Lymphology 58 (2025) 11-22

FEASIBILITY AND POTENTIAL BENEFITS OF MODERATE INTENSITY CYCLING IN PEOPLE LIVING WITH LOWER LIMB LYMPHEDEMA: A PILOT RANDOMIZED CONTROLLED TRIAL

C. Jönsson, K. Johansson, M. Bjurberg, C. Brogårdh

Department of Health Sciences, Lund University, Lund, Sweden (CJ, KJ, CB); Department of Hematology, Oncology and Radiation Physics, Skåne University Hospital, Lund, Sweden (CJ, MB); Department of Clinical Sciences, Lund University, Lund Sweden (MB); Department of Neurology, Rehabilitation Medicine, Memory Disorders and Geriatrics, Skåne University Hospital, Lund, Sweden (CB).

ABSTRACT

The aim of this pilot randomized controlled trial (RCT) was to assess the feasibility of a moderate intensity cycling intervention in persons with lower limb lymphedema (LLL) and to explore its potential benefits. Thirty-three participants were included for an 8-week intervention of home-based exercise and randomized to an intervention group (IG) with cycling 3-5 times a week, 30-60 minutes, or to a control group (CG). Feasibility was assessed by recruitment and retention rates, adherence to training protocol, and adverse events. Potential benefits were physical fitness (submaximal bicycle ergometer test), volume, local tissue water, impedance of extracellular fluid, lymphedema-related disability (Lymph-ICF-LL) and health-related quality of life (Lymphedema Quality of Life Inventory). Assessments were performed at baseline and after 8 weeks. Non-parametric analyses were used. Twenty-seven participants (IG=16; CG=11), median age 63 years and time with LLL 9 years, completed the trial. Retention to group allocation was 82%, training protocol adherence was 81% and only one adverse event occurred. Significant between-group improvement was found for lymphedema-related disability favoring the IG. Within-group improvements regarding physical fitness, local tissue water and health-related quality of life were found in the IG, but not in the CG. In conclusion, this study shows that moderate intensity cycling is feasible with potential benefits in functioning and health-related quality of life for persons with chronic LLL.

Keywords: lymphedema, lower limb, aerobic exercise, cycling, quality of life, RCT

Lower limb lymphedema (LLL) is a well-known side effect to extensive inguinal and/ or pelvic lymph node dissection in gynecological cancer (1-3), malignant melanoma (4-6) and prostate cancer (7). Reported incidence of LLL secondary to cancer treatment varies widely depending on type and extent of cancer treatment, assessment method used, criterion for the diagnosis, and length of follow-up (1,3,7). According to recent reports, incidence varies from 0% to 56% in gynecological cancer (1-3,8), from 27% to 33% in malignant melanoma (4-6), and from 18% to 27% in prostate cancer (7). The impairment in the lymphatic system can also be caused by congenital defects, i.e., primary lymphedema, but this condition is very rare (9). LLL can also occur secondary to trauma or other diseases leading to an accumulation of interstitial fluid and enlargement

of affected limb or limbs (10). Irrespective of etiology, the treatment goal is to limit the swelling and maintain a stable condition using compression garments and self-care routines (11).

Research has shown that LLL not only has a negative impact on physical function (12-14), but also on physical activity (13-17), social activities (16), and quality of life (12-17). Traditionally, prescription for physical activity and exercise in persons with lymphedema were remedial movements to stimulate the lymphatic system. Vigorous exercise was avoided as there was a fear that it would exacerbate lymphedema, although there was no strong evidence to support this. Nowadays, recommendations for physical activity and exercise are based on research concluding no worsening of the lymphedema but showing improvements in pain, fatigue, upper-body function, strength, and quality of life (18). These results are, however, based mainly on persons with breast cancer-related upper limb lymphedema. Therefore, results may not be generalized to persons with LLL, as the muscles of the lower limbs have a greater circulatory impact than the muscles in the upper limbs, and as gravity has a greater effect on pooling in the lower limbs. Knowledge about the impact of exercise specifically on LLL is limited, as is the feasibility of moderate intensity exercise in this population. Thus, the objective of this pilot randomized controlled trial (RCT) was to assess the feasibility of a moderate intensity cycling intervention in persons with LLL and to explore its potential benefits.

MATERIALS AND METHODS

The study was approved by the regional ethical committee review board in Lund, Sweden, Dnr 2016/136, and was carried out in accordance with the Declaration of Helsinki. All eligible participants received written and verbal information about the study and gave written informed consent. The trial has been registered in ISRCTN10242104. When reporting the data, the Consolidated Standards of Reporting Trials (CONSORT) checklist was followed.

Study Design

The study was designed as a pilot RCT. Eligible participants were contacted by CJ by phone within two weeks after they had received information about the study. For those who were interested in participating, inclusion and exclusion criteria were checked and an appointment for consent, inclusion, and baseline measurements was booked. If existing compression garments were older than 2 months, new ones were provided (at least two sets) and used according to usual care for at least 2 weeks before inclusion in the study and throughout the intervention. After the assessments at test occasion 1 (T1), the participants were randomized to an intervention group (IG) or control group (CG) with an allocation ratio of 2:1, by opening the sealed envelope in sequential order. The random allocation was done using a computer software program administered by one of the authors (KJ). The ratio of 2:1 was chosen due to the limited number of suitable participants and the assumption that a higher opportunity to be randomized to exercise would attract participants to enroll. The participants were told not to discuss their group assignment with the blinded assessor at test occasion 2 (T2).

Participants

Participants were recruited from an outpatient Lymphedema Unit at Skåne University Hospital (SUH), and from two regional Hospital outpatient Rehabilitation Clinics, in the Southern Health Care Region of Sweden between November 2018 and November 2022. The inclusion was paused every year from May to September to avoid the influence of hot summer weather affecting the lymphedema and also between March 2020 and March 2022 due to the COVID pandemic. Participants diagnosed with LLL were identified through patient records by the first author (CJ) at SUH and by the physiotherapists at the two regional hospitals. Inclusion criteria were: 1) unilateral or bilateral, primary, or

secondary LLL, 2) persistent volume for at least 6 months with a palpable thickness of the subcutaneous tissue (19) in the lymphedema limb, 3) a volume variation of less than 5% for each affected limb during the last 6 months, 4) and treatment with compression stockings daytime or day and night according to usual care. Exclusion criteria were: 1) recurrence of cancer, 2) language limitations or cognitive impairments, 3) presence of concurrent diseases or medication affecting the limb volume. The diagnosis of LLL was set by a medical specialist based on clinical history and physical examination. The criteria for the diagnosis were an excess volume difference of >5% (20) and palpated increased skinfold thickness on the affect limb compared to the non-affected or the less affected limb (19). Lymphoscintigraphy was performed to verify the diagnosis for those with primary lymphedema or secondary not cancer-related LLL.

Assessments

All participants were assessed before and after the 8-week intervention (i.e., at T1 and T2, respectively). In addition, participants in the IG were also assessed every two weeks for the lower limb volume to capture any exacerbation of the lymphedema during the intervention and to promote continued cycling by discussing the logbook data. At T1, data were collected in the following order: demographics including age, body weight and height, professional or retired; clinical characteristics including physical activity level the previous 6 months (21), lymphedema location, cause and onset, subjective lymphedema symptoms (perception of heaviness and/ or tightness) during the last week assessed by Visual Analogue Scale (VAS) (22). Assessments for potential benefits started with the questionnaires Lymph-ICF-LL for lymphedema-related disability (23) and Lymphedema Quality of Life Inventory (LyQLI) for health-related quality of life (24), respectively. After taking off the compression garments and then resting in a supine position for 10 minutes assessments of extracellular fluid (25), volume (10) and local tissue water (26) were made, followed by putting on the compression garments. Lastly, assessment of physical fitness (submaximal bicycle ergometer test) (27) was made. The measures for potential benefits were repeated at T2 and are described below.

Outcome Assessments for Feasibility and Adverse events

Feasibility was assessed by recruitment and retaining, adherence to training protocol, and adverse events. Recruitment rate was defined as the number (proportion) of persons agreeing to participate out of potential eligible. Retention rate was defined as the number (proportion) of those enrolled at T1 who were finally measured at T2. Adherence to training protocol was defined as the number (proportion) of participants in the IG who performed cycling at least 3 sessions/week for at least 30 minutes each time, within the prescribed or higher intensity. Adverse events related to lymphedema were defined as a volume increase in the affected limb/ limbs of more than 5% compared to T1 and an accumulation of increased symptoms of heaviness and tightness in the lymphedema limb/ limbs, after each session compared to before. The symptoms were documented in the logbook on a 100-mm VAS ranging from “no heaviness and tightness” to “maximal heaviness and tightness”. The ratings were done in a sitting position with the compression garments on.

Outcome Assessments for Potential benefits

At T1 all the assessments were conducted by CJ. At T2 a physiotherapist (AJ) blinded to participants’ group allocation performed all the assessments except circumferential measurements for volume and markings for TDC measurements which were performed by CJ. The T1 data were not available for the assessors at T2.

Physical fitness

Physical fitness was assessed by the submaximal Åstrand test on a Monark Bicycle Ergometer (27), to get an estimation of maxi-

mal oxygen uptake (VO2max, L/min). During the test, the cadency was 50 revolutions per minute with the resistance workload individually adjusted to reach steady state after 6 minutes. Every minute the HR and the person's perceived exertion using the Borg RPE-scale was monitored (28). The coefficient of variation for this test is 9.8% (29).

Volume

Circumference measurements (CMs) every 4th cm along the limb were taken and the truncated cone formula was used to calculate volume (10). Each lower limb was assessed separately due to bilateral involvement for some participants, thus the term "the most affected limb (MA)" with the greatest volume and "the least affected limb (LA)" with the smallest volume were designated. The method has shown high intra-rater reliability (ICC 0.99) and low measurement errors (SEM%: 1.2-1.3%, SRD%: 3.4-3.6%) for persons with LLL (30). A standardized measurement protocol was used to identify and mark the measuring points (31). CMs to the nearest millimeter were taken once at each marking.

Local tissue water

Tissue dielectric constant (TDC) measurements were taken with the MoistureMeterD (Delfin Technologies Ltd, Finland) and probe M25 for assess local tissue water (26). The TDC method has shown fair to excellent reliability (ICC 0.68-0.96) and acceptable measurement errors (SEM%: 4.2%-9.7%, SRD%: 11.7%-26.8%) in persons with LLL (31). A standardized measurement protocol was used to mark 14 different points on the lower limbs (31). The measurements were repeated two or three times at each point, to achieve two values differing less than 1.0 units and the mean value was used (31).

Extracellular fluid

Impedance of extracellular fluid was calculated by BIS using SEAC SFB7 monitor (SEAC Australia, Impedimed) (25). The BIS method has shown high reliability (ICC 0.79-0.90) and acceptable measurement errors (SEM%: 5.0%-5.2%; SRD%: 14.0% -14.4%) in persons with LLL (31). A standardized measurement protocol was used for the electrodes on the upper limbs (25) and the lower limbs (32). Each limb segment was measured once, and the R(0) of the lower limbs was used in the analyses.

Perceived lymphedema-related disability

Perceived lymphedema-related disability was assessed by the Lymph-ICF-LL (23), a questionnaire based on the International Classification of Function, Disability and Health, ICF (33). The questionnaire comprises 28 items in five domains: physical function, mental function, general tasks/ household activities, mobility activities and life domains/ social life. The impact of LLL is scored on a 100-millimeter VAS where a higher score indicates a more negative impact. The Lymph-ICF-LL has shown good validity and reliability (23).

Health-related quality of life

Disease specific health-related quality of life was assessed by the LyQLI (24). The questionnaire comprises 45 items in three domains: physical, psychosocial, and practical. The impact of lymphedema is scored on a 4-point Likert scale, ranging from 0 to 3, where higher scores indicate a more negative impact. The LyQLI has shown good validity, reliability (24) and responsiveness (34).

Intervention

The exercise in the IG consisted of home-based cycling 3-5 times a week, with a mean intensity of 40-59% of the Heart Rate Reserve, HRR (estimated maximum HR minus resting HR) x (%HRR) + resting HR) corresponding to moderate intensity. The exercise was performed on an indoor spinning bike (*Fig. 1*) provided by the research team, or on a private bicycle either indoors or outdoors, or at a gym. A HR monitor (Polar FS1) was provided to check the correct exercise intensity and time. A log-

Fig. 1. *Photograph of a spinning bike used in the intervention.*

book was provided for ratings of perceived heaviness and tightness in the lymphedema limb/ limbs before and after each session on VAS (22), total time with the HR monitor and the average HR. Each session started with a 5-minute warm-up of cycling, then the monitor was switched on to check the correct intensity and cycling continued for 30-60 minutes. Thereafter the monitor was switched off, followed by cooling down for 5 minutes with slow cycling, and stretching. Verbal and written information about the target HR, completion of the logbook data, and stretching was given at T1. Also, recommendations on appropriate cadency of 60-90 revolutions /min. To promote a high retention rate, the range of exercise frequency, intensity and duration was chosen so that the exercise level could be individually adapted based on the participant´s conditions and exercise habits but still within moderate intensity. For participants already exercising, advice was given to either replace some of their previous exercise with the cycling or simply add the cycling on top of their existing exercise habits.

The participants in the CG were advised to continue with their habitual daily physical activity routines or exercise during the 8 weeks. After the trial, an offer was given to receive the same instructions to perform cycling as the IG.

Statistical Analysis

Demographics and clinical characteristics are presented as median, and quartiles (Q1 and Q3) or frequencies. Feasibility, adverse events, completion rates and perceived symptoms related to the exercise sessions are presented as numbers and proportions. As data were not normally distributed, Mann-Whitney U test was used for evaluating differences between the groups at T1 and for evaluating differences in changes (T1-T2) between the groups. Wilcoxon signed rank test was used for evaluating changes between T1 and T2 within each group. A p-value of ≤0.05 was considered statistically significant. For statistical analysis IBM SPSS Statistics version 29 (IBM, Armonk, New York, USA) was used.

RESULTS

Feasibility and adverse events

Seventy-one persons were identified as potentially eligible participants. Of these, 11 (15%) were excluded based on criteria, 27 (38%) declined due to lack of interest or lack of time, resulting in 33 (46%) who agreed to participate. After consenting, two participants withdrew due to lack of time and in spring 2020 three participants were aborted due to COVID-19 restrictions (*Fig. 2*). In total, 27 participants (82%) (IG n=16; CG n=11) completed the 8-week intervention. Demographics and characteristics of those are presented in *Table 1*. Their median (Q1, Q3) age was 63 (54, 73) years and time since onset of LLL was 9 (4, 18) years. Twelve of them (44%) had underwent gynecological cancer treatment. All participants had a palpable thickness of the subcutaneous tissue in the MA limb.

In the IG, 12 participants used a spinning bike, indoors or at a gym, while 4 participants used a private bike outdoors. Thirteen partici

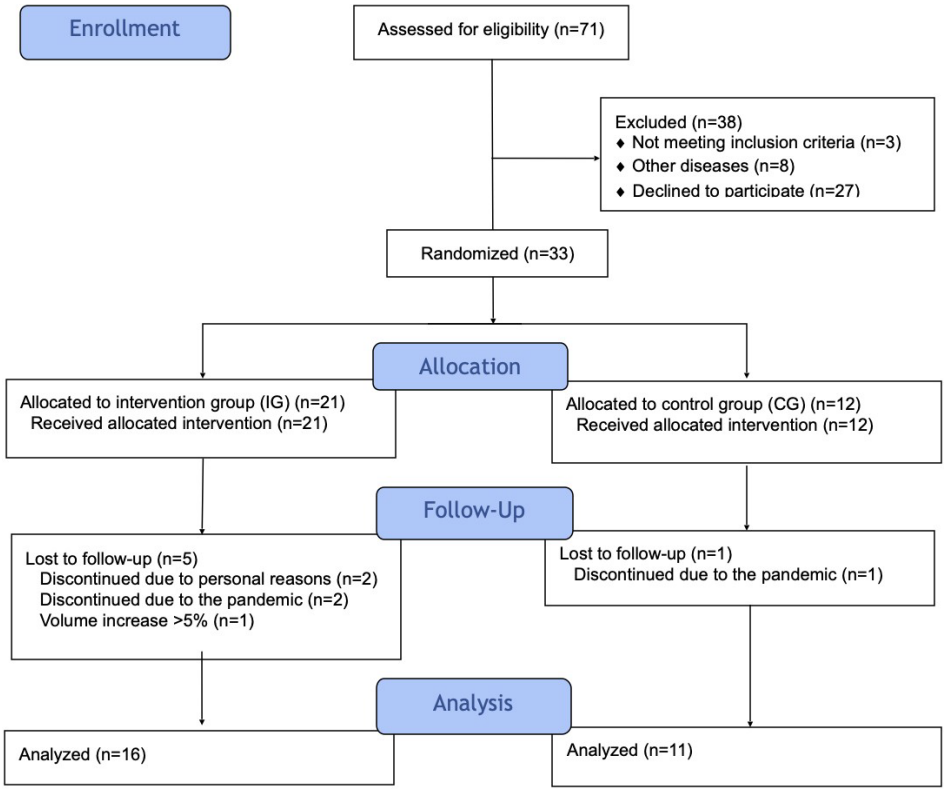

Fig. 2. *Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the study.*

pants (81%) adhered to training protocol by fulfilling the prescribed exercise dose (i.e., at least 30 minutes of moderate intensity cycling at least 3 times a week during the 8 weeks). Three participants reached the prescribed exercise dose for only 4 weeks each, with shorter and/ or fewer sessions in the remaining weeks. All the fortnightly follow-up sessions were attended by 14 participants whereas two participants preferred phone calls for two of their follow-ups due to lack of time.

One adverse event occurred after 6 weeks, consisting of a volume increase of >5% in one of the limbs in one participant. Seven participants reported increased symptoms in more than half of their sessions, but without accumulation over time. Six participants reported no change after cycling compared to before, whereas three participants reported decreased symptoms in more than half of their sessions.

Potential benefits

In *Table 2*, data for the IG and CG at T1 and T2 are presented. At T2, BIS data were incomplete in three participants due to calibration problems with the device. At T1, no between-group differences existed except for volume which was significantly larger in the IG compared to the CG. Regarding changes (T1-T2), a significant difference between the groups was found in perceived lymphedema-related disability after cycling in favor of the IG (-1.1 points, p=0.050). Within the IG, significant improvements for physical fitness (+0.5 L/min, p=.019), TDC (-2.2, p=.013, in one point with a high T1 value) and in health-related quality of life (-0.1 points, p=.049) were found. Also, a statistically significant decrease in R0 of ECF (-13.2, p=.004) in the MA limb was found after the intervention (*Table 3*).

TABLE 1
Demographic and clinical characteristics of participants who provided follow-up data in the intervention group and control groups

	Intervention group (n=16)	Control group (n=11)
Age, years, median (Q1, Q3)	60 (54, 71)	71 (58, 75)
Gender, women/ men, n	11/ 5	6/ 5
BMI, kg/m^2, median (Q1, Q3)	27.4 (24.3, 31.3)	24.8 (20.5, 26.4)
Physical activity, exercise, and housework, n		
Hardly any to easy PA	5	6
Moderate to high PA and exercise	11	5
Working/ retired, n	9/ 7	5/ 6
Diagnosis, n		
Gynecological cancer	10	2
Melanoma	2	2
Urological cancer	1	3
Other	0	1
Primary lymphedema	3	3
Duration of lymphedema, mo, median (Q1, Q3)	132 (67, 206)	83 (33, 216)
Lymphedema, bilateral/ unilateral, n	5 / 11	2/ 9
Palpated thickness of subcutaneous tissue, (n)		
MA limb	16	11
LA limb	0	0
Heaviness, n/ VAS, median (Q1, Q3)		
MA limb	8/ 8 (0, 37)	5/ 1 (0, 20)
LA limb	0	0
Tightness, n/ VAS, median (Q1, Q3)		
MA limb	7/ 0 (0, 32)	3/ 0 (0, 3)
LA limb	0	0

Values are presented as median (quartile Q1, Q3) or n (number). BMI=body mass index; PA=physical activity; MA=more affected; LA=less affected; VAS= visual analogue scale

DISCUSSION

This pilot RCT demonstrated that recruiting and retaining people with LLL to moderate intensity homebased cycling was feasible. Adherence to the training protocol was high, fulfilling at least 3 weekly sessions of moderate intensity cycling, for at least 30 minutes. Only one adverse event occurred which consisted of a temporary volume increase in one participant. Potential benefits were found in the IG which were not found in the CG, such as improvements in physical fitness, local tissue water, lymphedema-related disability, and health-related quality of life. These results support the implementation of a well powered RCT.

The recruitment rate of 46% should be considered acceptable according to Reynolds et al (35) who showed a median rate of 38% in exercise trials in cancer survivors. A higher recruitment rate would however be desirable considering the substantial amount of research supporting physical activity and exercise to be important in oncological rehabilitation (36,37). Several factors were considered to attract persons to enroll: active recruitment by an informative letter followed by telephone contact;

TABLE 2
Data for potential benefits in the intervention group (n=16) and the control group (n=11) at baseline (T1) and post intervention (T2)

	Intervention group		Control group	
	T1	T2	T1	T2
Bicycle ergometer test, L/min				
VO2max	2.7 (1.8, 3.1)	3.1 (2.3, 3.4)	2.4 (1.8, 2.8)	2.6 (2.2, 3.0)
Volume, ml				
MA limb	9574* (8582, 10518)	9492 (8810, 10662)	7926 (7210, 8695)	7853 (7113, 8480)
LA limb	8676* (7349, 9878)	8694 (7357, 9794)	7009 (6405, 7969)	7102 (6600, 8141)
TDC, high				
MA limb	42.5 (39.6, 48.9)	37.4 (32.1, 47.8)	39.0 (35.9, 48.3)	40.1 (34.3, 46.3)
LA limb	32.4 (28.5, 41.7)	31.9 (26.9, 40.8)	32.8 (29.3, 39.8)	30.5 (29.4, 34.7)
BIS, R(0)[a]				
MA limb	286.1 (214.8, 565.3)	233.7 (199.5, 320.4)	285.4 (253.5, 319.3)	278.3 (246.5, 332.3)
LA limb	308.8 (256.6, 568.0)	292.6 (240.4, 367.7)	315.7 (263.5, 368.3)	296.6 (246.7, 363.1)
Lymph-ICF-LL				
Sum score	14.6 (6.1, 27.1)	12.2 (2.6, 19.9)	6.4 (2.7, 13.4)	5 (2.8, 21.6)
LyQLI				
Sum score	0.7 (0.2, 1.1)	0.4 (0.2, 1.1)	0.3 (0.1, 0.6)	0.3 (0.2, 0.6)

Values are presented as median (quartile Q1, Q3).
MA=more affected; LA=less affected; TDC=tissue dielectric constant; TDC high=highest value at T1 compared to reference values in healthy persons (45); BIS=bioimpedance spectroscopy (R0); Lymph-ICF-LL=perceived lymphedema-related disability; LyQLI=lymphedema quality of life inventory.
**Between group differences at T1: volume, MA limb p=0.008, LA limb p=0.03; [a]BIS: n=24*

TABLE 3
Potential benefits evaluated as differences in changes in the intervention group (n=16) and the control group (n=11), within the groups (WG) and between the groups (BG)

	Intervention group	p-value WG	Control group	p-value WG	p-value BG
Bicycle ergometer test, L/min					
VO2max	0.5 (0, 0.7)	0.019*	0.2 (-0.2, 0.4)	0.238	0.197
Volume, ml					
MA limb	63 (-28, 178)	0.171	93 (-121, 221)	0.320	1.00
LA limb	69 (-60, 242)	0.083	46 (-45, 195)	0.240	0.952
TDC, high					
MA limb	-2.2 (-5.8, -.2)	0.013*	-0.4 (-3.8, 1.0)	0.320	0.311
LA limb	-1.2 (-3.1, .3)	0.072	0.1 (-1.6, 1.1)	0.621	0.961
BIS, R(0)[a]					
MA limb	-13.2 (-147.1, -3.8)	0.004*	-11.9 (-16.6, .11.4)	0.570	0.194
LA limb	-10.0 (-24.8, 17.9)	0.359	-19.1 (-35.6, 23.7)	0.570	0.558
Lymph-ICF-LL					
Sum score	-2.4 (-8.7, -0.4)	0.029*	0.2 (-1.8, 4.7)	0.465	0.050*
LyQLI					
Sum score	-0.1 (-0.2, 0.0)	0.049*	0.1 (-0.1, 0.1)	0.576	0.101

Values are presented as median (quartile Q1, Q3); *p< 0.05
MA=more affected; LA=less affected; TDC=tissue dielectric constant; TDC high=highest value at T1 compared to reference values in healthy persons (45); BIS=bioimpedance spectroscopy; Lymph-ICF-LL=perceived lymphedema-related disability; LyQLI=lymphedema quality of life inventory; [a]BIS, n=24

making exercise easily accessible by lending bicycles; minimizing travel time by performing the measurements at a hospital nearby; and the opportunity to receive exercise instructions after the trial for those in the CG. Despite this, half of those eligible declined participation due to lack of time, no interest, or already exercising. These reasons are in line with those presented in review articles about physical activity participation in cancer survivors (35,38). One factor to consider in future RCTs is to recruit participants sooner after the onset of LLL and not several years later.

In this study there was high adherence to the training protocol (81%). Reasons for this could be easy access to exercise using a private spinning bike or one provided by the research team which was accepted by almost half of the participants. The high adherence to the follow-up sessions (14 participants had 100% attendance) supported the study design with regular controls for limb volume and individual feedback on the logbook data. High adherence was also found for self-monitoring using VAS and the HR monitor. Self-monitoring with a logbook and feedback from an HR monitor are addressed as important behavior change techniques by Mazzoni et al (39) and are thus recommended in a full-scale RCT.

Only one adverse event occurred in one participant consisting of a volume increase of +9% in one of the limbs compared to baseline measurements. When intervention was stopped and decongestive treatment was given, baseline measurements were achieved after some weeks. Possible reason for deterioration could be intensive cycling 5 times each week, two weeks before the worsening and an increase in body weight of +3kg which gave a change of volume in the contralateral limb (+3.5%). Thus, regular follow-ups with weight and volume controls are important during the intervention.

That a volume increase in the limbs of more than 5% was considered to be a real clinical change, was based on consensus in our research group when planning this intervention. At that time, knowledge about changes in lower limb volume and limits for a real clinical change was limited (40). Only one study had evaluated the measurement error in persons with LLL using the tape measurement method (41). They reported the intra-rater difference to be 264 ml, but not the relative change. Based on this our research group evaluated the test-retest reliability using CMs every 4th cm for volume in persons with LLL (30,31). The results showed that the relative smallest real difference (SRD%) was 3.6% (30), indicating that our consensus of a lower limb volume increase of more than 5% was reasonable.

Furthermore, the logbook data revealed that 7 participants experienced increased symptoms in their lymphedema limb/ limbs after cycling compared to before in more than half of their sessions. These experiences of deterioration were only temporary and can be explained by increased blood circulation in combination with well-fitted compression stockings. Interestingly, three participants experienced decreased heaviness or tightness in more than half of their sessions, whereas the remaining participants reported no change. To be aware of the experiences of deterioration as well as improvements in the lymphedema limb/ limbs related to exercise could serve as helpful information for participants in future RCTs.

The tape measurement method using CMs for volume is well established for persons with lymphedema. Normally the method is used to calculate a difference between the limbs (10), but since we also included persons with bilateral LLL, changes in each lower limb were evaluated separately. Our findings indicate that this measurement method was feasible and acceptable by the participants. A weakness however is the large inter-observer variability (41) which needs to be considered in a future study.

The assessments of local tissue water and impedance of ECF were exploratory since these two measurement methods have been used preferably in early diagnosis of upper limb lymphedema (42) or LLL (31). Our findings support the use of the TDC method for assessing changes in LLL status based on the within-group analysis indicating a significant decrease in a point with a high TDC in the IG at T2. However, the change in TDC was small and thus not considered clinically relevant.

For the ECF, our finding showed a significant decrease in the within group analysis of the R(0) values indicating a worsening of the ECF in the IG at T2. This result is opposite to other exercise studies where improvements were found after exercise in persons with LLL (43,44). A deterioration of the LLL was not supported by the tape measurement method, suggesting another explanation to the decreased R(0). One reason could be that an increase in muscle volume due to the exercise could change the muscle-fluid component in the limbs and thus change the amount of ECF. Another reason could be that the sensitivity of the BIS data may alter in persons who have had LLL for several years. Whether this measurement method is suitable for evaluating changes in LLL in exercise studies including persons with stable LLL needs to be further investigated.

The potential benefit of cycling in this study was the significant between-group improvement in lymphedema-related disability favoring the IG. Even though this improvement was small it seems like persons with LLL could benefit from moderate intensity cycling not only as a way of improving their physical fitness but also as a way of improving lymphedema-related disability and health-related quality of life. These findings are consistent with a systematic review and meta-analysis (18) supporting exercise as a part of lymphedema symptom management in persons with cancer-related lymphedema.

A limitation of the present study was that more participants in the IG reported moderate to high physical activity and exercise at baseline compared to the CG. Cycling habits were not recorded as baseline data, which could be considered as a limitation. An already established routine to regular exercise may have biased the retention to group allocation and the adherence to exercise protocol. It is therefore recommended to control for physical activity and exercise before inclusion in a full-scale RCT.

Another limitation was that the follow-up sessions with volume control and feedback on the logbook data were given only to the IG. Receiving this attention may have affected motivation and adherence to exercise protocol and thus the results. More equal attention between the groups is something to consider in future RCTs.

Furthermore, the assessments of volume were not performed by the blinded assessor due to limited experience in CMs which could be considered a limitation. To engage a blind assessor familiar with the measurement methods in a future trial is therefore recommended. More participants would also have been desirable, although we are convinced that the number of participants was large enough for a pilot RCT focusing on feasibility, adherence and potential benefits.

CONCLUSION

This pilot study shows that moderate intensity cycling is feasible with potential benefits in functioning and health-related quality of life for persons with chronic LLL. These findings support implementation of a well-powered RCT in the future.

ACKNOWLEDGMENTS

We thank the persons who volunteered to participate and the physiotherapists at the regional hospitals who helped us to identify eligible participants and book a room for assessments. We also thank physiotherapist, PhD Anna Johnsson with all the blinded assessments and physiotherapist, PhD Michael Miller for language editing.

CONFLICT OF INTEREST

All authors declare no competing financial interests exist.

REFERENCES

1. Biglia, N, A Librino, MC Ottino, et al: Lower limb lymphedema and neurological complications after lymphadenectomy for gynecological cancer. Int. J. Gynecol. Cancer. 25 (2015), 521-525.
2. Hayes, SC, M Janda, LC Ward, et al: Lymphedema following gynecological cancer: Results from a prospective, longitudinal cohort

study on prevalence, incidence and risk factors. Gynecol, Oncol. 146 (2017), 623-629.
3. Lindqvist, EM, M Wedin, M Fredrikson, et al: Lymphedema after treatment for endometrial cancer - A review of prevalence and risk factors. Eur. J. Obstet. Gynecol. Reprod. Biol. 211 (2017), 112-121.
4. Hyngstrom, JR, YJ Chiang, KD Cromwell, et al: Prospective assessment of lymphedema incidence and lymphedema-associated symptoms following lymph node surgery for melanoma. Melanoma Res. 23 (2013), 290-297.
5. Friedman, JF, B Sunkara, JS Jehnsen, et al: Risk factors associated with lymphedema after lymph node dissection in melanoma patients. Am. J. Surg. 210 (2015),1178-1184.
6. Söderman, M, JB Thomsen, JA Sørensen: Complications following inguinal and ilioinguinal lymphadenectomies: A meta-analysis. J. Plast. Surg. Hand Surg. 50 (2016), 315-320.
7. Clinckaert, A, K Callens, A Cooreman, et al: The prevalence of lower limb and genital lymphedema after prostate cancer treatment: A systematic review. Cancers (Basel). 14 (2022), 5667.
8. Carlson, JW, J Kauderer, A Hutson, et al: GOG 244-the lymphedema and gynecologic cancer (LEG) study: Incidence and risk factors in newly diagnosed patients. Gynecol. Oncol. 156 (2020), 467-474.
9. Rockson, SG, KK Rivera: Estimating the population burden of lymphedema. Ann. N.Y. Acad. Sci. 1131 (2008), 147-154.
10. Brorson H, B Svensson, K Ohlin: Volume measurements and follow-up. In: Greene, AK, SA Slavin, H Brorson, (Eds): Lymphedema, Presentation, Diagnosis, and Treatment. Springer, Cham, 2015.
11. Svensk förening för lymfologi (SFL). Available at https://lymfologi.se. Accessed Aug, 2024.
12. Rowlands, IJ, VL Beesley, M Janda, et al: Quality of life of women with lower limb swelling or lymphedema 3-5 years following endometrial cancer. Gynecol. Oncol. 133 (2014), 314-318.
13. Klernäs, P, A Johnsson, V Horstmann, et al: Health-related quality of life in patients with lymphoedema - a cross-sectional study. Scand. J. Caring Sci. 32 (2018), 634-644.
14. Neuberger, M, L Schmidt, F Wessels, et al: Onset and burden of lower limb lymphedema after radical prostatectomy: A cross-sectional study. Support Care Cancer. 30 (2022), 1303-1313.
15. Ferrandina, G, G Mantegna, M Petrillo, et al: Quality of life and emotional distress in early stage and locally advanced cervical cancer patients: a prospective, longitudinal study. Gynecol. Oncol. 124 (2012), 389-394.
16. Dunberger, G, H Lindquist, AC Waldenström, et al: Lower limb lymphedema in gynecological cancer survivors--effect on daily life functioning. Support Care Cancer. 21 (2013), 3063-3070.
17. Stolldorf, DP, MS Dietrich, SH Ridner: Symptom frequency, intensity, and distress in patients with lower limb lymphedema. Lymphat. Res. Biol. 14 (2016), 78-87.
18. Hayes, SC, B Singh, H Reul-Hirche H, et al: The effect of exercise for the prevention and treatment of cancer-related lymphedema: A systematic review with meta-analysis. Med. Sci. Sports Exerc. 54 (2022), 1389-1399.
19. Thomis, S, L Dams, I Fourneau, et al: Correlation between clinical assessment and lymphoflouroscopy in patients with breast cancer-related lymphedema: A study of concurrent validity. Lymphat. Res. Biol. 18 (2020), 539-548.
20. International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2023 consensus document of the International Society of Lymphology. Lymphology 56 (2023), 133-151.
21. Frändin, K, G Grimby: Assessment of physical activity, fitness and performance in 76 year olds. Scan. J. Med. Sci. Sports 4 (1994), 41-46.
22. Scott J, EC Huskisson: Graphic representation of pain. Pain 2 (1976), 175-184.
23. Devoogdt, N, A De Groef, A Hendrickx, et al: Lymphoedema functioning, disability and health questionnaire for lower limb lymphoedema (Lymph-ICF-LL): Reliability and validity. Phys. Ther. 94 (2014), 705-721.
24. Klernäs, P, A Johnsson, V Horstmann, et al: Lymphedema quality of life inventory (LyQLI)-development and investigation of validity and reliability. Qual. Life Res. 24 (2015), 427-439.
25. Cornish, B: Bioimpedance analysis: Scientific background. Lymphat. Res. Biol. 4 (2006), 47-50.
26. Nuutinen, J, R Ikäheimo, L Lahtinen: Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. Physiol. Meas. 25 (2004), 447-454.
27. AstrandNEW.pdf. Accessed at https://monarksportsmed.com/wp-

content/uploads/2018/11/AstrandNEW.pdf. August, 2023.
28. Borg, GA: Psychophysical bases of perceived exertion. Med. Sci. Sports Exerc. 14 (1982), 377-381.
29. Ekblom-Bak, E, F Björkman, ML Hellenius, et al: A new submaximal cycle ergometer test for prediction of VO2max. Scand. J. Med. Sci. Sports 24 (2014), 319-326.
30. Jönsson, C, K Johansson, M Bjurberg, et al: Circumferential measurements to calculate lower limb volume in persons with lymphedema: What segment length is to be recommended? Lymphat, Res, Biol. 21 (2022), 275-282.
31. Jönsson, C, K Johansson, M Bjurberg, et al: Impedance of extracellular fluid, volume, and local tissue water can be reliably measured in people with lower limb lymphedema. Phys. Ther. 102 (2022), pzac025.
32. Steele, ML, M Janda, D Vagenas. et al: Normative interlimb impedance ratios: Implications for early diagnosis of uni- and bilateral, upper and lower limb lymphedema. Lymphat. Res. Biol. 16 (2018), 559-566.
33. Kostanjsek, N: Use of the international classification of functioning, disability and health (ICF) as a conceptual framework and common language for disability statistics and health information system. BMC Public Health 11 (2011), S3.
34. Klernäs, P, A Johnsson, J Boyages, et al: Test of responsiveness and sensitivity of the questionnaire lymphedema quality of life inventory. Lymphat. Res. Biol. 16 (2018), 300-308.
35. Reynolds, SA, L O´Connor, A McGee, et al: Recruitment rates and strategies in exercise trials in cancer survivorship: A systematic review. J. Cancer Surviv. 18 (2023), 1233-1242.
36. Cormie, P, EM Zopf, X Zhang: The impact on cancer mortality, recurrence, and treatment-related adverse effects. Epidemiol. Rev. 39 (2017), 71-92.
37. Friedenreich, CM, CR Stone, WY Cheung, et al: Physical activity and mortality in cancer survivors: A systematic review and meta-analysis. JNCI Cancer Spectr. (2019).
38. Gildea, GC, RR Spence, TL Jones, et al: Barriers, facilitators, perceptions and preferences influencing physical activity participation, and the similarities and differences between cancer types and treatment stages - A systematic rapid review. Prev. Med. Rep. 34 (2023), 102255.
39. Mazzoni, A, M Carlsson, S Berntsen, et al: "Finding my own motivation"- A mixed methods study of exercise and behavior change support during oncological treatment. Int. J. Behav. Med. 26 (2019), 499-511.
40. Hidding, JT, PB Viehoff, CHG Beurskens, et al: Measurement properties of instruments for measuring of lymphedema: A systematic review. Phys. Ther. 96 (2016), 1965-1981.
41. Sawan, S, R Mugnai, A de Barros Lopes, et al: Lower-limb lymphedema and vulvar cancer: Feasibility of prophylactic compression garments and validation of leg volume measurement. Int. J. Gynecol. Cancer 19 (2009), 1649-54.
42. Johansson, K, K Blom, L Nilsson-Wikmar, et al: Early intervention with a compression sleeve in mild breast cancer-related arm lymphedema: A 12-month prospective observational study. Cancers (Basel). 15 (2023), 2674.
43. Do, JH, KH Choi, JS Ahn, et al: Effects of a complex rehabilitation program on edema status, physical function, and quality of life in lower-limb lymphedema after gynecological cancer surgery. Gynecol. Oncol. 147 (2017), 450-455.
44. Dionne, A, S Goulet S, M Leone M, et al: Aquatic exercise training outcomes on functional capacity, quality of life, and lower limb lymphedema: pilot study. J. Altern. Complement. Med. 24 (2018), 1007-1009.
45. Jönsson, C, K Johansson, M Bjurberg, et al: Test-retest reliability of volume and local tissue water measurements in lower limbs of healthy women and men. Lymphat. Res. Biol. 18 (2020), 261-269.

Charlotta Jönsson, Registered Physiotherapist, PhD
Department of Health Sciences, Lund University, Lund, Sweden
Department of Oncology, Lymphedema Unit, Skåne University Hospital, Lund
Lasarettsgatan 23 A, S-221 85 Lund, Sweden
Phone: (+46) 46 17 75 18,
Fax number (+46) 046 17 17 45
E-mail: charlotta.jonsson@med.lu.se