Research Proposal

Title： To explore the effect of psychosomatic symptom intervention program on patients with differentiated thyroid cancer during the initial treatment period

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The Organizer: Harbin Medical University

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I. Research background

Thyroid cancer is the most common malignant tumor of the endocrine system, and differentiated thyroid cancer (DTC) accounts for more than 95% of thyroid cancers. The initial treatment period usually refers to the first year after a patient has received surgery, Thyroid stimulating hormone (TSH) suppression therapy, or radioiodine therapy. During this stage, patients are usually in a period of thyroid hormone disorder, which may have a variety of adverse effects. Studies have shown that patients may experience a variety of health-related problems during this stage. Most patients are not only prone to neck discomfort and pain after surgery, but also may face the risk of physical complications such as postoperative bleeding, nerve injury, hypoparathyroidism, and psychological problems such as anxiety, depression, sleep disorders, and fear of recurrence. These psychosomatic symptoms will directly or indirectly affect the patients' TSH target rate. When patients have low stress coping ability, poor self-management ability, and cannot adhere to long-term, scientific and reasonable medication, the level of thyroid hormone in the blood will be affected, which will lead to the reduction of treatment effect and quality of life, and the risk of disease recurrence may also be increased. Therefore, this study intends to design a psychosomatic symptom intervention program for patients with differentiated thyroid cancer in the initial treatment period based on the experience of psychosomatic

symptoms of patients in the initial treatment period, aiming to improve the physiological discomfort symptoms and negative psychological experience of patients in the initial treatment period, enhance the patients' self-management efficacy, and thus promote TSH suppression therapy to reach the target and physical and mental health.

Ⅱ、Study Protocol

1. Project basis

1.1 Research significance: Many scholars have studied postoperative DTC patients and found that patients with this disease have serious psychosomatic symptoms. At present, the intervention of postoperative psychosomatic symptoms of DTC patients at home and abroad mainly focuses on psychological intervention. Few scholars pay attention to the coordinated development of physical and psychological functions of DTC patients in the initial treatment period, especially the dynamic assessment of postoperative TSH level and the management of drug-induced symptoms. Psychosomatic medicine believes that while taking into account the comprehensive treatment of the disease, psychological intervention should also be used. The two aspects should be coordinated to carry out effective psychological and physiological intervention to maintain a good psychosomatic state of patients. In summary, this study was guided by stress inoculation training. The three stages of stress inoculation training (conceptualization, skill acquisition and repetition, application and completion) were used to simulate the different responses of patients under psychosomatic stress, and the intervention steps were designed. Guided by the theory

of symptom management, the psychosomatic symptoms of DTC patients in the initial treatment period were divided into physiological function management and psychological function management, and intervention measures were formulated to promote the synergistic effect of the positive development of the psychosomatic state of patients, so as to provide reference for clinical practice.

1.2 Design idea:

（1）Through literature review, qualitative research, Delphi expert letter consultation and pre-experiment, the psychosomatic symptom intervention program was constructed.

（2）A randomized controlled trial was conducted. The participants who met the inclusion criteria were randomly divided into the intervention group and the control group by block randomization method. The intervention group was intervened for psychosomatic symptoms to verify the effectiveness of the intervention program.

2. The research content and objectives of the project were analyzed

2.1 Research Content

（1）In the early stage, literature review and qualitative research were conducted to construct the psychosomatic symptoms intervention program. After that, the intervention program was modified through Delphi expert consultation and pre-experiment to form the final version of the intervention program.

（2）A randomized controlled trial was conducted to verify the effectiveness of the intervention program. Patients with DTC at the initial treatment stage were selected as the research objects, and the patients who met the inclusion criteria

were divided into the intervention group and the control group according to the block randomization method. The control group carried out routine nursing education + continuous support nursing, while the intervention group carried out routine nursing education + continuous support nursing + psychosomatic symptom intervention.

（3）The primary outcome indicator was TSH level, and the secondary outcome indicators were anxiety, depression, self-management efficacy, and shoulder joint function.

2.2 Research objectives

To verify the effectiveness of the psychosomatic symptom intervention program in patients with newly treated differentiated thyroid cancer in improving postoperative TSH, anxiety, depression, and self-management efficacy.

3. Proposed study protocol and feasibility analysis

3.1 Study Protocol:

3.1.1 Subjects: DTC patients who met the inclusion criteria in a cancer hospital in Heilongjiang Province.

Inclusion criteria: ① Differentiated thyroid cancer confirmed by pathological examination; ② Normal cognitive and language communication skills, with the ability to read and understand Chinese questionnaires; ③ able to use smart phones; ④ informed consent and voluntary participation in this study.

Exclusion criteria: ① previous history of neck and shoulder trauma (such as shoulder pain, tendinitis, tendon rupture, scapulohumeral periarthritis, or neuropathy); ② patients with severe heart, brain, lung diseases and cognitive dysfunction; ③ with

a history of serious mental illness or psychiatric disorders; ④ patients taking sleep medication or psychotherapeutic medication; And ⑤ those who had recently participated in similar interventions or were receiving other psychological interventions.

3.1.2 Benefits: all participants were reimbursements for a five-test thyroid function test and occasional small gifts.

3.1.3 Sample Size: PASS 15.0.5 software was used to calculate, Sample Size, Normal Approximation, Two-Sized, Z-Test(Unpooled) was selected, the test energy efficiency was set to 0.8, α was 0.05, N1=N2, and the effective rate of the intervention group was set to 0.8. The effective rate of the intervention group was set to 0.8, and the control group was set to 0.5, then the required sample size was 72 cases. Based on a 15% loss to follow-up rate, the required sample size was 83. To facilitate the design of block randomization in this study (1:1 group design), the block size was set to 4, so the sample size was preferably even, so at least 84 samples were required.

3.1.4 Trial procedure

Grouping: Participants were selected from the Department of Thyroid Surgery of a cancer hospital in Heilongjiang Province by convenience sampling method. Patients who met the inclusion criteria were randomly divided into intervention group and control group according to the type of surgery and BMI.

Routine nursing: 1) condition observation and vital signs monitoring; 2) Diet nursing: fasting water on the day of the operation, a small amount of water after the condition is stable, and the diet gradually changes from liquid to semi-liquid and soft food; 3) Posture: when the patient's condition was stable, he was given a

semi-recubuted position, encouraged to move in bed, and protected the neck when changing position. 4) Keep the neck drainage tube unobstructed, observe and record the drainage fluid; 5) closely observe patients' swallowing, pronunciation, incision and other conditions; 6) Prepare a tracheotomy kit beside the bed; 7) a unified health education lecture was conducted before discharge, including drug knowledge and review related precautions.

Control group: routine nursing + continuous support nursing. Contents of continuing care: after discharge, patients were provided with care through the Internet and wechat platform: ① establishing wechat group to answer patients' questions in time; ② Patients described their own recovery and condition in the group at any time, and the researchers regularly summarized the patient's condition data. ③ Using wechat public platform, push DTC disease management knowledge every week, such as the cause of the disease, treatment progress, disease recurrence, scar and postoperative home care tips.

Intervention group: routine nursing + continuous support nursing + psychosomatic symptom intervention program. Psychosomatic symptom intervention included three parts: psychological module, physiological module and psychosomatic common module. The intervention program for psychosomatic symptoms was constructed through literature review, semi-structured interview, Delphi expert consultation and pre-test before the intervention, and the program was scientific and feasible. Before the intervention, an expert group consisting of one oncology expert, one psychological expert and one nursing expert was hired to train the

intervention of patients after thyroid cancer surgery. The training method was on-site simulation teaching, and the training content included thyroid cancer related knowledge, psychological related knowledge, related intervention theories, methods and techniques used in this study. The training standards required that the intervention participants should be proficient in the knowledge of thyroid cancer and be able to use relevant theories combined with psychological practice and specific functional training. Finally, before the intervention, researchers wrote a manual for the intervention of psychosomatic symptoms in patients with DTC at the initial treatment stage.

3.1.5 Outcome measures

Main outcome measures: thyroid stimulating hormone (TSH) control rate;

The secondary outcome indicators included anxiety, depression, self-management efficacy and shoulder joint function.

3.2 Feasibility analysis

3.2.1 Preliminary Research Basis

This study was one of the sub-projects of "The psychosomatic mechanism and hospital-community collaborative management and time effect of TSH suppression treatment response in patients with postoperative differentiated thyroid cancer (DTC)" funded by the National Natural Science Foundation of China Youth Project approved in 2020.

3.2.2 Study conditions

The research site was a cancer hospital in Heilongjiang Province, which is a

third-grade class-A hospital. The thyroid surgery department has 106 standard beds and performs more than 2600 thyroid surgeries every year, ranking in the forefront of the same specialty in China. The research group has maintained a good cooperative relationship with the hospital in the early stage, which can ensure the smooth progress of the research.

3.2.3 Research Methods

The intervention program in this study was guided by stress inoculation training and symptom management theory, and the content design was feasible. A randomized controlled trial was used to intervene the psychosomatic symptoms of DTC patients in the initial treatment period, and scientific and effective statistical analysis methods were used to process and analyze the data, so as to increase the feasibility of the study and the credibility of the research results.

3.2.4 Statistical methods to be adopted

SPSS 26.0 software was used for statistical analysis. The general data and baseline characteristics were compared by independent sample t test and χ^2 test. Shapiro-Wilk's test was used to assess whether the data were normally distributed. The continuous variables conforming to normal distribution were described by mean ± standard deviation, and the measurement data not conforming to normal distribution were described by median and quartile. Two-factor repeated measures analysis of variance or generalized estimating equation were used for comparison between different groups at different time points. Main effect results were used when there was no interaction, and the simple effect of one factor was analyzed when there was

interaction. Categorical variables were described by frequency and percentage, and comparison between the two groups was χ^2 performed by test. Multiple imputation was used to account for missing data.

3.2.5 Acceptability of study subjects

Adhering to the principle of no harm and benefit, this study strives to improve the mental and physical health of patients and the quality of life of patients through the experiment, which is easy to be accepted by patients.

3.2.6 Research team

The research team of this study mainly included 1 master's tutor, 2 nursing master's students, 1 nursing staff, 1 head nurse and a clinician. The main researchers were two postgraduate students who had been fully trained in the early stage and were assisted by professional medical staff. The medical staff could fully mobilize the enthusiasm of the patients and cooperate with the researchers to complete the experiment successfully, which could effectively carry out psychosomatic intervention for the research objects.

In conclusion, the research protocol and technical route to be adopted in this project are practical and feasible.

Signature page of informed consent form

Subject Statement

The investigator has explained to me in detail the purpose of the study, the process, and the possible risks and benefits of participating in the study; I have carefully read the informed consent form, all questions have been answered to my satisfaction, and I fully understand it.

I consent to the collection and use of my health data by my researchers. I agree that the research center will have access to my data and the results of this study for scientific research purposes. I consent to the members of the Ethics Committee and the representatives of the government authorities to have access to my data under the principle of confidentiality. I understand that access to these records is necessary to ensure that the data collected from this study is true, complete and reliable.

I understand that my participation in this study is voluntary, and I can withdraw from the study at any time without affecting my subsequent legal rights and interests.

I have obtained a copy of my signed informed consent form. I did not give up any of my legal rights when I signed this consent form.

Patient signing _____ **Date** _____**Tele** _____

Signature of legal representative *_____ **Date** _____

Tele _____

Relationship with the patient _____

*** The signature of a legal representative is not required unless the subject is**

unable to read (such as illiterate or blind) or cannot sign on his or her own for some other reason.

Statement by the Investigator

I promise to strictly abide by the principles of GCP and the relevant regulations of the state and the hospital in this study, to protect the rights and interests of the subjects, and to ensure the authenticity, integrity and reliability of the research working time and research data. I agree that the research group can access the data and research results of this study for scientific research purposes.

I have fully explained the purpose of the study, the process, and the possible risks and benefits of participation, and she has received sufficient information to make a decision about participation in the study. I will provide the patient or his or her legal representative with a signed and dated copy of the informed consent form.

Investigator signing_____ **Date**_____

Tele _____