INFORMED CONSENT FORM

Effect of triple pre-rehabilitation on radiotherapy for head and neck cancer patients: a randomized controlled trial

Peking University

2022/10/20

Dear patient：

We will conduct **Effect of triple pre-rehabilitation on radiotherapy for head and neck cancer patients: a randomized controlled trial**. This study is a cooperative project with Peking University School of Nursing. You are eligible to participate in the study, so we would like to invite you to participate. This Informed Consent will introduce to you the purpose, steps, benefits, risks and possible inconvenience or discomfort of the study. Please carefully read this consent and make a decision on whether to participate in the study. When the researcher explains and discusses the informed consent form to you, feel free to ask questions and have him/her explain to you what you do not understand. You can discuss this with family, friends, and your primary care physician before making a decision. If you are currently participating in another clinical study, please inform your study physician or investigator.

The project leader of this study was Peiguo Wang (Department of Radiotherapy, Tianjin Medical University Cancer Hospital).

1 Objectives

1. To evaluate the intervention effect of triple pre-rehabilitation on head and neck cancer patients with radiotherapy.

2. Process evaluation to further optimize the intervention program.

1. Participants

This study plans to recruit adult patients with head and neck malignancies who are to undergo radiotherapy at Tianjin Medical University Cancer Institution and Hospital. Inclusion criteria: a) $18 \leqslant$ age $<$ 75 years old; b) The pathological diagnosis of HNC included nasopharyngeal cancer, oral cancer, oropharyngeal cancer, hypopharyngeal cancer, laryngeal cancer, salivary gland cancer; c) Plan to receive radiotherapy; d) Basic communication skills; and e) Volunteer to participate in this study. Exclusion criteria: a) Combined with other malignant tumors; b) distant metastasis; c) Inability to measure body composition, such as metal in the body or inability to stand alone; d) With contraindications to exercise (such as cardiovascular and cerebrovascular diseases, respiratory diseases, etc.); e) Complicated with severe liver and kidney function damage; f) Previous diagnosis of other cancers; and g) pregnant or lactation women.

If you meet the above criteria, you will be randomly divided into two groups on a 1:1 basis.

You will be randomly assigned to either the pre-rehabilitation group or the rehabilitation group (i.e., the likelihood of being assigned to both groups is equal), with 40 patients planned for each group. Patients in pre-rehabilitation group (Pre Group) received triple pre-rehabilitation from enrollment (2-4 weeks before radiotherapy), and the intervention lasted until the end of radiotherapy. Patients in the rehabilitation group (Re Group) received triple intervention from the beginning of radiotherapy to the end of radiotherapy. The triple pre-rehabilitation intervention consists of exercise, nutrition and psychology. Patients in the intervention group received face-to-face three-combination pre-rehabilitation intervention adjustment and intensive intervention measures, combined with weekly WeChat follow-up during the intervention process to review the intervention content formulated face-to-face last time, strengthen behaviors, and answer questions during the process.

2. Intervention

You will be followed up at the time of enrollment (T0), before radiotherapy (T1), in the middle of radiotherapy (T2), and at the end of radiotherapy (T3). During the follow-up, a questionnaire will be conducted. Combined with dietary score and body composition measurement, a comprehensive non-invasive physical function assessment (4m normal walking speed, 60s sitting and standing experiment, grip strength), nutritional assessment (body composition measurement, questionnaire) and psychological status assessment (questionnaire) will be conducted. Each time, it will take about 25 to 30 minutes. To facilitate contact, we will register your personal information (name and contact information) at the time of enrollment. This information will be kept strictly confidential and will only be used to contact you for subsequent assessment. During the last follow-up, you may be interviewed to understand your thoughts and suggestions on pre-rehabilitation. In order to facilitate the sorting out of interview materials, the interview process will be recorded, which will be kept by specially-assigned personnel and destroyed after the data is sorted out correctly.

To participate in this study, you are required to cooperate with the following matters: ① implement the pre-rehabilitation program as arranged by the investigator; ② You need to be evaluated by the investigator according to the follow-up time; ③ You need to inform the researchers about your health problems, even if you think that is not very important; ④ Please record your pre-recovery diary card as required and give it to your study doctor at your next

visit. In addition, it is necessary to pay attention to contraception during the study (age group). When you decide whether to participate in the study, please carefully consider the impact of the examinations and follow-up listed above on your daily work and family life. Consider the timing and transportation of each return visit. If you have any questions about the tests and procedures involved, please contact us.

3. Risk and control

There is no cost to participate in this study. The intervention program of this study was modified and improved by evidence-based and expert meetings to ensure the safety of the intervention program. However, participating in this study may still cause muscle strain, fall, hypoglycemia and other adverse events due to improper exercise, diarrhea and constipation due to improper dietary intake or improper use of oral dietary supplements. If you are lactose intolerant, please inform the investigator in advance and strictly follow the exercise and nutrition recommendations given by the investigator.

Exercise and nutrition risk control: During the first intervention, we will assess your exercise ability and exercise habits, and develop a personalized exercise plan for you. Elastic band matching corresponding strength according to your grip strength; The intensity and time of exercise gradually increase according to their own tolerance degree; It is advisable to not feel tired when doing physical exercise at home, and avoid doing exercise on an empty stomach. Be sure to be accompanied by family members. During the intervention period, we will conduct weekly WeChat follow-up to assess your exercise status and adverse events. The research team made personalized meal plans for the patients, and guided the patients and their families to learn how to use food exchange portions. Patients taking dietary supplements were given one-on-one guidance before their initial use, including the symptoms and management of common adverse reactions, and were instructed to contact the research team in time to resolve any discomfort symptoms.

If any discomfort occurs during the intervention, please stop immediately and inform us. We will follow up your situation through WeChat throughout the intervention. If you have any questions, you can contact us at any time. If you feel uncomfortable with some of the questions in the questionnaire or interview, you may refuse to answer them. In case of accidental injury caused by the implementation of research procedures for the purpose of the study, we will

provide necessary medical measures, bear the corresponding medical expenses and provide corresponding financial compensation in accordance with relevant laws and regulations of our country.

4. Benefit

To participate in this research could optimize your mental and physical health and reduce the adverse reaction during radiotherapy is happening at the same time, your participation will help researchers to further improve the rehabilitation program, introduced the concept of early rehabilitation and practice patients with head and neck malignant tumor radiation therapy, namely in head and neck malignant tumour patients before radiotherapy standardized intervention management, in order to improve clinical outcomes. However, the effect of the intervention will vary from person to person and will be related to your completion, and we cannot guarantee that your health will improve.

5. Expenses and compensation

There will be no payment for your participation in this study. To thank you for your participation, elastic bands suitable for your physical function will be issued to you at the beginning of the intervention (3 to 6 weeks before radiotherapy in the Pre group and at the beginning of radiotherapy in the Re group). At the same time, the researchers will provide you with free reports of physical function, nutritional status, psychological status and body composition measurement. According to the evaluation results, you can get targeted recommendations. During radiotherapy, you will be monitored for changes in nutritional status and get relevant guidance. If you have significant nutritional or psychological problems, the investigator will recommend that you seek help from a nutrition or psychological clinic.

6. Inclusion and withdrawal

All interventions in this study occurred during the waiting time caused by necessary medical procedures such as positioning. If you choose not to participate in this study, you only need to continue to wait for the start of radiotherapy according to the arrangement of the radiotherapy doctor. If you have questions about exercise and nutrition, you are also welcome to consult the study site.

Participation in the study is completely voluntary. You may refuse to participate or withdraw at any time during any stage of the study without any reason, without discrimination

or retaliation, and without affecting your current and future medical treatment and rights and interests. In principle, after your withdrawal, the researcher will preserve your relevant information until its final destruction. During this period, the researcher will not continue to use or disclose the information. However, in the following rare cases, the investigator will continue to use or disclose your relevant information, even if you have withdrawn from the study or the study has been concluded. These situations include: ① removing your information will affect the scientific nature of the research results or the evaluation of data security; ② Provide limited information for the results of the study (this information will not include your name, medical record number and other personal information that can identify you). We will inform you of any information that may affect your decision to continue to participate in the study.

7. Patients protection

If you decide to participate in the study, your participation in the study and your personal data during the study will be kept confidential. During the study period, your name, gender and other personally identifiable information will be replaced by code names or numbers and will be kept strictly confidential. Without your permission, any information that can identify you will not be disclosed to members outside the study group. All study members and study stakeholders are required to keep your identity confidential. Your files will be kept securely and accessible to researchers only. The results may be published in a journal, but will not reveal any personally identifiable information about you. The information collected will be used for this study only. At any time, you may request access to your personal information and modify it if necessary.

If you agree to participate in the study, all your medical data will be reviewed by the relevant personnel of the research institute that initiated the study, the relevant authorities or by an independent ethics committee to check whether the study was conducted properly. If you sign the informed consent form, you agree to be consulted by the above person.

If you have any questions related to this study, please feel free to contact Lichuan Zhang (Tel: 19822165454), the main author of this study. If you have any questions related to the subject's own rights and interests, you can contact the Ethics Committee of Tianjin Cancer Hospital at 15022109087.

Statement of the Investigator

"I informed the subject of the background, objectives, procedures, risks, and benefits of the study, and gave him/her enough time to read the informed consent form, discuss it with others, and answer his/her questions about the study; I have informed the subject that he/she can contact Professor Lu Qian at any time if he/she has any questions related to the study, and contact the Biomedical Ethics Committee of Peking University at any time if he/she has any questions related to his/her rights and interests, and provided accurate contact information. I have informed the subject that he/she may withdraw from the study; I have informed the subject that he/she will be provided with a copy of this informed consent form containing my signature and his/her signature."

Signature of the investigator Date

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Statement of the patient

"I have been informed of the background, objectives, procedures, risks, and benefits of the study. I have had plenty of time and opportunity to ask questions, and I am satisfied with the answers. I was also told who to contact when I had questions, wanted to report difficulties, concerns, suggestions for research, or wanted to get further information or help with research. I have read this informed consent form and agree to participate in this study. I understand that I can withdraw from the study at any time during the study without any reason. I was told that I would get a copy of the informed consent form with my signature and that of the investigator."

Signature of the patient Date

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