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Original Article

Preventing lower limb lymphedema after pelvic lymphadenectomy with progressive resistance exercise training: A randomized controlled trial

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ABSTRACT

Objective: This study aimed to assess the efficacy of a self-designed progressive resistance exercise training program for preventing the development of lower limb lymphedema.
Methods: An open-label randomized controlled trial was conducted in patients who underwent radical surgery for cervical cancer treatment in our department between October 7, 2019, and October 7, 2021. The participants were randomly assigned to one of three groups: progressive resistance exercise training, graduated compression stocking, and control group.
Results: A total of 267 patients were enrolled (89 in each group). The incidence of lower limb lymphedema was 9.0% ($n = 8$) in the progressive resistance exercise training group, 28.1% ($n = 25$) in the graduated compression stocking group, and 42.7% ($n = 38$) in the control group. Over the 2-year follow-up period, the risk of lower limb lymphedema was significantly lower in the progressive resistance exercise training group than in the control group, with a hazard ratio (HR) (95% confidence interval [CI]) of 0.156 (0.073–0.335). The study was underpowered to demonstrate a statistically significant reduction in risk in the graduated compression stocking group, with an HR (95% CI) of 0.624 (0.376–1.033).
Conclusions: Progressive resistance exercise training is an effective strategy for preventing lower limb lymphedema after pelvic lymphadenectomy for cervical cancer. It imposes no additional economic burden and can be performed conveniently without the need for dedicated exercise facilities. This makes it particularly accessible to patients in developing countries, allowing them to exercise at their convenience.
Trial registration: ChiCTR1800014905.

Introduction

Cervical cancer poses a significant global health challenge, particularly for women. It is the fourth most prevalent cancer among women worldwide, with approximately 85% of cases concentrated in developing nations. Cervical cancer is a prominent contributor to cancer-related fatalities in women living in these regions.[1] In early-stage cervical cancer treatment, radical hysterectomy combined with bilateral pelvic lymphadenectomy is the preferred approach, particularly when fertility preservation is not a priority.[2,3] Nevertheless, a prevalent postoperative complication associated with this procedure is lower limb lymphedema (LLL).[4]

The incidence of LLL after radical surgery for cervical cancer varies from 1.2% to 47.6%,[5–7] whereas the incidence of LLL in our center was 32.06%. The occurrence of LLL can be attributed to multiple factors, including cancer staging, surgical and radiological treatments, and other risk factors.[8,9] LLL occurs at a peak time of 3–6 months postoperatively[9,10] and is attributed to the accumulation of high-protein fluid in the interstitium due to the failure of lymphatic transport or dysfunction of interstitial protein processing.[11] Swelling is caused by the accumulation of excess water in the extracellular space, filtered or diffused plasma proteins in extravascular blood cells, and parenchymal stromal cell products. Failure to control lymphedema may lead to repeated cellulitis and lymphangitis, progressive elephantine trophic changes in

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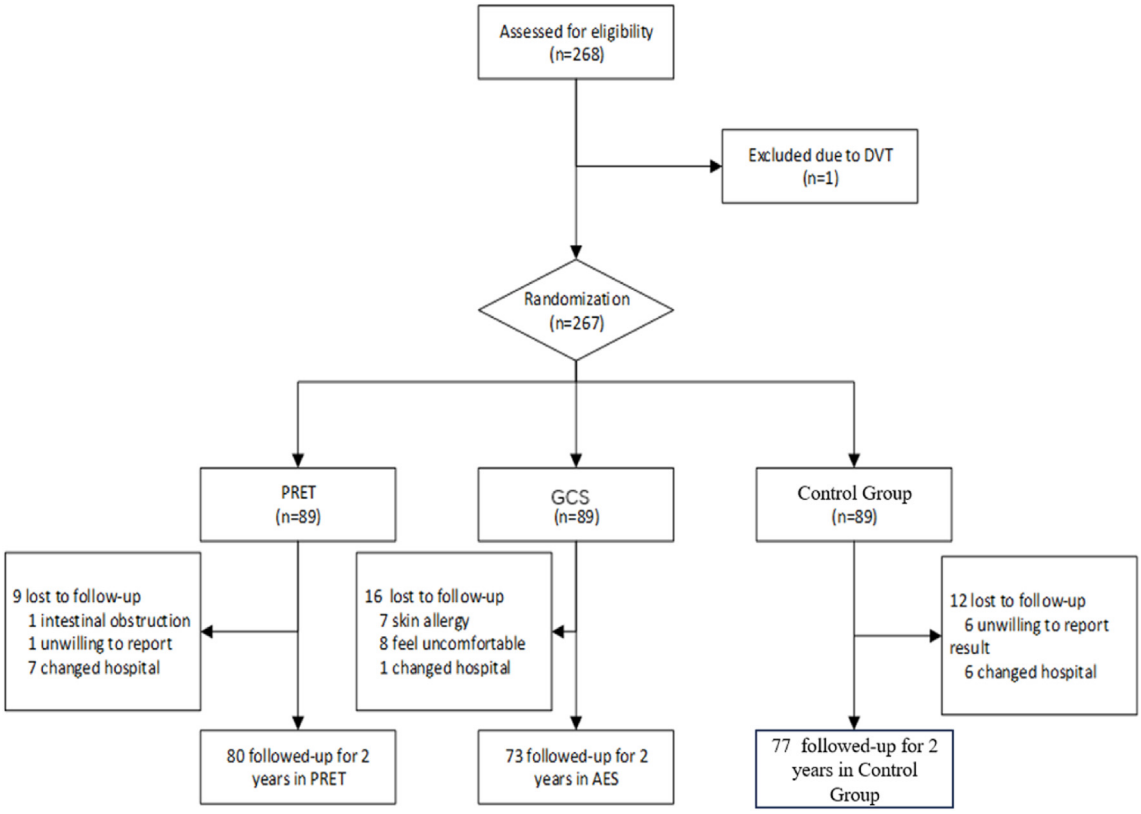

Fig. 1. Flow chart. DVT, deep venous thrombosis; PRET, progressive resistance exercise training; GCS, graduated compression stockings; AEs, adverse events.

the skin, and crippling invalidism. On rare occasions, the development of lymphangiosarcoma, widely known as Stewart–Treves syndrome,[12] can affect patients physically, psychologically, and socially. Moreover, LLL is difficult to cure, and therefore, the prevention of lymphedema has become an important issue in the care of patients who undergo lymphadenectomy.

Clinically, the method used to prevent lymphedema after radical hysterectomy is the use of graduated compression stockings (GCS) placed on the lower legs. These are generally available over the counter and are cost-effective. The function of GCS depends on the pressure exerted, the gradient of decreasing pressure from distal to proximal, and muscle activity.[13]

The mechanism of action of GCS involves intermittent pumping or compression during muscle activity, leading to a reduction in the risk of lymphedema.[14] Stockings exert constant pressure on the tissues, resting pressure, and pressure during muscle activity.[15] However, if stockings are folded while fitting patients, the pressure increases, making them more difficult to fit.[16] GCS stockings are made of nonbreathable yarns; therefore, patient compliance with compression therapy[17] may be affected by weather and temperature.

A systematic review indicated that resistance training under proper supervision could help to reduce the risk of lymphedema and ease its symptoms if it occurs.[18] However, research on progressive resistance exercise training (PRET) has mainly focused on upper limb function exercises in patients with breast cancer[19–21], and PRET designed for the upper limbs is inappropriate for lymphadenopathy of the lower limbs. In addition, some PRET programs reported in the literature were limited by their place of implementation and need for professional resistance exercise equipment. For example, Dionne's[22] aquatic exercise intervention involved yoga exercises, aqua-jogging, and pedaling on a water bike, and Katz[23] had patients perform weight training with variable resistance machines. These exercises may not be feasible for patients living in the rural areas of China. To address this gap in the literature, we created a PRET program that was not restricted by the need for special equipment or a dedicated exercise area so as to be accessible to most patients with cervical cancer in China. Our previous studies support the feasibility and safety of PRET for the prevention of LLL after radical pelvic lymphadenectomy for cervical cancer.[24] Therefore, we launched this randomized controlled trial (RCT) to evaluate the effectiveness of a self-designed PRET program in preventing the occurrence of LLL.

Methods

Study participants, recruitment, and randomization

An open-label randomized controlled trial was conducted on patients who underwent radical surgery for the treatment of cervical cancer in our department between October 7, 2019, and October 7, 2021. The primary objective of this study was to identify the effectiveness of a self-designed PRET program in preventing the occurrence of LLL.

The inclusion criteria were as follows: women aged 30–80 years, who were treated with radical hysterectomy and pelvic lymphadenectomy for cervical cancer, and were available to have their limb volume measured at the hospital each month. The exclusion criteria were living alone, extensive metastasis to distant organs, history of lymphedema, and deep venous thrombosis (DVT).

Adverse events that occurred during the PRET, including muscle strain, falls, and fractures, were carefully recorded.

Cluster randomization was applied, and each ward was considered a cluster. Participants were randomized into one of three groups: (1) Progressive resistance exercise training group (PRET group). (2) Graduated compression stocking group (GCS group). (3) Control group.

Sample size

Sample size was calculated using the log-rank module with Power Analysis and Sample Size software (PASS 15; NCSs, LLC. Kaysville, Utah, USA, 2017). The 2-year incidence of LLL in our center was 32%, equaling a 2-year LLL-free survival rate of 68%. The intervention was estimated to reduce the risk of developing LLL by 70% (hazard ratio [HR] = 0.3). After

Table 1
Baseline characteristic of participants.

Characteristics	PRET ($n = 89$)	GCS ($n = 89$)	Control group ($n = 89$)	χ^2/F	P
Age (years), median (range)	48 (29–78)	50 (27–77)	52 (29–79)	3.001	0.051
BMI (kg/m^2), mean ± SD	22.91 ± 3.29	23.14 ± 2.96	23.29 ± 3.67	0.308	0.735
Preoperative serum albumin level (g/dL), mean ±SD	42.99 ± 6.92	44.33 ± 7.27	43.66 ± 6.69	0.820	0.442
Preoperative DDI level (μg/mL), mean ± SD	0.48 ± 0.40	0.46 ± 0.28	0.55 ± 0.63	0.841	0.432
Duration of operation (h), mean ± SD	1.63 ± 0.68	1.74 ± 0.60	1.71 ± 0.60	0.647	0.524
Intraoperative blood loss (mL), mean ± SD	195.17 ± 164.90	198.88 ± 178.05	196.63 ± 154.81	0.011	0.989
Total amount of peritoneal drainage (mL), mean ± SD	781.69 ± 563.85	782.25 ± 1140.29	685.84 ± 421.44	0.458	0.633
No. of lymph nodes resected, mean ± SD	23.61 ± 6.91	24.81 ± 10.57	23.89 ± 8.44	0.458	0.633
Education, *n* (%)				3.780	0.437
Higher	53 (59.6)	58 (65.2)	63 (70.8)		
Medium	21 (23.6)	19 (21.3)	12 (13.5)		
Short	15 (16.9)	12 (13.5)	14 (15.7)		
Marital status, *n* (%)				8.645	0.071
Married	83 (93.3)	72 (80.9)	73 (82.0)		
Widowed	6 (6.7)	14 (15.7)	15 (16.9)		
Divorced	0 (0.0)	3 (3.4)	1 (1.1)		
Tumor size, *n* (%)				1.170	0.557
< 4 cm	49 (55.1)	47 (52.8)	42 (47.2)		
> 4 cm	40 (44.9)	42 (47.2)	47 (52.8)		
Hypertension, *n* (%)				1.348	0.510
Yes	15 (16.9)	10 (11.2)	11 (12.4)		
No	74 (83.1)	79 (88.8)	78 (87.6)		
Diabetes, *n* (%)				0.831	0.660
Yes	4 (4.5)	4 (4.5)	2 (2.2)		
No	85 (95.5)	85 (95.5)	87 (97.8)		
The Autar deep vein thrombosis scale, *n* (%)				5.043	0.283
Low risk	37 (41.6)	26 (29.2)	28 (31.5)		
Medium risk	52 (58.4)	61 (68.5)	59 (66.3)		
High risk	0 (0.0)	2 (2.2)	2 (2.2)		
Chemotherapy, *n* (%)				1.964	0.375
Yes	46 (51.7)	54 (60.7)	54 (60.7)		
No	43 (48.3)	35 (39.3)	35 (39.3)		
Radiotherapy, *n* (%)				1.295	0.523
Yes	46 (51.7)	45 (50.6)	52 (58.4)		
No	43 (48.3)	44 (49.4)	37 (41.6)		

DDI, D-Dimer; BMI, body mass index; LNs, lymph nodes.
Education: higher; graduate; Medium: vocational/undergraduate; Short: mandatory school only.

the calculation, 80 patients in each group were required with a power of 0.9, and α was adjusted to 0.025 (two sided); however, in consideration of the lost to follow-up rate, the sample size was increased by 10%, and 89 cases were ultimately included in each group (267 cases in total).

Intervention

We established a WeChat group (a messaging app that allows multiple people to communicate through mobile phones) for each group and regularly provided the patients with information on LLL. Patients could also communicate with each other and medical staff at any time.

Progressive resistance exercise training group (PRET group)

This PRET was originally designed with the purpose of preventing LLL after pelvic lymphadenectomy based on the characteristics of abdominal wound healing, the anatomy of the lower limb lymphatic circumfluence, and the adjacent lymph nodes.[21–24] The PRET was designed by a multidisciplinary expert group in China, and was discussed in terms of safety, scientific nature, feasibility, and applicability. The PRET program was authorized as a utility model patent by the Intellectual Property Office of China (2018-L-00658606).

The PRET program was divided into five phases: 1–7 (phase I), 8–14 (phase II), 15–30 (phase III), 31–60 (phase IV), and 61–180 days after surgery (phase V) (Supplementary Material). During the first month after surgery, the participants were instructed to perform the exercises in a supine position. One month after the surgery, they were asked to exercise in a standing position. On Day 61, the patients were able to perform resistance training of the lower limbs with a 10 kg elastic bandage while in the standing position. For the first three phases (within 1 month after surgery), each exercise took 20–25 min to complete. For the last two phases (after 1 month after surgery), each exercise consisted of a 10 min warm-up and 10 min relaxation period. It took 40 min to complete.[24]

The exercises were performed under supervision in the hospital for the first 2 weeks. During this period, we urged the patients to exercise regularly and monitored their actions. Fourteen days later, after the patients were discharged, each was asked to set an alarm as a reminder to perform the exercises regularly.

Health education was similar to that for the Control group.

Graduated compression stocking group (GCS group)

The lower limb size of each participant was measured. Each patient in this group received medical grade 15–22 mmHg graduated off-the-shelf compression stockings (Level I). Graduated compression above the knee stockings were selected for this study, and the patients were asked to wear them for no less than 23 h per day.[17] The stockings were manufactured by Haoshide Medical Co., Ltd. (Zhende Medical Corporation, Zhejiang, China).

Health education was similar to that for the Control group.

Control group

In adherence to routine nursing care for the LLL in our gynecological oncology department, a paper education booklet was provided to the participants. The health education included the following: information about the anatomy and physiology of the lymphatic system; definition and risk factors for lower extremity lymphedema; symptoms and signs as well as complications and impact of lower extremity lymphedema; general advice for prevention: avoiding scratches, bites, and trauma; avoiding standing or sitting for long periods; wearing properly fitting shoes; and maintaining toenail and skin care; and instructions on measuring and recording leg circumference in the booklet.

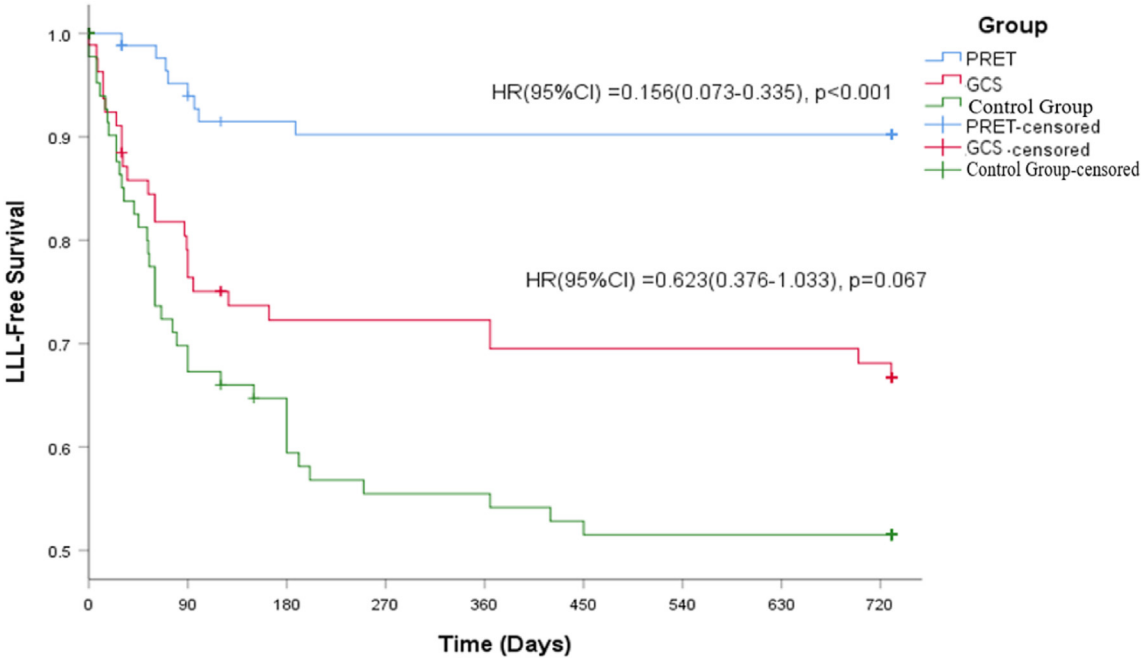

Fig. 2. Risk comparison among three groups. LLL, lower limb lymphedema; HR, hazard ratio; CI, confidence interval; PRET, progressive resistance exercise training; GCS, graduated compression stockings.

We also asked them to report their steps on the WeChat app for the first 6 months after surgery.

Follow-up

The baseline limb volume was measured before surgery. Regular follow-up visits were scheduled at 1, 2, 3, 4, 5, 6, 12, and 24 months postoperatively. We encouraged patients to self-report when they had swelling, lower limb discomfort, or any problems outside the routine follow-up. At each follow-up visit, an experienced lymphedema management specialist blinded to the group allocation performed the follow-up assessments.

The assessment includes the following four steps:

1. Volume of bilateral lower limb measurement
2. Bioelectrical impedance analysis
3. Case histories (data collection) were recorded, including weight on the day of follow-up, number of footsteps per month, and Gynecologic Cancer Lymphedema Questionnaire (GCLQ) score.
4. Health education

Once a patient was diagnosed with lower extremity lymphedema, follow-up was interrupted, and the patient was referred to the lymphedema clinic.

Diagnosis of LLL

In clinical practice, lower limb lymphedema not only occurs on one side of the lower limb, but may also occur on both sides of the lower limb. Therefore, it is obviously not appropriate to diagnose whether a patient has lower limb lymphedema solely through self-comparison before and after the occurrence of lymphedema.

In addition, leg circumference changes with one's own weight easily. So, we think that only using the variable of lower limb circumference as the primary outcome indicator is not scientifically feasible. It needs to combine with the patient's self-report. Therefore, before each evaluation, we conduct symptom screening for patients, and then combine objective data measurement. Based on clinical practice, we adopt this comprehensive diagnostic method that combines subjective and objective factors to define the occurrence of the LLL.

LLL was diagnosed if the patient GCLQ $\geq$ 4 and met any of the following criteria.

1. Limb volume greater than 10% of the preoperative volume.
2. According to BIA, the %ECW value exceeded 40.0%.
3. With signs of thickening of the skin and subcutaneous tissue, and deep fascia effusion.

Measures

Demographic characteristics

Sociodemographic and clinical characteristics of the patients were obtained from their electronic medical records.

Physical measures

Circumferential assessments are the usual way to calculate limb volume. The circumference was measured beginning at ankle level and continued every 10 cm for 60 cm. The shape of the lower limb is described in terms of the shape of six cylinders. Lymphedema was diagnosed if the limb volume was greater than 10% of the preoperative volume.[22]

The total volume (V) was calculated by taking the sum of the volumes of all 10 cm cylinders, that is:[25] $v = \frac{C1+C2+C3+C4+C5+C6+C7+C8}{\pi}$. Here, C1 is the circumference at the metatarsophalangeal joint, C2 is the circumference at the ankle level, and C3–C8 are the circumferences every 10 cm along the lower limb. π is a constant, approximately 3.14159. The volumes are given in cm^3. The limb volume measurements took approximately 5 min to complete. Certified lymphedema therapists performed all the measurements.

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

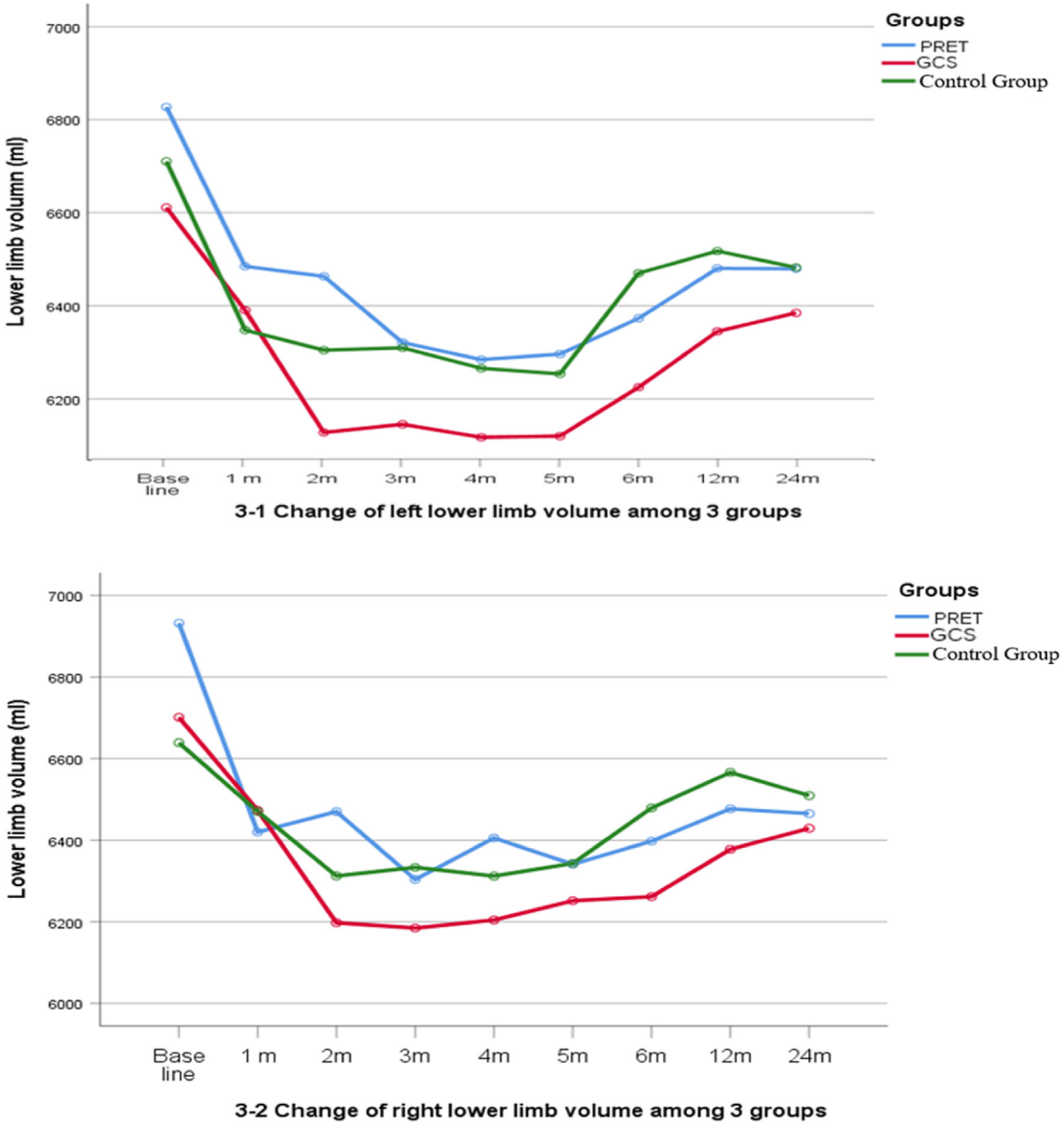

Fig. 3. The follow-up for the lower limb volume. PRET, progressive resistance exercise training; GCS, graduated compression stockings.

The number of footsteps in the first 6 months after surgery was recorded using WeChat or an electronic bracelet.

Daily training; physical data such as heart rate during exercise; and special sports such as yoga, swimming, and Taiji were recorded.

Lymphedema-related symptoms

The GCLQ was used to assess symptoms associated with LLL. The GCLQ is a validated self-report measure that assesses seven symptom domains in both lower extremities. The seven domains include heaviness, general swelling, limb-related swelling, infection, aching, numbness, and physical function. Participants reporting ≥ four symptoms of the lower extremities within the seven domains were classified as having LLL. The survey took approximately 5–10 min to complete.

The GCLQ can effectively distinguish between gynecological cancer patients with and without LLL. Cronbach's alpha was 0.95, the kappa value was 0.759, and the sensitivity and specificity of ≥ 4 were 86% and

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

	Phase 1, *n* (%)	Phase 2, *n* (%)	Phase 3, *n* (%)	Phase 4, *n* (%)	Phase 5, *n* (%)
Very light	64 (71.9)	32 (36.0)	19 (21.3)	44 (49.4)	58 (65.2)
Fairly light	21 (23.6)	49 (55.1)	24 (27.0)	23 (25.8)	25 (28.1)
Somewhat hard	3 (3.4)	6 (6.7)	42 (47.2)	20 (22.5)	5 (5.6)
Hard	1 (1.1)	2 (2.2)	4 (4.5)	2 (2.2)	1 (1.1)
Very hard	0 (0.0)	0 (0.0)	0(0.0)	0 (0.0)	0 (0.0)
Total No.	89 (100.0)	89 (100.0)	89 (100.0)	89 (100.0)	89 (100.0)

PRET, progressive resistance exercise training.

Table 3
Satisfaction with wearing the GCS.

	Blisters, *n* (%)	Hot, *n* (%)	Pruritus, *n* (%)
Yes	19 (21.3)	29 (32.6)	35 (39.3)
No	70 (78.7)	60 (67.4)	54 (60.7)
Total No.	89 (100.0)	89 (100.0)	89 (100.0)

GCS, graduated compression stockings.

83.33%, respectively. When the kappa value was 0.758, the sensitivity and specificity of ≥ 5 were 85.71% and 90.00%, respectively. Thus, we can distinguish between patients with and without lymphedema.[26]

Bioelectrical impedance analysis (BIA)

Body water composition was assessed by bioelectrical impedance analysis (BIA) using the InBody S10 multifrequency bioelectrical impedance analyzer (InBody Co., Ltd., Seoul, Korea). For patients with symptoms but limb volume less than 10% of the preoperative volume, we provide BIA for the diagnosis of LLL, Electrodes were placed at eight precise tactile points on the body, and 30 impedance measurements were obtained for six different frequencies (1, 5, 50, 250, 500, and 1000 kHz) at the following five segments of the body: the right and left arms, trunk, and right and left legs. The measurements included intracellular water (ICW), extracellular water (ECW), total body water (TBW; the sum of ICW and ECW), and the ratio of ECW to TBW (%ECW) for each of the five body segments without empirical estimations based on age, sex, weight, or body type.[27] Extracellular water ratio (%ECW) measurements can predict the presence of unilateral or bilateral leg lymphedema in a single measurement without the need for arm, contralateral leg, or previous measurements as controls.[28] A cutoff %ECW of 40.0% can predict the presence of leg lymphedema, with a sensitivity of 81.6% and specificity of 97.4%.[29,30]

Data analysis

Data analyses were performed using IBM SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, N.Y., USA). The mean ± SD and median (range) were applied to describe the quantitative variables, while counts (percentages) were applied to describe categorical variables. One-way ANOVA was used to test differences between groups for variables that followed a normal distribution, while the Kruskal–Wallis H test was used for variables that did not follow a normal distribution. The χ^2 test was used to examine significant differences between categorical variables. Kaplan–Meier curves were used to perform survival analysis, while the log-rank test was used to test for differences between groups. Repeated-measures ANOVA was used to analyze the lower limb volume on both sides.

Registration and ethical considerations

This study was approved by the Institutional Review Board of FUSCC (IRB No. 1801180-11). All participants signed an informed consent form before participating in the study. The RCT was registered online (ChiCTR1800014905).

Results

From October 7, 2019 to October 7, 2021, all eligible patients were recruited for the study. A total of 268 participants from 15 wards were randomized into three groups: five wards in the PRET group, five in the GCS group, and five in the Control group (See Supplementary Group Allocation). Of these, one patient in the GCS group was excluded because of DVT. A total of 267 patients signed informed consent forms to participate in the study. Among them, 37 dropped out (9 in the PRET group, 16 in the GCS group, and 12 in the Control group) (Fig. 1).

Baseline characteristics of participants

The median age of the patients in the PRET, GCS, and Control group was 48, 50, and 52 years, respectively. The median number of removed lymph nodes was 23.61 ± 6.91, 24.81 ± 10.57, and 23.89 ± 8.44 in each group, respectively. No significant differences in baseline sociodemographic or clinical characteristics were found between the three groups (Table 1).

Risk of developing LLL in the three groups

The incidence of LLL in the PRET, GCS, and Control group was 9.0 % ($n = 8$), 28.1 % ($n = 25$), and 42.7% ($n = 38$), respectively. There was a significant difference in the incidence of LLL among the three groups after surgery ($P < 0.05$). Compared with the Control group, the PRET group had a significantly lower risk of developing LLL, with an HR (95% CI) of 0.156 (0.073–0.335), $P < 0.001$. While GCS and Control group showed a protective trend, with an HR (95% CI) of 0.624 (0.376–1.033), it was underpowered to show that there was a significant difference between GCS and Control group under the current sample size ($P = 0.067$) (Fig. 2).

The incidence of bilateral involvement in the GCS group was higher than that in the other two groups, with 2 (25.0%) of 8 patients in the PRET group and 13 (34.2%) of 38 patients in the Control group with bilateral involvement, and 18 (72.0%) of 25 patients in the GCS group.

During a 2-year follow-up period, there was a significant decrease in the measured values at the fifth postoperative month in all three groups (Fig. 3). The participants in the PRET group were diagnosed with LLL within 61–90 days (4/8, 50.0%), whereas the other two groups had the highest number of cases within 30 days after surgery, with 8 (32.0%) of 25 patients in the GCS group and 10 (26.3%) of 38 patients in the Control group. In addition, in terms of long-term effects, after 181 days, only one patient underwent PRET, 6 patients were treated, and 8 patients received Control group.

Satisfaction at each phase of the PRET and with wearing GCS

We assessed the perceived difficulty level using the Likert 5-level scoring method after each phase of the PRET. We found that 71.9% of the patients felt that the first phase (postoperative days 1–7) was very light, and 49.4% and 65.2% of the patients felt that the last two phases (fourth and fifth, respectively) were very light. Some patients felt that these three phases were very light, while only a few felt that the phases were hard, and none felt that they were very hard (Table 2).

We classified symptoms based on patient satisfaction with the GCS. A blister is a painful swelling of the skin surface. The roots of the stockings were covered with small silicone dots to prevent slippage. Blisters contain clear liquid and are usually caused by the silicone dots that repeatedly rub the skin. As a result, 19 (21.3%) participants had small blisters, of which 4 had exudation. Twenty-nine (32.6%) participants felt hot, and 35 (39.3%) had pruritus (Table 3).

Discussion

In 2019, the 10-year overall survival rate of patients diagnosed with cervical cancer from 2005 to 2009 at our center was 77%. LLL is one of the most disabling adverse effects of radical hysterectomy for cervical cancer.[31] Patients are likely to experience pain (67%) or skin tightness (43%) in the affected limb,[32] thereby affecting their quality of life during their survival period. In the treatment of LLL, Wright et al showed that daily use of medical grade 20–30 mmHg or 30–40 mmHg graduated off-the-shelf compression stockings from foot to waist reduced the circumference of swollen lower limbs but did not significantly improve physical functioning and that there was no statistically significant difference in pain scores.[33] Wearing a GCS can alleviate swelling and pain in the limbs; however, for patients who have not yet suffered from lymphedema, continuous wearing of a GCS not only increases the economic cost but also increases discomfort. Therefore, we expect to find an effective intervention that does not affect the patient's quality of life while preventing the occurrence of lymphedema.

The incidence of LLL in the PRET group was significantly lower than that in the other two groups. PRET has been demonstrated to have a preventive effect on postoperative LLL. In addition, the incidence of LLL peaks at 3–6 months after surgery.[9,10] In our study, seven patients in the PRET group developed lymphedema before 120 days, and only one patient developed LLL between 121 days and 2 years after surgery. Compared to the other two interventions, PRET had a long-term preventive effect on the occurrence of postoperative LLL. We believe that this may be due to the initiation of PRET in the early postoperative period (the first day after surgery), which enhances contraction of the lower limb smooth muscle, promotes lymphatic centripetal flow and lymphatic reflux, and ultimately forms a new lymphatic collateral pathway to shunt the lymph, thereby preventing the occurrence of lymphedema. However, for how long does LLL occur after stopping exercise? We believe that a follow-up period of 5–10 years is required to observe the long-term effects of PRET. However, we suggest that continuing PRET after surgery may be beneficial for patients. In addition, our perceived difficulty level was similar to that of a previous study, and patients felt that it was acceptable and feasible.[24] They could exercise at any time and place without increasing their time or economic costs.

During 2 years of follow-up, there were changes in the volume and circumference of the lower limbs. Significant decrease in the measured values occurred at the 5th postoperative month in the three groups. These observations may be attributed to multiple factors. First, in the initial 4 months after surgery, lymphedema occurred more frequently but subsided by the 5th month. Second, at 5 months postoperatively, most patients have completed all adjuvant treatments. Some patients may experience various discomforts caused by adjuvant therapy during this period, thereby causing their weight to be lower than that in the previous few months.

During this period, the overall volume of the lower limbs decreased. However, the diagnostic standard for LLL is a comprehensive diagnosis in which leg circumference and volume are not the only factors considered when diagnosing LLL, and the main outcome measure of this study was whether LLL occurred rather than changes in leg circumference. Therefore, we believe that the sudden decrease at this point is nonspecific and can be explained.

Medical-grade graduated off-the-shelf compression stockings are widely used in clinical practice because they are off-the-shelf products. Many studies have demonstrated that compression therapy has a positive impact on the lymph pumping function, including reducing initial lymphatic vessel pressure, limiting filtration, improving lymphatic reabsorption, and stimulating lymphatic contraction and anti-inflammatory activity of the parasympathetic (vagal) system.[34,35] However, wearing stockings is influenced by factors such as weather,[17] economic conditions, comfort when wearing clothing, and clothing matching (whether stockings match clothing), which limit patient compliance in practical clinical work to a certain extent. Our research shows that, compared with the GCS group, patients were often dissatisfied with their stockings, particularly those with pruritus, heat, and blisters, during the summer in Shanghai. Therefore, we believe that this can explain why the GCS group had a higher dropout rate than the other two groups. This may also be one reason why the effectiveness of wearing stockings in preventing LLL in this study was not significant. In addition, pressure guarantees compression therapy. We advise patients to replace stockings promptly if they notice that their elasticity has weakened. To ensure the pressure value, each patient was required to use cold water for cleaning, avoid exposure to sunlight, and avoid the use of alkaline detergents. Even if stockings are appropriately cared for, it is difficult to maintain a pair of stockings for 6 months without replacing them. This increases the overall treatment cost for patients. Therefore, some patients continue to wear stockings even when the compression decreases, resulting in unsatisfactory preventive effects.

Limitations

This RCT was a single-tertiary cancer center-based study. In addition, we only followed up patients for 2 years after surgery, and further observation is needed to assess the preventive effect for a longer period after surgery.

Conclusions

In conclusion, PRET can effectively prevent LLL after pelvic lymphadenectomy for cervical cancer. It has no economic burden and does not require a dedicated exercise space, making it convenient for patients to perform at any time.

CRediT authorship statement

Jiajia Zhang: Conceptualization, Methodology, Data curation, Formal analysis, Writing, Data statistical analysis. Changming Zhou: Methodology, Writing – Original draft preparation, Data statistical analysis. Qin Ma: Formal analysis, Data collection. Yi Zhang: Conceptualization, Methodology, Supervision. Xiaoju Zhang: Conceptualization, Methodology, Supervision, Writing – Revised. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding authors attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Declaration of competing interest

The authors declare no conflict of interest.

Ethics statement

This study was approved by the Institutional Review Board of FUSCC (IRB No. ID: 1801180-11). All participants signed an informed consent form before participating in the study.

Data availability statement

The data that support the findings of this study are openly available at [doi: https://doi.org/10.1016/j.apjon.2023.100333].

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Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

Supplementary materials

Supplementary data to this article can be found online at https://doi.org/10.1016/j.apjon.2023.100333.

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