Original Article
Application of prerehabilitation nursing practice before radiotherapy in patients with liver cancer: a single-center prospective randomized controlled study

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Abstract: Objective: To investigate the applicability of prerehabilitation nursing practice before radiotherapy for patients with liver cancer. Methods: Ninety patients with primary liver cancer who were admitted to The Fifth Medical Center of PLA (Chinese People's Liberation Army) General Hospital from December 2019 to May 2020 and received stereotactic body radiotherapy (SBRT) were selected. On the day of the outpatient visit, all patients were assigned to the observation or control group using a random number table, with 45 patients in each group. Patients in the control group received preoperative instructions before radiotherapy for liver cancer, while those in the observation group received prerehabilitation interventions until the start of radiotherapy. Prerehabilitation interventions included microecological agents for enteral nutrition, *Baduanjin* exercise, and psychological support for 10-15 days. Quality of life instrument for patients with liver cancer (QOL-LC), gripping power weighting index (GPWI), serum albumin (ALB), lymphocyte count, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) at admission (baseline) and the first day after radiotherapy were compared between the two groups. The GPWI, ALB, QOL-LC and lymphocyte counts were primary measurs, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) were secondary. Furthermore, we analyzed the correlations between QOL-LC and the HGP/BW ratio, ALB, lymphocyte counts, NLR, and PLR in the two groups. Results: There were no significant differences in baseline QOL-LC scores, GPWI, ALB, lymphocyte counts, NLR and PLR at admission between the two groups (*P*>0.05). On the first day after radiotherapy, QOL-LC scores, GPWI, ALB, and lymphocyte counts in the observation group were higher than those in the control group (*P*<0.05), while NLR and PLR levels were lower than those in the control group (*P*<0.05). The correlation study revealed that QOL-LC scores were positively correlated with the GPWI, ALB and lymphocyte counts in liver cancer patients (*P*<0.05), but negatively correlated with NLR and PLR (*P*<0.05). Conclusion: Quality of life in patients with primary liver cancer is significantly associated with nutritional status and immune activity conditions. The application of prerehabilitation nursing practice before radiotherapy in patients with liver cancer can ameliorate their nutritional status and immune activity conditions, increase resistance to radiotherapy and improve perioperative quality of life. Therefore, it is worthy of promotion in clinical practice.

Keywords: Prerehabilitation, liver cancer, radiotherapy, nursing

Introduction

Liver cancer is a tumor malignancy that severely threatens human health, globally its morbidity ranks sixth and mortality ranks fourth [1, 2]. Treatment options include radical surgeries, such as hepatectomy and liver transplantation, and radiotherapy, particularly stereotactic body radiotherapy (SBRT), which has gradually gained prominence as a treatment for liver cancer [3]. However, radiotherapy kills both tumor and normal blood cells, resulting in decreased immune function and complications including fatigue, poor appetite and gastrointestinal dysfunction. All these reduce patients' quality of life and contribute to a poor prognosis. Therefore, for medical experts at the Department of Radiotherapy for Liver Cancer, optimizing preoperative management of patients, increasing tolerance to radiotherapy, and improving quality of life have all become research hotspots. Conventionally, rehabilitation intervention re-

sumes after surgery. However, there are still issues, such as wound pain, vexations at wound healing, and anxiety [4, 5]. Because patients frequently have higher compliance with prerehabilitation nursing before surgery, along with a certain length of period before a selected operation at most medical institutions, this period is appropriate for the preoperative intervention of prerehabilitation nursing. Prerehabilitation therapy is a new preoperative management concept based on an emerging strategy, fast-track rehabilitation for surgery. It promotes the improvement of the functional status of patients before surgery and optimization of physiological reserves to better adapt to and tolerate surgical stress [6]. Prerehabilitation therapy has been used in several occasions before surgeries, including gastrointestinal and urologic surgeries, which has proven beneficial to patients. However, there is yet to be an agreement on the methodology and timing of prerehabilitation interventions, and many problems still need addressing. Furthermore, it is primarily used before abdominal surgeries, and its application before radiotherapy for liver cancers is yet to be reported. In our study, we investigated the applicability of prerehabilitation therapy before to radiotherapy for liver cancer.

Materials and methods

Clinical characteristics

Ninety patients with primary liver cancer who were admitted at The Fifth Medical Center of PLA General Hospital from December 2019 to May 2020 and who received SBRT were selected. The inclusion criteria were defined as follows: (1) patients who were diagnosed with liver cancer based on images and laboratory results [7] and willing to receive SBRT; (2) those with Child-Pugh class A/B liver function; (3) those with favorable underlying medical conditions, and with the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score of 0-2 points [8]; (4) patients with normal renal function; (5) those with white blood cell (WBC) count >2.0×10^9/L, and platelet (PLT) count >60×10^9/L; and (6) patients who were over 18 years old. The exclusion criteria were as follows: (1) patients who underwent any surgery within three months prior; (2) patients who could not tolearate oral food delivery; (3) those

with Child-Pugh class C liver function; (4) patients with lymphatic or distant organ metastasis; (5) patients with psychonosema who were unable to communicate with others; (6) patients with limb dysfunction, or unable to exercise normally. On the day of an outpatient visit, all patients were assigned to the observation or control group using a random number table, with 45 patients in each group. The Ethics Committee of The Fifth Medical Center of PLA General Hospital approved this study, with approval numbers (2020-057-D). All the included patients were informed of the details in the research protocol and signed an informed consent form.

Preoperative interventions

Preparations before routine radiotherapy for liver cancer in the control group included preoperative education, general dietary guidelines, and preoperative counseling. Patients in the observation group also received prerehabilitation interventions as follows. First, nurses and nutritionists analyzed patients' nutrition status, and those with an NRS2002 score of r3 points were administered oral microecological agents for enteral nutrition supplements. However, patients with an NRS2002 score <3 points were exempted from nutritional support, and their nutrition status was evaluated every three days for adjustments. Second, exercise interventions: the Baduanjin exercise procedures [9] were repeated 2-3 times per day. To ensure the effectiveness and consistency of exercise, certified nurses guided patients to do Baduanjin exercises. Third, preoperative counseling: patients and their families received health education and counseling services. We instructed them to positively meditate and decompress by watching videos of meditation every day [10]. All these interventions lasted for 10-15 days. **Figure 1** illustrates the Baduanjin exercise procedures.

Observation and measurements

The following indices were recorded at admission (baseline) and the first day after radiotherapy, including (1) Grip strength body mass index (GPWI) and serum albumin (ALB) for assessments of patients' physical strength and nutrition status. Gripping power weighting index (GPWI) = grip power/weight (kg/kg). We measured the gripping power using an electronic

Procedures of Baduanjin exercise

Step 1 Hands holding the sky to harmonize the triple energizer

Step 2 Drawing bow to shoot the hawk

Step 3 Separating the heaven and earth to benefit the spleen

Step 4.Wise owl gazing backwards to treat strains and injuries

Step 5 Puching with an angry gaze to boost energy

Step 6 Touching toes than bending backwards to strengthen

Step 7 Shaking head and swinging tall to remove firelight

Step 8 Standing on toes and bouncing for seven times to remove diseases

Figure 1. The Baduanjin exercise procedures.

hand grip force meter (WCS-100). The display screen was outward so as not to contact the body and clothes. Gripping power weighting index (GPWI) = gripping power/weight (kg/kg).

The gripping power meter was held once and the reading was recorded. Serum albumin (ALB) levels were collected by the nurse in accordance with the regulations and sent to the laboratory for testing. (2) The lymphocyte count, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) for assessments of immune function, were collected by the nurse in accordance with the regulations and sent to the laboratory for testing. (3) The quality of life instrument for patients with liver cancer (QOL-LC) [11], which was developed by Dr. Wan Chonghua in 1998 (after he combined the widely accepted Functional Living Index-Cancer and the European Organization for Research and Treatment of Cancer with the cultural characteristics of our nation and specific conditions of patients with liver cancer) was used for analysis. The *Journal of Clinical Oncology* published the QOL-LC scale in 2009, which contains four dimensions: physical function (six items), psychological function (six items), symptomatic adverse events (five items), and social function (five items), making a total of 22 items. With an additional item for self-evaluating the overall quality of life, there were 23 items on the formal scale (V2.0). Each item could be scored from zero to ten, with a maximum of 220 points for the first 22 items. The full mark of the last item, self-evaluation for overall quality of life, was 100 points. The higher the total score was, the better the quality of life.

Statistical analysis

We performed all statistical analyses using SPSS v.20.0 software. Measurement data were presented as mean ± standard deviation and analyzed using a *t*-test. Further, we analyzed the enumeration data using the Chi-square test. A *P*-value of <0.05 was considered statistically significant.

Results

Basic clinical characteristics

Among the 93 eligible patients, three withdrew from our study, leaving 90 patients with primary liver cancer who were included for further analysis. Each group had 45 participants, including 33 males and 12 females in the observation group, with a mean age of 68.76±9.85 years and an average radiation dose of 40.87± 12.21 Gary (Gy); and there were 30 males and 15 females in the control group, with a mean age of 69.15±9.06 years and an average radiation dose of 40.96±12.47 Gy. In the observation group, 41 subjects showed Child-Pugh class A liver function and four had Child-Pugh class B liver function, while the control group had 43 cases of Child-Pugh class A liver function and two of Child-Pugh class B liver function. There were no significant differences in gender and Child-Pugh classification (X^2=0.157, 0.718, both *P*>0.05), as well as age and doses (*t*=-0.206, -0.192, both *P*>0.05) between the two groups.

QOL-LC scores, GPWI, ALB, lymphocyte counts, NLR, and PLR in patients with liver cancer before and after SBRT

Compared with baseline levels, QOL-LC scores, GPWI, ALB levels, and lymphocyte counts significantly decreased (all *P*<0.05), and NLR and PLR significantly increased in the two groups after SBRT (all *P*<0.05). There were no significant differences between the two groups (all *P*>0.05) in QOL-LC scores, GPWI, ALB levels, lymphocyte counts, NLR, and PLR. The mentioned indices (except ALB) significantly differed after SBRT between the two groups (all *P*<0.05), as shown in **Table 1**.

Correlations between QOL-LC scores and GPWI, ALB, lymphocyte counts, NLR, and PLR in the two groups

After SBRT, QOL-LC scores in patients with liver cancer were positively correlated with the GPWI, ALB and lymphocyte counts (*P*<0.05), but negatively correlated with NLR and PLR (*P*<0.05), as shown in **Table 2**.

Discussion

This study investigated whether protocols of prerehabilitation were suitable for patients with liver cancer and their applicability. The concept of prerehabilitation therapy was derived from exercise interventions before surgery at first, and researchers [12, 13] later discovered that preoperative multi-interventions which include medication instructions, quitting smoking and alcohol use, dietary guidelines, nutrition supplements, psychological support, and patient education are more effective than single exercise interventions. Most often prerehabilitation interventions used in clinical practice were

Table 1. Comparison of QOL-LC, GPWI, ALB, Lymphocyte Count, NLR, PLR Levels of Liver Cancer Patients between Baseline and Post-SBRT

		observation group	control group	t	P
		45	45		
Baseline	QOL-LC	163.35±22.39	165.35±21.56	-0.432	0.6671
	GPWI	0.55±0.21	0.54±0.18	0.243	0.8089
	ALB	33.35±3.25	34.15±3.09	-1.197	0.2346
	the lymphocyte count (10*9/L)	1.15±0.09	1.12±0.12	1.342	0.1832
	NLR	4.89±1.09	5.02±1.16	-0.548	0.5852
	PLR	122.25±23.82	121.43±21.76	0.17	0.865
Post-SBRT	QOL-LC	154.98±26.52	142.87±24.57	2.247	0.0271
	GPWI	0.45±0.12	0.39±0.13	2.275	0.0253
	ALB	31.24±4.21	32.09±3.76	-1.01	0.3152
	the lymphocyte count (10*9/L)	0.58±0.03	0.39±0.04	25.41	0.0001
	NLR	6.72±1.32	8.62±1.65	-6.032	0.0001
	PLR	143.62±27.09	158.56±26.21	-2.659	0.0093

Note: QOL-LC: Quality of life instrument for patients with liver cancer; GPWI: Gripping power weighting index; ALB: Albumin; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

Table 2. Correlation of QOL-LC with GPWI, serum albumin (ALB), lymphocyte count, NLR, PLR

Indicators	QOL-LC	
	r	P
GPWI	0.732	0.001
ALB	0.658	0.015
The Lymphocyte Count (10*9/L)	0.532	0.026
NLR	-0.213	0.0001
PLR	-0.267	0.0001

Note: QOL-LC: Quality of life instrument for patients with liver cancer; GPWI: Gripping power weighting index; ALB: Albumin; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

single exercise interventions, which were unsuitable for patients with cancer. Therefore, for intervention, our study adopted *Baduanjin* exercise, traditional Chinese *qigong*, which promotes *qi*-blood circulation by stretching and bending the body with dynamic and static exercises [14, 15]. Despite improvements in muscle strength and range of motion, *Baduanjin* exercise can also promote *qi* and activate blood, with movements such as "hands holding the sky to harmonize the triple energizer, wise owl gazing backward to treat strains and injuries, and standing on toes and bouncing for seven times to remove diseases" all of which can regulate *qi* activity, which enhances the emotional catharsis and function of the liver, including the emotional release of anxiety and depression. The movement of "separating the heaven and earth to benefit the spleen and stomach" can tonify the spleen and stomach, alleviate symptoms, such as dyspepsia and stomach discomforts, and improve psychological activity and mental flexibility.

Weight loss is an immediate consequence of malnutrition. Studies [16-18] have discovered that compared with individuals having stable weights, those with weight loss showed a shorter survival, which is an independent risk factor for surgical complications, mortality, duration of hospital stay, and, inpatient hospitalization fees. Preoperative nutrition assistance, including oral administration of microecological agents for enteral nutrition support, is recommended for patients with malnourishment, despite nutrition requirements based on patients' dietary status. Microecological agents consist of whey proteins and probiotics that provide high-level nutrition, which balance the intestinal microbiota, facilitate protein synthesis and muscular endurance, suppress inflammatory responses, and enhance immune activity. Preoperative psychology interventions for surgical patients, particularly for patients with cancer with distinct levels of anxiety and depressive emotions, can relieve anxiety through 60-minute consultations with psychologists, which encompass relaxation training based on visual mental imagery and respiratory training.

Besides, videos provided by psychologists are used for self-learning at home. Another goal of psychological interventions is to ensure the patient's compliance with exercise and nutrition interventions so that prerehabilitation nursing practice can be implemented effectively.

As treatment patterns shift from a single biological model to a bio-psycho-social model with changes in the disease spectrum, the aim of health care not only focus on higher survival rates or longer survival time but also on the quality of life (QOL), including physical, psychological, and social self-restoring [19, 20]. Previous efficacy evaluations of liver cancer treatments primarily appraise the comprehensive healing rate, survival rates and survival time. Recently, QOL reflecting an overall recovery and feelings of patients has received more attention and is universally used in efficacy assessments of the treatment of cancers and chronic diseases. In our study, the QOL-LC scale was employed to assess the efficacy of prerehabilitation nursing in patients with liver cancer. Due to liver function impairments after radiotherapy for liver cancer, the exacerbating somatic symptoms may reduce QOL, but prerehabilitation nursing can reduce these adverse reactions with ameliorated QOL. Because lymphocytes are critical tumor immune cells, decreased lymphocyte counts in the peripheral circulation or deficiency of lymphocyte function can impair immune responses. Serum lymphocyte levels directly reflect the immune activity and tumor progression [21, 22]. Because neutrophils, lymphocytes and platelets vary with tumor development, NLR and PLR can reflect not only the degree of inflammatory responses but also the severity of the body's antitumor effects [23]. Our results revealed that NLR and PLR after radiotherapy were lower in the observation group than in the control group. This indicates that prerehabilitation nursing can be applied in patients with liver cancer and be beneficial to them, which is consistent with the study by Ayman Alsebaey, *et al*. [24].

Another study [25] reports that prerehabilitation therapy for 2-8 weeks before surgery accelerates recovery and improves patient prognosis. At our hospital, the period before an operation is approximately 2-4 weeks, during which prerehabilitation therapy can be used to intervene to improve threatment and recovery efficacy.

Conclusively, prerehabilitation nursing is safe and effective for patients with liver cancer before radiotherapy, which improves nutrition conditions, immune responses, tolerance to radiotherapy, and perioperative QOL of patients. Therefore, it is worthy of promotion in the clinic. However, there were some limitations to this trial, including limited sample size, being a single-center study, and lacking long-term follow-up results. In the future, a larger sample size and multicenter controlled long-term follow-up study are necessary for further confirmation of results.

Disclosure of conflict of interest

None.

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