Hindawi
European Journal of Cancer Care
Volume 2024, Article ID 9494994, 9 pages
https://doi.org/10.1155/2024/9494994

Research Article

Clinical Study of Preoperative Prehabilitation Synchronized Neoadjuvant Chemotherapy for Gastric Cancer Patients

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Received 10 September 2023; Revised 8 December 2023; Accepted 12 March 2024; Published 21 March 2024

Academic Editor: Mohammad Reza Kalhori

Background. To investigate the effectiveness of prehabilitation in improving physical and nutritional status in patients undergoing gastric cancer resection. *Methods*. A total of 136 locally advanced gastric cancer patients who planned to undergo neoadjuvant chemotherapy (NAC) plus transabdominal radical surgery were involved. All participants were divided into the prehabilitation group and the control group using the odd-even method, with 68 cases in each group. Intervention consisted of preoperative exercise and nutrition optimization. Participants were adults awaiting elective gastric resection for cancer. The primary outcomes were changes in functional ability and nutritional status, as measured by relative changes in 6 minute walking distance (6MWD) and scores on the albumin and prealbumin. Preoperative (end of the prehabilitation period) and postoperative (from 4 to 6 weeks after surgery) data were compared between the two groups. *Results*. All 136 patients were randomized in this study. Compared with the control group, the prehabilitation group exhibited improved functional capacity both before surgery (6MWD change) and after surgery. Furthermore, it demonstrated significantly higher levels of albumin and prealbumin before and after surgery than the control group. *Conclusion*. Prehabilitation in gastric cancer patients can improve preoperative functional capacity and nutritional status. Maintaining a patient's physical function and nutritional status may have a significant impact on the continuity of cancer care.

1. Introduction

Gastric cancer is a prevalent gastrointestinal malignancy in China, ranking third in terms of incidence and mortality among malignant tumors. It exhibits a higher prevalence among middle-aged and elderly populations. Locally advanced stage is already present in approximately 70% of gastric cancer cases identified [1]. However, these patients are often diagnosed with malnutrition [2] and reduced cardiopulmonary exercise capacity [3]. Currently, radical surgical resection serves as the cornerstone for curative treatment of locally advanced gastric cancers [4]. Nevertheless, it is associated with significant adverse events.

Current optimal surgical practice involves the implementation of the Enhanced Recovery after Surgery (ERAS) program, showing promising results in reducing hospital stay duration, resource utilization, and complications [5]. Despite these advancements, gastric cancer patients still experience short-term and long-term adverse effects, such as high rates of postoperative complications and mortality, decreased muscle strength and cardiorespiratory fitness, fatigue, depression, emotional distress, anxiety, and poor quality of life [6]. The postoperative prognosis depends not only on tumor staging but also on patients' nutritional status and functional capacity [7]. Therefore, optimizing perioperative nutrition and function is crucial in managing these patients.

Prehabilitation, which refers to enhancing physical fitness prior to surgery in order to improve patients' ability to withstand surgical stress, has emerged as a valuable intervention [8]. It involves preoperative physical training, nutritional optimization and psychological intervention,

and it has been shown to enhance preoperative physical function in major abdominal surgeries. Furthermore, evidence supports the effectiveness of prehabilitation in aiding the recovery of patients undergoing surgery for esophageal cancer [9], lung cancer [10], colorectal cancer [11], and gastric cancer [12] due to its focus on modifiable factors such as physical, nutritional status, and psychiatric status.

Extensive evidence suggests that neoadjuvant chemotherapy prior to surgery confers a survival advantage for the majority of patients with locally advanced gastric cancer [13]. However, this treatment approach does not improve malnutrition and cardiopulmonary exercise function in these patients [14]. Prehabilitation during neoadjuvant chemotherapy may enhance nutritional parameters and operative recovery in women with ovarian cancer who are candidates for surgery [15]. Prehabilitation during neoadjuvant chemotherapy in oesophageal cancer has the potential to reduce inflammation, enhance immune function, and improve body composition [16]. Prehabilitation during Neoadjuvant Therapy Prior to Esophagogastric Cancer Resection may help preserve physiological parameters (peak VO_2) and muscle mass, as well as improve quality of life in patients undergoing prehabilitation [17]. Bausys et al.'s study on the impact of home-based prehabilitation on postoperative complications in gastric cancer revealed that prerehabilitation prior to surgery significantly enhances compliance with neoadjuvant therapy, physical condition, nutritional status, and quality of life [12].

Therefore, we conducted a study on patients diagnosed with locally advanced gastric cancer who required neoadjuvant chemotherapy. We effectively utilized the 7~9 week neoadjuvant chemotherapy period and interchemotherapy intervals to implement prehabilitation hypothesis suggests that integrating prehabilitation during neoadjuvant chemotherapy for gastric cancer patients has the potential to enhance perioperative functional capacity and optimize nutritional status.

2. Materials and Methods

2.1. Trial Design. This study was a parallel-group, randomized, single-blind, pragmatic clinical trial conducted at Anyang Tumor Hospital. The trial protocol (AZLL2020122708) received approval from the Scientific Ethics Review Committee of Anyang Tumor Hospital, and written informed consent was obtained from each patient prior to randomization. The study enrolled patients diagnosed with locally advanced gastric cancer who were scheduled to undergo neoadjuvant chemotherapy (NAC) followed by radical gastrectomy at the Department of Abdominal Oncology, Anyang Cancer Hospital, between January 2021 and August 2022. The study was completed on 31 January 2023. This study adhered to the principles outlined in the Declaration of Helsinki.

2.2. General Information. Inclusion criteria of the study subjects were as follows: ① patients' gastric cancer was confirmed by gastroscopy without invading the esophagogastric junction, and the pathological examination confirmed the diagnosis of adenocarcinoma, and the clinical stage before treatment was cT3~4aN1~3M0; ② patients aged 40–75 years; ③ NAC + radical total/distal gastrectomy and D2 abdominal lymphadenectomy were proposed, with no absolute contraindications to chemotherapy and surgery; ④ two courses (total 5 weeks) of NAC with SOX 3 week treatments were given, and surgery was performed 2–4 weeks after the completion of chemotherapy; and ⑤ patients signed the consent form for chemotherapy, surgery, and the clinical study. Exclusion criteria were as follows: ① patients with severe bronchial asthma, emphysema, cardiac insufficiency, unstable angina pectoris and other underlying diseases that cannot tolerate prehabilitation; ② patients with severe malnutrition and inability to eat through the mouth; ③ patients with malignant tumors in other organs; and ④ those with physical or cognitive impairments hindering cooperations. Rejection criteria included: ① tumor progression was observed after two cycles of NAC, but no surgical treatment was performed and ② abdominal and pelvic implants were found during operation.

Following informed and written consent for trial participation, patients underwent relevant baseline study procedures. A total of 136 cases were enrolled and divided into two groups based on their admission order: the control group (receiving conventional preoperative neoadjuvant chemotherapy + radical total/distal gastrectomy and D2 abdominal lymphadenectomy) and the prehabilitation group (undergoing prehabilitation, nutritional optimization, and psychological intervention in addition to conventional treatment).

2.3. Methods. The SOX regimen (oxaliplatin + S-1) was administered to all patients as neoadjuvant chemotherapy, with a treatment cycle of 3 weeks. This treatment was repeated for a total of 2 cycles. Following neoadjuvant chemotherapy, all patients underwent enhanced CT scans, ultrasound gastroscopy, tumor marker assessments, pathological biopsies, and other examinations for comprehensive evaluation. In cases where the tumor had advanced significantly, second-line chemotherapy was considered while surgical intervention was abandoned. Also, for patients with nonadvanced tumors, standard radical total/distal gastrectomy and D2 abdominal lymphadenectomy (D2) were performed 2–4 weeks after the completion of oral chemotherapeutic drugs (i.e., 7–9 weeks after the first chemotherapy).

Preoperative prehabilitation: Patients in both groups received routine preoperative training and underwent health and functional ability assessments, including walking, endurance, strength, joint mobility, and posture evaluations, starting from the day of initial admission. The control group followed the conventional preoperative preparation program for gastric cancer in the department, including preoperative smoking and alcohol cessation pulmonary function exercises, and no additional exercise interventions were performed. Patients in the prehabilitation group were prescribed an individualized, home-based exercise training

program four times per week by a dedicated nurse practitioner for rehabilitation training, following the guidelines provided by the American College of Sports Medicine [18] (3–5 days per chemotherapy cycle in the hospital for health level functional capacity assessment and exercise training instruction, and the remaining 16–18 days at home for exercise training supervision).

The prehabilitation training for patients in the prehabilitation group included abdominal breathing exercises, deep inspiration training with a breathing coach, aerobic exercise, and strengthening exercise. These exercises were implemented from the day following initial admission until one day prior to surgery [19]. Patients with preoperative sputum underwent coughing and sputum evacuation training. The duration of prehabilitation training was 7~9 weeks.

Abdominal breathing exercises, which included effective cough breathing exercises, were performed 10 times in each group, four sessions a day. Patients sat down, leaned forward slightly, took a deep breath, and used the strength of abdominal muscles to cough quickly and forcefully. According to the actual situation, patients should make appropriate adjustments without experiencing obvious fatigue.

Respiratory trainer deep inhalation training: Patients in both groups performed the training 10 times per session, four sessions per day. Deep inhalation makes the disc float upwards as much as possible. Patients should adjust the intensity according to their individual capacity, without experiencing significant fatigue.

Aerobic exercise was 30 minutes of continuous moderate intensity training (including 5 minutes of warm-up and 5 minutes of relaxation), 3 days per week. Exercises included brisk walking, jogging, or cycling, depending on the individual's fitness level and preferences. Patients selected their own rated perceived exercise intensity, up to 12 to 13 (rated perceived exercise scale Borg score range of 6 to 20) under the guidance of a nurse practitioner dedicated to rehabilitation training [20].

A 30-minute strengthening exercise (including 5 minutes of flexibility and 5 minutes of stretching) was given once a week using an elastic band as resistance for three sets of 8 to 12 repetitions for 8 muscle groups. The resistance level was determined by the full-time nurse practitioner specializing in rehabilitation training to achieve moderate intensity efforts, rated 5 to 6 on a 10-point scale [21]. A logbook was provided to participants to record all their training activities. An athletic training specialist provided supervision through weekly phone or in-person visits to record training results, monitor adherence, and resolve problems or concerns. No specialized rehabilitation was given in either group postoperatively.

Preoperative prehabilitation nutritional support: The nutrition specialist nurse assessed the nutritional status and eating habits of all patients using the NRS-2002 scale and measured various body data. According to the NRS-2002, an NRS score of <3 is considered a low risk of malnutrition, and a score ≥3 is considered a high risk of malnutrition [22]. In the control group, routine nutritional nursing guidance was given according to the department's routine gastric cancer preoperative preparation program. This meant that the responsible nurse informed patients of the purpose of perioperative chemotherapy and surgery and various precautions after admission, and provided advice on nutrition, such as preparing their own liquid or semiliquid food, having small and frequent meals, increasing the intake of high-quality protein, fresh vegetables, and fruits. Any discomfort, such as poor nausea or abdominal distension, was promptly addressed by physicians. On the first postoperative day, tube feeding was started and gradually increased, followed by a liquid diet starting on the fifth postoperative day once the anastomotic fistula was excluded. No additional nutritional interventions were performed.

The nutrition specialist nurse practitioner estimated the amounts and proportions of the various nutrients required for both prehabilitation groups [23]. All patients in the prehabilitation group received nutritional therapy to improve their dietary habits and control blood glucose if necessary. They were also encouraged to take daily preoperative whey protein supplementation (1.2–1.5 g/kg ideal body weight or 20% of total energy requirements) [24] to provide high nutritional supplementation and promote muscle synthesis. Additionally, patients were recommended to take oral nutritional supplementation (ONS) on top of their daily diet, with a calorie range of 400–900 kcal/d. If ONS is contraindicated, parenteral nutrition support therapy was considered. A logbook was provided to the participants, and a professional dietitian supervised their nutritional intake, monitored compliance, and addressed questions or problems through weekly phone calls. Patients in both groups were given only routine postoperative management without nutritional interventions.

Preoperative prehabilitation psychological intervention: All patients were visited the day after their first admission. In the control group, routine health education was given to inform all precautions for NAC and surgical treatment. In the prehabilitation group, on this basis, cases of successful previous surgeries were cited to enhance patients' confidence in treatment and reduce anxiety [23]. For patients with anxiety or depression, psychological counseling, meditation, and other cognitive-behavioral training were provided; if necessary, psychologists were consulted and pharmacological interventions were given.

Following the surgical procedure and subsequent discharge, all patients received standard postoperative care protocols. On the first day after surgery, they remained in bed and received back patting to facilitate phlegm expulsion, along with gradual administration of a small amount of nutrient solution through a feeding tube. From the second day onwards, exercise and tube feeding were gradually increased. On the fifth day after the operation, after excluding anastomotic fistula, they began to consume liquid food by mouth. Over the course of two weeks, the diet transitioned to semiliquid food, and three weeks after the operation, a small amount of regular food was introduced. Patients gradually resumed normal activities). No additional interventions were implemented.

2.4. Observation Indexes. Measurements were recorded at 3 time points for all participants. These included at baseline (beginning of the prehabilitation period for the intervention group), immediately before surgery (end of the prehabilitation period for the intervention group), and after surgery (4 weeks postsurgery). The primary outcome was change in functional capacity over time, assessed by the difference in absolute change in 6 minute walk distance (6MWD) between baseline and the preoperative visit (primary analysis) and between baseline and the postoperative visit. Secondary outcomes were serological nutritional indexes, length of hospital stay (LOS) after surgery, length of stay in the intensive care unit (ICU), postoperative human albumin input, postoperative complications, and morbidity and mortality rate. The incidence of each serious complication and the morbidity and mortality rate within 4 weeks after surgery were recorded. The 6MWD and serological nutritional parameters were measured and collected from patients discharged from the hospital at 4 weeks postoperatively.

The 6MWD assessment followed a double-blind method with the assessor (rehabilitation training allied nurse practitioner) and the subjects unaware of the grouping. Subjects were familiarized with the test procedure and environment prior to the test and were informed of various precautions. The subjects wore comfortable shoes and walked back and forth for 6 minutes in a flat corridor of 20 meters without outside interference. The distance walked (meter, m) was measured, and subjects turned back without hesitation at a speed that made them feel fatigued by the end of the walk. Subjects stopped the test as soon as symptoms such as dizziness and shortness of breath became apparent during the test. Assessors supervised all tests, following standardized procedures to minimize potential errors due to bias or varying degrees of encouragement.

Postoperative pulmonary complications (PPCs) were defined according to the guidelines from the European Society of Anesthesiology and the European Society of Intensive Care Medicine. PPCs included respiratory infections, respiratory failure, pleural effusion, atelectasis, pneumothorax, bronchospasm, and aspiration pneumonitis [25]. Additional outcomes included the severity score and incidence of major pulmonary complications (grade ≥ 3).

Patients' serum albumin and prealbumin levels were measured on the second day of initial admission, 1 day before surgery, and 4 weeks after surgery. When patients' postoperative serum albumin levels were below 35 g/L, they were supplemented with human albumin until their albumin levels reached or exceeded 35 g/L, and the amount of human albumin input (gram, g) was recorded.

2.5. Statistical Analysis. Statistical analysis was performed using *SPSS* statistical software (version 22.0 for Windows, SPSS Inc., Chicago, IL, USA). All measurement data were reported as mean ± SD. Baseline characteristics were compared between groups using an independent-samples t test. Chi-squared tests were employed for analyzing count data. Differences between groups at all follow-up times (baseline, preoperative, and postoperative) were assessed using repeated measures analysis of variance. All statistical tests were two-tailed and a significance level of $P < 0.05$ was considered statistically significant.

3. Results

3.1. Clinical Characteristics of the Study Participants. There were no statistically significant differences in age, sex, body mass index (BMI), clinical stage, comorbidity ratio, 6MWD, serum albumin level, or serum prealbumin level at baseline between the control group and prehabilitation group; furthermore, there were no statistically significant differences in the extent of gastrectomy between the two groups (see Table 1). There were 5 cases with tumor progression and no surgical treatments were identified, and 6 cases with abdominal and pelvic implant metastasis were found during the operation. 65 cases in the control group (including 3 cases with tumor advanced without surgery) and 66 cases in the prehabilitation group (including 2 cases with tumor advanced without surgery) participated in the preoperative evaluation.

3.2. Data on the Adherence to the Prehabilitation. A prehabilitation intervention was implemented for a total of 68 patients in the prehabilitation group. The adherence rate for physical training was 83.8% (57/68), while the adherence rate for nutritional support was higher, reaching 92.6% (63/68). Those who did not complete the designated training emphasis or did not adhere to the nutritional requirements were considered to have poor adherence. Among the participants in the prehabilitation group, it was observed that 25 patients experienced varying degrees of anxiety and/or depression. To address these psychological concerns, counseling and meditation were provided as interventions with an impressive compliance rate of 92% (23/25).

3.3. Comparison of 6MWD between the Two Groups. Postoperative 6MWD assessment was not performed in 11 of the operated patients (7 in the control group and 4 in the prehabilitation group): 2 patients died and 9 (6 in the control group and 3 in the prehabilitation group) failed to participate in the postoperative assessment due to frailty (4 of them had severe complications and were hospitalized for more than 30 days). 58 cases in the control group and 62 cases in the prehabilitation group participated in the postoperative evaluation. The prehabilitation group had higher preoperative 6MWD levels than the control group after undergoing prehabilitation ($P < 0.01$), especially in the postoperative period ($P < 0.001$) (see Table 2). After 7–9 weeks of neoadjuvant chemotherapy, the control group did not exhibit any significant alteration in 6MWD levels ($P = 0.799$). However, following 4 weeks of surgical trauma, a notable decrease in 6MWD levels was observed ($P = 0.009$). In contrast, the prehabilitation group showed a significant improvement in 6MWD after undergoing neoadjuvant chemotherapy combined with prehabilitation for 7–9 weeks ($P = 0.036$). Although there was a significant

Table 1: Comparison of general conditions of gastric cancer patients in two groups.

Item	Control	Prehabilitation	x^2/t value	P value
Gender				
Male	48	45	0.306	0.580
Female	20	23		
Age				
<65	58	59	0.061	0.803
≥65	10	9		
BMI				
<24	55	52	0.394	0.530
≥24	13	16		
Clinical stages				
IIIa	47	44	0.299	0.585
IIIb	21	24		
Comorbidities				
Without	44	46	0.131	0.717
With	24	22		
Extent of gastrectomy				
Distal	28	35	1.802	0.179
Total	35	27		
6MWD (meters)	454.5 ± 79.8	447.8 ± 83.8	0.473	0.637
Serum albumin (g/L)	38.13 ± 3.92	37.58 ± 4.05	0.808	0.420
Serum prealbumin (mg/L)	286.2 ± 67.0	283.3 ± 61.5	0.268	0.789

decrease in 6MWD levels compared to preoperative levels at week four postsurgery, the levels still remained higher than baseline ($P = 0.049$), as depicted in Figure 1.

3.4. Comparison of the Nutritional Status of the Patients in the Two Groups. The levels of albumin and prealbumin in the prehabilitation group were significantly higher than those in the control group both before and after the operation ($P < 0.05$), (see Tables 3 and 4). The dose of postoperative albumin supplementation (grams) in patients from the prehabilitation group (58.34 ± 9.717), on the other hand, was significantly lower than that in the control group (77.23 ± 10.565), with a statistically significant difference ($t = 9.869$, $P < 0.001$).

3.5. Perioperative Complications Occurred in Both Groups. One case of death occurred in the prehabilitation group due to anastomotic fistula combined with sepsis, while another case of death in the control group was attributed to pulmonary embolism. The remaining patients were cured after active treatment. The difference between the two groups in terms of abdominal complications was not statistically significant (11/65 vs. 9/66, $\chi^2 = 0.273$, $P = 0.601$). However, the incidence of pulmonary infection (grade ≥ 3) in the prehabilitation group was lower than that in the control group, with a statistically significant difference (16/65 vs. 6/66, $\chi^2 = 5.648$, $P = 0.017$).

3.6. Length of Hospital Stay (LOS) after Surgery and ICU Stay in Both Groups. The LOS after surgery (days) for the control group was significantly longer compared to the prehabilitation group (13.24 ± 5.358 vs. 10.74 ± 3.608), exhibiting a statistically significant difference ($t = 3.015$, $P = 0.003$). Furthermore, the duration of ICU stay (hours) in the control group also demonstrated a significantly longer period than that in the prehabilitation group (29.36 ± 6.619 vs. 25.61 ± 6.349), with a statistically significant distinction observed ($t = 3.167$, $P = 0.002$).

4. Discussion

Poor physical fitness has an incidence of 43.8% in patients with progressive gastric cancer [26], and it [27] is closely associated with increased incidence of postoperative complications and a poor prognosis in gastric cancer patients. Among patients undergoing surgery, malnourished patients have longer hospital stays and high complication rates [28], while malnutrition is highly prevalent in patients with progressive gastric cancer, reaching up to 48% [29], which severely affects patients' quality of life, increases chemotherapy toxicity, and decreases overall survival. Radical total/distal gastrectomy and D2 abdominal lymphadenectomy for gastric cancer pose challenges to patients' normal activities, leading to negative nutritional nitrogen balance and a corresponding upregulation of nutritional requirements [29]. Thus, radical total/distal gastrectomy and D2 abdominal lymphadenectomy will aggravate malnutrition and decrease the physical quality of patients. The physical fitness and nutritional status of gastric cancer patients in the perioperative period strongly influence their quality of life, treatment compliance, and overall survival. Most studies have focused on the safety and efficacy of rehabilitation treatments such as sports nutrition after tumor surgery. In contrast to these traditional approaches, preoperative prehabilitation aims to prevent functional decline caused by cancer treatment by addressing modifiable risk factors, such as physical fitness, nutritional status, and psychological status.

Table 2: Comparison of 6MWD after intervention between two groups of gastric cancer patients (m, $\overline{x} + s$).

Group	Cases	Preoperation		Postoperation	
		m, $\overline{x} + s$	95% CI	m, $\overline{x} + s$	95% CI
Control	58	460.7 ± 82.3	446.113–488.094	403.4 ± 74.9	386.447–421.312
Prehabilitation	62	499.9 ± 86.3	473.617–514.222	478.8 ± 74.6	465.736–499.458
t value		2.662		5.524	
P value		0.009		<0.001	

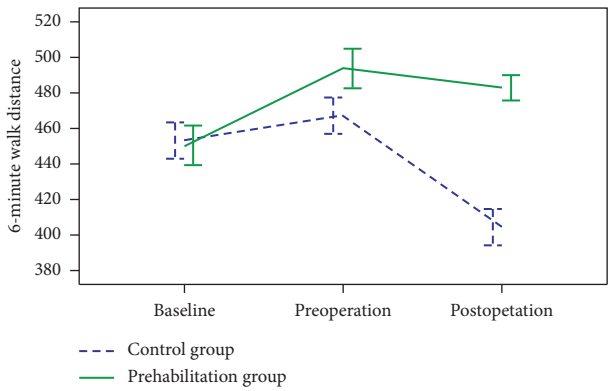

Figure 1: Trajectory of change in functional capacity in the perioperative period.

Table 3: Comparison of serum albumin levels between two groups of gastric cancer patients after intervention (g/L, $\overline{x} + s$).

Group	Cases	Serum albumin	
		Preoperation	Postoperation
Control	65	38.69 ± 5.05	34.36 ± 3.82
Prehabilitation	66	42.96 ± 3.36	38.57 ± 4.11
t value		5.704	5.805
P value		<0.001	<0.001

Table 4: Comparison of serum prealbumin levels between two groups of gastric cancer patients after intervention (mg/L, $\overline{x} + s$).

Group	Cases	Serum prealbumin	
		Preoperation	Postoperation
Control	65	300.5 ± 71.5	249.5 ± 71.6
Prehabilitation	66	328.9 ± 67.1	283.0 ± 69.7
t value		2.348	2.601
P value		0.020	0.010

Liu et al. [30] conducted a two-week exercise-based prehabilitation program for lung cancer patients who planned to undergo thoracoscopic lobectomy. The results showed that the prehabilitation group's average 6MWD before operation was 41.3 meters larger than that of the control group, and 57.6 meters larger one month after operation. Lau et al. [31] found through a meta-analysis that compared with the control group, preoperative prehabilitation significantly improved the preoperative 6MWD and the postoperative 6MWD at 4–8 weeks in patients with gastrointestinal cancer. In this study, 6MWD was also used as indicator of patients' physical function. The results showed that after undergoing preoperative prehabilitation, the prehabilitation group had significantly higher levels of 6MWD before operation and 4 weeks after operation than the control group (39.2 meters and 75.4 meters, respectively). It can be seen that prehabilitation can significantly improve the patients' physical function before operation, and it is also conducive to the recovery of postoperative physical function.

Nutritional interventions in oncology patients undergoing chemotherapy [32] revealed that all nutritional indicators (albumin, prealbumin, transferrin, etc.) were significantly higher in the intervention group compared to the control group. Recent randomized controlled trials [33] have also shown that nutritional supplementation leads to significant improvements in various nutritional indicators (serum albumin, serum prealbumin, etc.). In our study, we found that patients in the prehabilitation group also had significantly improved preoperative serum albumin and prealbumin levels after undergoing prehabilitation, and they remained at baseline levels for 4 weeks postoperatively. In contrast, patients in the control group did not have a significantly improved preoperative nutritional status and experienced a rapid decline in the 4 weeks after surgery. These findings are consistent with previous literature [19]. The results of our trial also showed that the dose of perioperative albumin use was significantly lower in the prehabilitation group than in the control group, suggesting that prehabilitation can effectively save health care resources. This finding contradicts the results of previous studies [34], and the discrepancy may be attributed to the duration of prehabilitation.

The effectiveness of preoperative prehabilitation was found to improve with longer prehabilitation period. NAC combined with radical total/distal gastrectomy and D2 abdominal lymphadenectomy is the standard treatment protocol for clinical stage III gastric cancer. NAC usually lasts for more than 6 weeks, and it is crucial to optimize patients' physical and nutritional status through prehabilitation during this period to reduce surgery risks and improve outcomes. Therefore, there is an urgent need for randomized clinical trials with multidisciplinary interventions to optimize patients' cardiopulmonary adaptability [35] and improve their nutritional status, thereby enabling them to pass through the preoperative period and creating conditions for postoperative follow-up treatment. The average duration of our prehabilitation care was 8 weeks, which is consistent with two cycles of three-week preoperative NAC treatment. This duration alighs with

a reasonable prehabilitation timeframe for patients undergoing NAC. The extended duration of prehabilitation, without delaying the treatment of the tumor, distinguishes this trial from other studies [36]. The preoperative physical functional status and nutritional status of most patients were substantially improved, more so than in previous studies [19]. Moreover, these improvements in physical functional and nutritional status continued up to 4 weeks postoperatively, which created favorable conditions for comprehensive postoperative treatment.

The results of our trial showed that the rate of pulmonary infections in patients in the prehabilitation group was significantly lower than that in the control group, indicating that the prehabilitation interventions can reduce the occurrence of perioperative pulmonary infections, which is also consistent with existing literature [37]. In contrast, there was no significant difference in the incidence of abdominal complications between the two groups, indicating that the improvement of physical function and the improvement of nutritional level had no significant effect on the prevention of abdominal complications. Furthermore, our findings indicate that combining prehabilitation with NAC resulted in shorter postoperative hospital stays and ICU stays for patients, highlighting the potential of prehabilitation to expedite patient recovery, which is consistent with existing literature [38].

5. Limitations

This study has several limitations that should be acknowledged. As previously mentioned, the variability of neoadjuvant treatment in terms of duration and regimen may limit the consistency, generalizability, and applicability of our findings. In addition, the exclusion of patients who were not willing to participate in a physical intervention may introduce a potential selection bias. Additionally, the short follow-up time of the study prevented the assessment of progression-free survival and overall survival after surgery. Other considerations for future research include the introduction of a supervised training sessions, a consistent duration of the intervention, better integration into the medical treatment plan, and a larger sample size.

6. Conclusions

It can be seen that a longer duration of prehabilitation for gastric cancer patients along with NAC can reduce physical dysfunction, improve nutritional status, reduce postoperative pulmonary infection complications, and expedite patient recovery. Its value may be considerable in the cancer treatment process. However, the effect of prehabilitation on the medium- and long-term outcomes in gastric cancer patients remains unknown and requires further investigation in subsequent studies.

Data Availability

All authors agree to share their data and material for further research purposes.

Ethical Approval

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments, or comparable ethical standards. This article does not contain any studies with animal subjects performed by any of the authors.

Consent

All the authors provided their consent to participate in this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Li LI and Jiaxin LIU designed the study and wrote the paper. Li LI, Jiaxin LIU, Yong ZHANG, and Shoumiao LI collected and analyzed the data. Jing WANG and Shoumiao LI revised the paper. All authors agreed to publish the results of this study. Li Li and Jiaxin Liu made equal contributions to this work as co-first authors.

Acknowledgments

We would like to express our gratitude to the medical records staff at Anyang Tumor Hospital for their support in this study. This study was funded by the Henan Province Science and Technology Tackling Key Project (232102310090) and the Medical Science and Technology Project of Henan Province (SBGJ202002129).

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