemorrhage after surgery, summarized as below.

## 2. Materials and Methods

**2.1. General Information.** 116 ICU patients with severe cerebral hemorrhage treated in Taian Maternal and Child Health Hospital from June 2018 to June 2020 were selected as the research objects and randomly divided into the control group and experimental group, with 58 patients in each group.

**2.2. Inclusion Criteria.** (1) The patient met the diagnostic criteria in the *Guidelines for the Management of Spontaneous Intracerebral Hemorrhage* [13] and was confirmed by head CT and MRI examinations. (2) It was the first time that the patients had the disease, and if not the first time, there should be no residual neurological impairment after the first onset. (3) The onset time was no more than 24 hours. (4) The patients had clear consciousness and were able to cooperate with examination and treatment. (5) This study was approved by the ethics committee of Taian Maternal and Child Health Hospital, and the patients and their families accepted the treatment plan and signed informed consent.

**2.3. Exclusion Criteria.** (1) The patients had severe heart, lung, kidney, and liver dysfunction and were complicated with autoimmune diseases, hematological diseases, connective tissue diseases, or malignant tumors. (2) The patients had severe hypertension that could not be effectively controlled. (3) The patients had taken drugs affecting inflammatory response in the past one month. (4) The patients were allergic to drugs used in the study. (5) The patients refused to cooperate with researchers.

**2.4. Methods.** The control group received routine treatment measures immediately after admission, specifically as follows. (1) Dehydration: the patients with cerebral edema received 250 ml of 20% mannitol injection (specification: 250 ml/bottle; manufacturer: Shandong Wego Pharmaceutical Co., Ltd.; SFDA approval no. H20053865) by intravenous drip, 1–2 times a day. The dosage and treatment courses could be adjusted according to the severity of cerebral edema [14]. (2) Anticoagulation: 5000 IU of low-molecular-weight heparin calcium (1.0 ml: 5000 Axa unit; manufacturer: Shenzhen Scriprogen Biopharmaceutical Co., Ltd.; SFDA approval no. H20060190) was injected subcutaneously into the abdominal wall around the umbilicus every 12 hours. 80 mg of ozagrel sodium (specification: 40 mg; manufacturer: Youcare Pharmaceutical Group Co.,

Ltd.; SFDA approval no. H20063851) and 250 ml of sodium chloride injection were injected into the patients by intravenous drip, twice a day. The patients also orally took 0.1 g of aspirin enteric-coated tablets (specification: 100 mg/tablet; manufacturer: Bayer Schering Pharmaceutical Health Co., Ltd.; SFDA approval no. J20130078) once a day and continuously for 12 months. (3) Brain protection: the patients received 30 mg of edaravone injection (specification: 30 mg/vial; manufacturer: Nanjing Simcere Dongyuan Pharmaceutical Co., Ltd.; SFDA approval no. H20031342) and 250 ml of 0.9% sodium chloride injection by intravenous drip, twice a day. (4) Hyperbaric oxygen: hyperbaric oxygen therapy (HBOT) at atmospheric pressure ( $2.026 \times 10^5$  Pa) was performed at 1 hour after thrombolysis, and each time lasted for 1 hour, once a day. (5) Symptomatic treatment: patients with hypertension and diabetes received antihypertensive and hypoglycemic treatment, respectively. In addition, it was necessary to prevent infection and maintain the water-electrolyte balance of patients.

The experimental group was additionally treated with cinpezide maleate. The patients received 240 mg of cinpezide maleate injection (specification: 320 mg/vial; manufacturer: Beijing Sihuan Pharmaceutical Co., Ltd.; SFDA approval no. H20061204) and 250 ml of 0.9% sodium chloride injection by intravenous drip, once a day. The routine treatment was the same with that in the control group. During the treatment, all patients were prohibited from using other cerebral vasodilators,  $\text{Ca}^{2+}$  antagonists, or nootropic agents. The treatment lasted for 14 days in both groups.

## 2.5. Observation Indexes

**2.5.1. Clinical Efficacy.** According to the *Clinical Neural Function Deficit Score Criteria for Stroke* [15], the neurological deficit score of patients decreased by more than 90% after treatment, with the disability grade as 0, which was cured. The neurological deficit score decreased by 46%–90%, with the disability grade as levels 1–3, which was markedly effective. The neurological deficit score decreased by 18%–45%, which was improved. The neurological deficit score decreased by less than 17%, which was ineffective. Total effective rate = (improved + markedly effective + cured)/total number  $\times$  100%.

**2.5.2. Evaluation of Neurological Function.** Glasgow Coma Scale (GCS) was used to evaluate the coma degree, including eye opening response (4 points), verbal response (5 points), and motor response of the nonhemiplegia side (6 points), with a total score of 15 points. A score of 8 or less was considered as coma, and a higher score represented a lower level of coma in patients. The National Institutes of Health Stroke Scale (NIHSS) was used to evaluate the neurological deficits, including 11 large dimensions (consciousness, gaze, visual field, facial paralysis, upper limb movement, lower limb movement, ataxia, sensation, language, dysarthria, and neglect), with a total score of 42 points. A higher score represented more serious neurological deficits. Fugl-Meyer

motor function measure scale was used to evaluate the comprehensive motor function of patients, with 17 items and a total score of 100 points. The score <50 was considered as severe dyskinesia, 50–84 as obvious dyskinesia, 85–95 as moderate dyskinesia, and 96–99 as mild dyskinesia.

**2.5.3. Oxidative Stress Indexes.** Fasting venous blood from the elbow was taken in the morning and centrifuged at 4000 r/min for 5 min. After the supernatant was placed in an Eppendorf tube, the total antioxidant capacity (T-Aoc) kits (specification: 50T/48S; brand: Solarbio) were used to detect the T-Aoc levels, superoxide dismutase (SOD) activity kits (specification: 50T/24S; brand: Solarbio) were used to detect the SOD level, glutathione peroxidase (GSH-PX) kits (specification: 50T/343T; manufacturer: Shanghai Caiyou Industrial Co., Ltd.) were used to detect the GSH-PX level, and malondialdehyde (MDA) kits (specification: 100T/96S; brand: Solarbio) were used to detect the MDA level of patients.

Venous blood was collected from patients, and serum was separated. Enzyme-linked immunosorbent assay (ELISA) was used to detect the total antioxidant capacity (T-Aoc), superoxide dismutase (SOD), glutathione peroxidase (GSH-PX), and malondialdehyde (MDA) levels of patients.

**2.5.4. Inflammatory Factor Levels.** Venous blood was collected from patients to separate serum. Chemiluminescent immunoassay was used to detect the level of high-sensitivity C-reactive protein (hsCRP), and ELISA was used to detect the levels of interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ).

**2.5.5. Cerebrovascular Function.** A hemodynamic analyzer (model: HM 81-01) was used to detect the vascular function of patients, including the mean cerebral blood flow volume ( $Q_{\text{mean}}$ ), mean cerebral blood flow velocity ( $V_{\text{mean}}$ ), peripheral vascular resistance ( $R$ ), and dynamic resistance.

**2.6. Statistical Treatment.** In this study, SPSS 20.0 was selected as data processing software, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw pictures of the data. Enumeration data and measurement data were included in the study, tested by  $\chi^2$ ,  $t$ -test, and normality test. The difference was statistically significant when  $P < 0.05$ .

### 3. Results

**3.1. Comparison of General Data.** There was no significant difference in gender, age, bleeding sites, and other basic information between the two groups ( $P > 0.05$ ), suitable for comparative study, as shown in Table 1.

**3.2. Comparison of Clinical Efficacy between the Two Groups.** The total effective rate in the experimental group was higher than that in the control group ( $P < 0.05$ ), with a statistically significant difference, as shown in Table 2.

**3.3. Comparison of Neurological Function between the Two Groups.** After treatment, the GCS, NIHSS, and Fugl-Meyer scores in both groups were better than those before treatment, and the scores in the experimental group were better than those in the control group, with statistical differences ( $P < 0.05$ ), as shown in Table 3.

**3.4. Comparison of Oxidative Stress Indexes between the Two Groups.** Compared with the control group, T-Aoc, SOD, and GSH-PX in the experimental group were obviously higher, while MDA was lower ( $P < 0.05$ ). All the oxidative stress indexes after treatment were better than those before treatment, with statistical significance ( $P < 0.05$ ), as shown in Table 4.

**3.5. Comparison of Inflammatory Factor Levels between the Two Groups.** After treatment, the hsCRP, IL-6, IL-8, and TNF- $\alpha$  levels in both groups were obviously lower than those before treatment, and the levels in the experimental group were lower than those in the control group ( $P < 0.05$ ), with statistical significance, as shown in Table 5.

**3.6. Comparison of Cerebrovascular Function between the Two Groups.** After treatment, the cerebrovascular function in both groups was obviously improved, and the function in the experimental group was obviously better than that in the control group ( $P < 0.05$ ), as shown in Table 6.

### 4. Discussion

Hypertensive cerebral hemorrhage (HICH) is a common high-risk disease in clinics, and most patients in clinics mainly receive medical treatment. If patients with surgical indications have more serious condition or their secondary cause is found, surgical treatment will be adopted to mainly reduce intracranial pressure, remove hematoma, and save the life of patients. In addition, patients need to control blood pressure to reach the standard and be stable for life [16]. The prognosis of the disease is often related to the amount of bleeding, bleeding sites, and complications. Patients are considered to have good prognosis if they experience a small amount of blood loss with no bad complications during treatment, and their bleeding sites do not affect the neurological function. Patients have poor prognosis if they suffer from complications such as pulmonary infection and gastrointestinal bleeding [17–20]. Clinical statistics suggest that severe intracerebral hemorrhage can account for about half of intracerebral hemorrhage cases. Failure to take timely and effective measures will directly affect the recovery of patients after intervention, leading to sequelae or even death. In recent years, the medical research about cinepazide maleate mostly focuses on its effect on HICH and lacks studies on severe cerebral hemorrhage. Therefore, this paper retrospectively analyzed the clinical data of 116 ICU patients with severe cerebral hemorrhage treated in our hospital, observed their serum inflammatory factor levels, and explored the clinical effect of



TABLE 1: Comparison of basic data between the two groups.

Items	Control group ( $n = 58$ )	Experimental group ( $n = 58$ )	$t/X^2$	$P$
Age (years old)	$63.5 \pm 7.32$	$62.8 \pm 7.09$	0.523	0.602
BMI ( $\text{kg}/\text{m}^2$ )	$25.57 \pm 5.18$	$25.51 \pm 5.06$	0.063	0.950
Amount of bleeding (ml)	$42.85 \pm 4.57$	$43.04 \pm 4.77$	0.219	0.827
Systolic pressure (mmHg)	$121.36 \pm 9.73$	$120.68 \pm 9.67$	0.378	0.707
Diastolic pressure (mmHg)	$95.32 \pm 6.24$	$94.81 \pm 6.33$	0.437	0.663
Gender	—	—		
Male	37 (63.79%)	39 (67.24%)	0.153	0.696
Female	21 (36.21%)	19 (32.76%)		
Bleeding sites				
Basal ganglia	43 (74.14%)	45 (77.59%)	0.188	0.664
Thalamus	11 (18.97%)	10 (17.24%)	0.058	0.809
Others	4 (6.90%)	3 (5.17%)	0.152	0.691
Concomitant diseases				
Hypertension	17 (29.31%)	20 (34.48%)	0.357	0.550
Diabetes mellitus	11 (18.97%)	10 (17.24%)	0.058	0.809

TABLE 2: Comparison of clinical efficacy between the two groups ( $n$  (%)).

Group	Ineffective	Improved	Markedly effective	Cured	Total effective rate
Control group ( $n = 58$ )	15 (25.86)	16 (27.59)	14 (24.14)	13 (22.41)	43 (74.14)
Experimental group ( $n = 58$ )	6 (10.34)	11 (18.97)	20 (34.48)	21 (36.21)	52 (89.66)
$X^2$	—	—	—	—	4.710
$P$	—	—	—	—	0.030

TABLE 3: Comparison of neurological function between the two groups ( $n = 58$ ,  $\bar{x} \pm s$ ).

Group	GCS score		NIHSS score		Fugl-Meyer score	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	$6.25 \pm 0.58$	$10.98 \pm 1.33$	$16.97 \pm 1.74$	$10.41 \pm 1.09$	$43.88 \pm 4.25$	$60.64 \pm 6.71$
Experimental group	$6.18 \pm 0.61$	$14.71 \pm 1.37$	$17.32 \pm 1.78$	$7.46 \pm 0.73$	$44.15 \pm 4.31$	$71.57 \pm 7.47$
$t$	0.633	14.877	0.071	17.126	0.340	8.290
$P$	0.528	<0.05	0.287	<0.05	0.735	<0.05

TABLE 4: Comparison of oxidative stress indexes between the two groups ( $\bar{x} \pm s$ ).

Indexes		Control group ( $n = 58$ )	Experimental group ( $n = 58$ )	$t$	$P$
T-Aoc (U/L)	Before treatment	$0.94 \pm 0.08$	$0.96 \pm 0.08$	1.346	0.181
	After treatment	$1.78 \pm 0.22$	$3.15 \pm 0.36$	24.730	<0.05
SOD (U/L)	Before treatment	$14.05 \pm 1.19$	$13.68 \pm 1.17$	1.689	0.094
	After treatment	$55.71 \pm 5.72$	$86.19 \pm 8.85$	22.029	<0.05
GSH-PX (U/L)	Before treatment	$89.65 \pm 9.43$	$90.12 \pm 9.52$	0.267	0.790
	After treatment	$150.41 \pm 15.07$	$197.36 \pm 19.86$	14.342	<0.05
MDA (nmol/L)	Before treatment	$3.74 \pm 0.38$	$3.69 \pm 0.35$	0.737	0.463
	After treatment	$2.14 \pm 0.25$	$1.61 \pm 0.18$	13.103	<0.05

cinapazide maleate on the patients, neurological function, inflammatory response, and oxidative stress injury, aiming to provide a reference for the optimization of clinical therapeutic schedules for ICU patients with severe cerebral hemorrhage.

Cinapazide maleate injection is a  $\text{Ca}^{2+}$  antagonist that can prevent  $\text{Ca}^{2+}$  from penetrating into vascular smooth muscle cells across the membrane and relax the vascular smooth muscle, thereby expanding cerebral, peripheral, and coronary

vessels to relieve vasospasm, reduce vascular resistance, and increase blood flow. In addition, cinapazide maleate can enhance the role of cyclic adenosine monophosphate and adenosine, reduce oxygen consumption, and increase the content of cyclic adenosine monophosphate by inhibiting cAMP phosphodiesterase. In addition, it can improve the deformability and flexibility of red blood cells to enhance their ability to pass through small blood vessels, thereby reducing blood viscosity and improving microcirculation [21–24]. This

TABLE 5: Comparison of inflammatory factor levels between the two groups ( $\bar{x} \pm s$ ).

Indexes		Control group ( $n = 58$ )	Experimental group ( $n = 58$ )	$t$	$P$
hsCRP (mg/L)	Before treatment	$3.14 \pm 0.53$	$3.26 \pm 0.58$	1.163	0.247
	After treatment	$1.59 \pm 0.20$	$1.04 \pm 0.15$	16.755	<0.05
IL-6 (ng/L)	Before treatment	$124.09 \pm 12.38$	$123.85 \pm 12.51$	0.104	0.918
	After treatment	$89.42 \pm 8.71$	$45.31 \pm 8.03$	29.315	<0.05
IL-8 (ng/L)	Before treatment	$5.61 \pm 0.55$	$5.68 \pm 0.57$	0.673	0.502
	After treatment	$1.98 \pm 0.35$	$1.35 \pm 0.23$	11.456	<0.05
TNF- $\alpha$ ( $\mu$ g/L)	Before treatment	$2.18 \pm 0.43$	$2.17 \pm 0.40$	0.130	0.897
	After treatment	$1.29 \pm 0.31$	$0.92 \pm 0.22$	7.413	<0.05

TABLE 6: Comparison of cerebrovascular function between the two groups ( $\bar{x} \pm s$ ).

Indexes		Control group ( $n = 58$ )	Experimental group ( $n = 58$ )	$t$	$P$
$Q_{\text{mean}}$ (ml/s)	Before treatment	$8.4 \pm 0.6$	$8.5 \pm 0.7$	0.826	0.411
	After treatment	$10.3 \pm 7.1$	$14.7 \pm 7.8$	3.177	0.0019
$V_{\text{mean}}$ (cm/s)	Before treatment	$12.2 \pm 1.2$	$12.3 \pm 1.3$	0.430	0.668
	After treatment	$15.7 \pm 1.5$	$18.2 \pm 1.9$	7.865	<0.05
$R$ (kPa·s/m)	Before treatment	$1963.1 \pm 164.2$	$1968.4 \pm 165.1$	0.173	0.823
	After treatment	$991.8 \pm 90.2$	$874.1 \pm 88.3$	7.101	<0.05
Dynamic resistance (kPa·s/m)	Before treatment	$472.3 \pm 47.1$	$469.7 \pm 45.6$	0.302	0.763
	After treatment	$385.9 \pm 40.1$	$311.5 \pm 32.2$	11.018	<0.05

study showed that the total effective rate in the experimental group was higher than that in the control group, indicating that cinpezide maleate can improve the postoperative therapeutic effect of patients with cerebral hemorrhage compared with routine treatment. After treatment, the GCS, NIHSS, and Fugl-Meyer scores in both groups were better than those before treatment, and the scores in the experimental group were better than those in the control group ( $P < 0.05$ ). GCS was mainly used to evaluate the coma degree of patients with cerebral hemorrhage, NIHSS was to evaluate the neurological deficits, and Fugl-Meyer reflected the comprehensive motor function. It can be seen that cinpezide maleate can effectively enhance the postoperative neurological function of patients, improve brain metabolism, and promote the recovery of brain function. The oxidative stress indexes such as T-Aoc, SOD, and GSH-PX in the experimental group were higher than those in the control group, while MDA in the experimental group was lower than that in the control group. The hsCRP, IL-6, IL-8, and TNF- $\alpha$  levels in the experimental group were lower than those in the control group. Compared with the control group, the cerebrovascular function in the experimental group was significantly improved. Oxidative stress response and inflammatory response are closely related to the pathological changes of nerve injury and edema in patients with cerebral hemorrhage. After cerebral hemorrhage, hematoma occurs rapidly in the lesion area, resulting in the death of a large number of brain nerve cells around the lesions. At the same time, the blood supply area of the bleeding vessel forms reperfusion injury which produces lots of inflammatory factors and then leads to systemic inflammatory response. The further development of inflammation will bring about microglia activation, infiltration of inflammatory cells around the lesions, and release of proinflammatory mediators, eventually resulting in cell death

and brain injury. If the inflammatory response is not timely controlled, it will also aggravate the risk of secondary injury after cerebral hemorrhage. When cerebral hemorrhage occurs, the brain tissue will also suffer from oxidative damage, which is a potential damage state in which the oxides and antioxidants in the body lose their dynamic balance. Under the common effect of inflammatory factors, lots of oxygen free radicals are generated in the lesion area, aggravating the damage of surrounding nerve cells. In addition, oxygen free radicals can also form the blood-brain barrier, causing systemic oxidative stress injury. Therefore, it is of great significance to improve the inflammatory factor levels and oxidative stress response for the postoperative treatment of patients. In summary, the implementation of cinpezide maleate-combined routine treatment after surgery has a positive effect on patients with severe cerebral hemorrhage, which can improve the cerebral blood flow, promote microcirculation, and have good anti-inflammatory effect, thereby reducing cerebral damage. Jia et al. [25] believed that cinpezide maleate had the effect of reducing serum inflammatory factor levels and blood viscosity and had a good clinical therapeutic effect on cerebral hemorrhage, which is consistent with the results of this study. The study has some shortcomings. For example, it is a single-center study with a small sample size, and the clinical efficacy of cinpezide maleate needs to be further verified by multicenter studies with an expanded sample size. In addition, this study lacks the observation and analysis of the long-term efficacy of patients.

In conclusion, cinpezide maleate can effectively reduce the serum inflammatory factor levels of ICU patients with severe cerebral hemorrhage after surgery, alleviate the oxidative stress response in the body, and improve the cerebrovascular function and cerebral nerve function, which is worthy of clinical promotion.



## Data Availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Research Article

# Clinical Evaluation of Pinggan Yiqi Yangshen Recipe Combined with Labetalol Hydrochloride and Magnesium Sulfate in the Treatment of PIH

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**Background.** To observe the clinical effect of Pinggan Yiqi Yangshen recipe combined with labetalol hydrochloride and magnesium sulfate in the treatment of pregnancy-induced hypertension (PIH). **Methods.** A total of 126 patients with PIH diagnosed in our hospital from January 2016 to May 2018 were randomly divided into the control group and the experimental group, with 63 cases in each group. The control group was treated with labetalol combined with magnesium sulfate. On the basis of the control group, the experimental group was treated with Pinggan Yiqi Yangshen recipe. Clinical efficacy, blood pressure, renal function, and biochemical indexes were compared between the two groups. Moreover, pregnancy outcomes and adverse reactions were compared between the two groups. **Results.** After treatment, the total effective rate in the experimental group was higher than in the control group. Blood pressure and mean arterial pressure in the experimental group were more significantly downregulated than the control group. Renal function indexes and biochemical indexes in the experimental group were more significant than those in the control group. The incidence of cesarean section, preterm birth, and abnormal fetal heart rate in the experimental group was significantly lower than that in the control group. There was no difference in the incidence of fetal distress, postpartum hemorrhage, neonatal asphyxia, and adverse reactions between the two groups. **Conclusion.** Pinggan Yiqi Yangshen recipe combined with labetalol hydrochloride and magnesium sulfate can effectively reduce the blood pressure of patients with PIH, help patients to return to normal levels of biochemical indexes and renal function indexes, and improve pregnancy outcomes with high safety, which is worthy of further promotion and application in clinical practice.

## 1. Introduction

Pregnancy-induced hypertension (PIH) is a disease that occurs more frequently in pregnant women. PIH usually refers to a pregnancy complication with hypertension, nausea, vomiting, edema, and proteinuria as the main clinical symptoms after 20 weeks of pregnancy [1, 2]. If not treated timely, patients will suffer from convulsion, coma, heart failure, kidney failure, and other serious conditions and can also cause fetal distress, premature delivery, and even death. PIH seriously threatens the life safety of the mother and child and is one of the main causes of maternal

death at present [3]. In recent years, the incidence of PIH has been increasing year by year [4], which has aroused great attention from doctors and patients. Clinically, western medicine is mainly used to treat patients with PIH, among which magnesium sulfate and labetalol hydrochloride are the most common [4, 5]. However, long-term use may lead to some adverse reactions in patients, such as weakened knee reflex and muscle weakness [6]. At present, western medicine combined with traditional Chinese medicine has been gradually used to treat PIH, and its advantages have been reported in clinical practice. It can not only play the advantage of the rapid therapeutic effect of western medicine

but also reflect the characteristics of the overall adjustment and treatment of both symptoms and root causes of traditional Chinese medicine [7, 8].

In this study, Pinggan Yiqi Yangshen recipe was used in combination with labetalol hydrochloride and magnesium sulfate to treat PIH in order to observe its clinical effect on PIH and the occurrence of adverse outcomes during pregnancy.

## 2. Materials and Methods

**2.1. General Information.** A total of 126 patients with PIH admitted to Zhangqiu Maternity and Child Care Hospital from January 2016 to May 2018 were randomly divided into the experimental group (63 cases) and control group (63 cases). There was no significant difference in general data between the two groups ( $P > 0.05$ , Table 1). The inclusion criteria were as follows: all patients met the diagnostic criteria of PIH in “Obstetrics & Gynecology” [9]; all patients were singleton pregnancies; all patients were treated for the first time. The exclusion criteria were as follows: patients with serious heart, brain, kidney, liver, and other important viscera-related diseases; patients who are allergic to the treatment drugs in this study; patients who do not cooperate with the researcher. This study was approved by the ethics committee of Zhangqiu Maternity and Child Care Hospital, and all patients signed informed consent.

**2.2. The Treatment.** The patients in both groups were treated with 0.25–5 g methyl dopa (H11020968, China Resources Shuanghe Pharmaceutical Co., Ltd.), twice a day. The control group was treated with basic treatment combined with labetalol hydrochloride and magnesium sulfate. The usage and dosage of labetalol hydrochloride were as follows: the patients received an intravenous infusion of 50 mg labetalol hydrochloride (H32026120, Jiangsu Desano Pharmaceutical Co., Ltd.) dissolved in 250 ml of 5% glucose solution at 2 mg/min, once a day, for 7 days. Severe patients were given 30 ml 10% glucose solution containing 25 mg labetalol hydrochloride by an intravenous drip. The usage and dosage of magnesium sulfate were as follows: the patients received an intravenous infusion of 60 ml magnesium sulfate injection (national drug approval H33021961, Hangzhou Minsheng Pharmaceutical Co., Ltd.) dissolved in 500 ml 5% glucose injection at 1–2 g/h, once a day, for 7 days. The experimental group was added with Pinggan Yiqi Yangshen recipe on the basis of the control group. The prescription of Pinggan Yiqi Yangshen recipe was as follows: 15 g *Eucommia ulmoides*, 10 g *Uncaria rhynchophylla*, 30 g *Astragali Radix*, 20 g *Semen Cassiae*, 20 g *Chrysanthemum morifolium*, 15 g *Poria cocos*, 15 g *Atractylodes macrocephala*, 15 g *Bupleurum chinense*, 20 g *Curcuma Radix*, 30 g *Radix Codonopsis*, 10 g *Rhizoma Alismatis*, 6 g *Pinelliae Rhizoma*, 20 g *Angelica*, 15 g *Angelica dahurica*, 10 g *Gardenia jasminoides*, 10 g *Citri Reticulatae Pericarpium*, 10 g *Cyperus rotundus*, 10 g *Paeoniae Alba Radix*, 5 g *Cortex Phellodendri*, 15 g donkey-hide gelatin, and 15 g *Herba Taxilli* were decocted with water every morning and evening for 7 days, one course of treatment for light patients and two courses of treatment for severe patients.

**2.3. Observation Indexes.** The clinical effect of patients in two groups after treatment was observed. The criteria were as follows: (1) special effect: the patient's symptoms and signs were disappeared, the systolic blood pressure (SBP) was decreased  $>30$  mmHg, the diastolic blood pressure (DBP) was decreased  $>20$  mmHg, the blood pressure was normal, and 24 h urine protein (Upro) was decreased; (2) valid effect: the patients' symptoms and signs were disappeared or improved, SBP was decreased  $<10$  mmHg, DBP was decreased  $<120$  mmHg, blood pressure was basically normal, and Upro was decreased; (3) invalid effect: the patients' symptoms, signs, blood pressure, and Upro were not changed or worse. Total effective rate = (special + valid)/total cases.

The improvement of blood pressure and mean arterial pressure before and after treatment was observed. The biochemical indexes of the two groups were detected. Biuret colorimetry (BT 2000 Plus Biochemical Analyzer, Italy BT) was used to detect the level of 24 h Upro. The level of superoxide dismutase (SOD) was measured by the xanthine oxidase assay (Xanthine Oxidase Test Kit, Shenzhen Zike Biotechnology Co., Ltd.). The plasma nitric oxide (NO) level was determined by nitric acid reductase (Nitric Oxide Test Kit, Shanghai Yisen Biological Technology Co., Ltd.). The level of malondialdehyde (MDA) was determined by the thiobarbituric acid method (Shanghai Mingbo Biological Technology Co., Ltd.). The plasma endothelin-1 (ET-1) level was determined by the radioimmunoassay (Shanghai Hengyuan Biological Technology Co., Ltd.). Renal function indexes were detected in both groups. The normal range of blood urea nitrogen (BUN) was 3.2–7.1 mmol/L; serum creatinine (Cr) was 70–106  $\mu$ mol/L; serum uric acid (UA) was 89–357  $\mu$ mol/L; serum urea (SU) was 1.78–7.14 mmol/L. The adverse reactions and maternal and infant outcomes of the two groups were observed.

**2.4. Statistical Analysis.** SPSS 22.0 software was used to analyze the data. The measurement data was expressed as  $\bar{x} + s$ , and the counting data were expressed as  $n$  (%) and analyzed by  $\chi^2$  test.  $P < 0.05$  was considered statistically significant.

## 3. Results

**3.1. Comparison of Clinical Efficacy between the Two Groups.** The total effective rate of the experimental group was 93.65%, and that of the control group was 71.43%. The clinical efficacy of the treatment group was significantly higher than that of the control group ( $\chi^2 = 16.211$ ,  $P < 0.01$ , Table 2).

**3.2. Comparison of Renal Function Indexes and Biochemical Indexes in Two Groups.** There was no significant difference in renal function and biochemical indexes between the two groups before treatment. After treatment, renal function indexes and biochemical indexes in both groups decreased compared with those before treatment, and the reduction in the experimental group was more significant than that in the control group ( $P < 0.01$ , Tables 3 and 4).

TABLE 1: Comparison of general clinical data between the two groups.

Clinical parameters	Experimental group ( <i>n</i> = 63)	Control group ( <i>n</i> = 63)	$\chi^2$	<i>P</i> value
<i>Age (years)</i>				
≤32	37	40	0.301	0.584
>32	26	23		
<i>BMI (kg/m<sup>2</sup>)</i>				
<18.5	6	8	0.725	0.696
18.5–24.9	45	46		
≥25	12	9		
<i>Gestational age (weeks)</i>				
<28	7	8	0.076	0.783
≥28	56	55		
<i>Parity</i>				
1	41	39	0.137	0.711
>1	22	24		
<i>Severity degree</i>				
Mild	8	9	0.469	0.791
Moderate	49	50		
Severe	6	4		

TABLE 2: Comparison of clinical efficacy between the two groups.

Group	<i>n</i>	Special effect	Valid effect	Invalid effect	Total effective rate
Experimental group	63	57.14% (36/63)	36.51% (23/63)	6.35% (4/63)	93.65% (59/63)
Control group	63	26.98% (17/63)	44.44% (28/63)	28.57% (18/63)	71.43% (45/63)
$\chi^2$					16.211
<i>P</i>					<0.01

TABLE 3: Comparison of biochemical indexes between two groups.

Group		NO (mmol/L)	SOD (U/ml)	24 h Upro (g)	ET-1 (ng/L)	MDA (nmol/L)
Experimental group	Before treatment	523.46 ± 72.84	63.21 ± 8.73	4.22 ± 1.14	93.56 ± 17.73	21.84 ± 6.12
	After treatment	971.43 ± 104.57* <sup>Δ</sup>	124.37 ± 17.84* <sup>Δ</sup>	1.25 ± 0.82* <sup>Δ</sup>	48.65 ± 8.97* <sup>Δ</sup>	10.76 ± 4.11* <sup>Δ</sup>
Control group	Before treatment	525.71 ± 71.66	61.28 ± 8.16	4.18 ± 1.09	94.11 ± 18.06	21.63 ± 6.34
	After treatment	747.23 ± 79.47*	92.64 ± 13.92*	2.71 ± 0.94*	73.24 ± 12.69*	15.93 ± 4.45*s
$\chi^2$		13.542	9.416	6.631	11.723	7.264
<i>P</i>		<0.01	<0.01	<0.01	<0.01	<0.01

Compared with the same group before treatment, \**P* < 0.01; compared with the control group after treatment, <sup>Δ</sup>*P* < 0.01.

**3.3. Comparison of Blood Pressure and Mean Arterial Pressure in Two Groups.** Before treatment, there was no significant difference in blood pressure between the experimental group and control group (*P* > 0.05). After treatment, SBP was 127.63 ± 11.45 mmHg, DBP was 78.34 ± 15.71 mmHg, and MAP was 101.66 ± 6.23 mmHg. In the control group, SBP was 151.32 ± 13.16 mmHg, DBP was 90.57 ± 16.63 mmHg, and MAP was 121.37 ± 7.54 mmHg. SBP, DBP, and MAP in both groups were lower than before treatment (*P* < 0.05), and the experimental group was more significantly decreased than the control group (*P* < 0.05, Figures 1 and 2).

**3.4. Comparison of the Incidence of Adverse Reactions and Pregnancy Outcomes between the Two Groups.** After treatment, the incidence of cesarean section, preterm birth, and abnormal fetal heart rate in the experimental group was significantly lower than that in the control group (*P* < 0.05). There was no significant difference in the incidence of fetal

distress, postpartum hemorrhage, and neonatal asphyxia between the two groups (*P* > 0.05). There was no significant difference in the incidence of adverse reactions between the two groups (*P* > 0.05, Tables 5 and 6).

## 4. Discussion

PIH is caused by many factors, such as family genetic history, age, obesity, and hypertension. At the same time, insufficient nutritional intake and recurrent mood fluctuations during pregnancy can also lead to the occurrence of PIH [10, 11]. The main clinical manifestations of PIH are abnormally elevated blood pressure, proteinuria, edema, etc., accompanied by dizziness, nausea, systemic small vessel spasm, and other clinical symptoms. Furthermore, due to the high blood pressure of patients, there will be insufficient blood supply in the uterus and placenta, which will affect the uptake of oxygen and nutrients in the uterus of the fetus and be prone to fetal intrauterine growth retardation and other



TABLE 4: Comparison of renal function indexes between two groups.

Group		Cr ( $\mu\text{mol/L}$ )	SU ( $\text{mmol/L}$ )	BUN ( $\text{mmol/L}$ )	UA ( $\mu\text{mol/L}$ )
Experimental group	Before treatment	$123.47 \pm 12.56$	$9.61 \pm 1.67$	$8.97 \pm 1.54$	$433.74 \pm 52.67$
	After treatment	$83.96 \pm 8.44^{*\Delta}$	$4.54 \pm 1.22^{*\Delta}$	$4.26 \pm 0.73^{*\Delta}$	$236.71 \pm 39.82^{*\Delta}$
Control group	Before treatment	$122.76 \pm 12.41$	$9.58 \pm 1.72$	$8.83 \pm 1.45$	$430.95 \pm 53.74$
	After treatment	$99.42 \pm 9.26^*$	$6.87 \pm 1.53^*$	$5.64 \pm 0.89^*$	$314.85 \pm 42.36^*$
$X^2$		11.124	6.173	8.265	13.814
$P$		<0.01	<0.01	<0.01	<0.01

Compared with the same group before treatment,  $^*P < 0.01$ ; compared with the control group after treatment,  $^{\Delta}P < 0.01$ .

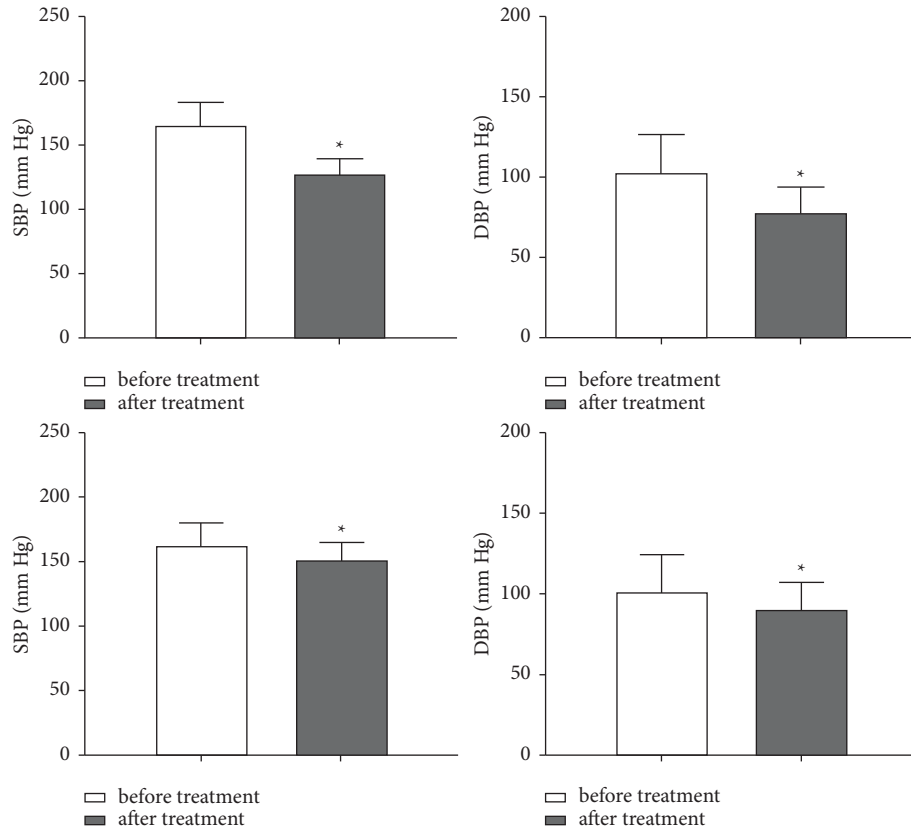


FIGURE 1: Comparison of the blood pressure between the two groups. (a) SBP in the experimental group was compared before and after treatment. (b) DBP in the experimental group was compared before and after treatment. (c) SBP in the control group was compared before and after treatment. (d) DBP in the control group was compared before and after treatment.  $^*P < 0.05$ .

phenomena. Severe cases are forced to terminate pregnancy or even die, which poses a serious threat to the life safety of pregnant women and fetus [12, 13]. Through effective intervention to control pregnant women's blood pressure, the occurrence of cardiovascular and cerebrovascular diseases can be avoided, which is of great significance to ensure the healthy development of the fetus and guarantee the life safety of pregnant women. At present, a single antihypertensive drug combined with lifestyle improvement is used to treat patients with PIH, but the treatment effect is not ideal [14]. Due to the poor physical quality of pregnant women, this situation is easy to cause adverse effects in the fetus [15, 16]. Labetalol hydrochloride is one of the antihypertensive drugs commonly used in the treatment of PIH, which can dilate blood vessels, reduce cardiac load and myocardial oxygen

consumption, and increase cardiac output, so as to achieve the purpose of lowering blood pressure [17, 18]. Magnesium sulfate has the antagonistic effect of  $\text{Ca}^{2+}$  and is mainly used for anticonvulsion. It can reduce blood pressure by causing vascular dilation, further improve human microcirculation, and can be used for the treatment of hypertensive crisis [19, 20].

According to the traditional Chinese medicine system, due to the pregnancy of the fetus in the pregnant woman, all organs of the body cannot function normally, which will lead to the deficiency of the spleen and kidney yang deficiency, resulting in the disorder of water and moisture functions in the body [21]. Kidney yang deficiency leads to poor water flow in pregnant women and obstruction of fetal gas, resulting in the fetal and maternal deficiency of blood.

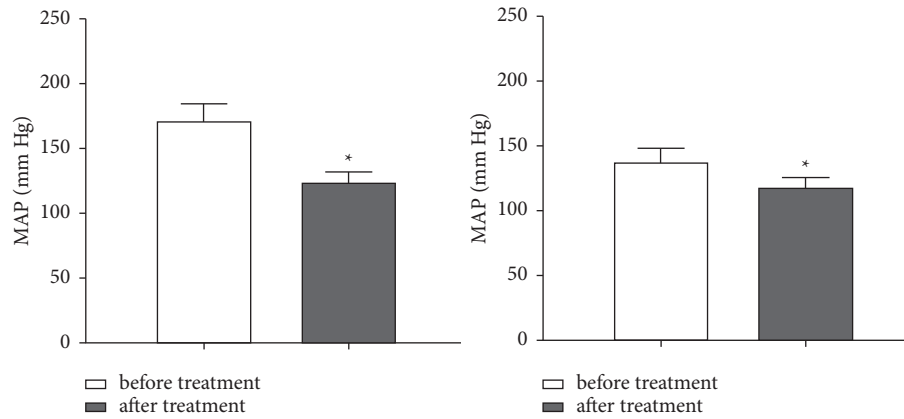


FIGURE 2: Comparison of the mean arterial blood pressure between the two groups. (a) MAP in the experimental group was compared before and after treatment. (b) MAP in the control group was compared before and after treatment. \*\* $P < 0.05$ .

TABLE 5: Comparison of the incidence of adverse reactions between two groups.

Group	<i>n</i>	Headaches	Nausea	Swelling	Vomiting	Muscle weakness
Experimental group	63	5	3	2	4	7
Control group	63	8	4	3	7	9
$X^2$		0.513	0.207	0.161	0.446	0.737
<i>P</i>		>0.05	>0.05	>0.05	>0.05	>0.05

TABLE 6: Comparison of pregnancy outcomes between the two groups after treatment.

Group	<i>n</i>	Caesarean section	Premature birth	Fetal distress	Postpartum hemorrhage	Abnormal fetal heart rate	Neonatal asphyxia
Experimental group	63	23	11	2	2	3	3
Control group	63	42	26	6	8	15	7
$X^2$		5.623	4.216	0.451	0.782	7.667	0.486
<i>P</i>		<0.05	<0.05	>0.05	>0.05	<0.05	>0.05

Therefore, patients with PIH should tonify the kidney and qi [22]. In this paper, we study a TCM prescription of Pinggan Yiqi Yangshen recipe. Among them, *Astragali Radix* has the functions of tonifying qi, replenishing wei, and consolidating the exterior. *Radix Codonopsis* has the functions of tonifying qi and nourishing blood. *Cortex Phellodendri* and *Gardenia jasminoides* have the effects of clearing away heat, purging fire and dampness, and detoxification. *Paeoniae Alba Radix* and *Cyperus rotundus* have the effects of nourishing blood, softening the liver, and relieving pain. *Pinelliae Rhizoma* can dry wet and reduce phlegm. *Citri Reticulatae Pericarpium* has the function of regulating qi and dispelling phlegm. *Atractylodes macrocephala* and *Poria cocos* have the functions of moistening water, invigorating the spleen and stomach, and relieving the heart and placenta. *Curcumae Radix* and *Angelica* have the actions of supplementing blood, promoting blood circulation, and opening the meridians. *Chrysanthemum morifolium* and *Semen Cassiae* have the actions of calming liver wind. *Bupleurum chinense*, *Angelica dahurica*, and *Uncaria rhynchophylla* have the functions of relieving liver depression, calming liver wind, reinforcing qi, and elevating yang. *Rhizoma Alismatis*

has the effect of inducing diuresis to alleviate edema. *Eucommia ulmoides*, donkey-hide gelatin, and *Herba Taxilli* have the actions of eliminating dampness, calming the liver, reinforcing the kidney, and preventing miscarriage. *Citri Reticulatae Pericarpium* has the functions of invigorating the spleen and regulating the stomach. The whole prescription can reinforce qi, strengthen the spleen, calm the liver, and reinforce the kidney [23–28]. Recent research has reported that *Atractylodes macrocephala* and *Poria cocos* can enhance human immunity [29, 30]. *Uncaria rhynchophylla* and *Eucommia ulmoides* have strong antihypertensive, sedative, spasmodic, and diuretic effects [31, 32]. *Chrysanthemum morifolium* extract solution can dilate blood vessels, reduce blood pressure, and reduce the cardiac output [33]. On the basis of western medicine use in hypertension, Chinese medicine can improve the possible adverse outcomes during pregnancy, improve human microcirculation, and can achieve the safe hypotension effect.

This study showed that, after treatment, both groups had certain clinical treatment effects. Our results showed that the combination of traditional Chinese and western medicine could effectively reduce the blood pressure and improve the



clinical symptoms of pregnancy hypertension. After treatment, the levels of BUN, UA, Cr, and SU in the experimental group were lower than those in the control group. We identified that this was closely related to the efficacy of *Astragali Radix*, *Herba Taxilli*, and *Eucommia ulmoides* in these prescriptions, such as nourishing qi and nourishing yuan, tonifying the kidney, calming the liver, and strengthening body resistance to eliminate pathogenic factors. Pinggan Yiqi Yangshen recipe can improve the renal blood circulation and increase the blood flow, and it significantly decreased the level of renal function indicators. After treatment, the incidences of cesarean section, premature birth, and abnormal fetal heart rate in the experimental group were significantly higher than those in the control group. However, there was no difference in the incidence of fetal distress, postpartum hemorrhage, and neonatal asphyxia between the two groups, which may be related to the small number of cases included. NO, an important diastolic factor produced by endothelial cells, is a new type of transport molecule with free radical properties with the effect of vascular dilation. SOD is an antioxidant enzyme to defend against the damage and destruction of oxygen free radical in metabolism and other life activities. MDA is a major metabolite reflecting lipid peroxidation in the body. The level of MDA in plasma can reflect the content of free radicals in tissues and the degree of lipid peroxidation damage. ET-1 exists in vascular endothelial cells and is one of the most vital vasoconstrictor factors. Plasma ET-1 is associated with hemodynamic changes during normal pregnancy. ET-1 showed no significant difference in the first and second trimester, but increased significantly in the third trimester, interacting with other vasoactive substances to regulate blood pressure and hemodynamic changes [34–37]. In this study, the levels of NO and SOD increased in both groups after treatment, and the experimental group was significantly higher than the control group. The levels of MDA, RT-1, and Upro in the experimental group were significantly lower than those in the control group. The results showed that the combination of integrated Chinese and western medicine is effective in treating PIH and can adjust the level of each index to the normal range.

In conclusion, Pinggan Yiqi Yangshen recipe combined with labetalol hydrochloride and magnesium sulfate can effectively improve the clinical symptoms of PIH patients, restore the damaged liver and kidney function, and improve the adverse outcomes during pregnancy in the mother and infant, which is worthy of further clinical promotion.

### Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

### Authors' Contributions

Ping Li and Jie Zhao contributed equally to this work.

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## Research Article

# Comparative Study on Diagnosis Value of Contrast-Enhanced Ultrasound and Contrast-Enhanced Computed Tomography after Treating Advanced Renal Cancer Patients with Yiqi Jiedu Decoction

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**Objective.** To compare and analyze the diagnosis value of contrast-enhanced ultrasound (CEUS) and contrast-enhanced computed tomography (CECT) after treating advanced renal cancer patients with Yiqi Jiedu decoction. **Methods.** The case data of 60 patients diagnosed with advanced renal cancer from January 2013 to January 2021 at the Affiliated People's Hospital of Ningbo University were retrospectively analyzed, 30 patients who accepted the conventional treatment were included in the control group, and the rest treated with Yiqi Jiedu decoction on the basis of conventional treatment were included in the study group. After treatment, patients in both groups received the CEUS and CECT examinations, the diagnosis efficacy of both examinations was evaluated with the ROC curve, and the overall survival (OS) of patients was analyzed. **Results.** No significant between-group differences in the general information were observed ( $P > 0.05$ ); the clinical remission rate and disease control rate were not significantly different between the two groups ( $P > 0.05$ ); the enhancement and attenuation, degree of enhancement, uniformity of enhancement, and pseudocapsule sign of the CEUS and CECT examinations were not remarkably different ( $P > 0.05$ ); according to the results of CEUS and CECT examinations, the maximum diameters of tumor after treatment were smaller in the study group than in the control group, but with no significant between-group difference ( $P > 0.05$ ); in addition, there were no obvious differences in determining the maximum diameter of tumor by CEUS and CECT ( $P > 0.05$ ), and the results of the maximum diameter of tumor determined by CEUS, CECT, and pathological specimen were not statistically different ( $P > 0.05$ ); as for the diagnosis efficacy, the result was CEUS + CECT > CEUS > CECT; and the OS of patients in the study group was longer than those in the control group. **Conclusion.** The patients treated with Yiqi Jiedu decoction obtain longer OS, and the application value of CEUS combined with CECT in the treatment effect and prognosis of patients with advanced renal cancer is higher.

## 1. Introduction

The incidence of kidney cancer in urinary tract tumors in China is second only to that of bladder tumors, which accounts for 3-4% of malignant tumors in adults and is increasing year by year. Currently, the clinical diagnosis of renal cancer mainly relies on imaging examination because there is no generally accepted tumor marker available. Contrast-enhanced ultrasound (CEUS) and contrast-

enhanced computed tomography (CECT) are emerging technologies in ultrasound diagnostics in recent years, which can reflect the blood perfusion characteristics of pathological tissue and have high diagnostic values in the early renal cancer, progressive renal cancer, and recurrent renal cancer [1-4]. Yiqi Jiedu decoction has the efficacy of invigorating qi, promoting diuresis, and removing toxicity, and it has been applied clinically as an adjuvant regimen of traditional Chinese medicine for renal cancer patients in our hospital

for many years, achieving better clinical outcomes [5]. Some studies found that both CEUS and CECT can effectively evaluate cancer patients' treatment performance by determining the intratumoral blood perfusion parameters before and after treatment, which can be used to guide subsequent treatment options [6–8]. Based on this, CEUS and CECT examinations were carried out for 60 patients with advanced renal cancer treated in our hospital, and the diagnostic value of both after treating such patients with Yiqi Jiedu decoction was further evaluated in this study.

## 2. Data and Methods

**2.1. Inclusion Criteria.** (1) The patients had parenchymatous space-occupying lesion in the kidney; (2) the patients' estimated survival was more than 6 months; (3) the clinical data of patients were complete; (4) the patients and their family members agreed to join the study and signed the informed consent; (5) the lesion was on the one side; and (6) the patients met the TCM treatment indications of Yiqi Jiedu decoction.

**2.2. Exclusion Criteria.** (1) The patients had simple cyst of the kidney; (2) the patients had other severe organic diseases or coagulation disorder; (3) the patients suffered from other malignant tumors; (4) the follow-up time was less than 1 month; (5) pregnant or lactating women; (6) the patients presented communication disorders or cognitive disorders; and (7) the patients had contraindication of CEUS and CECT examinations.

**2.3. Grouping.** The case data of 60 patients diagnosed with advanced renal cancer at the Affiliated People's Hospital of Ningbo University from January 2013 to January 2021 were retrospectively analyzed, 30 patients who accepted the conventional treatment were included in the control group, and the rest treated with Yiqi Jiedu decoction on the basis of conventional treatment were included in the study group. The implementation of the study was monitored by the Ethics Committee of the Affiliated People's Hospital of Ningbo University.

**2.4. Methods.** All patients received the conventional chemoradiotherapy according to their condition, and on this basis, those in the study group took one dose of Yiqi Jiedu decoction (20 g of Mongolian milkvetch root, 20 g of Largehead Atractylodes Rhizome, 30 g of Solomonseal Rhizome, 15 g of tuber of multiflower knotweed, 30 g of *Hedyotis*, 15 g of Barbated Skullcup herb, 15 g of Giant Knotweed Rhizome, 15 g of *Isatis* root, and 15 g of Danshen root) daily in two split times (in the morning and the evening) for 60 days [9, 10]. After that, all patients received the CEUS and CECT examinations.

**2.4.1. CEUS Test.** Two focus points under the lesion were set with the ultrasonography (model: Siemens Sequoia 512) and probes (model: 4C1; frequency: 2.0–4.5 MHz) under MI 0.21

[11, 12], which were applied for all patients. The freeze-dried powder of the SonoVue contrast agent was dissolved and shaken with 5 ml of normal saline into milk white liquid; then, the patients were administered with 1.2 ml of it via elbow vein bolus injection and flushed with 5 ml of normal saline (i.e., the contrast agent was completely injected within 3–5 s); meanwhile, the CPS mode and timekeeping were initiated to observe the start time of ultrasound contrast enhancement and attenuation of kidney cortex, medulla, and lesion, record the lesion form, size, blood flow, and boundary, and videotape the whole process. The TIC curve was obtained by the analysis software to analyze various parameters and compare the enhancing intensity between lesion and surrounding normal renal parenchyma to determine the enhancing intensity of ultrasound contrast. For patients with a poor imaging effect or incomplete image, a second CEUS could be carried out 10 min after the first contrast.

**2.4.2. CECT Test.** The patients were in the spine position and scanned with the Siemens SOMATOM Sensation 64-Slice CT from their porta hepatis plane to lower pole of the kidney with routine plain scan first and then contrast-enhanced scan. During the contrast-enhanced scan, 80 ml of nonionic iodine contrast agent (specification: 300 mgI/ml) was administered via elbow vein injection with the binocular high-pressure syringe under the rate of 3–4 ml/s; then, 30 ml of normal saline was injected under the rate of 3 ml/s, and after that, the arterial phase, portal venous phase, and scanning were delayed for, respectively, 28 s, 70 s, and 180 s. The scan conditions were set as follows: gantry rotation was 0.33 s per rotation, reference current was 500 mAs, tube potential was 120 kVp, detector straight line was  $32 \times 0.6$  mm, and thread interval was 0.65–1.3 mm; for the conventional reconstruction images, both the slice thickness and slice interval were 8 mm, and for the thin reconstruction images, 1 mm, and sagittal or coronal scanning was performed on thin slice reconstructed images with a thickness of 4–6 mm and FOV of 35–45 cm [13].

## 2.5. Observation Indexes

**General information:** the patients' general information included their age, tumor diameter, gender, affected side of tumor, tumor location, clinical manifestations, and pathological type.

**Clinical efficacy:** according to the Response Evaluation Criteria in Solid Tumors (RECIST) [14], the clinical efficacy was classified into complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). The clinical remission rate =  $(CR + PR) / \text{total number} \times 100\%$ , and the disease control rate =  $(CR + PR + SD) / \text{total number} \times 100\%$ .

**Follow-up observation:** the follow-up visits were conducted after the first month of treatment, mainly including imaging examination, serum tumor marker, and routine physical examinations such as the routine



TABLE 1: Statistics of patients' general information of the two groups ( $n = 30$ ).

Observation indicator	Control group	Study group	$t/X^2$	$P$
Age (years)	50.48 ± 8.36	51.13 ± 8.52	0.298	0.767
Tumor diameter (cm)	3.51 ± 2.23	3.47 ± 2.31	0.068	0.946
Gender (male)	11 (36.67%)	13 (43.33%)	0.278	0.596
Affected side			0.268	0.605
Left	17 (56.67%)	15 (50%)		
Right	13 (43.33%)	15 (50%)		
Tumor position				
Upper pole of the kidney	7 (23.33%)	6 (20%)	0.098	0.754
Midpole of the kidney	12 (40%)	14 (46.67%)	0.272	0.602
Lower pole of the kidney	11 (36.67%)	10 (33.33%)	0.073	0.787
Clinical manifestation				
Painless hematuria	11 (36.67%)	9 (30%)	0.300	0.584
Lumbago	4 (13.33%)	5 (16.67%)	0.131	0.718
Hematuria with lumbago	15 (50%)	16 (53.33%)	0.067	0.796
Pathological type			0.341	0.559
Locally advanced renal cell carcinoma	23 (76.67%)	21 (70%)		
Metastatic renal cell carcinoma	7 (23.33%)	9 (30%)		

blood test, routine urinalysis, erythrocyte sedimentation rate (ESR), and hepatic and kidney function.

**2.6. Statistical Processing.** In this study, the between-group differences in data were calculated by SPSS22.0, the picture drawing software was GraphPad Prism 7, the enumeration data were expressed by ( $n$  (%)) and examined with the  $X^2$  test, the measurement data were expressed by ( $\bar{x} \pm s$ ) and examined with the  $t$ -test, and differences were considered statistically significant at  $P > 0.05$ .

### 3. Results

**3.1. General Information.** No significant differences in the general data between the two groups were observed ( $P > 0.05$ ), indicating no statistical significance. Table 1 provides the specific data.

**3.2. Clinical Efficacy of Patients in Both Groups.** No statistical differences in the clinical remission rate and disease control rate of patients between the two groups were observed ( $t = 0.073, 0.082$ ;  $P = 0.787, 0.774$ ) (Figure 1).

The control group had 2 CR cases, 8 PR cases, 12 SD cases, and 8 PD cases, and the clinical remission rate and disease control rate were 33.33% (10 cases) and 73.33% (22 cases), respectively.

The study group had 2 CR cases, 9 PR cases, 10 SD cases, and 9 PD cases, and the clinical remission rate and disease control rate were 36.67% (11 cases) and 70% (21 cases), respectively.

**3.3. Imaging Characteristics of Patients with Advanced Renal Cancer on CEUS and CECT Scans.** No significant differences in the ultrasound characteristics including enhancement and attenuation, degree of enhancement, uniformity of enhancement, and pseudocapsule sign on CEUS and CECT scans of 60 advanced renal cancer patients were observed ( $P > 0.05$ ) (Table 2 and Figure 2).

**3.4. Changes in the Maximum Diameters of Tumor before and after Treatment.** According to the CEUS and CECT tests, the maximum diameters of tumor in patients were smaller in the study group than in the control group, but the between-group differences were not significant ( $P > 0.05$ ); in addition, there were no obvious differences in determining the maximum diameter of tumor by CEUS and CECT ( $P > 0.05$ ) (Table 3); the results of the maximum diameter of tumors determined by CEUS, CECT, and pathological specimen were not statistically different ( $P > 0.05$ ) (Table 4).

**3.5. Diagnosis Efficacy of CEUS and CECT for Advanced Renal Cell Carcinoma Patients.** Taking the postoperative pathological examination as the golden standard, the diagnosis efficacy of CEUS and CECT for advanced renal cell carcinoma was evaluated with the ROC curve, and the result was CEUS + CECT > CEUS > CECT (Figure 3 and Table 5).

**3.6. Comparison of Patients' OS between the Two Groups.** The difference in the follow-up visit time (months) between the study group and the control group was not significant ( $13.68 \pm 2.11$  vs.  $13.94 \pm 2.30$ ,  $t = 0.456$ ,  $P = 0.650$ ); the patients' OS was longer in the study group than in the control group, as shown in Figure 4.

### 4. Discussion

Renal cell carcinoma has an incidence rate second only to bladder cancer among urinary tract tumors in China. According to epidemiological investigation, renal cell carcinoma accounts for approximately 2-3% of malignant tumors in adults, with an average standardized morbidity of 3.7/100,000 that is obviously increasing in recent years [15, 16]. Renal cell carcinoma has a very rapid disease progression and is the most lethal malignancy of all urinary tumors. Although surgery is the optimal treatment for renal cell carcinoma, nearly half of the patients are advanced at the time of first diagnosis and lose the opportunity of surgery,

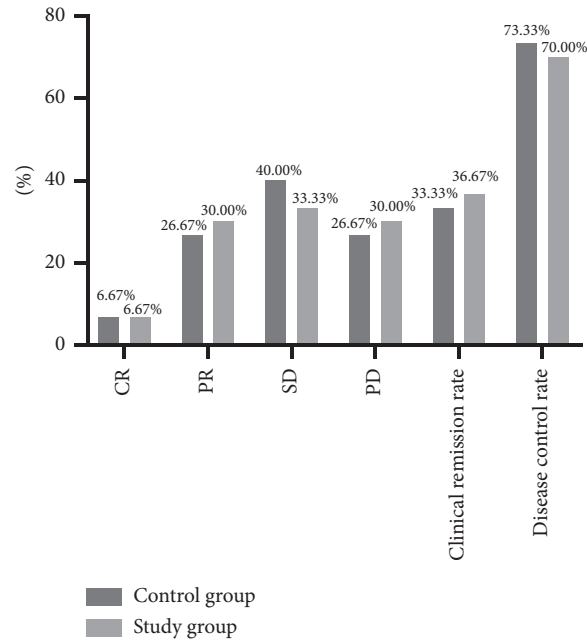


FIGURE 1: Comparison of patients' clinical efficacy between the two groups (%). Note: the horizontal axis indicates the evaluation dimensions, and the vertical axis indicates the percentage (%).

TABLE 2: Imaging characteristics of patients with advanced renal cancer on CEUS and CECT scans ( $n$  (%)).

Characteristic dimension	CEUS	CECT	$X^2$	$P$
Enhancement and attenuation			1.905	0.168
Fast enhancement and fast attenuation	7 (11.67)	10 (16.67)		
Fast enhancement and slow attenuation	39 (65)	38 (63.33)		
Slow enhancement and fast attenuation	4 (6.67)	7 (11.67)		
Slow enhancement and slow attenuation	10 (16.67)	5 (8.33)		
Degree of enhancement			0.745	0.388
High	44 (73.33)	45 (75)		
Low	16 (26.67)	12 (20)		
None	0 (0)	3 (5)		
Uniformity of enhancement			0.534	0.465
Yes	27 (45)	31 (51.67)		
No	33 (55)	29 (78.33)		
Pseudocapsule sign			0.310	0.577
Yes	26 (43.33)	23 (38.33)		
No	34 (56.67)	37 (61.67)		

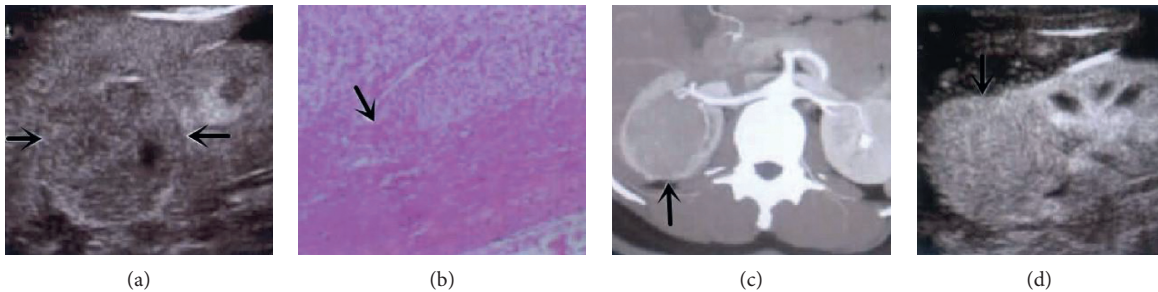


FIGURE 2: CEUS and CECT scans imaging of patients with advanced renal cancer note. (a) CEUS scan for renal clear cell carcinoma with pseudocapsule sign around. (b) The image of the pseudocapsule formation in a case with renal clear cell carcinoma. (c) CEUS scan for renal cell carcinoma with no tumor enhancement. (d) CEUS scan for renal cell carcinoma showing uniform hyperenhancement of the tumor.



TABLE 3: Changes in the maximum diameters of tumor before and after treatment (mm).

Group	CEUS		CEUS	
	Before treatment	After treatment	Before treatment	After treatment
Control group	45.66 ± 10.81	28.59 ± 7.08	46.17 ± 10.98	28.01 ± 7.05
Study group	45.16 ± 10.75	25.81 ± 6.15	46.20 ± 11.04	25.19 ± 6.27
<i>t</i>	0.180	1.624	0.011	1.637
<i>P</i>	0.858	0.110	0.992	0.107

TABLE 4: Comparison of the maximum diameters of tumor after treatment determined by CEUS, CECT, and pathological specimen (mm).

Method	Maximum diameter of tumor
CEUS	26.55 ± 6.23
CECT	26.38 ± 6.25
Pathological specimen	26.11 ± 6.19
<i>t</i> <sub>CEUS-pathological</sub> / <i>P</i> <sub>CEUS-pathological</sub>	0.274/0.785
<i>t</i> <sub>CEUS-pathological</sub> / <i>P</i> <sub>CEUS-pathological</sub>	0.168/0.867

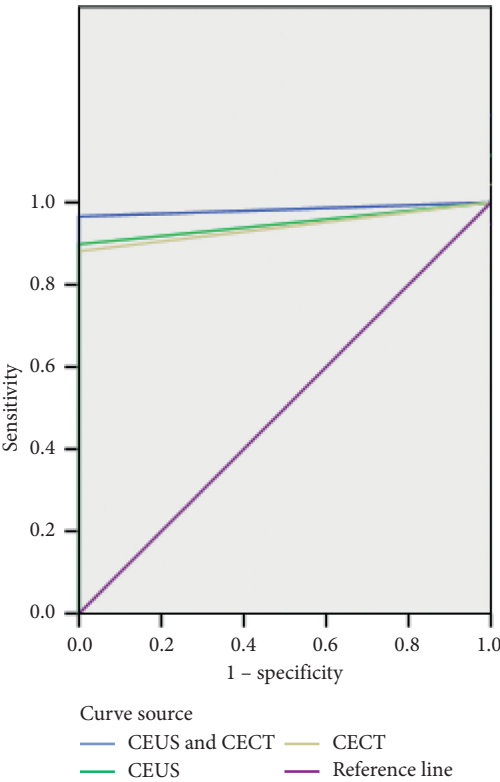


FIGURE 3: ROC curve.

TABLE 5: Area under the curve.

Variable of test result	Area	Standard error	Asymptotic Sig.	Asymptotic 95% CI	
				Lower limit	Upper limit
CEUS + CECT	0.983	0.019	0.100	0.000	1.000
CEUS	0.949	0.041	0.126	0.000	1.000
CECT	0.941	0.046	0.133	0.000	1.000

and a large number of clinical studies have shown that the disease is not sensitive to radiation therapy, so postoperative chemoradiotherapy is not a significant predictor of

improved patient survival [17–20]. Therefore, Yiqi Jiedu decoction is commonly used in the clinic to assist renal cancer treatment, in the hope of enhancing drug efficacy,

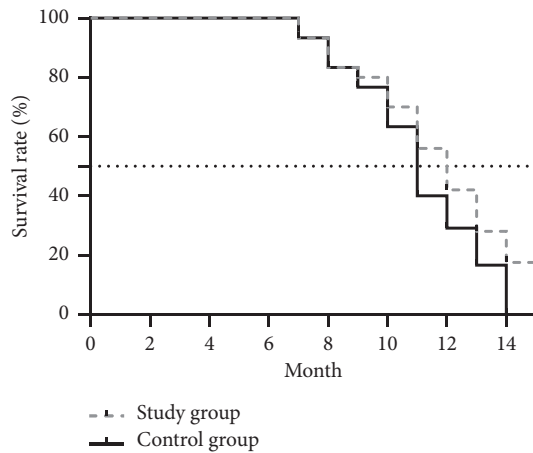


FIGURE 4: Patients' OS of the two groups. Note: the horizontal axis indicates the survival time (month), the vertical axis indicates the survival rate (%), and ..... indicates the survival time corresponding to the median survival rate of patients in both groups.

reducing drug toxic and side effects and tumor volume, and lowering the clinical stage, so as to enable the inoperable patients to receive surgery and even prolong their survival. To better control the condition of renal cancer patients, especially those in the advanced stage, effective diagnostic modalities must be adopted to evaluate their treatment performance, guide subsequent treatment options, and prevent remetastasis and recurrence. With the continuous development of ultrasound contrast agents and contrast imaging technology, CEUS can observe the intratumoral blood perfusion in real-time, dynamically and continuously, which makes up for the deficiency of two-dimensional ultrasound, color ultrasound, CT, and other examinations in the diagnosis of renal cell carcinoma, and provides a new method for qualitative diagnosis.

In this study, the clinical remission rate and disease control rate of patients were not significantly different between the two groups ( $P > 0.05$ ), which was consistent with the report of Choi et al. [15]. In addition, according to the results of CEUS and CECT examinations, the maximum diameters of tumor after treatment were smaller in the study group than in the control group, but the between-group difference was not significant ( $P > 0.05$ ), indicating that Yiqi Jiedu decoction could reduce the maximum diameter of tumor for advanced renal cell carcinoma patients, but the result was not statistically significant. The results of the maximum diameter of tumor determined by CEUS, CECT, and pathological specimen were not statistically different ( $P > 0.05$ ); the diagnosis efficacy of CEUS and CECT on renal cell carcinoma was evaluated by the ROC curve, and the result was  $\text{CEUS} + \text{CECT} > \text{CEUS} > \text{CECT}$ , implying that the CEUS obtained a better diagnosis efficacy than CECT, both of them could be used as the imaging examination for measuring the size of renal tumor, and the correctness of their combination was higher. Also, the enhancement and attenuation, degree of enhancement, uniformity of enhancement, and pseudocapsule sign in CEUS and CECT scans for 60 patients with advanced renal cancer were not

significantly different ( $P > 0.05$ ), denoting that both CEUS and CECT could identify the renal cell carcinoma by enhancing the diffusivity and centrality.

Compared with CECT, CEUS is simple to operate, and the contrast medium used is iodine-free gas-filled microbubbles, which is noninvasive, nonallergic, nonradiating, and safer, and can be discharged all over the lung in about 10 min without liver and kidney toxicity; moreover, the ultrasound contrast agent is essentially the blood pool imaging agent that stays only intravascularly, thus accurately reflecting the characteristics of tissue microvascular perfusion; finally, CEUS is also capable of real-time, dynamic, and continuous monitoring of the phasic changes in blood perfusion in tumor lesions; in particular, its display of the microvasculature of tumors and low blood flow is better than CT [21–24]. However, for double renal lesions or multiple lesions on the one side, CEUS can only obtain contrast perfusion imaging of relatively local or adjacent lesions, and lesions in different parts are difficult to show simultaneously; for deep or superficially special tumors, multiple contrasts are necessary to achieve better results; besides, contrast agents are expensive, so it is difficult to widely promote their application. The study also has the following deficiencies. For example, it was a single center study with a small sample size, and the in-depth exploration of study dimensions with insignificant differences still requires a larger sample size. In addition, the analysis of patients' quality of prognosis survival and time to disease progression was not addressed.

In conclusion, patients treated with Yiqi Jiedu decoction obtain longer OS, the diagnostic sensitivity and accuracy of CEUS for advanced renal cancer are better than those of CECT, but the combination of CEUS and CECT is more valuable in the treatment effect and prognosis of patients with advanced renal cancer.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Chinese Medicine on the Biological Behavior and Magnetic Resonance Imaging of Bladder Cancer

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**Objective.** This study aimed to investigate the effects of traditional Chinese medicine (TCM) on biological behavior and magnetic resonance imaging and recurrence rate of patients with bladder cancer. **Method.** Forty-seven postoperative bladder cancer patients treated in our hospital who met the criteria were selected and randomly divided into the TCM treatment group (observation group) and the group without TCM treatment (control group). In the TCM treatment group, the prescription was slightly adjusted according to the different symptoms, and the main prescription remained unchanged. According to the treatment plan, patients continued to undergo bladder irrigation chemotherapy plus TCM treatment, while the control group was only treated with bladder irrigation chemotherapy. The number of patients with recurrence at 3 and 6 months and 1 year, the effects on patients' clinical symptoms, and quality of life were observed, respectively. The changes in MRI images, blood routine, immune function, and leukocyte level and other related indexes before and after treatment were compared between the two groups. **Results.** After the patients in the observation group were treated with traditional Chinese medicine, the patients' quality of life significantly improved. The patients' CD3+, CD4+, and CD4+/CD8+ indexes were significantly higher than those of the control group. The levels of Hb and PLT of the patients in the observation group were significantly lower than those of the patients in the control group. Patients in the observation group had higher leukocyte levels and a lower recurrence rate than patients in the control group. **Conclusion.** TCM with chemotherapy drugs can effectively improve patients' immune function, increase the level of T-lymphocyte subpopulation, and improve bone marrow hematopoietic function, which has a significant effect on the prevention and treatment of bladder cancer recurrence after surgery.

## 1. Introduction

Bladder cancer is one of the most common malignant tumors of the genitourinary system, which seriously endangers human physical and mental health [1, 2]. Globally, bladder cancer is the ninth most prevalent malignant tumor, ranking sixth in men and about tenth in women [3–5]. Clinically, bladder cancer is often divided into nonmuscle invasive bladder cancer and muscle invasive bladder cancer. Non-muscle invasive bladder cancer accounts for approximately 70%–75% of primary bladder tumors [6, 7], and it is

generally less differentiated, more malignant, and more likely to develop into muscle invasive bladder cancer [8]. Bladder cancer often recurs, with its recurrence rate ranging from 20% to 70%, and up to 30% of patients eventually experience bladder cancer progression [8, 9]. And it is highly prone to recurrence after surgery, which has become a challenge for current clinical treatment [10–13].

Bladder cancer survival is approximately 16–20 months [14], and some patients with advanced bladder cancer do not achieve the expectation of controlling their disease after extensive radiotherapy and chemotherapy, and even aggravate

their disease. The intervention of Chinese medicine can accelerate the recovery of patients, reduce the recurrence rate of surgery, improve the symptoms of side effects of surgery and perfusion therapy, and also play a more desirable consolidation role. TCM is a holistic approach to identifying and examining the causes of bladder cancer. It is believed that the pathogenesis of bladder cancer is mainly due to weakness of vital qi, and blood stasis, dampness, and heat toxicity are entangled with each other, resulting in a tangible mass over time. Pathogenesis based on root deficiency and branch excess: root deficiency presents with spleen-liver-kidney insufficiency and branch excess with phlegm and qi-blood stagnation. From the perspective of the four types of evidence, namely, dampness and heat, blood stasis and internal obstruction, spleen and kidney deficiency, and yin deficiency and internal heat, the dialectical use of Chinese medicine in the treatment of bladder cancer has achieved satisfactory outcomes.

Surgery, chemotherapy, and radiotherapy can play a certain role in bladder cancer, but not sufficient and high incidence of adverse reactions after the participation of radiotherapy and chemotherapy; it seriously reduces patients' quality of life and affects their confidence in actively accepting treatment, which in turn affects the desired outcomes. Therefore, in recent years, clinical practice has gradually strengthened the attempts to use Chinese medicine combined with Western medicine in the treatment of bladder cancer and has achieved better efficacy. The application of chemotherapy drugs is often accompanied by serious gastrointestinal reactions, bone marrow suppression, neurological damage, and other toxic side effects, and many patients often end their treatment midway because they have difficulty in tolerating the severe side effects of chemotherapy. In the treatment of bladder cancer, the application of bladder irrigation with Chinese medicine tonics has an inhibitory effect on white corpuscle.

With the continuous development and improvement of medical technology, diagnostic imaging technology has been widely used. At present, imaging technology has become an essential method for diagnosing bladder cancer. In clinical experiments, the application of imaging technology can be used to identify patients' bladder cancer lesions, so that medical personnel can better understand patients' physical conditions and thus adopt suitable treatment plans, so that bladder cancer patients can receive timely and effective treatment. There are two types of magnetic resonance imaging, diffusion-weighted imaging, and MR elastography. Diffusion-weighted imaging is an imaging technique obtained by the difference in the motion of water molecules between tissues. The problems concerning motion have been overcome by the application of MRI, which is mainly used to examine the imaging data of the abdomen. Diffusion-weighted imaging does not involve other contrast agents and the acquisition time is relatively short compared to ultrasound diagnosis. In clinical trials, MRI diffusion-weighted imaging is mainly used for imaging detection of bladder cancer tumors. In addition, it can make effective detection of bladder cancer lesions, so that the corresponding treatment plan can be formulated for the histological grading of bladder cancer, and the recurrence of bladder cancer can be prevented.

MRI scans have wide use nowadays. In recent years, with the continuous development of hardware and software, functional magnetic resonance imaging (fMRI) has been gradually applied to the study of abdominal organs and lesions. In this study, we selected "bladder cancer patients" as the study objects and initially investigated the effect of Chinese medicine on the recurrence of bladder cancer after surgery, as well as the improvement of clinical symptoms and quality of life. As an important supplement to conventional MRI scanning, functional magnetic resonance imaging has now become a popular research and application direction.

## 2. Materials and Methods

**2.1. Research Objects.** 47 patients at the Oncology and Gynecology Departments of Zhangqiu District People's Hospital, Jinan, Shandong, China, between January 1, 2020, and May 31, 2021, were included in this study, and all patients had complete clinical data. Among them, there were 35 male patients and 12 female patients, aged 35–80 years, with a mean age of 58.2 years. There were 5 cases at clinical stage T0, 31 cases at stage T1, and 11 cases at stage T2. There were 15 cases of pathological grade I and 32 cases of grade II, all of which underwent resection of bladder tumor with pathological diagnosis reports. There were 29 cases of noninvasive bladder cancer and 18 cases of invasive bladder cancer. All patients were treated with TURBT surgery and bladder perfusion chemotherapy. The patients were divided into the TCM treatment group (observation group, 24 cases) and the group without TCM treatment (control group, 23 cases). Some patients were found to have recurrence after treatment, and the number of recurrences ranged from 2 to above 30. This study was approved by the ethics committee of Zhangqiu District People's Hospital, Jinan, Shandong, China, and all patients gave informed consent.

### 2.2. Inclusion Criteria

- (1) Patients who had been diagnosed with bladder cancer, had pathological diagnoses, and underwent surgery.
- (2) Patients between the ages of 35 and 70 years.
- (3) Patients who voluntarily participated in the study and had signed the informed consent form.
- (4) Performance status (KPS) score >60 and expected survival >12 months.
- (5) Patients with no psychiatric or psychiatric history that would affect informed consent and who had some communication and language skills.
- (6) Patients with no other malignancies and severe comorbidities.
- (7) Patients with complete medical information.

### 2.3. Exclusion Criteria

- (1) Patients with significant preoperative inflammatory reactions, combined with severe primary diseases of

the heart, liver, kidney, blood or endocrine system, and psychiatric and immune disorders

- (2) Patients who had not undergone postoperative bladder irrigation or who had not been treated with formal irrigation.
- (3) Patients who had other malignant systemic diseases.
- (4) Patients with a perioperative application of antibiotics, long-term use of drugs that suppressed the immune system, and hormonal drugs.
- (5) Poor patient compliance and reluctance to accept surveys.
- (6) Patients lost to follow-up.

**2.4. General Information.** The patient's clinical information mainly covered basic personal information, history, blood test results about one week before surgery, surgical records, pathology reports, and so on. Basic personal information includes the patient's age, gender, contact information (for follow-up), and blood results about one week before surgery. History includes a history of smoking and a history of diseases. Contents of surgical records include tumor size and number, tumor shape, and location. Pathology report includes the degree of pathological differentiation and whether it is infiltrating muscle layer (Table 1).

**2.5. Treatment Method.** The basic formula of Chinese medicine was as follows: glabrous greenbrier rhizome, Yuge, chrysanthemum flower, prepared rehmannia root, villous amomum fruit, asiatic cornelian cherry fruit, common yam rhizome, tree peony root bark, oriental water plantain rhizome, milkvetch root, cassia bark, common selfheal fruit-spike, and gecko.

The above herbs were taken by decoction with water twice a day, 1 dose/day, for at least six months. The patients did not eat cold and greasy food during the medication period, with recording the change of symptoms and followed up every two weeks at the outpatient clinic.

Bladder irrigation is routine intravesical chemotherapy drug and immunosuppressant irrigation therapy.

**2.6. Observation Time and Follow-Up.** From the 1<sup>st</sup> dose of Chinese medicine, follow-up was conducted by regular outpatient review and telephone follow-up.

Review time: patients were reviewed once every 3 months in the first year after surgery and once every 6 months from the second year onwards.

Review items: physical examination, MRI-based imaging, abdominal CT or ultrasound and cystoscopy, etc., combined with cystoscopy biopsy for pathology if necessary, and the number of patients with recurrence was derived from the collected follow-up data.

## 2.7. Observation Contents

**2.7.1. Tumor Recurrence.** The patient was treated with transurethral bladder tumor electrosurgery and returned to the hospital for follow-up urological CT and cystoscopy in the 3<sup>rd</sup>, 6<sup>th</sup>, and 12<sup>th</sup> months after surgery to observe the postoperative recurrence.

**2.7.2. Adverse Drug Reactions.** Patients were observed to receive bladder irrigation chemotherapy followed by treatment with Chinese medicine for drug side effects, including symptoms such as carnal hematuria, urinary frequency, urinary urgency, urinary pain, and lower abdominal pain.

**2.7.3. Changes in Immune Function.** Before and after the treatment, 5 mL of fasting venous blood was taken from the patients and placed on our automatic blood centrifuge for centrifugation, the speed of the centrifuge was adjusted to 3000 r/min for 10 min, and the supernatant was placed in a refrigerator at  $-20^{\circ}\text{C}$  for examination. The T-lymphocyte subsets in the serum were detected.

**2.7.4. Blood Routine Examination.** Before and after the treatment, 5 mL of fasting venous blood was taken from the patients and placed on our automatic blood centrifuge for centrifugation, the speed of the centrifuge was adjusted to 3000 r/min for 10 min, and the supernatant was placed in a refrigerator at  $-20^{\circ}\text{C}$  for examination. The hemoglobin (Hb) and platelet (PLT) count of the patients was tested before and after the treatment.

**2.7.5. Leukocyte Level.** The efficacy was evaluated according to the grading criteria for myelosuppression by chemotherapy: degree I,  $3.0 \times 10^9/\text{L} \leq \text{WBC} < 4.0 \times 10^9/\text{L}$ ; II,  $2.0 \times 10^9/\text{L} \leq \text{WBC} < 3.0 \times 10^9/\text{L}$ ; III,  $1.0 \times 10^9/\text{L} \leq \text{WBC} < 2.0 \times 10^9/\text{L}$ ; and IV,  $\text{WBC} < 1.0 \times 10^9/\text{L}$ .

**2.7.6. Magnetic Resonance Imaging.** The patient was put in the supine position with a proper bladder filling by fasting for 6 h before the examination with a 1.5 T (MAGNETOM Avanto) scanner. The parameters were set as follows: HR-T2WI (TR of 7000–8 000 ms, TE of 90–102 ms, layer thickness of 3 mm, layer spacing of 1 mm); DWI (TR of 4 000 ms, TE of 78 ms, layer thickness of 4 mm, layer spacing of 0.4 mm); and DCE (TR of 180–300 ms, TE of 1.7–4, layer thickness of 6 mm, layer spacing of 2 mm, reversal angle  $70^{\circ}$ ). The patient was injected with Magenvixen through the elbow vein at a uniform rate, the multiphase dynamic enhancement images were obtained at 20, 30, 40, 60, 80, and 100 s after the injection, and the delayed phase scan was performed 3 min later. The MRI was performed by two senior physicians in the imaging department of our hospital.



TABLE 1: General characteristics of the patients.

Characteristics		Observation group (24 cases)	Control group (23 cases)
Gender	Male	17 (70.8%)	18 (78.3%)
	Female	7 (29.2%)	5 (21.7%)
Age		59.2 ± 5.01	57.3 ± 6.24
Number of tumors	Single	7 (29.2%)	8 (34.8%)
	Multiple	17 (29.2%)	15 (5.2%)
Maximum tumor diameter		37.21	36.67
Clinical stage	T0	2 (8.3%)	3 (13.0%)
	T1	16 (66.7%)	15 (65.2%)
	T2	6 (25.0%)	5 (21.7%)

**2.8. Statistical Analysis.** SPSS 22.0 software was applied to process and analyze the data in this study, and the measurement data were described by mean ± standard deviation ( $\bar{x} \pm s$ ). A *t*-test was used for comparison, the count data were described by rate or percentage (%), and the chi-square test was used for comparative analysis.  $P < 0.05$  was a statistically significant difference.

### 3. Results

**3.1. Recurrence of Bladder Cancer One Year after Surgery.** The number of recurrences within 3 months was 2 cases, both in the control group (8.7%), and there was no recurrence in the observation group (Table 2). The recurrence rate in the control group was 13.0% within 6 months, and the recurrence rate in the observation group was 4.2%, which was significantly lower than the recurrence rate in the control group. Seven cases recurred within 12 months: two in the observation group, with a recurrence rate of 8.3%, and five in the control group, with a recurrence rate of 21.7%. This indicated that the combined treatment of Chinese and Western medicine was effective in preventing the recurrence of bladder cancer after surgery.

**3.2. MRI of Patients after Chinese Medicine Treatment.** Postoperative MRI showed that T1WI signal was increased to different degrees, 3 of which had uniform high signal, 1 had uniform isointensity signal, and the rest had mixed signal. For T2WI, 1 had uniform high signal, 4 had uniform low signal, and 1 had uniform isointensity signal. DWI showed that 9 lesions had high signal, and the rest had varying degrees of signal decrease. Dynamic enhancement scans showed no significant arterial phase enhancement within any of the 25 treated areas, one marginal arterial phase enhancement, and seven delayed scans showed mild marginal enhancement (Figure 1). The pathological picture of 400 times a different installment of bladder cancer is shown in Figure 2.

MRI image of patient A showed a small amount of cancer involvement in the smooth muscle and fibrous connective tissue (of the bladder tumor base) and the pathological diagnosis indicated that patient A was high-grade invasive uroepithelial carcinoma with a small percentage of micropapillary carcinoma (about 2%) (Figure 1A). The MRI image of patient B is shown in

Figure 1B. The pathologic diagnosis showed mucosal ulcer formation in the right side of the bladder wall within the total cystectomy specimen, reaching deep into the muscular layer, with interstitial edema and necrosis with more chronic inflammatory cell infiltration. After adequate sampling (11 wax blocks), no cancer residue was seen, and no cancer involvement was seen in the prostate and bilateral seminal vesicle glands and vas deferens. No metastasis was observed in the left pelvic (0/5) and right pelvic (0/1) lymph nodes.

MRI image of patient C (Figure 1C) showed bladder tissue, prostate, and bilateral vesicoureteral glands and vas deferens. The bladder size was 5 \* 4 \* 4.5 cm, and a rough mucosal area (3 \* 2 cm) was seen on the right side, which seemed to invade the muscle layer. The prostate size was 3.5 \* 3.5 \* 2.7 cm. The size of the left seminal vesicle gland was 2.4 \* 1.5 \* 0.7 cm, the length of the left vas deferens was 7 cm and the maximum diameter was 0.5 cm, the size of the right seminal vesicle gland was 3.2 \* 2 \* 0.7 cm, and the length of the right vas deferens was 7.5 cm and the maximum diameter was 0.7 cm. The left pelvic lymph nodes were covered with grayish-yellow fatty tissue with a combined size of 4.5 \* 3 \* 1.5 cm and several enlarged lymph nodes with a maximum diameter of 1–1.7 cm. The right pelvic lymph nodes were covered with one grayish-yellow fatty tissue and one enlarged lymph node with a maximum diameter of 2 cm. Combined with pathological diagnosis, this patient was diagnosed with high-grade uroepithelial carcinoma (microscopic diameter of approximately 0.3 cm) with squamous. The invasion reached the lamina propria and did not involve the urethral margin, prostate, bilateral seminal vesicle glands, and vas deferens. No metastasis was found in the lymph nodes of the left pelvis (0/6) and right pelvis (0/3).

**3.3. Adverse Reactions to Bladder Irrigation Drugs.** Adverse reactions during treatment were recorded and evaluated in 47 patients in both groups using the Common Terminology Criteria for Adverse Reactions, version 5.0. Two patients in the observation group were recorded with malaise, one with hypothermia, and zero with weight loss after treatment, while five patients in the control group were recorded with malaise, three with hypothermia, and one with weight loss after treatment. In the control group, 2 patients showed mild gastrointestinal reactions with decreased appetite and no vomiting symptoms, and 1 patient showed constipation during treatment. In the observation group, there were 8 cases of gastrointestinal reactions. 11

TABLE 2: Bladder cancer recurrence rate.

Time	Group	Cases	Recurrence	No. of recurrence	Recurrence rate (%)
3 months	Observation group	24	0	24	0
	Control group	23	2	21	8.7
6 months	Observation group	24	1	23	4.2
	Control group	23	3	20	13.0
12 months	Observation group	24	2	22	8.3
	Control group	23	5	18	21.7

patients in both groups had symptoms such as urinary frequency, urinary urgency, urinary pain, hematuria, and lower abdominal pain, the incidence of which was 12.5% in the observation group and 34.8% in the control group. None of the 47 patients experienced toxic reactions other than gastrointestinal symptoms and systemic symptoms, and no urethral strictures occurred (Table 3). The results showed that Chinese medicine did not aggravate or persist in adverse reactions and significantly reduced the incidence of adverse reactions in patients after bladder irrigation chemotherapy.

**3.4. Leukocyte Levels.** The recurrence rate of bladder cancer after surgery is high, so the method of camptothecin bladder infusion is mainly used after surgery to prevent its post-operative recurrence or metastasis. The application of chemotherapeutic drugs is often accompanied by severe gastrointestinal reactions, bone marrow suppression, nerve damage, and other toxic side effects. Many patients often end their treatment midway because they have difficulty tolerating the toxic side effects of chemotherapy. However, the bone marrow suppression of camptothecin local chemotherapy is mostly the suppression of leukocytes, so the application of Chinese medicine treatment to improve the suppression of leukocytes by camptothecin is of great clinical significance. After the application of traditional Chinese medicine in this study, it could be seen from Figure 3 that the leukocyte level in the control group was  $3.21 \pm 1.24$ , and after traditional Chinese medicine treatment, the leukocyte level was  $4.37 \pm 1.23$ , and there was a significant difference in the leukocyte count between the two groups ( $P < 0.05$ ). Results showed that the leukocyte count after traditional Chinese medicine treatment was significantly higher than that of the patients in the control group, suggesting that traditional Chinese medicine could effectively enhance the body's immune and the bone marrow hematopoietic capacity of bladder cancer patients after surgery.

**3.5. Comparison of Indicators Related to T-Lymphocyte Subsets.** Although radiotherapy and chemotherapy for bladder cancer after surgery can prolong patients' disease-free survival and reduce mortality, most patients have apparent adverse effects and suppressed immune function. Immunological studies have shown that the occurrence, development, and prognosis of tumors are directly related to the immune function of the body, especially the T cell-mediated cellular immunity.

T cells mainly include two subpopulations: CD4+ and CD8+. Traditionally, CD4+ is considered as helper T cells and CD8+ as suppressor T cells, so the ratio of CD4+, CD8+, and CD4+/CD8+ cells is measured to directly reflect the cellular immune function of patients.

The level of CD3+ was  $53.12 \pm 6.24$  in the control group and  $60.23 \pm 7.14$  in the observation group, and the level of CD3+ was elevated by Chinese medicine treatment. The CD4+ in the control group was  $40.21 \pm 5.12$  and  $49.01 \pm 3.48$  in the observation group. The CD8+ and CD4+/CD8+ in the control group were  $35.23 \pm 4.87$  and  $1.14 \pm 0.17$  and  $31.68 \pm 3.92$  and  $1.55 \pm 0.16$  in the observation group, respectively. The results showed that the levels of CD3+ and CD4+ were significantly increased, the CD8+ level was decreased, and CD4+/CD8+ was significantly increased compared with the control group ( $P < 0.05$ ), suggesting that the use of traditional Chinese medicine can effectively enhance the immune function of the body of bladder cancer patients after surgery (Figure 4).

**3.6. Comparison of Blood Routine Related Indexes between Two Groups of Patients before and after Treatment.** The platelet, neutrophil, and hemoglobin levels of patients with bladder cancer after surgery were normal, indicating that traditional Chinese medicine did not cause abnormal changes in blood routine and adverse reactions. In addition, the application of traditional Chinese medicine could effectively reduce the side effects produced by chemotherapy. The Hb and PLT levels of patients in the control group were  $121.33 \pm 12.32$  g/L and  $209.31 \pm 11.97$  10<sup>9</sup>/L, respectively, and the Hb and PLT levels of the observation group were  $102.34 \pm 6.14$  g/L and  $161.21 \pm 9.74$  10<sup>9</sup>/L, respectively. After treatment with traditional Chinese medicine, the Hb and PLT levels were significantly lower in the control group than the observation group ( $P < 0.05$ , Figure 5).

**3.7. Improvement in Quality of Life.** Patients' symptom improvement and quality of life were scored from the first day of treatment to the end, with reference to the clinical symptom score (Figure 6) and Carlsbad score (Figure 7) in both groups. The clinical symptom scores of patients in the observation group were  $(21.32 \pm 3.01)$  significantly increased compared to the patients in the control group ( $8.72 \pm 2.87$ ), which illustrated that Chinese medicine could improve the quality of life of patients (Figure 6).

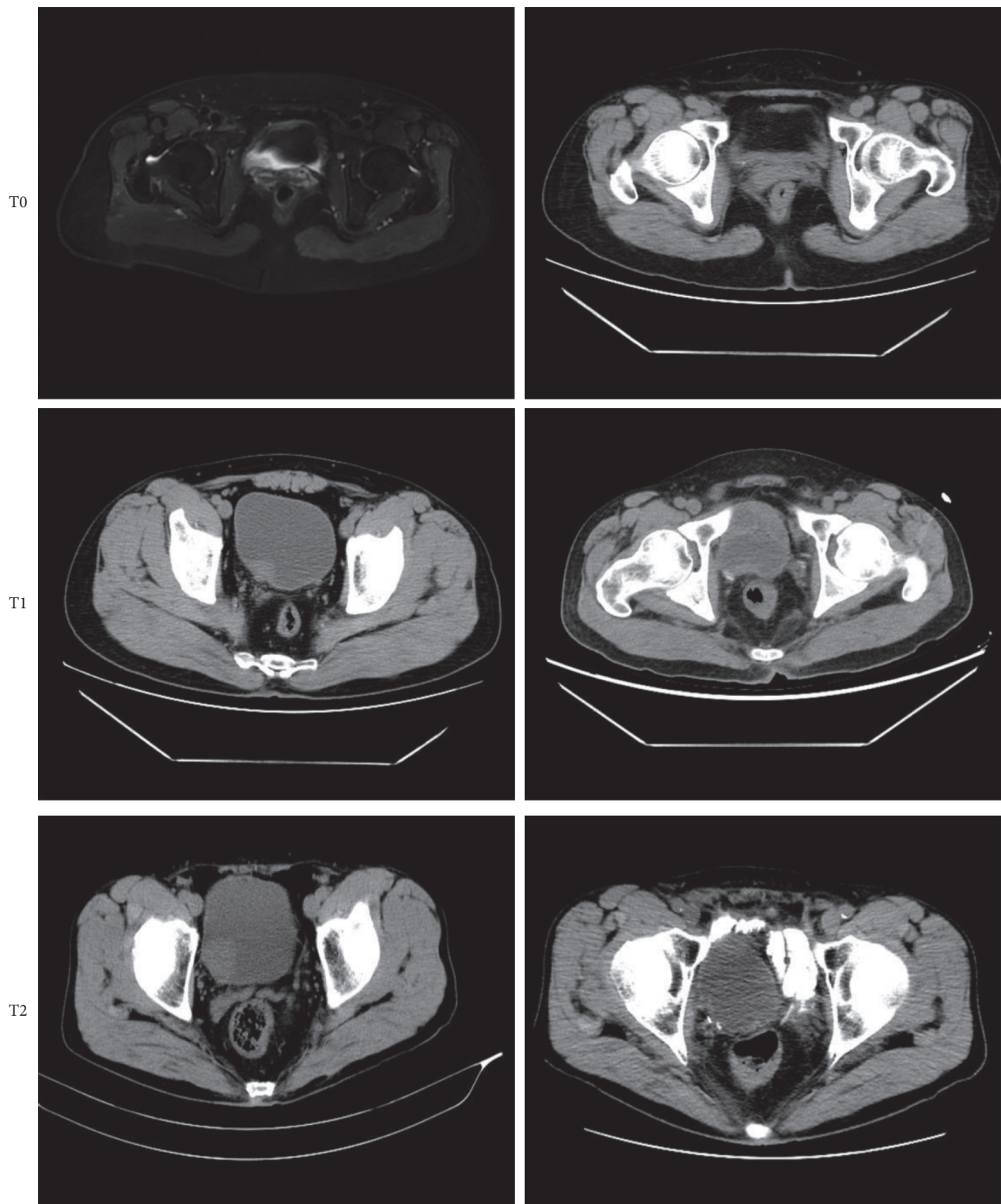


FIGURE 1: MRI image of the patient. Uppercase letters represented the patient's preoperative images and lowercase letters represented the patient's postoperative images.

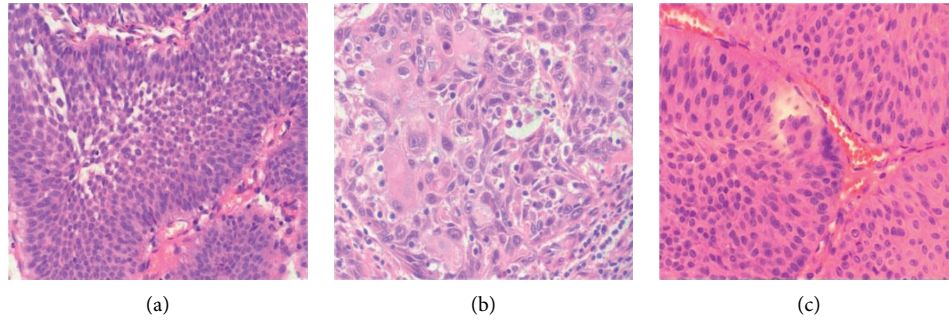


FIGURE 2: Pathological pictures of different stages of bladder cancer (×400). (a) T0. (b) T1. (c) T2.

TABLE 3: Incidence of adverse reactions to bladder irrigation chemotherapy.

Characteristics	Observation group	Control group
Systemic symptoms		
Malaise	2 (8.3%)	5 (21.%)
Hypothermia	1 (4.2%)	3 (13.0%)
Weight loss	0	1 (4.3%)
Skin reaction	0	1 (4.3%)
Gastrointestinal reactions	0	1 (4.3%)
Vomiting	0	1 (4.3%)
Anorexia	1 (4.2%)	3 (13.0%)
Constipation	1 (4.2%)	4 (17.4%)
Other adverse reactions		
Frequent urination	3 (12.5%)	8 (34.8%)
Urinary urgency		
Painful urination		
Lower abdominal pain		

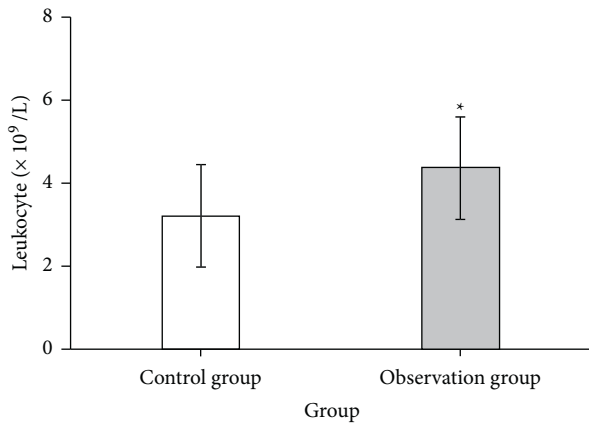


FIGURE 3: Comparison of leukocyte levels between the observation group and the control group. \* $P < 0.05$ .

#### 4. Discussion

Bladder cancer is one of the most common urinary system cancers and is receiving increasing attention because of its high incidence and recurrence rate. Moreover, due to the improvement of living standards and related auxiliary examinations such as urological CT and cystoscopy, bladder tumors have been diagnosed earlier and more sensitively. NMIBC is preferred to be treated with TURBT, and MIBC is mostly treated with radical cystectomy or bladder-preserving combination therapy.

Recurrence occurs in 60% to 70% of NMIBC patients within 1 to 2 years after TURBT treatment, and tumor

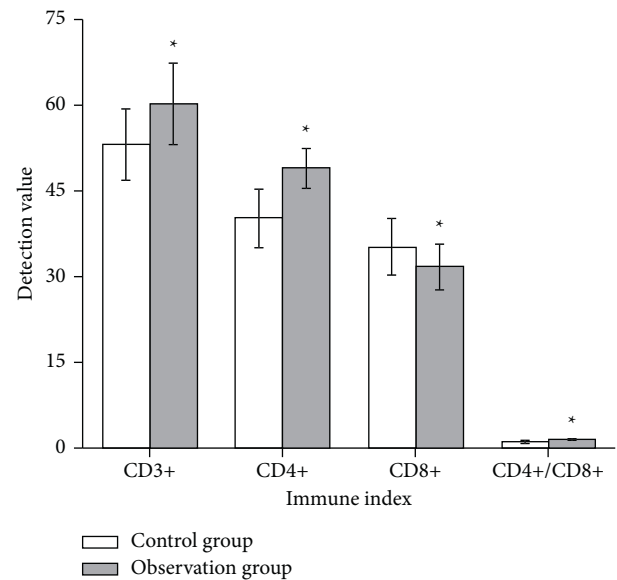


FIGURE 4: Comparison of indicators related to T-lymphocyte subsets in two groups of patients. \* $P < 0.05$ .

recurrence may be at risk for higher malignancy and greater invasive and metastatic capabilities [15]. The occurrence of bladder cancer is multicentric, and the possibility of cancer cell shedding and implantation inevitably exists preoperatively and intraoperatively. The possibility of incomplete tumor removal exists in both TURBT and partial cystectomy, which may be partly responsible for the recurrence and progression of bladder tumors. Moreover, the higher

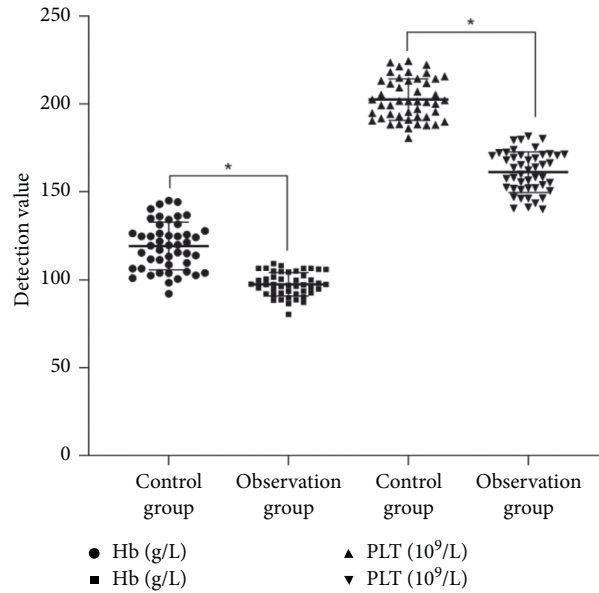


FIGURE 5: Comparison of routine blood-related indicators between two groups of patients.  $*P < 0.05$ .

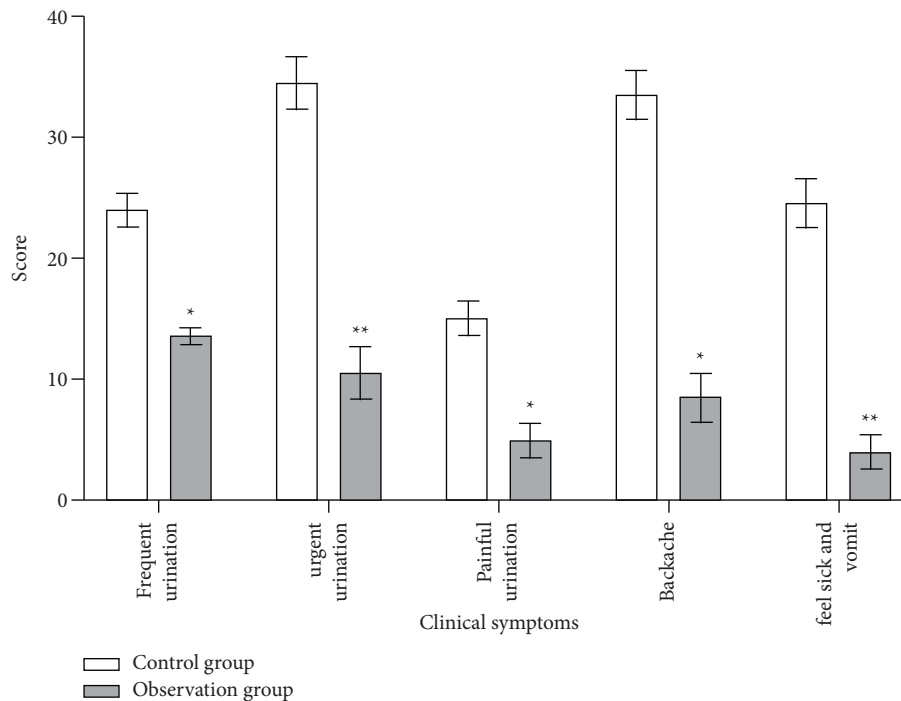


FIGURE 6: Clinical symptom score of each clinical symptom between two groups of patients.  $*P < 0.05$ ;  $**P < 0.01$ .

recurrence rate and possible accompanying tumor progression are important reasons affecting their prognosis. Therefore, to improve the prognosis of bladder cancer, complete removal of the tumor and the shed and grown cancer cells become the main purpose.

A safe, noninvasive, and relatively accurate way of preoperative diagnosis, postoperative outcome assessment, and prediction is sought to improve long-term survival. CT and MRI are now commonly used for imaging to evaluate efficacy. However, CT has limitations due to radiation and

false negatives and difficulty in characterizing some recurrent lesions. In contrast, MRI is free of radiation concerns and has a high soft-tissue resolution. MRI provides more diagnostic information and facilitates the detection of residual or recurrent lesions. Magnetic resonance diffusion-weighted imaging (MRI-DWI) is a noninvasive imaging technique that belongs to functional imaging. It reflects the information of living tissue structure and cell density by detecting the diffusion motion of water molecules. It is the only method to observe the movement of water molecules in

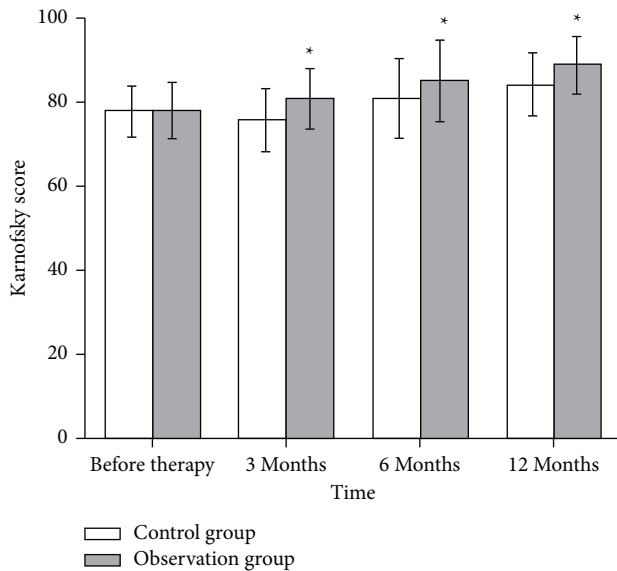


FIGURE 7: Carlsbad score of patients in both groups. \* $P < 0.05$ .

the body and has been maturely applied to imaging neurological diseases.

The results of this study showed that the percentage of CD4+ and CD3+ cells and the CD4+/CD8+ ratio of patients in the observation group were significantly increased compared with the control group ( $P < 0.05$ ). Better clinical results were achieved, and no adverse effects were observed throughout the drug administration. Our findings suggest that the use of traditional Chinese medicine treatment could significantly improve the cellular immune function of the body, improve the hematopoietic function of bone marrow, and have fewer toxic side effects, which has a certain effect on the prevention of recurrence and metastasis after bladder cancer surgery. For postoperative residual or recurrent lesions, through long-term follow-up review and MRI-DWI image control analysis, most of the residual or recurrent tumors were located in the marginal part of the original cancer foci; the appearance of slightly longer signals at the margins after TURBT often suggested recurrence; dynamic enhancement scans showed fast-in and fast-out performance; the scope of recurrent lesions would increase with longer follow-up time; and the time of recurrence was mainly 12 months after surgery. Long-term follow-up review and MRI-DWI image control analysis revealed that most of the tumor residuals or recurrences were located in the marginal part of the original cancer foci. The appearance of slightly longer signals at the margins after TURBT often suggested recurrence; dynamic enhancement scans showed fast-in and fast-out manifestations; the scope of recurrent lesions increased with longer follow-up time; and the recurrence time was mainly 12 months after surgery. However, the number of cases in this study was small and the observation and follow-up period was short. In addition to the continued follow-up of existing cases, a larger, multicenter, prospective, and longer-term clinical study was needed to confirm the value of the application of Xiaoji Shenqi Decoction.

## 5. Conclusion

The efficacy of Chinese medicine in preventing the recurrence of bladder cancer after surgery was satisfactory, and it had a higher recurrence-free survival with a higher safety profile. Hence, it merits encouragement in clinical application.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Hengxin Qi and Yuefeng Pan contributed equally.

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## Research Article

# Efficacy of Applying Kanglaite Injection under Incentive Nursing Intervention in Treating Patients with Advanced Penile Carcinoma and Its Effect on Treatment Compliance

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**Objective.** To explore the efficacy of applying Kanglaite (KLT) injection under incentive nursing intervention (INI) in treating patients with advanced penile carcinoma and its effect on patient treatment compliance. **Methods.** The clinical data of 120 patients with advanced penile carcinoma treated in the Affiliated Hospital of Southwest Medical University from February 2019 to February 2020 were retrospectively analyzed, and the patients were equally divided into the experimental group ( $n=60$ ) and control group ( $n=60$ ) according to their admission order. All patients received the KLT injection treatment; those in the control group accepted the conventional nursing; and on this basis, those in the experimental group accepted INI, including psychological nursing intervention, which was conducted concurrently with the treatment, to compare their short-term efficacy, treatment compliance, degree of cancer-related fatigue (Brief Fatigue Inventory), and negative emotion scores (Hospital Anxiety and Depression Scale) between the two groups. **Results.** Compared with the control group, the experimental group presented a significantly higher objective remission rate (58.3%) ( $P<0.05$ ), higher rates of excellent and good treatment compliance ( $P<0.05$ ), and lower degree of cancer-related fatigue and negative emotion scores ( $P<0.001$ ). **Conclusion.** INI can improve the negative emotions in patients with advanced carcinoma of the penis, alleviate their degree of cancer-related fatigue, promote their treatment compliance, and achieve a more significant efficacy of applying the KLT injection treatment, so it should be promoted in practice.

## 1. Introduction

Carcinoma of the penis is a malignant tumor that originates from the glans penis, coronal sulcus, the mucosa of the prepuce inner plate, and the skin of the penis, with an incidence accounting for more than 90% of all penile tumors [1, 2]. At present, academia has not clarified the pathogenic factor, but it is believed that smegma, chronic inflammatory stimulation, and so on are closely related to its incidence [3, 4]. In general, early penile cancer is less malignant, and patients can achieve a surgical cure rate of 75% [5]. However, advanced penile cancer patients with inguinal lymph node metastasis only have a 5-year survival rate of 20%, and may even die within 2 years in case of no comprehensive therapeutic measures [6, 7]. Therefore, additional therapeutic

measures should be performed for such patients based on chemotherapy. Kanglaite (KLT) injection is a common drug used in the clinic for treating malignant tumors, which mainly contains coix seed oil, granulesten, and glycerol for injection, of which coix seed is a bidirectional broad-spectrum anticancer injection emulsion that can effectively enhance the patients' immune function and at the same time inhibit the proliferation of malignant tumor cells [8]. Clinical studies have shown that KLT injection can improve the quality of life and increase the short-term survival rate of patients, but it has no obvious improvement on the psychological condition of patients [9].

Affected by social culture, medical conditions, family conditions, and other subjective and objective factors, patients with advanced penile cancer usually face great physical

and mental stress, and long-term psychological stress will lead to neurological disorders in patients, which will eventually trigger somatic symptoms and result in decreased treatment effect. To improve the psychological status of patients, some scholars have proposed the incentive nursing intervention (INI) in practice [10], which refers to effective education, guidance, and emotional support for the specific physical and mental conditions of patients and high-quality nursing personnel, thereby helping patients with building confidence and improving treatment compliance [11]. No studies on the application of INI in treating advanced penile cancer patients with KLT injection have been conducted in previous literature. Based on this, the efficacy of adopting KLT injection treatment under INI in treating such patients and its effect on patient treatment compliance were explored herein, with the results reported below.

## 2. Data and Methods

**2.1. Study Design.** It was a retrospective study and conducted from February 2019 to February 2020 in Affiliated Hospital of Southwest Medical University to explore the efficacy of adopting KLT injection treatment under INI in treating patients with advanced carcinoma of the penis and its effect on patient treatment compliance.

**2.2. Enrolment of Research Objects.** The clinical data of patients with advanced carcinoma of the penis treated in Affiliated Hospital of Southwest Medical University from February 2019 to February 2020 were retrospectively analyzed. The patients were included according to the following criteria: (1) the patients were diagnosed with penile carcinoma after biopsy [12] and were in stage III or IV according to the Jackson staging method [13]; (2) the patients were treated in our hospital throughout, with no occurrence of death, transfer, and discontinuation of therapy; (3) the patients had complete clinical data; and (4) the patients did not have other serious complications. The patients were excluded according to the following criteria: (1) the patients were unable to communicate with others because of hearing disorder, language disorder, unconsciousness, or mental diseases; (2) during treatment, the patients quit, died, changed the treatment regimen, or were found missing in the follow-up visit; (3) the patients suffered from other serious organic diseases; and (4) the patients' clinical data were incomplete.

**2.3. Steps.** A total of 120 patients were included in the study and equally divided into the experimental group and control group according to their admission order, with 60 cases each. On the day that the patients agreed to join the study, the study team collected their sociodemographic data and clinical performance data, and the nursing personnel made no implications except for explaining the questionnaires; after filling, the questionnaires were taken back and verified for completeness, and such process was repeated after the end of nursing. In case of any omissions, the patients were

encouraged to complete the questionnaires based on no violation of the voluntary principle to ensure integrity and authenticity.

**2.4. Moral Consideration.** The study met the principle of the World Medical Association Declaration of Helsinki [12] and was approved by the ethics committee of Affiliated Hospital of Southwest Medical University. The study team explained the purpose, meaning, content, and confidentiality of the study to the enrolled patients, and the patients signed the informed consent.

**2.5. Criteria of Quitting the Experiment.** For the patients with one of the following situations and who were judged unsuitable for continuously accepting the experiment by the study team, their case records would be reserved but not used for data analysis: (1) those who experienced adverse events or serious adverse events; (2) those who presented condition worsened during the experiment; (3) subjects developed certain severe comorbidities or complications; and (4) subjects were unwilling to continue with the clinical trial and proposed the request of withdrawal from the clinical trial to the study team.

**2.6. Methods.** All patients received two courses of KLT injection treatment; that is, 200 ml of KLT injection (manufactured: Zhejiang Kanglaite Pharmaceutical Co., Ltd.; NMPA approval no. Z10970091) was administered once daily via slow intravenous infusion for 21 d as one course, and the next course was proceeded 5 days after the end of the first course.

Meanwhile, the patients in the control group received conventional nursing; namely, their vital signs were closely monitored and guidance for diet, exercise, drug use, and so on was given, with the specific methods. (1) Drug use: the patients with carcinoma of the penis usually felt pain at the penis and scrotum, so the nursing personnel could administer the paracetamol oxycodone sustained-release tablets (manufactured: China National Pharmaceutical Industry Corporation Ltd.; NMPA approval no: J20171086) to the patients under medical supervision and at the same time perform continuous infusion with a micro analgesic pump, establish the nursing record on observation of micro analgesic pump and multipurpose administration to effectively monitor the patients' condition, and pay special attention to the adverse reactions after administration, and for patients with local swelling, their infusion part should be changed in time. According to the medical advice, the nursing personnel needed to help the patients with perineal tumor rupture in changing their dressings twice a day in strict accordance with the aseptic operation; the dressings were fully soaked with 0.9% normal saline before changing to avoid pain sensation and bleeding, the thickness of sterile gauze for cover should be appropriate to avoid infection, and the frequency of dressing changing could be increased if necessary based on the dressing status. The dressing condition at the tumor was observed regularly after dressing

change, and the corresponding records were made. (2) Preventing adverse reactions: for patients with constipation, the nursing personnel could give them laxatives and glycerine enema (if necessary), help them with forming a normal bowel evacuation habit, repeatedly advise them to eat more food with crude fiber, fresh fruits, and vegetables, and increase exercise frequency, and in case of diarrhea, the patients should inform the nursing personnel immediately. For patients with edema of both lower limbs, the nursing personnel should give them diuretic drugs, help them with massage and turning over, and repeatedly advise them to avoid sitting for a long time to prevent skin rupture. For patients with vomiting, the nursing personnel should give them drugs that inhibit gastric acid, ask the family members of the patients to prepare light food, and inform the patients of avoiding hypertense. (3) Health education: the nursing personnel distributed the health education handbooks prepared by our hospital to the patients and popularized the relevant knowledge about carcinoma of the penis to the patients and their family members to improve their self-care ability and alleviate their negative emotions.

On this basis, INI was implemented to the patients in the experimental group with the following methods: (1) the nursing personnel were trained by a professional psychologist to comprehensively learn to help the patients with alleviating their negative emotions by incentive methods such as making use of target, emotion, and materials and to promote the scientific nature and professionalism of INI with evidence-based nursing. (2) After admission, the one-on-one mental intervention by nursing personnel was conducted on the patients in the experimental group. The nursing personnel first carefully read the patients' basic information and then prepared corresponding nursing plans according to the patients' condition, educational degree, personality, and mental state, to provide them with specific health education and emotional support with individual differences. (3) The patients with advanced carcinoma of the penis were prone to negative emotions such as dysesthesia and anxiety, so the nursing personnel should pay attention to the changes in their mental state and emotions, increase the frequency of communicating with them, and explain relevant knowledge about the disease in one-on-one communication, thereby relieving their negative emotions and promoting their treatment compliance. (4) Before chemotherapy, the nursing personnel should carefully listen to the patients' demands, encourage them through verbal communication, and help them with solving their reasonable demands, to reduce their anxiety and enable them to build confidence; after solving the problems, praises and encouragement were given to the patients, so that they could bravely share their problems, fully understand their value, face the difficulties and challenges brought by treatment in a more positive way, and reduce their worries. (5) The nursing personnel set phased targets and good examples for the patients and praised the patients when they finished every small target and made any progress. (6) The nursing personnel needed to think about the patients, keep a sincere and caring attitude, and feel for the patients during communication, thus enabling the patients to promote their trust in the nursing personnel and then increase treatment compliance.

## 2.7. Observation Criteria

**2.7.1. General Information.** The general information extraction forms were created by the patients themselves, including the in-patient number, name, age, body mass, BMI, cancer stage, method of paying medical fees, marital status, monthly income, educational degree, place of residence, and living habits.

**2.7.2. Short-Term Efficacy.** According to the Response Evaluation Criteria in Solid Tumors (RECIST) established by WHO in 2000 [14], the patients' condition was classified into complete response (CR, disappearance of lesions, no new lesions, and tumor markers restored to normal for over one month), partial response (PR,  $\geq 30\%$  decrease in SLD (the sum of the longest diameters of target lesion) for over one month), stable disease (SD, no PR-no PD), and progressive disease (PD,  $\geq 20\%$  increase in SLD, or new lesions). The treatment effect of patients was compared by the objective remission rate (ORR, CR + PR) and disease control rate (DCR, CR + PR + SD).

**2.7.3. Treatment Compliance.** It was considered as excellent compliance in case that the patients fully accepted the treatment regimen established by the physician and the nursing regimen established by the nursing personnel, went through the treatment smoothly, and cooperated with various nursing measures; good compliance in case that the patients basically accepted the treatment regimen established by the physician and the nursing regimen established by the nursing personnel, finished the most of the treatment and cooperated with various nursing measures from time to time; and poor compliance in case that the patients only cooperated with the treatment when the disease was aggravated or, once in a while, could not understand various adverse reactions occurred during treatment and failed to cooperate with the nursing measures. After nursing, the treatment compliance of patients in both groups was compared.

**2.7.4. Degree of Cancer-Related Fatigue.** The degree of cancer-related fatigue of patients before and after treatment was evaluated by the Brief Fatigue Inventory (BFI) [15], which has been validated in international literature for its credibility and sensitivity. On a scale of 0–10 points, 0 points indicated no fatigue, 1–3 points indicated mild fatigue, 4–6 points indicated medium fatigue, and 7–10 points indicated severe fatigue.

**2.7.5. Negative Emotion Scores.** The emotional state of patients before and after treatment was evaluated by Hospital Anxiety and Depression Scale (HAD) [16], which has been validated in international literature for its credibility and sensitivity. On a scale of 0–42 points, 0 points indicated no anxiety, and higher scores indicated the more serious anxiety and depression.

TABLE 1: Comparison of patients' general information.

Group	Experimental ( $n = 60$ )	Control ( $n = 60$ )	$X^2/t$	$P$
Age (years)				
Range	35–74	34–76		
Mean age	$60.12 \pm 3.65$	$59.87 \pm 3.54$	0.381	0.704
Mean body weight (kg)	$59.56 \pm 2.54$	$59.17 \pm 2.57$	0.836	0.405
BMI ( $\text{kg}/\text{m}^2$ )	$23.98 \pm 1.65$	$23.88 \pm 1.58$	0.339	0.735
Cancer stage			0.139	0.709
III	35	37		
IV	25	23		
Payment method for medical fee				
Medical insurance	32	30	0.134	0.715
Commercial insurance	20	18	0.154	0.695
Others	8	12	0.960	0.327
Marital status			0.196	0.658
Married	46	48		
Unmarried/divorced/widowed	14	12		
Place of residence			0.034	0.855
Urban area	28	27		
Rural area	32	33		
Monthly income (yuan)			0.035	0.853
$\geq 4000$	25	24		
$< 4000$	35	36		
Life habit				
Smoking history	30	28	0.134	0.715
Drinking history	27	29	0.134	0.714
Educational degree			0.034	0.854
Senior high school and below	26	27		
College and above	34	33		

**2.8. Statistical Processing.** In this study, the data processing software was SPSS20.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), items included were enumeration data and measurement data, methods used were  $X^2$  test and  $t$ -test, and differences were considered statistically significant at  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Patients' General Information.** No statistical differences in the patients' general information between the two groups were observed ( $P > 0.05$ ). See Table 1.

**3.2. Comparison of Patients' Short-Term Efficacy.** The ORR of the experimental group was 58.3%, which was remarkably higher than that of the control group ( $P < 0.05$ ). See Table 2.

**3.3. Comparison of Patients' Treatment Compliance.** The rates of excellent and good treatment compliance of patients were higher in the experimental group than in the control group ( $P < 0.05$ ). See Figure 1.

The numbers of patients with excellent, good, and poor treatment compliance in the experimental group were 48 (80.0%), 10 (16.7%), and 2 (3.3%), respectively; and the numbers of patients with excellent, good, and poor treatment compliance in the control group were 35 (58.3%), 13 (21.7%), and 12 (20.0%), respectively.

**3.4. Comparison of Patients' Degree of Cancer-Related Fatigue and Negative Emotion Scores.** Compared with the control group after treatment, the patients' degree of cancer-related fatigue and negative emotion scores of the experimental group were significantly lower ( $P < 0.001$ ). See Figure 2.

Figure 2(a) shows the BFI scores. The horizontal axis from left to right denotes before and after nursing; the lines with dots indicated the experimental group, and the lines with blocks indicated the control group. Before nursing, the BFI scores between the two groups were not statistically different ( $7.21 \pm 1.23$  vs.  $7.23 \pm 1.20$ ,  $P > 0.05$ ); and after nursing, the BFI scores were significantly lower in the experimental group than in the control group ( $5.10 \pm 0.54$  vs.  $6.15 \pm 0.65$ ,  $P < 0.001$ ).

Figure 2(b) shows the HAD scores. The horizontal axis from left to right denotes before and after nursing; the lines with dots indicated the experimental group, and the lines with blocks indicated the control group. Before nursing, the HAD scores between the two groups were not statistically different ( $34.65 \pm 2.21$  vs.  $34.68 \pm 2.23$ ,  $P > 0.05$ ); and after nursing, the HAD scores were significantly lower in the experimental group than in the control group ( $19.65 \pm 1.68$  vs.  $26.98 \pm 2.54$ ,  $P < 0.001$ ).

### 4. Discussion

Penile cancer is the most common malignant neoplasm of the penis. At present, academia has not clarified the pathogenic factor of penile cancer, but it is generally assumed

TABLE 2: Comparison of patients' short-term efficacy ( $n$  (%)).

Group	CR	PR	SD	PD	ORR	DCR
Experimental	5 (8.3)	30 (50.0)	15 (25.0)	10 (16.7)	35 (58.3)	50 (83.3)
Control	0 (0.0)	24 (40.0)	18 (30.0)	18 (30.0)	24 (40.0)	42 (70.0)
$X^2$	5.217	1.212	0.376	2.981	4.034	2.981
$P$	0.022	0.271	0.540	0.084	0.045	0.084

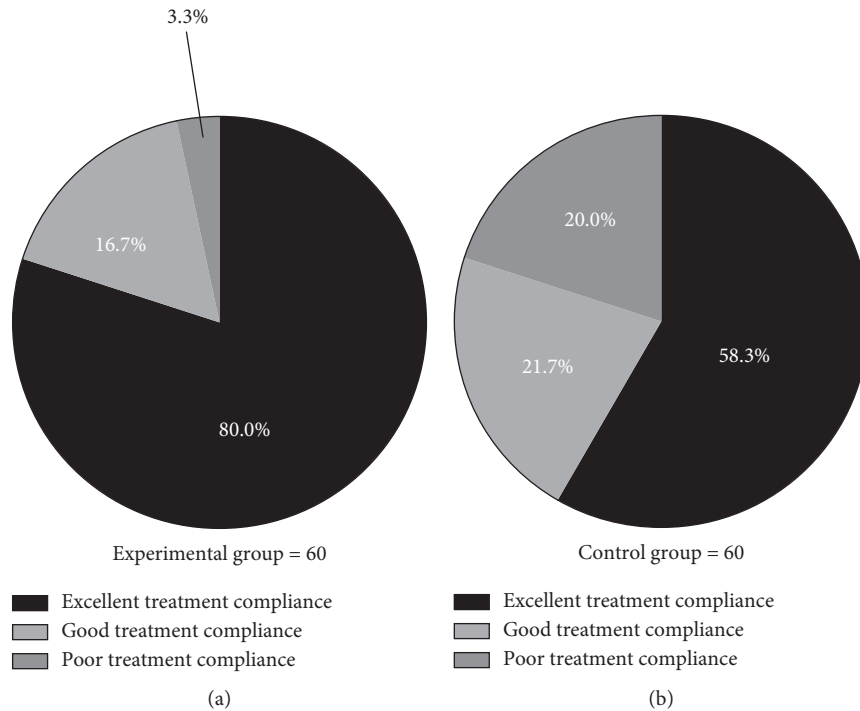


FIGURE 1: Comparison of patients' treatment compliance ( $n(\%)$ ). The black areas indicated excellent treatment compliance, the light gray areas indicated good treatment compliance, and the dark gray areas indicated poor treatment compliance. (a) Experimental group and (b) control group.

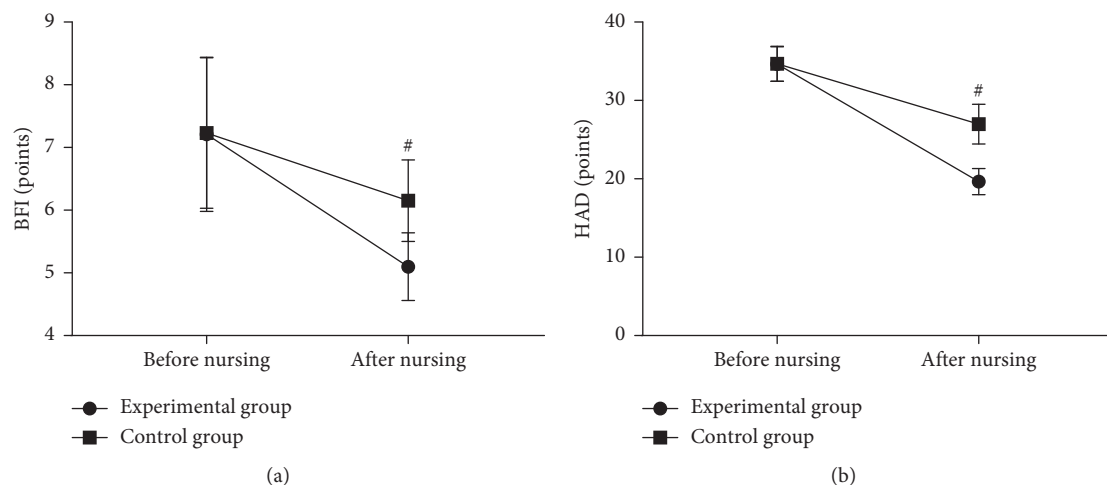


FIGURE 2: Comparison of patients' degree of cancer-related fatigue and negative emotion scores ( $\bar{x} \pm s$ , points). # means  $P < 0.001$ .

that phimosis, redundant prepuce, smegma, chronic inflammation, and so on are closely related, and country and region, ethnic folklore, religion, and life habits also affect the incidence to a certain extent [17]. In the 1950s, the incidence

of penile cancer in China ranked first in the male reproductive system malignancies, while, with increasing medical and health technologies nowadays, penile cancer has become a rare male tumor, with an incidence that accounts for only



1.0% of all male malignancies [18]. Clinical practice shows that most penile cancers are less malignant, and the cure rate can reach up to 80.0% in patients at the early stage of the disease, but advanced penile cancer patients with distant metastasis have a 5-year survival rate of only 20% [19] and poor prognosis. Chemotherapy is the main treatment modality for patients with advanced penile cancer because it can prolong the survival time of the patients, but it usually triggers organic responses in patients and leads to more serious psychological stress. Compared with conventional chemotherapeutic agents including pingyangmycin and 5-fluorouracil, KLT injection is safer and can accelerate the apoptosis of malignant cells, reduce the frequency of mitosis, and be beneficial in improving the comprehensive efficacy based on chemotherapy. However, advanced penile cancer usually causes severe mental irritation to patients, who will not only feel anxious and tense due to the medical economic burden, but also develop negative and hostile feelings caused by the ulcerated and malodorous penis, and some patients will even experience somatic symptoms due to the long-term poor mental health, leading to further reduced treatment adherence that is not conducive to the performance of clinical treatment and nursing.

As the concept of medical treatment has been changed in Chinese residents, the psychological state of patients with advanced cancer has become a recognized evaluation criterion for efficacy in the academic community [20], the nursing model solely centered on treatment can no longer meet the needs of clinical care, and the more targeted nursing based on humanities care and with remodeling of the patients' personality and dignity as an essence has become the important development direction in the care of such patients. INI is the more common nursing model for cancer patients in recent years, which aims to integrate emotional and physical support into all aspects of nursing, to make patients fully feel the care of nursing personnel, and thus be more cooperative with the nursing personnel's actions during clinical treatment [21]. The study by scholars Patel et al. showed that performing INI for patients with malignant tumors could reduce their scores of Anxiety Self-Rating Scale and Depression Self-Rating Scale [22], and this study also found that patients in the experimental group had a significantly lower degree of cancer-related fatigue and negative emotion scores after nursing than those in the control group ( $P < 0.001$ ), indicating that the nursing model was people-centered, practically felt for the patients, and stimulated the patients' positive mental state, thereby keeping their body in a highly excited state, enhancing their confidence in conquering the disease, and relieving their negative emotions. In many references, it was shown that negative emotions were important factors affecting patient treatment compliance, which was the key to ensuring the implementation of medical behaviors and nursing measures, and poor compliance could result in tumor recurrence and metastasis and seriously affect patient prognosis [23]. With INI, the penile cancer-related knowledge could be popularized through one-to-one communication for patients to form a more clear perception of the condition, which was beneficial for enhancing the clinical management efficacy of

the nursing personnel, and therefore the rates of excellent and good treatment compliance were significantly higher in the experimental group than in the control group ( $P < 0.05$ ). The studies by scholars Mehta et al. showed that a good nurse-patient relationship was the basis of treatment [24], and INI could enhance patients' trust in nursing personnel, maintain their correct expectations during treatment, and promote their cooperation, so the ORR of the experimental group was significantly higher than that of the control group ( $P < 0.05$ ), denoting INI could sufficiently mobilize patients' enthusiasm and reduce the adverse effects of their negative emotions and hostility to the treatment, thus achieving better therapeutic outcomes.

## 5. Conclusion

Based on KLT injection treatment, INI can ease the negative emotions in patients with advanced carcinoma of the penis, improve their degree of cancer-related fatigue, promote their treatment compliance, and achieve a more desirable treatment effect so such nursing method should be promoted in practice.

## Data Availability

The data used to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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## Research Article

# Effect of Psychological Intervention Combined with Dietary Guidance on Quality of Life and Long-Term Efficacy of Bushen Quyu Decoction in Treatment of Patients with Advanced Ovarian Cancer

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**Objective.** To study the effects of psychological intervention combined with dietary guidance on the quality of life and long-term efficacy of Bushen Quyu Decoction in the treatment of patients with advanced ovarian cancer. **Methods.** 220 patients with advanced (stages III to IV) ovarian cancer in our hospital from May 2015 to October 2018 were selected and randomly divided into a control group and an observation group, with 110 cases in each group. The patients in the control group received basic nursing care and treatment with Bushen Quyu Decoction, and the patients in the observation group were combined with psychological intervention and dietary guidance on the basis of the treatment of the patients in the control group. The clinical efficacy, nursing satisfaction, treatment compliance, quality of life, negative emotion comparison, and long-term efficacy of the two groups were compared. Moreover, the changes of immune function indexes and the content of tumor markers were compared between the two groups. **Results.** The total effective rate of treatment in the observation group (64.55%) was higher than that in the control group (31.82%). The nursing satisfaction of the observation group was 94.55%, the nursing satisfaction of the control group was 84.55%, and the difference was statistically significant ( $p < 0.01$ ). The treatment compliance of the observation group was 98.18%, the treatment compliance of the control group was 82.73%, and the difference was statistically significant ( $p < 0.0001$ ). After nursing, the Anxiety Self-Rating Scale (SAS) score and Self-Rating Depression Scale (SDS) score of the two groups of patients were decreased ( $* p < 0.05$ ), and the score of the observation group decreased more significantly ( $\Delta p < 0.05$ ). After nursing, the scores of the two groups of patients in social/family status, physical function, physiological function, and emotional status increased ( $* p < 0.05$ ), and the observation group was significantly higher than the control group ( $\Delta p < 0.05$ ). After nursing, the CD3+, CD4+, CD4+/CD8+ levels of the observation group were significantly higher than the control group ( $p < 0.05$ ). The CD8+ level of the observation group was significantly lower than the control group ( $p < 0.05$ ). After nursing, the levels of tumor markers in the two groups were decreased ( $* p < 0.05$ ), and the observation group was downregulated more significantly than the control group ( $\Delta p < 0.05$ ). The two-year cumulative survival rate of the observation group was 78.18%, and the two-year cumulative survival rate of the control group was 54.55%. The observation group was significantly higher than the control group ( $p < 0.05$ ). **Conclusions.** Psychological intervention combined with dietary guidance can significantly improve the quality of life and mental state of patients with advanced ovarian cancer, enhance the patient's immune function, reduce the serum tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen (CA199) levels, and improve survival rate and survival time, which has important clinical significance.

## 1. Introduction

Ovarian cancer is one of the common gynecological malignancies in clinic with high morbidity and mortality [1]. In recent years, the incidence of ovarian cancer in young women has been increasing year by year, and it is the fifth leading cause of cancer-related death in women worldwide and also the main cause of death of gynecological malignant tumors, attracting more and more social attention [2]. Ovarian cancer has no obvious clinical symptoms in the early stage and is easily ignored by patients. As time goes by and the condition deteriorates, it is often in the middle and late stages when diagnosed. Advanced ovarian cancer is prone to spread and metastasis, which seriously threatens the health and life safety of women [3]. So far, the most effective way to treat advanced ovarian cancer is chemotherapy, which can inhibit the growth and spread of tumor cells through the pharmacological effects of chemotherapeutic drugs. However, chemotherapy takes a long time, and the process is more painful, which will bring health to the patient. The double burden of economy affects the physical and mental health of patients and is not conducive to the recovery of patients [4, 5]. In recent years, Chinese medicine adjuvant therapy has been widely used in the clinical treatment of ovarian cancer. By regulating the immune function of the body, it can improve the toxic and side effects caused by chemotherapy, thus inhibiting the metastasis and recurrence of cancer cells, improving the clinical efficacy, and prolonging the survival time [6, 7]. Clinical experience has shown that most patients with ovarian cancer will have different degrees of psychological problems, such as anxiety, anger, depression, giving up, and other psychological changes, so it is very necessary to implement appropriate psychological care interventions for patients [8]. Malnutrition in patients with ovarian cancer can also lead to an increase in their mortality, which can be corrected by standardized nutritional therapy [9]. Therefore, the continuous psychological intervention and the formulation of a reasonable diet plan for the patients can help improve the patients' negative psychological mood, increase the patients' confidence and courage to treat the disease, so as to improve the clinical efficacy, improve the patient's quality of life, and prolong the patient's survival time. In this study, 220 patients with advanced ovarian cancer treated in our hospital from May 2015 to October 2018 were selected as the research objects, aiming to explore the effects of psychological intervention combined with dietary guidance on the quality of life and long-term efficacy of Bushen Quyu Prescription in the treatment of advanced ovarian cancer patients. The report is as follows.

## 2. Materials and Methods

**2.1. General Information.** 220 cases of advanced ovarian cancer patients treated in our hospital from May 2015 to October 2018 were randomly divided into the control group and observation group, each with 110 cases. Control group included 34 to 70 years old, average ( $55.23 \pm 7.14$ ) cases;

clinical stage included 68 cases of stage III and 42 cases of stage IV; tumor type included 12 cases of undifferentiated carcinoma, 41 cases of mucinous carcinoma, 9 cases of embryonic carcinoma, 14 cases of granular carcinoma, and 34 cases of serous carcinoma; observation group included 33–72-year-old cases; clinical stage included 65 cases of stage III and 45 cases of stage IV; tumor types included 14 cases of undifferentiated carcinoma, 37 cases of mucinous carcinoma, 11 cases of embryonic carcinoma, 13 cases of granular carcinoma, and 35 cases of serous carcinoma. Inclusion criteria were as follows: all patients who were diagnosed by pathological diagnosis and met the diagnostic criteria in the "Guidelines for the Diagnosis and Treatment of Ovarian Malignant Tumors" [10] and patients  $\geq 18$  years old and able to communicate normally; the survival time of patients was predicted to exceed 6 months. Those who were treated for the first time were also included. Exclusion criteria were as follows: patients with heart damage or liver and kidney abnormalities; patients with mental disorders, mental disorders, or loss of consciousness; patients with other types of malignant diseases; and women in pregnancy and lactation. There was no statistically significant difference between the two groups of patients in general information, such as age, tumor type, and clinical stage ( $p > 0.05$ ), and they were comparable. The research goals and procedures of this study have been clarified by patients and their families, and they have voluntarily signed an informed consent form, which has been approved and supported by the medical ethics committee of Affiliated Hospital of Shaoxing University (Approval No. 20150112-3).

**2.2. Treatment Method.** Patients in the control group were treated with conventional nursing and Bushen Quyu Decoction, and the observation group was treated with psychological intervention and dietary guidance on the basis of the control group.

Recipe for invigorating the kidney and removing blood stasis was as follows: *Astragalus* 25 g, *Taizishen* 20 g, *Shan Ci* mushroom 10 g, *Scutellaria barbata* 20 g, *Ligustrum lucidum* 15 g, *Codonopsis* 20 g, *Polygonatum* 15 g, *Atractylodes macrocephala* 20 g, *Poria* 20 g, chicken internal gold 10 g, and *Scrophulariaceae* 20 g. Decoction and extract were about 300 ml of juice, 1 dose/d, divided into two warm doses in the morning and evening, 4 weeks as a course of treatment, and two consecutive courses of treatment.

Psychological nursing methods were as follows. Nursing staff in the observation group took the initiative to communicate with patients and their families patiently before treatment, understand the patients' condition, personality, psychology, family situation, disease cognition, and other conditions, and listen to their feelings carefully, popularize the knowledge of ovarian cancer-related diseases for patients, improve their understanding of ovarian cancer, eliminate the doubts of patients and their families, pay attention to the patient's emotional changes and psychological state, inform the patient in advance of the possible adverse reactions during the treatment, and avoid causing the patient's emotional



fluctuations, actively communicate with patients, avoid talking about sensitive topics, encourage patients to express their feelings, and listen to them patiently and comfort them, so that they can feel the care and attention of medical staff, so as to improve the compliance of patients with treatment. Family members of patients should strengthen emotional support, so that patients can feel the support and care from family members, relieve anxiety and depression, and illustrate the positive effect of a good attitude on the recovery of the disease. Besides, regular lectures on successful cases should be held to encourage patients to build up their confidence and determination to overcome the disease.

Diet care method was as follows. According to the characteristics of the patient's condition and their own conditions, the observation group was made a personalized diet plan. The patients were instructed to maintain a light diet, ate more high-fiber, high-vitamin, low-fat, and low-salt foods, and ate more fruits and vegetables during bed rest, avoided irritating foods, avoided tobacco and alcohol, and avoided intake of foods that are too high in sugar or fat. The dietary principle was to eat small and frequent meals, chew slowly, and avoided overeating.

**2.3. Observation Index.** (1) We compare the clinical efficacy of the two groups. According to the relevant content in "Evaluation Criteria for Treatment Efficacy of Solid Tumors-RECIST" [11], the efficacy is determined 4 weeks after the end of treatment. Regarding complete remission, the tumor continues to disappear for  $\geq 4$  weeks or completely disappear; for partial remission, tumor shrinkage was  $>70\%$ ; for stable cases, tumor shrinkage was  $30\%$  to  $70\%$ ; for progression, after treatment, the extent of the lesion cannot be controlled, and the increase was  $>20\%$  or new lesions. The total effective rate of treatment (%) = (complete remission + partial remission)/total number of cases  $\times 100\%$ . (2) We compare the nursing satisfaction and treatment compliance of the two groups. A satisfaction survey questionnaire was used to evaluate the patient's satisfaction with the nursing staff's service attitude, operational skills, and humanistic care. The full score is 100 points: 90 points or more are considered very satisfactory, 70–90 points are considered relatively satisfactory, and less than 70 points are considered dissatisfied. The full score for compliance is 100 points: 90 points or more are full compliance, 70–90 points were for partial compliance, which refers to patients' incomprehension and resistance to some treatments and nursing procedures, and noncompliance was below 70 points, which refers to patients' serious resistance and noncompliance. (3) We compare the negative emotional state of the two groups of patients before and after intervention and using the anxiety self-rating scale and depression self-rating scale to evaluate [12]. The SAS is a self-rating scale used to evaluate the anxiety of patients. It has 20 items and is scored in reverse from 4 to 1 point. The higher the score, the higher the degree of anxiety. The 20 items of the SDS are scored on a scale of 1 to 4. The higher the score, the deeper the depression. (4) We compare the quality of life of the two groups of patients. The ovarian cancer specific scale (Functional Assessment of Cancer TherapyOvarycancerV4.0,

FACT-OV4) was used to evaluate the quality of life [13], including social/family status, emotional status, functional status, and physiological status. The higher the score, the better the quality of life. (5) We compare the long-term efficacy of the two groups of patients. The follow-up was 2 years, the follow-up frequency was 2 months, the patient's survival time was recorded, and the two-year cumulative survival rate was calculated. (6) We compare the levels of T cell subsets of the two groups of patients after treatment. (7) We compare the changes of tumor markers in the two groups before and after treatment. 5 ml of fasting cubital venous blood was collected from the patient and then centrifuged at a radius of 12.5 cm, 3 000 r/min for 10 min. The flow cytometry fluorescent antibody alkaline phosphatase staining method was used to detect T lymphocyte subsets (CD3+, CD4+, CD8+, and CD4+/CD8+ cell ratio) levels, and ELISA method was used to detect tumor markers, including CEA and CA199.

**2.4. Statistical Method.** All statistical data are analyzed using SPSS23.0 statistical software (IBM, NY, USA) at least three times. Measurement data are expressed as mean  $\pm$  standard deviation (SD), using *t*-test. Counting data are expressed as rate [n (%)], using  $\chi^2$  test.  $p < 0.05$  was evaluated as statistically significant.

### 3. Results

**3.1. Comparison of the Clinical Efficacy between the Two Groups of Patients.** As shown in Table 1, the total effective rate (64.55%) in the observation group after treatment was higher, than that of total effective rate in the control group (31.82%) ( $p < 0.001$ ), indicating that the clinical efficacy of the observation group is better.

**3.2. Comparison of Nursing Satisfaction and Patient Treatment Compliance between the Two Groups.** The nursing satisfaction of the observation group was 94.55%, and that of the control group was 84.55%; the difference was statistically significant ( $p < 0.01$ ) (Table 2). The treatment compliance of the observation group was 98.18%, and the treatment compliance of the control group was 82.73%; the difference was statistically significant ( $p < 0.001$ ) (Table 3).

**3.3. Comparison of the Immune Function of the Two Groups of Patients after Nursing.** After nursing, the CD3+, CD4+, and CD4+/CD8+ levels of the observation group were  $73.04 \pm 7.63$ ,  $33.25 \pm 6.31$ , and  $1.52 \pm 0.31$ , which were significantly higher than those of the control group ( $*p < 0.05$ ). The level of CD8+ in the observation group was  $22.84 \pm 6.36$ , which was significantly lower than the control group ( $*p < 0.05$ ) (Figure 1).

**3.4. Comparison of the Negative Emotional State of the Two Groups of Patients.** After nursing, the SAS score and SDS score of the two groups were significantly decreased ( $*p < 0.05$ ), and the scores of the observation group were

TABLE 1: Comparison of clinical efficacy between the two groups [n (%)].

Group	Cases	Complete remission	Partial remission	Stable	Progression	Total effective rate
Observation group	110	14 (12.73)	57 (51.82)	29 (26.36)	10 (9.09)	71 (64.55)
Control group	110	3 (2.73)	32 (29.09)	48 (43.64)	27 (24.54)	35 (31.82)
$\chi^2$						26.639
$p$						<0.001

TABLE 2: Comparison of nursing satisfaction between the two groups [n (%)].

Group	Cases	Very satisfied	Relatively satisfied	Dissatisfied	Nursing satisfaction
Observation group	110	33	71	6	104 (94.55)
Control group	110	15	78	17	93 (84.55)
$p$					<0.01

TABLE 3: Comparison of treatment compliance between the two groups [n (%)].

Group	Cases	Full compliance	Partial compliance	Noncompliance	Compliance
Observation group	110	41	67	2	108 (98.18)
Control group	110	28	63	19	91 (82.73)
$p$					<0.001

decreased more significantly ( $\Delta p < 0.05$ ), as shown in Table 4.

**3.5. Comparison of the Quality-of-Life Scores between the Two Groups of Patients.** Before nursing, there was no statistically significant difference in the quality-of-life scores between the two groups ( $p > 0.05$ ). After nursing, the scores of the two groups of patients in terms of social/family status, physical function, physiological function, and emotional status were increased ( $*p < 0.05$ ), and the observation group was significantly higher than the control group ( $\Delta p < 0.05$ ) (Table 5).

**3.6. Comparison of Tumor Marker Levels between the Two Groups of Patients.** Before nursing, there was no significant difference in serum CA199 and CEA levels between the two groups of patients ( $p > 0.05$ ). After nursing, the levels of tumor markers in the two groups were significantly decreased ( $^{##}p < 0.01$ ), and the observation group was downregulated more significantly than the control group ( $\#p < 0.05$ ) (Figures 2 and 3).

**3.7. Comparison of the Two-Year Cumulative Survival Rate of the Two Groups of Patients.** The two-year cumulative survival rate of the observation group was 78.18%, and the two-year cumulative survival rate of the control group was 54.55%. The observation group was significantly higher than the control group ( $p < 0.05$ ) (Figure 4).

## 4. Discussion

Ovarian cancer is a malignant tumor with high clinical incidence [14]. With the improvement of people's living standards, women's pressure from work and life is increasing, coupled with environmental pollution and other factors, the incidence of ovarian cancer is increasing year by

year, and the death rate is also increasing, which has been highly concerned by the medical community [15]. At present, there is no accurate and effective early diagnosis method for ovarian cancer, and it has progressed to the middle and late stage when it is diagnosed. Meanwhile, the treatment method is still based on traditional surgical resection, supplemented by radiotherapy and chemotherapy [16]. However, not only do patients have to suffer painful side effects during radiotherapy and chemotherapy, but also the rapid spread of tumor cells may lead to a high recurrence rate, which greatly reduces the patient's quality of life and life safety, bringing great trouble to the physical and mental health of patients [17]. As a treatment method that has been widely used in the treatment of ovarian cancer in recent years, traditional Chinese medicine (TCM) has the advantages of simple operation, less toxic side effects, and high security advantage. It can effectively control the development of the disease, alleviate the suffering of patients, and improve the quality of the patient's quality of life and survival. In clinical cancer treatment, it has been widely recognized by patients [18]. However, when patients with ovarian cancer learn that they have advanced cancer, they will generally experience nervousness, anxiety, denial, depression, and even resistance to treatment. At the same time, studies have confirmed that these negative psychological emotions can lead to a decrease in the immune function of patients with malignant tumors, which in turn will affect the treatment effect and quality of life of the patients [19]. Other studies have shown that ovarian cancer patients need to have a light diet and a reasonable diet control, and poor dietary habits will adversely affect the treatment of advanced ovarian cancer patients. Therefore, it is of great significance to improve the quality of life and prolong the survival time of ovarian cancer patients to pay attention to the changes of their psychological state and control their dietary habits while providing effective treatment for ovarian cancer patients [20]. Nursing should be based on the patient's



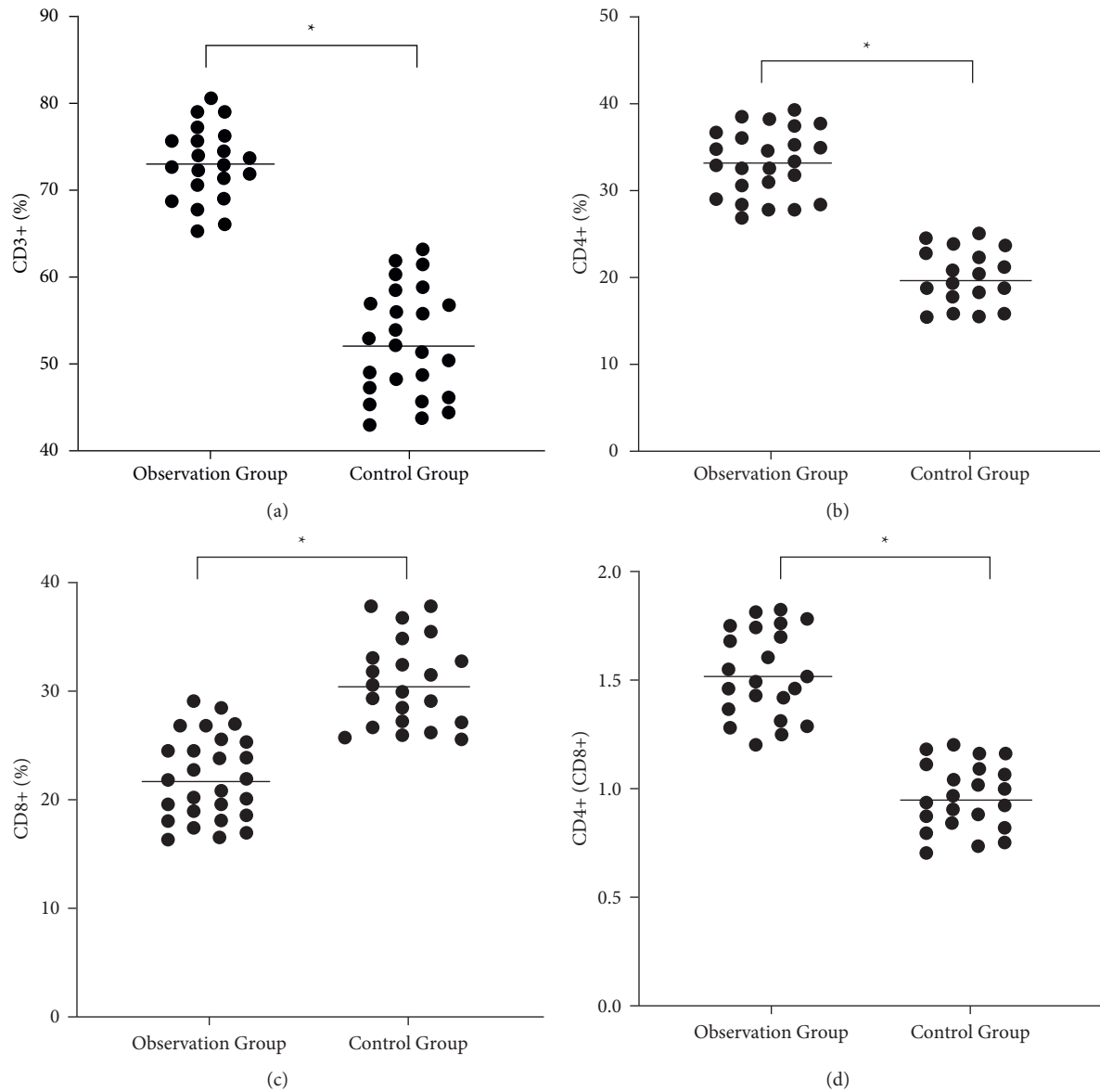


FIGURE 1: Comparison of immune function between two groups after nursing. (a) Comparison of CD3+ level between the two groups. (b) Comparison of CD4+ level between the two groups. (b) Comparison of CD8+ level between the two groups. (b) Comparison of CD4+/CD8 level between the two groups. \* $p < 0.05$ .

TABLE 4: Comparison of negative emotional state between the two groups ( $x \pm s$ ).

Group	Cases	SAS scores		SDS scores	
		Before care	After care	Before care	After care
Observation group	110	72.56 $\pm$ 7.13	34.67 $\pm$ 5.23* $\Delta$	69.78 $\pm$ 7.65	37.66 $\pm$ 5.17* $\Delta$
Control group	110	71.42 $\pm$ 7.36	47.24 $\pm$ 6.71*	70.54 $\pm$ 7.82	52.03 $\pm$ 6.21*
$t$		0.362	11.423	0.278	13.754
$p$		>0.05	<0.05	>0.05	<0.05

condition and actual conditions, implement high-quality psychological interventions and high-quality diet care, and provide guidance on TCM, which reflects the comprehensiveness and individualization of the treatment process [21]. The implementation of psychological care for patients can

improve patients' bad mood, promote their confidence in treatment, and improve treatment compliance, thereby enhancing the treatment effect.

This present study showed that the clinical efficacy of the observation group after nursing was significantly higher than

TABLE 5: Comparison of quality-of-life scores between the two groups ( $\bar{x} \pm s$ ).

Group	Cases		Social/family status	Physical function	Physiological function	Emotional status
Observation group	110	Before care	$32.54 \pm 3.66$	$28.97 \pm 2.13$	$31.72 \pm 3.75$	$29.61 \pm 3.48$
		After care	$72.63 \pm 4.47^{*\Delta}$	$73.32 \pm 5.96^{*\Delta}$	$76.84 \pm 4.21^{*\Delta}$	$71.24 \pm 5.33^{*\Delta}$
Control group	110	Before care	$31.87 \pm 3.72$	$29.46 \pm 2.34$	$32.26 \pm 3.41$	$28.77 \pm 3.73$
		After care	$54.52 \pm 6.13^*$	$56.26 \pm 5.74^*$	$61.37 \pm 5.42^*$	$57.12 \pm 6.37^*$
$t$			5.632	4.541	6.125	4.723
$p$			<0.05	<0.05	<0.05	<0.05

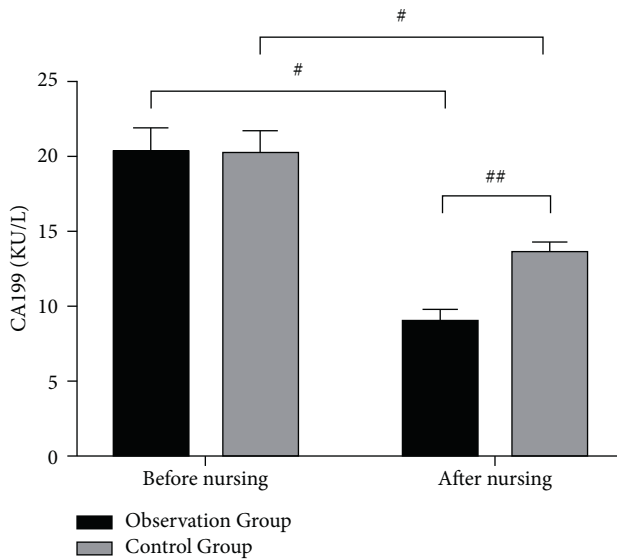


FIGURE 2: Comparison of serum CA199 levels between the two groups before and after nursing.

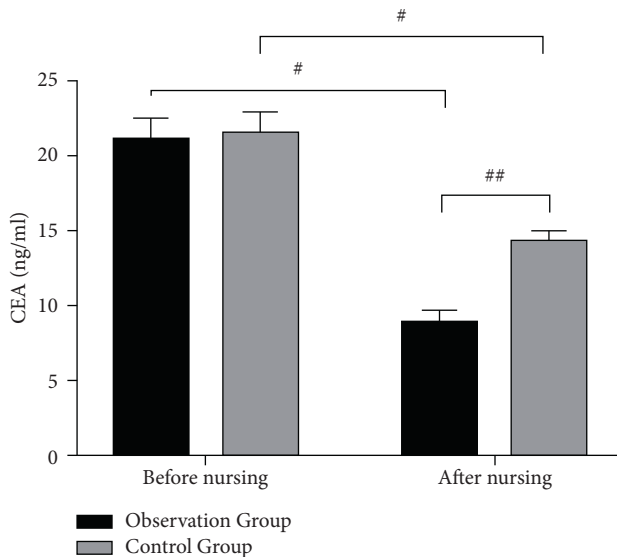


FIGURE 3: Comparison of serum CEA levels in the two groups before and after nursing.

that of the control group ( $p < 0.001$ ), and the nursing satisfaction and treatment compliance of the observation group after nursing were significantly higher than that of the control group ( $p < 0.01$ ), indicating that the nursing staff's practice of

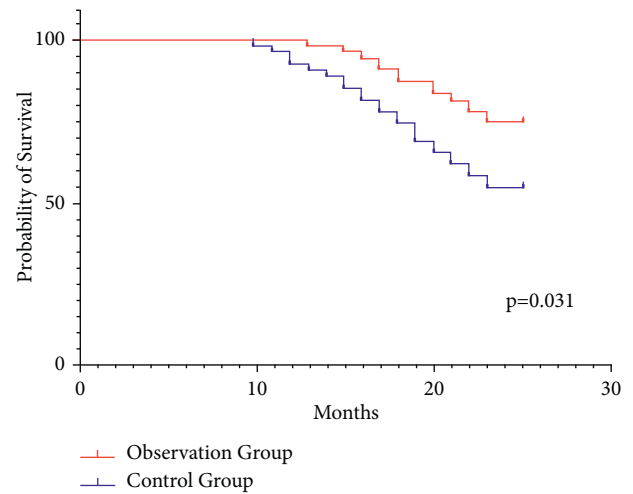


FIGURE 4: Comparison of two-year cumulative survival rate between the two groups.

psychological intervention and dietary guidance for patients with advanced ovarian cancer provides positive psychological support to patients, establishes a good doctor-patient relationship with patients, strengthens patients' trust in medical staff, and is willing to actively cooperate with treatment, thereby improving clinical efficacy. Tumor markers are produced during the proliferation of tumor cells and are of great value for tumor diagnosis and prognosis. Meanwhile, the growth of malignant tumors has a greater relationship with the body's immune function. Immune function is an important indicator for evaluating the therapeutic effect of malignant tumors [22, 23]. The results of this study showed that 4 weeks after treatment, the CD3+, CD4+, CD4+/CD8+ levels in the observation group were higher than those in the control group ( $p < 0.05$ ). The CD8+ level was lower than the control group ( $p < 0.05$ ). The CA19-9 and CEA levels in the observation group were lower than the control group ( $p < 0.05$ ), consistent with the results of studies reported by Hao et al. [24], suggesting that the prescription of tonifying kidney and removing blood stasis can disperse the masses and strengthen the body, clear heat and detoxify, invigorate the kidney, and replenish qi [25]. The prescriptions of *Astragalus*, *Codonopsis*, *Atractylodes*, and *Poria* have the functions of invigorating the spleen and qi, diuresis and swelling, and strengthening the body. ZZ nourishes the liver and kidney and can enhance the immune function against tumors. Taizishen can invigorate the spleen and stomach and improve immunity. Huangjing nourishes qi, replenish lung yin, and replenish kidney yin. Scrophulariaceae and *Scutellaria barbata* can detoxify, clear away heat and dispel blood stasis,

nourish the yin, and cool the blood; *Gallus gallus domesticus* invigorates the spleen, eliminates food, and promotes dampness; Shansi mushroom dissipates nodules and eliminates carbuncle, clears heat, and detoxifies [26–30]. In modern pharmacology, the combination of various drugs can promote the body to secrete immune factors, reduce the level of tumor markers, and improve the therapeutic effect. The combined use of psychological intervention and dietary guidance can significantly improve the body's immune function and significantly reduce the level of tumor markers [31]. Results showed that the patients' negative emotions, such as depression and anxiety, were significantly improved after continuous psychological intervention in the observation group. Moreover, the functional status, physical status, emotional status, and social and family status scores in the observation group were significantly better than those of the control group. The two-year cumulative survival rate of the observation group was also significantly higher than that of the control group ( $p < 0.05$ ), which further illustrates that the patients with advanced ovarian cancer who are treated with Bushen Quyu Decoction can be given continuous psychological intervention and reasonable dietary guidance, which can effectively eliminate the patient's negative emotions, such as anxiety and depression, effectively improve the patient's nursing effect, ultimately improve the patient's quality of life, and effectively extend the patient's survival time.

## 5. Conclusion

In summary, the Bushen Quyu Decoction combined with psychological intervention and diet guidance to treat patients with advanced ovarian cancer can effectively alleviate the patients' negative emotions, improve the patient's immune function, reduce the level of tumor markers, further improve the patient's quality of life and nursing satisfaction, improve the treatment effect, and promote the rehabilitation of patients; it is worthy of clinical application.

## Data Availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

## Disclosure

The funding body had no role in the design of the study, collection, analysis, interpretation of data, or writing of the manuscript.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# The Effects of Chinese Herbal Decoction Combined with Recombinant Human Interferon $\alpha 2b$ on MRI Imaging, Tumor Markers, and Immune Function in Patients with Renal Cell Carcinoma

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**Background.** To explore the clinical efficacy of traditional Chinese medicine decoction combined with recombinant human interferon  $\alpha 2b$  in the treatment of renal cell carcinoma (RCC). **Methods.** 68 RCC patients were divided into the control group and treatment group ( $n = 34$ ). The control group was treated with recombinant human interferon  $\alpha 2b$ , and the treatment group was treated with traditional Chinese medicine decoction on the basis of the control group. The clinical efficacy and life quality were observed. At the same time, the changes of immune function before and after treatment were compared. **Results.** After one course of treatment, the effective rate and clinical benefit rate of the treatment group were higher than those of the control group. The Karnofsky score in the treatment group was better than that in the control group. In improving the immune function, the treatment group was better than the control group in increasing CD3+ and CD4+ and reducing CD8+. **Conclusion.** Traditional Chinese medicine decoction combined with recombinant human interferon  $\alpha 2b$  has a good effect on the treatment of RCC. It can not only improve the common clinical symptoms of patients but also improve the quality of life and cellular immune function of patients.

## 1. Introduction

Renal cell carcinoma (RCC) is one of the common malignant tumors in the urinary system. Its incidence accounts for about 3% of clinical cancer patients [1–3], and it is increasing year by year. The etiology of RCC is not clear and may be related to smoking, obesity, and hypertension [4]. Clinically, patients with low back pain, hematuria, and abdominal masses are typical symptoms, which may be accompanied by hypertension, fever, anemia, and abnormal coagulation function [5, 6]. There are no obvious symptoms in the early stage of RCC. When there are obvious symptoms, a small number of patients have lesions confined to the kidneys. Most patients have unpredictable metastases. Metastatic

RCC seriously affects the life quality of patients, and its therapeutic effect and prognosis are not ideal. Moreover, RCC is not sensitive to radiotherapy and chemotherapy but is more sensitive to immunotherapy and targeted therapy [7].

At present, the modern medical treatment of RCC is mainly based on radical nephrectomy [8–12], postoperative adjuvant targeted therapy, and immunotherapy. However, targeted therapy and immunotherapy are expensive and have large side effects, which cannot effectively delay disease progression [13]. The long-term effect is not good. In the past 20 years, the 5-year survival rate of patients with advanced RCC has been very low. The main reason is the lack of effective treatments. Clinically, most advanced RCC have



metastasized far away and cannot be treated with surgery. Although immunotherapy and targeted therapy have certain short-term effects, they have serious side effects and poor long-term effects [14]. The clinical effect of the combination of Chinese and Western medicine in the treatment of RCC is better. The multifaceted and multilayered mechanism reflects the unique advantages of Chinese medicine. Previous studies have shown that [15–18] TCM adjuvant therapy emphasizes syndrome differentiation and has multilevel, multitarget, and multidirectional effects. Adjuvant treatment of Chinese medicine has a positive effect on improving clinical symptoms, improving immunity, reducing toxicity, improving life quality, preventing recurrence and metastasis, and prolonging survival time.

Surgery is currently the most effective way to treat RCC. At the same time, interferon adjuvant therapy should be given to patients with RCC [19]. Interferon  $\alpha 2b$  has obvious antitumor effects, which can inhibit cell proliferation and improve the immune function [16]. After interferon  $\alpha 2b$  binds to the cell surface receptors, it can significantly improve the immune function and enhance the phagocytosis of macrophages. It can also accelerate the apoptosis of cancer cells and exert a powerful inhibitory effect. However, patients often have symptoms, such as fever, chills, body aches, cytopenias, nausea, and indigestion after the application of interferon [20]. This will lead to interferon reduction or even discontinuation, thereby affecting the standard treatment of RCC patients.

In view of this, patients were given the adjuvant therapy of recombinant human interferon  $\alpha 2b$  combined with Chinese medicine decoction. This study aimed to explore the effects of recombinant human interferon  $\alpha 2b$  combined with Chinese medicine decoction on MRI imaging manifestations, tumor markers and immune function in patients with RCC.

## 2. Materials and Methods

**2.1. Clinical Data.** This study is a retrospective study. The cases were all RCC patients who were admitted to Qingdao Hospital of Traditional Chinese Medicine, Qingdao Hiser Hospital from January 2019 to December 2020. 71 RCC patients who met the criteria were selected and all met the relevant diagnostic criteria for renal cancer in the “practical oncology.” Renal surgery specimens were confirmed by cytopathology or histopathology. Examinations, such as abdominal MRI, CT, or PET-CT, showed the existence of space-occupying lesions. Patients have typical clinical manifestations, such as hematuria, abdominal masses, and waist and abdomen pain. The age of the patients was 18 to 75 years old. Physical status Karnofsky (KPS) score was  $\geq 60$  points. Patients did not receive other antitumor treatment one month before the experiment. All patients voluntarily signed informed consent forms. This study was approved by the Institutional Ethics Committee of Qingdao Hospital of Traditional Chinese Medicine, Qingdao Hiser Hospital. Patients with metastatic RCC, severe liver, cardiovascular and hematopoietic system, and other primary diseases, patients receiving other treatments, psychiatric patients,

patients with obvious bleeding tendency and severe electrolyte disorders, patients with immunotherapy contraindications, patients with allergic physique, and pregnant or lactating women were excluded from this study.

Case rejection and dropout were as follows. After inclusion, those cases that did not meet the inclusion criteria or did not use the drugs according to the experimental protocol should be eliminated. The included cases that have serious adverse events or complications and are not suitable for continuing to accept the experimenter, withdrawing by themselves, or failing to complete the entire treatment process shall be regarded as dropped cases. Those that fail to check in accordance with regulations or whose main indicators are missing shall be eliminated.

According to the case rejection and dropout criteria, 68 cases finally completed the entire treatment process. There was no significant difference in staging between the two groups. According to the treatment method, the patients were divided into a control group and a treatment group, with 34 cases in each group. General data balance test is shown in Table 1.

As shown in Table 1, gender, age, Karnofsky score, tumor location, Robson tumor stage, and case classification were all  $P > 0.05$  between the two groups. It indicates that there is no significant difference between the two groups of data, and the data are well balanced and comparable.

**2.2. Treatment Methods.** Patients in the control group were injected subcutaneously with recombinant human interferon  $\alpha 2b$ . The dosage is 3 million IU/day  $\times$  2 weeks (1–2 weeks), 6 million IU/day  $\times$  2 weeks (3–4 weeks), and 9 million IU/day  $\times$  2 weeks (5–6 weeks). Six weeks is a course of treatment, and all patients are treated for 1 course.

The treatment group was treated with Lishen Huazhuo Decoction on the basis of the control group. Lishen Huazhuo Decoction contains 30 g of *Salvia miltiorrhiza*, 30 g of Chinese yam, 20 g of cattail yellow, 15 g of malt, 15 g of Taizi ginseng, 15 g of *Pteris vulgaris*, 10 g of *Ulmus pumila*, 10 g of *Imperata* root, 10 g of licorice, and 3 g of rhubarb. Lishen Huazhuo Decoction was prepared according to the above ratio (1 dose/d). During the medication period, the diet should be strictly in accordance with the doctor’s advice, fasting spicy, and irritating food.

**2.3. MR Inspection Method.** Patients fasted for 4 h before the MR examination. Before the patient enters the scanning room, all metal materials outside the body should be removed. It should be confirmed that there are no contraindications to MR examination. All patients took the supine position and received end-inspiratory breath-holding and breathing amplitude consistency training.

Siemens SKYRS 3.0T MR scanner is used for MR inspection. The patient is in the supine position, and an end-inspiratory breath-hold scan is performed to keep the baseline level of each sequence the same. The scan range includes all kidneys. After the regular scan is completed, a dynamic enhanced scan is performed. The conventional scanning sequence includes axial T2WI, axial T2WI fat



TABLE 1: Comparison of general information between the control group and the treatment group ( $n = 34$ ).

Features		Control group	Treatment group
Age		$58.97 \pm 12.33$	$60.23 \pm 13.79$
Male/female		19/15	20/14
Karnofsky score		$75.37 \pm 7.324$	$73.674 \pm 3.086$
Tumor location	Left	17	18
	Right	17	16
Robson tumor stage	I	11	11
	II	15	16
	III	8	7
Case classification	Clear cell carcinoma	17	16
	Granular cell carcinoma	10	10
	Papillary RCC	7	8

suppression sequence, coronal T2WI, and axial T1WI (positive phase, reverse phase). The layer thickness of the axial T12WI, T2WI, and T2WI fat suppression sequence is 5.0 mm, and the layer spacing is 1.1 mm. The layer thickness of coronal T2WI is 6.0 mm, and the layer spacing is 1.0 mm. Multiphase dynamic enhancement scanning adopts three-dimensional volume interpolation fast spoiling VIBE (GRE T1WI) technology. Scans of early medullary cortex, late cortex medulla, renal parenchymal phase, and excretory phase were performed at 20–30 s, 45–70 s, 100–260 s, and 200–360 s after the injection of the contrast agent. The contrast agent Gd-DTPA injection should be injected through the cubital vein with a high-pressure syringe at a speed of 2.5 ml/s, with a dose of 0.1 mmol/kg. After the contrast agent is injected, 20 ml of normal saline was added.

**2.4. MR Image Analysis and Data Processing.** The images are observed and analyzed by two experienced MR diagnostic physicians. When there is a disagreement on the analysis results, two MR diagnostic physicians negotiate and reach a consensus. The main analysis included the following: (1) the location of the lesion, (2) signal characteristics, which compared with normal renal parenchyma, is divided into low signal, low signal-based mixed signal, high-level low-mix signal, and high signal-based mixed signal and high signal, (3) edge condition, which should confirm whether there is a thin ring high (low) signal or whether there is a nodular or irregular shape abnormal signal, and (4) the characteristics of dynamic strengthening, which are divided into no strengthening, ring-shaped strengthening, irregular edge shape, and nodular strengthening. Compared with the renal cortex, the degree of enhancement is divided into obvious enhancement, moderate enhancement, and mild enhancement.

## 2.5. Observation of Curative Effect

**2.5.1. Short-Term Objective Curative Effect (Solid Tumor Size).** According to the latest evaluation standards for the efficacy of solid tumors, the short-term efficacy evaluation of renal cancer is divided into complete remission (CR), partial remission (PR), stable (SD), and progress (PD). The short-term curative effect CR + PR is defined as effective. The

percentage of all cases that can be evaluated is effective rate. The solid tumor of kidney cancer was selected as the measurement lesion, and the lymph node, bone, liver, or lung metastasis lesions were not used as the measurement lesion. ① Complete remission is as follows: it can be seen that the tumor lesions disappeared completely and remained for more than 4 weeks. ② Partial remission is as follows: the maximum diameter of the tumor lesion has been reduced by  $\geq 50\%$ . No new lesions appeared, which maintained for more than 4 weeks. ③ Stable cases are as follows: the maximum diameter of the tumor lesion is reduced by less than 25% or increased by no more than 50%. No new lesions appeared, which maintained for more than 4 weeks. ④ Progress is as follows: the maximum diameter of tumor lesions increased by  $\geq 20\%$  or new lesions appeared.

**2.5.2. Improvement of Common Clinical Symptoms.** The clinical effect of patients is divided into three categories: improvement, stability, and ineffectiveness. According to the standards of “Guiding Principles for Clinical Research of New Chinese Medicines (Practice),” the efficacy of patients is identified. Among them, there are five standard test indicators, such as fatigue, dry mouth and throat, lumbar muscle soreness, five upset and hot, and abnormal stool. Each indicator includes 0 to 3 points. Improvement means that the score after treatment is 0–30% of that before treatment. Stable means that the score after treatment is 30% to 70% of that before treatment. Invalid means that the score after treatment is 70% to 100% of the score before treatment. The total effective rate is the ratio of (improvement + stability) to the total effective rate.

**2.5.3. Quality of Life.** Quality of life is evaluated once before and after treatment. The KPS physical status scoring standard is used to evaluate and record the quality of life (QOL). ① Improvement means that the KPS value increased by  $>10$  points. ② Stability means that the fluctuation range of KPS value  $<10$  points. ③ Decrease means that the KPS value decreased by  $>10$  points:

$$\text{improvement rate} = \frac{(\text{improvement} + \text{stability})}{\text{total number of cases}}. \quad (1)$$

## 2.6. Index Measurement

**2.6.1. Changes in Cellular Immune Function (CD3+, CD4+, CD8+, and CD4+/CD8+) before and after Treatment (Flow Cytometry).** Before and after treatment, 5 mL of fasting venous blood was drawn from the patient and centrifuged in an automatic blood centrifuge. The centrifuge speed was adjusted to 3000 r/min and centrifuged for 10 min. The supernatant was taken and placed in a refrigerator at  $-20^{\circ}\text{C}$  for inspection. Flow cytometry was used to detect the relevant indicators of T lymphocyte subsets in serum. CD3+, CD4+, CD8+, and other T lymphocyte subsets were detected by Beckman Coulter EpicsXL flow cytometer.

**2.6.2. Detection of Tumor Markers (Electrochemiluminescence Immunoassay).** Enzyme-linked immunoassay was used to determine the levels of neuron-specific enolase (NSE), carcinoembryonic antigen (CEA), human  $\beta$ 2 microglobulin ( $\beta$ 2-MG), and ferritin (FERR) tumor markers before and after treatment.

## 2.7. Observation Time.

- (1) Symptoms and signs are recorded once a week
- (2) Imaging tumor examination (MRI) was performed before treatment and once after the end of the first course of treatment

**2.8. Statistical Analysis.** SPSS 22.0 statistical analysis software was used to process and analyze the data. The measurement data is described by the mean  $\pm$  standard deviation, and the independent sample *t*-test is selected for comparison. The count data is expressed as a ratio or percentage (%), and the comparative analysis was performed by chi-square test. The difference was statistically significant at  $P < 0.05$ .

## 3. Results

**3.1. MRI Features before and after Treatment.** Among the 34 cases in the control group, MRI judged 10 cases of septal thickening (cancer wall thickness,  $2.89 \pm 0.70$  mm), 16 cases of calcification, and 8 cases of solid component. MRI T1WI examination showed that 27 cases had clear boundary and 7 cases had blurred boundary. T2WI showed 26 cases of high signal, 5 cases of slightly high signal, and 3 cases of equal signal. Among the 34 patients in the treatment group, MRI judged 11 cases of septal thickening (cancer wall thickness,  $2.86 \pm 0.56$  mm), 17 cases of calcification, and 6 cases of solid component. MRI T1WI examination showed that 28 cases had clear borders and 6 cases had blurred borders. T2WI showed 25 cases of high signal, 6 cases of slightly high signal, and 3 cases of equal signal.

After treatment, the complete ablation zone showed iso-high signal on T1WI in the treatment group. The signal intensity tended to be lower than before treatment, showing a high level of low-confounding signal. The T2WI fat suppression image showed low signal in the ablation zone.

The residual cavity shadow left by the ablation antenna was a strip of high signal. After treatment, the ablation zone of the T2WI fat suppression image showed a mixed signal dominated by low signal, and the ablation zone gradually shrank. The signal had a tendency to increase unevenly, which was manifested as a mixed signal (Tables 2 and 3).

**3.2. Observation of Recent Objective Curative Effect.** The objective response rate (CR + PR) of the treatment group and the control group was 23.53% and 14.71%, respectively. The disease control rate (CR + PR + SD) was 55.88% and 41.18%, respectively. There was no statistically significant difference in the objective efficacy between the treatment group and the control group ( $P > 0.05$ , Table 4).

**3.3. Improvement of Common Clinical Symptoms.** As shown in Table 5, the symptoms of loose stools were significantly worsened after treatment in the control group ( $P < 0.01$ ). The symptoms of dry mouth and throat improved after treatment in the control group ( $P < 0.05$ , Table 5). The symptoms of hematuria, fatigue, dry mouth and throat, and five upset fever in the treatment group were significantly improved after treatment ( $P < 0.05$ , Table 5). After treatment, the soft symptoms of lumbar creatine were significantly improved in the treatment group ( $P < 0.05$ , Table 5). Comparing the two groups after treatment, the symptoms of poor appetite and obesity in the treatment group were significantly lighter than those in the control group ( $P < 0.05$ , Table 5). Compared with the two groups after treatment, the fatigue symptoms of the treatment group were lighter than those of the control group ( $P < 0.05$ , Table 5).

**3.4. Karnofsky Score.** The Karnofsky score in the treatment group was significantly higher after treatment than before treatment ( $P < 0.05$ , Figure 1), indicating that Chinese herbal decoction combined with recombinant human interferon  $\alpha$ 2b can significantly improve the life quality of patients. The Karnofsky score in the control group was higher than that before the treatment ( $P < 0.05$ , Figure 1), indicating that recombinant human interferon  $\alpha$ 2b also can improve the life quality of patients. Compared with the two groups after treatment, the treatment group was better than the control group in the improvement of Karnofsky score ( $P < 0.05$ , Figure 1). These results show that the combination of Chinese medicine decoction combined with recombinant human interferon  $\alpha$ 2b can increase the Karnofsky score and improve the physical status of patients compared with the use of recombinant human interferon  $\alpha$ 2b alone.

**3.5. Comparison of White Blood Cell and Neutrophil Test Results between the Two Groups of Patients before and after Treatment.** Recombinant human interferon  $\alpha$ 2b is a first-line immune drug for the treatment of RCC. However, patients will suffer varying degrees of blood cell reduction as well as clinical manifestations [21]. These adverse symptoms will lead to the reduction of interferon dosage or even the

TABLE 2: MRI manifestations of patients in the control group ( $n = 34$ ).

Time	Enhanced scan		
	Ring reinforcement	Strengthened Irregularities or enhancement of marginal nodules	No reinforcement
Before treatment	19	5	10
After treatment	14	3	17

TABLE 3: MRI manifestations of patients in the treatment group ( $n = 34$ ).

Time	Enhanced scan		
	Ring reinforcement	Strengthened Irregularities or enhancement of marginal nodules	No reinforcement
Before treatment	20	5	9
After treatment	12	2	20

TABLE 4: Comparison of short-term objective curative effect between the two groups of patients (case (%)).

Group	CR	PR	SD	PD	CR + PR	CR + PR + SD
Treatment group	2 (5.88%)	6 (17.65%)	11 (32.35%)	15 (22.12%)	8 (23.53%)	19 (55.88%)
Control group	1 (2.94%)	4 (11.76%)	9 (26.47%)	20 (58.82%)	5 (14.71%)	14 (41.18%)

TABLE 5: Comparison of common symptoms' improvement between the two groups of patients after treatment.

Common symptoms	Control group		Treatment group	
	Before	After	Before	After
Hematuria	$1.54 \pm 0.87$	$1.06 \pm 0.89$	$1.58 \pm 0.91$	$0.66 \pm 0.51^*$
Languid	$1.63 \pm 0.75$	$1.45 \pm 0.63$	$1.64 \pm 0.69$	$0.89 \pm 0.33^*$
Dry mouth and throat	$1.86 \pm 1.02$	$0.86 \pm 0.42^*$	$1.98 \pm 0.99$	$0.73 \pm 0.72^*$
Lumbar muscle soreness	$1.54 \pm 1.04$	$1.38 \pm 0.92$	$1.59 \pm 1.17$	$0.88 \pm 0.93^*$
Five upset fever	$1.27 \pm 0.85$	$1.03 \pm 0.74$	$1.31 \pm 0.89$	$0.59 \pm 0.74^*$
Abnormal stool	$1.08 \pm 0.43$	$1.36 \pm 0.64$	$0.98 \pm 0.39$	$1.64 \pm 0.77^*$
Poor appetite	$1.61 \pm 0.65$	$1.35 \pm 0.21$	$1.63 \pm 0.48$	$0.97 \pm 0.37^{* \#}$

\*  $P < 0.05$  compared with this group before treatment; #  $P < 0.05$  compared with the control group.

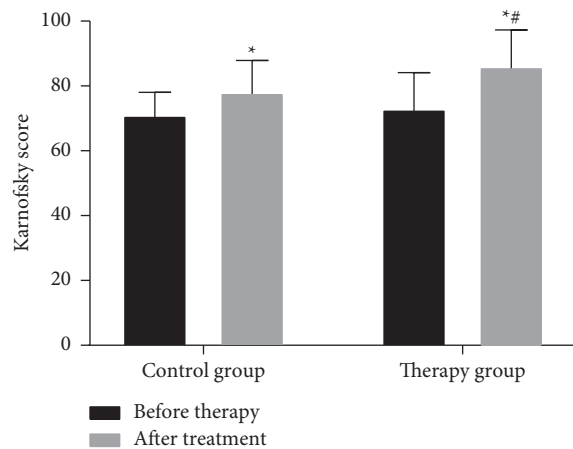


FIGURE 1: Comparison of Karnofsky scores between two groups of patients before and after treatment ( $x \pm s$ ). \*  $P < 0.05$  (compared with before treatment); #  $P < 0.05$  (compared with the control group).

discontinuation of the drug, which will have a certain impact on the standard treatment of RCC patients. Therefore, the changes in the levels of white blood cells and neutrophils between the treatment group and the control group were detected (Figures 2 and 3).

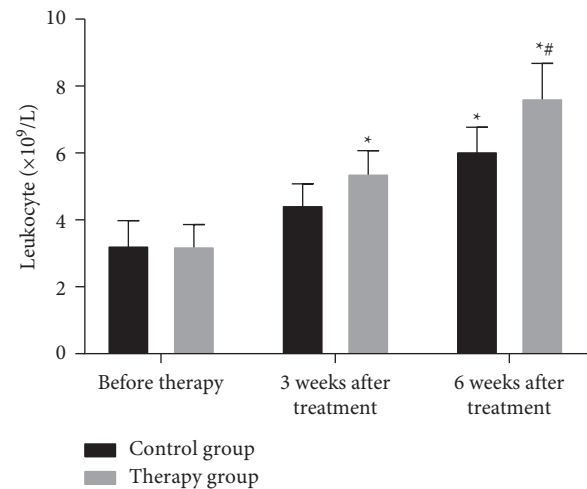


FIGURE 2: Comparison of peripheral blood leukocytes and counts between the two groups. \*  $P < 0.05$  (compared with before treatment); #  $P < 0.05$  (compared with the control group).

As shown in Figures 2 and 3, the recovery rate of white blood cells and neutrophils in the treatment group was significantly higher than that in the control group ( $P < 0.05$ ). The results indicate that the number of white blood cells can increase after giving patients oral Chinese medicine

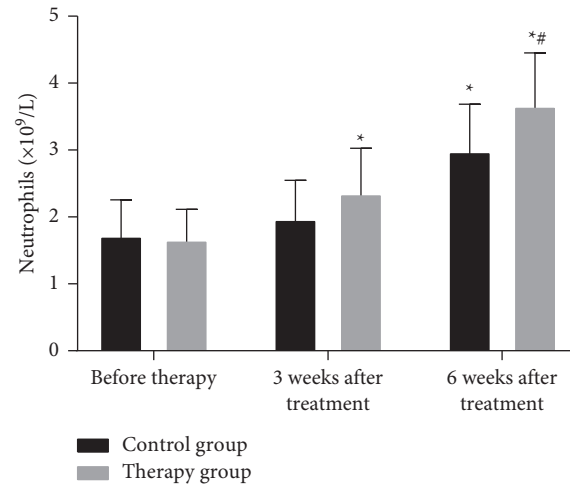


FIGURE 3: Comparison of neutrophil counts in peripheral blood between the two groups. \* $P < 0.05$  (compared with before treatment); # $P < 0.05$  (compared with the control group).

decoction. The possible reason is that the drug can enhance bone marrow hematopoietic function after being absorbed by the intestine. By monitoring the number of white blood cells in patients, it is found that the drug can indeed increase the number of white blood cells in patients, but the increase in some patients is not obvious.

**3.6. The Changes of Tumor Marker Levels in Patients before and after Treatment.** Before treatment, there was no significant difference in the levels of tumor markers between the two groups ( $P > 0.05$ , Table 6). After treatment, the levels of NSE and  $\beta 2$ -MG in the two groups were significantly reduced. The NSE values in the treatment group and the control group were significantly reduced after treatment ( $P < 0.05$ , Table 6). Compared with the two groups after treatment, the treatment group was better than the control group in reducing NSE levels ( $P < 0.05$ , Table 6). The  $\beta 2$ -MG values in the treatment group and the control group were decreased after treatment ( $P < 0.05$ , Table 6). But after treatment, there was no significant difference in the reduction of  $\beta 2$ -MG levels between the treatment group and the control group ( $P > 0.05$ , Table 6).

**3.7. Changes in the Proportion of T-Lymphocyte Factor Subgroups of Patients before and after Treatment.** The CD4+/CD8+ ratio after treatment in the control group was significantly higher than before treatment ( $P < 0.01$ , Figure 4). The CD3+ and CD4+ values were higher than before treatment ( $P < 0.05$ , Figure 4). The CD8+ value was lower than before treatment ( $P < 0.05$ , Figure 4). After treatment, the CD3+, CD4+, and CD4+/CD8+ ratios in the treatment group were significantly increased ( $P < 0.05$ , Figure 4), and the CD8+ value was significantly decreased ( $P < 0.05$ , Figure 4). After treatment, the increase in the ratio of CD4+/CD8+ in the treatment group was significantly better than that in the control group ( $P < 0.05$ , Figure 4). After treatment, the treatment group was

better than the control group in increasing CD3+ and CD4+ values and decreasing CD8+ value ( $P < 0.05$ , Figure 4). These results indicate that Chinese herbal decoction can improve the immune function of patients.

**3.8. Quality of Life Score.** The scores of nausea and vomiting, loss of appetite, and diarrhea in the control group were significantly higher than those before treatment ( $P < 0.05$ , Table 7), indicating that these 4 items all deteriorated significantly after treatment. The scores of physical functions, role function, and social function were all higher than those before treatment ( $P < 0.05$ , Table 7), indicating that all 3 items were improved after treatment. The score of dyspnea was higher than that before treatment ( $P < 0.05$ , Table 7), indicating that this item aggravated after treatment. The role function and emotional function of the treatment group were significantly higher than before treatment ( $P < 0.05$ , Table 7), indicating that these two items were significantly improved after treatment. Both physical function and social function were improved compared with before treatment ( $P < 0.05$ , Table 7). The scores of fatigue and insomnia were lower than before treatment ( $P < 0.05$ , Table 7). It shows that all 4 items are improved after treatment. Nausea, vomiting, and diarrhea were all higher than before treatment ( $P < 0.05$ , Table 7), indicating that these two items aggravated after treatment.

After treatment, symptoms such as fatigue and nausea and vomiting in the treatment group were significantly lighter than those in the control group ( $P < 0.05$ , Table 7). After treatment, the treatment group was better than the control group in improving the patient's role function ( $P < 0.05$ , Table 7). The symptoms of insomnia and appetite loss in the treatment group were lighter than those in the control group ( $P < 0.05$ , Table 7). The emotional function and overall health of patients in the treatment group were better than those in the control group ( $P < 0.05$ , Table 7).

TABLE 6: Changes of NSE, FERR,  $\beta$ 2-MG, and CER levels of patients before and after treatment.

Indicator	Control group		Treatment group	
	Before	After	Before	After
NSE	19.38 $\pm$ 2.77	14.68 $\pm$ 2.53*	19.29 $\pm$ 3.01	10.55 $\pm$ 2.13* <sup>#</sup>
FERR	331.97 $\pm$ 86.03	268.43 $\pm$ 75.96	329.62 $\pm$ 90.31	265.27 $\pm$ 77.83
$\beta$ 2-MG	2714.85 $\pm$ 501.33	2035.17 $\pm$ 478.88*	2702.31 $\pm$ 498.35	2006.64 $\pm$ 485.41*
CER	3.10 $\pm$ 1.57	2.93 $\pm$ 2.01	3.08 $\pm$ 1.73	2.82 $\pm$ 1.78

\* Compared with before treatment,  $P < 0.05$ ; <sup>#</sup> compared with the control group,  $P < 0.05$ .

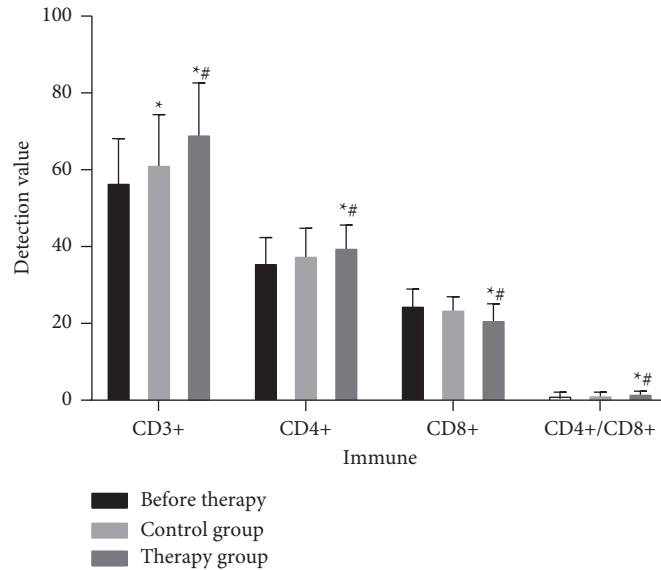


FIGURE 4: The changes of patients' CD3+, CD4+, CD8+, and CD4+/CD8+ before and after treatment. \*  $P < 0.05$  (compared with before treatment); <sup>#</sup>  $P < 0.05$  (compared with the control group).

TABLE 7: Comparison of EORTC QLQ-C30 quality of life scores before and after treatment between the two groups.

Item	Control group		Treatment group	
	Before	After	Before	After
Functional subscale				
Physical function	45.75 $\pm$ 16.38	55.69 $\pm$ 18.35*	45.77 $\pm$ 17.93	60.34 $\pm$ 19.81*
Role function	59.43 $\pm$ 18.23	72.36 $\pm$ 20.19*	60.44 $\pm$ 20.37	82.68 $\pm$ 21.52* <sup>#</sup>
Cognitive function	58.03 $\pm$ 18.95	62.37 $\pm$ 20.06	57.91 $\pm$ 16.99	63.71 $\pm$ 18.82
Emotional function	51.36 $\pm$ 14.38	60.34 $\pm$ 19.97	54.39 $\pm$ 16.37	71.38 $\pm$ 21.79* <sup>#</sup>
Social function	52.67 $\pm$ 16.57	64.77 $\pm$ 16.38*	51.97 $\pm$ 14.39	67.03 $\pm$ 16.29*
Symptom subscale				
Weak	44.07 $\pm$ 23.65	41.97 $\pm$ 19.06	43.98 $\pm$ 22.44	31.43 $\pm$ 18.73* <sup>#</sup>
Pain	25.34 $\pm$ 19.25	32.76 $\pm$ 25.34	25.57 $\pm$ 21.79	29.14 $\pm$ 20.33
Nausea and vomiting	15.69 $\pm$ 12.12	47.38 $\pm$ 16.42*	17.03 $\pm$ 5.63	32.58 $\pm$ 13.46*
Breathing difficulties	38.23 $\pm$ 19.37	55.83 $\pm$ 28.71*	38.04 $\pm$ 18.23	45.57 $\pm$ 23.31
Agrypnia	42.76 $\pm$ 21.83	48.21 $\pm$ 19.34	42.42 $\pm$ 21.39	24.39 $\pm$ 14.23 <sup>#</sup>
Appetite loss	27.86 $\pm$ 19.34	57.14 $\pm$ 34.25*	28.67 $\pm$ 20.47	40.26 $\pm$ 24.37
Constipation	37.45 $\pm$ 18.67	38.14 $\pm$ 20.00	36.71 $\pm$ 19.73	42.39 $\pm$ 21.37*
Diarrhea	34.43 $\pm$ 22.37	59.37 $\pm$ 21.23	35.58 $\pm$ 19.19	54.38 $\pm$ 23.33
General health	55.27 $\pm$ 16.67	56.89 $\pm$ 20.41	55.83 $\pm$ 19.27	68.79 $\pm$ 20.43 <sup>#</sup>

\*  $P < 0.05$ , compared with this group before treatment; <sup>#</sup>  $P < 0.05$ , compared with the control group.

#### 4. Discussion

At present, the toxic and side effects of RCC biological treatment are relatively large. The use of traditional Chinese medicine has a certain effect on reducing its toxic and side

effects [22]. Interferon  $\alpha$ 2b has obvious effects of antitumor, which can inhibit cell proliferation and improve the body's immune function. After interferon  $\alpha$ 2b binds to the cell surface receptors, it can significantly improve the immune function of the patient's body, enhance the phagocytosis of macrophages,



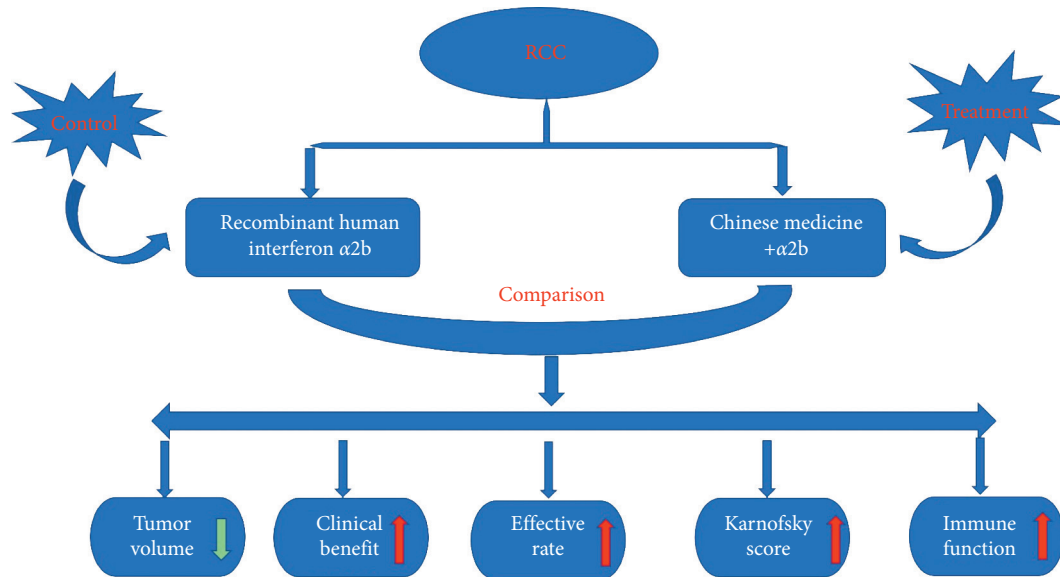


FIGURE 5: The graphical abstract.

and accelerate cell apoptosis [23, 24]. However, after the application of interferon, patients often have symptoms such as fever, chills, body aches, cytopenias, nausea, and indigestion in varying degrees, leading to a reduction in interferon dose or even withdrawal. Therefore, this study explored the efficacy of Lishen Huazhuo Decoction combined with biological therapy in the treatment of RCC patients.

In recent years, due to the strengthening of people's awareness of physical examination and the improvement of inspection equipment, the detection rate of RCC has increased year by year. Percutaneous thermal ablation guided by image (ultrasound, CT, MR) is affected by factors, such as the operator's technical level, the limitations of imaging technology, the size, shape, location, and adjacent relationship of the tumor in the actual operation. This may lead to incomplete ablation and recurrence, and the ablation effect directly affects the patient's prognosis and quality of life. Among them, MRI has high soft tissue resolution and can be used for multisequence, multiparameter, and multidirectional imaging. MRI also has a variety of functional imaging methods, such as perfusion weighted imaging (PWI), diffusion weighted imaging (DWI), and magnetic resonance spectroscopy (MRS). Therefore, MRI is widely used in the treatment of RCC.

The results of this study show that the treatment group has a significant effect compared with the control group (Figure 5). After treatment, the clarity of lesion boundaries and MRI T1WI tumor marker levels in the treatment group were significantly lower than those in the control group. The objective remission rate, improvement of common symptoms, Karnofsky score, quality of life score, white blood cell and neutrophil count, and T lymphocyte factor subgroup ratio were significantly higher than those of the control group.

## 5. Conclusion

In summary, the treatment of RCC patients with recombinant human interferon  $\alpha 2b$  plus Chinese medicine

decoction has obvious antitumor effect. Its components can also enhance the body's immunity and hematopoietic function and can greatly reduce the adverse reactions caused by hormone therapy. Chinese medicine decoction improves the patient's immunity and enhances the immunosuppressive effect of interferon  $\alpha 2b$ . At the same time, Chinese medicine decoction reduces the toxic and side effects caused by the application of immunosuppressive agents, improves the patient's life quality, and reduces the incidence of related adverse reactions. Therefore, recombinant human interferon  $\alpha 2b$  plus Chinese medicine decoction has obvious clinical therapeutic effects and is worthy of application in clinical work. However, the regulatory mechanism of recombinant human interferon  $\alpha 2b$  plus Chinese medicine decoction still needs to be further explored.

## Data Availability

The datasets used during the present study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# The Effect of Resveratrol on Blood Glucose and Blood Lipids in Rats with Gestational Diabetes Mellitus

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**Background.** Previous studies have reported that resveratrol has various biological effects such as anti-inflammatory, antioxidant, and antitumor. This study aimed to investigate the effects of resveratrol on blood glucose and blood lipids in rats with gestational diabetes mellitus (GDM). **Methods.** The rat diabetes model was prepared by one-time intraperitoneal injection of streptozotocin (STZ, 35 mg/kg). Fasting blood glucose was measured by using a blood glucose meter. The ELISA method was used to detect the levels of insulin, leptin, adiponectin, resistin, TNF- $\alpha$ , and IL-6. The content of TC, TG, LDL-C, and HDL-C was determined by using an automatic biochemical detector. **Results.** Compared with the GDM group, the insulin level in the resveratrol (120 and 240 mg/kg) treatment group was significantly increased. But, the blood glucose level and body weight were significantly reduced. The content of TC, TG, and LDL-C in the resveratrol (240 mg/kg) treatment group was significantly reduced, and the content of HDL-C was significantly increased. In addition, leptin, resistin, TNF- $\alpha$ , and IL-6 levels in the 240 mg/kg resveratrol treatment group were significantly reduced, and adiponectin was significantly increased. Also, resveratrol (240 mg/kg) was stronger than metformin hydrochloride in improving insulin secretion and regulating blood lipids and adipokine content. **Conclusion.** Resveratrol has a dose-dependent effect on GDM rats to increase insulin secretion, reduce blood glucose and body weight, and regulate blood lipids and plasma adipokines.

## 1. Introduction

Gestational diabetes mellitus (GDM) refers to diabetes or impaired glucose tolerance that occurs or is first discovered during pregnancy [1]. Although the abnormal glucose metabolism of GDM patients can return to normal after delivery, the chance of developing type 2 diabetes will increase in the future [2]. GDM is extremely harmful to mothers and babies and may cause preeclampsia, premature rupture of membranes, and premature delivery [3]. The incidence of fetal malformations is 3 to 4 times that of the normal control group [4]. Therefore, timely treatment of

GDM is of great significance to the health of mothers and infants and can also effectively reduce the incidence of diabetes in the future.

The etiology and pathogenesis of GDM are extremely complex and have not yet been fully elucidated. The main features of glucose metabolism during pregnancy are increased glucose demand, increased insulin resistance, and relatively insufficient insulin secretion [5]. This may cause GDM in some pregnant women. GDM is more common in people who are obese or overweight, people who have a long-term high-sugar and high-fat diet, people who have a family history of diabetes, and elderly pregnant women [6].

Hyperglycemia can cause abnormal embryonic development and even death, and the incidence of miscarriage can reach 15% to 30% [7]. GDM patients are 2 to 4 times more likely to develop high blood pressure during pregnancy than non-diabetic pregnant women. This may be related to the presence of severe insulin resistance and hyperinsulinemia [8]. In addition, it has been found that obesity, lipid metabolism disorders, and abnormal secretion of adipocytokines in adipose tissue play a very critical role in the pathogenesis of GDM [9]. Therefore, it is very important for GDM patients to find drugs that can lower blood glucose and blood lipids and have fewer side effects.

Resveratrol is a kind of polyphenol compounds, mainly derived from peanuts, grapes (red wine), knotweed, mulberries, and other plants [10]. Resveratrol is a natural antioxidant that can reduce blood viscosity. Resveratrol can also inhibit platelet coagulation and vasodilation and maintain blood flow [11]. Resveratrol has an effect on inhibiting atherosclerosis and preventing coronary heart disease, ischemic heart disease, and hyperlipidemia [12]. Because resveratrol has a variety of biological and pharmacological activities, it is widely used in food, medicine, health-care products, and cosmetics [13]. In addition, it has been found that resveratrol can control and reduce the body weight of obese rats [14]. Therefore, we speculate that resveratrol may play a role in reducing blood glucose and blood lipids in patients with GDM.

In this study, a one-time intraperitoneal injection of streptozotocin (STZ) was used to prepare a 5-day GDM rat model. The purpose of this study is to explore the regulating effect of resveratrol on blood glucose and blood lipid levels in GDM rats.

## 2. Materials and Methods

**2.1. Animals.** Female and male SD rats (SPF, 180–220 g) were purchased from the Hebei Experimental Animal Center (Shijiazhuang, China). All rats were reared in the animal room in a suitable breeding environment (temperature 23 ~ 25°C, relative humidity 65 ~ 70%). The photoperiod was 12 h: 12 h. The animal experiment was approved by the Experimental Animal Committee of Jinan Central Hospital.

**2.2. GDM Model.** After the female rats were fed a high-fat diet for 8 weeks in the animal room, the estrus cycle was measured by the vaginal smear method. Female rats and male rats in pre-estrus were caged overnight at a ratio of 1 : 2. Next day, the vaginal smear was examined under a microscope, and the sperm observed was determined to be a pregnant mouse. After 5 days of pregnancy, STZ (35 mg/kg, Yi Sheng Biotechnology Co., LTD, Shanghai, China) was injected intraperitoneally to make a GDM model. After 72 h, when the fasting blood glucose stabilized at 13.5 mmol/L, the model was established successfully. 100 GDM rats were randomly divided into 5 groups: the GDM model control group (GDM-NC), resveratrol 60, 120, and 240 mg/kg treatment group, and metformin hydrochloride (200 mg/kg) positive control group. Another 20 SD rats with 5 days

gestation were taken as the normal pregnancy control group. Rats in each group were given continuous administration for 2 weeks (1 time/day). The normal pregnancy control group and GDM-NC group were given equal volume of normal saline. After 2 weeks of treatment, the rats in each group were weighed and recorded with an electronic balance.

**2.3. Blood Glucose and Insulin Level.** A blood glucose meter (ACCU-CHEK, Shanghai, China) was used to measure the abdominal blood glucose of each group on the 0th, 7th, and 14th day of treatment. The insulin level in rat plasma was measured with an ELISA kit (MILLIPORE, Beijing, China).

**2.4. Detection of TC, TG, LDL-C, and HDL-C in Serum.** Two weeks after the drug treatment, urethane (Beijing Chemical Reagent Company, Beijing, China) was injected intraperitoneally for anesthesia. Blood was collected from the abdominal aorta, and the upper serum was collected after centrifugation at 2000 rpm for 5 min. An automatic biochemical detector (Wuhan Jingcheng Weiye Medical Instruments Co., Ltd., Wuhan, China) was used to determine the serum levels of TC, TG, LDL-C, and HDL-C in each group.

**2.5. Detection of Leptin, Adiponectin, Resistin, TNF- $\alpha$ , and IL-6 Levels in Plasma.** After 2 weeks of treatment, urethane was injected intraperitoneally for anesthesia. Blood was taken from the abdominal aorta and anticoagulated with heparin. An ELISA kit (MILLIPORE, Beijing, China) was used to determine the levels of leptin, adiponectin, resistin, TNF- $\alpha$ , and IL-6 in plasma.

**2.6. Statistical Analysis.** All experiments were repeated 3 times. SPSS 22.0 (IBM Corp.) was used for statistical analysis. All experimental data were displayed as mean  $\pm$  SD. Paired Student's *t* test was used to analyze the parameter comparison between the two groups.  $P < 0.05$  was considered to indicate a statistically significant difference.

## 3. Results

**3.1. The Effects of Resveratrol on Fasting Blood Glucose and Insulin Levels in GDM Rats.** Compared with the normal pregnancy control group, the fasting blood glucose level of the GDM-NC group was significantly increased ( $P < 0.01$ , Table 1). After 2 weeks of treatment with resveratrol (120 and 240 mg/kg) and metformin hydrochloride (200 mg/kg), blood glucose levels were significantly lower than those in the GDM-NC group ( $P < 0.05$ , Table 1). Compared with the normal pregnancy control group, the insulin level of the GDM-NC group was significantly reduced ( $P < 0.01$ , Table 2). After 2 weeks of treatment with resveratrol (120 and 240 mg/kg) and metformin (200 mg/kg), insulin levels were significantly increased compared with the GDM-NC group ( $P < 0.05$ , Table 2). The abovementioned results indicate that resveratrol can increase insulin levels and lower blood glucose in GDM rats.

TABLE 1: The effect of resveratrol on fasting blood glucose level in GDM rats.

Group	Dosage (mg/kg)	0 <sup>th</sup> day (mmol/L)	7 <sup>th</sup> day (mmol/L)	14 <sup>th</sup> day (mmol/L)
Normal pregnancy		6.1 ± 0.7**	6.2 ± 0.6**	6.3 ± 0.5**
GDM-NC		16.3 ± 2.2	16.4 ± 2.3	16.1 ± 2.5
Resveratrol	60	16.6 ± 2.3	15.4 ± 2.1	14.9 ± 2.1
	120	16.3 ± 2.0	13.5 ± 1.8*	12.8 ± 1.8*
	240	16.2 ± 1.8	12.2 ± 1.6*	9.7 ± 1.5**
Metformin hydrochloride	200	16.4 ± 2.2	10.9 ± 1.5*	8.8 ± 1.3**

Compared with the GDM-NC group, \* $P < 0.05$ , \*\* $P < 0.01$ .

TABLE 2: The effect of resveratrol on insulin level in GDM rats.

Group	Dosage (mg/kg)	0 day (mmol/L)	7 day (mmol/L)	14 day (mmol/L)
Normal pregnancy		13.2 ± 2.3**	13.3 ± 2.1**	13.1 ± 2.4**
GDM-NC		5.6 ± 1.1	5.5 ± 0.9	5.6 ± 1.0
Resveratrol	60	5.6 ± 1.2	6.8 ± 1.4	7.1 ± 1.5
	120	5.5 ± 0.9	7.6 ± 1.5*	8.5 ± 1.3*
	240	5.4 ± 1.0	10.3 ± 1.6*	12.2 ± 1.2**
Metformin hydrochloride	200	5.5 ± 2.2	7.4 ± 1.5*	8.6 ± 1.6*

Compared with the GDM-NC group, \* $P < 0.05$ , \*\* $P < 0.01$ .

### 3.2. The Effect of Resveratrol on the Weight of Rats with GDM.

Compared with the normal pregnancy control group, the body weight of the GDM-NC group was increased significantly ( $P < 0.01$ , Figure 1). After 2 weeks of treatment with resveratrol (120 and 240 mg/kg) and metformin hydrochloride (200 mg/kg), the body weight of GDM rats was significantly reduced compared with the GDM-NC group ( $P < 0.05$ , Figure 1). These results indicate that resveratrol can reduce the body weight of GDM rats.

**3.3. The Effect of Resveratrol on the Content of TC, TG, LDL-C, and HDL-C in the Serum of GDM Rats.** Compared with the normal pregnancy control group, the serum levels of TC, TG, and LDL-C in the GDM-NC group were significantly increased, and the content of HDL-C was significantly decreased ( $P < 0.01$ , Figures 2(a)–2(d)). After 2 weeks of treatment with resveratrol (120 and 240 mg/kg), serum levels of TC and TG were lower than those in the GDM-NC group ( $P < 0.05$ , Figures 2(a), 2(b)). Among them, the LDL-C content of the resveratrol (240 mg/kg) treatment group was significantly reduced. Also, the HDL-C content of the resveratrol (240 mg/kg) treatment group was significantly increased ( $P < 0.05$ , Figures 2(c), 2(d)). Compared with the metformin hydrochloride treatment group, the resveratrol (240 mg/kg) treatment group had a better effect on lowering blood lipids. These results indicate that resveratrol can effectively reduce blood lipid levels in GDM rats.

**3.4. The Effect of Resveratrol on the Levels of Leptin, Adiponectin, Resistin, TNF- $\alpha$ , and IL-6 in the Plasma of Rats with GDM.** Compared with the normal pregnancy control group, the plasma levels of leptin, resistin, TNF- $\alpha$ , and IL-6 in the GDM-NC group were significantly increased, and the adiponectin level was significantly reduced ( $P < 0.01$ , Figures 3(a)–3(e)). After 2 weeks of treatment with resveratrol (240 mg/kg), compared with the GDM-NC group, the plasma

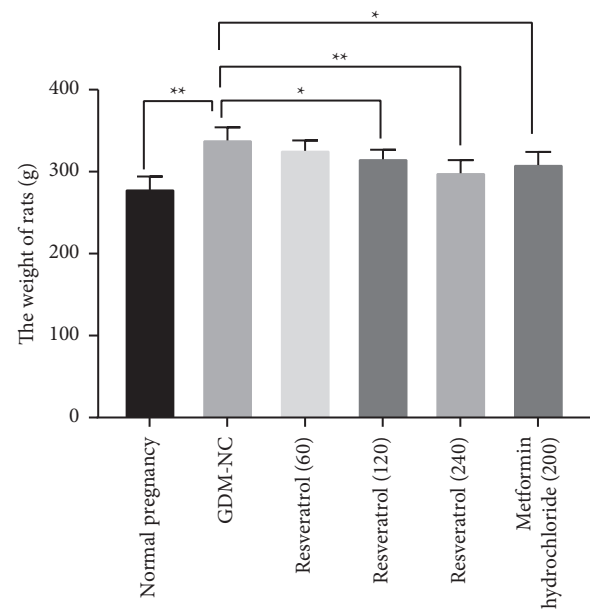


FIGURE 1: The effect of resveratrol on the weight of rats with GDM. The body weight of rats with GDM in the resveratrol (60, 120, 240 mg/kg) treatment group and metformin hydrochloride treatment group was compared with that in the GDM-NC group. \* $P < 0.05$ , \*\* $P < 0.01$ .

levels of leptin, resistin, TNF- $\alpha$ , and IL-6 in GDM rats were significantly reduced ( $P < 0.05$ , Figures 3(a), 3(c)–3(e)). In addition, adiponectin was significantly increased in the 240 mg/kg resveratrol treatment group, while resistin was significantly decreased ( $P < 0.05$ , Figure 3(b)). Compared with the metformin hydrochloride treatment group, the plasma levels of leptin, resistin, TNF- $\alpha$ , and IL-6 in the resveratrol (240 mg/kg) treatment group were significantly increased. Also, the adiponectin level was apparently decreased (Figures 3(a)–3(e)). The abovementioned results indicate that resveratrol may reduce blood lipids in GDM rats by regulating these adipocytokines.

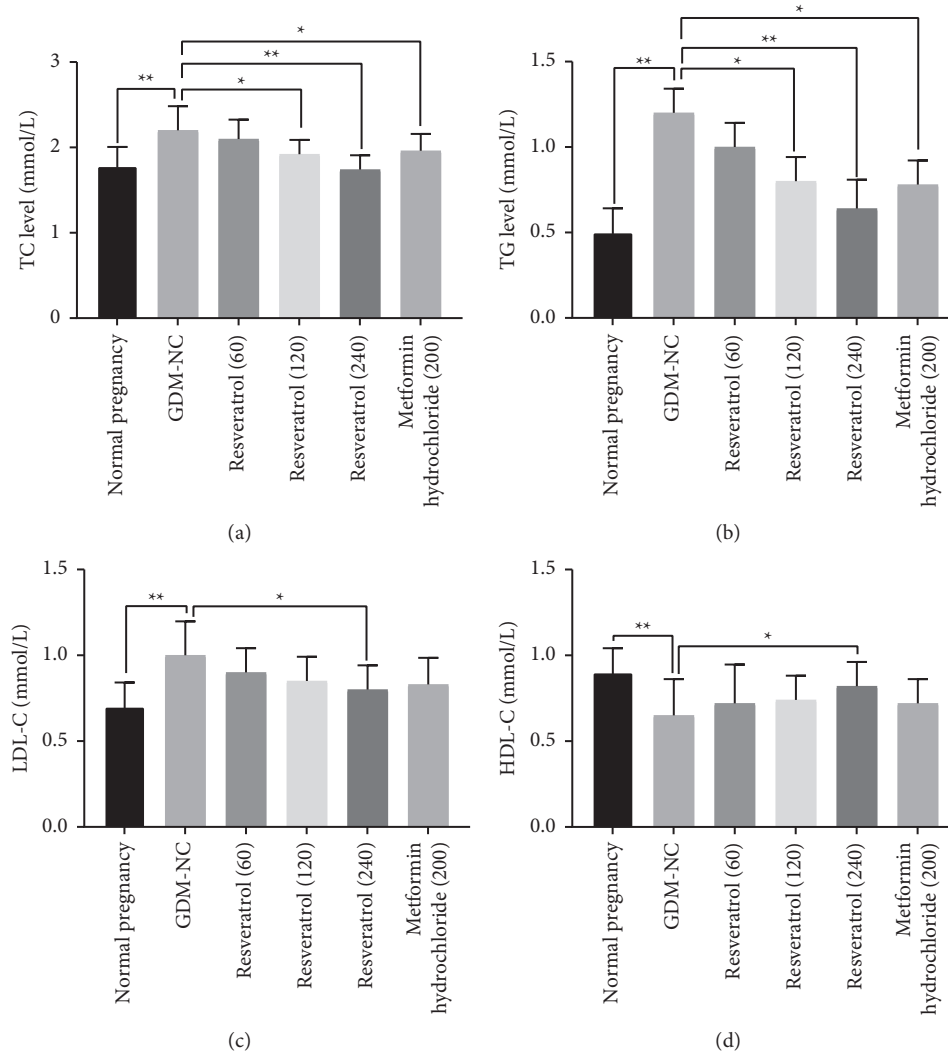


FIGURE 2: The effect of resveratrol on the content of TC, TG, LDL-C, and HDL-C in the serum of GDM rats. (a–d) The TC, TG, LDL-C, and HDL-C levels in of rats with GDM in the resveratrol (60, 120, 240 mg/kg) treatment group and metformin hydrochloride treatment group were compared with those in the GDM-NC group. \* $P < 0.05$ , \*\* $P < 0.01$ .

#### 4. Discussion

GDM is one of the common complications of pregnancy. Hyperglycemia during pregnancy not only endangers the health of the mother but also has an adverse effect on the fetus [15]. At present, the main clinical treatments for GDM are insulin and oral hypoglycemic drugs metformin and thiazolidinedione. However, these drugs have large side effects and easily pass through the placental barrier [16]. Therefore, the development of hypoglycemic drugs suitable for pregnant women has important clinical significance.

Resveratrol is a naturally occurring nonflavonoid polyphenol compound, which is widely present in natural plants such as grape, knotweed, cassia seed, and peanut [17]. Previous studies have reported that resveratrol has various biological effects such as anti-inflammatory, antioxidant, and antitumor [18, 19]. In this study, we found that insulin secretion levels and fasting blood glucose levels in GDM rats were significantly increased after 2 weeks of resveratrol

treatment. The levels of TC, TG, and LDL-C in the resveratrol group were significantly reduced, while the level of HDL-C was significantly increased. In addition, the weight of rats in the resveratrol group was significantly reduced. It has been shown that obesity and lipid metabolism disorders are very dangerous predisposing factors for diabetes [20]. Therefore, the hypolipidemic effect of resveratrol is of great significance to the treatment of GDM.

In addition, we also found that the levels of leptin, TNF- $\alpha$ , and IL-6 in the plasma of resveratrol GDM rats were significantly reduced. Leptin has been reported to inhibit the secretion of insulin and exert a negative feedback effect between blood insulin and adipose tissue [21]. TNF- $\alpha$  and IL-6 can affect the phosphorylation of insulin-sensitive cells, block insulin signal transduction, and cause abnormal glucose metabolism [22]. This study also found that resveratrol can increase adiponectin levels and reduce resistin levels. Resistin can reduce the uptake of glucose by adipose tissue and inhibit the signal transduction pathway of



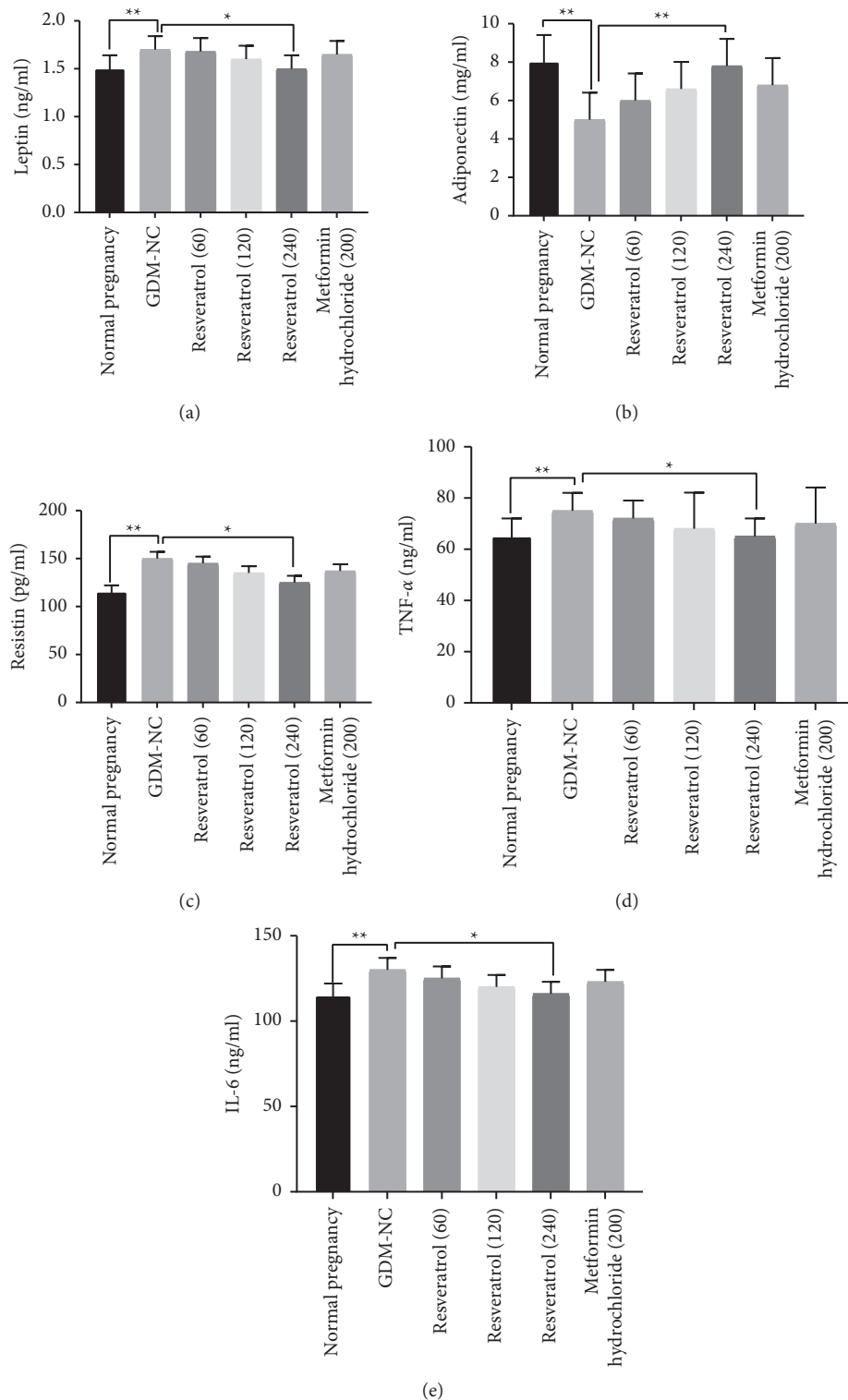


FIGURE 3: The effect of resveratrol on the levels of leptin, adiponectin, resistin, TNF- $\alpha$ , and IL-6 in the plasma of rats with GDM. (a-e) The leptin, adiponectin, resistin, TNF- $\alpha$ , and IL-6 levels of rats with GDM in the resveratrol (60, 120, 240 mg/kg) treatment group and metformin hydrochloride treatment group were compared with those in the GDM-NC group. \* $P < 0.05$ , \*\* $P < 0.01$ .

insulin [23]. Adiponectin can reduce the occurrence and development of diabetes by improving insulin sensitivity [24]. These results indicate that resveratrol has a dose-dependent effect on GDM rats to increase insulin secretion,

reduce blood glucose, reduce body weight, and regulate blood lipids and plasma adipokines. Moreover, resveratrol was stronger than metformin hydrochloride in improving insulin secretion and regulating blood lipids and adipokines.



However, the specific mechanisms of resveratrol for regulating blood sugar and blood lipids are still unclear. This is also the main problem that we need to solve in the future.

## 5. Conclusions

Resveratrol has a dose-dependent effect on reducing blood glucose and blood lipids in GDM rats. Resveratrol can also treat GDM by promoting insulin secretion and regulating adipokines. However, this study has not yet elucidated the specific regulatory mechanism of resveratrol in GDM. Therefore, the regulatory mechanism of resveratrol in GDM will be explored in the future.

## Data Availability

The datasets used during the present study are available from the corresponding author upon reasonable request.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Research Article

# The Efficacy of *Tripterygium* Glycosides Combined with LMWH in Treatment of HSPN in Children

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**Objective.** This study aimed to explore the clinical efficacy and relevant mechanism of *Tripterygium* glycosides combined with low molecular weight heparin calcium (LMWH) in the treatment of Henoch–Schönlein purpura nephritis (HSPN) in children. **Methods.** 64 cases of children patients with HSPN treated at Qilu Hospital (Qingdao) from January 2015 to May 2020 were selected and randomly divided into the control group and the observation group and 32 cases in each group. Conventional medical treatment was applied in the two groups, besides which the control group was given LMWH while the observation group was given *Tripterygium* glycosides based on the control group. The clinical efficacy and the indexes of clinical symptoms of the two groups were compared. Immune globulin level, fibrinogen content (FIB), prothrombin time (PT), platelet level (PLT), and activated partial thromboplastin time (APTT) level of the two groups were compared before and after the treatment. **Results.** The total effective rate in the observation group was significantly higher than that of the control group, and the recurrence rate in the observation group was lower than that in the control group. After treatment, urine red blood cell count and 24 h urine protein were obviously better than those of the control group. There was no statistically significant difference in PT between the two groups of children before and after treatment. The levels of PLT and FIB in the two groups of patients after treatment were significantly lower than before treatment, and the PLT levels in the observation group were lower than those in the control group. **Conclusion.** The combination of *Tripterygium* glycosides and LMWH had good clinical effects in the treatment of children with HSPN, and it could improve the clinical symptoms, the mechanism of which might be related to the increase of PT, a decrease of PLT, and the improvement of coagulation function.

## 1. Introduction

Henoch–Schönlein purpura (HSP) in children is a systemic inflammatory vascular disease mediated by immunoglobulin A. The clinical manifestations of children with HSP include skin purpura, arthritis, hemorrhagic gastroenteritis, and renal damage, and in some cases, manifest as asymptomatic urine abnormalities [1]. Kidney damage is a common secondary injury in HSP, with a higher incidence of

Henoch–Schönlein purpura nephritis (HSPN), often transient hematuria, accompanied by varying degrees of renal disease and functional impairment [2, 3]. HSPN tends to occur in children under 10 years of age, and it accounts for about 8% of pediatric urinary system patients [4]. The incidence rate in boys is higher than that in girls [5]. Most of the children show self-limiting characteristics and can be cured within a few weeks after the onset. However, about one-half of the children still have recurrent attacks [6].

Recent studies have shown that about 15% of children with HSPN develop persistent nephropathy, and 8% of children with HSPN develop renal failure. Therefore, the treatment of children with HSPN should be taken seriously to get the desired outcomes [7]. At present, glucocorticoids, immunosuppressants, and other drugs are often used to treat pediatric HSPN, but these treatments have obvious defects such as prolonged treatment course, severe adverse reactions, and recurrence [8].

*Tripterygium wilfordii* is a vine-like plant that grows in southeastern of China and has been used in traditional Chinese medicine for thousands of years. *Tripterygium* glycosides are natural active ingredient extracted from *Tripterygium wilfordii* [9]. It has a variety of pharmacological functions, such as detoxification, invigorating blood, preventing inflammation, and antifertility [10]. *Tripterygium* glycosides have been used in the treatment of HSPN in China. A previous study has suggested that *Tripterygium* glycosides can relieve hematuria and proteinuria in immunoglobulin A deposition nephropathy and diabetic nephropathy [11]. In addition, *Tripterygium* glycosides can enhance the effect of thiamazole and prednisone in the treatment of hyperthyroidism [12]. Moreover, *Tripterygium* glycosides have been used to reduce proteinuria and protect the kidney for more than 20 years [13, 14].

In this study, *Tripterygium* glycosides and low molecular weight heparin calcium (LMWH) were used to treat HSPN to evaluate its clinical efficacy on HSPN. At the same time, the changes in the levels of immunoglobulin and thrombin in patients were compared, and the related mechanisms of clinical efficacy were explored, which aims to provide a scientific basis for clinically formulating reasonable and effective treatment plans.

## 2. Materials and Methods

**2.1. Clinical Information.** Sixty-four children with HSPN admitted at Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, Qingdao, Shandong, China, from January 2015 to May 2020, were selected and divided into the control group and observation group, with 32 cases in each group. In the control group, there were 20 males and 12 females; they were 4–15 years old, with an average of  $(9.1 \pm 2.8)$  years old; the course of the disease was 5–30 days, with an average of  $(17.5 \pm 8.0)$  d. In the observation group, there were 22 males and 10 females; the age was 3–13 years, with an average of  $(7.9 \pm 2.7)$  years; the course of the disease was 7–25 days, with an average of  $(14.4 \pm 5.9)$  d. There is no statistical difference of children in the above clinical data ( $P > 0.05$ ).

### 2.2. Inclusion Criteria and Exclusion Criteria

Inclusion criteria: (I) children aged 2–15 years; (II) no immunosuppressive agents, glucocorticoids, and nonsteroidal drugs were used 2 weeks before treatment, such as *Tripterygium* glycoside, cyclophosphamide, or mycophenolate mofetil; (III) the course of the disease was less than 2 months; (IV) kidney pathological grade

is grade I-II; (V) all guardians of the children signed the informed consent form; (VI) patients had no surgical operation history caused by HSPN.

Exclusion criteria: (I) severe heart and cerebrovascular diseases and insufficient liver and kidney function; (II) children with D-dimer or fibrinase less than normal; (III) children with allergies to the drugs used in this study; (IV) switch to or add with another immunosuppressive agent (mycophenolate mofetil, cyclosporine A, and tacrolimus) during treatment; (V) diagnosed with hypercalciuria; (VI) diagnosed with other systemic diseases that may affect renal function (systemic lupus erythematosus).

The study got the approval of the Ethics Committee of Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, Qingdao, China. Patients' family members fully knew the study process and they signed informed consent forms.

**2.3. Interventions.** Both groups of patients were given conventional medical treatments such as antihistamine therapy, hormone therapy, antiplatelet aggregation therapy, and supportive medical therapy, and dipyridamole tablets were taken orally (Shanghai Xinyi Jiufu Pharmaceutical Co., Ltd., National Medicine Standard H44020689, 25 mg/tablet), 1 mg/kg each time, 3 times a day.

On this basis, children in the control group were given low molecular weight heparin calcium (Shenzhen Saibaoer Biopharmaceutical Co., Ltd., 0.5 mL: 5000 AXaU) 100 IU/kg subcutaneously, once a day, for continuous use of 12 weeks. Children in the observation group were given *Tripterygium* glycosides tablets (Zhejiang Prokangyu Natural Medicine Co., Ltd., National Medicine Standard Z33020778, 10 mg) on the basis of control group, 1.5 mg/kg each time, and it was given 30 minutes after breakfast, lunch, and dinner, respectively. The treatment course of both groups was 12 weeks.

**2.4. Clinical Treatment Effect.** The clinical efficacy evaluation criteria are as follows [15]: (I) if clinical symptoms and signs, biochemical tests, blood pressure, and urine protein return to normal, hematuria disappears, and no recurrence within 3 months, it was considered to be cured; (II) if clinical symptoms and signs, biochemical tests, blood pressure, and urine protein have basically returned to normal, hematuria disappears, and a small number of recurrences within 3 months, it was considered to be excellent; (III) if clinical symptoms and signs, biochemical tests, blood pressure, and urine protein are all normal, and as a result, hematuria has disappeared, it was considered to be effective; (IV) if clinical symptoms and signs, biochemical tests, blood pressure, urine protein, and hematuria have not improved and the condition even worsened, it was considered to be invalid. Total effective rate = (cure + excellent + effective) number of cases / total number of cases  $\times 100\%$ .



### 2.5. Renal Function Index and Coagulation Functional Index.

The fasting elbow venous blood and morning urine were collected before and after the treatment of the child, and a fully automatic biochemical analyzer (American Beckman AU-5800) was used to detect renal function indicators (24-hour urine protein). Urine microscopic was used to count the red blood cell (urine RBC). The automatic coagulation analyzer (model: ACL7000; Beckman Coulter Co., Ltd., USA) and supporting kits were used to detect coagulation function indexes: fibrinogen content (FIB), prothrombin time (PT), platelet level (PLT), and activated partial thromboplastin time (APTT). Record the occurrence of adverse reactions during the hospitalization. The treatment course of the two groups was 12 weeks, and the follow-up was one year.

**2.6. Judgment Criteria for Kidney Damage.** After 4 weeks of follow-up treatment and 3 months, urine was tested to determine the kidney damage. The normal value of urinary transferrin is 0.001–5 mg/L. The normal value of urinary N-acetyl- $\beta$ -D-glucosaminidase is 0.3–12 IU/L. The normal value of urinary  $\beta$ 2-microglobulin is 0.1–25 mg/L. If any of the indicators is abnormal, it is considered that there is kidney damage.

**2.7. Statistical Methods.** SPSS 19.0 was used for data analysis, data were expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), comparison between two groups was by the *t*-test, and comparison between groups was by the  $\chi^2$  test.  $P < 0.05$  indicates that the difference is statistically significant.

## 3. Results

**3.1. Comparison of Baseline Data.** As given in Table 1, after treatment in the observation group, there were 15 children with HSPN cured patients, 8 excellent patients, 7 effective patients, and 2 invalid patients; the total effective rate was 94%. In the control group after treatment, there were 10 cases of HSPN cured patients, 8 cases of excellent patients, 4 cases of effective patients, and 10 cases of invalid patients; the total effective rate was 69%. The total effective rate in the observation group was significantly higher than that in the control group ( $P < 0.05$ ). After the treatment, all children were followed up for one year, and it was found that 15 cases in the control group relapsed, while 4 cases in the observation group relapsed. The recurrence rate in the observation group was significantly lower than that in the control group ( $P < 0.05$ ).

**3.2. Comparison of Urine Red Blood Cell Count and 24-Hour Urine Protein.** It can be seen from Table 2 that, before treatment, there was no statistically significant difference in urine red blood cell count and 24-hour urine protein between the two groups ( $P > 0.05$ ). After treatment, the above indicators of the two groups were significantly reduced ( $P < 0.05$ ), and the two indexes of the observation group

were significantly lower than those of the control group (all  $P < 0.05$ ).

**3.3. Comparison of Coagulation Function Index.** There was no statistically significant difference in PT between the two groups of children before and after treatment ( $P > 0.05$ ). After treatment, the APPT levels of the control group did not change significantly from before treatment ( $P > 0.05$ ), while the APPT levels of the observation group were significantly increased ( $P < 0.05$ ), and the difference between the two groups was significant ( $P < 0.05$ , Table 3). The levels of PLT and FIB in two groups of patients after treatment were lower than before treatment ( $P < 0.05$ ), and the PLT levels in the observation group were lower than those in the control group ( $P < 0.05$ ). There was no significant difference in the FIB level between the two groups after treatment ( $P > 0.05$ ) (Table 4).

**3.4. Comparison of Adverse Reactions and Kidney Function Damage.** During the treatment period, 2 cases of adverse reactions occurred in the observation group (1 case of nausea and 1 case of diarrhea and were resolved spontaneously); the incidence rate in the observation group was 6.25%. 3 cases of adverse reactions occurred in the control group (2 cases of nausea and 1 case of dizziness, all of them spontaneously); the incidence rate of adverse reactions in the control group was 9.37%. There was no significant difference in the incidence of kidney damage between the two groups of children before treatment and after 4 weeks of treatment ( $P > 0.05$ ). Two cases in the observation group were found lost to follow-up after 3 months of treatment. The incidence of kidney damage in the control group was significantly higher than that in the observation group ( $P < 0.05$ , Table 5).

## 4. Discussion

According to a survey on the spectrum of childhood glomerular diseases performed in China from 2004 to 2014, HSPN (13%) and lupus nephritis (9%) are the most common secondary glomerular diseases in children. Purpuric nephritis (23%) is the most common pathological pattern observed in young children (0–12 years old) [16]. The clinical features of HSPN are hematuria and urine protein, some of which are accompanied by hypertension and renal insufficiency, which seriously affect children's physical and mental health. The increasing incidence of HSPN has attracted great attention in clinical treatment, and previous studies reported that the immature immune system of infants and young children will trigger HSPN, and the younger the child, the greater the probability of HSPN [17]. Long-term persistent proteinuria and hematuria can cause renal failure and cause irreversible damage to patients. Therefore, early diagnosis and early treatment are essential for children with HSPN.

HSPN is a systemic inflammatory response of small blood vessels, and its pathogenesis is not yet clear. There is direct evidence that food, environmental factors, infections, chemical exposure, drug allergies, insect bites, and other factors are all related to HSPN [18]. Some scholars believe

TABLE 1: Comparison of clinical efficacy between two groups.

Group	Cases ( <i>n</i> )	Cure	Excellent	Effective	Invalid	Total effective rate (%)	Recurrence rate
Control group	32	10 (31%)	8 (25%)	4 (12.5%)	10 (31%)	69	15 (47%)
Observation group	32	15 (47%)	8 (25%)	7 (22%)	2 (6%)	94	4 (12.5%)

TABLE 2: Comparison of the indexes of urine RBC and 24 h urine protein between two groups.

Group	Cases ( <i>n</i> )	Urine RBC ( <i>n</i> /μl)		24 h urine protein (g)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	32	219.9 ± 33.01	94.83 ± 8.28 <sup>a</sup>	0.17 ± 0.02	0.13 ± 0.01 <sup>a</sup>
Observation group	32	205.0 ± 20.28	43.40 ± 9.22 <sup>a</sup>	0.17 ± 0.01	0.07 ± 0.02 <sup>a</sup>
<i>T</i>		0.6661	7.191	0.7276	5.376
<i>P</i>		0.5418	0.002	0.5072	0.0058

<sup>a</sup>Compared with before treatment, *P* < 0.05.

TABLE 3: Comparison of the indexes of PT and APTT between two groups.

Group	Cases ( <i>n</i> )	PT (s)		APTT (s)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	32	12.4 ± 1.01	12.7 ± 0.96	23.73 ± 0.80	25.07 ± 0.48
Observation group	32	12.63 ± 0.74	13.87 ± 0.35	23.73 ± 0.97	28.27 ± 0.57 <sup>a</sup>
<i>T</i>		0.3222	1.969	0	7.496
<i>P</i>		0.7634	0.1203	>0.99	0.0017

<sup>a</sup>Compared with before treatment, *P* < 0.05.

TABLE 4: Comparison of the indexes of PLT and FIB between two groups.

Group	Cases ( <i>n</i> )	PLT (× 10 <sup>10</sup> /L)		FIB (g/L)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	32	28.67 ± 0.99	26.39 ± 0.48 <sup>a</sup>	3.38 ± 0.10	2.78 ± 0.07 <sup>a</sup>
Observation group	32	28.68 ± 1.22	24.15 ± 0.44 <sup>a</sup>	3.4 ± 0.11	2.70 ± 0.06 <sup>a</sup>
<i>T</i>		0.011	5.959	0.2437	1.488
<i>P</i>		0.9917	0.004	0.8194	0.2109

<sup>a</sup>Compared with before treatment, *P* < 0.05.

TABLE 5: Comparison of kidney damage between the two groups.

Group	Cases ( <i>n</i> )	Before treatment		After 4 weeks of treatment		After 3 months of treatment	
		Kidney damage	No kidney damage	Kidney damage	No kidney damage	Kidney damage	No kidney damage
Control group	32	3 (9.37%)	29 (90.62%)	8 (25%)	24 (75%)	13 (40.62%)	19 (59.38%)
Observation group	32	2 (6.25%)	30 (93.75%)	6 (18.75%)	26 (81.25%)	3 (10%) <sup>a</sup>	27 (90%)

<sup>a</sup>Compared with the control group, *P* < 0.05.

that the above factors may cause the activated complement and immune complexes to be deposited in the glomerular mesangium and ultimately affect the normal physiological and metabolic mechanisms of blood coagulation to trigger the disease [19]. The most manifested is the hypercoagulable state of the blood and the disorder of the coagulation and fibrinolysis system. In addition, platelet activation and aggregation complement activation and abnormal humoral immune mechanisms are closely related to the occurrence and development of the disease [20, 21]. Disorders of the coagulation and fibrinolysis system cause abnormal elevation of PT and APTT and a significant decrease in D-D and FIB, which are risk factors for abnormal coagulation and

hemostasis, platelet aggregation, inflammatory effects, and glomerular diseases [22]. Therefore, the primary goal of clinical treatment should be to improve coagulation function.

According to traditional Chinese medicine (TCM) dialectics, HSPN belongs to the categories of “purpura” and “hematuria” [23, 24]. Its pathogenesis is mainly due to blockage of the collaterals and blood-heat delusion, which is a symptom of deficiency and excess. Children are the body of immature Yin and Yang, with innate endowment and insufficient Qi machine, the onset of the disease is rapid, and the disease is difficult to heal [25]. *Tripterygium wilfordii* has the effects of bitter, cold, cool in nature, with great toxicity, and



returns to the liver and kidney meridians. It has the effects of dispelling wind and dampness, promoting blood circulation, dredging collaterals, reducing swelling and pain, killing insects, and detoxifying [26]. *Tripterygium* glycosides are a glycoside extracted from the roots of *Tripterygium*, and its main component is epoxy diterpene lactones. Previous reports showed that *Tripterygium* glycosides had potent anti-inflammatory and immunosuppressive effects [27]. *Tripterygium* glycosides tablets have been indicated to reduce the inflammatory response in rat lung tissue [28]; it can upregulate IL-10 expression and TNF- $\alpha$  levels in the rat arthritis model [29].

This study shows that the observation group has better efficacy than the control group, and the recurrence rate is significantly lower than that of the control group. It shows that *Tripterygium* glycosides combined with LMWH are more effective than LMWH in treating children with HSPN. After treatment, the improvement of clinical symptoms of the observation group was better than that of the control group, indicating that *Tripterygium* glycosides combined with LMWH had a better effect on improving the clinical symptoms of HSPN. The total effective rate of *Tripterygium* glycosides combined with LMWH treatment was significantly higher than that of LMWH treatment alone, indicating that the combination of Chinese and Western medicines is more effective than treatment with Western medicines. After treatment in the two groups, the urine red blood cell and 24-hour urine protein content were significantly reduced, indicating that *Tripterygium* glycosides combined with LMWH can further improve microcirculation and hemorheology, effectively alleviate the symptoms of proteinuria and hematuria, and improve renal function. PLT and FIB were significantly reduced, APTT was significantly increased, and the improvement of various indicators in the observation group was significantly better than that of the control group after treatment, indicating that the combination of *Tripterygium* glycosides combined with LMWH has a stronger effect of promoting blood circulation and removing blood stasis than LMWH. LMWH and *Tripterygium* glycosides have a synergistic effect, which significantly improves the patient's hypercoagulable state, hemorheology, and microcirculation, and prevents the exacerbation of the disease. The possible reasons are as follows: (1) *Tripterygium* glycosides significantly improve glomerular capillary permeability, can effectively reduce the level of urinary protein, and effectively reverse its pathological changes; (2) LMWH can produce various coagulation factors. At the same time, inhibition has a significant improvement effect on the permeability of the filter membrane and improves kidney function. However, there is still room for improvement in this study. To begin with, the insufficient sample size may lead to a large probability of error in data deviation, so we hope to increase the sample size in future research to reduce the deviation of results. Moreover, the reasons for the decrease of adverse drug reactions shall be further explored to stabilize the efficacy of drugs better. These are the directions of our follow-up and improvement, so as to find a better treatment for this disease.

The results of this study showed that the total effective rate of treatment in the observation group was significantly higher than that in the control group, and the recurrence rate of the observation group was lower than that in the control group. After treatment, the urine red blood cell count and 24-hour urine protein were significantly lower than that in the control group. The levels of PLT and FIB in two groups of patients after treatment were lower than before treatment; the PLT levels in the observation group were lower than those in the control group. There was no significant difference in the incidence of kidney damage between the two groups of children before treatment and after 4 weeks of treatment. The incidence of kidney damage in the control group was significantly higher than that in the observation group. It shows that the combination of *Tripterygium* glycoside tablets and LMWH in the treatment of children with HSPN has significant efficacy and high safety and has the potential for clinical application.

### Data Availability

The datasets used to support the findings of this study are available from the corresponding author upon request.

### Ethical Approval

The study got the approval of the Ethics Committee of Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University.

### Consent

Patients' family members fully knew the study process, and they signed informed consent forms.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

### Authors' Contributions

Yan Jin and Yanzheng Wang contributed equally to this work.

### Supplementary Materials

The flowchart of *Tripterygium* glycosides combined with LMWH in treatment of HSPN in children. (*Supplementary Materials*)

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## Research Article

# Effect of Amoxicillin and Clavulanate Potassium Combined with Bazhengsan on Pediatric Urinary Tract Infection

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**Objective.** To explore the therapeutic effect of amoxicillin and clavulanate potassium combined with Bazhengsan on pediatric urinary tract infection (UTI). **Methods.** The data of 120 UTI children treated in Wuhan Xinzhou District People's Hospital from February 2019 to February 2020 were retrospectively analyzed. They were equally split into experimental group (EG) and control group (CG) according to the order of admission. All children were treated with amoxicillin and clavulanate potassium for suspension (twice a day), and EG was additionally treated with one dose of Bazhengsan daily. Both groups were treated for 10 days. After treatment, the immune function indexes, inflammatory factor levels, and clinical efficacy were compared before and after treatment. **Results.** No remarkable differences in the general data such as blood routine and urine routine results were observed between the two groups before treatment ( $P > 0.05$ ). After treatment, EG achieved obviously better immune function indexes ( $P < 0.001$ ) and lower levels of inflammatory factors ( $P < 0.05$ ) compared with CG. Besides, the treatment effective rate in EG (96.7%) was higher than that in CG ( $P < 0.05$ ). **Conclusion.** Amoxicillin and clavulanate potassium combined with Bazhengsan can improve the immune function of UTI children and reduce the levels of inflammatory factors, with remarkable effects, which should be popularized in practice.

## 1. Introduction

Pediatric urinary tract infection (UTI) refers to urinary tract inflammation caused by pathogens invading urinary tract mucosa or tissue. Its clinical manifestations mainly include abnormal urination such as frequency and urgency of urination, as well as urinary incontinence and retention in some children [1, 2]. If not treated in time, it may trigger chronic urinary system infection and lead to renal fibrosis, seriously endangering children's physical and mental health. Antibiotics are the main treatment measures in clinic since UTI is mostly caused by bacteria. However, the wide application of antibiotics results in antibiotic resistance in more than half of the strains due to the production of  $\beta$ -lactamase [3, 4]. Therefore, children can be treated with  $\beta$ -lactamase inhibitors in practice to protect the activity of  $\beta$ -lactamase

antibiotics. Amoxicillin and clavulanate potassium is a mixture of the  $\beta$ -lactam antibiotic (amoxicillin) with the  $\beta$ -lactamase inhibitor (clavulanate potassium), which can enhance the sensitivity of pathogens to amoxicillin and inhibit the production of drug-resistance bacteria [5]. At present, many reports have shown that amoxicillin and clavulanate potassium can reduce the clinical symptoms of UTI children, and especially oral administration of this drug can reduce the incidence of complications such as phlebitis, with definite efficacy [6, 7]. However, UTI can recur in children due to factors such as immunocompromise, and recurrence is an important reason for the development of UTI into chronic renal failure [8, 9]. However, amoxicillin and clavulanate potassium cannot improve the immune function of children, so it is extremely important to combine it with other therapeutic drugs.

In recent years, traditional Chinese medicine (TCM) with the holistic view has shown unique advantages in the treatment of urinary tract diseases. TCM classifies UTI into the category of stranguria and holds that the disease in children is caused by excessive milk and food and accumulation of heat and stagnation, which triggers disturbance of qi transformation and urinary tract obstruction, resulting in frequent urination and pain [10, 11]. The treatment should be based on clearing heat, eliminating accumulation, promoting urination, and removing stranguria. Ning treated pediatric UTI with Bazhengsan and found that *Polygonum aviculare* and fringed pink in the medicine inhibited *Staphylococcus* and *Bacillus* and turned bacteriuria negative [12]. In addition, scholars Changli Xue found that the total effective rate (98.3%) of children was significantly improved compared with the control group after the addition and subtraction treatment of Bazhengsan, suggesting the remarkable effects of this drug on UTI [13]. However, the research of Bazhengsan in UTI treatment focuses on the short-term efficacy, and its impact on immune function and inflammatory factor levels in children remains unclear. Besides, there is no study on the application of Bazhengsan combined with amoxicillin and clavulanate potassium. Based on this, this paper will explore the actual effect of the combined treatment on pediatric UTI, reported as follows.

## 2. Materials and Methods

**2.1. Study Design.** This retrospective study was conducted in Wuhan Xinzhou District People's Hospital from February 2019 to February 2020, aiming to explore the efficacy of amoxicillin and clavulanate potassium combined with Bazhengsan in the treatment of pediatric UTI.

**2.2. Recruitment of Research Subjects.** The data of UTI children treated in Wuhan Xinzhou District People's Hospital from February 2019 to February 2020 were retrospectively analyzed. Children meeting the following criteria were included: (1) children who were diagnosed with UTI by examination, meeting the criteria of Guidelines for the Clinical Research of Chinese Medicine New Drugs [14] and Zhu Futang Practical Pediatrics (7th Edition) [15], that is, white blood cell (WBC) in urine routine  $>5/\text{HP}$ , and midstream urine culture colony count  $>1 \times 10^6/\text{mL}$ ; (2) children with typical urinary tract irritation symptoms; (3) children who were treated throughout the whole period in our hospital without transferring or stopping treatment; (4) children with complete clinical; and (5) children between 1–12 years old. Children were excluded according to the following criteria: (1) children with urinary calculi, urinary deformity, deformity of kidney, chronic pyelonephritis, or other serious organic diseases; (2) children quitting the treatment halfway and changing the treatment plans; (3) children with simple urethral syndrome; (4) children who were allergic to the drugs involved in the study; (5) children with missing clinical data; and (6) children who received antibacterial drug therapy before participating in the study.

**2.3. Steps.** A total of 120 children were enrolled in this study and were equally split into experimental group (EG) and control group (CG) according to the order of admission. On the day when the family members agreed to participate in the study, the research group collected social demographic data and clinical data of the children and tested their blood routine, urine routine, immune function, and inflammatory factor levels. At 10 days after treatment, the research group tested their immune function and inflammatory factor levels again.

**2.4. Ethical Considerations.** This study is in line with the principles of Declaration of Helsinki (as revised in 2013) [16] and approved by the ethics committee of Wuhan Xinzhou District People's Hospital. After the children were recruited, the research group explained the purpose, significance, content, and confidentiality of the study to their families and asked them to sign the informed consent.

**2.5. Withdrawal Criteria.** Judged by the research group, the children with the following conditions were unsuitable to continuously participate in the experiment, and their medical records would be kept but not for data analysis: (1) adverse events or serious adverse events occurred; (2) the condition deteriorated during the experiment; (3) the subjects had some serious comorbidities or complications; and (4) the families of the children were unwilling to continue the clinical trial and requested the research group for withdrawal.

**2.6. Methods.** All children took amoxicillin and clavulanate potassium for suspension (Guangzhou Baiyunshan Pharmaceutical Co., Ltd., Baiyunshan Pharmaceutical General Factory, National Medical Products Administration approval no. H20041109, each containing 200 mg of amoxicillin and 28.5 mg of clavulanate with the ratio as 7:1), with the specific administration methods as follows: (1) 14.3 mg/kg each time for children with the body weight less than 13 kg and age less than 2 years old; (2) one pack each time for children with the body weight of 13–21 kg; and (3) 2 packs each time for those with body weight over 21 kg. After the symptoms disappeared, children continued to take the suspension orally. The total treatment time was 10 days.

EG was additionally treated with Bazhengsan consisting of plantain seed, *Polygonum aviculare*, fringed pink, talc, ural licorice root tip, *Gardenia*, rhubarb, dandelion, and *Hedyotis diffusa*. With the addition and subtraction of herbs in Bazhengsan, Cortex Phellodendri and *Bupleurum* were added for children with fever and chills, Lalang Grass Rhizome and field thistle were added for children with hematuria, peony and *Cyperus rotundus* were added for children with abdominal distention, and *Astragalus mongholicus* and *Codonopsis* were added for those with qi deficiency. Bazhengsan was decocted by the research group and administrated specifically as follows: (1) 1 dose every 2 days with frequent administration every day for children aged under 2 years old; (2) 1 dose every 2 days and three



times a day for children aged 2–5 years old; and (3) 1 dose every day and three times a day for children over 5 years old. The total treatment time was 10 days.

## 2.7. Observation Criteria

**2.7.1. General Data.** The general data extraction forms were established by the children's families, including inpatient number, name, gender, age, urine culture results, blood routine results, urine routine results, residence, family monthly income, parents' marital status, and parents' educational level.

**2.7.2. Immune Function Indexes.** Five milliliter of fasting venous blood was taken from children before treatment ( $T_1$ ), 5 days after treatment ( $T_2$ ), and 10 days after treatment ( $T_3$ ). The levels of T lymphocyte subsets ( $CD8^+$  and  $CD4^+/CD8^+$ ) were detected by flow cytometry (ACEA BIO Hangzhou Co., Ltd, Zhejiang Medical Products certified no. 20142400581), and the levels of immunoglobulin (IgA and IgG) were measured by nephelometry immunoassay kit (Nanjing Getein Bio-Pharmaceutical Co., Ltd., Jiangsu Medical Products certified no. 20122400146).

**2.7.3. Inflammatory Factor Levels.** Five milliliter of fasting venous blood was collected at  $T_1$ ,  $T_2$ , and  $T_3$ . The levels of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), and procalcitonin (PCT) were measured by enzyme-linked immunosorbent assay (Beijing Kewei Clinical Diagnostic Reagent Inc., National Medical Products Administration approval no. S20060028).

**2.7.4. Clinical Efficacy.** The therapeutic efficacy of the children was evaluated according to the Guidelines for Clinical Research on Antibiotics [17] issued by the Pharmaceutical Administration of the Ministry of Health. If the symptoms, signs, laboratory tests, and etiological tests were normal, the children were regarded as cured; if the condition of the children was remarkably improved while one index did not return to a normal level, the treatment was deemed as markedly effective; if the condition was improved while more than one index did not return to normal levels, the treatment was classified as effective; if the condition was not improved, or even aggravated, the treatment was ineffective.

**2.8. Statistical Processing.** The data in this study were processed by SPSS20.0 software and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The data included in the study were enumeration data (clinical efficacy) and measurement data (immune function indexes and inflammatory factor levels), tested by  $X^2$  and  $t$ -test. The differences were statistically significant at  $P < 0.05$ .

## 3. Results

**3.1. Comparison of General Data of Children.** No remarkable differences in the general data such as blood routine and urine routine results were observed between the two groups before treatment ( $P > 0.05$ ) (see Table 1).

**3.2. Comparison of Immune Function Indexes of Children.** The immune function indexes were obviously better in EG than in CG ( $P < 0.001$ ) (see Figure 1).

Figure 1(a) shows IgA. With no remarkable difference in the IgA at  $T_1$  between the two groups ( $0.48 \pm 0.05$  vs  $0.49 \pm 0.04$ ,  $P > 0.05$ ), the IgA at  $T_2$  and  $T_3$  was obviously higher in EG than in CG ( $0.70 \pm 0.09$  vs  $0.53 \pm 0.06$ ,  $0.85 \pm 0.07$  vs  $0.69 \pm 0.04$ ,  $P < 0.001$ ).

Figure 1(b) shows IgG. With no remarkable difference in the IgG at  $T_1$  between the two groups ( $5.41 \pm 0.54$  vs  $5.43 \pm 0.56$ ,  $P > 0.05$ ), the IgG at  $T_2$  and  $T_3$  was obviously higher in EG than in CG ( $7.23 \pm 0.75$  vs  $6.21 \pm 0.60$ ,  $8.67 \pm 0.85$  vs  $6.54 \pm 0.65$ ,  $P < 0.001$ ).

Figure 1(c) shows  $CD8^+$ . With no remarkable difference in the  $CD8^+$  at  $T_1$  between the two groups ( $32.98 \pm 3.21$  vs  $32.96 \pm 3.24$ ,  $P > 0.05$ ), the  $CD8^+$  at  $T_2$  and  $T_3$  was obviously lower in EG than in CG ( $27.41 \pm 2.54$  vs  $30.58 \pm 2.45$ ,  $23.12 \pm 1.22$  vs  $25.87 \pm 1.35$ ,  $P < 0.001$ ).

Figure 1(d) shows  $CD4^+/CD8^+$ . With no remarkable difference in the  $CD4^+/CD8^+$  at  $T_1$  between the two groups ( $1.12 \pm 0.12$  vs  $1.14 \pm 0.13$ ,  $P > 0.05$ ), the  $CD4^+/CD8^+$  at  $T_2$  and  $T_3$  was obviously higher in EG than in CG ( $1.42 \pm 0.23$  vs  $1.21 \pm 0.20$ ,  $1.64 \pm 0.36$  vs  $1.32 \pm 0.35$ ,  $P < 0.001$ ).

**3.3. Comparison of Inflammatory Factors in Children.** The levels of inflammatory factors in EG were significantly lower than those in CG ( $P < 0.001$ ) (see Figure 2).

Figure 2(a) shows TNF- $\alpha$ . With no remarkable difference in the TNF- $\alpha$  at  $T_1$  between the two groups ( $125.65 \pm 12.10$  vs  $125.84 \pm 12.41$ ,  $P > 0.05$ ), the TNF- $\alpha$  at  $T_2$  and  $T_3$  was obviously lower in EG than in CG ( $109.98 \pm 10.14$  vs  $118.64 \pm 12.65$ ,  $101.98 \pm 9.65$  vs  $116.98 \pm 11.41$ ,  $P < 0.001$ ).

Figure 2(b) shows IL-6. With no remarkable difference in the IL-6 at  $T_1$  between the two groups ( $154.52 \pm 12.98$  vs  $154.60 \pm 12.48$ ,  $P > 0.05$ ), the IL-6 at  $T_2$  and  $T_3$  was obviously lower in EG than in CG ( $100.65 \pm 10.22$  vs  $115.98 \pm 11.50$ ,  $50.98 \pm 6.98$  vs  $70.41 \pm 7.68$ ,  $P < 0.001$ ).

Figure 2(c) shows hs-CRP. With no remarkable difference in the hs-CRP at  $T_1$  between the two groups ( $6.54 \pm 0.68$  vs  $6.55 \pm 0.67$ ,  $P > 0.05$ ), the hs-CRP at  $T_2$  and  $T_3$  was obviously lower in EG than in CG ( $4.26 \pm 0.54$  vs  $5.31 \pm 0.58$ ,  $3.10 \pm 0.35$  vs  $4.22 \pm 0.36$ ,  $P < 0.001$ ).

Figure 2(d) shows PCT. With no remarkable difference in the PCT at  $T_1$  between the two groups ( $154.44 \pm 21.68$  vs  $154.56 \pm 21.54$ ,  $P > 0.05$ ), the PCT at  $T_2$  and  $T_3$  was obviously lower in EG than in CG ( $121.98 \pm 12.21$  vs  $134.85 \pm 12.68$ ,  $104.98 \pm 10.68$  vs  $115.68 \pm 11.45$ ,  $P < 0.001$ ).

TABLE 1: Comparison of general data of children.

Group	EG ( $n = 60$ )	CG ( $n = 60$ )	$X^2/t$	$P$
Gender			0.035	0.853
Male	25	24		
Female	35	36		
Age (years)				
Range	1–10	1–11		
Average age	$6.54 \pm 1.22$	$6.59 \pm 1.20$	0.226	0.821
Urine culture			—	—
Positive	60	60		
Negative	0	0		
Blood routine			0.100	0.752
WBC $\leq (11 \times 10^9) \cdot L^{-1}$	54	55		
WBC $> (11 \times 10^9) \cdot L^{-1}$	6	5		
Urine routine			0.054	0.817
WBC $> 20/HP$	48	49		
$5/HP < WBC < 19/HP$	12	11		
Arterial blood gas indexes (mmHg)				
Residence			0.035	0.852
Urban area	36	37		
Rural area	24	23		
Family monthly income(yuan)			0.034	0.853
$\geq 5000$	35	34		
$< 5000$	25	26		
Marital status of parents			0.152	0.697
Married	56	57		
Single/divorced/widowed	4	3		
Education level of parents			0.141	0.707
High school and below	24	22		
University and above	36	38		

3.4. *Comparison of Clinical Efficacy in Children.* The clinical efficacy in EG was remarkably better compared with CG ( $P < 0.05$ ) (see Table 2).

#### 4. Discussion

The incidence of pediatric urinary tract infection (UTI) is 3%–5% in China [18], and the children present with different symptoms and signs due to different ages and urinary infection sites. Gram-negative bacteria are the most common pathogens, and the proportion of Gram-positive bacteria represented by *Streptococcus faecalis* and *Staphylococcus* has also increased in recent years. Antibiotics are still the main treatment measures. Antibiotics are secondary metabolites with antipathogen effects, which can selectively act on specific links in the synthesis of deoxyribonucleic acid and ribonucleic acid with protein in bacterial cells, so as to inhibit, kill, and dissolve bacteria. Early antibiotic treatment of pediatric UTI has achieved remarkable results. However, with the long-term administration of antibiotics, the drug-resistant bacteria have secreted a large amount of  $\beta$ -lactamase against  $\beta$ -lactam antibiotics, which can cleave the  $\beta$ -lactam ring, lose the antibacterial activity, and subsequently enhance the bacterial resistance to antibiotics such as penicillin and cephalosporin. In order to stabilize the antibacterial efficacy of antibiotics, children can be clinically treated with  $\beta$ -lactamase inhibitors that can irreversibly combine with  $\beta$ -lactamase to ensure the role of antibiotics [19]. Amoxicillin and clavulanate potassium are a mixture of the  $\beta$ -lactam antibiotic (amoxicillin) with the  $\beta$ -lactamase inhibitor (clavulanate potassium), in which

the former has an antibacterial effect on Gram-negative and Gram-positive bacteria, while the latter has strong broad-spectrum enzyme inhibitory function. Their combination can enhance the sensitivity of antibiotics and reduce the possibility of drug-resistant bacteria. It has been well documented that amoxicillin and clavulanate potassium can alleviate the clinical symptoms of UTI children and improve the short-term efficacy [20], but it cannot reduce the recurrence rate of pediatric UTI. About 50% of children will relapse after 1 month of treatment due to complex factors, and kidney scars can be formed in severe cases, triggering secondary hypertension and chronic renal failure [21], with poor prognosis.

There are many reasons for the recurrence of pediatric UTI, and low immune function is one of the most critical factors. Once the immune balance is damaged, normal bacteria can become opportunistic pathogens, triggering the recurrence of UTI. Carmen and Maria and have shown in their study that the levels of T lymphocyte subsets in patients with chronic UTI are markedly lower than those in healthy people. They also have stated that the imbalance of  $CD4^+/CD8^+$  is an important factor leading to immune disorders, and immunoglobulin also plays an important role in resisting bacterial invasion [22]. Bazhengsan in this study is derived from an ancient prescription, including plantain seed, *Polygonum aviculare*, fringed pink, talc, ural licorice root tip, *Gardenia*, rhubarb, dandelion, and *Hedyotis diffusa*. Plantain seed promotes urination, removes stranguria, clears heat, and brightens the eye because its outer epidermal cell wall contains a large number of hydrophilic polysaccharide



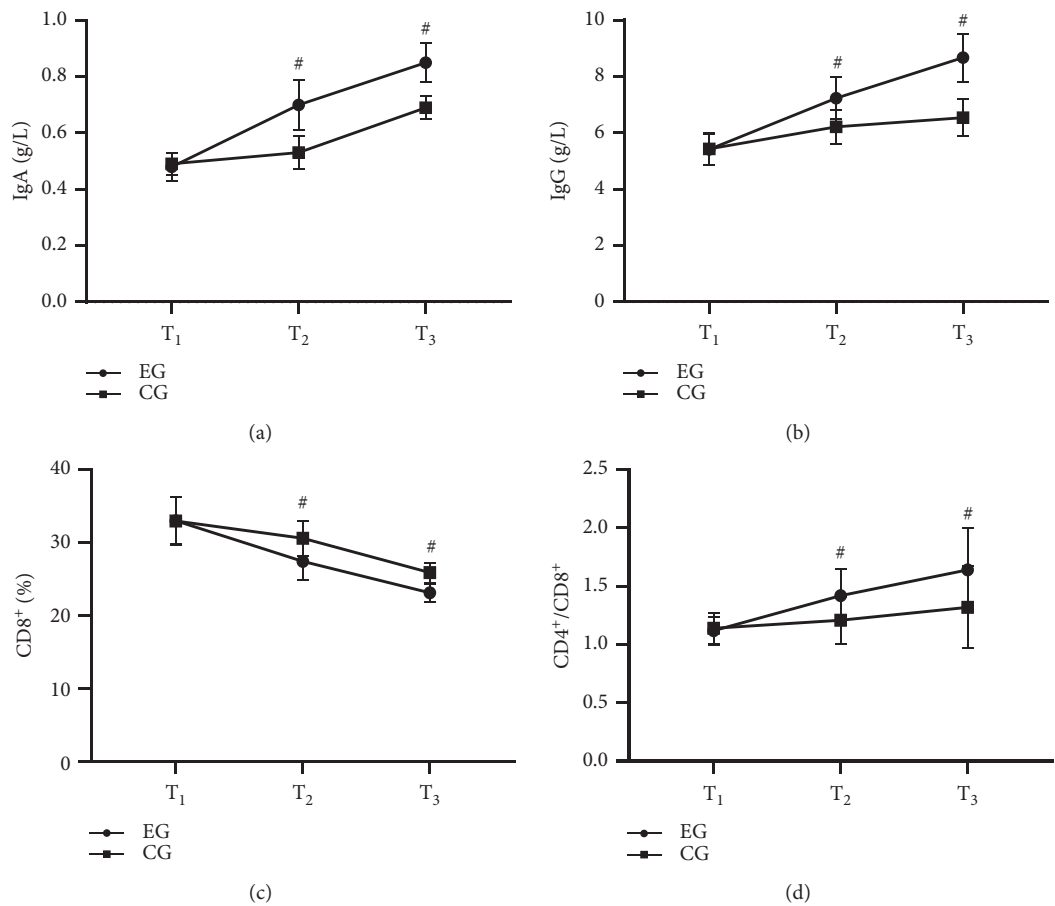


FIGURE 1: Comparison of immune function indexes of children ( $\bar{x} \pm s$ ). Note: the abscissa from left to right was T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>. The lines with dots were EG while those with squares were CG. # indicated  $P < 0.001$ .

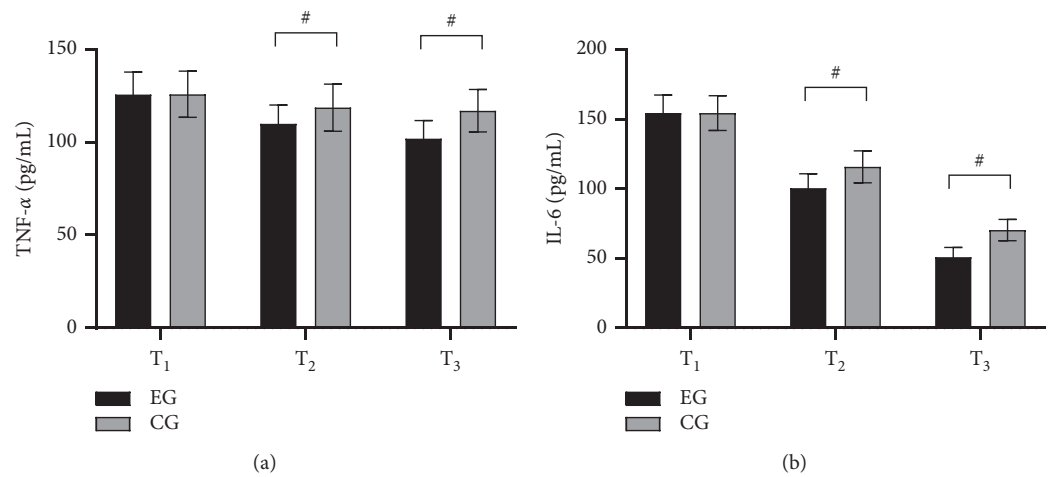


FIGURE 2: Continued.

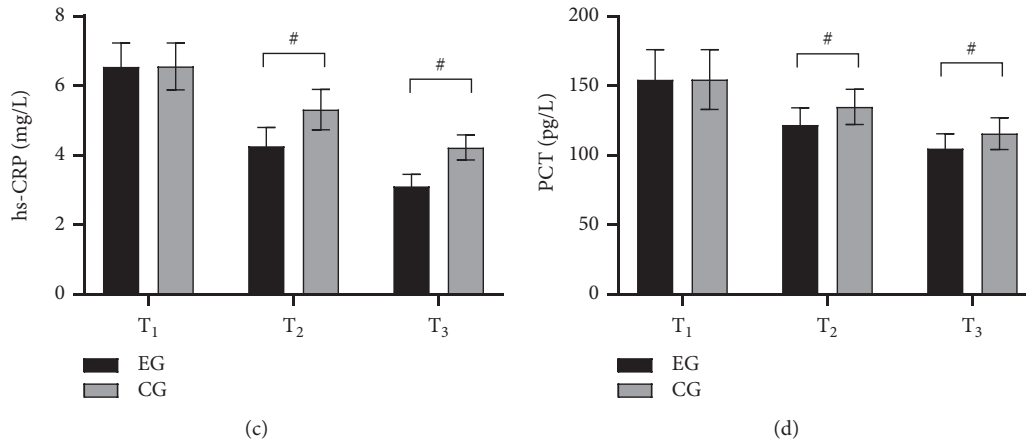


FIGURE 2: Comparison of inflammatory factors in children ( $\bar{x} \pm s$ ). Note: the abscissa from left to right was T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>. The black area was EG and the gray area was CG. # indicated  $P < 0.001$ .

TABLE 2: Comparison of clinical efficacy in children ( $n(\%)$ ).

Group	N	Cured	Markedly effective	Improved	Ineffective	Total effective rate
EG	60	30 (50.0)	18 (30.0)	10 (16.7)	2 (3.3)	58 (96.7)
CG	60	24 (40.0)	10 (16.7)	16 (26.7)	10 (16.7)	50 (83.3)
$\chi^2$		1.212	2.981	1.768	5.926	5.926
P		0.271	0.084	0.184	0.015	0.015

colloids that can improve the intensity of delayed allergic reaction and increase the level of hemolysin in mice with low immune function, indicating that the substance can enhance the immune function. In addition to plantain seed, water extract and low polarity extract can also regulate the secretion of human immunoglobulin, while rhubarb can enhance the IgA level secreted by the intestinal tract of burned mice and accelerate the secretion of immune-related substances [23]. Therefore, Bazhengsan has an immune enhancement effect, and the immune function indexes of EG after treatment were significantly better compared with CG ( $P < 0.001$ ).

At present, scholars have studied the application of Bazhengsan in pediatric UTI, but the effect of the drug on the levels of inflammatory factors in children remains unclear. *Polygonum aviculare* in Bazhengsan significantly inhibits *Shigella flexneri*, *Escherichia coli*, *Staphylococcus aureus*, and *Staphylococcus*, while the water and ethanol extracts of fringed pink also restrain *Escherichia coli* and *Salmonella paratyphi*. Moreover, dandelion and *Hedyotis diffusa* have strong inhibitory effects on a variety of bacteria and cocci, while rhubarb can also hinder the nucleic acid synthesis of bacterial cells and plays an anti-anaerobic role. Cao et al. have shown in their study that rhubarb can improve serum TNF- $\alpha$  and IL-6 levels, indicating that the drug can effectively prevent the amplification of inflammatory mediators and avoid their biological effects [24]. Therefore, the levels of inflammatory factors after treatment in this study were lower in EG than in CG ( $P < 0.001$ ), with markedly better clinical efficacy in EG ( $P < 0.05$ ).

It is worth noting that some scholars have found that rhubarb can inhibit the expression of intercellular attachment molecules in glomerulus, reduce the proliferation of

human renal fibroblasts induced by mitogen PMA, and hinder the secretion of IL-6, thereby preventing renal fibrosis [25] or protecting the renal function of UTI children. This study did not discuss the renal function of children, and the protective effect of Bazhengsan on renal function of UTI children needs to be further explored.

In addition, amoxicillin and clavulanate potassium combined with Bazhengsan can enhance the comprehensive efficacy of children, which should be popularized in practice.

## Data Availability

The data used to support the findings of this study are available upon reasonable request from the corresponding author.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect of Danqi Buxin Decoction on Chronic Function Indexes and Life Quality in Patients with Chronic Heart Failure of Yang Deficiency Type

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**Objective.** The purpose was to explore the clinical effect of Danqi Buxin decoction on chronic heart failure (CHF) with yang deficiency and its effect on cardiac function and life quality of patients. **Methods.** 106 CHF patients with yang deficiency treated in Jinan Municipal Hospital of Traditional Chinese Medicine from February 2019 to February 2020 were selected as the research objects and divided into the treatment group and reference group according to the odd and even admission numbers, with 53 cases in each group. The reference group was treated with routine antiheart failure drugs, while the treatment group was additionally treated with Danqi Buxin decoction to compare the clinical effect and cardiac function changes between the two groups. **Results.** The clinical effective rate in the treatment group was significantly higher than that in the reference group ( $P < 0.05$ ). The TCM symptom scores at T1, T2, and T3 in the treatment group were significantly higher than those in the reference group ( $P < 0.05$ ). After treatment, the LVEDV levels in both groups were significantly higher than those before treatment, while the BNP levels were significantly lower than those before treatment ( $P < 0.001$ ). The LVEDV level in the treatment group after treatment was higher than that in the reference group, while the BNP level in the treatment group was significantly lower than that in the reference group ( $P < 0.001$ ). The life quality scores in the treatment group after treatment were significantly higher than those in the reference group ( $P < 0.05$ ). **Conclusion.** Danqi Buxin decoction on the basis of conventional drugs can significantly improve the cardiac function and life quality of CHF patients with yang deficiency type. Its further research is helpful to establish a good treatment plan for CHF patients.

## 1. Introduction

Chronic heart failure (CHF) is a syndrome in which heart disease develops to the end stage due to various causes. With a high mortality rate, a high hospitalization rate, poor clinical prognosis, and high treatment cost, it brings heavy burden to the family of patients [1, 2]. At present, Western medicine mainly adopts a conservative treatment including angiotensin receptor blockers,  $\beta$ -blockers, and other drugs to improve patients' congestion and alleviate the condition. Although significant progress has been made in the treatment of heart failure, there are still many shortcomings, such as side effects

caused by vasodilators or diuretics. Besides, long-term administration will lead to lower treatment compliance of patients, failing to achieve the expected therapeutic effect and prolong the survival of patients [3]. Therefore, exploring safe and efficient treatment methods is of great significance to improve the life quality and prolong survival time of patients. Traditional Chinese medicine (TCM) has high safety, and its components and unique combination can play a role of multitarget and comprehensive dialectical treatment [4, 5]. TCM classifies CHF as heart impediment, palpitation edema, and other categories and believes that the disease is a heart qi insufficiency syndrome that occurs mainly in the heart but

involves important organs such as the kidney, spleen, and lung [6, 7]. In patients with heart yang deficiency, lack of warm nourishing in blood vessels affects qi-blood circulation and causes qi disorder, resulting in qi stagnation, blood deficiency, and endogenous turbid dampness. Therefore, in the treatment of CHF, especially for patients with heart yang deficiency, the basic principle should be activating blood, dissolving stasis, dredging collaterals, inducing diuresis, and supplementing qi to warm yang [8]. Based on this, to analyze the therapeutic effect of Danqi Buxin decoction on CHF with yang deficiency type, 106 CHF patients with yang deficiency treated in our hospital from February 2019 to February 2020 were selected as the research objects, summarized, and reported as follows.

## 2. Materials and Methods

**2.1. General Information.** 106 CHF patients with yang deficiency treated in Jinan Municipal Hospital of Traditional Chinese Medicine from February 2019 to February 2020 were selected as the research objects and divided into the treatment group and reference group according to the odd and even admission numbers, with 53 cases in each group. The treatment group had 29 males and 24 females, with an average age of  $(54.38 \pm 3.49)$  years old and an average disease course of  $(3.08 \pm 0.32)$  years. The number of cases with cardiac functions II, III, and IV was 8, 34, and 11, while the average Lee's score of heart failure was  $(13.46 \pm 1.27)$ . The reference group had 28 males and 25 females, with an average age of  $(54.42 \pm 3.45)$  years old and an average disease course of  $(3.11 \pm 0.26)$  years. The number of cases with cardiac functions II, III, and IV was 6, 37, and 10, while the average Lee's score of heart failure was  $(13.53 \pm 1.32)$ . There was no significant difference in the baseline data between the two groups ( $P < 0.05$ ) indicating comparability. The flow diagram is shown in Figure 1.

**2.2. Inclusion Criteria.** ① The patients met the diagnostic criteria of CHF in Guidelines for Diagnosis and Treatment of Chronic Heart Failure [9], with the clinical manifestations such as edema of both lower limbs, exertional dyspnea, and fatigue; ② the patient met the TCM diagnostic criteria of yang deficiency type in Guidelines for the Clinical Research of Chinese Medicine New Drugs [10], including fatigue, shortness of breath, and edema, with subsymptoms such as abdominal distension, cold body, and cold limbs; ③ the cardiac function of the patients were grades II–IV according to New York Heart Association (NYHA) classification of cardiac function; and ④ this study was approved by the Ethics Committee of Jinan Municipal Hospital of Traditional Chinese Medicine, and all patients had signed the informed consent.

**2.3. Exclusion Criteria.** ① The patients had severe liver and kidney dysfunction; ② the patients were complicated with malignant arrhythmia or acute myocardial infarction; ③ the patients were allergic to Danqi Buxin decoction and other drug ingredients used in this study; and ④ the patients were complicated with malignant tumors.

## 3. Methods

Both groups of patients were given basic treatment (diuretic, oxygen inhalation, cardiogenic, and antiinfection treatment), limiting the intake of water and sodium, paying attention to rest, correcting arrhythmia, and maintaining electrolyte and acid-base balance. The reference group was treated with routine antiheart failure drugs, including 20 mg of oral spironolactone (SFDA approval no.: H33020070; manufacturer: Hangzhou Minsheng Pharmaceutical Co., Ltd.; specification: 20 mg \* 100 s), 0.125 mg of digoxin (SFDA approval no.: H37020332; manufacturer: Shandong Xinhua Pharmaceutical Co., Ltd.; specification: 0.25 mg), and 0.5 mg of nitroglycerin (SFDA approval no.: H13022503; manufacturer: Hebei Medical University Pharmaceutical Factory; specification: 0.5 mg \* 100 tablets/bottle). The above three drugs were taken once daily. On this basis, the treatment group was additionally treated with Danqi Buxin decoction with the formula including 15 g of Bighead Atractylodes Rhizome, 15 g of dried tangerine peel, 15 g of root of red-rooted *Salvia*, 15 g of Chinese angelica, 15 g of Rhizoma Chuanxiong, 15 g of Cassia Twig, 10 g of sun-dried ginseng, 10 g of dwarf lilyturf tuber, and 30 g of *Astragalus mongholicus*, one dose each day. Cooked in water to obtain 150 ml of juice, the decoction was warmly taken three times a day, with 50 ml each time. Both groups of patients were continuously treated for 14 days.

**3.1. Evaluation Indexes.** Clinical efficacy evaluation: relevant criteria in Guidelines for the Clinical Research of Chinese Medicine New Drugs were used to evaluate the clinical efficacy. After treatment, all clinical symptoms disappeared, and NYHA classification reached grade I, which was cured; The symptoms were significantly improved, and NYHA classification reached grade I or increased by 2 grades, which was markedly effective. The symptoms were improved, and NYHA classification increased by 1 grade, which was effective. The symptoms and NYHA classification were not improved, or the condition was aggravated, which was ineffective. Treatment effective rate = cured rate + markedly effective rate + effective rate.

According to TCM scores corresponding to the degree of clinical symptoms, the TCM symptom scores of patients before treatment (T0), 5 days after treatment (T1), 10 days after treatment (T2), and 14 days after treatment (T3) were calculated and compared between the two groups.

Echocardiography was used to detect the left ventricular end-diastolic volume (LVEDV) levels of both groups before and after treatment. 5 ml of fasting venous blood was collected from the two groups before and after treatment. After anticoagulation with heparin sodium and centrifugation, the serum was extracted for detection. BNP-Triage kits (manufacturer: Shanghai Westang Biotech Co., Ltd.) were used to determine the BNP level.

The daily quality of life scale for patients with chronic heart failure made by our department was used to evaluate the life quality of both groups after treatment, including disease condition, physical strength, living function, social



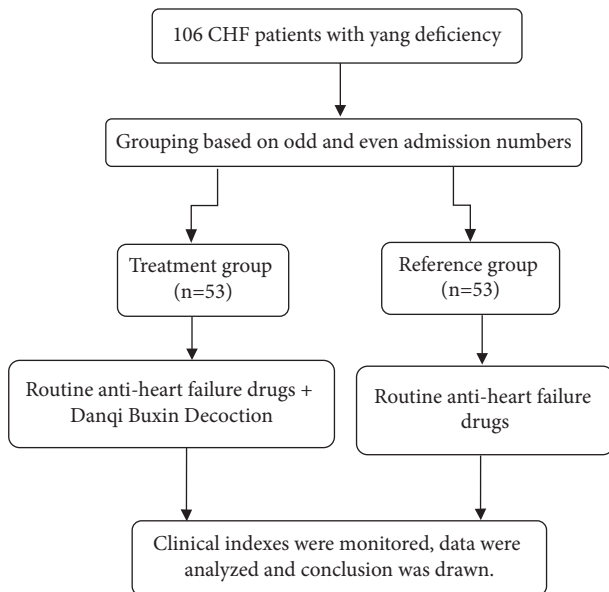


FIGURE 1: Flow diagram of the study.

psychological function, and working condition. The total score was 30 points in condition and social psychological function, 100 points in physical strength, 20 points in living function, and 15 points in working condition. A higher score indicated higher life quality of patients.

**3.2. Statistical Methods.** All the experimental data were statistically analyzed and processed by SPSS 21.0 software, and the data were graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The count data were tested by  $\chi^2$ , expressed by ( $n$  (%)), and the measurement data were measured by the  $t$ -test, expressed by ( $\bar{x} \pm s$ ). The difference was statistically significant when  $P < 0.05$ .

## 4. Results

**4.1. Comparison of Demographic Characteristics between the Two Groups.** No notable differences in demographic characteristics were observed between the two groups ( $P < 0.05$ ; Table 1).

**4.2. Comparison of Clinical Efficacy between the Two Groups.** The total clinical effective rate in the treatment group was significantly higher than that in the reference group ( $P < 0.05$ , Table 2).

**4.3. Comparison of TCM Symptom Scores at Different Time between the Two Groups.** The TCM symptom scores at T1, T2, and T3 in the treatment group were significantly higher than those in the reference group ( $P < 0.05$ , Figure 2).

**4.4. Comparison of LVEDV and BNP Levels before and after Treatment between the Two Groups.** After treatment, the LVEDV levels in both groups were significantly higher than those before treatment, while the BNP levels were

significantly lower than those before treatment ( $P < 0.001$ , Figures 2 and 3). The LVEDV level in the treatment group after treatment was higher than that in the reference group, while the BNP level was significantly lower than that in the reference group ( $P < 0.001$ , Figures 3 and 4).

**4.5. Comparison of Life Quality Scores after Treatment between the Two Groups.** After treatment, the scores of disease condition, physical strength, living function, social psychological function, and working condition in the treatment group were significantly higher than those in the reference group ( $P < 0.05$ , Table 3).

## 5. Discussion

Clinical investigation shows that CHF is a chronic progressive disease, and about 25% of patients have the risk of secondary hospitalization, which seriously affects their life quality. Since decreased myocardial contractility and cardiac hemodynamic overload are the main causes of CHF, the basic treatment principle in clinics is to rebuild myocardial cells and restore cardiac function [11]. TCM has accumulated a lot of experience in the treatment of cardiovascular diseases and believes that heart yang deficiency is the root of heart failure. Heart failure has gradually evolved from heart qi insufficiency to heart yang deficiency, which is caused by the weakness of heart qi and yang, and runs through the whole process of disease occurrence and development [12]. Although Western medicine has made significant progress in CHF treatment, there are still many shortcomings, such as the side effects of drugs which lead to malignant arrhythmia, affecting the therapeutic effect [13, 14]. TCM believes that attention should be paid to yin-yang balance and the recovery of various organ functions in treatment, thus improving clinical symptoms and life quality.

TCM believes that CHF is mostly due to damage of viscera caused by congenital deficiency or acquired pathogenic factors [15]. In this study, the CHF patients with yang deficiency were treated with Danqi Buxin decoction on the basis of routine antiheart failure drugs. After treatment, the LVEDV levels in both groups were significantly higher than those before treatment ( $P < 0.001$ ), and the LVEDV level in the treatment group was significantly higher than that in the reference group ( $P < 0.001$ ). In Danqi Buxin decoction, root of red-rooted *Salvia* cools blood, eliminates carbuncle, improves blood circulation, and disperses stasis; dwarf lilyturf tuber tonifies the stomach, promotes fluid, and nourishes yin to moisten the lung; sun-dried ginseng has the effect of invigorating primordial energy, nourishing blood, and tranquilizing mind by nourishing the heart. Therefore, it is speculated that the whole prescription has the effect of reducing myocardial oxygen consumption and improving coronary blood flow, which effectively reduces the clinical symptoms and improves prognosis of CHF patients [16]. Moreno-Suarez et al. [17] pointed out in their study that after CHF patients were treated with Shenqi Fumai decoction based on the routine Western medicine treatment, the LVEDV level after treatment was significantly higher



TABLE 1: Comparison of demographic characteristics between the two groups.

Items	Treatment group	Reference group	$\chi^2/t$	$P$
Education level				
Primary school	10 (18.87)	11 (20.75)	0.059	0.807
Junior high school	27 (50.94)	30 (56.60)	0.342	0.559
Senior high school	11 (20.75)	9 (16.98)	0.247	0.620
University and above	5 (9.43)	3 (5.66)	0.541	0.462
Occupation				
Peasant	23 (43.40)	26 (49.06)	0.342	0.559
Worker	18 (33.96)	15 (28.30)	0.396	0.529
Teacher	8 (15.09)	5 (9.43)	0.789	0.374
Others	4 (7.55)	7 (13.21)	0.913	0.339
Residence			0.604	0.437
Urban area	25 (47.17)	29 (54.72)		
Rural area	28 (52.83)	24 (45.28)		
Marital status				
Married	49 (92.45)	47 (88.68)	0.442	0.506
Unmarried	2 (3.77)	1 (1.89)	0.343	0.558
Divorced	2 (3.77)	5 (9.43)	1.377	0.241

TABLE 2: Comparison of clinical efficacy between the two groups ( $n$  (%)).

Group	$n$	Cured	Markedly effective	Effective	Ineffective	Total effective rate
Treatment group	53	23 (43.40%)	25 (47.17%)	2 (3.77%)	3 (5.66%)	90.57% (48/53)
Reference group	53	15 (28.30%)	20 (37.74%)	8 (15.09%)	10 (18.87%)	66.04% (35/53)
$\chi^2$						4.296
$P$						<0.05

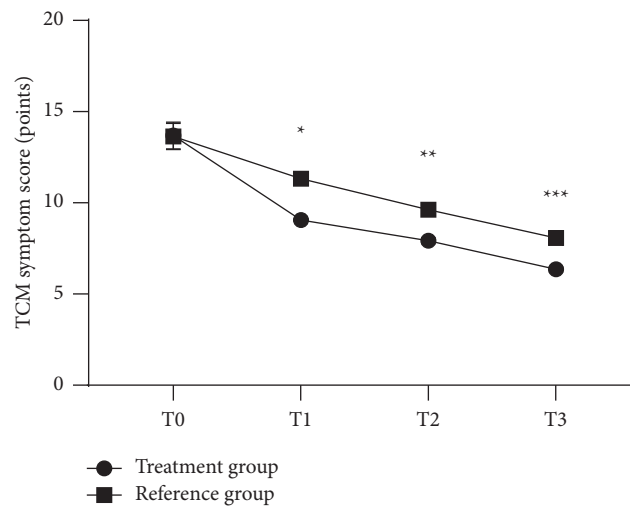


FIGURE 2: Comparison of TCM symptom scores at different time between the two groups ( $\bar{x} \pm s$ ). Note: the abscissa represents T0, T1, T2, and T3, and the ordinate represents the TCM symptom score (points). The TCM symptom scores of the treatment group at T0, T1, T2, and T3 were (13.69 ± 0.74), (9.05 ± 0.34), (7.92 ± 0.17), and (6.35 ± 0.14), respectively. The TCM symptom scores of the reference group at T0, T1, T2, and T3 were (13.64 ± 0.71), (11.32 ± 0.29), (9.63 ± 0.23), and (8.07 ± 0.25), respectively. \*Significant difference in the TCM symptom scores at T1 between the two groups ( $t = 36.981$ ,  $P < 0.001$ ). \*\*Significant difference in the TCM symptom scores at T2 between the two groups ( $t = 45.527$ ,  $P < 0.001$ ). \*\*\*Significant difference in the TCM symptom scores at T3 between the two groups ( $t = 43.701$ ,  $P < 0.001$ ).

than that before treatment, indicating that TCM decoction can activate blood, remove stasis, dredge collaterals, induce diuresis, and supplement qi to warm yang, thereby improving the cardiac function and clinical symptoms of CHF patients. Improving the quality of life of CHF patients is not only one of the goals of clinical treatment but also an

important indicator to measure the therapeutic effect of heart failure. This study evaluated the effect of different treatment regimens on the quality of life of CHF patients by using self-made quality of life scale, and the results showed that the scores in the treatment group after treatment were notably higher compared with the reference group

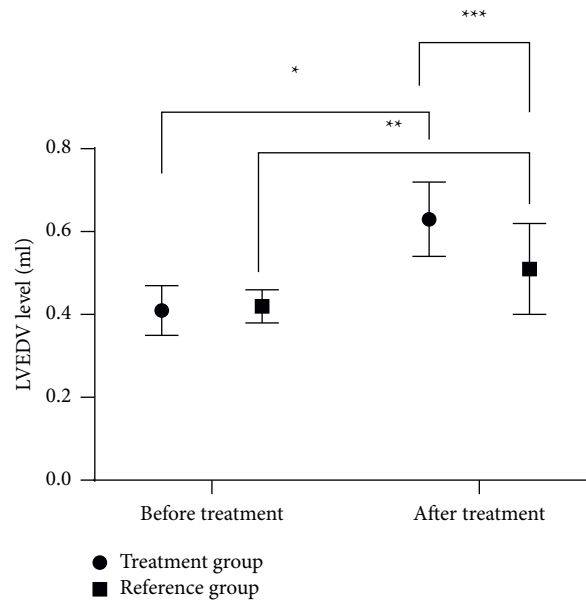


FIGURE 3: Comparison of LVEDV levels before and after treatment between the two groups ( $\bar{x} \pm s$ ). Note: the abscissa represents before treatment and after treatment, and the ordinate represents the LVEDV level (ml). The LVEDV levels of the treatment group before and after treatment were (0.41 ± 0.06) ml and (0.63 ± 0.09) ml, respectively. The LVEDV levels of the reference group before and after treatment were (0.42 ± 0.04) ml and (0.51 ± 0.11) ml, respectively. \*Significant difference in the LVEDV levels of the treatment group before and after treatment ( $t = 14.807$ ,  $P < 0.001$ ). \*\*Significant difference in the LVEDV levels of the reference group before and after treatment ( $t = 5.598$ ,  $P < 0.001$ ). \*\*\*Significant difference in the LVEDV levels between the two groups after treatment ( $t = 6.147$ ,  $P < 0.001$ ).

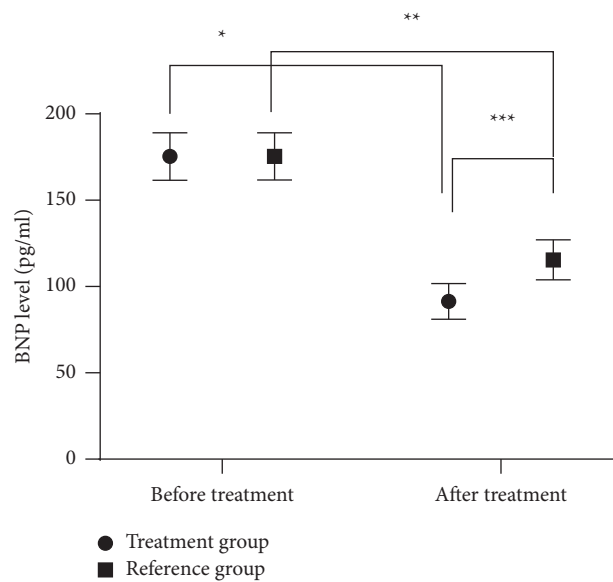


FIGURE 4: Comparison of BNP levels before and after treatment between the two groups ( $\bar{x} \pm s$ ). Note: the abscissa represents before treatment and after treatment, and the ordinate represents the BNP level (pg/ml). The BNP levels of the treatment group before and after treatment were (175.34 ± 13.78) pg/ml and (91.44 ± 10.33) pg/ml, respectively. The BNP levels of the reference group before and after treatment were (175.41 ± 13.69) pg/ml and (115.48 ± 11.62) pg/ml, respectively. \*Significant difference in the BNP levels of the treatment group before and after treatment ( $t = 34.466$ ,  $P < 0.001$ ). \*\*Significant difference in the BNP levels of the reference group before and after treatment ( $t = 24.297$ ,  $P < 0.001$ ). \*\*\*Significant difference in the BNP levels between the two groups after treatment ( $t = 11.257$ ,  $P < 0.001$ ).

( $P < 0.001$ ). It is possibly because Danqi Buxin decoction has the effects of warming yang, invigorating qi, and inducing diuresis to alleviate edema, thereby alleviating clinical symptoms and improving the life quality of patients. The study includes the following deficiencies. (1) This study is a

clinical trial including 106 cases and 2 weeks of treatment, with short observation cycle, small sample size, and patients all coming from our hospital. Therefore, it is necessary to carry out more multicenter studies with a larger sample size and longer follow-up. (2) This study only includes

TABLE 3: Comparison of life quality scores after treatment between the two groups ( $\bar{x} \pm s$ , points).

Group	<i>n</i>	Disease condition	Physical strength	Living function	Social psychological function	Working condition
Treatment group	53	21.43 $\pm$ 1.18	57.82 $\pm$ 2.76	15.22 $\pm$ 2.26	23.68 $\pm$ 1.98	7.61 $\pm$ 0.69
Reference group	53	16.52 $\pm$ 1.23	50.47 $\pm$ 2.33	10.49 $\pm$ 2.17	16.92 $\pm$ 1.65	4.62 $\pm$ 0.52
<i>t</i>		20.971	14.814	10.991	19.094	25.194
<i>P</i>		<0.001	<0.001	<0.001	<0.001	<0.001

preliminary observation on the curative effect and lacks the research on the readmission rate and the long-term quality of life, which needs further clinical verification.

In conclusion, Danqi Buxin decoction can significantly improve the cardiac function and life quality of CHF patients with yang deficiency type, with a significant effect, which is worthy of clinical promotion and application.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Effect Observation on Modified Zishen Tongguan Decoction Combined with Acupuncture in Treatment of Urinary Retention after Cervical Cancer Surgery and Its Influence on the Incidence of Adverse Reactions

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**Objective.** To explore the effect observation on modified Zishen Tongguan decoction combined with acupuncture in the treatment of urinary retention after cervical cancer surgery and its influence on the incidence of adverse reactions. **Methods.** The clinical data of 84 patients suffered from urinary retention after radical resection of cervical cancer (December 2018–December 2019) in the oncology department of Jinan Municipal Hospital of Traditional Chinese Medicine were selected for retrospective analysis. According to the order of admission, they were divided into group A ( $n = 42$ ), treated with conventional therapy, modified Zishen Tongguan decoction, and acupuncture, and group B ( $n = 42$ ), treated with conventional therapy. The clinical efficacy of the two groups was observed, the urination function indexes after therapy were recorded, and the clinical efficacy and incidence of adverse reactions were analyzed. **Results.** After therapy, compared with group B, the average urinary flow rate, maximum urinary flow rate, bladder compliance (BC) level value, and the number of patients with good recovery of bladder function of group A were obviously higher ( $P < 0.05$ ), and the urination time and detrusor pressure were obviously lower ( $P < 0.001$ ). There was no significant difference in the average scoring of overactive bladder syndrome score (OABSS) between the two groups at 7 days of therapy ( $p > 0.05$ ). The average OABSS of group A at 14 days of therapy was obviously lower than that of group B ( $P < 0.001$ ). Compared with group B, the total clinical effective rate of group A was obviously higher ( $P < 0.05$ ), while the total incidence of adverse reactions was obviously lower ( $P < 0.05$ ). **Conclusion.** Modified Zishen Tongguan decoction combined with acupuncture is a reliable method to treat urinary retention after cervical cancer surgery, which greatly improves the urination function of patients, as well as the clinical efficacy. Further research will help create a better solution for patients with urinary retention after cervical cancer surgery.

## 1. Introduction

Cervical cancer is the primary malignant tumor of cervix, ranking first among women's malignant tumors in our country, with clinical manifestations of vaginal bleeding, swelling and pain of lower limbs, and unpleasant smell [1, 2]. Surgery is a common method to treat cervical cancer, but it affects a wide range of lesions and easily damages ligamentum and nerve fibers. Because of the long recovery time

of bladder contraction after surgery, the incidence of urinary retention is very high. The symptom is that the urine in the bladder is filled to capacity and cannot discharge by itself, which is a common complication after cervical cancer surgery [3–5]. Urinary retention can cause urinary tract infection, resulting in dysuria. In addition, because the bladder cannot be emptied, bacterial infection is easy to occur and cystitis is caused. Currently, indwelling urinary catheter is mostly adopted in the clinic as a routine treatment

method [6], which, although can alleviate the symptoms to a certain extent, has poor treatment effect due to the fact that long indwelling period can easily cause infection. Therefore, an effective treatment program for urinary retention after cervical cancer surgery is urgently needed. Some scholars have pointed out in their research [7] that the addition of traditional Chinese medicine (TCM) treatment on the base of conventional therapy such as urinary catheterization has significant effect, and the use of TCM to treat urinary retention has received widespread attention. TCM believes that the patients' vitality is badly sapped after surgery, their lung, spleen, and kidney are weak, and their waterways cannot be regulated, causing difficulty in urination [8]. Therefore, the treatment should be based on tonifying the kidney and qi and dissipating heat and stasis. Zishen Tongguan decoction has the effect of promoting blood circulation to remove blood stasis, tonifying the kidney, and inducing diuresis for treating stranguria, which can improve the urination function after surgery and accelerate rehabilitation of patients. Previous studies have shown that acupuncture can promote the voluntary movement of bladder to reduce the urinary dysfunction [9]. However, there are few reports about the combination of TCM and acupuncture in treating urinary retention after cervical cancer surgery. This study aims to provide more accurate data for the studies of Zishen Tongguan decoction combined with acupuncture in the treatment of urinary retention after cervical cancer surgery and provide some clinical reference.

## 2. Materials and Methods

**2.1. General Data.** The clinical data of 84 patients suffered from urinary retention after radical resection of cervical cancer (December 2018–December 2019) in the oncology department of Jinan Municipal Hospital of Traditional Chinese Medicine were selected for retrospective analysis. According to the order of admission, they were divided into group A ( $n=42$ ) and group B ( $n=42$ ). See Figure 1 for details.

**2.2. Inclusion and Exclusion Criteria.** The inclusion criteria were as follows: (1) all the enrolled patients met the diagnostic criteria for cervical cancer of *Guidelines for Diagnosis and Treatment of Cervical Cancer (4<sup>th</sup> edition)* [10] and were diagnosed by histopathology, and the clinical manifestations included contact bleeding, abnormal vaginal bleeding, abnormal vaginal discharge, and urgency of micturition; (2) all patients underwent radical resection of cervical cancer; (3) the patients suffered from postoperative urinary retention, and their residual urine volume was  $>100$  ml; (4) the patients were diagnosed with urinary retention by ultrasonography and reproductive system examination; and (5) the patients were conscious, and their clinical data were complete.

The exclusion criteria were as follows: (1) the patients with urinary calculus; (2) the patients with liver and kidney dysfunction and immune disease; (3) the patients with other severe postoperative complications such as pelvic infection, lymphocyst, postoperative bleeding, and urethrovaginal

fistula; (4) the patients with bladder dysfunction; and (5) the patients who were allergic to the medicine in this study.

The study was approved by the ethics committee of Jinan Municipal Hospital of Traditional Chinese Medicine, and all the patients and their families knew the study and signed the informed consent.

**2.3. Methods.** After surgical treatments including extensive hysterectomy and laparoscopic pelvic lymph node resection, all patients had urinary retention after surgery, received indwelling urethral catheter, and orally took the prazosin hydrochloride tablets (manufactured by Changzhou Pharmaceutical Factory Co., Ltd., NMPA approval no. H32023906; specification:  $1\text{ mg} \times 100$  tablets/bottle). Meanwhile, physical stimulation, such as hot compress, massage of bladder area, and listening to the sound of water flow, was applied to patients. The urine bag was changed and perineum was disinfected once a day [11].

Patients in group A were additionally treated with modified Zishen Tongguan decoction combined with acupuncture. Zishen Tongguan decoction included, respectively, 20 g of Chinese yam, Cortex Phellodendri, Rhizoma Anemarrhenae, cowherb seed, and Poria; 10 g of Rhizoma Alismatis, lycopodium herb, Cortex Moutan Radicis, *Polyporus umbellatus*, and *Cornus officinalis*; 50 g of Radix Astragali; 15 g of Fructus aurantii, Prepared Radix Rehmanniae, Peach Kernel, and *Achyranthes* root; 8 g of Radix Aconiti Carmichaeli and Cortex Cinnamomi; 12 g of Rhizoma Sparganii and Rhizoma Curcumae; and 6 g of liquorice root. The patients were administrated with the decoction for 50 ml each time and 3 times a day (the decoction was decocted with water). If the patients were accompanied by red complexion, irritability, red urine, constipation, and yellow tongue with red coating, the illness was diagnosed as toxic heat. 10 g of Hemp Fruit and mirabilite, respectively, should be added. If the patients had heaviness sensation in the limbs and head, recessive fever, bitter taste, yellow urine, little urinary volume, chest fullness, and red tongue with yellow coating, the illness was diagnosed as internal damp-heat. 20 g of capillary *Artemisia* and 30 g of gentian should be added. If the patients were accompanied by tiredness, abdominal distension, epigastric discomfort, diarrhea, and pale tongue with white coating, the illness was diagnosed as stagnancy of cold-dampness. 6 g of Manchurian Wildginger, 15 g of parasitic *Loranthus*, and 10 g of Chinese teasel root should be added. If the patients had feverish sensation over the palm and sole, pale complexion, tiredness, and red tongue with little coating, the illness was diagnosed as deficiency of qi and yin. 15 g of Radix Scrophulariae and 20 g of Polygonatum odoratum, *Ophiopogon japonicus*, Radix Rehmanniae, and *Dendrobium* should be added.

**2.3.1. Acupuncture Therapy.** The patients received acupuncture therapy from the 4<sup>th</sup> day after surgery. The lateral position was taken. Yinlingquan, Qihai, Guanyuan, Zusanli, Baihui, bilateral Sanyinjiao, and bladder meridian acupoints were selected for acupuncture. After routine disinfection, twirling-reinforcing- and uniform reinforcing-reducing

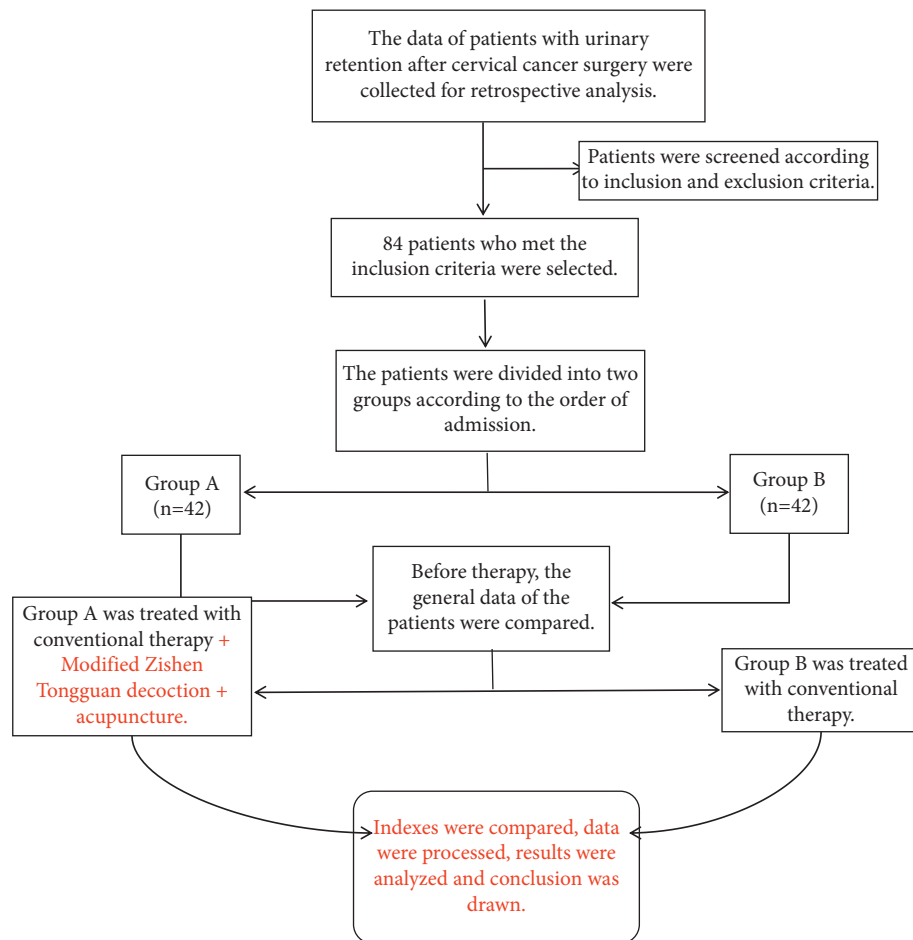


FIGURE 1: Route of experimental technique.

needling methods were used. The retaining needle time for the above acupoints was 30 min. The acupuncture was conducted once a day. Both groups were treated for 21 consecutive days, and the therapeutic outcome was observed [12, 13].

**2.4. Observation Indexes.** An intelligent urinary flow rate detector (manufacturer: Beijing Zhongxi Huada Technology Co., Ltd.; model: CN202M272181) was used to detect the average urinary flow rate, maximum urinary flow rate, and urination time of the two groups after therapy. Urodynamic analyzer (manufacturer: Beijing Haifuda Technology Co., Ltd.; model: ZN999-Nidoc970A) was used to detect detrusor pressure and bladder compliance (BC) level value.

Residual urine volume  $\leq 100$  ml indicated good recovery of bladder function. The number of patients with good recovery of bladder function in both groups after therapy was evaluated.

Urination situation at 7 days and 14 days of therapy of the two groups was evaluated according to overactive bladder syndrome score (OABSS) [14]. The scale included urination frequency during daytime, urination frequency at night, urinary urgency, and urge urinary incontinence, with the total score of 15 points. The higher the score, the more severe the overactive bladder syndrome.

Evaluation of clinical symptoms: (1) if the urinary retention disappeared, urination was smooth, and residual urine volume was not more than 50 ml, it was cured. If the urinary retention basically disappeared, urination was a little blocked, and residual urine volume was 51–100 ml, it was markedly effective. If the urinary retention was reduced, urination lasted longer, there was painful and uncomfortable urination, and residual urine volume was 51–100 ml, it was effective. If the patients could not urinate by themselves, it was invalid.

The incidence of adverse reactions of the two groups was recorded, including rash, salivation, urinary system infection, and nausea and vomiting.

**2.5. Statistical Methods.** The data processing software selected in this study was SPSS21.0, and the selected drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA). The count data were tested by the  $X^2$  test and described by ( $n$  (%)). The measurement data were tested by the  $t$  test and described by mean  $\pm$  SD.  $P < 0.05$  indicated that the difference had statistical significance.

### 3. Results

**3.1. Comparison of the Baseline Data.** There was no significant difference in baseline data including mean age, BMI,



TABLE 1: Comparison of baseline data ( $n = 42$ ).

Items	Group A	Group B	$\chi^2/t$	$P$
Mean age (mean $\pm$ SD, years old)	42.18 $\pm$ 3.46	42.23 $\pm$ 3.42	0.067	0.947
BMI (mean $\pm$ SD, kg/m <sup>2</sup> )	21.82 $\pm$ 1.03	21.76 $\pm$ 1.06	0.263	0.793
<i>Disease types (n (%))</i>				
Squamous cell carcinoma	28 (66.67%)	25 (59.52%)	0.460	0.498
Adenocarcinoma	7 (16.67%)	9 (21.43%)	0.309	0.578
Squamous cell carcinoma and adenocarcinoma	5 (11.90%)	7 (16.67%)	0.389	0.533
Small cell carcinoma	2 (4.76%)	1 (2.38%)	0.346	0.557
<i>Clinical stages (n (%))</i>				
Stage IB2	13 (30.95%)	11 (26.19%)	0.233	0.629
Stage IIA1	17 (40.48%)	19 (45.24%)	0.194	0.659
Stage IIA2	9 (21.43%)	11 (26.19%)	0.263	0.608
Stage IIB1	3 (7.14%)	1 (2.38%)	1.050	0.306
Surgery time (mean $\pm$ SD, min)	155.48 $\pm$ 29.18	155.36 $\pm$ 30.19	0.019	0.985
Bladder urinary retention (mean $\pm$ SD, ml)	473.46 $\pm$ 36.74	475.25 $\pm$ 35.62	0.227	0.821
<i>Physical work (n (%))</i>			0.441	0.507
Yes	26 (61.90%)	23 (54.76%)		
No	16 (38.10%)	19 (45.24%)		
<i>Surgical approaches (n (%))</i>			0.202	0.653
Laparoscopic surgery	27 (64.29%)	25 (59.52%)		
Laparotomy	15 (35.71%)	17 (40.48%)		
<i>Marital status (n (%))</i>				
Married	6 (14.29%)	8 (19.05%)	0.343	0.558
Unmarried	34 (80.95%)	31 (73.81%)	0.612	0.434
Divorced	2 (4.76%)	3 (7.14%)	0.213	0.645
<i>Residence (n (%))</i>			0.778	0.378
Cities and towns	16 (38.10%)	20 (47.62%)		
Countryside	26 (61.90%)	22 (52.38%)		
<i>Education level (n (%))</i>				
College and above	8 (19.05%)	7 (16.67%)	0.081	0.776
High school	25 (59.52%)	21 (50.00%)	0.769	0.381
Middle school and below	9 (21.43%)	14 (33.33%)	1.497	0.221

disease types, and clinical stages between the two groups ( $P > 0.05$ ), as shown in Table 1.

### 3.2. Comparison of the Urination Situation after Therapy.

After therapy, compared with group B, the average urinary flow rate and maximum urinary flow rate of group A were obviously higher, while the urination time and detrusor pressure were obviously lower ( $P < 0.001$ ). See details in Table 2.

**3.3. Comparison of the Number of Patients with Good Recovery of Bladder Function and BC Level Values after Therapy.** After therapy, the BC level value and the number of patients with good recovery of bladder function of group A were obviously higher compared with group B ( $P < 0.05$ ), as shown in Figure 2.

**3.4. Comparison of the OABSS Scores at 7 and 14 Days of Therapy.** There was no significant difference in the average OABSS scores between the two groups at 7 days of therapy ( $P > 0.05$ ). The average OABSS score of group A was obviously lower compared with group B at 14 days of therapy ( $P < 0.001$ ). See details in Figure 3.

**3.5. Comparison of the Clinical Efficacy.** The total clinical effective rate of group A was obviously higher compared with group B ( $P < 0.05$ ), as shown in Table 3.

**3.6. Comparison of the Incidence of Adverse Reactions.** The total incidence of adverse reactions of group A was obviously lower compared with group B ( $P < 0.05$ ), as shown in Table 4.

## 4. Discussion

Cervical cancer is one of the most common diseases affecting women's health, and the continuous infection with high-risk human papillomavirus (HPV) is the most important pathogenic factor in the occurrence and development of it [15, 16]. Surgical resection is often used clinically, which has better therapeutic effect. However, because of the large trauma area of the surgery and intraoperative free ureter lower end, the peripheral nerve of the bladder may be removed when upper pushing the bladder, thereby causing postoperative bladder dysfunction and then the occurrence of urinary retention [17]. In addition, because of the mental stress caused by postoperative pain, being unaccustomed to urinating in bed, and urinary tract infection caused by urinary catheter insertion, the possibility of urinary

TABLE 2: Comparison of urination situation after therapy (mean  $\pm$  SD,  $n = 42$ ).

Items	Average urinary flow rate (cm/s)	Maximum urinary flow rate (cm/s)	Urination time (s)	Detrusor pressure (cm·H <sub>2</sub> O)
Group A	8.32 $\pm$ 1.36	16.27 $\pm$ 2.27	34.18 $\pm$ 4.63	22.17 $\pm$ 3.18
Group B	6.27 $\pm$ 1.42	12.96 $\pm$ 2.31	41.26 $\pm$ 4.73	28.12 $\pm$ 3.21
<i>t</i>	6.757	6.623	6.932	8.534
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001

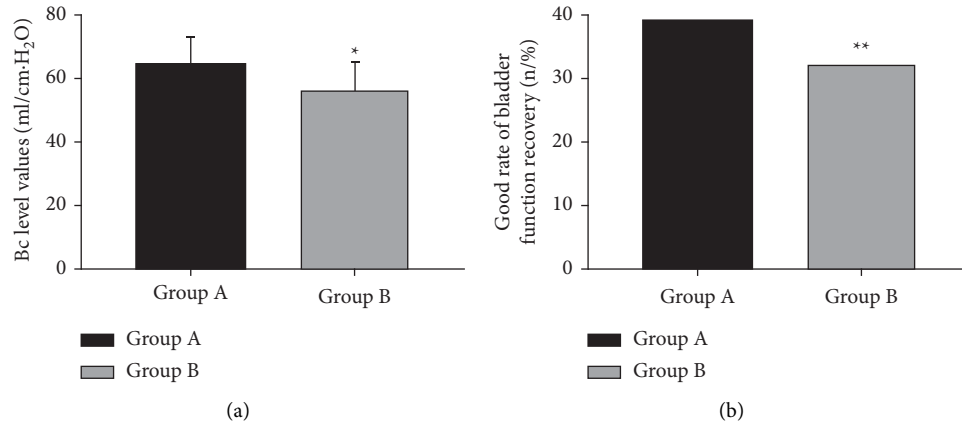


FIGURE 2: Comparison of the number of patients with good recovery of bladder function and BC level values after therapy ( $n$  (%), mean  $\pm$  SD). (a) Comparison of BC level values between the two groups after therapy. The horizontal axis represents group A and group B, and the vertical axis represents BC level value (ml/H<sub>2</sub>O). After therapy, the BC level values in group A and group B were  $64.35 \pm 8.34$  ml/H<sub>2</sub>O and  $56.23 \pm 8.46$  ml/H<sub>2</sub>O, respectively. \*There was a significant difference in BC level values between the two groups after therapy ( $t = 4.430$ ,  $P < 0.001$ ). (b) Comparison of the number of patients with good recovery of bladder function between the two groups after therapy. The horizontal axis represents group A and group B, and the vertical axis represents the number of patients with good recovery of bladder function ( $n$  (%)). After therapy, the number of patients with good recovery of bladder function in group A and group B were 39 (92.86%) and 32 (76.19%), respectively. \*\*There was a significant difference in the number of patients with good recovery of bladder function between the two groups after therapy ( $X^2 = 4.459$ ,  $P < 0.05$ ).

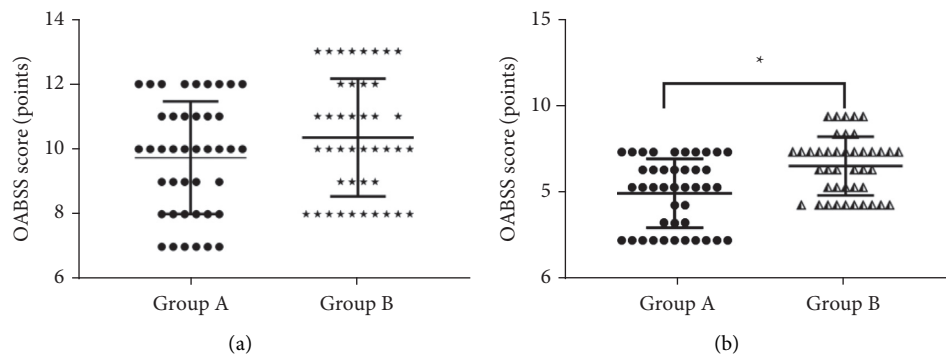


FIGURE 3: Comparison of OABSS scores at 7 d and 14 d of therapy (mean  $\pm$  SD,  $n = 42$ ). (a) Comparison of OABSS scores between the two groups at 7 d of therapy. The average OABSS scores of group A and group B at 7 d of therapy were  $9.17 \pm 1.72$  points and  $10.40 \pm 1.67$  points, respectively. (b) Comparison of OABSS scores between the two groups at 14 d of therapy. The average OABSS scores of group A and group B at 14 d of therapy were  $5.58 \pm 1.50$  points and  $7.98 \pm 1.60$  points, respectively. The horizontal axis represents group A and group B, and the vertical axis represents OABSS score (points). \*There was a significant difference in average OABSS scores between the two groups at 14 d of therapy ( $t = 7.092$ ,  $P < 0.001$ ).

retention will also increase, which may result in pyelitis, obstruction of the ureter, ureteral fistula, and other complications, affecting the postoperative recovery. At present, indwelling urinary catheter combined with Western medicine is often used as a conventional therapy. Although it can

relieve clinical symptoms to a certain extent, urinary tract infection may be caused by long-term indwelling catheter, with limited efficacy [18].

It has been reported [19] that the implementation of TCM treatment in patients with urinary retention after

TABLE 3: Comparison of clinical efficacy ( $n$  (%)).

Items	$n$	Cured	Markedly effective	Effective	Invalid	Total clinical effective rate
Group A	42	23 (54.76)	11 (26.19)	6 (14.29)	2 (4.76)	95.24% (40/42)
Group B	42	17 (40.48)	9 (21.43)	8 (19.05)	8 (19.05)	80.95% (34/42)
$\chi^2$						4.087
$P$						<0.05

TABLE 4: Comparison of incidence of adverse reactions ( $n$  (%)).

Items	$n$	Rash	Salivation	Urinary tract infection	Nausea and vomiting	Total incidence
Group A	42	1 (2.38)	0 (0.00)	0 (0.00)	2 (4.76)	7.14% (3/42)
Group B	42	2 (4.76)	1 (2.38)	4 (9.52)	3 (7.14)	23.81% (10/42)
$\chi^2$						4.459
$P$						<0.05

mixed hemorrhoid surgery can stimulate the bladder and induce diuresis. TCM believes that urinary retention belongs to the category of uroschesis. Kidney qi deficiency, lack of vitality after surgery, and unregulated waterways can result in inability to urinate normally and retention of the bladder. Therefore, the therapy should be based on tonifying the kidney and qi, removing blood stasis, and alleviating water retention [20]. In this study, the therapeutic effect of modified Zishen Tongguan decoction combined with acupuncture on urinary retention after cervical cancer surgery was observed. Modern pharmacological studies have shown [21] that Radix Astragali has the effect of replenishing vitality, antiaging, enhancing immunity, and inducing diuresis. Rhizoma Anemarrhenae can nourish the kidney and yin, clear heat, and drain fire, which has antibacterial and antitumor effect. Rhizoma Alismatis is cold-natured, which can remove dampness and promote diuresis after entering the kidney and bladder meridian. Polyporus umbellatus plays a role of inducing diuresis and curing edema. Polyporus polysaccharide injection was subcutaneously injected to rats by some scholars [22], and significant increase of urine volume was found in the rats. The combined use of the above herbal medicine can make patients' kidney-qi sufficient, bladder gasification normal, and urination smooth. Acupuncture takes patients' acupoints as the point of penetration, which can treat disease of internal organs. Guanyuan, Yinlingquan, Zusanli, etc., are selected for regulating the bladder and assisting in gasification. Yilingquan is selected for promoting blood circulation to remove blood stasis and clearing heat and dampness. Acupuncture on the above points has the effect of dredging meridians, promoting qi to induce diuresis, solid off, and addendum [23].

This study showed that compared with group B, the average urinary flow rate and maximum urinary flow rate of group A after therapy were obviously higher, while the urination time and detrusor pressure were obviously lower ( $P < 0.001$ ). It is speculated that Zishen Tongguan decoction combined with acupuncture can affect neuronal activity, promote the contraction of sphincter and detrusor, and enhance urinary function. BC refers to the ability to maintain constant pressure or slightly increase pressure,

which is the tolerance of the bladder to the increased fluid [24]. This study showed that the BC level value of group A after therapy was obviously higher compared with group B ( $P < 0.001$ ). It is speculated that acupuncture plays a role during the treatment, which can regulate yin and yang of viscera and promote the functional recovery of bladder smooth muscle through stimulating acupoints. Cowherb seed and Rhizoma Alismatis included in the decoction can stimulate nerve conduction, increase the blood perfusion of the local vessels of the bladder detrusor, and promote the recovery of tissue, which has been confirmed in the study of Nardone et al. [25]. The study also showed that the incidence of adverse reactions of group A was obviously lower compared with group B ( $P < 0.05$ ), indicating that Chinese herbal decoction combined with acupuncture had high safety and could improve the therapeutic effect. Deficiencies of this study were as follows. The clinical trial lasted for 3 weeks due to the limitation of the research cycle, and the long-term efficacy of the patients after therapy could not be completely followed up. Therefore, the experimental design scheme needed to be improved. There was a lack of research on emotional changes and quality of life of patients. It is hoped that the impact on the life and mental health of such patients could be evaluated in future studies.

In summary, the modified Zishen Tongguan decoction combined with acupuncture can significantly improve the therapeutic effect, bladder compliance, and urinary function in patients with urinary retention after cervical cancer surgery. Therefore, the combined use of modified Zishen Tongguan decoction and acupuncture has high clinical value.

## Data Availability

The data used to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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## Research Article

# Effect of Combining Traditional Chinese Medicine with Hormonal Therapy on Quality of Life and Tumor Markers of Prostate Cancer Patients

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**Objective.** To explore the effect of combining traditional Chinese medicine (TCM) with hormonal therapy on the quality of life and tumor markers of prostate cancer patients. **Methods.** A total of 60 prostate cancer patients treated in Zibo Central Hospital from June 2017 to June 2021 were selected for the retrospective analysis study and divided into the control group and experimental group based on whether applying TCM treatment, with 30 cases each. The patients in the experimental group received the combined treatment of TCM and hormonal therapy, and those in the control group only accepted the hormonal therapy, so as to analyze their clinical efficacy and tumor marker levels after treatment. **Results.** The patients' general information were not statistically different ( $P > 0.05$ ); after treatment, the levels and ratios of total prostate-specific antigen (TPSA) and free prostate-specific antigen (FPSA) of patients in both groups were improved, and the experimental group obtained significantly lower TPSA and FPSA levels ( $P < 0.05$ ) and higher TPSA/FPSA ratios ( $P < 0.05$ ); the incidence of androgen-independent prostate cancer was significantly lower in the experimental group than in the control group (8 vs. 16,  $P < 0.05$ ); in addition, the time to develop into the androgen-independent prostate cancer was longer in patients of the experimental group than those of the control group ( $P < 0.05$ ); the treated patients in the experimental group obtained obviously higher Functional Assessment of Cancer Therapy-Prostate (FACT-P) quality of life scores and Karnofsky score (KPS) than those in the control group ( $P < 0.05$ ), and the number of patients with recovered PSA levels was significantly higher in the experimental group than in the control group ( $P < 0.05$ ). **Conclusion.** Combining self-made TCM formula with hormonal therapy can effectively improve the levels of prostate tumor markers and postpone the progress of developing from prostate cancer to androgen-independent prostate cancer, which is conducive to promoting the patients' quality of life.

## 1. Introduction

Although the level of medical diagnosis and treatment in China has been increasing in recent years, cancer, with a high incidence and fatality rate, remains an important disease that threatens human health. Prostate cancer is one of the more frequent cancers in men [1, 2]. According to the regional registration statistics, the incidence of prostate cancer in China ranked the sixth of malignant tumors in men and increases with age [3–6]. Currently, hormonal therapy is an important and effective means of prostate

cancer treatment because androgens are the source of prostate cancer cell growth, and cutting off the supply of androgens leads to slow cancer cell growth and even death. In general, hormonal therapy is only effective at the beginning, but most patients will gradually develop hormone-independent prostate cancer, adding difficulties to clinical treatment [7–10]. TCM has gradually accumulated a great deal of clinical practice experiences in the field of tumor treatment and achieved certain efficacy results for a long time, and thus, its value and significance in the treatment of prostate cancer has also received increasing attention, but

the relevant mechanisms of action are still in the stage of active exploration [11, 12]. Since 2019, the authors have implemented a comprehensive program of self-made TCM formula combined with hormonal therapy for treating prostate cancer patients, which presents better efficacy, convenient and rapid administration, and high clinical acceptance of patients. To further clarify its efficacy and related mechanism of action, a retrospective analysis study was carried out on the patients treated in our hospital, which is summarized and reported as follows.

## 2. Study Plan

**2.1. Patient Screening and Grouping.** According to the screening criteria for patients, 60 prostate cancer patients treated in Zibo Central Hospital from June 2017 to June 2021 were selected for the retrospective analysis study and divided into the control group and the experimental group based on whether adopting TCM treatment, with 30 cases each. The study was approved by the Ethics Committee of Zibo Central Hospital.

**2.2. Inclusion Criteria.** ① The patients met the clinical diagnosis criteria for prostate cancer in the Chinese Standard for Diagnosis and Treatment of Common Malignant Tumors [13]; ② the patients were diagnosed after prostate MRI examination and prostate biopsy pathological examination; ③ the patients met the indications of hormonal therapy; ④ the patients were highly compliant and had complete clinical data; and ⑤ the patients and their family members understood the study and signed the informed consent.

**2.3. Exclusion Criteria.** ① The patients presented other severe organic diseases or malignant tumors; ② the condition of the patients was extremely severe and uncontrollable; ③ the estimated survival of the patients was less than 6 months; ④ the patients had severe complications; and ⑤ the patients had communication disorders, limb motor disorders, or cognitive dysfunction.

**2.4. Methods.** All patients received the conventional treatment regimen, and on this basis, those in the control group received the hormonal therapy; i.e., those who were diagnosed with metastasis after general check-up according to the pathological score of prostate biopsy and those who presented surgical indications and received surgery were treated with goserelin acetate (specification: 3.6 mg/tube; manufactured: AstraZeneca UK Limited; registration no. H20100314) and bicalutamide (specification: 50 mg; manufactured: AstraZeneca GmbH; registration no. H20100390) [14–16]. In addition to the hormonal therapy, the patients in the experimental group adopted TCM treatment. To ensure the stable quality of Chinese herbs and avoid affecting the efficacy due to decocting, Huarun Sanjiu TCM concentrate granules were selected, which contained 20 g of prepared *Rehmannia* root, 20 g of common yam rhizome, 15 g of Asiatic Cornelian cherry fruit, 20 g of glossy privet fruit, 20 g

of malaytea scurfpea fruit, 20 g of plantain seed, 30 g of tuckahoe, 20 g of Mongolian milkvetch root, 15 g of zhuling, 20 g of paniculate bolbostemma, 30 g of hedyotis, 15 g of black nightshade herb, 10 g of manyleaf *Paris* rhizome, and 15 g of zedoary rhizome. The patients orally took one dose daily with boiled water in two split times (in the morning and evening) after meal, and the total administration time of TCM needed to be over 12 months.

**2.5. Observation Indexes.** Before treatment, the patients' general information including their age, Karnofsky scores (KPS), scores of the fourth edition of Functional Assessment of Cancer Therapy-Prostate (FACT-P), duration of disease, the frequency of chemotherapy, prostate volume, Gleason score, TNM stage, and pathological examination results was recorded.

By drawing patients' blood, their levels and ratios of total prostate-specific antigen (TPSA) and free prostate-specific antigen (FPSA) were measured (with the enzyme-linked immunosorbent assay), and the kits were purchased from Shanghai Tellgen Life Science Co., Ltd. (NMPA Certified No. 20153401695/NMPA Certified No. 20153401809); mean time for developing from advanced prostate cancer to androgen-independent prostate cancer and the number of affected patients were recorded.

The quality of life of the prostate cancer patients was evaluated by the FACT-P scale, which included 12 items and mainly evaluated the prognostic quality of life from the dimensions of patients' physical well-being, social/family well-being, emotional well-being, functional well-being, and prostate cancer subscale, with higher scores indicating better quality of life; the patients' performance status was evaluated by the KPS scale, with higher scores indicating that the patients had better physical health and could bear some adverse reactions caused by treatment; see Table 1 for the specific scoring standards. The patients' prostate-specific antigen (PSA) levels were measured, and the clinical observation point was 4 ng/ml; i.e., less than 4 ng/ml was considered as normal, and PSA between 4 and 10 ng/ml was called the gray interval.

**2.6. Statistical Processing.** In this study, the between-group differences in data were calculated by the SPSS22.0 software, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), the items included were the enumeration data and the measurement data, which were expressed by (n (%)) and ( $\bar{x} \pm s$ ) and examined by the  $\chi^2$  test and *t*-test, respectively, and differences were considered statistically significant at  $P < 0.05$ .

## 3. Results

**3.1. General Information.** After statistical processing, no statistical differences in the patients' general information between the two groups were observed ( $P > 0.05$ ). See Table 2 for specific values.



TABLE 1: Scoring standards of KPS.

Clinical symptom	Percentage method (points)
No evidence of disease	100
Minor signs or symptoms of disease; able to carry on normal activity	90
Some signs or symptoms of disease; normal activity with effort	80
Cares for self; unable to carry on normal activity or to do active work	70
Requires occasional assistance but is able to care for most personal needs; unable to do active work	60
Requires considerable assistance and frequent medical care	50
Disabled; requires special care and treatment	40
Severely disabled; hospital admission indicated	30
Very sick; completely disabled; hospital admission necessary; active supportive treatment necessary	20
Moribund; fatal processes progressing rapidly	10
Dead	0

TABLE 2: Analysis of patients' general information ( $n = 30$ ).

Observation indicator	Control group	Experimental group	$X^2/t$	$P$
Age (years)	$57.42 \pm 6.38$	$58.04 \pm 6.40$	0.376	0.708
KPS score	$64.02 \pm 6.04$	$63.77 \pm 6.12$	0.159	0.874
FACT-P score	$69.84 \pm 6.65$	$70.15 \pm 6.83$	0.178	0.859
Duration of disease (months)	$12.51 \pm 2.56$	$12.84 \pm 2.67$	0.489	0.627
Number of chemotherapy (times)	$8.05 \pm 1.72$	$8.17 \pm 1.69$	0.273	0.786
Prostate volume (ml)	$71.86 \pm 3.28$	$71.93 \pm 3.35$	0.082	0.935
Gleason score	$8.25 \pm 1.17$	$8.34 \pm 1.26$	0.287	0.775
TNM stage				
II	11 (36.67)	9 (30)	0.300	0.584
III	18 (60)	19 (63.33)	0.071	0.791
IV	1 (3.33)	2 (6.67)	0.351	0.554
Pathological examination				
Good differentiation	7 (23.33)	8 (26.67)	0.089	0.766
Poor differentiation	16 (53.33)	17 (56.67)	0.067	0.795
No differentiation	7 (23.33)	5 (16.67)	0.417	0.519
CEA ( $\mu\text{g/L}$ )	11 (36.67)	9 (30)	0.376	0.708
NSE ( $\mu\text{g/L}$ )	18 (60)	19 (63.33)	0.159	0.874
CYFRA21-1 ( $\mu\text{g/L}$ )	1 (3.33)	2 (6.67)	0.178	0.859

**3.2. Levels and Ratios of TPSA and FPSA.** After treatment, the levels and ratios of TPSA and FPSA in patients of both groups were improved, and the experimental obtained significantly lower TPSA and FPSA levels ( $P < 0.05$ ) and higher TPSA/FPSA ratios ( $P < 0.05$ ) than the control group, indicating statistically significant differences. See Table 3.

**3.3. Situation of Developing into Androgen-Independent Prostate Cancer.** The incidence of androgen-independent prostate cancer was significantly lower in the experimental group than in the control group (8 vs. 16,  $P < 0.05$ ); in addition, the time to develop into the androgen-independent prostate cancer was longer in patients of the experimental group than that in patients of the control group ( $P < 0.05$ ). See Table 4.

**3.4. FACT-P Quality of Life Scores and KPS Scores.** After treatment, the experimental group obtained obviously higher FACT-P quality of life scores and KPS scores than the control group ( $P < 0.05$ ); see Figure 1 for specific data.

**3.5. PSA Level.** After treatment, the number of patients with PSA level restored to normal was significantly higher in the experimental group than in the control group ( $P < 0.05$ ); see Table 5.

## 4. Discussion

Prostate cancer is a cancer specific to men, with cancer cells either growing slowly and leading to late onset or growing rapidly and difficult to control, seriously threatening the physical health and quality of life of a large number of men. Hormonal therapy is the usual means of treating prostate cancer in the clinic, which mainly includes orchiectomy and the use of antiandrogen drugs and GnRH-agonist. Generally, hormonal therapy has better short-term outcomes, but in the longer term, its efficacy mainly rests with the androgen dependence of cancer cells; i.e., the higher the dependence, the better the inhibitory effect on cancer cells of the therapy [17–20]. Based on the analysis on TCM theory, the authors believe that prostate cancer is a renal disease, which is mostly found in middle- and old-aged men, and prostate cancer patients mainly have dysuria, rectal pain, hematuria, and other

TABLE 3: Analysis of levels and ratios of TPSA and FPSA ( $\bar{x} \pm s$ ).

Test indicator		Control group	Experimental group	t/P
TPSA (ng/ml)	Before treatment	80.47 $\pm$ 15.23	81.15 $\pm$ 15.81	0.191/0.849
	After treatment	55.71 $\pm$ 10.66	46.73 $\pm$ 10.28	3.321/0.002
FPSA (ng/ml)	Before treatment	8.26 $\pm$ 3.19	8.33 $\pm$ 3.53	0.091/0.928
	After treatment	5.14 $\pm$ 1.53	3.45 $\pm$ 1.28	4.640/<0.001
TPSA/FPSA	Before treatment	0.11 $\pm$ 0.06	0.12 $\pm$ 0.05	0.789/0.433
	After treatment	0.15 $\pm$ 0.06	0.20 $\pm$ 0.11	2.186/0.033

TABLE 4: Comparison of the situation of developing into androgen-independent prostate cancers of patients between the two groups.

Group	n	Number of affected patients	Time (months)
Control group	30	16 (53.33)	30.85 $\pm$ 7.24
Experimental group	30	8 (26.67)	39.71 $\pm$ 8.13
$X^2/t$		4.444	4.458
P		0.035	<0.001

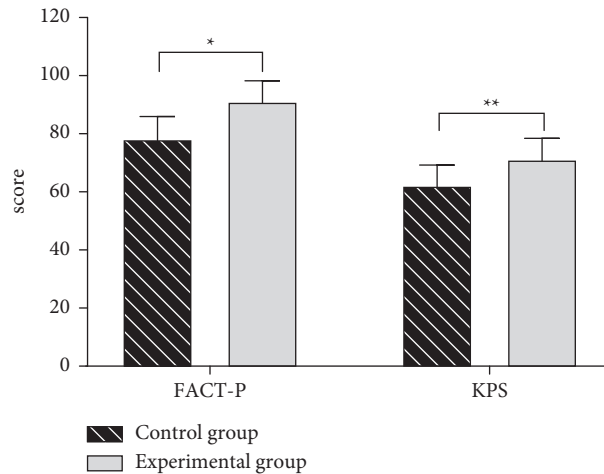


FIGURE 1: Analysis of patients' FACT-P quality of life scores and KPS scores ( $\bar{x} \pm s$ ). Note: the horizontal axis indicates the scoring indicators, and the vertical axis indicates the value (points); after treatment, the FACT-P score and KPS score of the control group were (78.12  $\pm$  7.85) and (62.18  $\pm$  7.09), respectively; after treatment, the FACT-P score and KPS score of the experimental group were (91.03  $\pm$  7.18) and (71.17  $\pm$  7.23), respectively; \* indicates a significant difference in FACT-P scores between the two groups ( $t = 6.647$ ,  $P < 0.001$ ); \*\* indicates a significant difference in KPS scores between the two groups ( $t = 4.863$ ,  $P < 0.001$ ).

TABLE 5: Analysis of patients' PSA level.

Group	n	<4 ng/ml	$\geq 4$ ng/ml
Control	30	17 (56.67)	13 (43.33)
Experimental	30	25 (83.33)	5 (16.67)
t		5.079	
P		0.024	

symptoms accompanied by different degrees of lumbar, hip, and lower abdominal pain, which are associated with dysfunctions of the kidney storing essence, kidney governing water, and kidney governing bones. Medium-elderly male patients mostly suffer from deficiency of kidney essence, blockage of sanjiao and shuidao, disorder of bladder functioning, poor drainage of lower jiao water, and stagnation of fluid-dampness, which, after a long time, will produce phlegmatic toxin that blocks meridian and qi-blood circulation and then generates blood stasis, and finally, intermingled phlegm and stasis will block the seminal orifice and lead to

prostate cancer. Therefore, TCM mainly treats prostate cancer by invigorating the kidney and using the Chinese herbs with the efficacy of being antitumor, promoting blood circulation to remove blood stasis, and removing phlegm to promote diuresis because the tumorigenesis is associated with phlegm and stasis. Combined with part of clinical experience, a comprehensive program of self-made TCM formula combined with hormonal therapy for prostate cancer patients was implemented by the authors to make up for the shortage of hormonal therapy and try to balance the treatment of prostate cancer, thereby guiding future prognosis and improving the quality of life for patients.

In this study, the levels and ratios of TPSA and FPSA of patients in both groups were improved after treatment, and the experimental group obtained significantly lower TPSA and FPSA levels ( $P < 0.05$ ) and higher TPSA/FPSA ratios ( $P < 0.05$ ) than the control group; it was found that prostate epithelial cells could secrete a protease, the specific antigen, which was very low in normal body serum but would be significantly elevated in patients with prostate cancer due to the destruction of normal prostate tissue. The results were consistent with the study results of Khachaturov [21], which proved that, on the basis of hormonal therapy, the combined application of self-made TCM formula could effectively inhibit the specific antigen levels in patients with prostate cancer and present significant efficacy. The incidence of androgen-independent prostate cancer was significantly lower in the experimental group than in the control group (8 vs. 16,  $P < 0.05$ ), in addition, the time to develop into the androgen-independent prostate cancer was longer in patients of the experimental group than that in patients of the control group ( $P < 0.05$ ), implying that combining the self-made TCM formula with hormonal therapy presented a certain efficacy in treating prostate cancer, especially in prolonging the transformation to androgen-independent prostate cancer. After treatment, the FACT-P quality of life scores and KPS scores of patients were obviously higher in the experimental group than in the control group ( $P < 0.05$ ), indicating that performing additional TCM treatment could improve the overall physical condition of prostate cancer patients, alleviate the symptom impact, and promote quality of life. The number of patients with PSA level restored to normal after treatment was significantly higher in the experimental group than in the control group ( $P < 0.05$ ). PSA, a serine proteinase involved in sperm and semen formation, is derived from the epithelial cells of the prostatic duct and acinus and often used for the identification of benign and malignant neoplasms and as the important indicator in the postoperative follow-up to determine the progression of the disease and the condition of surgical treatment. This study demonstrated that the effect of combined treatment with TCM on PSA was more obvious.

In the hormonal therapy, bicalutamide is an anti-androgen agent that achieves the purpose of treatment by preventing the action of endogenous androgens on the prostate, and goserelin acetate is a GnRH-agonist that can cause a dramatic increase in testosterone in early treatment, exert a combined effect with bicalutamide, and block androgens after testosterone decrease, thereby inhibiting tumor growth. However, side effects may occur in patients after hormonal therapy, which mostly belong to deficiency of both the kidney and spleen, as well as qi and yin. It is described in Huangdi Neijing that “With vital qi inside, your body will not be affected by pathogenic qi” and “Attack of pathogen will lead to deficiency of qi.” TCM treatment is dominated by supporting healthy energy to eliminate pathogenic factors, which can improve patients’ immunity and alleviate the side effects of chemoradiotherapy, while also having an important role in ameliorating cancer

symptoms and protecting immune system function, and thus, combining TCM with Western medicine in the treatment of malignant tumors has attracted much attention [22–25]. The TCM formula herein can strengthen kidney and spleen, invigorate qi and yin, and ameliorate the side effects from hormonal therapy, which presents the overall efficacy of strengthening vital qi with the additional effects including clearing heat and removing toxicity, promoting blood circulation to remove blood stasis, diuresis, and diffusing dampness, and dissipating phlegm and resolving masses. In the formula, paniculate *bolbostemma*, *hedyotis*, black nightshade herb, manyleaf *Paris* rhizome, and zedoary rhizome are Chinese herbs with the effects of clearing heat, removing toxicity and diuresis, and promoting blood circulation to remove blood stasis and have the direct effects of anti-inflammation and antitumor demonstrated in pharmacological research; in addition, the herbs including malaytea scurfpea fruit, Asiatic Cornelian cherry fruit, glossy privet fruit, and plantain seed can ameliorate patients’ symptoms such as dysuria, and pharmacological research demonstrated that they have the estrogen-like effect and act synergistically with hormonal therapy drugs to resist the androgen activity; particularly for those with intractable prostate cancer, they can mildly strengthen the renal yang, greatly nourish the renal qi, relieve the clinical symptoms, and improve the quality of life; using prepared *Rehmannia* root, common yam rhizome, Asiatic Cornelian cherry fruit, glossy privet fruit, malaytea scurfpea fruit, tuckahoe, zhuling, plantain seed, Mongolian milkvetch root, and other herbs together can invigorate the kidney for nourishing semen and strengthen the spleen to invigorate qi, improve the systematic symptoms in patients, and enhance the body immunity; some of the kidney-nourishing herbs also have the functions of bidirectionally regulating the hypothalamic-pituitary-adrenal axis (HPA axis), ameliorating the side effects caused by hormonal therapy and prolonging the time for patients to progress to androgen-independent prostate cancer. This study also has the following deficiencies. For example, the sample size was small due to the limited research cost, so a multicenter study with larger sample size is still in need. In addition, the follow-up period was short, and statistics on the long-term survival of the patients were lacking.

In conclusion, the combination of self-made TCM formula and hormonal therapy effectively improves the prostate tumor marker levels in patients with prostate cancer and slows down the time for developing from prostate cancer to androgen-independent prostate cancer and contributes to the improvement of quality of life.

## Data Availability

Data supporting the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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## Research Article

# Clinical Efficacy of Treating Endometrial Cancer with Xiaoaiping Tablets under Comprehensive Nursing Intervention and Their Effect on Quality of Life

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**Objective.** To explore the clinical efficacy of treating endometrial cancer with Xiaoaiping tablets under comprehensive nursing intervention and their effect on quality of life. **Methods.** The clinical data of 120 endometrial cancer patients treated at the Affiliated Hospital of Southwest Medical University from February 2019 to February 2020 were retrospectively analyzed, and the patients were split into the experimental group and the control group according to their admission order, with 60 cases each. Conventional treatment and Xiaoaiping tablet regimen were received by all patients, those in the control group accepted the general nursing, and those in the experimental group accepted the comprehensive nursing intervention for 12 months, so as to compare their clinical efficacy, quality of life (Functional Assessment of Cancer Therapy, FACT), negative emotion scores (Hospital Anxiety and Depression Scale, HAD), and Medical Coping Modes Questionnaire (MCMQ) scores between the two groups. **Results.** No statistical differences in the patients' general information between the two groups were observed ( $P > 0.05$ ); compared with the control group after nursing, the experimental group obtained a significantly higher objective remission rate (80.0%), significantly higher disease control rate (90.0%) ( $P < 0.05$ ), significantly better QOL ( $P < 0.001$ ), significantly lower negative emotion scores ( $P < 0.001$ ), and significantly better MCMQ scores ( $P < 0.001$ ). **Conclusion.** Adopting Xiaoaiping tablets under comprehensive nursing intervention can improve the negative emotions of patients with endometrial cancer, enhance their confidence in medical treatment, present better efficacy, and obviously promote their QOL. Therefore, comprehensive nursing intervention should be promoted and applied in practice.

## 1. Introduction

Endometrial cancer is an epithelial malignancy that occurs in the endometrium, with an incidence accounting for 7% in female malignancies and 25%–30% in genital malignancies [1, 2]. The number of new patients with endometrial cancer per year in China is around 200,000 [3], whose risk level is second only to that of cervical cancer. With the rising incidence of endometrial cancer, clinical research on its treatment measures is also continuously deepening. At the present stage, surgery and chemotherapy are mainly adopted to treat the disease. To be specific, early-stage endometrial cancer is mainly treated by surgery, chemoradiotherapy and other treatment measures can be performed jointly after

surgery according to the pathological stage of patients, and comprehensive treatment is conducted for patients at the advanced stage [4, 5]. Generally, surgery supplemented with chemoradiotherapy is the conventional treatment for malignant tumors, but endometrial cancer belongs to reproductive system tumors, which has a significant impact on female physical and mental health, so the treatment effect of patients is subject to many factors such as physiological conditions and mental states. Also, some of the middle-aged and elderly patients with underlying diseases have a particularly poor quality of life (QOL) [6, 7], low body tolerance, and serious hostile and negative mentality, which are not conducive to obtaining the best surgical treatment effect. To solve the problems such as poor treatment tolerance of

endometrial cancer patients, some scholars treated such patients with Xiaoaiping tablets and found that the drug can significantly improve the body immunity of patients, thereby reducing the toxic side effects caused by chemotherapy [8], and that the medication will not increase the pain sensation of patients and presents exact efficacy. However, endometrial cancer can cause strong mental stimulation, so patients are prone to mental system dysfunction, and some even have suicidal tendencies [9]. Such negative coping style seriously affects the psychological defense mechanism of patients and significantly reduces their treatment compliance. Therefore, jointly adopting routine nursing on the basis of Xiaoaiping tablet treatment cannot improve the patients' psychological state, and more comprehensive nursing intervention measures should be adopted jointly.

Comprehensive nursing intervention is an all-round and high-quality nursing model capable of rising nursing intervention for cancer from traditional adjuvant therapy to humanities care so that patients can obtain more targeted quality nursing during treatment, which in turn changes their medical coping attitudes and improves treatment compliance [10]. In previous literature, no study has applied comprehensive nursing in endometrial cancer patients treated with Xiaoaiping tablets. Based on this, the actual effect of the comprehensive nursing intervention was explored herein, with the results reported as follows.

## 2. Data and Methods

**2.1. Study Design.** The study was a retrospective study and conducted at the *Affiliated Hospital of Southwest Medical University* from February 2019 to February 2020 to explore the clinical efficacy of treating endometrial cancer with Xiaoaiping tablets under comprehensive nursing intervention and their effect on QOL. This study was a double-blind study, meaning that neither the study subjects nor the researchers were aware of trial grouping, and the study designer was responsible for arranging and controlling the full trial.

**2.2. Recruitment of Study Objects.** The clinical data of patients with endometrial cancer treated at the *Affiliated Hospital of Southwest Medical University* from February 2019 to February 2020 were retrospectively analyzed, and the patients were included and excluded according to the following criteria. Inclusion criteria included the following: (1) the patients were diagnosed with endometrial cancer after B-mode ultrasound, hysteroscope, and magnetic resonance imaging (MRI) examinations and met the diagnosis criteria in the fourth version of *Guidance for Diagnosis and Treatment of Endometrial Cancer* [11] published in 2018; (2) the patients had measurable lesions; namely, the diameter of lesions was not less than 20 mm under routine imaging examination; (3) the patients were under the age of 80 years; (4) the estimated survival of the patients was over 3 months; (5) the patients' KPS scores were not less than 65 points [12]; and (6) throughout the treatment, no death, transfer, or treatment discontinued occurred to the patients. Exclusion

criteria included the following: (1) the patients could not communicate with others due to hearing disorders, language disorders, unconsciousness, mental diseases, or other factors; (2) the patients quit the treatment, died, changed the treatment regimen, or were found missing in follow-up visit; (3) the patients suffered from other severe organic diseases; (4) tumor distant metastasis occurred; and (5) the patients were alcohol dependent.

**2.3. Steps.** A total of 120 patients were included in the study and equally divided into the experimental group and the control group according to their admission order, with 60 cases each. On the day that the patients agreed to join the study, the study team collected the sociodemographic data and clinical performance data and distributed the questionnaires for all patients to fill in under unified guidance, the nursing personnel made no implications except for explaining the questionnaires, and after filling, the questionnaires were taken back and verified for completeness; after the end of nursing, the imaging examination was performed to the patients, and the questionnaires were distributed again and taken back after filling for completeness verification. In case of any omissions, the patients were encouraged to complete the questionnaires on the basis of no violation of the voluntary principle to ensure integrity and authenticity.

**2.4. Moral Consideration.** The study met the principle of the World Medical Association Declaration of Helsinki [13] and was approved by the Ethics Committee of the *Affiliated Hospital of Southwest Medical University*. After the patients were recruited, the study team explained the purpose, meaning, content, and confidentiality of the study to them and asked them to sign the informed consent.

**2.5. Criteria of Quitting the Experiment.** For patients who had one of the following situations and were judged unsuitable for continuously accepting the experiment by the study team, their case records were reserved but not used for data analysis: (1) those experienced adverse events or severe adverse events; (2) progression of disease and so on occurred during the experiment; (3) subjects developed some serious comorbidities or complications; and (4) subjects were unwilling to continue the clinical trial and proposed the demand to quit.

**2.6. Methods.** Conventional treatment combined with Xiaoaiping tablets (manufactured: Jilin Jichun Pharmaceutical Co., Ltd., NMPA approval no. Z20063564) was performed on patients in both groups. The patients orally took 8 Xiaoaiping tablets (0.3 g per tablet) three times daily for a total of 4 courses, with 3 weeks as 1 course.

The patients in the control group accepted the general nursing as follows: (1) The nursing personnel paid close attention to related indicators of the patients and dynamically monitored the changes in their vital signs. (2) The nursing personnel guided the patients to take drugs



according to medical advice and gave diet guidance and health guidance to the patients, thereby promoting their treatment compliance.

The comprehensive nursing intervention was conducted on patients in the experimental group as follows: (1) The nursing personnel carefully read the patients' basic information, prepared targeted nursing plans with individual differences according to the patients' educational degree, condition, dietary preference, and so on, made the nursing plans more scientific and professional by evidence-based nursing, and adjusted the plans at any times according to the feedback from the patients during nursing, thus ensuring that the patients accepted high-quality comprehensive nursing. (2) Psychological nursing: the nursing personnel accepted the training by a professional psychological consultant to promote the accuracy of psychological nursing and, in particular, made psychological nursing plans for specific psychological situations of patients with endometrial cancer, mainly including the following aspects: ① The nursing personnel had one-on-one communication with the patients daily, informed the patients about the influence of their psychological status on treatment, increased their degree of recognition for psychological intervention, and at the same time evaluated their mental status and gave emotional support. ② For patients with poor psychological status, the nursing personnel helped them in relieving their stress and negative emotions such as anxiety and hostility by the means of cognitive therapy and imagery communication. ③ In case that patients presented serious negative emotions and even mental diseases or somatic symptoms, relevant treatment should be intervened upon immediately. (3) Health education: ① The nursing personnel carried out health education to patients according to their educational degree, the senior medical staff introduced the basic knowledge of the disease through lectures, distributed corresponding health education handbooks to the patients after lecture, and informed the patients about the characteristics of endometrial cancer, so that the patients understood that the disease is progressing slowly but often has a good prognosis and then enhanced their confidence in treatment. ② The nursing personnel taught the family members of the patients at the same time, informed them that endometrial cancer will not affect their sexual life or accelerate the aging of women, and advised them to promote their degree of attention to the patients and be more caring and encouraging, and for those with poorer family nursing ability, the nursing personnel explained the nursing methods to them privately. ③ The nursing personnel could organize patients' exchange meeting and arrange the patients who obtained the ideal treatment effect to be the speaker, thereby exerting the peer effect and helping the patients in correctly recognizing cancer and accepting the treatment and nursing regimen. (4) Other nursing measures: ① The patients with endometrial cancer often complained of pain, so the nursing personnel needed to administer them with ibuprofen and other drugs according to the doctor's advice, closely monitor their drug reaction, and if necessary adopt the psychological adjustment method for distraction. ② Endometrial patients should eat foods that contain rich protein, so the nursing

personnel prepared healthy recipe according to their dietary habits and advised them about eating fewer foods with high cholesterol and calories and keeping off spicy food. ③ The cancer patients had different degrees of sleep disorders, so the nursing personnel should keep the hospitalization environment clean and tidy and tell the patients to take a hot bath and massage before sleep to improve their sleep quality.

## 2.7. Observation Criteria.

- (1) General information: the general information extract form was established by the patient, covering the inpatient number, name, age, body weight, BMI, cancer stage, pathological stage, pathological type, number of lesions, KPS scores, marital status, and educational degree.
- (2) Clinical efficacy: one month after the end of medication, patients in both groups accepted the pelvis CT scan and MRI examination, and their short-term efficacy was evaluated by the Response Evaluation Criteria in Solid Tumors (RECIST) [14] and classified as complete response (CR, complete endometrial retraction, interstitial decidua degeneration, and no endometrial hyperplasia or cancer focus for more than one month), partial response (PR, reduced level of endometrial lesions or residual cancer focus, accompanied by gland degeneration and atrophy for over one month), stable disease (SD, no changes in endometrium, residual cancer focus, and no degeneration and atrophy seen in endometrium), and progressive disease (PD, clear muscular invasion or extrauterus lesions). The objective remission rate (ORR) = CR + PR, and the disease control rate (DCR) = CR + PR + SD.
- (3) QOL: the patients' QOL before and after nursing was evaluated based on the Functional Assessment of Cancer Therapy-General (FACT-G) [15], including physical well-being (PWB), social/familial well-being (SWB), emotional well-being (EWB), and functional well-being (FWB), and a total of 27 evaluation items. The scores of PWB, SWB, and FWB ranged from 0 to 28 points, and the score of EWB ranged from 0 to 24 points, with 0 points indicating the best score for QOL.
- (4) Negative emotion scores: the patients' negative emotions before and after nursing were evaluated based on the Hospital Anxiety and Depression Scale (HAD) [16], which was divided into the scales for anxiety and depression (HAD-A and HAD-D). With the credibility and validity that have been proved in domestic literature, HAD can be used to evaluate the negative emotions in patients with endometrial cancer in China. The scores of both scales ranged from 0 to 15 points, with 0 points indicating the best score of no anxiety and higher scores indicating more serious anxiety and depression.
- (5) Medical Coping Modes Questionnaire (MCMQ) scores: the patients' medical coping attitude before

and after nursing was evaluated by the MSMQ scores [17], which was mainly used for patients with fatal diseases or nonfatal diseases. With the credibility and validity that have been proved in domestic literature, MSMQ can be used to evaluate the medical coping attitude of patients with endometrial cancer in China. MSMQ covered three coping strategies, that is, confrontation, avoidance, and acceptance-resignation, of which the confrontation dimension was in direct ratio with the medical coping, whereas the dimensions of avoidance and acceptance-resignation were in inverse ratio with the medical coping. Each strategy contained different items, and a total of 20 items were included in the Chinese version.

**2.8. Statistical Processing.** In this study, the data processing software was SPSS20.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), items included were enumeration data and measurement data, methods used were  $X^2$  test and  $t$ -test, and differences were considered statistically significant at  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Patients' General Information.** No statistical differences in patients' general information between the two groups were observed ( $P > 0.05$ ); see Table 1.

**3.2. Comparison of Patients' Clinical Efficacy.** The ORR and DCR of the experimental group were significantly higher than those of the control group ( $P < 0.05$ ) (see Table 2).

**3.3. Comparison of Patients' QOL.** Compared with the control group after nursing, the patients' QOL was significantly better in the experimental group ( $P < 0.001$ ) (see Figure 1).

Figure 1(a) shows the PWB scores. Before nursing, the PWB scores of the experimental group and the control group were not statistically different ( $21.80 \pm 2.12$  versus  $21.81 \pm 2.65$ ,  $P > 0.05$ ), and after nursing, the PWB scores were significantly lower in the experimental group than in the control group ( $12.45 \pm 1.65$  versus  $17.52 \pm 1.60$ ,  $P < 0.001$ ).

Figure 1(b) shows the SWB scores. Before nursing, the SWB scores of the experimental group and the control group were not statistically different ( $22.10 \pm 2.23$  versus  $22.12 \pm 2.24$ ,  $P > 0.05$ ), and after nursing, the SWB scores were significantly lower in the experimental group than in the control group ( $12.14 \pm 1.20$  versus  $16.11 \pm 1.58$ ,  $P < 0.001$ ).

Figure 1(c) shows the EWB scores. Before nursing, the EWB scores of the experimental group and the control group were not statistically different ( $19.21 \pm 1.58$  versus  $19.23 \pm 1.50$ ,  $P > 0.05$ ), and after nursing, the EWB scores were significantly lower in the experimental group than in the control group ( $11.28 \pm 1.65$  versus  $16.21 \pm 1.20$ ,  $P < 0.001$ ).

Figure 1(d) shows the FWB scores. Before nursing, the FWB scores of the experimental group and the control group were not statistically different ( $19.87 \pm 1.65$  versus  $19.88 \pm 1.57$ ,  $P > 0.05$ ), and after nursing, the FWB scores were significantly lower in the experimental group than in the control group ( $9.65 \pm 0.98$  versus  $13.12 \pm 1.54$ ,  $P < 0.001$ ).

**3.4. Comparison of Patients' Negative Emotion Scores.** Compared with the control group after nursing, the negative emotion scores were significantly lower in the experimental group ( $P < 0.001$ ) (see Figure 2).

Figure 2(a) shows the HAD-A scores. Before nursing, the HAD-A scores of the experimental group and the control group were not statistically different ( $11.10 \pm 1.23$  versus  $11.12 \pm 1.20$ ,  $P > 0.05$ ), and after nursing, the HAD-A scores were significantly lower in the experimental group than in the control group ( $6.74 \pm 0.68$  versus  $8.01 \pm 0.87$ ,  $P < 0.001$ ).

Figure 2(b) shows the HAD-D scores. Before nursing, the HAD-D scores of the experimental group and the control group were not statistically different ( $10.87 \pm 1.65$  versus  $10.89 \pm 1.58$ ,  $P > 0.05$ ), and after nursing, the HAD-D scores were significantly lower in the experimental group than in the control group ( $6.54 \pm 0.68$  versus  $7.98 \pm 0.98$ ,  $P < 0.001$ ).

**3.5. Comparison of Patients' MCMQ Scores.** Compared with the control group after nursing, the MCMQ scores were significantly better in the experimental group ( $P < 0.001$ ) (see Figure 3).

Figure 3(a) shows the confrontation scores. Before nursing, the confrontation scores of the experimental group and the control group were not statistically different ( $19.12 \pm 1.23$  versus  $19.15 \pm 1.20$ ,  $P > 0.05$ ), and after nursing, the confrontation scores were significantly higher in the experimental group than in the control group ( $22.87 \pm 1.68$  versus  $20.10 \pm 1.58$ ,  $P < 0.001$ ).

Figure 3(b) shows the avoidance scores. Before nursing, the avoidance scores of the experimental group and the control group were not statistically different ( $16.12 \pm 1.35$  versus  $16.08 \pm 1.36$ ,  $P > 0.05$ ), and after nursing, the avoidance scores were significantly lower in the experimental group than in the control group ( $12.08 \pm 1.11$  versus  $15.45 \pm 1.25$ ,  $P < 0.001$ ).

Figure 3(c) shows the acceptance-resignation scores. Before nursing, the acceptance-resignation scores of the experimental group and the control group were not statistically different ( $16.11 \pm 1.28$  versus  $16.09 \pm 1.23$ ,  $P > 0.05$ ), and after nursing, the acceptance-resignation scores were significantly lower in the experimental group than in the control group ( $6.48 \pm 0.87$  versus  $10.11 \pm 1.00$ ,  $P < 0.001$ ).

### 4. Discussion

In China, endometrial cancer is the second leading female reproductive malignancy with an incidence second only to cervical cancer. With the popularity of xenoestrogen in recent years, the incidence of endometrial cancer shows an obvious upward trend, so deepening the research on its

TABLE 1: Comparison of patients' general information.

Group	Experimental ( <i>n</i> = 60)	Control ( <i>n</i> = 60)	$\chi^2/t$	<i>P</i>
Age (years)				
Range	42–76	40–74		
Mean age	50.98 ± 3.65	51.23 ± 3.20	0.399	0.691
Mean body weight (kg)	55.10 ± 2.65	55.14 ± 2.48	0.085	0.932
BMI (kg/m <sup>2</sup> )	22.15 ± 1.20	22.25 ± 1.43	0.415	0.679
Tumor stage				
G1	32	30	0.134	0.715
G2	18	20	0.154	0.695
G3	10	10	0.000	1.000
Pathological stage				
I	24	25	0.035	0.853
II	16	15	0.044	0.835
III	12	13	0.051	0.822
IV	8	7	0.076	0.783
Pathological type				
Adenocarcinoma	36	35	0.035	0.853
Adenosquamous carcinoma	10	8	0.261	0.609
Clear cell carcinoma	8	10	0.261	0.609
Papillary adenocarcinoma	6	7	0.086	0.769
Number of lesions			0.069	0.793
<3	52	51		
≥3	8	9		
KPS scores (points)	71.98 ± 3.65	72.15 ± 3.54	0.259	0.796
Marital status			0.046	0.831
Married	45	46		
Unmarried/divorced/widowed	15	14		
Educational degree				
Senior high school and below	25	26	0.034	0.853
Junior college	18	19	0.039	0.843
College and above	17	15	0.171	0.680

TABLE 2: Comparison of patients' short-term efficacy (*n* (%)).

Group	CR	PR	SD	PD	ORR	DCR
Experimental	18 (30.0)	30 (50.0)	6 (10.0)	6 (10.0)	48 (80.0)	54 (90.0)
Control	10 (16.7)	18 (30.0)	17 (28.3)	15 (15.0)	28 (46.7)	45 (75.0)
$\chi^2$	2.981	5.000	6.508	4.675	14.354	4.675
<i>P</i>	0.084	0.025	0.011	0.031	<0.001	0.031

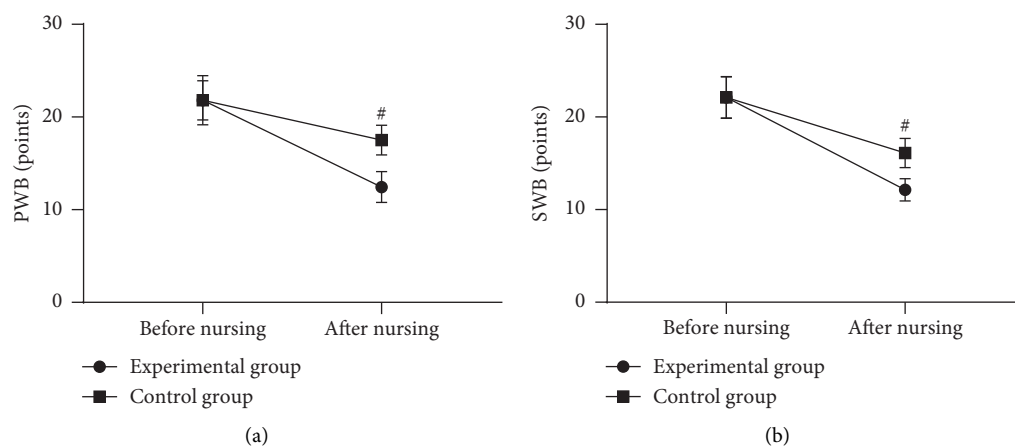


FIGURE 1: Continued.

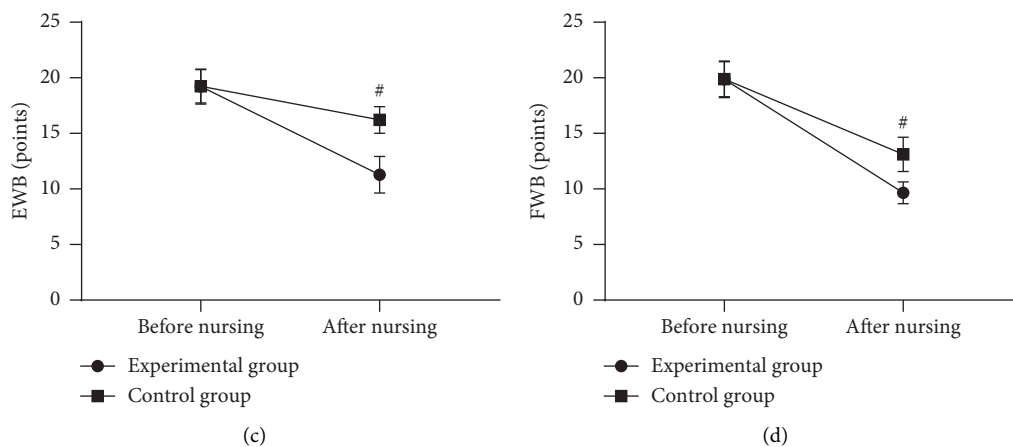


FIGURE 1: Comparison of patients' QOL ( $\bar{x} \pm s$ , points). *Note.* The horizontal axes from left to right indicate before and after nursing, the lines with dots indicate the experimental group, the lines with blocks indicate the control group; and # indicates  $P < 0.001$ .

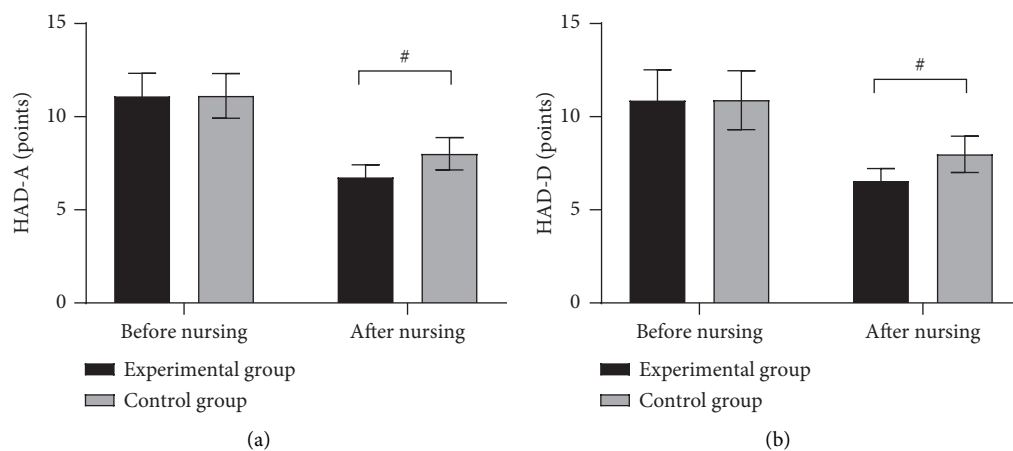


FIGURE 2: Comparison of patients' negative emotion scores ( $\bar{x} \pm s$ , points). *Note.* The horizontal axes from left to right indicate before and after nursing, the black areas indicate the experimental group, the gray areas indicate the control group, and # indicates  $P < 0.001$ .

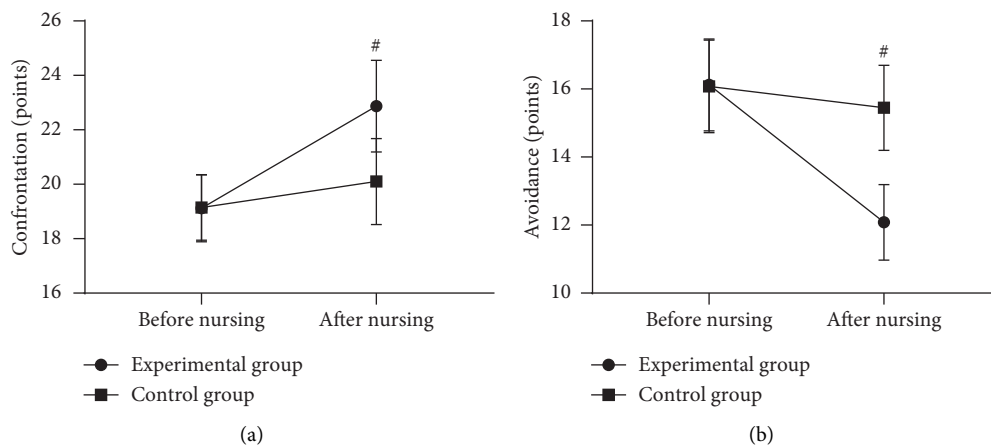


FIGURE 3: Continued.

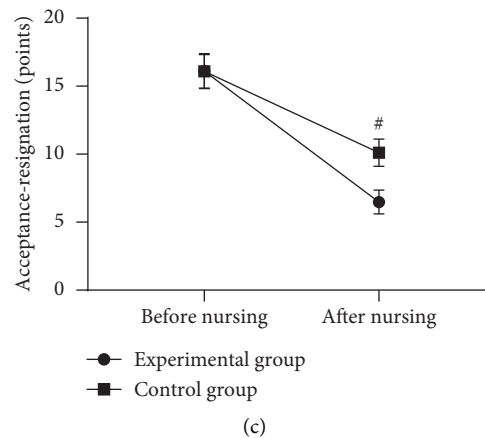


FIGURE 3: Comparison of patients' MCMQ scores ( $\bar{x} \pm s$ , points). *Note.* The horizontal axes from left to right indicate before and after nursing, the lines with dots indicate the experimental group, the lines with blocks indicate the control group; and # indicates  $P < 0.001$ .

therapeutic measures is an urgent task. At the present stage, surgery and chemotherapy are mainly adopted to treat endometrial cancer, and surgical treatment is curative for most patients, achieving a 5-year overall survival rate of 98% and a disease-free survival rate of over 90% [18]. But surgical treatment alone does not improve the 5-year survival for patients with combined core muscles and lymphatic vessel clearance invasion and those at the advanced stage when diagnosed, so chemotherapy regimens are recommended according to relevant guidelines to treat such patients [19]. Chemotherapy can prolong the survival time of patients, but this treatment modality has significant toxic effects. In addition, it often works poorly in patients with endometrial cancer, because such disease often occurs in perimenopausal and postmenopausal women who have poor tolerance, which is not conducive to exerting the effect of chemotherapy. To assist in the chemoradiotherapy and postoperative treatment of patients with endometrial cancer, some scholars administered 134 endometrial cancer patients with Xiaoaiping tablets and found that those in the observation group after administration had significantly improved immune function and achieved a 2-year survival rate of 52.8% [20], which was significantly higher than the statistical result of the international Gynecologic Oncology Group in 2010, suggesting that Xiaoaiping tablets could significantly prolong the survival time of patients. However, endometrial cancer is closely related to female reproductive organs and will cause the lack of physiological structure, seriously affecting patients' social role function, so patients often present negative emotions such as anxiety and depression after diagnosis. In particular, after surgical treatment and chemotherapy, patients suffer from organic trauma again, resulting in significantly reduced treatment compliance and failure to cooperate with the implementation of adjuvant treatment [21, 22]. Therefore, it is extremely important to adopt comprehensive nursing intervention to enhance the therapeutic effects of patients.

Comprehensive nursing intervention refers to integrating humanities care throughout nursing under the guidance of nursing diagnosis and based on the theory of

special science, which can provide patients with high-quality and all-round nursing care, fully motivate patients' potential of rehabilitation, and improve patients' psychological and mental status and physical function [23]. In this study, the social psychology-based comprehensive nursing intervention was adopted, and the negative emotion scores after nursing were significantly lower in the experimental group than in the control group ( $P < 0.001$ ), indicating that the psychological nursing in this model could relieve anxiety and depression in patients and improve their psychological function. In the study by scholars David et al., it was shown that psychological intervention could reduce the levels of cortisol and adrenaline in endometrial cancer patients with diabetes, demonstrating that psychological intervention was an important measure to reduce the stress reaction of patients [24]. Stress reaction will lead to various kinds of somatic symptoms in patients and then cause potential organ injury during treatment, so controlling stress reaction is beneficial to protect the body tolerance of endometrial cancer patients and avoid posttraumatic stress disorder (PTSD).

In addition, the psychological and mental status of endometrial cancer patients are closely related to their treatment compliance, and according to American Association for Cancer Research, patients' medical coping style, social support degree, and QOL all affect their will to live. With a reduced sense of survival, patients present poorer treatment compliance and refuse to cooperate with clinical treatment [25]. After the comprehensive nursing intervention, patients in the experimental group had a more optimal level of health knowledge, more scientific daily living habits, and increased social support, and therefore they obtained significantly better MCMQ scores ( $P < 0.001$ ) and better QOL. Hence, comprehensive nursing intervention can improve not only the patients' subjective treatment willingness and treatment compliance but also their objective organism conditions, so the ORR and DCR in the experimental group were significantly higher than those in the control group ( $P > 0.05$ ), indicating that comprehensive nursing intervention incorporated both the inner core of

humanism and the strictness of evidence-based nursing and could effectively improve the treatment outcomes of patients with endometrial cancer.

In conclusion, adopting Xiaoaiping tablets under comprehensive nursing intervention can improve the negative emotions of patients with endometrial cancer and enhance the treatment effect of Xiaoaiping tablets, presenting a good clinical application value.

## Data Availability

The data used to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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## Research Article

# Chinese Medicine *Leptochloa chinensis* Inhibits the Malignant Behaviors of Renal Cell Carcinoma 786-O Cells by Regulating the mTOR Pathway

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**Background.** Renal cell carcinoma (RCC) is a common malignant tumor of the urinary system that seriously threatens human life and health. This study aims to explore the role of the traditional Chinese medicine *Leptochloa chinensis* in the pathogenesis of RCC. Meanwhile, this study also revealed the molecular biological mechanism of its antitumor activity. **Methods.** Human RCC 786-O cells were cultured in the RPMI-1640 medium, which contains different concentrations of *Leptochloa chinensis* (1,000, 3,000, and 9,000  $\mu\text{g}/\text{ml}$ ). MTT and flow cytometry assays were used to detect the viability of 786-O cells. Transwell and wound healing assays were used to detect cell metastasis. The protein expression was observed by western blot analysis. **Results.** *Leptochloa* can inhibit cell proliferation and induce apoptosis in RCC 786-O cells. In addition, *Leptochloa* can weaken the migration and invasion of 786-O cells. More importantly, *Leptochloa* can block the mTOR pathway by inhibiting the protein expression of p-mTOR. Moreover, the high concentration of *Leptochloa chinensis* has a better inhibitory effect on 786-O cells. **Conclusion.** The traditional Chinese medicine *Leptochloa chinensis* inhibits the viability and metastasis of 786-O cells by blocking the mTOR pathway.

## 1. Introduction

Renal cell carcinoma (RCC) is a common malignant tumor of the urinary system, which seriously threatens human life and health [1]. RCC accounts for 2% to 3% of adult systemic malignant tumors, and its incidence is increasing at a rate of 2.5% per year [2]. In addition, RCC is relatively insidious and lacks sensitivity to radiotherapy and chemotherapy. Even with surgical treatment, there are still 20% to 40% of patients with postoperative invasion and distant metastasis

[3]. Most RCC patients are already at an advanced stage when they are diagnosed. And the cause of death is related to tumor metastasis [4]. Therefore, seeking a new RCC treatment method is of great significance for prolonging the life of patients and improving the life quality of patients.

Isolating effective anticancer active ingredients from plants is one of the ways to find new anticancer drugs, and the antitumor effect of Chinese medicine has been recognized [5]. Previous studies have confirmed that the anti-tumor effects of some Chinese medicines have ideal effects

[6, 7]. *Leptochloa chinensis*, also known as “Pusa bean, Qianliangjin,” is the dry mature seed of *Euphorbia lathyris* L. [8]. As early as the 1920s, foreign scholars conducted relevant research on the Chinese medicine *Leptochloa chinensis* [9]. At present, it has also been found that *Leptochloa chinensis* has pharmacological activity on a variety of tumor cells. It has been reported that *Leptochloa chinensis* is used to treat esophageal cancer [10], skin tumors [11], and acute lymphocytic leukemia [12], with good curative effects.

It has been shown that the mTOR pathway is closely related to tumor proliferation, invasion, and metastasis [13]. Blocking the PI3K/AKT/mTOR signaling pathway can inhibit tumor cell proliferation and metastasis and even induce cell apoptosis [14]. Li et al. found that plumbagin can block the PI3K/AKT/mTOR signaling pathway, leading to lung cancer cell apoptosis [15]. However, the specific anticancer mechanism between *Leptochloa chinensis* and mTOR signaling pathway is still unclear.

Therefore, this study explored whether *Leptochloa chinensis* can inhibit the proliferation, invasion, and migration of 786-O RCC cells. The anticancer mechanism of *Leptochloa chinensis* was also investigated in 86-O RCC cells. This study aims to provide more theoretical basis for the anti-tumor of Chinese medicine.

## 2. Materials and Methods

**2.1. Preparation of Lathyrol.** The experimental drug of lathyrol was purchased from Sichuan Weikeqi Biological Technology Co., Ltd., with a purity of 99% (no. 20190023, 20 mg/bottle). The drug was dissolved in 200  $\mu$ l dimethyl sulfoxide (DMSO), and then PBS was added to 2 ml. RPMI-1640 culture medium containing 10% fetal bovine serum (FBS) was used to dilute lathyrol to the experimental design concentration (0, 1000, 3000, and 9000  $\mu$ g/ml).

**2.2. Cell Culture.** First, 786-O RCC cells were divided into 4 groups (one of which is a blank control). After digesting the cells with 0.25% trypsin, a single cell suspension was prepared with the RPMI-1640 medium containing 10% FBS. The cell concentration was adjusted to  $6 \times 10^5$  cells/ml, and the cells were seeded in a 96-well plate with 100  $\mu$ l per well. After culturing in an incubator with 5% CO<sub>2</sub> at 37°C for 24 h, the medium was added to each well to make up to 100  $\mu$ l.

**2.3. MTT Assay.** Four groups of 786-O RCC cells were cultured with 0, 1000, 3000, and 9000  $\mu$ g/ml lathyrol. The dose was added once a day for 5 consecutive days. 24 h after the last dose, 10  $\mu$ l of 5 mg/ml MTT solution was added to each well. After incubating for 4 h, the supernatant was discarded. 110  $\mu$ l DMSO was added to each well, and the cells were incubated for 10 min at room temperature. The absorbance value (OD value) was measured at 490 nm by the enzyme-linked immunosorbent assay. Inhibition rate (%) = (OD value of the blank group – OD value of the experimental group)/OD value of the blank group  $\times$  100%.

**2.4. Flow Cytometric Analysis.** 786-O RCC cells ( $6 \times 10^5$  cells/ml) were evenly added into a 6-well cell culture plate. Then, it was placed in a constant temperature cell incubator for 24 h. After adherence, different concentrations of lathyrol (0, 1000, 3000, and 9000  $\mu$ g/ml) were added to the cells. After regular incubation for 24 h, they were digested with 5% trypsin without EDTA. Next, 500  $\mu$ l buffer, 5  $\mu$ l annexin V, and 5  $\mu$ l PI were added to the cells in sequence. After 30 minutes of reaction in the dark at room temperature, the flow cytometer detected cell apoptosis within 1 h. The results obtained were analyzed with FlowJo software.

**2.5. Wound Healing Assay.** 786-O RCC cells were immediately seeded into a 6-well plate with a density of  $6 \times 10^5$  per well. After the cells adhered, the cells were starved with a serum-free medium for 6 h. Next, a 200  $\mu$ l pipette tip was used to make a “1”-shaped scratch in the direction perpendicular to the 6-well plate. Different concentrations (0, 1000, 3000, and 9000  $\mu$ g/ml) of lathyrol were then added. After 24 h, the width of the scratch was observed under an inverted microscope. Cell migration rate (%) = (0 h scratch spacing – 24 h scratch spacing)/0 h scratch spacing  $\times$  100%.

**2.6. Transwell Assay.** Transwell chamber assay was used to detect the invasion ability of 786-O RCC cells *in vitro*. First, 500  $\mu$ l of the RPMI-1640 cell culture medium without FBS was added to the bottom well. The upper chamber was added with 100  $\mu$ l cell suspension, Matrigel (BD Biosciences), and different concentrations of lathyrol. Then, the cells were placed in a cell incubator with saturated humidity at 37°C with 5% CO<sub>2</sub> for 48 h. Next, the cells were fixed with 4% paraformaldehyde for 30 min and then stained with 0.1% crystal violet for 20 min. The invasive cells were observed and counted under a microscope.

**2.7. Western Blot Assay.** RIPA Lysis Buffer (Beyotime, Shanghai, China) was used to extract total protein from 786-O RCC after treatment with lathyrol. The BCA kit was used to detect protein concentration. Then, 50  $\mu$ g protein was used for the SDS-PAGE experiment. The protein sample was transferred to the PVDF membrane and blocked with 5% skimmed milk at 37°C for 1.5 h. The membrane was washed 5 times with TBST. The protein samples were then incubated with Bax, Bcl-2, mTOR, and p-mTOR primary antibodies in a refrigerator at 4°C overnight. Next, the protein was incubated with secondary antibodies for 2 h at room temperature. Subsequently, ECL exposure and development were performed in the ChemiDoc imaging system.  $\beta$ -Actin was used as an internal control. Quantity One 4.52 analysis software was used to measure the gray value of the bands. The relative expression of the target protein (IOD) = the gray value of the target protein/the gray value of the internal reference  $\beta$ -actin.

**2.8. Statistical Analysis.** Statistical analysis was performed using SPSS 24.0 software. The data are shown as mean  $\pm$  SD. All experiments are repeated three times. The differences

were analyzed by Student's *t*-test or one-way ANOVA followed by Tukey's post hoc test.  $P < 0.05$  indicates a significant difference.

### 3. Results

**3.1. *Leptochloa* Inhibits the Growth of RCC 786-O Cells.** First, the effect of *Leptochloa* on the viability of RCC cells was investigated in 786-O cells. MTT assay showed that *Leptochloa* can inhibit the proliferation of 786-O cells ( $P < 0.05$ , Figure 1, Table 1). In addition, we also found that the inhibitory effect of *Leptochloa* on the proliferation of 786-O cells was enhanced with the increase of *Leptochloa* concentration. 9000  $\mu\text{g/ml}$  *Leptochloa* has the highest inhibitory effect, with a growth inhibition rate of 76.03% ( $P < 0.01$ , Figure 1, Table 1). These results indicate that high concentrations of *Leptochloa* can significantly inhibit cell proliferation in RCC.

**3.2. *Leptochloa* Promotes the Apoptosis of RCC 786-O Cells.** Compared with the blank group, the apoptotic rate of 786-O cells increased after the treatment with *Leptochloa*. The higher the concentration of *Leptochloa*, the higher the apoptosis rate of 786-O cells ( $P < 0.05$ , Figure 2(a)). The apoptotic rate of 786-O cells reached the highest at 9000  $\mu\text{g/ml}$  *Leptochloa*, which was 53.06% (Figure 2(a)). In addition, compared with the blank group, the expression of proapoptotic protein Bax was significantly increased after 786-O cells were treated with *Leptochloa*, while the expression of antiapoptotic protein Bcl-2 was significantly decreased ( $P < 0.05$ , Figure 2(b)). These results indicate that *Leptochloa* can induce apoptosis of 786-O cells.

**3.3. *Leptochloa* Inhibits the Metastasis of RCC 786-O Cells.** To investigate whether *Leptochloa* affects the metastasis of 786-O cells, wound healing assay and transwell assay were performed. Wound healing assay showed that the migration distance of 786-O cells treated with *Leptochloa* was significantly shorter compared with the blank group ( $P < 0.05$ , Figure 3(a)). Among them, the 9000  $\mu\text{g/ml}$  group had the shortest migration distance (Figure 3(a)). Transwell assay showed that the number of invasive 786-O cells treated with *Leptochloa* was significantly reduced compared with the blank group ( $P < 0.05$ , Figure 3(b)). The higher the concentration of *Leptochloa*, the smaller the number of cells invaded (Figure 3(b)). These results indicate that *Leptochloa* can weaken the migration and invasion ability of 786-O cells.

**3.4. *Leptochloa* Regulates the mTOR Pathway in RCC 786-O Cells.** Western blot assay showed that, after treating 786-O cells with different concentrations of *Leptochloa* (1000, 3000, and 9000  $\mu\text{g/ml}$ ), the mTOR protein expression of each drug group was not statistically different from that of the blank group ( $P > 0.05$ , Figure 4). However, the expression of p-mTOR protein was decreased with increasing concentration of *Leptochloa* ( $P < 0.05$ , Figure 4). The above results

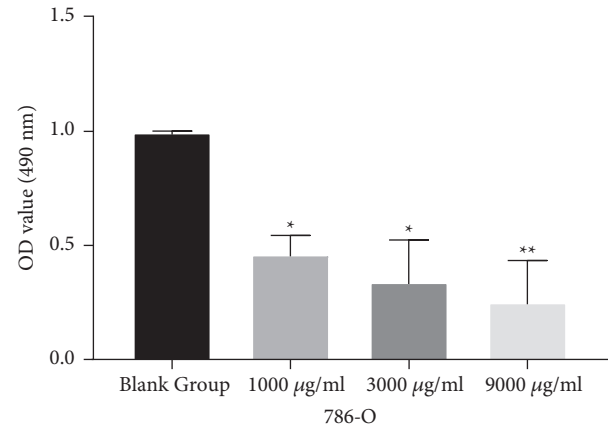


FIGURE 1: *Leptochloa* inhibits the growth of RCC 786-O cells. Cell proliferation was detected in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000  $\mu\text{g/ml}$ ). \* $P < 0.05$  and \*\* $P < 0.01$ .

TABLE 1: The inhibitory effect of different concentrations of *Leptochloa* on the proliferation of 786-O cells.

<i>Leptochloa</i> concentrations	OD value	Inhibition rate (%)	<i>P</i> value
0 (blank group)	0.999	—	—
1000 $\mu\text{g/ml}$	0.463	53.65	0.018*
3000 $\mu\text{g/ml}$	0.337	66.27	0.012*
9000 $\mu\text{g/ml}$	0.241	75.88	0.008**

\* $P < 0.05$  and \*\* $P < 0.01$ .

indicate that *Leptochloa* can block the mTOR pathway by inhibiting the protein expression of p-mTOR.

### 4. Discussion

RCC ranks second in malignant tumors of the urinary system, accounting for 3% of all solid tumors. With the continuous advancement of modern diagnostic technology, clinical cases of RCC have gradually increased [16]. However, 50% of RCC patients will metastasize after surgery. These patients require biological and immunotherapy [17]. Although great progress has been made in recent years, the overall effective rate of RCC is still low [18]. Therefore, people strive to explore the biological characteristics of RCC and possible effective treatments of Chinese medicine from the molecular biology level to significantly improve the prognosis of RCC.

In recent years, previous studies have found that *Leptochloa chinensis* has an inhibitory effect on a variety of tumor cells. For example, it was discovered earlier that *Leptochloa chinensis* had obvious anti-mouse ascites sarcoma cell activity [19]. This study found that *Leptochloa chinensis* had an inhibitory effect on the proliferation of 786-O cells. And the higher the concentration of *Leptochloa chinensis*, the stronger the anticancer effect. Choene et al. found that, with the increase of *Leptochloa chinensis* concentration, the number of human renal cancer cells in the G0 phase increases [20]. This also shows that *Leptochloa*

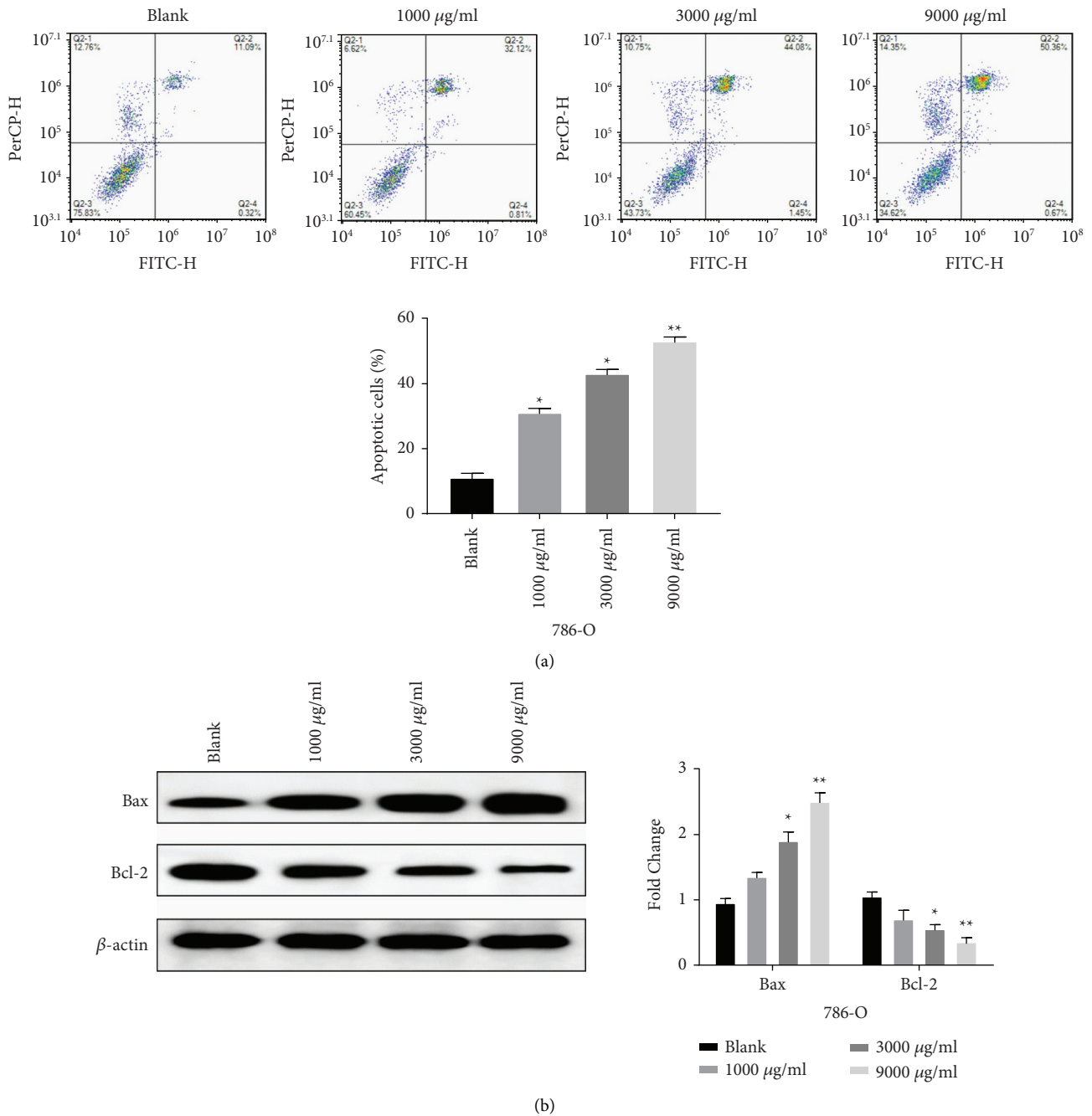


FIGURE 2: *Leptochloa* promotes the apoptosis of RCC 786-O cells. (a) Cell apoptosis was detected in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000  $\mu\text{g/ml}$ ). (b) The protein expression of Bax and Bcl-2 was measured in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000  $\mu\text{g/ml}$ ). \* $P < 0.05$  and \*\* $P < 0.01$ .

*chinensis* has an inhibitory effect on the growth of human RCC cells. In addition, cell invasion and migration are other important factors that affect the prognosis and the main reason for the failure of tumor treatment [21]. In this study, transwell and wound healing assays showed that *Leptochloa chinensis* can effectively inhibit cell migration and invasion in RCC cells. Yang et al. also showed that *Leptochloa chinensis* suppressed the invasion and metastasis of human lung cancer A549 cells [22], similar to the results of this study. These results indicate that traditional

Chinese medicine *Leptochloa chinensis* can inhibit the progression of RCC.

Recent studies have shown that the PI3K/AKT/mTOR signaling pathway is widely present in a variety of cells and is involved in the regulation of cell proliferation, apoptosis, invasion, metastasis, and angiogenesis [23]. The dysregulation of the PI3K/AKT/mTOR signaling pathway is related to the occurrence and development of many human cancers. Han et al. found that L-securinine promoted human acute myeloid leukemia cell HL-60 apoptosis through the PI3K/

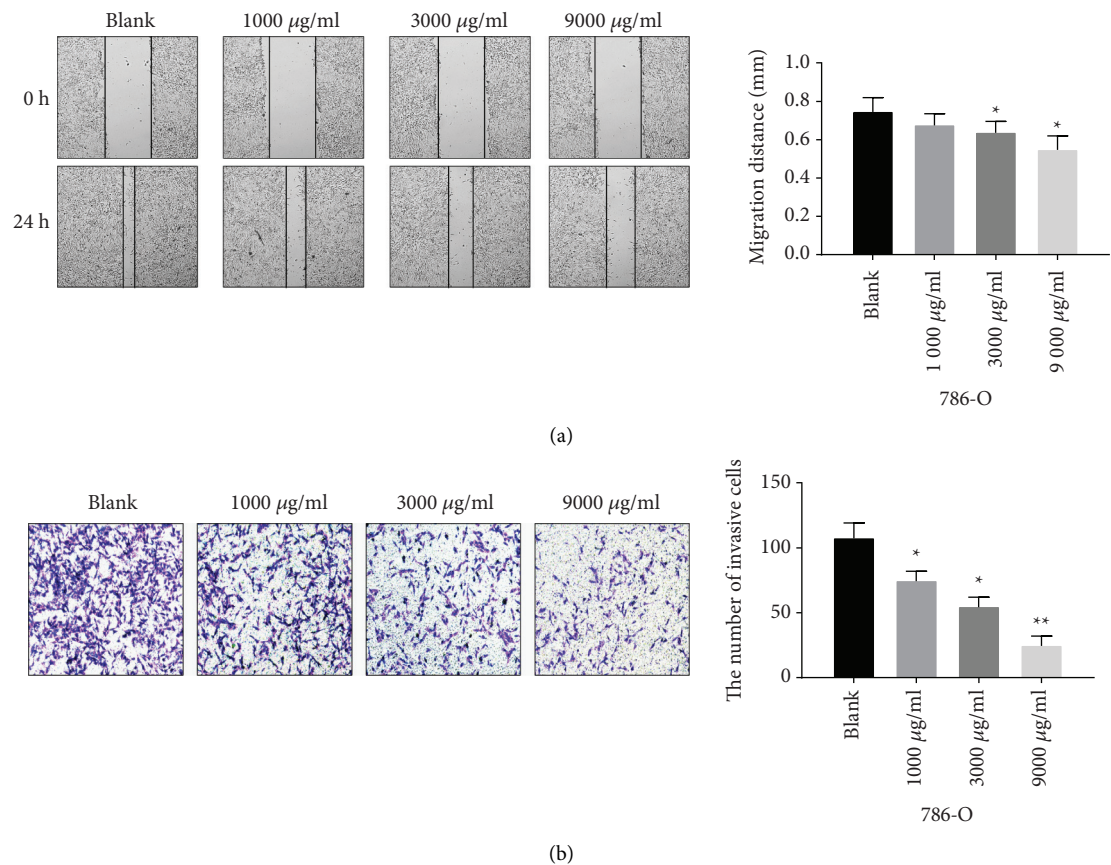


FIGURE 3: *Leptochloa* inhibits the metastasis of RCC 786-O cells. (a) Cell migration was detected by the wound healing assay in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000 µg/ml). (b) Cell invasion was detected by the transwell assay in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000 µg/ml). \* $P < 0.05$  and \*\* $P < 0.01$ .

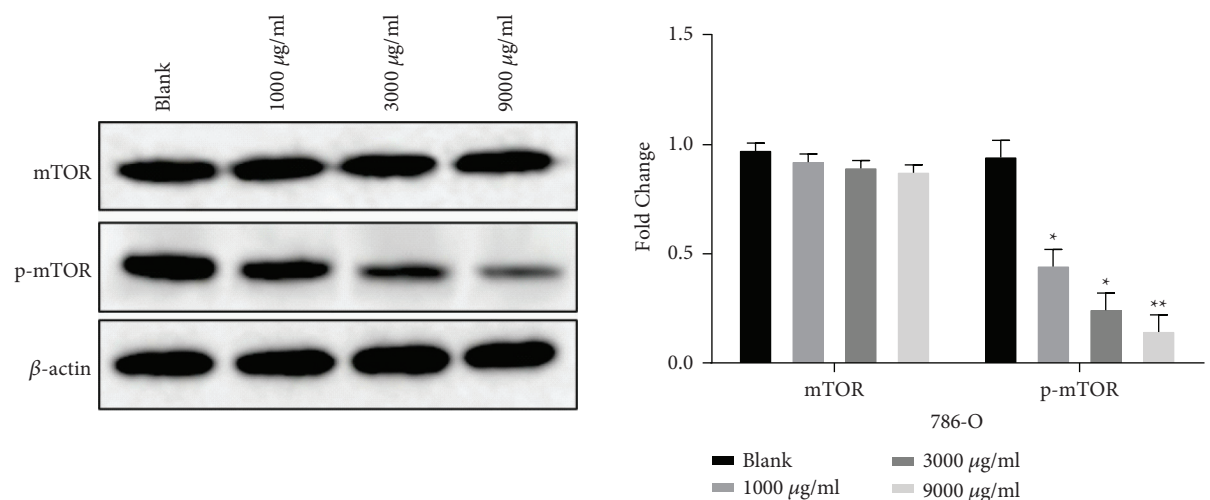


FIGURE 4: *Leptochloa* regulates the mTOR pathway in RCC 786-O cells. The protein expression of mTOR and p-mTOR was measured in 786-O cells treated with different concentrations of lathyrol (0, 1000, 3000, and 9000 µg/ml). \* $P < 0.05$  and \*\* $P < 0.01$ .

AKT/mTOR pathway [24]. In addition, Li et al. showed that traditional Chinese medicine curcumin downregulated mTOR to promote autophagy and apoptosis of lung cancer A549 cells [15]. These studies indicate that the antitumor effect of traditional Chinese medicine *Leptochloa chinensis*

may also be achieved by inhibiting the protein expression of mTOR or p-mTOR. As we predicted, *Leptochloa chinensis* can significantly downregulate the expression of p-mTOR, but has no significant effect on the expression of mTOR. The results indicate that *Leptochloa chinensis* may inhibit cell



proliferation, invasion, and migration by regulating the expression of p-mTOR.

## 5. Conclusion

In summary, *Leptochloa chinensis* can inhibit cell viability, invasion, and migration of 786-O cells. And the higher the concentration of *Leptochloa chinensis*, the stronger its inhibitory effect on RCC. We also found that *Leptochloa chinensis* exerts its anticancer effect in RCC by preventing the activation of mTOR phosphorylation. These results provide more theoretical basis for Chinese medicines to fight cancer. As for the other antitumor mechanisms of *Leptochloa chinensis*, further research is needed.

## Data Availability

The datasets used during the present study are available from the corresponding author upon reasonable request.

## Disclosure

Yongshun Tan and Lingyun Li are co-first authors.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Yongshun Tan and Lingyun Li contributed equally.

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## Research Article

# Application of Jianpi Xiaoi Recipe Combined with Cisplatin and Adriamycin in the Treatment of Endometrial Cancer and Its Effect on Disease Control Rate

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**Objective.** To explore the application of Jianpi Xiaoi recipe combined with cisplatin and Adriamycin in the treatment of endometrial cancer (EC) and its effect on the disease control rate (DCR). **Methods.** The data of 120 EC patients treated in People's Hospital of Rizhao from February 2019 to February 2020 were retrospectively analyzed. They were equally split into experimental group and control group according to the order of admission. All patients were treated with neoadjuvant intra-arterial chemotherapy (continuous infusion of the uterine artery for 5 days before surgery, with 20 mg of cisplatin mixed with 2000 mg of normal saline and 10 mg of Adriamycin mixed with 500 ml of normal saline daily), while the experimental group was treated with Jianpi Xiaoi recipe at the same time to compare the short-term efficacy, immune function indexes, incidence of adverse reactions, and HEC-1-B (human endometrial adenocarcinoma cells) cell inhibition rates between the two groups. **Results.** The DCR and objective remission rate (ORR) in the experimental group were markedly higher compared with the control group ( $P < 0.05$ ). The immune function indexes after treatment were remarkably better in the experimental group than in the control group ( $P < 0.05$ ). Compared with the control group, the incidence of adverse reactions in the experimental group was notably lower ( $P < 0.05$ ), while the HEC-1-B inhibition rates after treatment were obviously higher ( $P < 0.05$ ). **Conclusion.** Jianpi Xiaoi recipe combined with cisplatin and Adriamycin can increase the HEC-1-B cell inhibition rate in EC patients, improve their immune function, reduce the possibility of adverse reactions, and enhance the therapeutic effect, which is worthy of clinical application and popularization.

## 1. Introduction

Endometrial cancer (EC) is an epithelial malignant tumor that occurs in the endometrium. According to the statistics from the American Cancer Society (ACS) in 2017, EC is the sixth most common female cancer, with the highest incidence in South America, Northern Europe, and Eastern Europe during 2006–2007. The risk of EC in Southeast Asia has surged in the past decade, with an increasing incidence in Japan, Singapore, and the Philippines year by year [1]. The EC incidence in China has also reached 10/100,000, becoming a female reproductive system malignant tumor only after cervical cancer [2]. Since the early symptoms of the

disease are not obvious, and patients often suffer from symptoms such as vaginal bleeding, menstrual disorders, and lumbar-abdominal pain only after the disease progresses [3, 4], the diagnosis time of EC is often late and application of chemotherapy will cause serious adverse reactions due to gradually reduced immune function of patients [5, 6], affecting the overall therapeutic effect. Therefore, the selection of appropriate drugs to meet the maximum killing effect of cancer cells while minimizing its toxicity to normal cells has become the focus of the studies on chemotherapy.

Previous studies have shown that neoadjuvant intra-arterial chemotherapy (cisplatin and Adriamycin) has a remarkable effect on cervical cancer [7], Nasioudis et al.

applied it in the treatment of EC and found that this chemotherapy regimen can effectively reduce the mass volume and eliminate the possibility of subclinical metastasis [8]. A large number of international documents have confirmed that cisplatin and Adriamycin, like other antitumor drugs, kill cancer cells by inducing specific target molecule damage or dysfunction [9]. Although some studies have shown that they are safe and can reduce the incidence of complications in the subsequent surgery [10, 11], their effect on the incidence of adverse reactions in EC patients remains unclear. In recent years, Sugandha et al. found that based on the conventional chemotherapy regimens, dialectical application of Jianpi Xiaoi recipe can increase the disease control rate (DCR) of patients with advanced metastatic colorectal cancer and reduce the possibility of adverse reactions [11]. From the perspective of modern pharmacology, Jianpi Xiaoi recipe can also play a significant role in the treatment of EC because its components such as ginseng, *Astragalus*, poria, progesterone, and ginsenoside Rg3 can not only regulate the immune function of patients but also block the iron transport pathways of human endometrial adenocarcinoma cells (HEC-1-B), thus inducing apoptosis of cancer cells by inhibiting HEC-1-B and enhancing the therapeutic effect [12]. Therefore, this paper combined Jianpi Xiaoi recipe with cisplatin and Adriamycin to explore the application effect on EC patients, reported as follows.

## 2. Materials and Methods

**2.1. Study Design.** This retrospective study was conducted in People's Hospital of Rizhao from February 2019 to February 2020, aiming to explore the application of Jianpi Xiaoi recipe combined with cisplatin and Adriamycin in the treatment of endometrial cancer (EC) and its effect on the DCR.

**2.2. Enrollment of Research Subjects.** The data of 120 EC patients treated in People's Hospital of Rizhao from February 2019 to February 2020 were retrospectively analyzed. Patients were included according to the following criteria: (1) the patients were diagnosed with EC by preoperative fractional curettage pathology and postoperative pathological examination and met the diagnostic criteria in *Guidelines for the Diagnosis and Treatment of Endometrial Cancer (the 4<sup>th</sup> Edition)* [13]; (2) the patient had a good physical condition and could tolerate radiotherapy, chemotherapy, and surgical treatment; (3) the patients had no allergic reactions to the drugs involved in this study; and (4) the patients were expected to survive more than 3 months. Patients were excluded according to the following criteria: (1) the patients who were unable to communicate with others due to hearing impairment, language impairment, unclear consciousness, or mental illness; (2) the patients who quite the treatment halfway, died, changed the treatment regimens, and could not be followed up; (3) the patients complicated with serious heart, brain, liver, and kidney diseases or other malignant tumors; (4) the patients with incomplete clinical data; (5) the patients with low treatment

compliance; (6) the patients in pregnancy and lactation; and (7) the patients who were treated in other medical institutions or participated in similar studies.

**2.3. Steps.** One hundred and twenty patients were enrolled in this study and were equally split into experimental group and control group according to the order of admission. On the day when the patients agreed to participate in the study, the research team collected their sociodemographic and clinical data and found no significant difference in the general data between the two groups after analysis ( $P > 0.05$ ); see Table 1.

**2.4. Moral Consideration.** This study met the principles of the *Declaration of Helsinki* [14] and was approved by the hospital ethics committee. After enrollment, the research team explained the study purpose, significance, content, and confidentiality to the patients and asked them to sign the informed consent.

**2.5. Exit Criteria.** Judged by the research team, the patients with the following conditions were unsuitable to continuously participate in the experiment, and their medical records would be kept but not for data analysis: (1) the patients experienced adverse events or serious adverse events; (2) the patients had disease deterioration during the experiment; (3) the patients experienced severe comorbidities or complications; and (4) the patients who were unwilling to continue the clinical trial and requested for quitting the study during the experiment.

**2.6. Methods.** All patients were treated with neoadjuvant intraarterial chemotherapy, especially as follows: Seldinger technique was adopted to perform percutaneous puncture and intubation on one side of the femoral artery and insert a 5F catheter into the arteria iliaca communis. According to the tumor location and blood supply shown by the arterial angiography, the corresponding uterine artery was selected, and the catheter was retained to connect the infusion pump for continuous arterial infusion for 5 days. The patients daily received 20 mg of cisplatin (Qilu Pharmaceutical Co., Ltd.; National Medical Products Administration approval No. H20023460) mixed with 2000 mg of normal saline, and 10 mg of Adriamycin (Pfizer Wuxi Pharmaceutical Co., Ltd.; National Medical Products Administration approval No. H20013334) mixed with 500 ml of normal saline, with an infusion rate of 110 ml/h. In addition, the patients were daily given 3000 ml of 5% glucose saline for hydration, making the patients' daily urine volume more than 2000 ml. The angiography was performed again after chemotherapy, and then extubation was performed. Surgery was performed at 3–4 weeks depending on the patients' condition.

At the same time, the experimental group was treated with Jianpi xiaoai recipe consisting of 15 g of ginseng, 15 g of radix curcumae, 15 g of poria, 20 g of astragalus, 20 g of oldenlandia, 20 g of sculellaria barbata, 6 g of fructus aurantii, 6 g of liquorice, 10 g of rhizoma pinellinae praeparata,

TABLE 1: Comparison of patient general data.

Items	Experimental group ( $n = 60$ )	Control group ( $n = 60$ )	$\chi^2/t$	$P$
Age (years old)				
Range	28–70	27–68		
Average age	$54.68 \pm 5.21$	$54.56 \pm 5.23$	0.126	0.900
Pathological types				
Adenocarcinoma	52	50	0.261	0.609
Clear cell carcinoma	6	8	0.324	0.570
Adenoacanthoma	2	2	0.000	1.000
Muscular infiltration			0.135	0.714
Superficial muscular infiltration	26	28		
Deep myometrial invasion	34	32		
FIGO clinical stages				
I	12	14	0.196	0.658
II	32	30	0.134	0.715
II	16	16	0.000	1.000
Cytologic grades				
High differentiation	27	26	0.034	0.854
Middle differentiation	21	23	0.144	0.705
Poor differentiation	12	11	0.054	0.817
Menopause			0.035	0.853
Yes	35	36		
No	25	24		
Marital status			0.164	0.685
Married	42	44		
Unmarried/divorced/widowed	18	16		
Basic diseases				
Hypertension	20	18	0.154	0.695
Coronary heart disease (CHD)	12	11	0.054	0.817
Diabetes	12	12	0.000	1.000
Pulmonary diseases	13	10	0.484	0.487

and 5 g of epimedium. Radix ophiopogonis and dendrobium were added for patients with dry mouth; Fructus Amomi and bamboo shavings for patients with nausea and vomiting; fried *Evodia ruticarpa*, corydalis tuber, and Radix Paeoniae Alba for patients with gastrointestinal dysfunction; and angelica sinensis and spatholobus stem for those with blood deficiency. Jianpi Xiaoi recipe was decocted in warm water with one dose daily and was taken twice every day. Patients in the experimental group took the decoction for 2 months after the start of the neoadjuvant intraarterial chemotherapy.

## 2.7. Observation Criteria

- (1) General data: the general data extraction forms were established by the patients, including the in-patient number, name, age, pathological types, muscular infiltration, clinical staging, cytologic grades, menopause or not, marital status, and basic diseases.
- (2) Short-term efficacy: pelvic CT scan was performed in both groups at 1 month after treatment of the experimental group to evaluate the patient's short-term efficacy according to the response evaluation criteria in solid tumors (RECIST) [15] of the World Health Organization (WHO). The efficacy was classified as complete response (CR, complete endometrial withdrawal, stromal decidualization, and no

endometrial hyperplasia or carcinoma), partial response (PR, reduced grades of endometrial lesions with residual cancer foci accompanied by gland degeneration and atrophy), stable disease (SD, no changes in endometrium with residual cancer foci and no endometrial degeneration and atrophy), and progression disease (PD, the presence of clear muscular infiltration or extrauterine lesions). Objective response rate (ORR) = CR + PR; DCR = CR + PR + SD.

- (3) Immune function indexes: 5 ml of fasting venous blood was extracted from patients in the morning before treatment ( $T_1$ ), 1 month after treatment ( $T_2$ ), and 2 months after treatment ( $T_3$ ). The level of immunoglobulin A (IgA) was detected by rate nephelometry (Shijiazhuang Hipro Biotechnology Corp., Hebei Medical Products Administration certificate no. 20162400132), and the NK,  $CD4^+$ , and  $CD4^+/CD8^+$  levels were detected by flow cytometry (ACEA BIO Hangzhou Co., Ltd.; Zhejiang Medical Products Administration certificate no. 20142400581).
- (4) Incidence of adverse reactions: adverse reactions after treatment were evaluated based on the manifestations and grading criteria of acute and subacute adverse reactions [14] of the WHO.

- (5) HUC-1-B cell inhibition rates: 5 ml of fasting venous blood was collected from the patients in the morning before treatment ( $T_1$ ), 1 month after treatment ( $T_2$ ), and 2 months after treatment ( $T_3$ ). Flow cytometry (ACEA BIO Hangzhou Co., Ltd.; Zhejiang Medical Products Administration certificate no. 20142400581) was adopted to detect the apoptosis of HUC-1-B cells.

**2.8. Statistical Treatment.** In this study, the data were processed by SPSS 20.0 software and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). This study included enumeration data and measurement data, tested by  $X^2$  and  $t$ -test. The differences were statistically significant at  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Patients' General Data.** No remarkable differences in general data were observed between the two groups ( $P > 0.05$ ); see Table 1.

**3.2. Comparison of Patients' Short-Term Efficacy.** The DCR and ORR in the experimental group were higher compared with the control group ( $P < 0.05$ ); see Table 2.

**3.3. Comparison of Patients' Immune Function Indexes.** The immune function indexes after treatment were remarkably better in the experimental group than in the control group ( $P < 0.05$ ); see Figure 1.

Note: in Figure 1, the abscissa from left to right represented before treatment ( $T_1$ ), 1 month after treatment ( $T_2$ ), and 2 months after treatment ( $T_3$ ). The lines with dots indicated the experimental group, and those with squares indicated the control group. # indicated  $P < 0.05$ .

Figure 1(a) shows IgA. No statistical difference in IgA at  $T_1$  was found between the two groups ( $2.64 \pm 0.23$  vs.  $2.68 \pm 0.24$ ,  $P > 0.05$ ). The IgA at  $T_2$  and  $T_3$  in the experimental group was markedly lower than that in the control group ( $1.68 \pm 0.21$  vs.  $2.25 \pm 0.25$ ,  $1.44 \pm 0.18$  vs.  $2.04 \pm 0.20$ ,  $P < 0.001$ ).

Figure 1(b) shows NK. No statistical difference in NK at  $T_1$  was found between the two groups ( $7.99 \pm 0.45$  vs.  $8.10 \pm 0.46$ ,  $P > 0.05$ ). The NK at  $T_2$  and  $T_3$  in the experimental group was markedly higher than that in the control group ( $11.13 \pm 0.35$  vs.  $9.21 \pm 0.12$ ,  $13.00 \pm 0.48$  vs.  $11.10 \pm 0.54$ ,  $P < 0.001$ ).

Figure 1(c) shows  $CD4^+$ . No statistical difference in  $CD4^+$  at  $T_1$  was found between the two groups ( $34.58 \pm 2.12$  vs.  $34.64 \pm 2.13$ ,  $P > 0.05$ ). The  $CD4^+$  at  $T_2$  and  $T_3$  in the experimental group was remarkably higher than that in the control group ( $40.68 \pm 3.10$  vs.  $36.57 \pm 2.98$ ,  $44.68 \pm 3.23$  vs.  $40.12 \pm 3.24$ ,  $P < 0.001$ ).

Figure 1(d) shows  $CD4^+/CD8^+$ . No statistical difference in  $CD4^+/CD8^+$  at  $T_1$  was found between the two groups ( $1.24 \pm 0.12$  vs.  $1.23 \pm 0.13$ ,  $P > 0.05$ ). The  $CD4^+/CD8^+$  at  $T_2$  and  $T_3$  in the experimental group was remarkably higher

than that in the control group ( $1.32 \pm 0.24$  vs.  $1.20 \pm 0.20$ ,  $1.35 \pm 0.24$  vs.  $1.18 \pm 0.21$ ,  $P < 0.05$ ).

**3.4. Comparison of the Incidence of Adverse Reactions.** Compared with the control group, the incidence of adverse reactions in the experimental group was notably lower ( $P < 0.05$ ); see Table 3.

**3.5. Comparison of HEC-1-B Cell Inhibition Rates.** The HEC-1-B cell inhibition rates in the experimental group were remarkably higher compared with the control group ( $P < 0.05$ ); see Figure 2.

Note: in Figure 2, the abscissa from left to right represented before treatment ( $T_1$ ), 1 month after treatment ( $T_2$ ), and 2 months after treatment ( $T_3$ ), and the ordinate represented the HEC-1-B cell inhibition rate (%). The black area was the experimental group and the gray area was the control group. # indicated  $P < 0.05$ .

No statistical difference in the HEC-1-B cell inhibition rates at  $T_1$  was observed between the two groups ( $6.98$  vs.  $6.96$ ,  $P > 0.05$ ).

The HEC-1-B cell inhibition rates at  $T_2$  and  $T_3$  in the experimental group were remarkably higher compared with the control group ( $60.24$  vs.  $40.47$ ,  $72.58$  vs.  $53.68$ ,  $P < 0.001$ ).

### 4. Discussion

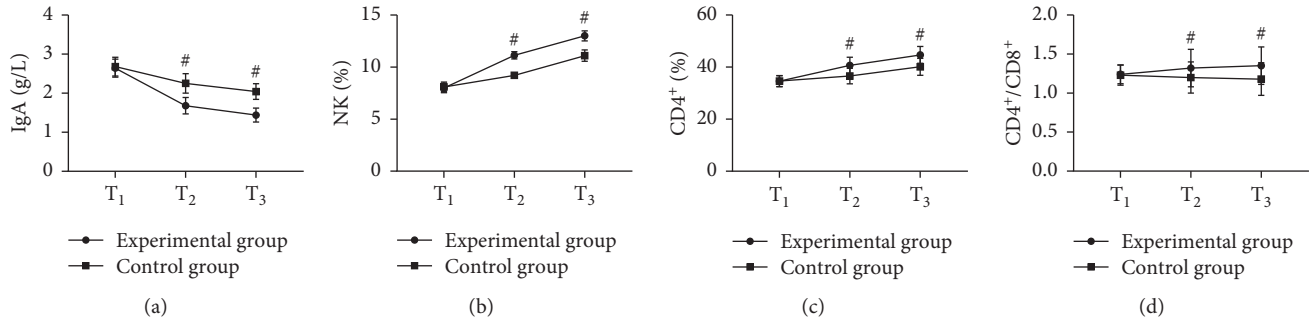
EC is a female reproductive systemic malignant tumor with the incidence second only to cervical cancer [16], which is common in perimenopausal women. The early symptoms of EC are nonspecific, and patients may present with symptoms such as abnormal leukorrhea and lumbar-abdominal pain as the disease progresses, seriously threatening their life health. Although the EC incidence has remained high in the past decade, the academic community has not clarified its pathogenesis. Modern Western medicine believes that lifestyle changes, obesity, and hypertension are all high-risk factors for the EC occurrence [17], and the main clinical treatment methods are surgery and chemotherapy. However, surgical treatment alone cannot improve the 5-year survival rate of patients with infiltration of deep muscular layer and lymphatic space [18], so adjuvant chemotherapy is essential. Neoadjuvant intraarterial chemotherapy is often adopted in the treatment of gynecological malignancies such as cervical cancer, which has been proven to inhibit the proliferative activity of cancer cells and accelerate their apoptosis [19]. Although bilateral uterine arteries supply blood for the EC patients, the dominant lateral uterine artery was selected for continuous perfusion in some studies to prolong the contact time between drugs and cancer cells, thereby improving the killing ability of the drugs. To enhance the therapeutic effect, this study also chose unilateral perfusion. After treatment, the HEC-1-B cell inhibition rates of both groups were improved, indicating the efficacy of neoadjuvant chemotherapy in the EC treatment.

Some previous studies have shown that preoperative neoadjuvant intraarterial chemotherapy can reduce the incidence of postoperative complications [20], but the effect



TABLE 2: Comparison of patients' short-term efficacy [ $n$  (%)].

Group	CR	PR	SD	PD	ORR	DCR
Experimental group	24 (40.0)	24 (40.0)	10 (16.7)	2 (3.3)	48 (80.0)	58 (96.7)
Control group	16 (26.7)	20 (33.3)	14 (23.3)	10 (16.7)	36 (60.0)	50 (83.3)
$X^2$	2.400	0.574	0.833	5.926	5.714	5.926
$P$	0.121	0.449	0.361	0.015	0.017	0.015

FIGURE 1: Comparison of patients' immune function indexes ( $\bar{x} \pm s$ ).TABLE 3: Comparison of the incidence of adverse reactions [ $n$  (%)].

Group	Experimental group ( $n = 60$ )	Control group ( $n = 60$ )	$X^2$	$P$
Leukopenia				
I-II	22 (36.7)	34 (56.7)	4.821	0.028
III-IV	10 (16.7)	22 (36.7)	6.136	0.013
Neutropenia				
I-II	18 (30.0)	30 (50.0)	5.000	0.025
III-IV	6 (10.0)	15 (25.0)	4.675	0.031
Thrombocytopenia				
I-II	5 (8.3)	20 (33.3)	11.368	0.001
III-IV	1 (1.7)	7 (11.7)	4.821	0.028
Decreased hemoglobin				
I-II	12 (20.0)	30 (50.0)	11.868	0.001
III-IV	2 (3.3)	8 (13.3)	3.927	0.048
Nausea and vomiting				
I-II	20 (33.3)	36 (60.0)	8.571	0.003
III-IV	10 (16.7)	22 (36.7)	6.136	0.013
Diarrhea				
I-II	12 (20.0)	24 (40.0)	5.714	0.017
III-IV	2 (3.3)	10 (16.7)	5.926	0.015
Anemia				
I-II	4 (6.7)	12 (20.0)	4.615	0.032
III-IV	0 (0.0)	6 (10.0)	6.316	0.012
Renal dysfunction				
I-II	0 (0.0)	4 (6.7)	4.138	0.042
III-IV	0 (0.0)	4 (6.7)	4.138	0.042

of this chemotherapy regimen on the adverse reactions of EC patients remains unclear. Therefore, reducing the incidence of adverse reactions of patients is the key to improve their quality of life. In recent years, the concept of holistic and dialectical treatment of traditional Chinese medicine (TCM) has achieved remarkable results in the treatment of

malignant tumors. Many studies have confirmed that TCM can improve the immunity of patients with chemotherapy, reduce the destruction of chemotherapy to normal tissues, and curb the further spread of cancer cells [21]. The Jianpi Xiaoi recipe selected in this study is often used in the treatment of colorectal cancer and colon cancer, which can

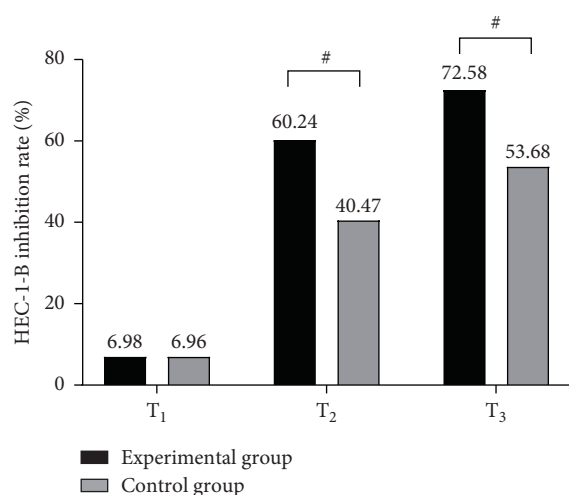


FIGURE 2: Comparison of HEC-1-B cell inhibition rates.

reduce the hematological and digestive tract adverse reactions of chemotherapy patients and improve the safety of chemotherapy [22]. Although the causes of EC and digestive system malignant tumors are different, TCM classifies them into categories of metrorrhagia and metrostaxis and accumulated diseases that are believed to be caused by dampness-heat and stasis, Qi-stagnation and blood stasis, and stagnation of liver Qi. The herbs in Jianpi Xiaoi recipe have significant effects on them because ginseng, as the principle drug in this recipe can replenish Qi to invigorate the spleen, percolate dampness and disinherit water, and support the healthy energy; astragalus, the minister drug, can benefit Qi and supplement the deficiency; fructus aurantii and radix curcumae can promote Qi, oldenlandia can detoxify the body, rhizoma pinellinae praeparata can dispel dampness, and epimedium can strengthen spleen, in which the five drugs are the assistant drugs. The herbs in the recipe are properly mixed to play the role of removing stasis and eliminating stagnation.

From the perspective of modern pharmacology, ginseng is rich in ginsenoside Rg3 (CS-Rg3) that can effectively inhibit the main pathways for the survival of cancer cells, namely, the activity of PI3K and AKT, and then induce HEC-1-B apoptosis. Wang et al. have found that the combination of cisplatin and astragalus in human endometrial cancer cell line HEC-1-B can significantly improve the lethality of HEC-1-B in vitro, which is stronger than the sum of the two drugs alone, with the cell inhibition rate as 2.7 times that of cisplatin alone [23]. Therefore, the HEC-1-B cell inhibition rates in the experimental group after treatment were significantly higher compared with the control group ( $P < 0.05$ ). In addition to HEC-1-B, the progesterone contained in *Astragalus* can also enhance the immune function of patients, so the experimental group had a lower incidence of adverse reactions and significantly better immune function indexes after treatment compared with the control group ( $P < 0.05$ ). Moreover, *poria* can affect the expression of caspase-3 and Bcl-2, in which caspase-3 can lead to cell apoptosis while Bcl-2 can inhibit apoptosis. A study has shown that *poria* decoction for nude mice bearing

EC can upregulate caspase-3 and downregulate Bcl-2 [24], indicating that *poria* have a positive effect on serum factor levels of EC patients. Therefore, in this study, the DCR and ORR in the experimental group were remarkably higher compared with the control group ( $P < 0.05$ ). It is worth noting that the effect of the herbs in Jianpi Xiaoi recipe on the molecular level of EC patients needs to be further investigated.

In conclusion, Jianpi Xiaoi recipe combined with cisplatin and Adriamycin can increase the HEC-1-B cell inhibition rate in EC patients, improve their immune function, reduce the possibility of adverse reactions, and enhance the therapeutic effect, which is worthy of clinical application and popularization.

## Data Availability

Data to support the findings of this study are available on reasonable request from the corresponding author.

## Conflicts of Interest

The authors have no conflicts of interest to declare.

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## Research Article

# Effect of Psychological Care Combined with Traditional Chinese Medicine on Postoperative Psychological Stress Response in Patients with Advanced Cervical Cancer

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**Objective.** To study the effects of psychological care combined with traditional Chinese medicine treatment on the postoperative psychological stress response and the expression levels of serum C-reactive protein (CRP) and interferon- $\gamma$  (IFN- $\gamma$ ) in patients with advanced cervical cancer. **Method.** 232 postoperative advanced cervical cancer patients treated in our hospital from December 2015 to December 2018 were selected as study objects and divided into the control group and study group using the random number table method. The control group was given basic care combined with traditional Chinese medicine treatment, while the study group was given psychological care treatment on the basis of the control group to compare the treatment effect, psychological stress response, pain level, quality of life, and long-term efficacy of the two groups. The serum CRP and IFN- $\gamma$  levels and their correlation with different psychological stress responses were compared between the two groups before and after treatment. **Result.** Comparing the clinical efficacy of the two groups, the total effective rate of the study group was higher than that of the control group. VAS scores in the study group were significantly lower than those in the control group 30 and 60 days after treatment. The SCL-90 scores of the study group after treatment were lower than those of the control group. After treatment, the differences between the two groups were statistically significant in the scores of emotional function, social function, and role function. The two-year cumulative survival rate in the study group (82.76%) was significantly increased compared to that in the control group (55.17%). The serum CRP and IFN- $\gamma$  expression levels in the two groups were significantly decreased after treatment compared to those before treatment, and the serum CRP and IFN- $\gamma$  expression levels in the study group were significantly decreased compared to those in the control group. **Conclusion.** Psychological care combined with traditional Chinese medicine in the treatment of advanced cervical cancer patients after surgery was effective in improving patients' psychological status, reducing their pain level, relieving postoperative negative emotions, increasing compliance, improving the quality of life, helping to prolong survival time, and controlling serum indexes back to normal, which was worth promoting in clinical practice.

## 1. Introduction

Cervical cancer is a serious common gynecologic malignant tumor disease located in the cervix, with high morbidity and mortality rates, and in recent years, the age of onset is

gradually younger and the incidence is showing an increasing trend [1]. The cure rate of early cervical cancer is high and the prognosis is good. Some research data show that the earlier the clinical stage of cervical cancer, the higher the cure rate. For example, the five-year survival rate of stage

late patients is as high as 97.5%. However, because the early onset of cervical cancer is more insidious, it is often at a locally advanced stage when diagnosed. Although modern medical technology is developing, the effect of surgery alone is poor and the survival rate is low, which seriously endangers the life of patients [2,3].

At present, one of the key approaches of treating cervical cancer is still surgery, supplemented by radiotherapy, and one of the important reasons affecting the prognosis is the late clinical stage [4]. Patients with intermediate and advanced cervical cancer often show symptoms such as cold and weakness, pallor, nausea and vomiting, and fat tongue during chemotherapy; cervical nodules; vaginal bleeding; and lower abdominal pain [5]. Surgical trauma, economic stress, and postoperative and disease pain may lead to severe psychological stress reactions in patients, which may lead to disruption of their physiological functions. Moreover, patients are prone to insomnia, fatigue, anorexia, and so on, which seriously degrades patients' quality of life and affects the clinical treatment outcome [6]. Therefore, postoperative psychological care is crucial to improve the level of psychological stress in patients. In recent years, the clinical application of traditional Chinese medicine has become more and more widespread, and traditional Chinese medicine has the efficacy of tonifying the spleen and kidney, tonifying qi and blood, activating blood circulation, removing blood stasis, and so forth and has less adverse effects and high safety profile, which is increasingly favored by doctors and patients [7].

In this study, 232 postoperative patients with advanced cervical cancer admitted to our hospital were divided into a study group and a control group. They were given basic care, traditional Chinese medicine treatment combined with psychological care treatment, respectively, to explore the effects of psychological care combined with traditional Chinese medicine treatment on the psychological stress response and serum indexes of patients with advanced postoperative cervical cancer.

## 2. Materials and Methods

**2.1. General Data.** A total of 232 postoperative patients with advanced cervical cancer treated at the Yantaishan Hospital, Yantai, Shandong, China, from December 2015 to December 2018 were included in this study. They were pathologically confirmed and randomly divided into a study group and a control group, with 116 cases in each group, using the random number table method. This study was approved by the ethics committee of the Yantaishan Hospital, Yantai, Shandong, China.

Inclusion criteria: all Chinese medicine diagnoses met the diagnostic criteria in the Guidelines for Clinical Research on New Chinese Medicines [8]; all Western medicine diagnoses met the diagnostic criteria in the Guidelines for the Diagnosis and Treatment of Common Gynecologic Malignancies [9]; the expected survival period was  $\geq 6$  months; and all patients were informed about the study purpose and signed an informed consent prior participation.

Exclusion criteria: pregnant and lactating women; patients with severe cardiac, hepatic, and renal dysfunction; patients with immune deficiency; patients with other tumor diseases; patients with impaired consciousness and uncooperative treatment; patients with intolerance or allergy to the study drugs and drug components; patients who had received antitumor treatment such as radiotherapy or chemotherapy in the 1 month before treatment.

There was no statistically significant difference between the general data of the two groups ( $P > 0.05$ , Table 1).

### 2.2. Treatment Methods

**2.2.1. Chinese Medicine Treatment.** Patients in both groups were given basic care combined with Chinese herbal medicine treatment. The Chinese herbal formula was as follows: galanga galangal fruit 10 g, white mulberry root-bark 10 g, heartleaf houttuynia herb 30 g, eucommia bark 20 g, poria 10 g, milkvetch root 30 g, largehead atractylodes rhizome 15 g, coix seed 20 g, garden burnet root 25 g, willowleaf rhizome 5 g, Chinese angelica 5 g, cassia bark 30 g, lightyellow sophora root 15 g, peony root 10 g, milkwort root 15 g, and atractylodes rhizome 25 g. Decoct the above herbs in water to 300 mL. Take one dose a day, divided into morning and evening. Fifteen days was a course of treatment, followed by four courses of treatment.

**2.3. Psychological Care Treatment.** Communicate properly in detail with patients and their families with no language barrier, make a comprehensive evaluation of the patient's psychological condition, understand the patient's condition and the patient's needs, encourage them to talk about their psychological concerns, and instruct their families to participate in the deescalation work to increase the patient's sense of security. Patients were relieved of adverse psychological emotions through music therapy, conversation method, emotional catharsis, and so on. Remove the misconceptions of patients and their families through health education and enhance the level of patients' knowledge about cervical cancer and their awareness about surgery. Tell patients about successful treatment cases at the right time to further enhance patients' confidence in treatment. Nursing staff should care for patients' inner feelings according to their personality characteristics, inform them about the operation in time and answer their questions patiently. In addition, patients can also be encouraged to participate in social activities appropriately according to their recovery. Special attention was given to those with more severe psychological stress. The patient's postoperative pain level was assessed, and the patient was helped to relieve pain and maintain a good state of mind through deep breathing, distraction, and analgesic drugs.

**2.4. Observation Indicator.** Efficacy evaluation: the evaluation was made by imaging the changes in tumor size of patients, and the tumor volume was calculated as length\*width\*radius. The efficacy evaluation was performed



TABLE 1: Comparison of general information between the two groups of patients.

Indicator	Control group	Study group	$X^2$	$P$ value
Case	116	116		
Age (years)			0.070	0.791
>43	67	65		
≤43	49	51		
Course of the disease (years)			0.322	0.570
<3	78	82		
3-4	38	34		
Educational level			0.078	0.780
High school and below	64	60		
Specialized degree and above	52	56		
BMI			0.088	0.957
<18.5	17	16		
18.5–24.9	84	86		
≥25	15	14		
Clinical stage			0.254	0.881
IIIa	47	48		
IIIb	45	47		
IVa	24	21		
Pathological type			0.248	0.618
Squamous cell carcinoma	92	95		
Adenocarcinoma	24	21		

according to the WHO solid tumor efficacy criteria [10]. The complete disappearance of all visible tumor lesions for more than 4 weeks was considered CR; a decrease of more than 50% in the product of two tumor diameters and no new lesions appearing was considered PR; a decrease of less than 50% in the product of two tumor diameters and an increase of no more than 25% was considered SD; and an increase of more than 25% in the product of two tumor diameters or the appearance of new lesions was considered PD. Total effective rate = (CR + PR)/total number of cases. A visual analogue scale [11] (VAS) was used to assess the pain level of cervical cancer patients at 1 d, 7 d, 30 d, and 60 d postoperatively, and patients were asked to mark the position representing their pain level in a 10 cm walking scale (with the scale face back to the patient), with a score of 0 being no pain and 10 being the most severe pain; the higher the score, the more severe the pain level.

The Symptom Checklist 90 (SCL-90) [12] was used to evaluate changes in patients' psychological stress levels. The scale has 10 factors, that is, reflecting the patient's psychological symptoms from somatization, obsessive-compulsive symptoms, interpersonal sensitivity, depression, anxiety, hostility, phobia, paranoia, psychoticism, and others (e.g., sleep and eating). There are 90 entries, each factor has 9 entries, each entry has 1 to 5 points, and each factor has 9 to 45 points, with 16 points as the standard cut-off value; the higher the score, the more severe the level of psychological stress. Quality of life scores were mainly measured using the SF-36 scale [13], which measured five dimensions of physical, emotional, social, cognitive, and role functioning, with higher scores indicating better quality of life.

The expression levels of serum CRP and IFN- $\gamma$  in the two groups of patients were compared before and after treatment. The long-term efficacy of the two groups was compared, and the two-year cumulative survival rate was

counted and calculated at the end of treatment with a two-year follow-up.

**2.5. Statistical Analysis.** Statistical analysis was performed using SPSS 23.0 statistical software, and the measurement data were compared using a  $t$ -test, expressed as mean  $\pm$  standard deviation. The count data were compared using the chi-square test, expressed as a percentage, with  $P < 0.05$  indicating a significant difference in statistical tests.

### 3. Results

**3.1. Comparison of Clinical Efficacy between Two Groups of Patients.** After treatment, the total effective rate of the study group (87.07%) was significantly increased compared with that of the control group (64.66%, Table 2).

**3.2. Comparison of VAS Scores after Treatment between the Two Groups.** The difference in VAS scores between the two groups was not statistically significant at 1 day of treatment ( $t = 0.415$ ,  $P = 0.852$ ) and 7 days of treatment ( $t = 0.423$ ,  $P = 0.556$ ); at 30<sup>th</sup> day of treatment, the VAS score was ( $4.80 \pm 0.323$ ) in the study group and ( $6.200 \pm 0.317$ ) in the control group, and the difference was statistically significant ( $t = 4.341$ ,  $P = 0.002$ ); on treatment day 60, the VAS score was ( $2.94 \pm 0.278$ ) in the study group and ( $5.32 \pm 0.271$ ) in the control group, and the difference was statistically significant ( $t = 8.577$ ,  $P \leq 0.001$ ) (Figure 1).

**3.3. Comparison of SCL-90 Scores between the Two Groups before and after Treatment.** Before treatment, there was no statistically significant difference between the SCL-90 scores of the two groups ( $P > 0.05$ ). After treatment, the SCL-90 scores of the two groups decreased ( $P < 0.05$ ), and the



TABLE 2: Comparison of clinical efficacy between two groups of patients ( $n$  (%)).

Group	$n$	CR	PR	SD	PD	Total effective rate
Control group	116	24	77	9	6	101 (87.07)
Study group	116	13	62	28	13	75 (64.66)
$\chi^2$						17.225
$P$ value						0.001

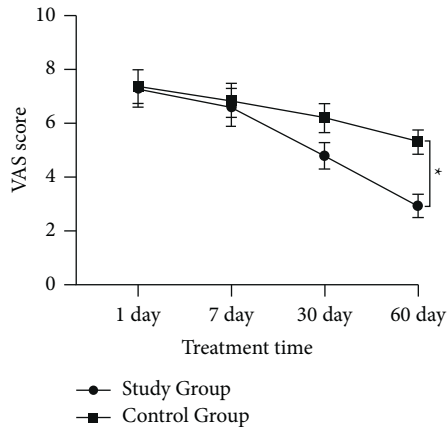


FIGURE 1: Comparison of VAS scores of the patients after treatment between the control group ( $n = 116$ ) and the study group ( $n = 116$ ). \* $P < 0.05$ .

decrease was more significant in the study group ( $P < 0.05$ ) (Table 3).

**3.4. Comparison of Serum CRP and IFN- $\gamma$  Expression Levels before and after Treatment between the Two Groups of Patients.** Before treatment, there was no statistically significant difference in the expression levels of serum CRP and IFN- $\gamma$  between the two groups ( $P > 0.05$ ); after treatment, serum CRP levels were downregulated in both groups compared with those before treatment ( $P < 0.05$ ), and the down-regulation was more significant in the study group. IFN- $\gamma$  levels were upregulated after treatment in both groups compared with pretreatment ( $P < 0.05$ ), and the upregulation was more significant in the study group ( $P < 0.05$ ) (Figure 2).

**3.5. Comparison of Quality of Life Scores between the Two Groups.** After treatment, the differences in emotional, social, and role function scores between the two groups were statistically significant ( $P < 0.05$ ), while the differences in physical and cognitive function scores were not statistically significant ( $P > 0.05$ ) (Table 4).

**3.6. Comparison of Long-Term Efficacy between the Two Groups of Patients.** The two-year cumulative survival rate in the study group (82.76%) was significantly increased compared to that in the control group (55.17%) ( $P < 0.05$ , Figure 3).

## 4. Discussion

Cervical cancer is a gynecologic malignancy with high morbidity and mortality, with many new cases every year. In recent years, some studies have reported that the incidence of the disease is gradually increasing in young age, and at an advanced stage, the treatment and prognosis are poor and the death rate is high [14]. With the progress of socioeconomic and medical science, more and more clinicians gradually realize that psychological factors have an important influence on the occurrence of tumor, disease progression, treatment effect, and prognosis and have a high clinical value [15]. At present, psychological intervention for tumor patients has become a hot topic in clinical research. Li et al. [16] found that due to the diagnosis of cervical cancer and the impact of surgical treatment, patients usually face tremendous physiological-psychological and social stresses after surgery. Coupled with postoperative physical pain and lack of understanding and uncertainty about the disease, patients will have serious psychological stress reactions, such as anxiety, depression, and insomnia. Psychological interventions are urgently needed to make them feel warm, comforted, and happy in the process of fighting cancer; safeguard patients' psychological health; and enhance their treatment confidence, which is conducive to enhancing treatment compliance and promoting recovery. Shi et al. [17] showed that psychological interventions could also reduce the levels of inflammatory factors, such as CRP, in patients with cervical cancer. As an inflammatory factor, CRP reflects the inflammatory condition and the degree of damage in the body. In normal human serum, the level of CRP is low, and when its level is abnormally elevated, it indicates that the patient's condition is worsening [18]. The results of this study showed that after treatment, the serum CRP levels of patients significantly decreased, indicating that psychological care combined with traditional Chinese medicine in the treatment of postoperative advanced cervical cancer patients can significantly reduce the level of the inflammatory factor CRP and enhance the immunity of the body, which is consistent with the results of our study [17]. IFN- $\gamma$  is a potent antiviral and antitumor interferon and mainly regulates the immune system, which can induce T cells to enhance their ability to recognize tumor antigens and ultimately, the body's ability to monitor tumors [19]. Studies have shown [20] that serum IFN- $\gamma$  levels are significantly downregulated with the aggravation of cervical lesions. The present study was consistent with these findings.

In the Chinese medicine health system, cervical cancer belongs to leukorrheal diseases and the dialectical treatment should focus on clearing heat and removing toxins [21]. The formula selected for this study consisted of 16 herbs. Chinese angelica has good effect on promoting blood circulation for regulating menstruation and relieving pain, which can effectively relieve acute pain; peony root has the effect of dispersing blood stasis, clearing heat, cooling blood, and relieving pain; lightyellow sophora root has the effect of invigorating spleen-stomach and replenishing qi; coix seed has the effect of detoxification and discharging pus; galanga galangal fruit has the effect of invigorating spleen and

TABLE 3: Comparison of SCL-90 scores before and after treatment in the two groups ( $\bar{x} \pm s$ ).

Group		<i>n</i>	Somatization	Interpersonal sensitivity	Anxiety	Phobia	Psychoticism
Study group	Before treatment	116	36.72 ± 3.45	39.16 ± 4.23	38.34 ± 4.71	35.96 ± 3.37	36.43 ± 4.52
	After treatment	116	12.56 ± 2.13	11.48 ± 2.76	12.14 ± 3.48	10.87 ± 2.26	10.93 ± 2.17
	<i>t</i>		11.263	13.861	23.654	4.782	7.665
	<i>P</i>		<0.05	<0.05	<0.05	<0.05	<0.05
Control group	Before treatment	116	35.63 ± 3.36	39.87 ± 3.94	37.81 ± 5.27	35.57 ± 3.44	35.67 ± 4.31
	After treatment	116	21.34 ± 2.71	22.51 ± 2.32	21.62 ± 4.47	19.26 ± 2.31	20.42 ± 3.32
	<i>t</i>		7.036	8.541	11.230	3.117	6.548
	<i>P</i>		<0.05	<0.05	<0.05	<0.05	<0.05
		<i>n</i>	Obsessive-compulsive symptoms	Depression	Hostility	Paranoia	Others
Study group	Before treatment	116	35.76 ± 4.41	38.97 ± 4.68	36.62 ± 5.53	37.73 ± 4.54	38.24 ± 4.21
	After treatment	116	11.05 ± 2.61	11.27 ± 2.46	10.92 ± 2.84	11.21 ± 2.53	12.57 ± 2.72
	<i>t</i>		15.423	8.662	11.346	12.951	7.652
	<i>P</i>		<0.05	<0.05	<0.05	<0.05	<0.05
Control group	Before treatment	116	35.78 ± 3.83	37.95 ± 5.19	36.15 ± 5.26	36.75 ± 5.66	38.87 ± 4.53
	After treatment	116	21.53 ± 2.44	21.66 ± 3.23	20.41 ± 3.27	21.58 ± 3.68	20.54 ± 3.17
	<i>t</i>		8.932	6.231	7.145	10.213	6.430
	<i>P</i>		<0.05	<0.05	<0.05	<0.05	<0.05

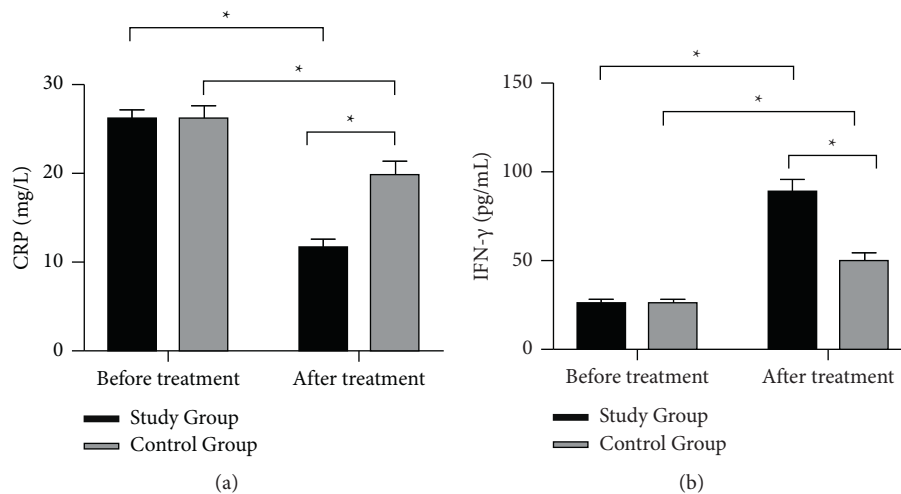


FIGURE 2: Comparison of serum CRP and IFN- $\gamma$  expression levels before and after treatment between the control group ( $n = 116$ ) and the study group ( $n = 116$ ). (a) The comparison of serum CRP expression levels before and after treatment between the control group ( $n = 116$ ) and the study group ( $n = 116$ ). (b) The comparison of serum IFN- $\gamma$  expression levels before and after treatment between the control group ( $n = 116$ ) and the study group ( $n = 116$ ). \* $P < 0.05$ .

TABLE 4: Comparison of quality of life scores between the two groups ( $\bar{x} \pm s$ ).

Group	<i>n</i>	Somatic function	Emotional function	Social function	Cognitive function	Character function
Study group	116	91.24 $\pm$ 5.67	88.36 $\pm$ 5.24	89.64 $\pm$ 6.53	90.77 $\pm$ 6.15	87.23 $\pm$ 7.96
Control group	116	86.14 $\pm$ 4.78	72.45 $\pm$ 4.57	74.23 $\pm$ 5.74	88.66 $\pm$ 5.36	71.41 $\pm$ 6.28
<i>t</i>		0.352	7.452	6.781	0.730	4.512
<i>P</i>		>0.05	<0.05	<0.05	>0.05	<0.05

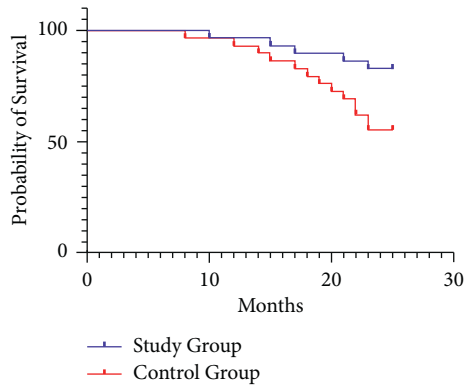


FIGURE 3: Comparison of long-term outcomes between the control group ( $n = 116$ ) and the study group ( $n = 116$ ).

resolving food stagnation, eliminating dampness and dispelling cold; white mulberry root-bark has the effect of purging lung for relieving asthma, diuresis, and detumescence; heartleaf houttuynia herb has the effect of clearing heat and removing toxicity, anti-inflammatory and antiviral; eucommia bark has the effect of nourishing liver and invigorating the kidney; poria can induce diuresis for removing edema, reinforce spleen, relieve diarrhea, reinforce heart and spleen, and nourish the heart to tranquilize; milkvetch root has the effect of reinforcing qi strengthening exterior defence and inducing diuresis for removing edema; largehead atractylodes rhizome has the effect of invigorating vital energy, invigorating spleen, and eliminating dampness and diuresis; garden burnet root has the effect of cooling blood for hemostasis, detoxication, and astringing sores; willowleaf rhizome has the effect of purging lung and descending qi; cassia bark and atractylodes rhizome have the effect of warmly invigorating kidney yang, dispelling cold for relieving pain, warming meridians, and activating blood; and milkwort root has the effect of tranquilization and expelling phlegm [22–26]. The combination of these drugs exerts the effects of clearing heat and removing toxicity, eliminating dampness, and promoting blood circulation.

The results of this study showed that the total effective rate of the study group was significantly higher than that in the control group ( $P = 0.001$ ). The pain level of patients in the study group was significantly lower than that in the control group after 30 days and 60 days of treatment ( $P < 0.05$ ). The level of psychological stress in the study group after care was significantly lower than that in the control group, indicating that psychological care combined with herbal treatment was effective in the treatment of postoperative advanced cervical cancer patients and could effectively improve the degree of postoperative pain and the adverse psychological reactions of patients. Breitbart et al. [27] showed that a positive and healthy state of mind was conducive to disease recovery. Cunningham [28] showed that psychological interventions could reduce postoperative pain and improve psychological status by reducing pain and oxidative stress factors in patients with cervical cancer. The results of this study showed that the serum IFN- $\gamma$  level of patients increased significantly after treatment and the IFN-

$\gamma$  level was negatively correlated with the degree of psychological stress of patients, indicating that psychological care combined with traditional Chinese medicine treatment could effectively increase the serum IFN- $\gamma$  level of patients, improve the antiviral ability of the body, and enhance the immunity of the body. After treatment, the patients in the study group had a significantly higher emotional function, social function, and role function scores than the control group ( $P < 0.05$ ). The two-year cumulative survival rate was significantly higher than that of the control group ( $P < 0.05$ ). Taken together, psychological care combined with traditional Chinese medicine treatment was more effective for postoperative advanced cervical cancer patients, which can significantly improve patients' quality of life and prolong their survival time.

## 5. Conclusion

In conclusion, psychological care combined with traditional Chinese medicine treatment could significantly improve the psychological stress response of patients with advanced cervical cancer, reduce the degree of the physical pain of patients, improve the quality of patients' life, and prolong the life of patients.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Xue Hou and Huajuan Zhang contributed equally to this work.

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## Research Article

# Clinical Effects of Chinese Herbal Decoction Combined with Basic Chemoradiotherapy and Nursing Intervention in the Treatment of Cervical Cancer and the Effect on Serum CEA, CA125, and TNF- $\alpha$ Levels

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**Objective.** This study was aimed to investigate the clinical effect of Chinese herbal decoction combined with basic chemoradiotherapy and nursing intervention in the treatment of cervical cancer and the effect on serum carbohydrate antigen 125 (CA125), carcinoembryonic antigen (CEA), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels. **Methods.** A total of 200 cervical cancer patients in our hospital from June 2015 to November 2018 were selected and randomly divided into a study group and a control group. The control group was given chemoradiotherapy and psychological nursing treatment, and the study group was given self-made Chinese herbal decoction on the basis of the control group. The clinical efficacy and serum CEA, CA125, and TNF- $\alpha$  levels were assessed. **Results.** After treatment, the total effective rate of the study group was significantly higher than that of the control group. The levels of serum CEA, CA125, and TNF- $\alpha$  were decreased in the two groups after treatment, and the decrease in the study group was more significant than that in the control group. After treatment, CD3<sup>+</sup> and CD4<sup>+</sup> levels were increased compared with those before treatment, and the increase in the study group was also more obvious than that of the control group. The level of CD8<sup>+</sup> was decreased compared with before treatment, and the decrease in the study group was more notable than that of the control group. The two-year cumulative survival rate of the study group was markedly higher than that of the control group. The quality-of-life of patients treated for 3 months, 1 year, and 2 years was dramatically improved compared to before treatment. The incidence of adverse reactions in the study group was lower than that of the control group. **Conclusion.** The treatment of basic chemoradiotherapy and psychological nursing intervention combined with Chinese herbal decoction on cervical cancer patients can improve the clinical treatment effects, improve the patient's body immunity, reduce serum CEA, CA125, and TNF- $\alpha$  levels, prolong survival time, improve life quality, and reduce the incidence of adverse reactions, and it is worthy of clinical promotion.

## 1. Introduction

Cervical cancer, which originates in the cervix of women, is a common clinical gynecological malignant tumor and currently accounts for the second highest incidence of gynecological malignancies [1]. Its early symptoms are vaginal

bleeding and increased leucorrhea, but there is no obvious specificity, and it is not easy to attract patients' attention, thus leading to the majority of patients often having developed to the middle or late stages when diagnosed [2]. Modern medical treatment methods for cervical cancer are surgery, radiotherapy, chemotherapy, immune gene therapy,



and so on [3–5]. However, the 5-year survival rate of patients after treatment is extremely low, indicating that it will have a certain negative impact on patients and seriously affect the life and health of patients [6]. Rogers et al. pointed out that chemoradiotherapy can be used to treat cervical cancer, which can kill tumor cells better and prolong the survival time of patients [7]. However, chemoradiotherapy will aggravate the adverse reactions of patients after treatment, and patients have poor tolerance to treatment, and the treatment effect is not ideal. Li et al. suggested that the combination of Chinese herbal decoctions and conventional treatment can effectively improve the immune function of patients, thereby reducing the toxic side effects of the treatment on patients [8]. With the development of the traditional Chinese medicine (TCM) industry in China, TCM has a unique advantage in treating cervical cancer and other gynecological tumors because of its characteristic of syndrome differentiation and rich experience in gynecological treatment [9]. However, the wide variety of TCM and the different compatibility methods make the current analysis of the cervical cancer prescriptions limited to the summary of the experience of famous doctors [10]. Therefore, this study explores the clinical effects of Chinese herbal decoction combined with basic chemoradiotherapy and nursing intervention on cervical cancer and the effects on CEA, CA125, and TNF- $\alpha$  levels. The report is as follows.

## 2. Materials and Methods

**2.1. General Information.** A total of 200 cervical cancer patients admitted at Zhangqiu District People's Hospital, Jinan, China, from June 2015 to November 2018 were included in the study and randomly divided into a study group and a control group, with 100 cases each. Inclusion criteria: (1) Western medicine diagnoses, all meet the relevant diagnostic criteria according to the "International Union of Obstetrics and Gynecology 2015 Guidelines for the Diagnosis and Treatment of Cervical Cancer" [11], (2) all patients diagnosed by pathological biopsy, (3) Chinese medicine diagnoses, all meet the diagnostic criteria of the "Guiding Principles for Clinical Research of New Chinese Medicines" [12], (4) all patients are the first treatment, (5) the expected survival period is  $\geq 6$  months, (6) patients with complete clinical data, and (7) all patients provided written informed consent. Exclusion criteria: (1) patients with liver and kidney dysfunction, (2) patients with other malignant tumors, (3) patients who are allergic to the drugs in this study, and (4) patients who are difficult to complete the study. This study was approved by the ethics committee of the Zhangqiu District People's Hospital, Jinan, China, and conducted in accordance with the Declaration of Helsinki. There was no statistically significant difference in general information between the two groups (Table 1) ( $P > 0.05$ ), which was comparable.

**2.2. Treatment Method.** The control group was treated with chemoradiotherapy. Cisplatin injection (30 mg/m<sup>2</sup>, H20010743, Howson Pharmaceutical Group Co., Ltd.,

TABLE 1: Comparison of general clinical data of the two groups of patients ( $n$ ).

Index	Study	Control	$X^2$	$P$
Cases	100	100		
Age (year)			0.082	0.774
>55	57	59		
$\leq 55$	43	41		
BMI (kg/m <sup>2</sup> )			1.456	0.483
<18.5	13	15		
18.5–24.9	69	73		
$\geq 25$	18	12		
Course (year)			0.357	0.550
2–4	32	36		
<2	68	64		
Pathological type			0.231	0.891
Squamous cell carcinoma	56	58		
Adenocarcinoma	29	26		
Adenosquamous carcinoma	15	16		
Clinical stage			0.245	0.885
I	26	23		
II	44	46		
III	30	31		

Jiangsu) was diluted with 250 ml of physiological saline, intravenous drip, 1 time/week, for total treatment 12 weeks. On this basis, the study group was given combined treatment with self-made Chinese herbal decoction. The composition of the soup is as follows: *Scutellaria barbata* (30 g), *Coix seed* (30 g), *Atractylodes macrocephala* (12 g), *Oldenlandia diffusa* (30 g), *Codonopsis pilosula* (9 g), *Poria cocos* (15 g), *Astragalus* (30 g), *Angelica* (9 g), *Radix Paeoniae Alba* (9 g), *Bupleurum* (9 g), and *Cyperus tuber* (9 g). Decoction method: all above medicine was put in a medicine pot with clear water, preferably 3 cm under the medicine, soaked for 30 minutes, and decocted 2 times to 300 ml concoction. Chinese herbal decoction started to be taken on the first day of chemotherapy, 1 dose/day, warm clothing in the morning and evening, 4 weeks as a course of treatment, a total of 3 courses of treatment. All patients were given certain psychological counseling to eliminate their worries. The patients will feel fear and anxiety, especially when the lower body feels pain or bleeding. The benefits and effects of TCM treatment should be introduced to patients to increase their confidence.

**2.3. Detection Methods of Serum Markers.** The serum tumor marker levels were detected one day before treatment and at the end of 3 treatment courses of the patients. 5 ml of fasting venous blood was extracted from the patient. After standing for 1 h, the blood was centrifuged at 3000 r/min for 10 min. The supernatant was drawn into the EP tube using a pipette. The enzyme-linked immunosorbent assay (ELISA) was performed to detect CA125, CEA, and TNF- $\alpha$  by the ARCHITECT i4000SR automatic immunoassay analyzer (Abbott, USA) and special kits according to the instructions.

**2.4. Observation Index.** The clinical efficacy of patients after treatment was evaluated, the evaluation criteria are complete remission (CR, the lesions completely subsided for more



than one month), partial remission (PR, the lesion has shrunk >50% for more than one month, and there is no trend of new lesions appearing, growing, or becoming serious), and uncontrolled (NC, the enlargement or reduction of the lesion is less than 50%, or discovery of the emergence, growth, and severity of new lesions) [13]. Total effective rate = (CR + PR)/total number  $\times$  100%. After 3 months of treatment, patients were reexamined to observe the immunological status of patients before and after treatment. Immunoglobulin tests were performed one day before treatment and after treatment. 5 ml of fasting venous blood was drawn from the patient. The test instrument was a flow cytometer (CyFlow® Cube 8, Partec, Germany). The levels of T lymphocyte subsets in peripheral blood including CD3<sup>+</sup>, CD4<sup>+</sup>, and CD8<sup>+</sup> were detected by fluorescent molecular labeling. Serum tumor markers were observed before and after treatment. The adverse drug reactions in 2 groups were recorded, including bone marrow suppression, alopecia, radioactive rectitis, cardiac function damage, gastrointestinal side effects, radioactive dermatitis, and renal dysfunction. We followed up the patients within 2 years after the end of treatment, evaluated the two-year survival rate, and conducted a quality-of-life survey (FACT-G). Before treatment, 3 months after treatment, 1 year after treatment, and 2 years after treatment, professional scorers were assessed according to the patients' true responses. The table includes four major items: physiological status, social/family status, emotional status, and functional status, and the total score is calculated. The lower the score, the worse the quality-of-life is affected by the disease.

**2.5. Statistical Methods.** SPSS 22.0 software was used for the statistical analysis. Measurement data are expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ), count data are expressed as  $n$  (%), and the comparison used the  $\chi^2$  test. The difference is statistically significant with  $P < 0.05$ .

### 3. Results

**3.1. Comparison of the Clinical Efficacy of the Two Groups Patients.** The total effective rate of treatment for patients in the study group was 81.00%, and it was 58.00% in the control group (Table 2). The clinical efficacy of patients in the study group was significantly higher than that of the control group ( $\chi^2 = 13.039$ ,  $P = 0.001$ ) (Table 2).

Comparison of serum CEA, CA125, and TNF- $\alpha$  levels between the two groups.

Before treatment, there was no significant difference in the levels of serum CEA, CA125, and TNF- $\alpha$  between the two groups of patients. The levels of serum CEA, CA125, and TNF- $\alpha$  were decreased after treatment in the two groups, and the study group decreased more significantly than the control group ( $P < 0.05$ ) (Figures 1–3).

**3.2. Comparison of Serum Immune Function between Two Groups.** There was no significant difference in CD3<sup>+</sup>, CD4<sup>+</sup>, and CD8<sup>+</sup> levels between the two groups before treatment. CD3<sup>+</sup> and CD4<sup>+</sup> levels were increased after treatment in two

TABLE 2: Comparison of clinical efficacy between the two groups of patients.

Group	Cases	CR	PR	NC	Total effective rate ( $n$ (%))
Study	100	43	38	19	81.00%
Control	100	27	31	42	58.00%
$\chi^2$					13.039
$P$					0.001

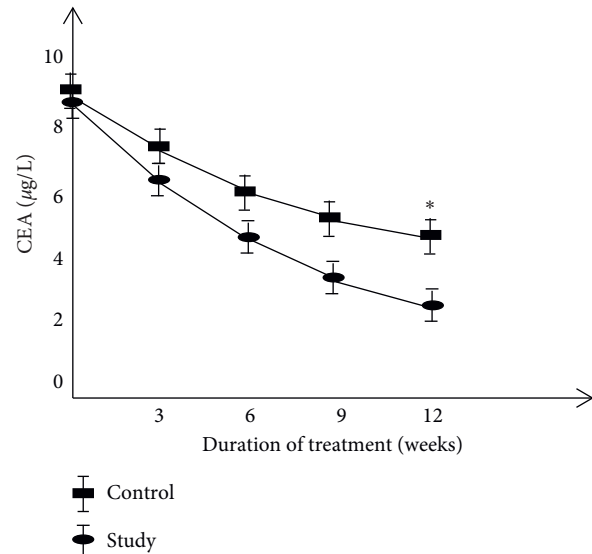


FIGURE 1: Comparison of serum CEA levels between two groups.

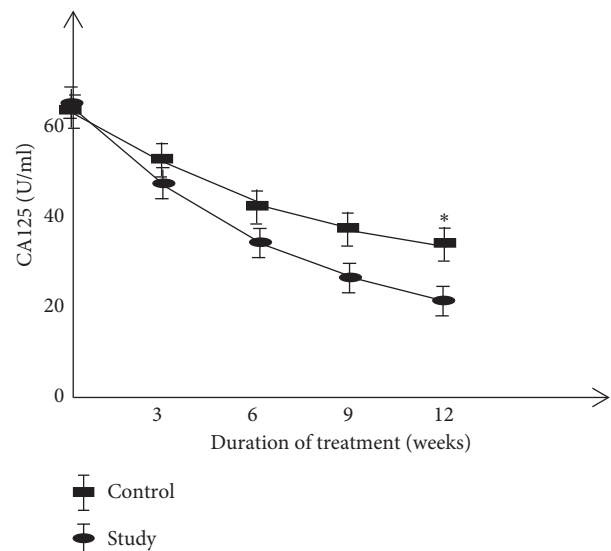


FIGURE 2: Comparison of serum CA125 levels between two groups.

groups, and the increase in the study group was more significant than that in the control group ( $P < 0.05$ ) (Figures 4(a) and 4(b)). CD8<sup>+</sup> levels were decreased compared with those before treatment, and the decrease in the study group was more significant than that in the control group ( $P < 0.05$ ) (Figure 4(c)).

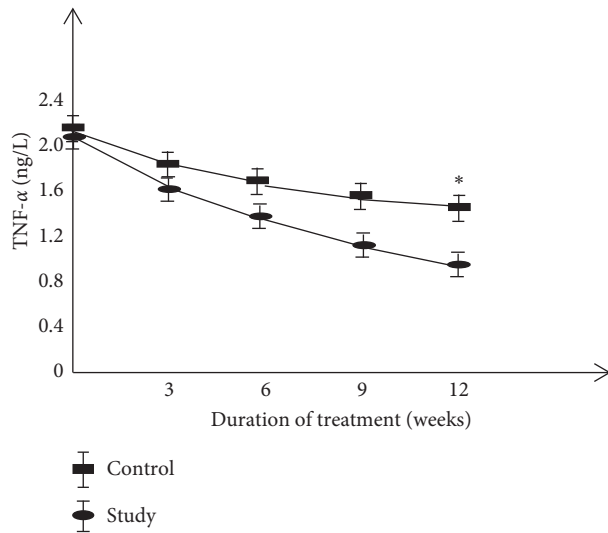


FIGURE 3: Comparison of serum TNF- $\alpha$  levels between two groups.

**3.3. Two-Year Cumulative Survival Rate and Quality-of-Life Were Compared between the Two Groups.** The two-year cumulative survival rate was significantly higher in the study group (70.83%) than in the control group (54.17%) ( $P < 0.05$ ) (Figure 5). There was no significant difference in the quality-of-life between the two groups before treatment ( $P > 0.05$ ). However, for 3 months after treatment, 1 year after treatment, and 2 years after treatment, the quality-of-life was significantly improved ( $P < 0.05$ ) (Table 3).

**3.4. Comparison of the Incidence of Adverse Reactions between the Two Groups of Patients.** The incidence of adverse reactions in the study group was 18% and 47% in the control group (Table 4). The difference was statistically significant ( $\chi^2 = 12.664$ ,  $P = 0.001$ ) (Table 4).

## 4. Discussion

Cervical cancer with high morbidity and mortality is a common malignant tumor that threatens the health and life safety of women [14]. The symptoms of early cervical cancer are concealed, and there are no specific clinical signs, which are easy to be ignored by patients. When clinical symptoms appear, they are often in the middle and late stages, missing the right for surgery [15]. Additionally, patients with advanced cervical cancer are often accompanied by cancer cell dissemination or lymph node metastasis, thus leading to radical surgery that cannot be carried out [16]. At present, chemoradiotherapy is often selected as the main treatment to improve the survival rate of patients [17]. Chemoradiotherapy for cervical cancer can shrink tumors and enhance paraurethral invasion [18]. Chemotherapy inhibits the repopulation of tumor cells during the interval of radiotherapy and the repair of sublethal tumor cell damage after radiotherapy, synchronizes the tumor cell cycle, inhibits the repopulation of tumor cells, improves the sensitivity of tumors to radiotherapy, and reduces the recurrence rate, thus improving the prognosis [19–21]. The standard

regimen of chemoradiotherapy is often based on cisplatin [22–25]. Cisplatin is one of the most effective drugs for the clinical treatment of metastatic cervical cancer [22]. Its response rate is as high as 50%. It can inhibit DNA replication and transcription, leading to DNA breaks and code errors. However, most patients with advanced cervical cancer have a certain degree of decline in immune function. Cisplatin synchronous radiotherapy will bring some toxic side effects to patients, such as nausea, vomiting, and bone marrow suppression, which further reduces the patient's immune function and affects the treatment effect, increases the patient's suffering, and further affects the patient's quality-of-life and treatment compliance. The psychological nursing intervention during chemoradiotherapy can improve the prognosis of patients and effectively reduce the incidence of complications. Research data prove that psychological care can make patients psychologically happy, effectively reduce the degree of unhappiness, patients can be in the best physical and mental state to cooperate with clinical treatment work, effectively control the incidence of complications, and accelerate the patient's early recovery process [26, 27]. While reducing the incidence of complications, patient care satisfaction increases.

TCM believes that cervical cancer belongs to the categories of “abdominal mass,” “uterine bleeding,” and “multicolored leucorrhea” [28]. The leading cause of the disease is menstruation, postpartum wind-cold-damp pathogen, and other evil poison invasions, coupled with the diet, seven emotions disorder, and other factors, resulting in weakness of the spleen and stomach, liver and kidney loss, deficiency of qi and blood, and damage the Chong channel and Ren channel [29]. When there is a problem with the Chong channel and Ren channel, the Du channel becomes weak, and the Dai channel is unstable, resulting in morbid vaginal discharge, and the blood stasis and damp toxin accumulate in the lower abdomen and the uterus to form a mass [30]. For a long time, evil poison is in depth, so that the healthy qi deficiency loss and internal and external evils result in qi stagnation and blood stasis and cancer toxin build-up [30]. In addition, Chinese medicine experts believe that chemotherapy drugs are toxic substances, which often further damage qi and blood, deplete qi and injure yin, and further damage the body's internal organs, causing spleen and kidney yang deficiency, spleen and stomach deficiency and cold, and stomach disharmony, insufficient qi and blood [31]. For cervical cancer, experts in Chinese medicine have confidence that treatment should be based on the theory of the spleen, stomach, and kidney, which can also lessen the adverse reactions caused by chemotherapy in patients to some extent [32]. Therefore, the clinical treatment should be based on strengthening vital qi to eliminate pathogenic factors, resolving toxins to transform stagnation and blood-enriching and supplementing qi. The basic prescription used by patients in this study included *Astragalus* and *Codonopsis pilosula* as the monarch drugs, which could invigorate spleen-stomach and replenish qi and raise yang and lift collapse [33]; *Atractylodes macrocephala* can tonify kidney essence, invigorate the spleen and kidney, effectively correct qi deficiency and weakness, and middle qi collapse [33];

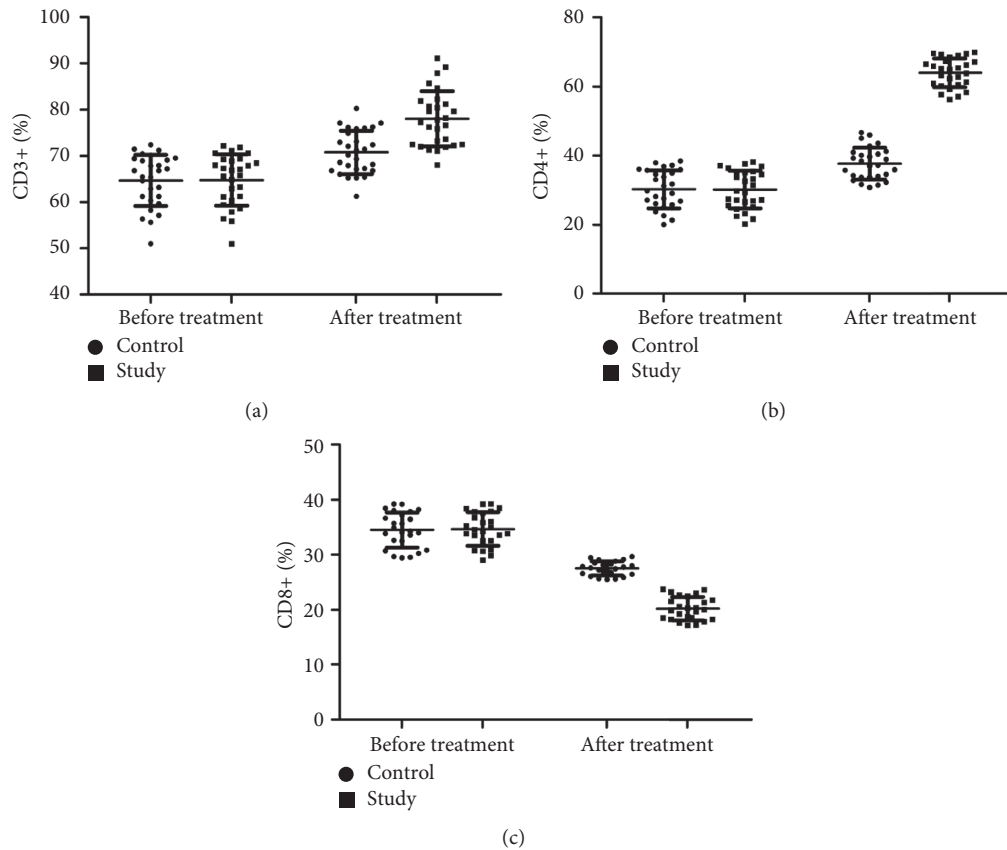


FIGURE 4: Comparison of CD3<sup>+</sup>, CD4<sup>+</sup>, and CD8<sup>+</sup> levels between the two groups.

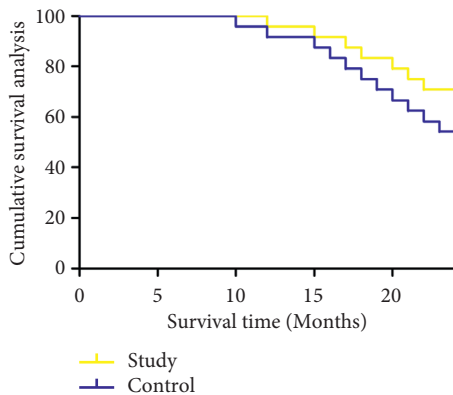


FIGURE 5: Comparison of two-year cumulative survival rate between the two groups.

*Scutellaria barbata* and *Coix seed* can clear heat and remove toxicity [33]; white *Radix Paeoniae Alba* and *Cyperus tuber* can enrich blood qi [33]; *Poria cocos* can nourish the spleen and disinherit dampness, eliminate dampness, and inhibit tumor [33]; *Oldenlandia diffusa* can clear heat and dissipate phlegm [33]; *Angelica* can not only invigorate blood but also activate blood, can not only dredge the meridian but also activate collaterals, and has the effect of pain-killing and anticancer [34]. The whole prescription is compatible with both symptoms and root causes, with the main function of

improving vital qi, supplemented by the elimination of evils, and it has the effects of strengthening the vitality and replenishing qi, detoxifying and removing blood stasis, dredging the meridian and eliminating symptoms, and anticancer and tumor suppressing.

The results of this study showed that the clinical efficacy of the study group after treatment was notably higher than that of the control group, and immune function was significantly increased while the incidence of adverse reactions was decreased. These results indicated that basic therapy combined with TCM in the treatment of cervical cancer could reduce the toxic and side effects of patients and improve the treatment tolerance of patients. Molecular immunology believes that the basis of maintaining the body's cellular immune function is T cell subsets [35]. The immune function of patients with cervical cancer is low, which makes the body's T cell subsets disorder, and the expression of each index is also abnormal. After treatment, the level of the patient's T cell subsets improved better, and the clinical symptoms were controlled. The results of this study showed that the two-year cumulative survival rate and improvement rate in quality-of-life after treatment were significantly higher in the study group than those of the control group. It is suggested that compared with cisplatin simultaneous radiotherapy treatment, combined with self-made Chinese herbal decoction adjuvant treatment can further improve the clinical efficacy of cervical cancer patients, enhance the

TABLE 3: Comparison of quality-of-life between the two groups.

Group	Before treatment	3 months after treatment	1 year after treatment	2 years after treatment
Study	51.43 ± 5.66	73.83 ± 7.92	95.46 ± 4.21	105.62 ± 4.67
Control	52.14 ± 5.71	62.34 ± 6.58	74.72 ± 6.11	81.73 ± 5.85
$\chi^2$	0.623	7.733	11.851	13.984
P	0.482	0.001	≤0.001	≤0.001

TABLE 4: Comparison of the incidence of adverse reactions between the two groups of patients (n).

Group	Cases	Bone marrow suppression	Alopecia	Radioactive rectitis	Cardiac function damage	Gastrointestinal side effects	Radioactive dermatitis	Renal dysfunction
Study	100	2	7	2	1	3	1	2
Control	100	6	12	7	5	7	4	6

body's immune function, thereby reducing the occurrence of serious drug toxicity, and exerting a good effect of increasing efficacy and reducing toxicity. The serum levels of CEA, CA125, and TNF- $\alpha$  in the study group were decreased more notably than those in the control group, which is consistent with the results of Huang et al. and Li et al. [36, 37], suggesting that the Chinese herbal formula has a better anti-tumor effect and can improve the abnormal expression of tumor markers.

## 5. Conclusion

In conclusion, certain psychological nursing interventions and chemoradiotherapy combined with traditional Chinese medicine decoction treatment for cervical cancer patients have good therapeutic effects, at the same time, improve the patient's serum tumor markers and immune level, and the treatment method is highly feasible.

## Data Availability

The data generated or analyzed during this study are included within this article.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Research Article

# Observation of Efficacy of Internet-Based Chronic Disease Management Model Combined with Modified Therapy of Bushenyiliu Decoction in Treating Patients with Type 2 Diabetes Mellitus and Prostate Cancer and Its Effect on Disease Control Rate

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**Objective.** To explore the efficacy of Internet-based chronic disease management model combined with the modified therapy of Bushenyiliu decoction in treating patients with type 2 diabetes mellitus (T2DM) and prostate cancer and its effect on disease control rate (DCR). **Methods.** 120 patients with T2DM and prostate cancer admitted to the Affiliated Hospital of Yangzhou University, Yangzhou First People's Hospital, from February 2019 to February 2020, were retrospectively analyzed and equally divided into the experimental group and the control group according to their admission order. Conventional treatment combined with the modified therapy of Bushenyiliu decoction was performed on all patients for 3 months, and the Internet-based chronic disease management model was adopted for patients in the experimental group additionally, so as to compare their short-term effect, survival time, disease progression, blood glucose indicators, immune function indicators, and type 2 Diabetes Self-Care Scale (2-DSCS) scores. **Results.** Compared with the control group, the experimental group obtained significantly higher DCR and objective remission rate (ORR) ( $P < 0.05$ ), higher survival time and disease progression ( $P < 0.001$ ), better blood glucose indicators and immune function indicators ( $P < 0.001$ ), and higher 2-DSCS scores ( $P < 0.001$ ) after treatment. **Conclusion.** Combining the Internet-based chronic disease management model with the modified therapy of Bushenyiliu decoction can effectively enhance the self-care ability of patients with T2DM and prostate cancer, improve their blood glucose level, promote their body immunity, and comprehensively optimize the cancer control effect, which should be promoted in practice.

Prostate cancer is an epithelial malignancy that occurs in the prostate with complex pathogenic factors, and patients with prostate cancer often present with abnormal urination, pelvic discomfort, and other symptoms. Its incidence and mortality rates, respectively, rank the 2nd and the 6th of male malignancies, and in European and American countries, the number of patients who die from this disease each year accounts for 6% of deaths from malignant tumors [1–3]. The incidence of prostate cancer in China is lower than the

world average, and the disease lethality was found to account for only 1.11% of the mortality from malignant tumors in China in the 2004–2005 sampling survey [4, 5]. However, China has seen the increase in the incidence of prostate cancer in the recent decade, with an annual increase of approximately 12.07% [6], as a result of which prostate cancer is likely to become the most prevalent urological malignancy among Chinese men [7]. Although the incidence of prostate cancer is increasing year by year, its early di-



agnosis rate has not been significantly improved, and patients are mostly in the metastatic or advanced stage when diagnosed. The role of radical surgery, chemotherapy, and endocrine therapy is limited, and treatment methods such as chemotherapy, like a double-edged sword, will greatly reduce the patients' body immunity, so screening a treatment method that is safer and highly effective has become a research hotspot in the field of prostate cancer treatment.

Recent clinical experiments have confirmed the unique advantages of traditional Chinese medicine (TCM) holism and the therapy with syndrome differentiation in treating the malignant tumors, and both Bushenyiqi decoction and Fuzhengyiliu decoction can improve the functional status of prostate cancer patients [8, 9]. The latest studies have shown that Bushenyiqi decoction can affect the Notch signaling pathway and regulate PC-3 cells [10], which has a precise efficacy and higher safety, indicating that TCM treatment is able to enhance the disease control effect of patients. However, clinical experiments usually focus on the treatment of the prostate and ignore the multiple complications that may exist in patients with prostate cancer, and the influence of different complications on the efficacy of TCM treatment is not clear. Type 2 diabetes mellitus (T2DM) is one of the most common complications of prostate cancer, and there are mixed opinions among academia regarding whether the disease is a risk factor predisposing to prostate cancer, but most of the literature have identified that T2DM is closely related to the prognosis of prostate cancer patients [11]. Bjornsdottir and other scholars suggested that T2DM can increase the mortality rate of prostate cancer patients [12], and the levels of blood glucose and glycosylated hemoglobin (HbA1c) can affect the division and apoptosis of prostate cancer cells, so the control of blood glucose level is the focus of treatment for patients with prostate cancer and T2DM. The World Health Organization (WHO) proposes that chronic disease management is a cosmopolitan conundrum [13], and even in Shanghai, where the level of self-care is high, the rate of blood glucose achievement is still under 10%. Some scholars have shown that the "Internet Plus" chronic disease management model based on mobile communication technology can improve the blood glucose control effect and enhance the patients' treatment compliance [14], which may work in both T2DM and prostate cancer at the same time.

Hence, 120 patients with T2DM and prostate cancer were included in the study to explore the efficacy of combining Internet-based chronic disease management model with the modified therapy of Bushenyiliu decoction in treating patients with T2DM and prostate cancer was explored herein, with the study reported as follows.

## 1. Materials and Methods

**1.1. Study Design.** This retrospective study was conducted in the Affiliated Hospital of Yangzhou University, Yangzhou First People's Hospital, from February 2019 to February 2020, and aimed to explore the efficacy of the combination of Internet-based chronic disease management model and the modified therapy of Bushenyiliu decoction in treating

patients with T2DM and prostate cancer and its effect on disease control rate (DCR).

**1.2. Enrollment of Research Objects.** Patients with T2DM and prostate cancer admitted to our hospital from February 2019 to February 2020 were retrospectively analyzed with the following inclusion and exclusion criteria. Inclusion criteria: (1) the patients met the diagnosis criteria for T2DM established by WHO in 1999 [10] and were diagnosed with prostate cancer after pathological examination and imaging examination; (2) the patients were 18 to 76 years old; (3) the patients accepted the insulin treatment and did not accept chemoradiotherapy before enrollment; and (4) the duration of diabetes of the patients was over 1 year. Exclusion criteria: (1) the patients presented mental problems or were unable to communicate with others; (2) the patients had various acute complications and dysfunction of important organs such as heart, brain, and kidney and abnormal hematopoietic function or suffered from malignant tumors; (3) the patients had gestational diabetes mellitus; (4) the patients' Karnofsky score (KPS) was less than 50 points [15]; and (5) the patients' condition was unstable and had the need for discontinuation of glucose lowering medications.

**1.3. Steps.** A total of 120 patients were enrolled in the study and equally divided into the experimental group and the control group according to their admission order. On the day that patients agreed to join the study, the study team collected the sociodemographic data and clinical manifestation data and found that there were no statistical differences in patients' general information between the two groups after analysis ( $P > 0.05$ ); see Table 1; before treatment, the study team measured the patients' blood glucose indicators and immune function indicators and recorded their type 2 Diabetes Self-Care Scale (2-DSCS) scores; 6 weeks and 12 weeks after treatment, the aforesaid indicators were measured again, and the 2-DSCS scores at the 36th week of follow-up visit were collected; and after 1 year of follow-up visit, the patients' survival time and disease progression were calculated.

**1.4. Moral Consideration.** The study met the principle of *World Medical Association Declaration of Helsinki* [16] and was approved by the ethics committee of the Affiliated Hospital of Yangzhou University, Yangzhou First People's Hospital. After enrollment, the study team explained the study purpose, meaning, content, and confidentiality to the patients and asked them to sign the informed consent.

**1.5. Criteria of Quitting the Experiment.** If the patients had the following situations and were determined as unsuitable to continuously accept the study judged by the study team, their case records were all retained for full data analysis: (1) those who experienced adverse events or serious adverse events; (2) those with condition worsened, etc. during the experiment; (3) those who developed certain severe comorbidities or complications; and (4) those who were

TABLE 1: Comparison of patients' general information.

Group	Experimental group ( <i>n</i> = 60)	Control group ( <i>n</i> = 60)	$\chi^2/t$	<i>P</i>
Age (years)				
Range	52–76	54–74		
Mean age	68.21 ± 2.65	68.26 ± 2.54	0.106	0.916
Duration of prostate cancer (months)				
Range	2–48	2–49		
Mean disease duration	30.24 ± 2.16	30.56 ± 2.15	0.813	0.418
Duration of T2DM (years)				
Range	1–12	1–11		
Mean disease duration	5.23 ± 1.22	5.26 ± 1.23	0.134	0.894
Blood pressure (mmHg)				
Diastolic blood pressure	78.65 ± 5.65	79.10 ± 5.10	0.458	0.648
Systolic blood pressure	132.65 ± 5.20	132.68 ± 5.23	0.032	0.975
FBG value (mmol)	10.62 ± 1.23	10.65 ± 1.20	0.135	0.893
Metastasis status				
Brain metastasis	3	4	0.152	0.697
Lung metastasis	4	5	0.120	0.729
Liver metastasis	4	3	0.152	0.697
Bone metastasis	6	8	0.323	0.570
T-PSA (μg/L)				
Range	50–456	52–470		
Mean T-PSA	220.25 ± 1.26	220.68 ± 1.25	1.877	0.063
Pathological type				
Adenocarcinoma	48	50	0.223	0.637
Squamous cell carcinoma	8	6	0.323	0.570
Undifferentiated carcinoma	4	4	0.000	1.000
KPS	62.98 ± 2.65	62.35 ± 2.41	1.362	0.176
Place of residence			0.134	0.715
Urban area	32	30		
Rural area	28	30		
Monthly income (yuan)			0.137	0.711
≥4000	24	26		
<4000	36	34		
Lift habits				
Smoking history	35	36	0.035	0.853
Drinking history	38	34	0.556	0.456
Educational degree			0.134	0.715
Senior high school and below	30	28		
College and above	30	32		

unwilling to continue the clinical trial and requested for quitting the experiment to the study team.

**1.6. Methods.** All patients accepted the conventional treatment combined with the modified therapy of Bushenyiliu decoction for three months. (1) ① Prostate cancer treatment: the total androgen deprivation therapy was adopted, intermittent endocrine blockade was performed after maximum androgen blockade, bilateral orchidectomy was conducted, and 250 mg of flutamide (manufactured: Jiangsu Tasly Diyi Pharmaceutical Co., Ltd.; NMPA approval no. H19990144) was taken after three meals every day; if the patients presented painful bone metastases, zoledronic acid (manufactured: Yangtze River Pharmaceutical (Group) Co., Ltd.; NMPA approval no. H20041975) was added; the chemotherapy project was intravenous infusion of 75 mg/m<sup>2</sup> of docetaxel (manufactured: Yangtze River Pharmaceutical

(Group) Co., Ltd.; NMPA approval no. H20058719) once every three weeks and orally taking 5 mg of prednisone (manufactured: Beijing Continent Pharmaceutical Co., Ltd.; NMPA approval no. H20058375) twice a day. ② T2DM treatment: the patients orally took 500 mg of metformin (manufactured: North China Pharmaceutical Co., Ltd.; NMPA approval no. H20113492) and 50 mg of vildagliptin (manufactured: Novartis Pharma Stein AG; NMPA approval no. J20180055) twice every day. (2) Bushenyiliu decoction: ① the formula included epimedium herb, malaytea scurpaea fruit, glossy privet fruit, phellodendri amurensis cortex, mongolian milkvetch root, tangshen, largehead atractylodes rhizome, indian bread exodermis, coix seed, hedyotis, and hawthorn fruit (30 g each) and common yam rhizome, cibot rhizome, himalayan teasel root, air potato, Chinese angelica, and snakegourd root (10 g each); the herbs were decocted with warm water and taken once every day. ② The formula was modified according to condition. 2-3 pieces of fresh

ginger were added in case of vomiting; 10 g of sanqi and 10 g of ophicalcite were added in case of internal blockade of static blood; 10 g of two-toothed achyranthes root and 10 g of Chinese taxillus herb were added in case of yin deficiency of liver and kidney; and 10 g of talc was added in case of internal exuberance of damp-heat.

The Internet-based chronic disease management model was adopted for patients in the experimental group additionally with the specific steps as follows. (1) Designing the chronic disease online management miniprogram: The Wechat miniprogram was developed by personnel from a software development company jointly with our hospital, which included the backstage management side and the patient side, being used by the medical workers and patients as well as their family members, respectively. (2) Building a chronic disease online management team: The team that included 2 endocrinologists, 2 prostate cancer physicians, 4 diabetes specialist nurses, 4 prostate cancer specialist nurses, and 2 nutritionists established a one-to-many management model with the patients, accepted the miniprogram training before the study, joined the theoretical examination and operational examination after training, and obtained the access to the backstage management side after getting the qualification certificate. (3) On the day of patients being enrolled in the experimental group, rehabilitation plans were proposed according to their actual condition, diagnosis, treatment, diet, and exercise plans with individual differences were made, one-to-one training was conducted aiming at the chemotherapy and insulin injection for patients, and then the team helped the patients to join the Wechat group, follow the Wechat miniprogram, and use the miniprogram correctly, to improve the utilization rate of the management platform. (4) Chronic disease online management miniprogram module: ① Electronic health records: The patients filled in the electronic health record that was updated once every two weeks with their basic information including blood pressure, blood glucose, weight, cancer stage, family history, and prior history, the system intelligently identified the health status of the patients and emphatically monitored their blood glucose values, hepatic and kidney function, etc., and then the physicians of the platform reminded the patients of physical examination and urged the patients to upload data, so as to dynamically monitor their condition changes in real time; the miniprogram could analyze the data sent by patients each time and reminded the patients with the risk of the deterioration of disease and at the same time sent message to the physicians of the platform; then the physicians gave proper advice and guidance to patients so that they could understand their own condition changes. ② Health consultation: the medical workers established the disease symptoms database for patients to do the self-service enquiry and find correspondent medical advice; in case the database could not satisfy the patient needs, the patients could enter the interface of physician service and raise questions, which the physicians needed to reply within 2 days. ③ Lifestyle assessment: it included the patients' dietary habits, exercise habits, and occupational habits, and by referring to the functional software such as Boohee, the miniprogram could help the patients record their daily diet

and exercise and self-screen their health status with the authoritative scales confirmed by international literature and automatically mark the patients with poor scale scores as the key intervention object; then the physicians pointed out their health risks in life and provided reasonable advice and guidance. ④ Sign-in: the sign-in module was based on the calendar and recorded the dates of logging in the miniprogram, return visits, and blood pressure recording, etc. of patients; the miniprogram pushed the sign-in reminder at 9 pm every day to the patients who did not record the information on time. ⑤ Health education: the knowledge resources about disease prevention and treatment were integrated according to the characteristics of diabetes and prostate cancer; information in popular and easy-to-understand language was screened from newspapers and scientific articles and pushed to Wechat in the form of articles, pictures, and short videos, so as to promote the patients' passive reading volume and increase their health knowledge. (5) All patients constantly recorded their data on the miniprogram and accepted telephone follow-up and clinical follow-up for a year.

#### 1.7. Observation Criteria

- (1) General information: the general information extraction forms were established by the patients themselves, including the in-patient number, name, age, duration of prostate cancer, duration of T2DM, blood pressure, fasting blood glucose (FBG) value, cancer metastasis status, level of total prostatic specific antigen (T-PSA), pathological type, Karnofsky score (KPS), place of residence, monthly income, life habits, and educational degree.
- (2) Short-term efficacy: the patients' condition was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) [17] established by WHO in 2000, which classified the condition as complete response (CR, disappearance of all lesions, no new lesions, and recovery of tumor markers for over one month), partial response (PR,  $\geq 30\%$  decrease in SLD (the sum of the longest diameters) of the target lesion for over one month), stable disease (SD, no PR, no PD), and progressive disease (PD,  $\geq 20\%$  increase in SLD or new lesions). The objective remission rate (ORR, CR + PR) and disease control rate (DCR, CR + PR + SD) were used to compare the treatment effect of patients.
- (3) Survival time and disease progression: the survival time and disease progression of patients in both groups were calculated.
- (4) Blood glucose indexes: before treatment ( $T_1$ ), 6 weeks after treatment ( $T_2$ ) and 12 weeks after treatment ( $T_3$ ), 5 ml of fasting vein blood was drawn from the patients in the morning to separate the supernatant under 3,000 r/min after letting it stand for 0.5 h, the FBG values were measured by the glucose oxidase method (Cobase 411 fully automatic biochemical analyzer and original supporting agents;

TABLE 2: Comparison of patients' overall efficacy ( $n(\%)$ ).

Group	CR	PR	SD	PD	ORR	DCR
Experimental group	18 (30.0)	30 (50.0)	6 (10.0)	6 (10.0)	48 (80.0)	54 (90.0)
Control group	10 (16.7)	20 (33.3)	12 (20.0)	18 (30.0)	30 (50.0)	42 (70.0)
$\chi^2$	2.981	3.429	2.353	7.500	11.868	7.500
$P$	0.084	0.064	0.125	0.006	0.001	0.006

NMPA (I) 20113402843), and the glycosylated hemoglobin (HbA1c) was measured by the cation-exchange high-performance liquid chromatography (EC-HPLC) method (with the machine and original supporting agents made by Tai'an City Kang Yu Medical Instrument Co., Ltd.; Shandong MPA (I) 20142400498) to calculate the standard deviation and absolute deviation of blood glucose.

- (5) Immune function indicators: at  $T_1$ ,  $T_2$ , and  $T_3$ , 5 ml of fasting vein blood was drawn from the patients in the morning, and their levels of T lymphocyte subsets, including  $CD3^+$ ,  $CD4^+$ , and  $CD8^+$ , were detected and their  $CD4^+/CD8^+$  values were calculated with the flow cytometer (FCM) (manufactured: Acea Bio (Hangzhou) Co., Ltd.; Zhejiang MPA Certified No. 20142400581).
- (6) 2-DSCS scores: the 2-DSCS [18] was made by Wang Jingxuan et al. and the 5-point Likert scale was adopted. The 2-DSCS included the aspects of dietary self-management, regular exercise, medication compliance, blood glucose monitoring, feet care, and prevention and treatment of hyperglycemia and hypoglycemia and a total of 26 items. Each item was evaluated on a scale of 0–5 points, respectively indicating never finished, seldom finished, sometimes finished, often finished, and completely finished. The range of the total score of 2-DSCS was 26–130 points, with higher scores indicating better self-care execution of T2DM patients. The 2-DSCS scores of patients were compared between the two groups at  $T_3$  and the 36th week of follow-up.

**1.8. Statistical Processing.** In this study, the data processing software was SPSS20.0, the picture drawing software was GraphPad Prism 7 (GraphPad Software, San Diego, USA), items included were enumeration data and measurement data, methods used were  $\chi^2$  test and  $t$ -test, and differences were considered statistically significant at  $P < 0.05$ .

## 2. Results

**2.1. Comparison of Patients' General Information.** No statistical differences were presented when comparing the patients' general information between the two groups ( $P > 0.05$ ); see Table 1.

**2.2. Comparison of Patients' Short-Term Efficacy.** The experimental group obtained significantly higher ORR and DCR than the control group ( $P < 0.05$ ); see Table 2.

**2.3. Comparison of Patients' Survival Time and Disease Progression.** The survival time and disease progression were significantly higher in the experimental group than in the control group ( $P < 0.001$ ); see Figure 1.

**2.4. Comparison of Patients' Blood Glucose Indicators.** After treatment, the experimental group achieved remarkably better blood glucose indicators than the control group ( $P < 0.001$ ); see Figure 2.

**2.5. Comparison of Patients' Immune Function Indicators.** After treatment, the immune function indicators were remarkably better in the experimental group than in the control group ( $P < 0.001$ ); see Figure 3.

**2.6. Comparison of Patients' 2-DSCS Scores.** After treatment, the 2-DSCS scores were remarkably higher in the experimental group than in the control group ( $P < 0.001$ ); see Table 3.

## 3. Discussion

Diabetes mellitus is the metabolic syndrome characterized by chronic increases in blood glucose levels. China has more than 100 million cases of diabetes mellitus, making the incidence of the disease ranking first in the world [19]. 90% of diabetes is T2DM, and recent epidemiological reports have confirmed that the disease is closely related to malignancy due to the facts that malignancy occurs in T2DM patients at a significantly increased risk than the general population and that there is an important relationship between patient prognosis and glycemic control [20]. Bjornsdottir and other scholars pointed out that T2DM increased mortality in patients with prostate cancer, with implicated factors including insulin-like growth factor I, insulin, blood glucose, and HbA1c. Insulin-like growth factor I and insulin are able to promote tumor development, long-term maintenance of high blood glucose levels increases the risk of prostate cancer recurrence, and prostate cancer patients with T2DM undergoing radical prostatectomy have a 50% increase in recurrence rate compared with prostate cancer patients with normal blood glucose values [21], suggesting that blood glucose levels may serve as a predictor of postoperative recurrence in T2DM patients with prostate cancer. Therefore, it is extremely important to strengthen the glycemic control of patients. However, the universal glycemic control rate across China is low, which is less than 10% even in Shanghai, where medical conditions and scientific research conditions are more advanced, and the

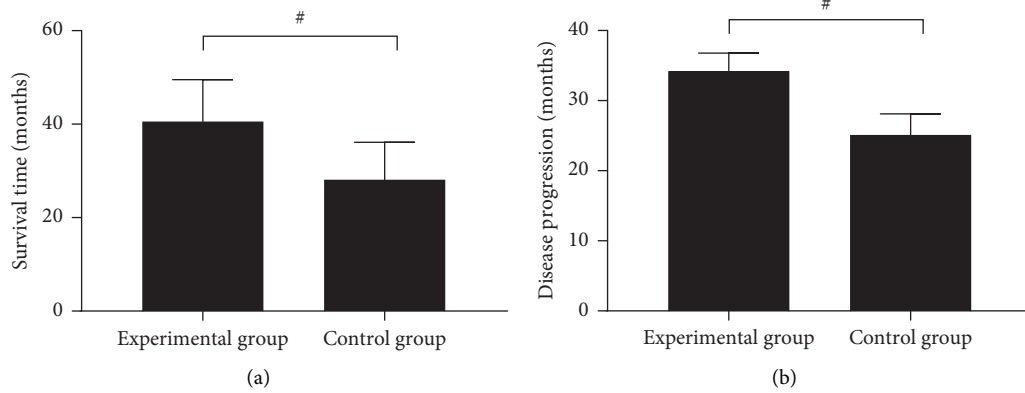


FIGURE 1: Comparison of patients' survival time and disease progression ( $\bar{x} \pm s$ , months). The horizontal axes from left to right denote the experimental group and the control group, and # denotes  $P < 0.001$ . In Figure 1(a), the vertical axis indicate the survival time, of which the experimental group was significantly higher than the control group ( $40.56 \pm 8.96$  vs.  $28.12 \pm 7.98$ ,  $P < 0.001$ ). In Figure 1(b), the vertical axis indicate the disease progression, of which the experimental group was significantly higher than the control group ( $34.21 \pm 2.56$  vs.  $25.12 \pm 2.98$ ,  $P < 0.001$ ).

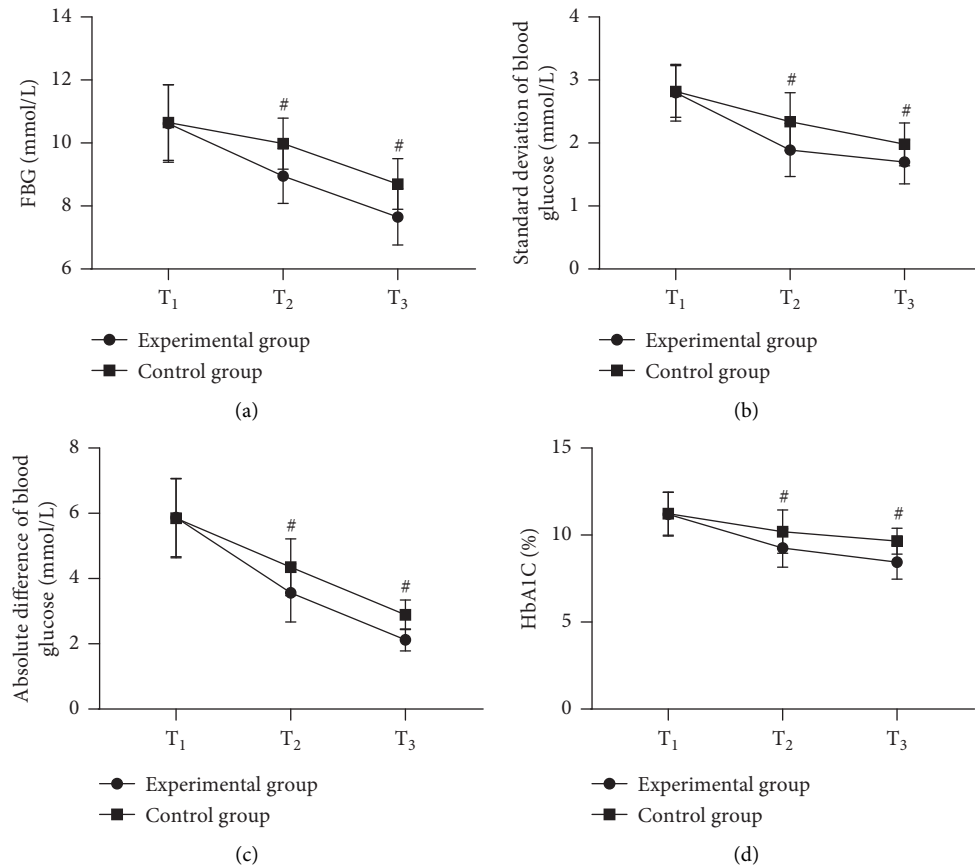


FIGURE 2: Comparison of patients' blood glucose indicators ( $\bar{x} \pm s$ ). The horizontal axes from left to right denoted  $T_1$ ,  $T_2$ , and  $T_3$ , the lines with dots denote group A, and the lines with blocks denote group B; and # denote  $P < 0.001$ . In Figure 2(a), the vertical axis indicate the FBG values; at  $T_1$ , the FBG values of the two groups were not statistically different ( $10.62 \pm 1.23$  vs.  $10.65 \pm 1.20$ ,  $P > 0.05$ ); and at  $T_2$  and  $T_3$ , the FBG values were significantly lower in the experimental group than in the control group ( $8.95 \pm 0.87$  vs.  $9.98 \pm 0.81$ ,  $7.65 \pm 0.89$  vs.  $8.70 \pm 0.80$ ,  $P < 0.001$ ). In Figure 2(b), the vertical axis indicate the standard deviation of blood glucose; at  $T_1$ , the standard deviations of blood glucose of the two groups were not statistically different ( $2.80 \pm 0.45$  vs.  $2.82 \pm 0.41$ ,  $P > 0.05$ ); and at  $T_2$  and  $T_3$ , the standard deviations of blood glucose were significantly lower in the experimental group than in the control group ( $1.89 \pm 0.42$  vs.  $2.34 \pm 0.46$ ,  $1.70 \pm 0.35$  vs.  $1.98 \pm 0.34$ ,  $P < 0.001$ ). In Figure 2(c), the vertical axis indicate the absolute deviation of blood glucose; at  $T_1$ , the absolute deviations of blood glucose of the two groups were not statistically different ( $5.87 \pm 1.20$  vs.  $5.85 \pm 1.21$ ,  $P > 0.05$ ); and at  $T_2$  and  $T_3$ , the absolute deviations of blood glucose were significantly lower in the experimental group than in the control group ( $3.56 \pm 0.89$  vs.  $4.35 \pm 0.87$ ,  $2.12 \pm 0.34$  vs.  $2.89 \pm 0.45$ ,  $P < 0.001$ ). In Figure 2(d), the vertical axis indicate the HbA1c level; at  $T_1$ , the HbA1c levels of the two groups were not statistically different ( $11.20 \pm 1.26$  vs.  $11.23 \pm 1.24$ ,  $P > 0.05$ ); and at  $T_2$  and  $T_3$ , the HbA1c levels were significantly lower in the experimental group than in the control group ( $9.26 \pm 1.10$  vs.  $10.20 \pm 1.24$ ,  $8.45 \pm 0.98$  vs.  $9.65 \pm 0.74$ ,  $P < 0.001$ ).

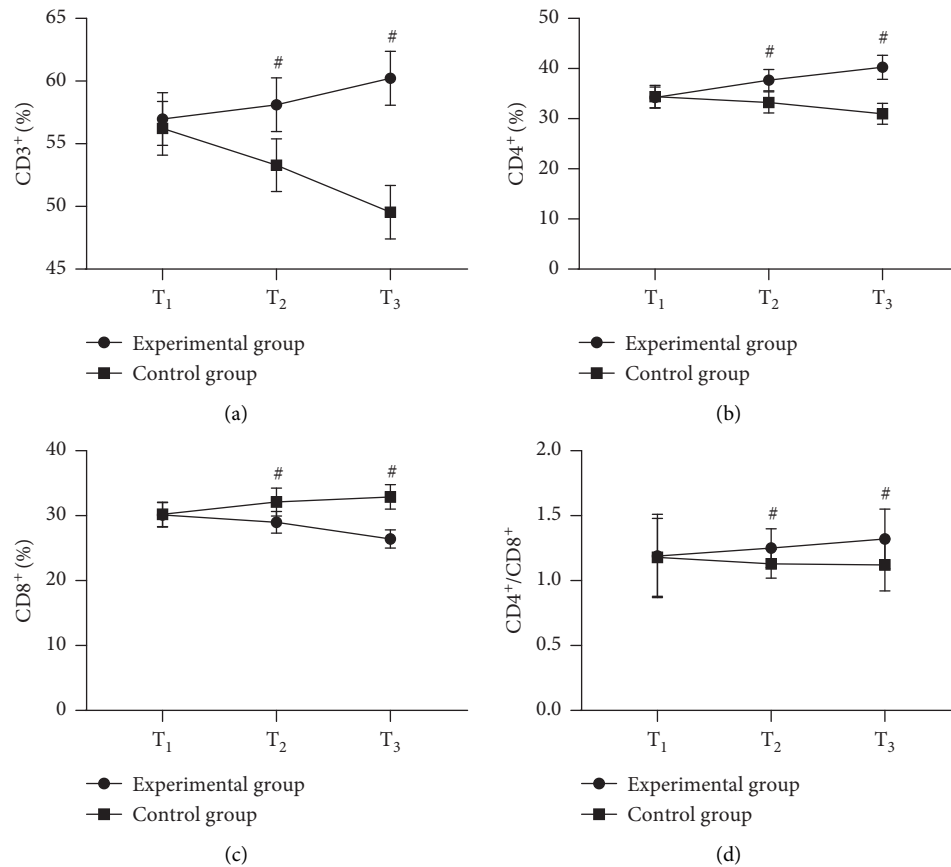


FIGURE 3: Comparison of patients' immune function indicators ( $\bar{x} \pm s$ ). The horizontal axes from left to right denote T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>, the lines with dots denote group A, and the lines with blocks denote group B; and # denote  $P < 0.001$ . In Figure 3(a), the vertical axis indicate the CD3<sup>+</sup> cells; at T<sub>1</sub>, the CD3<sup>+</sup> cells of the two groups were not statistically different ( $56.98 \pm 2.10$  vs.  $56.23 \pm 2.14$ ,  $P > 0.05$ ); and at T<sub>2</sub> and T<sub>3</sub>, the CD3<sup>+</sup> cells were significantly higher in the experimental group than in the control group ( $58.11 \pm 2.14$  vs.  $53.29 \pm 2.10$ ,  $60.23 \pm 2.15$  vs.  $49.54 \pm 2.13$ ,  $P < 0.001$ ). In Figure 3(b), the vertical axis indicate the CD4<sup>+</sup> cells; at T<sub>1</sub>, the CD4<sup>+</sup> cells of the two groups were not statistically different ( $34.21 \pm 2.10$  vs.  $34.41 \pm 2.23$ ,  $P > 0.05$ ); and at T<sub>2</sub> and T<sub>3</sub>, the CD4<sup>+</sup> cells were significantly higher in the experimental group than in the control group ( $37.68 \pm 2.12$  vs.  $33.24 \pm 2.11$ ,  $40.25 \pm 2.41$  vs.  $30.98 \pm 2.10$ ,  $P < 0.001$ ). In Figure 3(c), the vertical axis indicate the CD8<sup>+</sup> cells; at T<sub>1</sub>, the CD8<sup>+</sup> cells of the two groups were not statistically different ( $30.13 \pm 1.89$  vs.  $30.20 \pm 1.87$ ,  $P > 0.05$ ); and at T<sub>2</sub> and T<sub>3</sub>, the CD8<sup>+</sup> cells were significantly lower in the experimental group than in the control group ( $28.98 \pm 1.68$  vs.  $32.10 \pm 2.14$ ,  $26.41 \pm 1.41$  vs.  $32.89 \pm 1.88$ ,  $P < 0.001$ ). In Figure 3(d), the vertical axis indicate the CD4<sup>+</sup>/CD8<sup>+</sup> ratio; at T<sub>1</sub>, the CD4<sup>+</sup>/CD8<sup>+</sup> ratios of the two groups were not statistically different ( $1.19 \pm 0.32$  vs.  $1.18 \pm 0.30$ ,  $P > 0.05$ ); and at T<sub>2</sub> and T<sub>3</sub>, the CD4<sup>+</sup>/CD8<sup>+</sup> ratios were significantly higher in the experimental group than in the control group ( $1.25 \pm 0.15$  vs.  $1.13 \pm 0.11$ ,  $1.32 \pm 0.23$  vs.  $1.12 \pm 0.20$ ,  $P < 0.001$ ).

HbA1c control rate of Grade III Level A hospitals in Beijing is only 37.8% [22], showing that diabetes management is still an important problem in the management of chronic diseases in China.

Based on the Guiding Opinions on Actively Promoting the "Internet Plus" Action Plan released by the State Council, Han and other scholars proposed the "Internet Plus" chronic management model, aiming to make the most of the convenience of the Internet, improve the use efficiency of medical resources, reduce the medical cost of chronic disease management, and enable diabetic patients to obtain better medical services [23]. The results of Han et al. showed that the "Internet Plus" chronic management mode could improve metabolic parameters in T2DM patients, with significantly higher self-care scale scores in patients with diabetes than in those in the control group ( $P < 0.001$ ), which was similar to the results herein, in which the experimental group had significantly

higher posttreatment 2-DSCS scores than the control group ( $P < 0.001$ ), demonstrating that this chronic disease management model could achieve seamless docking of home care and hospital resources, promote the information sharing between doctors and patients, and fully address the decreasing regulatory efforts when patients were at home. To improve the efficiency of "Internet Plus" chronic management mode, Wechat miniprogram, with the advantages of real-time operation and convenience and the utilization better than computer-based platforms, was used as a tool in this study. For patients with prostate cancer, mobile phones are also a more practical tool. In this study, after regular entry of personal information, the patient's T2DM data and prostate cancer data were under dynamic regulation, so the improved glycemic control rate and posttreatment blood glucose indicators of the experimental group were significantly better than those of the control group ( $P < 0.001$ ).



TABLE 3: Comparison of patients' 2-DSCS scores ( $\bar{x} \pm s$ , points).

Item		Experimental group	Control group	<i>t</i>	<i>P</i>
Dietary self-management	$T_3$	23.68 $\pm$ 2.10	18.21 $\pm$ 1.52	16.344	<0.001
	36 weeks of follow-up	25.14 $\pm$ 2.33	15.42 $\pm$ 1.24	28.526	<0.001
Regular exercise	$T_3$	15.20 $\pm$ 1.20	10.10 $\pm$ 1.11	24.167	<0.001
	36 weeks of follow-up	17.23 $\pm$ 1.20	11.98 $\pm$ 1.23	23.665	<0.001
Medication compliance	$T_3$	12.10 $\pm$ 0.89	10.20 $\pm$ 1.23	9.694	<0.001
	36 weeks of follow-up	14.12 $\pm$ 0.21	9.84 $\pm$ 0.87	37.043	<0.001
Blood glucose monitoring	$T_3$	12.41 $\pm$ 1.52	10.95 $\pm$ 1.22	5.802	<0.001
	36 weeks of follow-up	14.23 $\pm$ 1.51	9.98 $\pm$ 0.87	18.890	<0.001
Feet care	$T_3$	18.24 $\pm$ 1.65	16.55 $\pm$ 1.42	6.013	<0.001
	36 weeks of follow-up	20.98 $\pm$ 1.23	14.32 $\pm$ 1.58	25.764	<0.001
Prevention and treatment of hyperglycemia and hypoglycemia	$T_3$	13.20 $\pm$ 1.52	11.87 $\pm$ 1.10	5.491	<0.001
	36 weeks of follow-up	15.01 $\pm$ 1.20	10.54 $\pm$ 1.02	21.985	<0.001

Improvement in blood glucose indicators is key to the consolidation of therapeutic effects in prostate cancer. Hyperglycemia inhibits docetaxel-induced apoptosis of prostate cancer cells, while there is a positive correlation between HbA1c and metastasis of prostate cancer, so the numerical reduction of both is beneficial for Bushenyiliu decoction to exert therapeutic effects. In Bushenyiliu decoction, epimedium herb, malaytea scurfpea fruit, glossy privet fruit, phellodendri amurensis cortex, and other herbs can inhibit proliferation and induce apoptosis of PC-3 cells and are conducive to slowing down the progression of prostate cancer, which has been proved in the in vitro study [24]; in addition, mongolian milkvetch root and tangshen have the effect of supplementing spleen to nourish lung, while largehead atractylodes rhizome can invigorate stomach, and fried orange fruit plays a role in regulating functional activities of vital energy and helping the patients to regulate their qi and blood; from the perspective of modern pharmacology, although tangshen cannot accelerate the rate of tumor cells apoptosis, it can promote the cellular metabolism in malignant tumor host, and there is a counter-promotion effect of largehead atractylodes rhizome, which can selectively inhibit the cell subset of malignant tumor responsible for metastasis; mongolian milkvetch root is able to accelerate protein synthesis, promote energy metabolism, and induce the generation of interleukin, the anticancer factor in the body, tuckahoe can affect the macrophage and lymphocyte, and coixenolide in the coix seed can fully enhance body immunity. Hence, the immune function indicators of the experimental group were significantly better than those of the control group after treatment ( $P < 0.001$ ).

In conclusion, with the combined action of multiple factors, the DCR and ORR of the experimental group were significantly higher than those of the control group ( $P < 0.05$ ), and so were the survival time and disease progression ( $P < 0.001$ ), indicating that the Internet-based

chronic disease management mode combined with the modified therapy of Bushenyiliu decoction can effectively enhance the self-care ability of patients with T2DM and prostate cancer, improve their blood glucose level, boost their body immunity, and comprehensively optimize the cancer control effect, which should be promoted in practice.

### Data Availability

Data to support the findings of this study are available upon reasonable request to the corresponding author.

### Conflicts of Interest

The authors have no conflicts of interest to declare.

### Acknowledgments

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## Research Article

# Diagnostic Value of Color Doppler Ultrasound Combined with Superb Microvascular Imaging in the Detection of Small Renal Tumors Less than 3 cm Treated with Jinkui Shenqi Pills

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The purpose of this study was to investigate the diagnostic value of color Doppler ultrasound combined with superb microvascular imaging (SMI) in the detection of small renal tumors less than 3 cm treated with Jinkui Shenqi pills. 50 cases were randomly selected from the patients with angioleiomyoma (a kind of small renal tumor) less than 3 cm confirmed by pathological examination and treated in our hospital from January 2018 to January 2020. All patients were treated with Jinkui Shenqi pills. All patients were first detected by color Doppler ultrasound and then by SMI. The results of color Doppler ultrasound were used as the control group, while those of color Doppler ultrasound combined with SMI were used as the experimental group. After that, the specificity, sensitivity, positive and negative detection results, and detection accuracy were compared between the two groups. The specificity and sensitivity in the experimental group were significantly higher than those in the control group, with statistical significance ( $P < 0.05$ ). The cases of positive and negative detection results in the experimental group were significantly higher than those in the control group, with statistical significance ( $P < 0.05$ ). The detection accuracy in the experimental group was significantly higher than that in the control group, with statistical significance ( $P < 0.05$ ). The specificity, sensitivity, positive and negative detection results, and detection accuracy of color Doppler ultrasound combined with SMI in the detection of small renal tumors less than 3 cm treated with Jinkui Shenqi pills were all significantly higher than those of color Doppler ultrasound; therefore, the application of color Doppler ultrasound combined with SMI for the diagnosis of small renal tumors is of high value.

## 1. Introduction

Small renal tumors including benign and malignant tumors are very common urinary diseases. The diameter of small renal tumors is generally no more than 3 cm at the early stage when the patients may not suffer from symptoms such as low back pain, odynuria, and hematuria, with little effect on their daily life. Therefore, it is highly likely that the early diagnosis and treatment will be missed, resulting in the aggravation of the patients' conditions and seriously affecting patients' life health [1–3]. Jinkui Shenqi pills are a kind of Chinese traditional medicine (CTM) mainly to treat edema due to kidney deficiency, soreness and weakness of waist and knees,

and other symptoms with the function of warming and invigorating kidney yang. The clinical symptoms of patients with small renal tumors can be alleviated to a certain extent after the treatment with Jinkui Shenqi pills. Color Doppler ultrasound is commonly used in the clinical diagnosis of small renal tumors. However, due to the small size of small renal tumors, the missed diagnosis and misdiagnosis may occur with single color Doppler ultrasound, adversely affecting patients' timely treatment [4–6]. Superb microvascular imaging (SMI) is a new type of imaging technology that detects human blood flow and displays the flow in a visual form, which can diagnose the vascular diseases of patients directly and accurately. It has been reported that the

sensitivity and specificity of SMI in the detection and diagnosis of small renal tumors are relatively high, which can greatly improve the detection rate and accuracy of small renal tumors [7–9]. To further study the application value of color Doppler ultrasound combined with SMI in the diagnosis of small renal tumors, patients with small renal tumors were selected as the research objects to compare the specificity, sensitivity, positive and negative detection results, and detection accuracy between color Doppler ultrasound and SMI combined with color Doppler ultrasound, aiming to clarify the application value and diagnostic effect of color Doppler ultrasound combined with SMI in clinical practice, with details reported as below.

## 2. Materials and Methods

**2.1. General Information.** 50 cases were randomly selected from the patients with angioleiomyoma (a kind of small renal tumor) less than 3 cm confirmed by pathological examination and treated in our hospital from January 2018 to January 2020. All patients were first detected by color Doppler ultrasound and then by superb microvascular imaging (SMI). The results of color Doppler ultrasound were used as the control group, while those of color Doppler ultrasound combined with SMI were used as the experimental group. The patients were aged 22–69 years, with an average age of  $46.22 \pm 5.89$  years, an average weight of  $69.95 \pm 4.70$  kg, an average height of  $168.82 \pm 5.79$  cm, and an average disease course of  $3.20 \pm 0.59$  months.

### 2.2. Inclusion/Exclusion Criteria

#### 2.2.1. Inclusion Criteria

- ① The patients had the clinical manifestation of angioleiomyoma (a kind of small renal tumor)
- ② The patients had normal heart and lung functions
- ③ The patients had no congenital diseases
- ④ The patients had no drug allergy history, drug abuse history, and bad addiction
- ⑤ This study was approved by the Hospital Ethics Committee, and the patients all voluntarily participated in the study and signed informed consent

#### 2.2.2. Exclusion Criteria

- ① The patients had coagulation disorder or were taking anticoagulants
- ② The patients' tumors were more than 3 cm in diameter
- ③ The patients had disturbance of consciousness and could not cooperate with this study

### 2.3. Methods

**2.3.1. Detection Methods.** All patients were first detected by color Doppler ultrasound and then by superb microvascular

imaging (SMI). The results of color Doppler ultrasound were used as the control group, while those of color Doppler ultrasound combined with SMI were used as the experimental group. At 1 hour before detection, patients drank enough water to suppress urine and keep the bladder in a filling state. A color Doppler ultrasound detector (Toshiba Aplio 400 with the probe model as PLT-1005BT) was adopted. With patients taking supine positions during detection, the medical staff moved the probe to scan patients' kidney areas, with the probe frequency of 3.0–7.0 MHz, and recorded the location and size of lesions or tumors [10–12]. After the detection by color Doppler ultrasound, the detector was adjusted to the CDFI, PD, and ADF modes with the color SMI mode. When the patients held their breath, SMI scanning was performed with the lesions as the center and samples selected in the area of 1 cm around the lesions. After the adjustment of color gain and the disappearance of artifact without any factors affecting the diagnostic results, the microvessels were clearly visible to determine the diagnostic results.

In this study, the detection was performed, and the detection results were read by two attending physicians with more than 7 years of experience in abdominal ultrasound examination. If there were any differences, agreement would be reached after the results were discussed.

**2.3.2. Treatment Methods.** All patients orally took Jinkui Shenqi pills (manufacturer: Pharmaceutical Factory of Beijing Tongrentang Technology Development Co., Ltd.; NMPA approval no. Z11020054) for treatment, with 20 pills each time for water-honey pills and 1 pill each time for big candied pills and 2 times a day.

**2.4. Observation Indexes.** With the pathological examination results as the “gold standard,” the specificity, sensitivity, positive and negative detection results, and detection accuracy were compared between the two groups.

Specificity = the cases of negative diagnostic results detected by color Doppler ultrasound/the cases of actual negative results detected by color Doppler ultrasound  $\times 100\%$ ; sensitivity = the cases of positive diagnostic results detected by color Doppler ultrasound/the cases of actual positive results detected by color Doppler ultrasound  $\times 100\%$ ; detection accuracy = the cases of both positive and negative results detected by color Doppler ultrasound and pathological diagnosis/the total number of patients  $\times 100\%$  [13–15].

All patients with positive results were detected twice. If the results were the same as those of the first detection, they were judged to be positive. If the results were different from those of the first detection, the patients were detected for the third time, and the third detection results were the final results.

**2.5. Statistical Treatment.** The selected data processing software for this study was SPSS 20.0, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw the

pictures of the data. Measurement data were expressed by ( $\bar{x} \pm s$ ) and tested by  $t$ -test. Enumeration data were expressed as ( $n$  (%)) and tested by  $\chi^2$  test. The differences had statistical significance when  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Positive and Negative Detection Results between the Two Groups.** The cases of both positive and negative detection results in the experimental group (39 and 9 cases) were significantly more than those in the control group (21 and 2 cases), with statistical significance ( $P < 0.05$ ), as shown in Table 1.

**3.2. Comparison of Specificity and Sensitivity between the Two Groups.** Figure 1 shows the detection image of positive tumors in this study, and Figures 2 and 3 show the imaging images of negative tumors. The diagnostic specificity and sensitivity of the experimental group (90.00% and 97.50%) were significantly higher than those of the control group (18.18% and 53.85%), with statistical significance ( $P < 0.05$ ), as shown in Table 2.

**3.3. Comparison of Detection Accuracy between the Two Groups.** The detection accuracy in the experimental group (96%) was significantly higher than that in the control group (46%), with statistical significance ( $P < 0.05$ ), as shown in Figure 4.

### 4. Discussion

Small renal tumors including benign and malignant tumors refer to intrarenal tumors less than 3 cm in diameter, and common benign tumors include angiomyolipoma [16–19]. Besides, malignant renal tumors, also known as renal cell carcinoma, commonly include Wilms' tumors and transitional cell carcinoma. Compared with benign renal tumors, renal cell carcinoma has lower incidence but poses a greater threat to patients' physical health. The infiltrative range, treatment, and prognosis of the tumors are closely related to the early diagnosis, and thus, exploring effective diagnostic methods has always been the focus in the research field of small renal tumors. All patients in this study were diagnosed with small renal tumors by pathological examination. The results of different detection methods showed that color Doppler ultrasound combined with SMI was more accurate, with higher specificity, sensitivity, and detection accuracy. The principle of SMI is to suppress blood vessels by clutter, so as to extract low-speed blood flow signals from blood vessels and express them as color overlaying images or monochromatic blood flow images. This shows that SMI can detect more blood flow signals and is more sensitive compared with color Doppler ultrasound. The results of this study showed that color Doppler ultrasound combined with SMI can obviously improve positive and negative detection rates. The specificity, sensitivity, and detection accuracy in the experimental group were significantly higher than those in the control group, with statistical significance ( $P < 0.05$ ),

TABLE 1: Comparison of positive and negative detection results between the two groups.

Group	Cases of positive detection results	Cases of negative detection results
Experimental group	39*	9**
Control group	21	2
$\chi^2$	13.50	5.01
$P$	<0.001	0.03

Note. \* indicated that the number of positive detection results was higher compared with the control group ( $P < 0.05$ ). \*\* indicated that the number of negative detection results was higher compared with the control group ( $P < 0.05$ ).

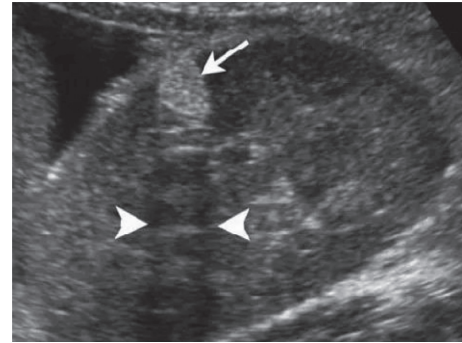


FIGURE 1: A detection image of positive tumors. Note. The black and white ultrasound image of the longitudinal section of the right kidney showed a cluster of echoes (as shown by the arrow) with a posterior sound shadow (as shown by the short arrow).

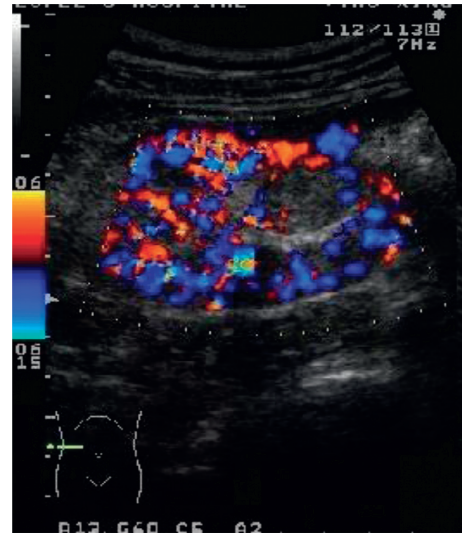


FIGURE 2: A detection image of negative tumors. Note. Yellow and blue represented different blood flow directions, in which the yellow part indicated the blood flow direction, while the blue part indicated the direction different from that of the blood flow.

indicating that color Doppler ultrasound combined with SMI can improve the diagnostic accuracy in patients with small renal tumors, which is worthy of application and popularization. Scholar Zhou et al. [20] pointed out in their study that color Doppler ultrasound combined with SMI could improve the positioning accuracy of the perforator



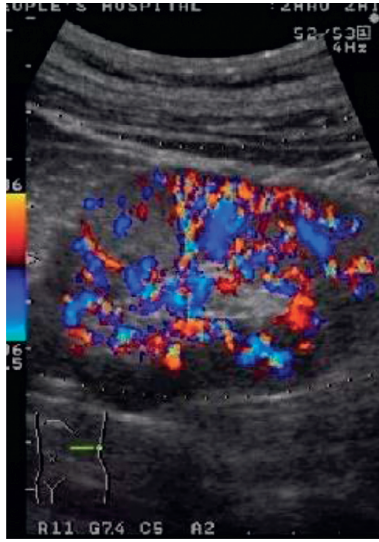


FIGURE 3: A detection image of negative tumors. *Note.* Yellow and blue represented different blood flow directions, in which the yellow part indicated the blood flow direction, while the blue part indicated the direction different from that of the blood flow.

TABLE 2: Comparison of specificity and sensitivity between the two groups.

Group	Specificity	Sensitivity
Experimental group	90.00%*	97.50%**
Control group	18.18%	53.85%
$\chi^2$	103.86	51.75
$P$	<0.001	<0.001

*Note.* \* indicated a significant difference in the specificity between the two groups ( $P < 0.05$ ). \*\* indicated a significant difference in the sensitivity between the two groups ( $P < 0.05$ ).

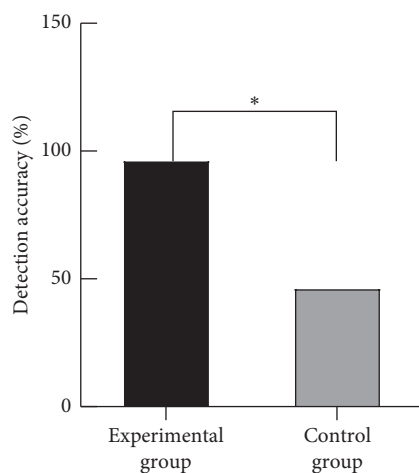


FIGURE 4: Comparison of detection accuracy between the two groups. *Note.* The abscissa represented the experimental group and control group, while the ordinate represented detection accuracy (%). \* denoted  $P < 0.05$ . \* represented the comparison of detection accuracy between the two groups. The detection accuracy was 96% in the experimental group and 46% in the control group, with statistical significance ( $\chi^2 = 60.71$  and  $P < 0.001$ ).

flap artery in patients with diabetes, which is consistent with the conclusion and proves the scientificity of results in this study.

At present, many scholars have affirmed the application value of color Doppler ultrasound in the diagnosis of small renal tumors in their research reports, but some clinical trials have revealed that the detection rate and accuracy of single color Doppler ultrasound for small renal tumors are not high, and its application effect remains unsatisfactory [21, 22]. SMI is an imaging test that mainly targets at blood flow velocity in microvessels as well as blood flow classification. In this study, the combination of SMI and color Doppler ultrasound was applied to the diagnosis of renal small tumors, further exploring the diagnostic effect, diagnostic specificity, sensitivity, and detection accuracy. Although this study confirmed the diagnostic value of color Doppler ultrasound combined with SMI in the detection of small renal tumors less than 3 cm treated with Jinkui Shenqi pills, its diagnostic efficacy was not absolute. In clinical practice, it is necessary to combine the results of urine routine, blood biochemistry, and blood tumor markers to further improve the diagnostic accuracy of the disease.

## 5. Conclusions

In conclusion, the detection mode of small renal tumors by color Doppler ultrasound combined with SMI can significantly improve the specificity, sensitivity, and detection accuracy. Therefore, color Doppler ultrasound combined with SMI has high application value and significant diagnostic effect, which is worthy of application and popularization in clinical practice.

## Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

## Ethical Approval

This study was approved by the Ethics Committee of Yichang Traditional Chinese Medicine Hospital, China.

## Consent

Signed written informed consent was obtained from the patients and/or guardians.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

YG designed the study and drafted the manuscript. SL was responsible for the collection and analysis of the experimental data. YG and SL revised the manuscript critically for important intellectual content. Both authors read and approved the final manuscript.



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## Research Article

# Effect of Yiqi Buxue Decoction on Hemodynamic Changes of the Uterine Artery and Fetal Umbilical Artery and Pregnancy Outcomes in Pregnant Patients with Pulmonary Arterial Hypertension

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**Objective.** To explore the effect of Yiqi Buxue decoction on hemodynamic changes of the uterine artery and fetal umbilical artery and pregnancy outcomes in pregnant patients with pulmonary arterial hypertension (PAH). **Methods.** 120 pregnant patients with PAH treated in our hospital (January 2019-January 2020) were chosen as the research objects, and randomly split into group A ( $n = 60$ ) and group B ( $n = 60$ ). Both groups received routine treatment, and group B was treated with sildenafil citrate, while group A was treated with Yiqi Buxue decoction combined with sildenafil citrate. Both groups received 6 weeks of treatment to analyze the hemodynamic changes of the uterine artery and fetal umbilical artery and compare the cardiopulmonary function indexes and pregnancy outcomes between the two groups. **Results.** The hemodynamic indexes of the uterine artery and fetal umbilical artery, cardiopulmonary function indexes, and pregnancy outcomes in group A after treatment were notably better compared with group B ( $P < 0.01$ ). **Conclusion.** Yiqi Buxue decoction can stabilize the hemodynamics of pregnant patients with PAH, improve their cardiopulmonary function, alleviate hypotension, and thus, reduce the possibility of adverse pregnancy outcomes, which should be popularized in practice.

## 1. Introduction

Pulmonary hypertension (PAH) during pregnancy refers to structural and functional changes in the pulmonary vessels caused by nonspecific causes, which is mainly characterized by elevated pulmonary vascular resistance (PVR). With obvious hemodynamic abnormalities and significantly increased cardiac load, patients are prone to heart failure under the influence of physiological changes during pregnancy, which seriously threatens maternal and child health [1–3]. Studies have shown that PAH is one of the leading important causes of perinatal death in patients, accounting for 12% of all causes of maternal death. With the continuous optimization of medical technology in recent years, the perinatal mortality rate of PAH has decreased from 33%–

42% to 4.2%–15.0% [4], indicating an increased survival rate of patients. However, for patients with Eisenmenger syndrome, the mortality rate remains about 25% [5, 6], suggesting a high possibility of adverse pregnancy outcomes. At present, Western medicine treatment is often adopted to improve the hemodynamics of patients in practice, and targeted PAH drugs are gradually introduced, including anticoagulant drugs such as sildenafil citrate to alleviate the hypercoagulable state of patients and enhance their cardiopulmonary function. However, most PAH drugs are expensive [7] and cannot be widely applied in the early stage of the disease, so it is extremely important to choose cheaper and more efficient drugs for treatment. Yiqi Buxue decoction is a common drug to regulate qi and blood in clinic, which is able to improve the obstructed blood flow of patients, reduce

the vascular resistance, enhance the cardiopulmonary function, optimize the microcirculation, enhance the anti-hypoxia ability of tissue, and stabilize the patients' internal environment. However, no research on the application of Yiqi Buxue decoction in PAH has been reported in academia. Based on this, Yiqi Buxue decoction was adopted in this paper for adjuvant treatment of PAH patients, summarized as follows.

## 2. Materials and Methods

**2.1. General Information.** The study is a randomized controlled trial. One hundred and twenty pregnant patients with PAH treated in Beijing ChuiYangLiu Hospital (January 2019-January 2020) were chosen as the research objects and randomly split into group A ( $n=60$ ) and group B ( $n=60$ ). No statistical difference was found in general information between the two groups ( $P>0.05$ ; Table 1). This study was approved by the hospital ethics committee, and all experiments conformed to the provisions of the Declaration of Helsinki.

**2.2. Inclusion Criteria.** The inclusion criteria of this study were as follows. (1) The patients or their families fully recognized the study process and signed the informed consent; (2) the patients were diagnosed with PAH during pregnancy after examination, according to the diagnostic criteria of ESC/ERS *Pulmonary Hypertension Guidelines* [8, 9]; and (3) the patients did not receive relevant treatment before enrollment [10, 11].

**2.3. Exclusion Criteria.** The exclusion criteria for patients in this study were as follows. (1) The patients had mental problems or could not communicate with others; (2) the patients had other organic diseases; (3) the patients were complicated with preeclampsia, endocrine system diseases, and other diseases; (4) the patients had chronic hypertension; and (5) the patients had placenta previa, or the fetuses had congenital malformation.

## 3. Methods

The patients in both groups received routine treatment, including introducing a low-salt and healthy diet, performing oxygen inhalation and cardiotonic treatment, limiting their physical activity of the patients, and arranging reasonable daily work for them. In addition, group B was treated with sildenafil citrate, while group A was treated with Yiqi Buxue decoction combined with sildenafil citrate. Both groups received 6 weeks of treatment, specifically as follows. (1) Sildenafil citrate: the patients took sildenafil citrate daily (Guangzhou Baiyunshan Pharmaceutical Holdings Co., Ltd., Baiyunshan Pharmaceutical General Factory; NMPA approval no. H20143255) before meals, 3 times a day and 25 mg each time. (2) Yiqi Buxue decoction: the decoction included 15 g of *Codonopsis pilosula*, 15 g of *Astragalus membranaceus*, 10 g of *Angelica sinensis*, 10 g of *Ligusticum*

*wallichii*, 10 g of *Radix Paeoniae Alba*, 10 g of prepared *Rehmannia* root, 10 g of *Poria cocos*, 10 g of Chinese yam, 10 g of motherwort, and 5 g of liquorice. The drugs were decocted in warm water, and the decoction was taken with one dose a day after breakfast and dinner.

### 3.1. Observation Criteria.

- (1) Hemodynamic changes of the uterine artery and fetal umbilical artery: all patients were examined by using a color Doppler ultrasound (Color ultrasound diagnostic instrument Voluson P6 produced by GE Healthcare; NMPA certified no. 20152062178) before and after treatment. With the probe frequency of 3 MHz and pulse sampling volume of 2 mm, the two-dimensional ultrasound diagnostic instrument was placed at the distal branch of the internal iliac artery to position the uterine artery and at 4 cm from the placenta to position the umbilical artery. Three stable arterial blood flow spectra were continuously measured to record the pulsatility index (PI), resistance index (RI), and the ratio of peak systolic velocity ( $S$ ) to end-diastolic peak velocity ( $D$ ) of the uterine artery and fetal umbilical artery.
- (2) Cardiopulmonary function indexes: fasting arterial blood and central venous blood were collected before and after treatment. Arterial oxygen saturation and arterial oxygen partial pressure were measured. The D-dimer level was detected by immunoturbidimetry (kits: Nanjing Getein Biotechnology Co., Ltd., Jiangsu Medical Products Administration No. 2400146). The level of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) was detected by radioimmunoassay (Cobase 411 electrochemiluminescence instrument with matching reagent; NMPA certified no. 3402843).
- (3) Pregnancy outcomes: pregnancy outcomes included fetal pregnancy outcomes and patient pregnancy outcomes. The number of adverse pregnancy outcomes was recorded.

**3.2. Statistical Treatment.** In this study, the data were processed by SPSS20.0 software and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The data included enumeration data and measurement data, tested by the  $X^2$  and  $t$ -test. The differences were statistically significant when  $P<0.05$ .

## 4. Results

**4.1. Comparison of Hemodynamic Changes of the Uterine Artery and Fetal Umbilical Artery.** After treatment, the hemodynamics indexes of the uterine artery and fetal umbilical artery in group A were notably better compared with those in group B ( $P<0.001$ ; Figures 1 and 2).

TABLE 1: Comparison of general data of patients.

Items	Group A ( <i>n</i> = 60)	Group B ( <i>n</i> = 60)	$X^2/t$	<i>P</i>
Age (years)				
Range	20–45	21–45		
Average age	32.98 ± 5.68	32.15 ± 5.98	0.780	0.437
Gestational age (weeks)				
Range	6–37	6–38		
Average gestational age	33.26 ± 5.98	33.45 ± 5.24	0.185	0.854
Number of multiparae	21	20	0.037	0.847
Number of primiparae	39	40		
Causes of PAH				
Congenital heart disease (CHD)	25	24	0.035	0.853
Rheumatic heart disease (RHD)	15	16	0.044	0.835
Hypertensive heart disease (HHD)	10	12	0.223	0.637
Other	10	8	0.261	0.609
Number of fetus			0.261	0.609
Single birth	50	52		
Multiple birth	10	8		
Number of patients who received cardiac therapy	2	3	0.209	0.648
Residence			0.040	0.841
Urban area	42	43		
Rural area	18	17		
Monthly income (yuan)			0.035	0.852
≥4000	36	37		
<4000	24	23		
PAH degree				
Mild	38	40	0.147	0.702
Moderate	16	15	0.044	0.835
Severe	6	5	0.100	0.752
Education			0.139	0.709
Senior high school and below	25	23		
University and above	35	37		

**4.2. Comparison of Cardiopulmonary Function Indexes.** The cardiopulmonary function indexes of group A after treatment were notably better compared with those of group B ( $P < 0.001$ ; Table 2).

**4.3. Comparison of Pregnancy Outcomes.** The pregnancy outcomes in group A were notably better compared with those in group B ( $P < 0.001$ ; Table 3).

## 5. Discussion

Occurring mostly in women of childbearing age, PAH will cause intimal hyperplasia of the pulmonary arteries, autochthonous thrombus, and increased pulmonary vascular resistance, ultimately increasing the right heart load of patients and leading to heart failure or death in severe cases. Both secondary PAH and primary PAH are absolute contraindications of pregnancy because patients in pregnancy will undergo a series of physiological changes that will greatly increase the mortality and the incidence of adverse pregnancy outcomes [6, 12–14]. For the patients, changes during pregnancy include increased blood volume, physiological anemia, the abnormal cardiac output that can

increase by about 50%, and a hypercoagulable state in the body of patients. In the third trimester, the returned blood volume of patients significantly decreases, significantly increasing the possibility of heart failure or death [15–17]. For the fetuses, PAH can reduce the placental blood perfusion. Imaging examination often shows increased resistance of the uterine artery and umbilical artery, so the fetuses cannot obtain nutrition from the placenta and suffer from long-term chronic hypoxia with the mothers, which seriously affects their life health. In this study, the results showed that the hemodynamics indexes of uterine artery and fetal umbilical artery in group A were notably better compared with those in group B after treatment. Yiqi Buxue decoction has been found to have the function to resist platelet aggregation and reduce vascular resistance [18]. Therefore, it suggested that Yiqi Buxue decoction could effectively improve the hemodynamics of the patient.

Due to the high risk of pregnant patients with PAH, clinical practice has been promoting contraception knowledge of PAH women, while improving PAH treatment methods [19]. Since 1990, some progress has been made in the treatment of PAH in China, and the mortality rate of patients with mild PAH has currently decreased to less than 10%, but the prognosis of

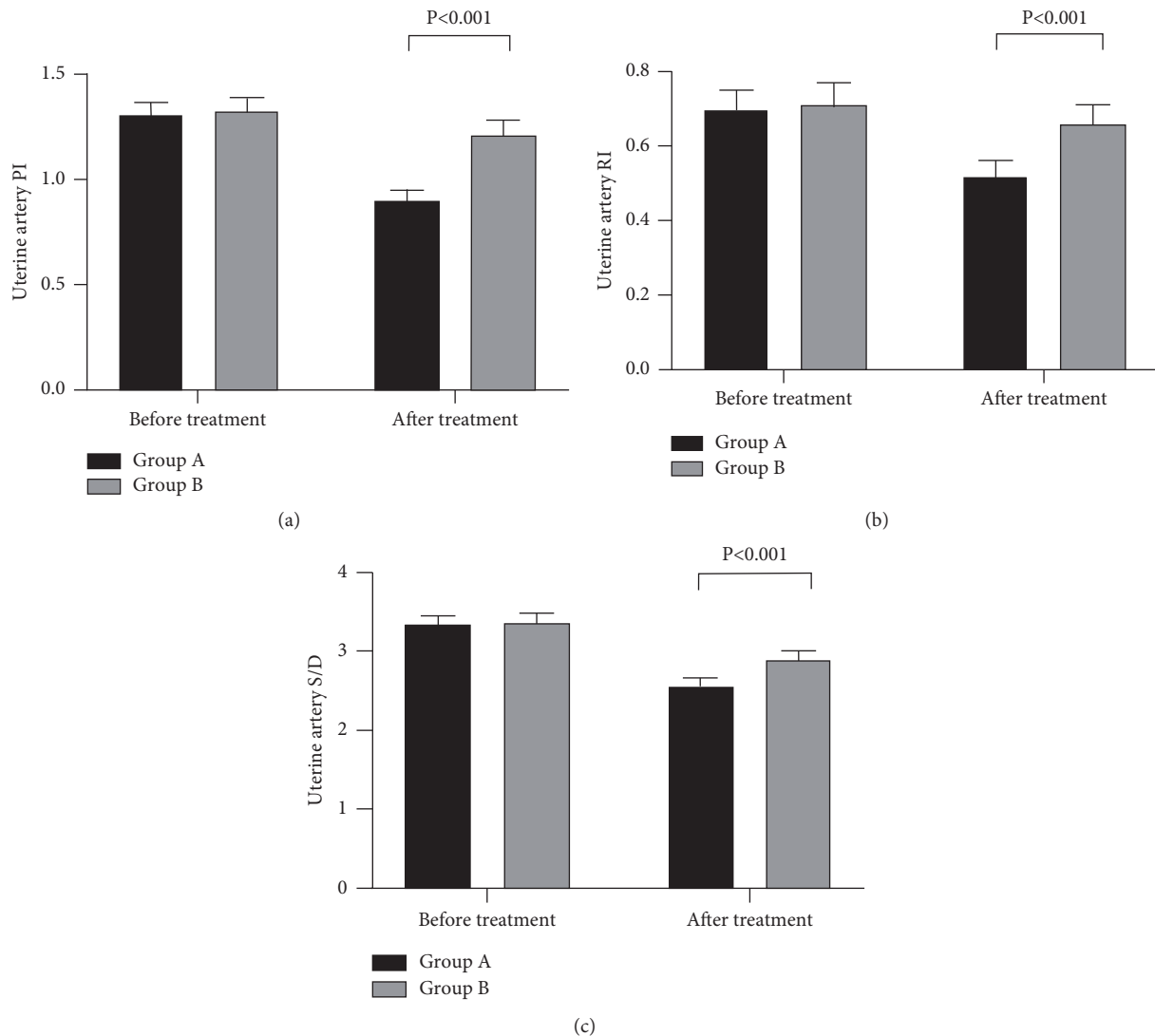


FIGURE 1: Comparison of hemodynamic changes in the uterine artery ( $\bar{x} \pm s$ ). The abscissa represents before and after treatment. The black area is group A, and the gray area is group B. (a) The uterine artery PI. With no statistical difference in the PI between the two groups before treatment ( $1.31 \pm 0.06$  and  $1.32 \pm 0.07$ ,  $P > 0.05$ ), the PI in group A after treatment was notably lower compared with that in group B ( $0.90 \pm 0.05$  and  $1.21 \pm 0.07$ ,  $P < 0.001$ ). (b) The uterine artery RI. With no statistical difference in the RI between the two groups before treatment ( $0.70 \pm 0.05$  and  $0.71 \pm 0.06$ ,  $P > 0.05$ ), the RI in group A after treatment was notably lower compared with that in group B ( $0.52 \pm 0.04$  and  $0.66 \pm 0.05$ ,  $P < 0.001$ ). (c) Uterine artery S/D. With no statistical difference in the S/D between the two groups before treatment ( $3.35 \pm 0.10$  and  $3.37 \pm 0.12$ ;  $P > 0.05$ ), the S/D in group A after treatment was notably lower compared with group B ( $2.56 \pm 0.11$  and  $2.89 \pm 0.12$ ,  $P < 0.001$ ).

patients with severe PAH remains unsatisfactory [20]. Although studies have shown that medication from early pregnancy can optimize the microcirculation of patients, drugs such as endothelin antagonists leave adverse effects on mothers and fetuses and cannot effectively improve maternal and fetal outcomes [21]. Sildenafil citrate selected in this study is a drug to treat PAH with high safety, which can reduce the hypoxemia of patients and optimize their cardiopulmonary function. Therefore, the results showed that the cardiopulmonary indexes and oxygen saturation of both groups were improved,

indicating that the maternal and fetal hypoxia was alleviated. Based on this, group A was additionally treated with Yiqi Buxue decoction that contained *Astragalus membranaceus*, *Angelica sinensis*, *Poria cocos*, motherwort, and *Ligusticum wallichii*. Among them, *Astragalus membranaceus* can resist platelet aggregation, reduce vascular resistance, enhance the pulmonary ventilation function, and boost the cardiopulmonary function of patients, thus improving their oxygen utilization and antihypoxia ability [22, 23]. *Angelica sinensis* can alleviate tissue damage caused by ischemia, reduce blood



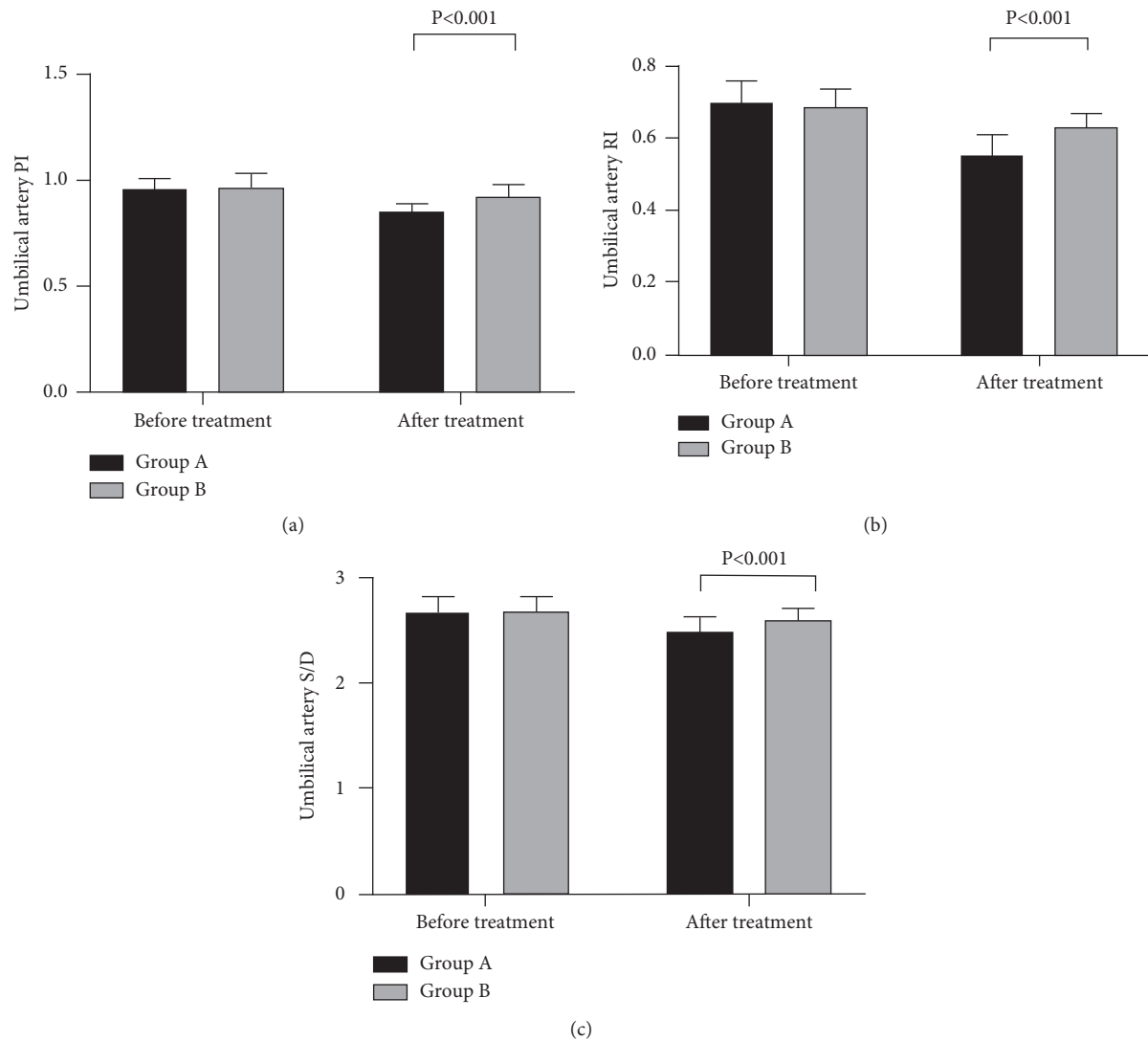


FIGURE 2: Comparison of hemodynamic changes in the fetal umbilical artery ( $\bar{x} \pm s$ ). The abscissa represents before and after treatment. The black area is group A, and the gray area is group B. (a) The umbilical artery PI. With no statistical difference in the PI between the two groups before treatment ( $0.96 \pm 0.05$  and  $0.97 \pm 0.06$ ,  $P > 0.05$ ), the PI in group A after treatment was notably lower compared with that in group B ( $0.85 \pm 0.04$  and  $0.92 \pm 0.06$ ,  $P < 0.001$ ). (b) The umbilical artery RI. With no statistical difference in the RI between the two groups before treatment ( $0.70 \pm 0.06$  and  $0.69 \pm 0.05$ ,  $P > 0.05$ ), the RI in group A after treatment was notably lower compared with that in group B ( $0.55 \pm 0.06$  and  $0.63 \pm 0.04$ ,  $P < 0.001$ ). (c) Umbilical artery S/D. With no statistical difference in the S/D between the two groups before treatment ( $2.67 \pm 0.15$  and  $2.68 \pm 0.14$ ,  $P > 0.05$ ), the S/D in group A after treatment was notably lower compared with that in group B ( $2.48 \pm 0.15$  and  $2.59 \pm 0.12$ ,  $P < 0.001$ ).

viscosity, and play a positive role in replenishing qi and enriching the blood. *Poria cocos* and motherwort promote blood circulation to remove blood stasis, with the effects of detumescence and diuresis. Therefore, group A after treatment had a lower D-dimer level and notably better microcirculation compared with group B. This demonstrated that the hemodynamic changes of the uterine artery and umbilical artery in group A were better, so the fetuses could obtain a stable source of nutrients, thus reducing the chance of low-birth-weight newborns. Zhu et al. have found that ligustrazine not only has a good effect of dilating arteries and reducing the pulmonary

arterial pressure of PAH patients but also has an antioxidant effect to scavenge oxygen free radicals and reduce the NT-proBNP level [24]. NT-proBNP, a common evaluation index of cardiac function in clinic, is positively correlated with pulmonary arterial pressure, so the decreased NT-proBNP indicated a lower degree of PAH in patients. Therefore, the lower NT-proBNP in group A represented more obvious improvement of PAH and a lower risk of patients during pregnancy. In addition, *Ligusticum wallichii* can alleviate pulmonary arteriospasm and further increase the placental blood supply and oxygen transportation by optimizing the blood circulation,



TABLE 2: Comparison of cardiopulmonary function indexes ( $\bar{x} \pm s$ ).

Indexes	Group A		Group B		<i>t</i>	<i>P</i>
Oxygen saturation (%)	Before treatment	85.45 ± 5.98	Before treatment	84.98 ± 5.45	0.450	0.654
	After treatment	97.68 ± 5.41	After treatment	90.22 ± 5.24	7.672	<0.001
	<i>t</i>	11.748	<i>t</i>	5.369		
	<i>P</i>	<0.001	<i>P</i>	<0.001		
Arterial oxygen partial pressure (mmHg)	Before treatment	49.21 ± 4.23	Before treatment	49.36 ± 4.25	0.194	0.847
	After treatment	62.65 ± 4.25	After treatment	53.65 ± 4.21	11.654	<0.001
	<i>t</i>	17.362	<i>t</i>	5.555		
	<i>P</i>	<0.001	<i>P</i>	<0.001		
D-dimer (mg/L)	Before treatment	2.05 ± 0.15	Before treatment	2.06 ± 0.17	0.342	0.733
	After treatment	1.78 ± 0.12	After treatment	1.89 ± 0.14	4.621	<0.001
	<i>t</i>	10.887	<i>t</i>	5.979		
	<i>P</i>	<0.001	<i>P</i>	<0.001		
NT-proBNP (pg/ml)	Before treatment	1100.65 ± 150.56	Before treatment	1115.65 ± 149.65	0.547	0.585
	After treatment	342.58 ± 40.68	After treatment	500.15 ± 50.23	18.883	<0.001
	<i>t</i>	37.651	<i>t</i>	30.203		
	<i>P</i>	<0.001	<i>P</i>	<0.001		

TABLE 3: Comparison of pregnancy outcomes [*n* (%)].

Outcomes	Group A ( <i>n</i> = 60)	Group B ( <i>n</i> = 60)	$\chi^2$	<i>P</i>
Fetal pregnancy outcomes				
Low birth weight	3 (5.0)	7 (11.7)	1.746	0.186
Neonatal asphyxia	5 (8.3)	10 (16.7)	1.905	0.168
Premature delivery	6 (10.0)	10 (16.7)	1.154	0.283
Death	2 (3.3)	5 (8.3)	1.365	0.243
Fetal distress	3 (5.0)	10 (16.7)	4.227	0.040
Premature rupture of membranes	5 (8.3)	6 (10.0)	0.100	0.752
Total	24 (40.0)	48 (80.0)	20.000	<0.001
Patient pregnancy outcomes				
Polyhydramnios	2 (3.3)	8 (13.3)	3.927	0.048
Postpartum hemorrhage	5 (8.3)	8 (13.3)	0.776	0.378
Death	0 (0.0)	2 (3.3)	2.034	0.154
Caesarean section	20 (33.3)	30 (50.0)	3.429	0.064
Total	27 (45.0)	48 (80.0)	15.680	<0.001

making the fetuses less likely to suffer from intrauterine distress or asphyxia and comprehensively reducing the adverse effect of PAH on the fetuses.

The results showed that Yiqi Buxue decoction could be taken in the early pregnancy to reduce the negative effect of physiological changes during pregnancy on PAH patients. However, the patients were not grouped in detail according to the gestational age in this study. Whether the patients can take Yiqi Buxue decoction alone, whether they can take it throughout the pregnancy, and its effect on different gestational weeks still need to be further explored.

In conclusion, Yiqi Buxue decoction can stabilize the hemodynamics of pregnant patients with PAH, improve their cardiopulmonary function, alleviate hypotension, and thus, reduce the possibility of adverse pregnancy outcomes, which should be popularized in practice.

## Data Availability

All data can be obtained from the corresponding authors.

## Consent

Consent was not applicable for this study.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Authors' Contributions

Rendong Han and Liya Gao contributed equally to this article.

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## Research Article

# Effect of Psychological Intervention Combined with Family Cooperation on the Perioperative Quality of Life and Psychological States of Elderly Patients with Prostate Cancer Treated with Compound Kushen Injection

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**Objective.** The purpose of the study was to investigate the nursing effect of psychological intervention combined with family cooperation on elderly patients with prostate cancer treated with compound kushen injection and put forward effective suggestions. **Methods.** 122 elderly patients with prostate cancer admitted to our hospital from June 2018 to June 2019 were selected and randomly divided into a control group ( $n = 61$ ) and experimental group ( $n = 61$ ). The patients in the control group received routine nursing intervention during the perioperative period, while the patients in the experimental group were treated with psychological intervention combined with family cooperation on the basis of routine nursing. The quality of life and psychological states of patients in the two groups were statistically analyzed. **Results.** The evaluation of psychological states at 24 hours before surgery and 24 hours before discharge in the experimental group was significantly better than that in the control group ( $P < 0.05$ ), with statistical significance. On comparing the basic conditions between the two groups in the perioperative period, the length of hospitalization, length of catheter retention after surgery, and incidence of complications in the experimental group were all significantly better than those in the control group ( $P < 0.05$ ), with statistical significance. The satisfaction of patients with the nursing process in both groups was recorded and statistically analyzed through questionnaires. The satisfaction with nursing process in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), with statistical significance. The quality of life of the patients was followed up at three months after discharge. The quality of life of the experimental group was significantly better than that of the control group ( $P < 0.05$ ), with statistical significance. **Conclusion.** Psychological intervention combined with family cooperation for the elderly patients with prostate cancer treated with compound kushen injection is beneficial to improve their psychological states, encourage them to face the disease in a more positive manner, effectively improve the quality of life after intervention, ensure the therapeutic effect during perioperative period, increase happiness index, and enhance their satisfaction with the nursing process, which is worthy of clinical application and popularization.

## 1. Introduction

According to relevant reports, with the aggravation of aging, people's life concept and quality of life have changed greatly, and the incidence of prostate cancer increases year by year [1–3]. Many studies have shown that compound kushen injection has a certain synergistic effect as an anticancer treatment, relieving pain, enhancing immunity, and stopping bleeding. It is an effective adjuvant drug for clinical

treatment of prostate cancer and can significantly improve the clinical benefit of patients. To further ensure good prognosis in elderly patients with prostate cancer, scientific nursing measures must be combined. In elderly patients, the social adjustment capacity is decreased, and they are shy of the arrival symptoms of this disease, which results in huge psychological burdens. Therefore, most elderly patients with prostate cancer face stressful psychological reactions in the perioperative period, including depression and anxiety,

which further adversely affect the therapeutic efficacy and physical recovery [4–6]. Based on this, in this study, psychological intervention combined with family cooperation was introduced to elderly patients with prostate cancer treated with compound kushen injection, and the patients' life quality and psychological states were evaluated, so as to further analyze the intervention's effect and provide data support for clinical research. The results of the study are summarized as follows.

## 2. Materials and Methods

**2.1. General Information.** One hundred and twenty-two elderly patients with prostate cancer admitted to our hospital from June 2018 to June 2019 were selected and randomly divided into control group ( $n = 61$ ) and experimental group ( $n = 61$ ), aging from 55 to 81 years, with the average age of 69.37 years. There were no statistical differences in the comparison of general data such as age in both groups ( $P > 0.05$ ), which was comparable, and the comparison of general data between the two groups is detailed in Table 1.

**2.2. Inclusion Criteria.** The inclusion criteria are as follows. (1) Patients met the clinical diagnostic criteria for prostate cancer according to the *Diagnostic Criteria for Prostate Cancer*. (2) All patients received compound kushen injection as an adjuvant therapy. (3) Patients had complete clinical records. (4) This study was approved by the Hospital Ethics Committee, and the patients and their families were informed of the purpose and process of this study and signed the informed consent.

**2.3. Exclusion Criteria.** The exclusion criteria are as follows. (1) Patients had other malignant and severe diseases. (2) Patients had other acute or long-term urinary system diseases. (3) Patients had cognitive impairment, such as mental disorders, or refused to cooperate with the study. (4) Patients had incomplete clinical data.

**2.4. Methods.** Patients in the control group were treated with the routine clinical nursing. According to the diagnosis results, preoperative examination and preparation were performed. The medical staff actively participated in the process of formulating the patients' surgical plans, reasonably evaluated patients' conditions, and made a scientific nursing intervention program. Besides, during the surgery, the medical staff cooperated with surgeon to complete the surgical process and paid close attention to the changes of patients' vital signs. After the surgery, routine index examination for patients was performed, and patients' dietary management and reasonable mix of nutrition were also taken into consideration [7–9].

Patients in the experimental group received psychological intervention combined with family cooperation. After patients' admission to hospital, psychological intervention was conducted on the basis of routine nursing by keeping an eye out for patient's psychological changes.

According to the patients' conditions, the medical staff informed patients and their family members of the cause of the disease, specific conditions, and treatment plan of prostate cancer in a gentle way. Additionally, the medical staff also explained the relevant knowledge of prostate cancer in detail, thoroughly understood the concerns of patients and their family members, and paid attention to emotional comfort. By describing similar successful cases, the medical staff increased the confidence of patients and their families and eliminated the fear before the surgery. After the surgery, patients and their families were informed of the results of the surgery in time and were encouraged to cooperate closely with the treatment. The patients' family members were told to conduct good supervision and support work to further increase the patients' confidence [10–12]. The nursing staff and family members cooperated with each other to perform the routine nursing and introduce psychological intervention during the perioperative period and observed the psychological changes of the patients acutely, so as to increase the patients' sense of security [13].

### 2.5. Observation Indexes

**2.5.1. Scores of Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) in Both Groups.** Self-rating anxiety scale (SAS) and self-rating depression scale (SDS) were adopted to evaluate the psychological states of patients at 24 hours after admission, 24 hours before the surgery, and 24 hours before discharge, with the total score of 100 points, and higher scores indicated patients' severer psychological conditions.

**2.5.2. Basic Conditions in Both Groups during the Perioperative Period.** The basic conditions of the patients in the two groups during the perioperative period were recorded in detail, including the length of the operation, bladder irrigation time, length of catheter retention after surgery, length of hospitalization, and incidence of complications.

**2.5.3. Nursing Satisfaction in Both Groups.** The nursing satisfaction of patients in the two groups was investigated with a self-made questionnaire from the hospital, which mainly included the nurses' attitudes, quality of work, professional degree, and so on, with the total score of 100 points. A score above 90 points indicated "very satisfied," a score of 70–90 points indicated "basically satisfied," and a score below 70 points indicated "unsatisfied." Total nursing satisfaction = basically satisfied + very satisfied.

**2.5.4. Statistical Analysis of the Postoperative Quality of Life in Both Groups.** The quality of life of the patients after surgery was evaluated by three evaluation indexes, international prostate symptom score, rehabilitation knowledge evaluation, and comprehensive evaluation of quality of life, so as to further record and analyze the patients' physical recovery, family emotion environment, body function, social skill and psychological states.

TABLE 1: General information of elderly patients with prostate cancer in both groups (n = 61).

	Experimental group	Control group	T or $X^2$	P
Age (years)	62.4 ± 5.63	63.6 ± 5.62	1.1781	0.2411
Education				
Below elementary education	20 (32.79%)	18 (29.51%)	0.1529	0.696
Elementary education and above	41 (67.21%)	43 (70.49%)		
Past medical history				
Hypertension	16 (26.23%)	14 (22.95%)	0.0331	0.856
Diabetes	12 (19.67%)	13 (21.31%)		
None	33 (54.09%)	34 (55.74%)		
Smoking				
Yes	50 (81.97%)	51 (83.61%)	0.0575	0.810
No	11 (18.03%)	10 (16.39%)		
Drinking				
Yes	49 (80.33%)	48 (78.69%)	0.0503	0.823
No	12 (19.67%)	13 (21.31%)		
Residence				
Urban area	42 (68.85%)	40 (65.57%)	0.1488	0.700
Rural area	19 (31.15%)	21 (34.43%)		

**2.6. Statistical Treatment.** The data obtained in this study were statistically analyzed and processed by SPSS20.0 software. Measurement data were expressed by ( $\bar{x} \pm s$ ) and tested by *t*-test. Enumeration data were expressed as [*n* (%)] and tested by  $X^2$  test. The differences had a statistical significance when  $P < 0.05$ .

### 3. Results

**3.1. Comparison of the SAS and SDS Scores between the Two Groups.** The SAS and SDS scores of patients at 24 hours after admission, 24 hours before the surgery, and 24 hours before discharge were compared and analyzed, and the results were as follows.

There were no significant differences in SAS and SDS scores of patients between the two groups at 24 hours after admission, as shown in Figure 1.

The SAS and SDS scores of the experimental group at 24 hours before the surgery were significantly better than those of the control group, as shown in Figure 2.

The SAS and SDS scores of the experimental group at 24 hours before discharge were significantly better than those of the control group, as shown in Figure 3.

**3.2. Comparison of the Basic Conditions between the Two Groups in the Perioperative Period.** According to the comparison between the basic conditions of the two groups in perioperative period, it is concluded that the length of hospitalization, length of catheter retention, and incidence of complications in the experimental group were significantly better than those in the control group ( $P < 0.05$ ), with statistically significant differences, as shown in Table 2.

**3.3. Comparison of the Nursing Satisfaction between the Two Groups.** The nursing satisfaction of the elderly patients with prostate cancer in the two groups was statistically

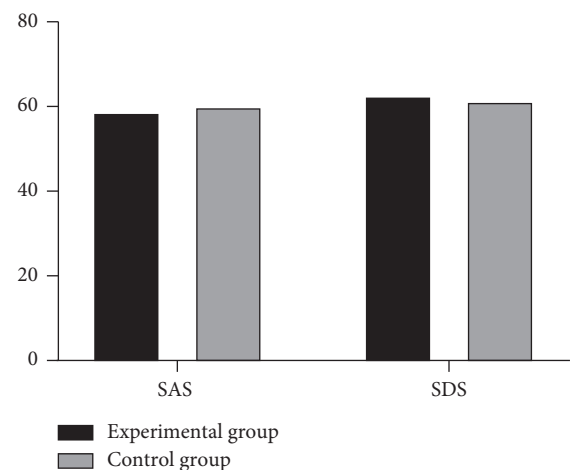


FIGURE 1: Comparison of SAS and SDS scores between the two groups at 24 hours after admission ( $n = 61$ ). The abscissa represents SAS and SDS, while the ordinate represents score. The SAS and SDS scores in the experimental group at 24 hours after admission were  $58.72 \pm 6.08$  and  $62.56 \pm 7.91$ , respectively. The SAS and SDS scores in the control group at 24 hours after admission were  $60.02 \pm 6.32$  and  $61.31 \pm 8.02$ , respectively. There were no significant differences in SAS and SDS scores between the two groups at 24 hours after admission ( $t = 1.7578$ ,  $P = 0.2493$ ).

analyzed in the form of questionnaires. According to the results, the total satisfaction of nursing in the experimental group was significantly higher than that in the control group ( $P < 0.05$ ), with statistically significant differences, as shown in Table 3.

**3.4. Comparison of the Quality of Life between the Two Groups after Surgery.** The quality of life of the two groups was investigated and evaluated at three months after surgery, as shown in Figure 4.



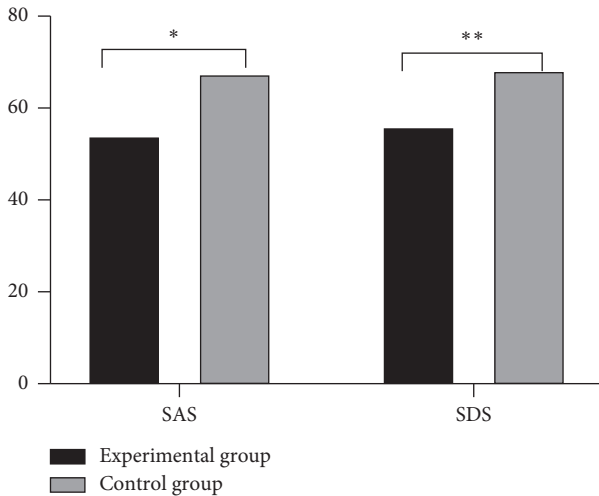


FIGURE 2: Comparison of SAS and SDS scores between the two groups at 24 hours before surgery ( $n = 61$ ). The abscissa represents SAS and SDS, while the ordinate represents score. The SAS and SDS scores of the experimental group at 24 hours before surgery were  $54.11 \pm 5.92$  and  $56.12 \pm 6.46$ , respectively. The SAS and SDS scores of the control group at 24 hours before surgery were  $67.63 \pm 8.67$  and  $68.37 \pm 7.13$ , respectively. \* indicates that the SAS score of the experimental group was significantly better than that of the control group ( $t = 10.0582$ ,  $P \leq 0.001$ ). \*\* indicates that the SDS score of the experimental group was significantly better than that of the control group ( $t = 9.9442$ ,  $P \leq 0.001$ ).

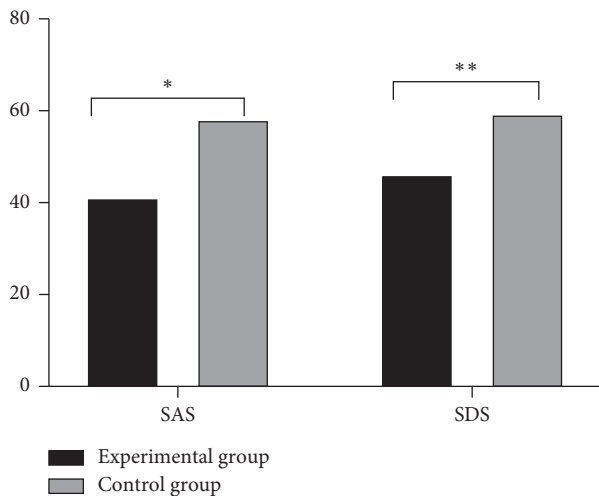


FIGURE 3: Comparison of SAS and SDS scores between the two groups at 24 hours before discharge ( $n = 61$ ). The abscissa represents SAS and SDS, while the ordinate represents score. The SAS and SDS scores of the experimental group at 24 hours before discharge were  $41.26 \pm 5.72$  and  $46.31 \pm 6.01$ , respectively. The SAS and SDS scores of the control group at 24 hours before discharge were  $58.33 \pm 6.08$  and  $59.48 \pm 7.11$ , respectively. \* indicates that the SAS score of the experimental group was significantly better than that of the control group ( $t = 15.9709$ ,  $P \leq 0.001$ ). \*\* indicates that the SDS score in the experimental group was significantly better than that in the control group ( $t = 11.0487$ ,  $P \leq 0.001$ ).

#### 4. Discussion

Prostate cancer is actually a relatively slow-growing tumor, and thus, patients may not be aware of the early-stage tumor growth. However, for patients with advanced cancer, the deterioration of the disease not only seriously impairs patients' physical function but also adversely affects patients' psychological states and quality of life [14–16]. With the development and progress of modern medical technology, the cure rate of the disease is increasing, and most patients with prostate cancer will receive compound kushen injection for comprehensive endocrine treatment in order to control the number of tumor cells, improve clinical symptoms, enhance the quality of life, and prolong survival time. However, the psychological changes of patients are often ignored in practice, and adverse psychological emotions or inadequate family support will also have a negative impact on the treatment effect of patients, leading to unsatisfactory results of compound kushen injection [17–20]. With the advancement of medicine, more attention has been paid to the psychological recovery of patients, especially in elderly patients with prostate cancer. Because the treatment method mainly targets the patients' special parts through the urinary system surgery, patients are prone to greater psychological burdens. Therefore, a scientific psychological intervention mode is more conducive to the postoperative rehabilitation of patients [21–24].

In this study, it was found that the evaluation of the psychological states of the experimental group was significantly better than that of the control group at 24 hours before surgery and 24 hours before discharge. On comparing the basic situations between the two groups during the perioperative period, the length of hospitalization, length of catheter retention after surgery, and incidence of complications in the experimental group were significantly better than those in the control group. According to the satisfaction in the two groups evaluated by the questionnaires, the satisfaction of the patients with the nursing process showed that the total satisfaction of nursing in the experimental group was significantly higher than that in the control group, and the quality of life score in the experimental group at three months after discharge was also significantly better than that in the control group. From the study results, it can be easily concluded that, due to the specificity of the surgery, the scores of preoperative psychological states in the two groups are high. When facing the upcoming surgery, the patients are easily restless, anxious, and stressed. However, the evaluation of patients' psychological states in the experimental group with the preoperative psychological intervention was significantly better than that in the control group, indicating that the psychological intervention combined with family cooperation can better help patients with good psychological construction, reduce the psychological stress of patients, and promote the postoperative rehabilitation of elderly patients with prostate cancer. The results of this study were similar to those of Beardo et al. [25], whose study showed that elderly patients with cancer were more



TABLE 2: Comparison of the basic conditions between the two groups in the perioperative period ( $n = 61$ ,  $\bar{x} \pm s$ ).

Group	Length of operation (min)	Bladder irrigation time (h)	Length of hospitalization (d)	Length of catheter retention after surgery (d)	Incidence of complications
Experimental group	$60.33 \pm 12.47$	$23.56 \pm 7.04$	$3.77 \pm 0.86$	$2.74 \pm 0.78$	18.03% (11/61)
Control group	$59.62 \pm 12.74$	$22.71 \pm 7.51$	$5.71 \pm 1.06$	$3.90 \pm 1.21$	34.43% (21/61)
$t/X^2$	0.3111	0.6449	11.1004	6.2933	4.2361
$P$	0.7563	0.5202	$P \leq 0.001$	$P \leq 0.001$	0.040

TABLE 3: Comparison of the nursing satisfaction between the two groups ( $n = 61$ ).

Group	Unsatisfied	Basically satisfied	Very satisfied	Total satisfaction
Experimental group	4.92% (3/61)	29.51% (18/61)	65.57% (40/61)	95.08% (58/61)
Control group	22.95% (14/61)	37.7% (23/61)	39.34% (24/61)	77.05% (47/61)
$X^2$				8.2700
$P$				0.004

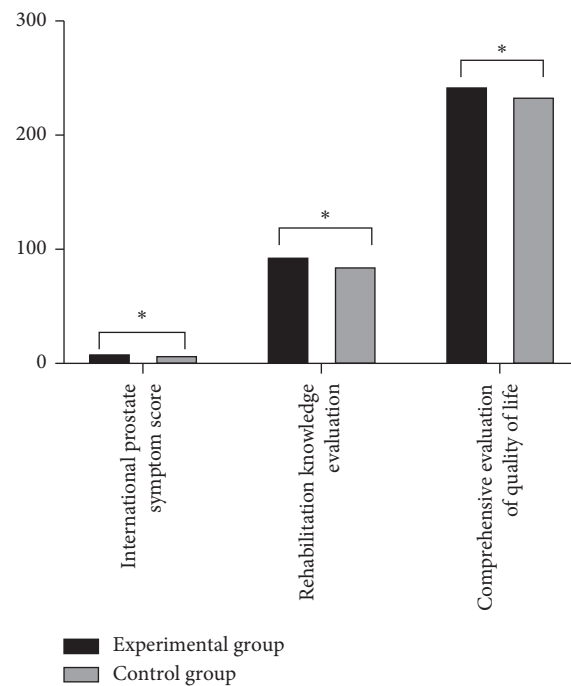


FIGURE 4: Comparison of the postoperative quality of life scores between the two groups ( $n = 61$ ,  $\bar{x} \pm s$ ). The abscissa represents international prostate symptom score, rehabilitation knowledge evaluation, and comprehensive evaluation of quality of life, while the ordinate represents score. The international prostate symptom score, rehabilitation knowledge evaluation, and comprehensive evaluation of quality of life in the experimental group were  $9.67 \pm 3.71$ ,  $94.47 \pm 3.12$ , and  $243.51 \pm 9.76$ , respectively. The international prostate symptom score, rehabilitation knowledge evaluation, and comprehensive evaluation of quality of life in the control group were  $8.21 \pm 3.02$ ,  $85.98 \pm 3.01$ , and  $234.72 \pm 10.49$ , respectively. \* indicates that there were significant differences in the international prostate symptom score, rehabilitation knowledge evaluation, and comprehensive evaluation of quality of life between the two groups ( $t = 2.3837, 15.2953, 4.7914, P < 0.05$ ).

prone to emotional fluctuations, and patients had a better therapeutic effect under the supervision of nursing staff during hospital treatment. It also pointed out that many elderly patients after discharge were subject to decreased medication compliance due to the various effects of mood and life, thus leading to the occurrence of adverse symptoms, slow recovery of physical health, or treatment failure in severe cases. However, perioperative psychological

intervention can effectively improve the patients' psychological states and enhance their treatment confidence.

In conclusion, psychological intervention combined with family support and adequate nursing care in the perioperative period for elderly patients with prostate cancer is more conducive to enhancing the patients' confidence in overcoming the disease. Both family support and care from the nursing staff can bring more psychological support to the

elderly patients, which is easier for the patients to accept their conditions and improve their life quality, especially in the recovery process after surgery.

## Data Availability

All primary data are available from the corresponding author upon a reasonable request.

## Conflicts of Interest

The authors declare that there are no conflicts of interest.

## Authors' Contributions

Jingyun Zhang and Caijian Li contributed equally to this article.

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## Research Article

# Effect of Perineum Block Anesthesia Combined with Unprotected Perineal Delivery on the Perineal Integrity Rate and Maternal-Infant Outcomes in Primiparas Taking Health Products Containing Traditional Chinese Medicine

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**Objective.** The purpose of the study was to investigate the effect of perineum block anaesthesia combined with unprotected perineal delivery on the perineal integrity rate and maternal-infant outcomes in primiparas taking health products containing traditional Chinese medicine (TCM). **Methods.** A total of 120 puerperae admitted to our hospital from July 2019 to July 2020 were selected as study subjects and divided into group A ( $n = 60$ ) and group B ( $n = 60$ ), according to the number table method. Both groups took health products containing TCM, and the puerperae in group A received perineum block anaesthesia combined with unprotected perineal delivery, while those in group B were treated with routine delivery combined with routine protected perineal delivery. After that, the effect of different delivery modes on the perineal integrity rate and maternal-infant outcomes in puerperae was analyzed by the comparison of delivery condition, perineal condition, and postpartum quality of life between the two groups. **Results.** There were no significant differences in average age and other general data between the two groups ( $P > 0.05$ ); the duration in first, second, and third stages of labor in group A was significantly lower than that in group B ( $P < 0.001$ ); the Apgar score in group A was significantly higher than that in group B ( $P < 0.001$ ); the number of puerperae with integrated perineum in group A was significantly higher than that in group B ( $P < 0.05$ ), while the number of puerperae receiving episiotomy in group A was significantly lower than that in group B ( $P < 0.05$ ); the quality of life score in group A was significantly higher than that in group B ( $P < 0.001$ ); the incidence of maternal postpartum complications in group A was significantly lower than that in group B ( $P < 0.05$ ). **Conclusion.** Perineum block anaesthesia combined with unprotected perineal delivery can effectively shorten maternal labor duration, improve perineal integrity rate, and reduce laceration of perineum, with a significant therapeutic effect, which is worthy of application and promotion.

## 1. Introduction

Natural delivery is a physiological process during which both mother and newborn actively participate in and complete the delivery, making it the optimal delivery mode [1], and in the process of natural delivery, maternal regular uterine contraction and birth canal extrusion can promote rhythmic contractions in fetal thoracic cavity, so that the pulmonary function of newborns can be exercised to induce their spontaneous breathing. In addition, fetal algesia, gustation,

and sense of touch can be stimulated in the birth canal, thus promoting the development of the brain and vestibular function area and benefiting later movement and the formation of personality; therefore, the natural delivery proves to be the most effective delivery mode to improve birth quality [2, 3]. Health products with traditional Chinese medicine (TCM) ingredients such as Yunkang Granules can effectively adjust the body of women during pregnancy, have a unique effect on the treatment of recurrent abortion, and promote fetal health. Cesarean section can adversely affect

maternal recovery and later neonatal development and subsequent pregnancy, even though it shows an improvement in maternal delivery safety to some extent. Clinical studies have confirmed that supine delivery affects maternal uterine blood supply and prolongs the duration in the second stage of labor, increasing the risks of episiotomy and dystocia. Episiotomy, a type of midwifery operation for smooth delivery, refers to the procedure of making an oblique incision in maternal perineum, so as to avoid perineal laceration and protect pelvic floor muscles [4–6]. Perineum block anaesthesia, serving the functions of relieving labor pain and reducing the risks of perineal laceration, has been widely used in obstetrics and has brought a boon to the majority of puerperae. Generally, traditional midwifery is performed by implementing artificial perineal dissection for puerperae, which can avoid perineal laceration occurring in puerperae during delivery but leaving pathological incisions affecting postpartum recovery; however, unprotected perineal delivery is aimed at reducing the rate of cesarean section, relieving maternal labor distress, and returning delivery to nature [6, 7]. Based on this, this study aimed to investigate the effect of perineum block anaesthesia combined with unprotected perineal delivery on the perineal integrity rate and maternal-infant outcomes in primiparas taking health products containing TCM, reported as follows.

## 2. Materials and Methods

**2.1. General Information.** A total of 120 puerperae admitted to our hospital from July 2019 to July 2020 were selected as study subjects and divided into group A ( $n = 60$ ) and group B ( $n = 60$ ), according to the number table method. This study was approved by the Hospital Ethics Committee, and the puerperae and their family members were informed of the purpose and process of this study and signed the informed consent.

**2.2. Inclusion Criteria.** Puerperae were all primiparas with singleton pregnancy. Puerperae had delivery certificate. Puerperae had no contraindications to perineum block anaesthesia.

**2.3. Exclusion Criteria.** Puerperae had abnormal fetal position, macrosomia, or placental abruption. Puerperae had organic lesions in the brain, heart, and liver. Puerperae had perineal inflammation, scars, and others seriously affecting perineal delivery. Puerperae had the history of pelvic surgery.

**2.4. Methods.** The puerperae in both groups before delivery orally took Yunkang Granules (NMPA approval no: Z19991100; manufacturer: Jilin Aodong Pharmaceutical Group Co., Ltd., Dalian Branch; specification: 8 g\*9 bags) on an empty stomach in the morning, at noon, and in the evening, 1 bag/time, 3 times/day, for 15 days continuously.

The puerperae in group B were treated with routine delivery combined with routine protected perineal delivery.

During surgery, after maternal uterine orifice was fully opened, the puerperae with supine positions on an obstetric table were instructed to rely on the rhythmic contractions of uterine to push the fetus out of the body, and meanwhile, 4 conventional surgical cotton pads were used to protect the maternal perineum [8, 9].

The puerperae in group A received perineum block anaesthesia combined with unprotected perineal delivery, and specific steps were as follows. After maternal uterine orifice was fully opened, the perineum block anaesthesia was performed in the way that 10 ml of 2% lidocaine hydrochloride injection (State Food and Drug Administration approval number: H61023138; manufacturer: Shaanxi Jianmin Pharmaceutical Co., Ltd.; specification: 5 ml: 50 mg) was taken by a syringe and then diluted with 10 ml of normal saline solution to 20 ml. After that, doctor's middle finger and forefinger entered into maternal vagina and could not stop until touching ischial spine, and then, puncture was conducted into the site about 0.5 cm from the inner side of the ischial spine with number 9 puncture needle along the surgical direction. After confirming that there was no blood when the needle was drawn back, the puerperae were injected with 5 ml of lidocaine, and then, the needle was withdrawn as the injection was slowly carried out. The remaining 5 ml of lidocaine was used for perineal local infiltration anaesthesia. During the process of unprotected perineal delivery, puerperae first took nonsupine positions and then took semireclining positions after the total opening of uterine orifice. When 2–3 cm of the fetal head was visible on vulval gapping, delivery was ready, and at the same time, with paying much attention to slowing the rate of fetal head delivered, medical staff should instruct the puerperae to practise abdominal pressure correctly and guide them to cooperate with breathing, so as to ensure smooth delivery.

**2.5. Observation Indexes.** The labor duration and maternal postpartum complications were recorded and compared between the two groups.

The neonatal conditions in both groups were evaluated by the Apgar [10] scale, with the total score of 10 points. The score of 8–10 points represented normal condition, the score of 4–7 points represented mild asphyxia, and the score of 0–3 points represented severe asphyxia.

**2.5.1. Evaluation Criteria.** First-degree laceration of perineum referred to that there was slight laceration occurring between perineal epidermis and vaginal mucosa, and there was no injury in the muscle layer. Second-degree laceration of perineum laceration referred to that laceration occurred in the perineal skin, mucosa of posterior vaginal wall, and muscle layer of vaginal mucosa. Third-degree laceration of perineum laceration referred to that there was severe laceration, involving the rupture of sphincter ani externa muscle, vaginal, anal, and rectal penetration, and rectal exposure.

The postpartum quality of life in both groups was evaluated by the Maternal Postpartum Quality of Life Rating Scale made by our department, which included the items of



mental state, sleep quality, appetite, and daily activity, with each item scoring 5 points, and higher scores indicated better postpartum quality of life.

**2.6. Statistical Treatment.** All the study data were processed for statistical analysis by SPSS21.0 software, and GraphPad Prism 7 (GraphPad Software, San Diego, USA) was used to draw the pictures of the data. Measurement data were expressed by  $(\bar{x} \pm s)$  and tested by the  $t$ -test. Enumeration data were expressed as  $(n (\%))$  and tested by the  $\chi^2$  test. The differences had statistical significance when  $P < 0.05$ .

### 3. Results

**3.1. Comparison of Clinical Information between the Two Groups.** There were no significant differences in average age, mean premature rupture of membranes time, mean gestational week, mean height, education level, and place of residence between the two groups ( $P > 0.05$ ), as given in Table 1.

**3.2. Comparison of Maternal Delivery between the Two Groups.** The duration in first, second, and third stages of labor in group A was significantly lower than that in group B ( $P < 0.001$ ), as given in Table 2.

**3.3. Comparison of Apgar Score between the Two Groups.** The Apgar score in group A was significantly higher than that in group B ( $P < 0.05$ ), as shown in Figure 1.

The abscissa represented group A and B, while the ordinate represented Apgar score points. The Apgar scores were  $(8.23 \pm 0.46)$  points in group A and  $(7.13 \pm 0.43)$  points in group B. \* indicated that there were significant differences in Apgar scores between the two groups ( $t = 13.532$ ,  $P < 0.001$ ).

**3.4. Comparison of Maternal Perineum Condition between the Two Groups.** The number of puerperae with integrated perineum in group A was significantly higher than that in group B ( $P < 0.05$ ), while the number of puerperae receiving episiotomy in group A was significantly lower than that in group B ( $P < 0.05$ ); there were no significant differences in the number of puerperae with first-, second-, and third-degree laceration of perineum between the two groups ( $P > 0.05$ ), as given in Table 3.

**3.5. Comparison of Postpartum Quality of Life Score between the Two Groups.** The scores of postpartum mental state, sleep quality, appetite, and daily activity in group A were significantly higher than those in group B ( $P < 0.05$ ), as given in Table 4.

**3.6. Comparison of Maternal Postpartum Complications between the Two Groups.** The incidence of maternal postpartum complications in group A was significantly lower than that in group B ( $P < 0.05$ ), as given in Table 5.

### 4. Discussion

Studies have found that natural delivery can generate a stress response, which is mainly stimulated by fetal birth canal pressure, hence leading to a series of endocrine alterations and promoting the production of neonatal immune factors to enhance immune function, providing more resistance for neonates than cesarean section. In addition, natural delivery can also promote postpartum milk secretion and improve the relationship between puerperae and fetuses [11, 12]. The study found that taking health products containing TCM before delivery could invigorate the spleen and kidney, nourish blood, and prevent abortion, which had a significant effect on pregnant women with habitual abortion. Cesarean section is suitable for puerperae with difficulties in delivery; although it can shorten labor duration, it brings more trauma to the maternal tissues, resulting in slow postpartum recovery. With continuous popularization of health knowledge, there have been more and more puerperae who prefer natural delivery; however, the own limitations of this delivery mode increase the difficulties in the obstetric work, and thus, how to improve the natural delivery rate and shorten the postpartum recovery duration has become the research focus in the medical community [13–15]. Unprotected perineal delivery, belonging to natural delivery, is a newly emergent delivery mode in recent years, which has broken the limitations of cesarean section. Additionally, this delivery mode can minimize maternal labor pain, reduce the risks of intraoperative bleeding and infection, promote rapid recovery of pelvic floor function, reduce sequelae caused by pelvic floor dysfunction, minimize perineal laceration, and improve perineal integrity rate, effectively facilitating delivery [14, 16, 17].

Pain in the second stage of labor is mainly caused by uterine contractions and forced distension of the pelvic floor during natural delivery, whereas perineum block anaesthesia can greatly reduce the pain caused by distension of the birth canal and pelvic floor during labor, so as to relax the perineum and vagina and effectively shorten the labor duration in the second stage [18]. In this study, after the primiparas with natural childbirth were treated with perineum block anaesthesia combined with unprotected perineal delivery, their perineal integrity rate was significantly higher than that of the puerperae undergoing the routine delivery and routine protected perineal delivery ( $P < 0.05$ ). The duration in first, second, and third stages of labor in group A was significantly lower than that in group B ( $P < 0.001$ ). Laudi and Peebles [19] have stated in their studies that after the primiparas with natural childbirth are treated with perineum block anaesthesia combined with unprotected perineal delivery, their perineal integrity rate is 23.45%, which is significantly higher than that of 6.12% in the routine group, indicating that perineum block anaesthesia combined with unprotected perineal delivery can improve maternal perineal integrity rate because unprotected perineal delivery can reduce the compression of maternal perineum and relax perineal musculature under the guidance of medical staff, so as to relieve delivery injuries. Clinical practice has confirmed [20] that maternal positions during delivery may affect fetal

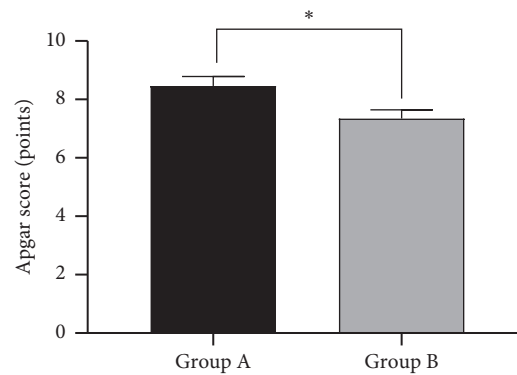


TABLE 1: Comparison of clinical information between the two groups.

Types	Group A ( $n=60$ )	Group B ( $n=60$ )	$\chi^2/t$	$P$
Average age (years old)	$27.64 \pm 2.31$	$27.68 \pm 2.29$	0.095	0.924
Mean premature rupture of membranes time ( $h$ )	$6.03 \pm 0.58$	$6.05 \pm 0.61$	0.184	0.854
Mean gestational week (weeks)	$39.06 \pm 0.53$	$39.08 \pm 0.56$	0.201	0.841
Mean height (cm)	$163.42 \pm 3.42$	$163.46 \pm 3.48$	0.064	0.950
Education level				
Undergraduate education	18 (30.00%)	20 (33.33%)	0.154	0.695
Secondary education	37 (61.67%)	36 (60.00%)	0.035	0.852
Primary education	5 (8.33%)	4 (6.67%)	0.120	0.729
Place of residence			0.033	0.855
Urban area	29 (48.33%)	30 (50.00%)		
Rural area	31 (51.67%)	30 (50.00%)		

TABLE 2: Comparison of maternal delivery between the two groups ( $\bar{x} \pm s$ , min).

Group	$n$	First stage of labor	Second stage of labor	Third stage of labor
Group A	60	$443.63 \pm 24.52$	$54.79 \pm 9.83$	$7.23 \pm 1.06$
Group B	60	$475.36 \pm 25.67$	$67.35 \pm 8.76$	$8.97 \pm 1.08$
$t$		6.924	7.389	8.907
$P$		<0.001	<0.001	<0.001

FIGURE 1: Comparison of Apgar score between the two groups ( $\bar{x} \pm s$ ).TABLE 3: Comparison of maternal perineum condition between the two groups ( $n$  (%)).

Group	$n$	Integrated perineum	Perineal side cut	First-degree laceration of perineum	Second-degree laceration of perineum	Third-degree laceration of perineum
Group A	60	12 (20.00%)	10 (16.67%)	35 (58.33%)	3 (5.00%)	0 (0.00%)
Group B	60	3 (5.00%)	20 (33.33%)	33 (55.00%)	4 (6.67%)	0 (0.00%)
$X^2$		6.171	4.444	0.136	0.152	0.000
$P$		0.013	0.035	0.713	0.697	1.000

TABLE 4: Comparison of postpartum quality of life score between the two groups ( $\bar{x} \pm s$ , points).

Group	$n$	Mental state	Sleep quality	Appetite	Daily activity
Group A	60	$3.84 \pm 1.05$	$3.75 \pm 0.86$	$3.64 \pm 0.53$	$3.73 \pm 0.63$
Group B	60	$2.93 \pm 0.97$	$3.21 \pm 0.74$	$2.83 \pm 0.49$	$3.14 \pm 0.58$
$t$		4.931	3.687	8.692	5.337
$P$		<0.001	<0.001	<0.001	<0.001

arterial blood pressure and neonatal growth as well as development to some extent. In the routine delivery mode, a supine position is often adopted, which can increase

maternal lumbar curvature and make uterus compress iliac arteries and inferior vena cava, thus affecting the abdominal aorta, leading to decreased uterine blood flow and increasing

TABLE 5: Comparison of maternal postpartum complications between the two groups ( $n$  (%)).

Group	$n$	Nausea and vomiting	Perineum edema	Puerperal infection	Postpartum hemorrhage	Total incidence
Group A	60	1 (1.67%)	0 (0.00%)	1 (1.67%)	0 (0.00%)	3.33% (2/60)
Group B	60	2 (3.33%)	3 (5.00%)	2 (3.33%)	1 (1.67%)	13.33% (8/60)
$X^2$						3.927
$P$						0.048

the risks of fetal distress. However, in unprotected perineal delivery, puerperae usually take semireclining positions, which can beneficially promote engagement of fetal head, decrease the resistance of pelvic floor soft tissues to descending fetal head, and increase the compliance of the fetus in the birth canal [21]. This study revealed that the Apgar score in group A was significantly higher than that in group B ( $P < 0.001$ ), demonstrating that perineum block anaesthesia combined with unprotected perineal delivery can reduce the incidence of neonatal asphyxia and improve delivery safety.

In conclusion, perineum block anaesthesia combined with unprotected perineal delivery can effectively shorten labor duration, improve perineal integrity rate and maternal quality of life in the postpartum period, and reduce the risks of delivery, which is worthy of application and promotion.

## Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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