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Retraction

Retracted: The Use of BT-ESD Technology under General Intravenous Anesthesia in the Treatment of Nonmuscle Invasive Bladder Cancer and the Effect of PI3K/Akt Signaling Pathway on Tumor Recurrence

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This article has been retracted by Hindawi, as publisher, following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of systematic manipulation of the publication and peer-review process. We cannot, therefore, vouch for the reliability or integrity of this article.

Please note that this notice is intended solely to alert readers that the peer-review process of this article has been compromised.

Wiley and Hindawi regret 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 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] H. Yan, S. Xia, D. Yao, J. Shi, and Z. Liu, "The Use of BT-ESD Technology under General Intravenous Anesthesia in the Treatment of Nonmuscle Invasive Bladder Cancer and the Effect of PI3K/Akt Signaling Pathway on Tumor Recurrence," *BioMed Research International*, vol. 2021, Article ID 8860745, 7 pages, 2021.

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Research Article

The Use of BT-ESD Technology under General Intravenous Anesthesia in the Treatment of Nonmuscle Invasive Bladder Cancer and the Effect of PI3K/Akt Signaling Pathway on Tumor Recurrence

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Objective. The objective is to investigate the effect of minimally invasive treatment of nonmuscle invasive bladder cancer (NMIBC) by transurethral endoscopic submucosal dissection of bladder tumor (BT-ESD) under general intravenous anesthesia and the expression of Akt in NMIBC and to study the effect of upregulation of intracellular phosphatidylinositol kinase (PI3K)/protein kinase B (Akt) on tumor recurrence. *Method*. 130 patients with NMIBC were selected as the research subjects, including 101 males and 29 females. The patients were divided into transurethral resection of bladder tumor (TURBT) group, BT-ESD learning group A (early 20 cases of chief surgeon), and BT-ESD learning group B (follow-up cases of the chief surgeon). The general information (male and female prevalence ratio and average age), operation duration, postoperative bladder irrigation duration, postoperative indwelling catheter time, postoperative hospitalization time, and postoperative complications were compared among the patients in all groups. The normal bladder tissues and pathological tissues of NMIBC patients were stained by immunohistochemistry. *Results*. No significant difference is identified in age among the three groups ($P > 0.05$), but there are significant differences in the operation duration, postoperative bladder irrigation time, postoperative indwelling catheter time, and postoperative hospital stay ($P > 0.05$). At the same time, compared with BT-ESD group A and BT-ESD group B, the number of postoperative complications in TURBT group is statistically different ($P < 0.05$). Akt has a strong positive expression in the nucleus of patients, which indicates that Akt activated by cellular PI3K will form the PI3K/Akt signaling pathway and reduce the recurrence rate of bladder tumor.

1. Introduction

Bladder tumor is one of the most common diseases in urogenital system tumors, which also poses a great threat to human health. According to statistics, in 2014, the number of bladder cancer cases in the United States exceeded 70000 and the number of deaths exceeded 15000 [1, 2]. In China, bladder tumor ranks the 7th in male tumors and 10th in female tumors, with a male to female ratio of more than 3 : 1. Therefore, in order to prevent the occurrence and recurrence of bladder tumor, early diagnosis and surgical treatment are of great significance. In clinical practice, currently available techniques for the treatment of bladder cancer include pelvic magnetic resonance imaging (MRI), urinary tract CT, cystoscopy, and tissue biopsy [3].

There are two types of tumor: nonmuscle invasive bladder tumor (NMIBC) and muscle invasive bladder tumor (MIBC). About 70% of the initial patients are in NMIBC at the time of diagnosis. Transurethral resection of bladder tumor (TURBT) is the internationally used technique for the treatment of NMIBC. Although this method has the advantages of short operation time and small trauma, it has a high probability of

complications due to different incision sizes. If the treatment frequency is not enough, the recurrence rate is also very high [4, 5]. Transurethral endoscopic submucosal dissection of bladder tumor (BT-ESD) is a minimally invasive technique, which uses the newly invented ERBE Hybrid knife to peel off bladder tumor. When all lesions are removed, it can provide clear tumor specimens for postoperative pathological diagnosis and provide effective information for the follow-up accurate treatment of disease at the same time [6, 7]. Bahria et al. (2016) [8] showed that Akt expression and activation can play a crucial role in NMIBC tumor recurrence, while Akt activation mainly depends on PI3K. Inhibition of PI3K can block the activation of Akt.

In this regard, by selecting the clinical data of MIBC patients, BT-ESD technology is used to treat the patients, and the advantages and disadvantages of different surgical methods in the treatment of NMIBC are evaluated. The normal bladder tissues and pathological tissues of NMIBC patients are selected for immunohistochemical staining to determine the expression of Akt in the cells, so as to provide the basis for the clinical accurate treatment of bladder cancer.

2. Materials and Methods

2.1. Research Subjects. 130 patients with NMIBC diagnosed were selected as the research subjects, including 101 males and 29 females. The data of all patients were complete. The study was also approved by the hospital ethics committee. All patients signed informed consent.

(1) Inclusion criteria: it was the first time the patients developed the disease. The patient had no history of other malignant tumor treatment. Bladder cancer was confirmed by cystoscopy and biopsy before operation, and NMIBC was confirmed by pathology after operation. The Tumor Node Metastasis (TNM) stage of bladder tumor was within T2 (tumor2). There was no underlying disease that makes it difficult to tolerate surgery. The patient was over 18 years old

(2) Exclusion criteria: patients with serious diseases could not tolerate surgery. The patient was diagnosed as having metastatic bladder malignant tumor before surgery. The age of the patients was less than 18 years old, and the statistical data were incomplete

2.2. General Information and Patient Grouping. The 130 patients were from 25 to 86 years old, and their median age was 64 years old. The patients were divided into a TURBT group, BT-ESD learning group A (early 20 cases of chief surgeon), and BT-ESD learning group B (follow-up cases of the chief surgeon). Three groups of patients were compared. The general information, operation duration, hemoglobin changes before and after operation, bladder irrigation time, catheter indwelling time, postoperative hospital stay, surgical complications, and tumor recurrence rate within 3 years were statistically analyzed.

2.3. Preoperative Work and Anesthesia Methods. The patient's medical history was studied. The patient's physical examination was conducted to master the patient's heart and kidney functions. Before the operation, the patient should carry out blood coagulation routine, hematuria and stool three routines, chest X-ray, electrocardiogram (ECG), and other examinations to exclude the contraindications of operation. Imaging and cystoscopy were performed, and biopsy was performed to confirm that the patient has bladder cancer. The patients were fasted for 12 hours and deprived of water for 6 hours. The patients were anesthetized by general intravenous anesthesia. The patients were kept breathing by endotracheal intubation during the operation. The vital signs were monitored by ECG monitoring and blood oxygen saturation.

2.4. TURBT Operation Method

(1) After intravenous anesthesia, all patients took bladder lithotomy position

(2) Under the guidance of the video, Fr26 bladder resectoscope (Shenzhen Xinfulin Electronics Co., Ltd., China) was put into the bladder from the urethra (if the external orifice of the urethra is too small for the patient to enter the bladder smoothly, urethral dilatation should be performed first). After the resectoscope entered the patient's bladder, the left and right ureteral orifices and urine spray were observed to determine the tumor size, location, number, whether the tumor has a pedicle, and whether there are stones in the bladder. The electric cutting power and coagulation power were maintained at 180 W and 90 W, respectively. If the tumor size was large and the base was wide, the tumor tissue of the bladder should be resected in a step-by-step manner (including the base of the tumor)

(3) If the diameter of the tumor was less than 2 cm, the number was small, and the base was narrow, the tumor should be cut from the tumor body and the base to the muscular layer at the same time. If the bladder tumor was close to the ureter, ureteral stent could be placed during the operation to prevent hydronephrosis and urinary extravasation caused by damage to the ureter

(4) In the process of resecting tumors on both sides of the bladder, because the lateral walls were relatively thin and the obturator nerve was taken into account, the electric cutting power was relatively small, so that obturator reflex or perforation would not occur. After tissue resection, it was necessary to ensure that there was no abnormal bladder mucosa within the tumor diameter of 2 cm. At the same time, the residual tumor was vaporized. The tissues removed during the operation should be analyzed pathologically

(5) After the operation, the patients should be given bladder perfusion chemotherapy. The Fr20-22 three-lumen catheter (Shanghai Qianshan Medical Science and Technology Co., Ltd., China) was placed and washed with normal saline at the same time

2.5. Operation Method of BT-ESD Technology

(1) After intravenous anesthesia, all patients took bladder lithotomy position. The cloth was disinfected

(2) ERBE Hybrid knife (Qingdao Dongfang Will Medical Science and Technology Co., Ltd., China) was fixed in the sheath of the electric resection mirror and was placed into the Fr26 electric resection mirror through the urethra with the assistance of the imaging system. Then, the size, location, pedicle, and distance from ureter of bladder tumor were observed. Electrocoagulation was used at the location of 15 mm or so of the tumor, and the surgical sites were marked at multiple sites near the tumor

(3) 10% glycerol fructose (Guangzhou brothers Biotechnology Co., Ltd., China) and indigo carmine (Chengdu Lianhe Chemical Medicine Co., Ltd., China) were mixed. Under appropriate pressure, a submucosal syringe (Shandong Zhushitang Medical Equipment Co., Ltd., China) was used to spray the preparation to the bladder mucosa without pathological findings near the tumor tissue. The degree and extent of dye dispersion were determined to ensure that the bladder mucosa was largely elevated and the lesion could be completely separated from the muscular layer

(4) The length of the head end of the Hybrid knife was adjusted, and submucosal uplifting operation was carried out continuously to ensure the tissue blunt separation between the bladder mucosa and the muscular layer, which greatly reduced the bleeding probability in the process of tumor dissection. The complete dissection from the mucosa to submucosa and lesion tissue was completed

(5) The tumor tissue stripped during the operation should be removed as much as possible. After the operation, bladder perfusion chemotherapy was given immediately, and the catheter was connected with the bladder for irrigation

2.6. Postoperative Management, Observation Index, and Follow-Up. All three groups were treated with gemcitabine (Zhejiang Qianzun Pharmaceutical Technology Co., Ltd., China) for bladder perfusion chemotherapy. A 50 ml syringe was used to inject the bladder perfusion fluid into the bladder cavity through the catheter, and then, the catheter was closed with a clamp. The patient was instructed to continuously adjust the body position (supine, left and right lateral, prone position) every 15 minutes, so as to increase the coverage of the infusion drug and make the liquid completely enter all parts of the bladder. After perfusion, it was necessary to release the clamp and drain the urine completely. The perfusion cycle was once a week for the first 10 weeks and once a month after 10 weeks, with continuous perfusion for 12 times, a total of 1 year and 3 months. The operation duration, bladder irrigation time, catheter placement time, intraoperative blood loss, postoperative hospital stay, and surgical complications (obturator nerve reflex and bladder perforation) were compared among the three groups. Then, the recurrence rates were recorded after 1, 2, and 3 years, respectively.

2.7. Immunohistochemical Staining. The prepared pathological tissue sections were baked in an oven (Suzhou Zhongjie Electrothermal Equipment Co., Ltd., China) for 1 hour and dewaxed with xylene (Zhejiang Qianzun Medical Technology Co., Ltd., China). After alcohol dehydration, the slices were incubated with 3% H_2O_2 methanol solution at room temperature for 10 minutes to remove endogenous peroxidase and then washed twice with distilled water and PBS. The slices were placed in 0.01 M citrate buffer solution (Shanghai Enzyme-linked Biotechnology Co., Ltd., China), repaired under high pressure for 2 minutes, and cooled at room temperature. Then, it was washed with PBS for 3 times and sealed with sheep serum at 37°C. After the first antibody was added, it was kept overnight at 4°C. At room temperature, it was washed with PBS three times. The second general antibody of pika (Tiangen Biochemical Technology Co., Ltd., China) was added, and the reaction time was one hour at 37°C. Then, it was rinsed with PBS for 3 times. The pathological tissues of the patients were stained with diaminobenzidine (DAB) (Alpha Henan Weitixi Chemical Technology Co., Ltd., China). The reaction was terminated after being observed under a microscope for a suitable time. It was rinsed with tap water twice, one minute each time. The cells were restained with light sappan (Chengdu Lianhe Chemical Medicine Co., Ltd., China) and then restained in PBS for 8 minutes, followed by rapid dehydration and transparent treatment. Then, neutral gum was used for sealing and DP2-BSW imaging system (HORIBA Scientific, France) was used for photographing.

2.8. Statistical Methods. All the observation data were analyzed by SPSS26.0 software. The measurement data were expressed by means ± standard deviation ($\bar{\chi} \pm s$). t-test was used to compare and analyze the data. The count data were compared by χ^2 test. If $P < 0.05$, the difference was statistically significant.

3. Result

3.1. Comparison Results of General Data of Three Groups of Patients. The general data of patients in the TURBT group, BT-ESD group A, and BT-ESD group B were compared and analyzed. Figure 1 shows the results.

Figure 1(a) revealed that there were 59 male patients and 20 female patients in the TURBT group and 15 males and 4 females in the BT-ESD group A, as well as 24 male patients and 8 female patients in the BT-ESD group B. As for the comparison among the three groups, $P = 0.7688 > 0.05$, indicating no significant difference in general ratio. Figure 1(b) suggested that the age of the TURBT group was 62.93 ± 12.19 years old, that of the BT-ESD group A was 63.08 ± 12.48 years old, and that of the BT-ESD group B was 62.73 ± 13.78 years old. The age of the TURBT group and BT-ESD group A was compared, $P = 0.9585 > 0.05$. The age of the TURBT group and BT-ESD group B was compared, $P = 0.9918 > 0.05$. The age of the BT-ESD group A was

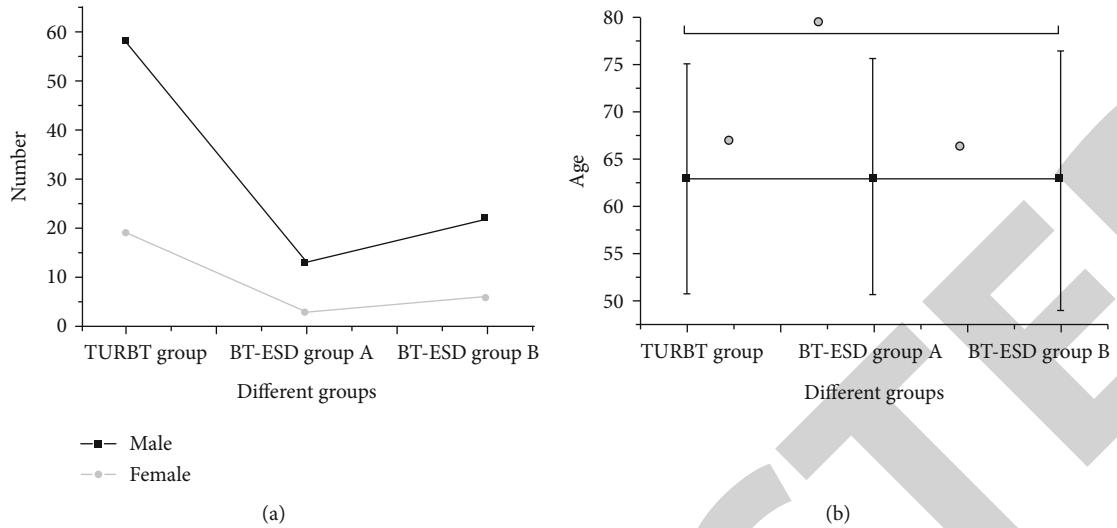

Figure 1: Comparison of general data of three groups of patients (the gray-shaded small circle indicated$P > 0.05$).

compared with the BT-ESD group B, $P = 0.9943 > 0.05$. Thus, no significant difference was identified in age among the three groups.

3.2. Comparison of Operation Duration. The operation duration of the patients in three groups was compared, as shown in Figure 2.

Figure 2 shows that the average operation duration of the TURBT group was 49.01 ± 28.05 minutes, that of the BT-ESD group A was 74.909 ± 23.98 minutes, and that of the BT-ESD group B was 53.01 ± 13.99 minutes. The TURBT group and BT-ESD group A were compared, $P = 0.0015 < 0.01$. The TURBT group and BT-ESD group B were compared, $P = 0.769 > 0.05$. The BT-ESD group A was compared with the BT-ESD group B, $P = 0.0299 < 0.05$. The above data identified the significant differences in the operation duration among the patients in three groups. The operation time of the TURBT group was significantly shorter than that of the BT-ESD group A. The operation duration of the BT-ESD group A was significantly longer than that of the BT-ESD group B. No significant difference was identified in operation time between the TURBT group and BT-ESD group B.

3.3. Comparison of the Duration of Bladder Irrigation after Operation. The duration of bladder irrigation was compared among the patients in the three groups, as shown in Figure 3.

The bladder irrigation time was 1.9 ± 0.73 days in the TURBT group, 1.73 ± 0.64 days in the BT-ESD group A, and 1.45 ± 0.69 days in the BT-ESD group B. The bladder irrigation time of the TURBT group was compared with the BT-ESD group A, $P = 0.6439 > 0.05$. The bladder irrigation time of the TURBT group was compared with the BT-ESD group B, $P = 0.0217 < 0.05$. The bladder irrigation time of the BT-ESD group A was compared with the BT-ESD group B, $P = 0.4988 > 0.05$. These data represented that there were significant differences in bladder irrigation time among the three groups. No significant difference was identified in bladder irrigation time between the TURBT group and BT-ESD group A. Bladder irrigation time in the TURBT group was significantly longer than that in the BT-ESD group B. No significant difference was identified in bladder irrigation time between the BT-ESD group A and BT-ESD group B.

3.4. Comparison of Indwelling Catheter Time after Operation. The time of indwelling catheter was compared among the patients in the three groups, as shown in Figure 4.

The indwelling catheter time was 3.89 ± 1.49 days in the TURBT group, 3.58 ± 1.47 days in the BT-ESD group A, and 2.39 ± 0.96 days in the BT-ESD group B. The TURBT group was compared with the BT-ESD group A, $P = 0.7098 > 0.05$. The TURBT group and BT-ESD group B were compared, $P < 0.0001$. The BT-ESD group A was compared with the BT-ESD group B, $P = 0.033 < 0.05$. Significant difference was identified in indwelling catheter time among the three groups. No significant difference was identified between the TURBT group and BT-ESD group A. Compared with the BT-ESD group B, the TURBT group increased significantly. The BT-ESD group A was significantly higher than the BT-ESD group B.

3.5. Comparison of Postoperative Hospital Stay. The postoperative hospital stay of the three groups was compared, as shown in Figure 5:

The postoperative hospital stay of the TURBT group was 4.89 ± 1.62 days, and that of the BT-ESD group A was 4.19 ± 0.92 days; the hospitalization time of the BT-ESD group B was 3.31 ± 0.91 days. The postoperative hospital stay of the TURBT group was compared with that of the BT-ESD group A, $P = 0.219 > 0.05$. The postoperative hospital stay of the TURBT group was compared with that of the BT-ESD group B, $P < 0.0001$. The postoperative hospital stay of the BT-ESD group A was compared with that of the BT-ESD group B, $P = 0.109 > 0.05$. Significant difference was identified in the length of hospital stay after surgery among the three groups. No significant difference was identified in postoperative hospital stay between the TURBT group and BT-ESD group A. Compared with the BT-ESD group B, the postoperative hospital stay in the TURBT group was

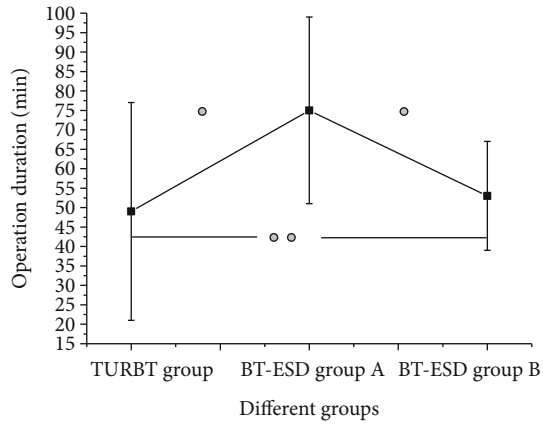

Figure 2: Comparison of operation duration among the patients in three groups (the single gray-shaded small circle indicated $P > 0.05$; the double gray-shaded small circle indicated $P < 0.05$).

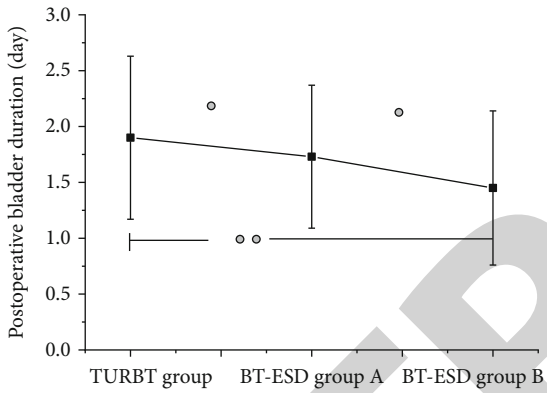

Figure 3: Comparison of bladder irrigation time among the patients in the three groups (the single gray-shaded small circle indicated $P > 0.05$; the double gray-shaded small circle indicated $P < 0.05$).

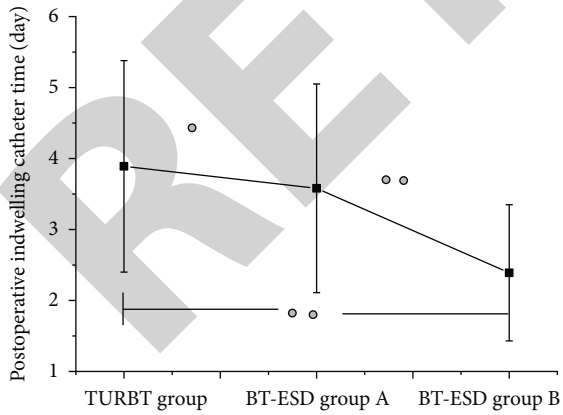

Figure 4: Comparison of indwelling catheter time among the patients in three groups (the single gray-shaded small circle indicated $P > 0.05$; the double gray-shaded small circle indicated $P < 0.05$).

significantly increased. No significant difference was identified in postoperative hospital stay between the BT-ESD group A and BT-ESD group B.

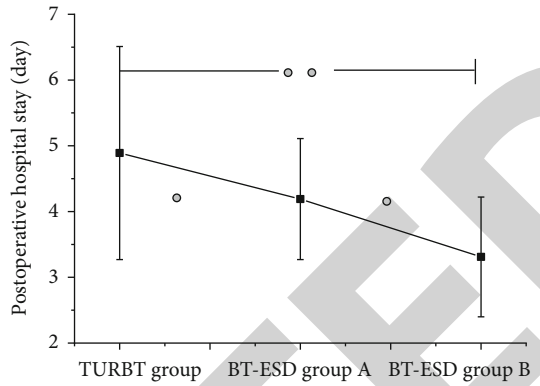

Figure 5: Comparison of postoperative hospital stay among the patients in three groups (the single gray-shaded small circle indicated $P > 0.05$; the double gray-shaded small circle indicated $P < 0.05$).

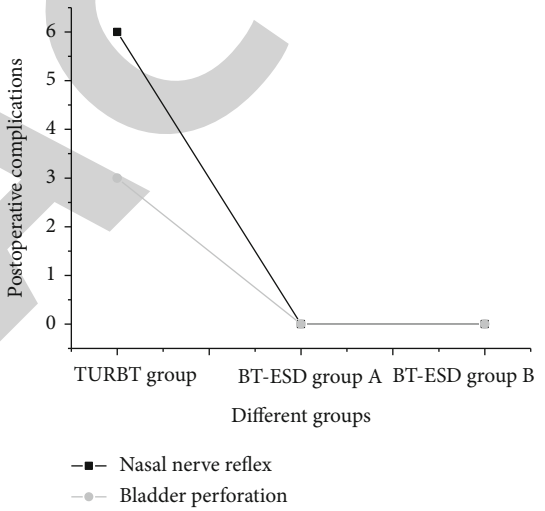

Figure 6: Comparison of postoperative complications among the patients in the three groups (the single gray-shaded small circle indicated $P > 0.05$; the double gray-shaded small circle indicated $P < 0.05$).

3.6. Comparison of Postoperative Complications. The postoperative complications of the patients in three groups were compared, as shown in Figure 6.

In the TURBT group, 6 cases had obturator nerve reflex and 3 cases had bladder perforation. There were no obturator nerve reflex and bladder perforation in the BT-ESD group A. There were no obturator nerve reflex and bladder perforation in the BT-ESD group B. There was no mortality in the three groups. Compared with the BT-ESD group A and BT-ESD group B, the number of postoperative complications in the TURBT group was statistically significant, $P = 0.0301 < 0.05$, which indicated that the postoperative complications of the TURBT group were significantly higher than those of the BT-ESD group A and BT-ESD group B.

3.7. Immunohistochemical Staining Results. Normal bladder tissues and pathological tissues of NMIBC patients were

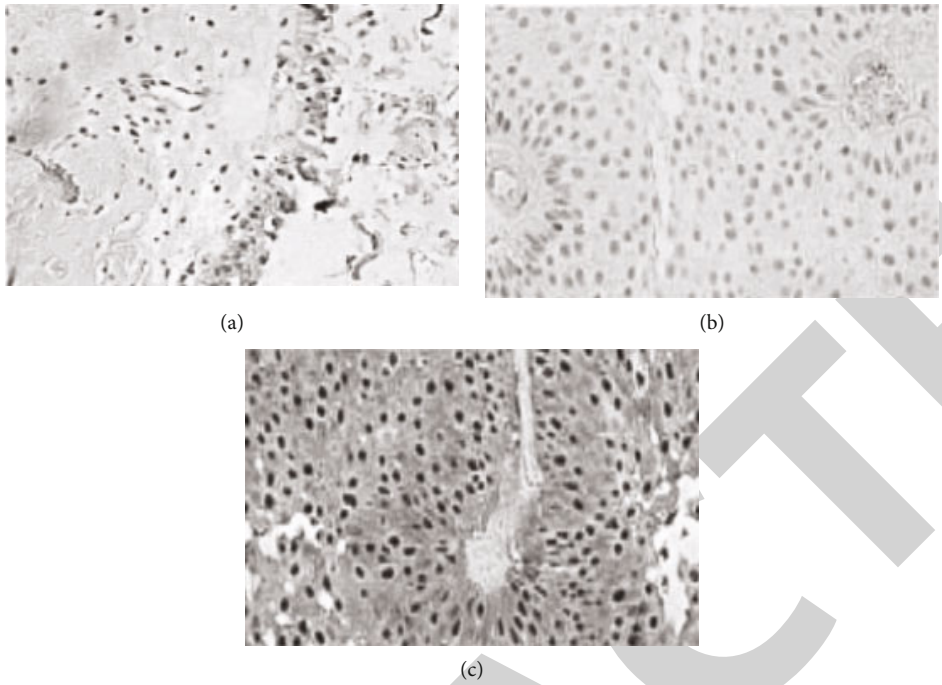

Figure 7: Different expression levels of Akt in NMIBC: (a) normal bladder tissue epithelium, (b) Akt negative staining, and (c) Akt staining.

selected for immunohistochemical staining, and the results are shown in Figure 7.

Figure 7 reveals that Akt staining was mainly concentrated in the cytoplasm. However, in the c diagram, Akt was strongly expressed in the nucleus.

4. Discussion

Bladder cancer is the most common malignant tumor of the urinary system in China, and about 70% of bladder tumors belong to NMIBC [9]. NMIBC is an early bladder tumor of the mucosa and submucosa, which is suitable for surgical treatment. With the continuous improvement of medical technology in China, the research and development of new treatment methods such as laparoscopic minimally invasive surgery and natural orifice translumenal endoscopic surgery (NOTES), the surgical treatment of bladder tumor has entered a mature stage [10, 11]. BT-ESD operation uses the technique of Hybrid knife from the urethra to the bladder. Compared with traditional TURBT operation, it can avoid the destruction of tumor tissue morphology and ensure the integrity of tumor tissue margin. The complete dissection of tumor tissue can help the attending doctors to evaluate the depth of tumor invasion more accurately and enhance the accuracy of bladder tumor pathology [12, 13].

There is no significant difference in bladder irrigation time among the three groups, but the indwelling catheter time is significantly reduced. Compared with TUEBT, the number of postoperative complications of BT-ESD is significantly reduced. This is consistent with the research results of Nojiri et al. [14], and the indwelling catheter time of BT-ESD patients is significantly reduced. The common complications of traditional TURBT include bladder bleeding, bladder perforation and obturator nerve reflex. Bleeding is a common complication of traditional TURBT, which is mainly caused by incomplete hemostasis during operation. Cases with larger tumor focus area will lead to bladder bleeding [15]. In the TURBT group, BT-ESD group A, and BT-ESD group B, the incidence of operative complications is 17.99%, 0%, and 0%, respectively. It indicates that BT-ESD technology can significantly reduce the incidence of operative complications compared with traditional surgical methods, which is consistent with the results of Abe et al. [16]. The BT-ESD technology can significantly reduce the incidence of surgical complications. The tumor tissues of the patients are studied by immunostaining. It is found that Akt staining intensity in recurrent tumors is significantly higher than that in corresponding primary lung tumors. This confirmed that the upregulation of Akt level is an important cause of bladder tumor recurrence. This is consistent with the research results of Shu and Michael [17], and the upregulation of Akt level is an inducing factor of cancer recurrence. On the other hand, it is indicated that when there is DNA damage effect, the PI3K/Akt signaling pathway is activated to inhibit apoptosis and promote cell survival. The specific molecular mechanism needs further study.

5. Conclusion

The BT-ESD technology and TURBT have an ideal effect in the treatment of NMIBC, but the BT-ESD technology can effectively reduce the postoperative bladder irrigation and indwelling catheter time and postoperative hospital stay and reduce the incidence of postoperative complications. Akt is highly expressed in NMIBC tumors. When facing DNA damage, cells mainly rely on the activation of the PI3K/Akt signaling pathway to continue metabolism.

Data Availability

All data generated or analyzed during this study are included in this published article.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authors' Contributions

Jinghui Shi and Zan Liu contributed equally to this work as cocorresponding author.

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