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Original Article

Progressive resistance exercise training to prevent lower-limb lymphedema after cervical cancer surgery: A feasibility study

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ABSTRACT

Objective: Radical hysterectomy with pelvic lymphadenectomy is the standard surgical treatment for early stage cervical cancer. One of the most common complications after this surgery is lower extremity lymphedema (LLL). Program of progressive resistance exercise training (PRET) is a possible way to prevent LLL for cervical cancer patients postoperatively. Before we start a randomized controlled trial to evaluate the preventive effect of PRET, we conducted this pilot study to assess the feasibility of PRET after cervical cancer surgery.

Methods: The primary purpose of the pilot study was the feasibility of PRET, as well as the satisfaction and adherence to the PRET assessed by a questionnaire. We conducted a single-arm prospective study involving cervical cancer patients who underwent radical hysterectomy with pelvic lymphadenectomy. Participants exercised twice a day for 24 weeks (two weeks of supervised in hospital and then 22 weeks of home-based training) after surgical treatment. All patients were followed up for 12 months. Information that included the limb volume, BMI, perceived difficulty level and adherence rate was collected.

Results: From February to April 2019, a total of 24 patients participated in the study. None of them dropped out. The adherence rate was more than 75% in majority of the patients, the perceived difficulty level of the PRET was high (for the first phase, the fourth phase and the fifth phase, more than half of the participants felt the intensity of the exercise appropriate), and no serious adverse events in the study were observed.

Conclusions: Exercise training was safe and feasible. The preliminary results offered us the possibility to further test the preventive effect of PRET in a full-scale randomized controlled trial.

Introduction

Globally, cervical cancer is the fourth most common cancer amongst women, ranking only after breast cancer, colorectal cancer, and lung cancer. According to the International Agency for Research on Cancer (IARC), there were approximately 600,000 cases of cervical cancer and 340,000 deaths in 2020.[1] Radical hysterectomy with pelvic lymphadenectomy is the standard surgical procedure for cervical cancer.[2] One of the most common complications that occur after this surgery was lower extremity lymphedema (LLL).[3] It is defined as a common non-curable chronic complication that results in psychological and esthetical complications that impact quality of life in women post-gynecological cancer treatment, occurring in 1–49% of survivors.[4,5]

Lower limb lymphedema occurred at a peak time of 3–6 months post-surgery.[6] It is the accumulation of high protein fluid in the interstitium due to the failure of lymphatic transport or dysfunction of interstitial protein processing,[7] leading to different negative consequences, such as skin changes, connective tissue fibrosis, loss of quality of life, or social retreat, and it manifests itself with the following symptoms in patients: swelling, pain, numbness, and limitation of movement, it affects patients physically, psychologically, and socially.[8] Hence, prevention of lymphedema has become an important issue in the care of patients who undergo lymphadenectomy.

A systematic review indicated that resistance training under proper supervision was able to reduce the risk of lymphedema and ease the symptoms.[9] Contemporary evidence, although limited, also suggests that moderate exercise under close supervision is feasible for patients with risk of lymphedema.[10,11] For instance, resistive exercise has been found to be beneficial in the treatment of lymphedema when used as an adjunct to compression therapy, result to an increase of muscular power and

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tension, stimulated pumping of the venous and lymphatic fluids, and the sympathetic nerves to contract the lymphatic vessels,[12] ultimately influenced lymphatic flow and reduced the risk of lymphedema.[13]

However, researches on progressive resistance exercise training (PRET) mainly focus on the upper limb function exercise of breast cancer patients,[14–16] the application of PRET to lower limb has not been reported. In addition, some PRET reported in literature was limited by the place of implementation and professional resistance exercise equipments. For example, Andre'e Dionne's aquatic exercise intervention involves yoga exercises, aqua-jogging, and pedaling on a water bike;[17] Katz asked patients to do the weight training with variable resistance machines.[18] All these exercises may not feasible for those patients who living in rural areas of China. To address this gap in the literature, we created a set of PRET which was not restricted by equipments and exercising area, and may fir for most patients with cervical cancer in China. The ultimate purpose will be evaluating the preventive effect against LLL of this PRET in post-operative cervical cancer patients. However, before we conduct a prospective randomize controlled trial to prove that, we conducted this pilot study to assess the feasibility and acceptability of the PRET in patients with cervical cancer. Also, this would lay a foundation for further prospective randomized controlled trials.

Methods

Participants, recruitment, and design

From 9th February to 1st April 2019, a total of 186 cervical cancer patients were treated in our department. However, the patients in our study were enrolled voluntarily. We explained our criteria to the eligible patients and stressed that this study would last six months. Finally, 33 patients signed informed consent to participate in the study. Among them, three participants were ineligible due to unavailable to measure the limb volume in hospital each month and two patients had history of lymphedema. The remaining 28 participants were invited and 24 accepted participation in this study. The inclusion criteria were: women aged from 30 to 80; after radical hysterectomy and pelvic lymphadenectomy for cervical cancer; available to measure the limb volume in hospital each month. The exclusion criteria were: patients living alone; extensive metastasis of distant organs; history of lymphedema. Adverse events during practicing PRET, for instance, muscle strain, fall down, fracture and so on were carefully recorded.

Sample size

The sample size was calculated by the single stage phase II clinical trials module using software Power Analysis and Sample Size (PASS 15, NCSs, LLC. Kaysville, Utah, USA, 2017). Final result showed that 23 samples were needed for calculation. If 15 adverse events occurred, the trial would be terminated immediately due to poor performance. Finally, 24 cases were included in this study (Figure 1).

Ethical considerations

This study was approved by the Ethical Committee of the FUSCC (ID: 1801180-11). All participants signed informed consent before entering the study.

PRET

This PRET was originally designed with the purpose to prevent lower limb lymphedema after pelvic lymphadenectomy, based on the characteristics of abdominal wound healing, the anatomy of the lower limb lymphatic circumfluence and the adjacent lymph nodes.[19–22]

The PRET was designed by an expert group composed of four persons (Zhu Hongmei, Ph.D. of sports rehabilitation medicine, Chinese University of Hong Kong; Lu Li, associate professor from Shanghai Sport University; Xiaohua Wu, chair of the department of gynecological oncology, FUSCC; Yaqiong Chen, chief nurse of the department of gynecological oncology, FUSCC). The expert argumentation towards the PRET was carried out in four aspects: safety, scientificity, feasibility, and applicability. Professor Lu Li recorded the PRET teaching video for patients education. The set of PRET was authorized as an utility model patent by Intellectual Property Office of China (2018-L-00658606).

The PRET was divided into five phases: 1–7 days after surgery (phase I), 8–14 days after surgery (phase II), 15–30 days after surgery (phase III), 31–60 days after surgery (phase IV), and 61–180 days after surgery (phase V) (Supplementary).

During the first month after surgery, participants were instructed to do this exercise in a supine position. One month after surgery, the participants were asked to do this exercise in a standing position. And from day 61, patients began to do resistance training of lower limbs with 10 kg elastic bandage in the standing position. For the first three phases (within one month after surgery), each took 20–25 min to complete. For the last two phases (one month after surgery), each exercise consisted of a 10 min of warm-up and 10 min of relaxation. It took 40 min in total.

Interventions

An educational booklet was issued to all participators. Patients were required to record the information of their daily exercise after they are discharged home. The contents of the education include: behaviors that should be avoided in the prevention of lymphedema, signs of infection, risk factors, nutrition.[23] The causes, signs and symptoms of lower extremity lymphedema, the symptoms of lower extremity lymphedema, how to self-monitor after the surgery and the way to report in time. The study also needs to ensure that each patient will measure the leg circumference by themselves or their relatives.

After the health education, we instruct the patient to do the PRET. Normally, patients were discharged home 14 days after surgery. They underwent exercise under supervision in hospital for the first two weeks and then practiced at home by themselves after they were discharged.

In hospital, we urged patients to exercise regularly, checked the action, and asked the main caregivers of each patient to learn how to measure the leg circumference. The main caregivers were usually patients' relatives and they were asked to report the change of leg circumference in time. Meanwhile, we emphasized the importance of preventing lymphedema and made patients to understand the possible causes, symptoms and signs of LLL. During this period, we taught them to

Two-Stage Phase II Clinical Trials

Possible Designs For P0=0.500, P1=0.750, Alpha=0.050, Beta=0.200

N1	R1	PET	N	R	Ave N	Alpha	Beta	Constrains Satisfied
23	15	0.000	23	15	23.00	0.047	0.196	Single Stage
14	7	0.605	23	15	17.56	0.046	0.198	Minimax
11	6	0.726	25	16	14.84	0.046	0.199	Optimum

Calculated by sofeware PASS 15, NCSs, LLC. Kaysville, Utah, USA, 2017

Figure 1. Sample size calculation. Calculated by software PASS 15, NCSs, LLC. Kaysville, Utah, USA, 2017.

record the training dairy and gradually developed a good nurse patient relationship.

After patients were discharged home, each of them were asked to set an exercise alarm to ensure regular exercise. We established a wechat group (a message app which allows multiple people to communicate through mobile phone) and constantly released education knowledge of LLL. In this way, patients can communicate with each other and medical staff any time they need.

Measures

Demographic characteristics

The socio-demographic and clinical characteristics of the patients were examined with electronic medical history of inpatients in our hospital.

Physical measures

Utilizing circumferential assessments was the usual way to calculate limb volume. The approach took readings at regular intervals along the limb and used a mathematical formula to calculate total volume. Circumference measurement began at the ankle level and continued every 10 cm for 60 cm. The shape of the lower limb being measured was simplified to six cylinders. If the actual limb volume was greater than 110% of its preoperative volume, lymphedema would be diagnosed.[24] The way to calculate the total volume (V) is to take the sum volume of all 10 cm cylinders, that is[25]: $V = \frac{(C+C+C+C+C+C+C)}{\pi}$, a lower limb with eight circumference readings. Here, C1 is the circumference at the metatarsophalangeal joint; C2 means the circumference of the ankle level, from C3 to C6 means the circumference every 10 cm along the lower limb. π is a constant, approximately 3.14159. Volumes are given in cm3. It took about 5 min to complete the limb volume measurements. All measurements were performed by certified lymphedema therapists. Volume of bilateral lower limb was measured among 1M, 2M, 3M, 4M, 5M, 6M, and 12M after surgery.

Body mass index (BMI) (kg/m^2) was calculated from self-reported data of height and weight.

Lymphedema-related symptoms

The Gynecologic Cancer Lymphedema Questionnaire (GCLQ) was used to assess symptoms associated with LLL. The GCLQ is a validated self-report measure that assesses seven domains of symptoms in both lower extremities. The seven domains include heaviness, general swelling, limb related swelling, infection, aching, numbness, and physical function. Participants reporting $\geq$ four symptoms of the lower extremities within the seven above-listed domains were classified as having LLL.[26] It took about 5–10 min to complete the study survey.

GCLQ can effectively distinguish gynecologic cancer patients with or without LLL. Cronbach's alpha was 0.95, kappa value was 0.759, and sensitivity and specificity of $\geq$ 4 were 86% and 83.33%, respectively. When kappa value was 0.758, the sensitivity and specificity of $\geq$ 5 were 85.71% and 90.00%. By this way, we can distinguish patients with or without lymphedema.[26]

Feasibility measure

Due to the feasibility of evaluating the small sample size, no statistical test was carried out. If no serious adverse effects were registered, or participants were satisfied with the program and adherence to the intervention was at least acceptable, then the exercise plan was considered feasible.

Likert five-level scoring method was used to assess perceived difficulty level after each phase of the PRET when participants scored various aspects of the test and intervention. The five levels were: 1 = very light, 2 = fairly light, 3 = medium, 4 = hard, 5 = very hard. At the end of each phase, the ratings of perceived difficulty level were carefully inquiry and record.

Intervention adherence was determined by calculating the average number of exercise sessions per month (exercise sessions/month = 30 days × 2 sessions/day, 60 sessions/month = 100%) and was divided into high (greater than 75% per month), acceptable (50%–75% per month) and low (less than 50% per month).

Training dairy, physical data (heart rate during exercise and the number of footsteps obtained by an electronic bracelet), special sports like yoga, swimming, and Taiji etc. were recorded daily (Figure 2).

Data analysis

Data analysis was performed using Statistical Package for Social Science SPSS 18. Kolmogrov–Smirnov test was used for all the quantitative variables. For those who met the criteria of normal distribution, we used mean ± SD to describe the data while for those who didn't, we used median (range) to describe the data. We reported the point prevalence of lymphedema at 24 weeks and used two diagrams to describe the change of each lower limb over time.

Results

Demographic characteristics

Eventually, 24 cervical cancer patients after radical hysterectomy and pelvic lymphadenectomy were voluntarily participated in the feasibility study. The median age at baseline of the 24 patients was 48.50 (38–75) years old. The median BMI was 23.83 (19.98–30.43) kg/m^2 at the beginning. 2.75% of the participants had the habit of sitting for more than 2 h per day. Lymph node metastasis was found in six patients, but none of them had distant metastasis. Thirteen participants received postoperative radiotherapy (Table 1).

Perceived difficulty level

We assessed perceived difficulty level by Likert 5-level scoring method after each phase of the PRET. As a result, 70.83% of patients felt the 1–7 days phase very light, 62.50% and 79.17% of patients felt that the last two phases were very light respectively. Compared with these three very light phase, 15–30 days phase is relatively balanced (Table 2).

Adherence rate

All participants were highly compliant with the adherence to supervised exercise (the first two weeks after the operation), however, the last two weeks of the first month, three participants were “acceptable” to insist on home-based exercise. Only in the second and fourth month, the compliance of one patient was lower, and the compliance rate of most patients was more than 75% (Table 3).

GCLQ score

The GCLQ scores were followed up every month after surgery. In the first month after surgery, majority of the patients complained of lower limb discomfort, mainly focus on tenderness 8 (33.33%) and heaviness 8 (33.33%). The median GCLQ score of the first month was 2.5 (0–7). However, as time went by, the lymphedema-related symptoms gradually relieved. But for some patients, symptoms of numbness may persist for years after surgery (Table 4).

Lower limb volume

The changes of lower limb volume were shown in Figure 3A and B. Compared with the baseline data, the leg volume of all patients

Table 1
Baseline characteristics of participants.

Characteristics	Mean (SD)/*n* (%)/ Median (range)
n	24
Sociodemographic and physical profile	
Age, Median (range)	48.50 (38–75)
BMI, Mean (range), kg/m^2	23.83 (19.98–30.43)
Education[a]	
Higher	4 (16.67)
Medium	6 (25.00)
Short	13 (54.17)
Illiteracy	1 (4.17)
Sitting for more than 2 h per day	
Yes	18 (75.00)
No	6 (25.00)
Living arrangement	
Living with partner	23 (95.83)
Living alone	1 (4.17)
Medical and surgical profile	
Stage	
IB1	10 (41.67)
IB2	3 (12.50)
IIa1	10 (41.67)
IIa2	1 (4.17)
Pathologic types	
Squamous cell carcinomas	17 (70.83)
Non-squamous cell carcinomas	7 (29.17)
LNs metastasis	
Yes	6 (25.00)
No	18 (75.00)
No. of lymph nodes resected, Mean (SD)	24.67 (8.12)
Duration of operation (h), Median (range)	1.5 (1–3)
Intraoperative blood loss (ml), Median (range)	200 (50–600)
Total amount of peritoneal drainage (ml), Median (range)	735 (0–1500)
Time of extubation of abdominal drainage tube (days), Median (range)	6 (5–15)
No. of postoperative radiotherapy	13 (54.17)
Time of postoperative radiotherapy (days), Median (range)	35 (0–79)
Postoperative radiotherapy times, Median (range)	25 (0–28)
Dose of postoperative radiotherapy, Median (range)	4500 (0–5040)

BMI: body mass index; LNs: lymph nodes.
[a] Education: higher:graduate; Medium: vocational/undergraduate; Short: mandatory school only.

Table 2
Perceived difficulty level at each phase of the PRET.

Perceived difficulty level	No.1 *n* (%)	No.2 *n* (%)	No.3 *n* (%)	No.4 *n* (%)	No.5 *n* (%)
Very light	17 (70.83)	11 (45.83)	8 (33.33)	15 (62.50)	19 (79.17)
Fairly light	6 (25.00)	10 (41.67)	5 (20.83)	6 (25.00)	4 (16.67)
Somewhat hard	0	2 (8.33)	10 (41.67)	3 (12.50)	1 (4.17)
Hard	1 (4.17)	1 (4.17)	1 (4.17)	0	0
Very hard	0	0	0	0	0
Total Number	24 (100.00)	24 (100.00)	24 (100.00)	24 (100.00)	24 (100.00)

PRET, progressive resistance exercise training.

Table 3
Adherence rate at each month of the PRET.

Training adherence	1M *n* (%)	2M *n* (%)	3M *n* (%)	4M *n* (%)	5M *n* (%)	6M *n* (%)
< 50%	0	1 (4.17)	0	1 (4.17)	0	0
50%–75%	3 (12.50)	1 (4.17)	2 (8.33)	2 (8.33)	1 (4.17)	1 (4.17)
> 75%	21 (87.50)	22 (91.67)	22 (91.67)	21 (87.50)	23 (95.83)	23 (95.83)

PRET, progressive resistance exercise training.

decreased significantly on the first month after surgery, and then maintained in a relatively stable level. One of the 24 patients had subjective and objective symptoms of lymphedema on day 188 after surgery (Figure 3A and B).

Discussion

In this study, we assessed the feasibility of recruiting cervical cancer patients after radical hysterectomy and pelvic lymphadenectomy into the PRET intervention study. The purpose of the pilot study was to determine the feasibility, acceptability and safety of the PRET intervention.

Gynaecological cancers represent 16.3% of total malignant diseases, cervical cancer, ovarian cancer, and endometrial cancer being the most common.[27] However, radical hysterectomy and pelvic lymphadenectomy was the standard surgical treatment for cervical cancer, while not all patients with ovarian cancer or endometrial cancer underwent lymphadenectomy. Lower limb lymphedema (LLL) represents one of the most common complications after pelvic lymphadenectomy. PRET has been proved to be effective in preventing upper limb lymphedema in breast cancer treatment,[16,28,29] but the research on PRET against LLL in cervical cancer was very much limited. We would like to conduct clinical trials, evaluating the preventive effect of PRET against LLL in cervical cancer patients postoperatively. However, there was no existing PRET exercise, which was unrestricted by equipment and area, and suitable for Chinese patients. Thus, we designed a set of PRET, and conducted this pilot study to determine the feasibility and safety in cervical cancer patients postoperatively.

The intensity of the exercise (PRET) was critical. The self-designed PRET should be scientific, and by the same time acceptable to patients. The oldest patient in this study was 75 years old. During the exercise, most patients thought that the level of perception difficulty was very light. It was undeniable that this was an affirmation of the safety of PRET. How to balance exercise intensity in different patients, as a 52 year old patient's training diary shows, the number of steps in the first week is 83, while the number of steps in the first week of another 40 year old patient was 20,000. Dionne et al.[17] suggested that an aquatic exercise intervention of moderate to vigorous intensity using short duration intervals was conducted twice a week. The 45-min circuit training session consisted of yoga exercises, aqua-jogging, and pedaling on a water bike. Muscular exercises were performed on an aqua step and a trampoline to stimulate muscle pumps of feet and ankles and play a fundamental role in the management of edema of the lower limbs by stimulating reabsorption of fluid and venous hemodynamics, which was the same as the principle of PRET. Katz[18] suggest that weight training should be given. Participants received instruction in performance of warm-up, stretching, diaphragmatic breathing, weight training, and additional stretching exercises. Twelve weight-training exercises were performed using variable resistance machines, free weights, and ankle weights. The exercises included seated row, chest, press, lateral raises, bicep curls, triceps pushdowns, leg press, leg extension, leg curl, hip flexion, leg abduction, prone, straight leg lifts, and calf raises. There may be more effective exercise methods and auxiliary equipment to prevent lymphedema of lower limbs, but in terms of feasibility and acceptance, PRET is more suitable for Chinese patients with cervical cancer, especially in rural area of China.

Patients' adherence to the exercise was the most difficult part of the study. PRET requires patients to start on the first day after surgery. By that time, abdominal drainage tube and catheter, wound pain, nausea, and dizziness made patients extremely uncomfortable. As a result, the adherence rate of the first month after surgery was lower than that of the following months. Even though, 87.5% (21/24) of the patients achieved high rate of intervention adherence (high adherence rate was defined as more than 75%) during the first month after surgery. The high adherence rate in our study might relate to the following points: Firstly, improving the cognition of postoperative lymphedema in patients with cervical

Table 4
The 12-month follow-up for LLL-related symptom.

LLL-related symptom	1M *n* (%)	2M *n* (%)	3M *n* (%)	4M *n* (%)	5M *n* (%)	6M *n* (%)	12M *n* (%)	Total *n* (%)
Limited movement of hip	2 (8.33)	0	0	1 (4.17)	0	0	0	3 (12.50)
Limited movement of knee	0	1 (4.17)	0	0	0	0	0	1 (4.17)
Limited movement of ankle	0	1 (4.17)	0	0	0	0	0	1 (4.17)
Limited movement of foot	0	0	0	0	0	0	0	0
Limited movement of toes	0	0	0	0	0	0	0	0
Leg or foot feel weak	4 (16.67)	5 (20.83)	2 (8.33)	2 (8.33)	1 (4.17)	0	2 (8.33)	16 (66.67)
Tenderness	8 (33.33)	3 (12.50)	3 (12.50)	2 (8.33)	0	0	3 (12.50)	19 (79.17)
Swelling	6 (25.00)	3 (12.50)	2 (8.33)	0	0	1 (4.17)	1 (4.17)	13 (54.17)
Swelling with pitting	0	0	0	0	0	0	1 (4.17)	1 (4.17)
Redness	0	0	0	0	0	0	0	0
Blistering	2 (8.33)	3 (12.50)	0	1 (4.17)	0	0	1 (4.17)	7 (29.17)
Tightness	2 (8.33)	1 (4.17)	0	1 (4.17)	1 (4.17)	0	1 (4.17)	6 (25.00)
Increased temperature	5 (20.83)	3 (12.50)	0	2 (8.33)	0	0	2 (8.33)	12 (50.00)
Heaviness	8 (33.33)	6 (25.00)	2 (8.33)	0	1 (4.17)	2 (8.33)	0	19 (79.17)
Numbness	2 (8.33)	2 (8.33)	5 (20.83)	2 (8.33)	4 (16.67)	2 (8.33)	1 (4.17)	18 (75.00)
Stiffness	3 (12.50)	3 (12.50)	0	1 (4.17)	0	0	2 (8.33)	9 (37.50)
Aching	1 (4.17)	1 (4.17)	1 (4.17)	1 (4.17)	0	0	1 (4.17)	5 (20.83)
Hip swelling	3 (12.50)	2 (8.33)	0	0	0	0	0	5 (20.83)
Groin swelling	0	1 (4.17)	2 (8.33)	1 (4.17)	0	0	0	4 (16.67)
Median (range)	2.5 (0–7)	1 (0–8)	0 (0–4)	0 (0–3)	0 (0–2)	0 (0–2)	0 (0–6)	

LLL, lower limb lymphedema.

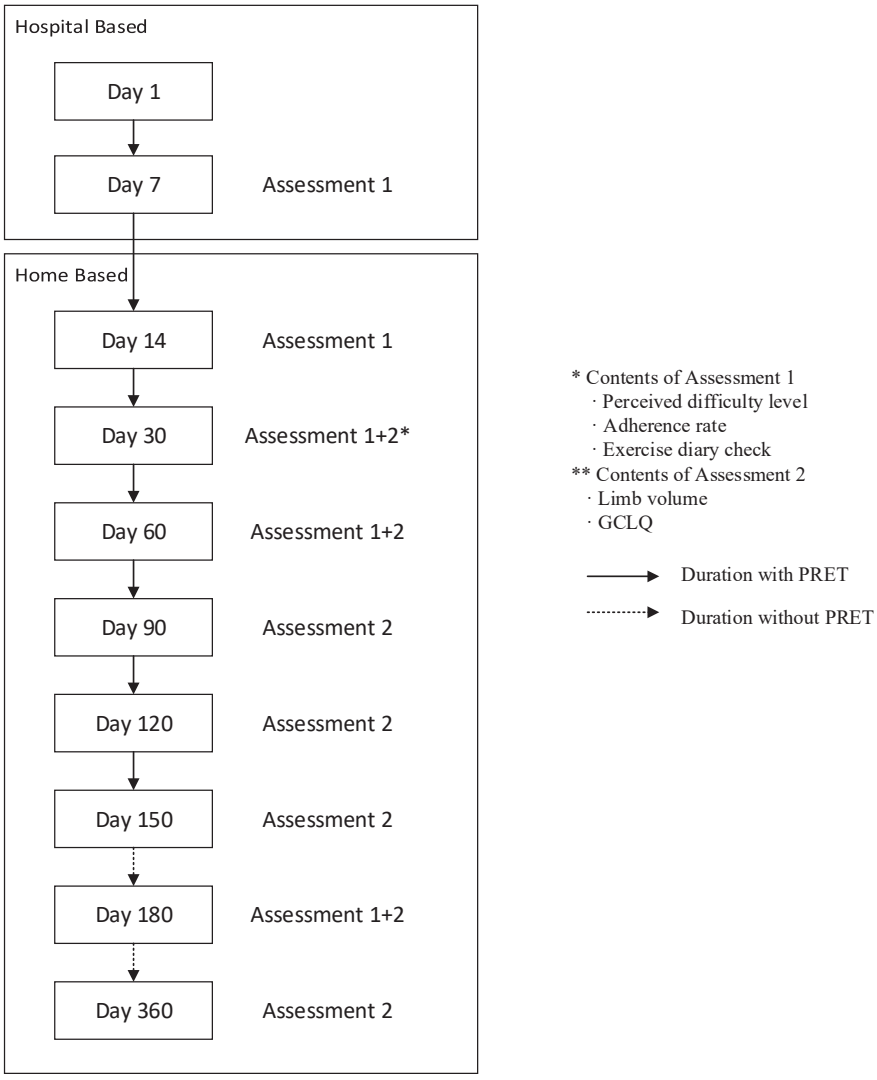

Figure 2. Flow chart of intervention and follow-up. PRET, progressive resistance exercise training; GCLQ, Gynecologic Cancer Lymphedema Questionnaire.

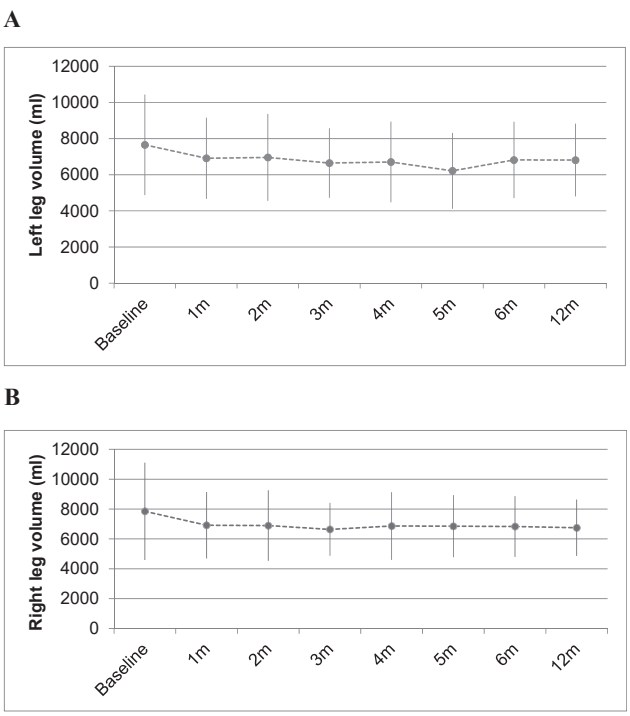

Figure 3. (A) The 12-month follow-up for the left leg volume. (B) The 12-month follow-up for the right leg volume.

cancer. There was an education booklet issued to patients in our department, describing the possible causes, the symptoms and signs of lymphedema. The understanding of the importance and benefits of preventing lymphedema helped to increase patients' adherence to the exercise. In our study, patients were required to record the information of their daily exercise after they were discharged home. They were also educated to self-monitor and report in time. The study also required each patient to measure the leg circumference by themselves or their relatives at home. Secondly, patients were willing to share their symptoms with us in time after discharged home once a good nurse–patient relationship was established during hospitalization. Patients regarded the PRET safe and important, and they completed it conscientiously. A good relationship between patients and medical staff could help to improve the adherence, which is consistent with the finding of Ida Åkerlund's study.[30] Last but not the least, we have set up a wechat group to encourage people with peer support, communicate frequently is the guarantee of high adherence rate of home-based exercise after discharge, and this way was also referred by Souliotis.[31]

Although the primary purpose of the study was to investigate the feasibility and safety of the PRET, we obtained some results regarding the prevention efficiency. One month after surgery, there was no difference in BMI, but the leg volume of all patients decreased almost as much as the baseline data, and what's more, there were symptoms related to lymphedema, mainly tenderness and heaviness, as time went on, the leg volume maintains relatively stable, but the lymphedema symptom (tenderness and heaviness) gradually reversed. This may be due to the fact that resistance exercise helps to enhance muscle strength and stimulant muscle pumping venous and lymphatic reflux.[32]

According to the literature, it is reported that LLL mostly occur within two years after surgery, and the most common median (range) onset time is 4 (1–11) months,[4,33] during the first 12-month follow-up, only one participant developed lymphedema. The incidence rate of lymphedema was 4.2% (1/24) in our study, compared to the incidence of 20–50% reported in literature.[4–6,27,28,34] Regarding the patient who developed LLL 188 days after surgery, it is critical to distinguish whether it was a result of PRET or caused by cancer treatment. However, the patient already completed the study and no longer practicing the exercise when she developed lymphedema. Since the development time in this case was in accordance with the peak onset of lymphedema, we believed the onset of lymphedema was the complication after surgery, rather than the consequences of PRET. We instructed the patient to keep doing PRET every day, increasing the time of raising the left lower limb. The lymphedema faded after 12 days and the symptoms related to lymphedema were improved.

Amendments

Minor amendments of the protocol to the future trial were made, and the attention was drawn to possible problems based on experiences with the present study. According to the assessment results of patients' satisfaction with the program, and considering the compliance of patients, we appropriately enhanced the intensity of the 5th and 6th phase to reach the level of “fairly light” or even the level of “somewhat hard” A weakness of the intervention is that we only focus on one aspect of the preventive effect on the lower limb lymphedema, namely the degree of leg circumference reduction, the time of occurrence and the incidence rate. However, some participants indicated that when the lymphedema occurs, they hope that the systematic treatment could be available in cancer centers, in addition, according to the rehabilitation experience of the patient who had presented lymphedema, PRET seems to help lymphedema, but it still needs to be confirmed in the randomized controlled trial (RCT).

Limitations

This was a pilot study with a small sample. The primary purpose was feasibility and safety evaluation. This was also a single-tertiary cancer center-based study. Before the results could be generalized to the population of women with cervical cancer in China, Further researches are needed.

Future perspectives

This feasibility study was a prospective single group study conducted prior to a RCT. After the original designed PRET was proved safe and feasible, we will conduct a large sample, prospective, multicenter randomized trial to verify the effect of PRET in the prevention of lower extremity lymphedema after cervical cancer surgery. The further RCT study was already registered online (ChiCTR1800014905).

Conclusions

In conclusion, the originally designed PRET in cervical cancer patients postoperatively was feasible and acceptable. This PRET was not restricted by equipment and area, and was suitable for most cervical cancer patients in China to carry out post-operatively. No serious adverse events were observed and the safety of the PRET intervention was proved. Based on the findings of this pilot study, a prospective, randomized clinical trial with large sample will be carried out to verify the preventive effect of PRET against LLL in cervical cancer patients in near future.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the Asia-Pacific Journal of Oncology Nursing at https://doi.org/10.1016/j.apjon.2021.12.002.

Declaration of competing interest

None declared.

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