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WATER EXERCISE COMPARED TO LAND EXERCISE OR STANDARD CARE IN FEMALE CANCER SURVIVORS WITH SECONDARY LYMPHEDEMA

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ABSTRACT

There are few studies showing that physical exercise can improve secondary lymphedema. We hypothesized that water exercise would be more effective than land exercise in reducing limb volume. Secondary objectives were joint movement, BMI, daily function, well-being, and body image. Limb volume was measured with circumference or was volumetric. Well-being and body image were measured with a study-specific questionnaire and daily function with DASH and HOOS questionnaires. Eighty-eight eligible patients with secondary lymphedema after breast or gynecological cancer participated in this controlled clinical intervention study. There was a higher proportion of women who participated in water exercises who reduced their secondary arm limb volume (p=0.029), and there were also significant differences for BMI (p=0.047) and self-reported frequency of swelling (p=0.031) in the water exercise group after intervention. Women with arm lymphedema in the land exercise group improved DASH scores (p=0.047) and outer rotation in the shoulder (p=0.001). Our results suggest that to reduce objective and self-reported swelling, lymphedema patients may be offered water exercise training while to improve daily shoulder function, land exercises are preferred. To guide female cancer survivors with lymphedema to effective exercise resulting in reduced limb volume and improved function, adequate evidenced-based programs are needed.

Keywords: physical exercise, water exercise, daily function, secondary lymphedema, breast/gynecologic cancer, limb volume, controlled trial, evidence-based

It is not known whether physical exercise improves lymphedema or if there are differences in improvements between different types of exercise settings, e.g., land-versus water-based physical exercise. There is also a lack of knowledge regarding if, and what kinds of, physical exercise may worsen lymphedema (1,2), and patients avoid physical exercise from fear of worsening the condition (3). The self-reported incidence of lymphedema after breast cancer has been reported to be up to 49% (4) with objective incidence of approximately 20% (5). There is, however, an increased risk with axillary dissection and postoperative radiation therapy (40%) (6). The incidence for lymphedema after cervical and endometrial cancer is approximately 30% (7,8); however, the incidence of leg lymphedema may be underrated as many women do not receive any information regarding the risk of developing it. Many women with secondary lymphedema have a reduced quality of life, severe heaviness in the affected limb, pain, and skin infections. They also experience decreased function in the limb, with reduced strength and mobility (1). The standard care for lymphedema patients, between treatments with Complex Decongestive Therapy (CDT), is so called self-care (9-11) in combination with occasional manual treatment (Manual Lymph Drainage, MLD).

It has been demonstrated that physical exercise may prevent the development of breast cancer-related lymphedema (12), and other studies have shown that land-based strength training, water exercise, and pole walking does not worsen the condition (13-17). However, to our knowledge, none or very little knowledge exists regarding whether physical exercise can actually reduce lymphedema volume. There is a lack of studies concerning the limb volume effects of exercise in lymphedema patients. In one study with breast cancer survivors with or without lymphedema, land exercise induced a greater decrease in body fat and increase in lean body mass than water exercise. However, water exercise was better for improving breast symptoms (18). Johansson et al (16) demonstrated that water-based exercise is feasible in lymphedema patients (n=25). The range of motion in the shoulder was improved in the exercising patients even years after cancer treatment had been completed while no reduction of limb volume was seen (17). Tidhar also studied lymphedema in patients (n=48) performing a special method including self-massage and slow motions in water (19); this special method is, however, not comparable with water exercise.

Since it is not known whether physical exercise can improve lymphedema or if there are differences between water-based versus land-based physical exercise compared to standard care only, we undertook this study to examine these issues. The aim was to examine if female cancer survivors with secondary lymphedema reduced limb volume, self-perceived swelling, and BMI (Body Mass Index) more after water exercise than after land exercise or standard care and also if the women improved daily function, joint mobility, general well-being, and body-image more after water exercise compared with land exercise and standard care.

METHODS

Study Design

The study was a controlled clinical intervention comparing female cancer survivors undergoing water exercise intervention, land exercise intervention, or standard care. The local Ethics Committee in Stockholm, Sweden, approved the research protocol and all participants were given oral and written information and signed an informed consent form.

Participants

In total, 109 female cancer survivors with secondary lymphedema were invited, and 88 participants were included from two hospitals and one primary health care unit in the middle, east, and north of Sweden. Feasibility of the inclusion procedure and data collection was evaluated for the first fourteen participants before the study continued. The women were consecutively invited by physiotherapists with special education in lymphedema treatment at each clinic, or recruited by way of advertisements in patient organization papers. Subjects were eligible for inclusion if they had a diagnosed secondary lymphedema in the arm after breast cancer or in the leg after gynecological cancer. Participating women had to speak and understand written Swedish. Exclusion criteria were ongoing intensive CDT, recurrence of cancer, ongoing active oncological treatment, or functional disorders hindering participation in exercise programs (this last criterion was not valid for participants recruited to standard care).

Comparison Groups

The subjects were placed into one of three treatment groups:

The water exercise group included 35 subjects who participated in 10 weeks of group intervention once a week, led by a physiotherapist. The water training was a standard program with the aim of increasing aerobic capacity, strength, and mobility. It was carried out in a 25 meter indoor pool, with 140 cm water depth at a water temperature of 28-29°C. The 50 minute program included the following components: warm-up exercises for ten minutes, mobility and stretch exercises for ten minutes, movements to increase the pulse for ten minutes, strength training for ten minutes, and slow-down mobility exercises for ten minutes. At the end we added hold/relax exercises of the muscles around the swollen limb and deep breathing in the slower parts. All women wore compression sleeves/hosiery during the exercises. If a woman participated seven times or more, she was defined as having complied with the intervention.

The land exercise group comprising 29 subjects participated in gymnastics in groups on land for 10 weeks of intervention once a week. The program included the same components as the water exercise. The only difference was that the leader adjusted the training to the women who could not jump, so that they could instead perform exercises near the floor. The same routines for compression and compliance were used.

The standard care group included 24 subjects receiving standard care, i.e., self-care as skin-care, mobility exercises for the arm or leg, placing the swollen limb above heart level, own massage of the arm and leg, compression sleeves/hosiery and occasional manual lymph drainage in health care.

Data Collection

In the intervention groups, all outcome measures (physiotherapist- and participant-delivered measurements) were assessed at baseline (one to two weeks before the start of the intervention) and after the study period of ten weeks exercise intervention (one to two weeks after the end). One assessor, not involved in the interventions, in each geographical area (north, middle, and east of Sweden) performed the physiotherapist-delivered measurements. The standard care group was assessed twice with a 10 week interval using participant-delivered measurements only. To maintain confidentiality, all physiotherapist- and participant-delivered outcome measure charts were given a number for identification. The cancer survivors were given a questionnaire along with a pre-paid envelope for return.

At baseline, the participants answered a study-specific questionnaire covering demographic and clinical data.

Outcome Measures

Limb swelling

Three physiotherapists measured the primary outcome measure limb volume in milliliters (ml) with either water displacement or circumference with tape measurement, depending on which method was established at that clinic. Both methods are reliable and valid (20,21) and well correlated with a coefficient of correlation of 0.813-0.915 (19). The participants graded their self-perceived frequency of limb swelling using the study-specific question: “How often are you swollen in your arm/leg?” graded 1-6, where 1 was “never” and 6 were “constantly.” The values were recorded in individual charts.

Body Mass Index

The participants’ BMI was self-reported as height and weight in a specific question in the study specific questionnaire before and after intervention. BMI was then calculated (weight [kilograms] / (length [meter]) 2).

Range of Motion

The physiotherapists measured active joint movement with goniometry according to usual standards in physiotherapy (22,23), and a clinical possible measurement error. Active hip and knee flexion in the lower extremity, and active elevation-abduction, and lateral rotation in the shoulder joint was measured.

Daily physical function

The participants graded physical function for the upper extremity with DASH – Disability of Arm, Shoulder and Hand questionnaires. DASH provides a summary score on a 100-point scale, with 100 indicating the most disability. DASH is a valid and reliable function test for the upper extremity (24,25). HOOS – Hip Osteoarthritis Outcome Score questionnaire – was used for function in the lower extremities. HOOS consists of questions on pain, function and range of motion. The HOOS score gives a maximum of 100 points, where a higher score means less dysfunction. The test has high reliability and validity (26,27).

Development of the study-specific lymphedema questionnaire

The participants delivered demographical, clinical, well-being, and health data using a study-specific questionnaire regarding their present situation. The study-specific questionnaire consisted of a total of 108 questions covering physical symptoms, sexuality, self-care, and body-image, as well as questions concerning information given by the health care system. The study-specific lymphedema questionnaire was developed and tested in accordance with a method used for more than 20 years in the Clinical Cancer Epidemiology research group at the Karolinska Institute (28-31). In summary, the questionnaire was developed during a qualitative phase. Female cancer survivors with secondary lymphedema (n=8) were interviewed about their condition. Based on the interviews, extensive literature searches and the authors' long clinical experience, the study-specific questionnaire was constructed. Validity and reliability was then tested on 12 female cancer survivors, not included in the present study, in face-to-face-validity interviews.

Well-being and body-image

The participants graded general well-being using the question: "How would you describe your well-being?" graded on a visual digital scale ranging from one to seven. To measure body-image, we used seven items from a validated body awareness verbal Likert scale (32). The statements asked about body-image were: "It is difficult for me to accept my body as it looks today." "I cannot trust my body," "My body feels damaged," "My body feels foreign," "I am ashamed over my body," "I do not like to see myself by the mirror when I am naked", and "Can you accept your body as it looks today?"

Statistical Analysis

For each category regarding demographic (*Table 1*) and clinical (*Table 2*) characteristics, we calculated mean volume difference between the edema limb and the healthy limb, with 95% confidence intervals (CI) assuming normal distribution.

For the outcomes for limb volume, BMI and joint movement, mean differences between before and after the intervention were reported with 95% CI. To compare these outcomes after the interventions compared to baseline within each group, paired samples t-tests were used. To compare the mean change between groups for these variables, a group by time interaction test from repeated-samples ANOVA was used. Ordinal categorical outcomes DASH and

TABLE 1
Demographics

	Land Exercise n=29 (%)	Water Exercise n=35 (%)	Standard Care n=24 (%)	Difference between groups, p-value*
All participants				
Age				
Mean [±SD]	65 [±11]	58 [±11]	63 [±12]	
29-57 years	8/29 (28)	14/30 (47)	7/24 (29)	0.430
58-67 years	9/29 (31)	9/30 (30)	10/24 (42)	
68-92 years	12/29 (41)	7/30 (23)	7/24 (29)	
Missing	0	5	0	
Level of education				
Elementary school	5/29 (17)	3/30 (10)	4/24 (17)	0.686
Secondary school	10/29 (34)	10/30 (33)	11/24 (46)	
University/College	14/29 (48)	17/30 (57)	9/24 (38)	
Missing	0	5	0	
Ethnicity				
Swedish	25/29 (86)	27/30 (90)	17/24 (71)	0.187
Other	4/29 (14)	3/30 (10)	7/24 (29)	
Missing	0	5	0	
Employment status				
Full-time employed	6/29 (21)	14/30 (47)	5/24 (21)	0.041
Part-time employed	1/29 (3)	2/30 (7)	1/24 (4)	
Unemployed	0/29 (0)	0/30 (0)	2/24 (8)	
Full-time sick leave	3/29 (10)	1/30 (3)	2/24 (8)	
Early retired	0/29 (0)	4/30 (13)	0/24 (0)	
Part-time time sick leave/ early retired	3/29 (10)	1/30 (3)	2/24 (8)	
Retired	16/29 (55)	8/30 (27)	12/24 (50)	
Missing	0	5	0	
Smoking				
Current smoker	3/29 (10)	0/18 (0)	1/24 (4)	0.623
Former smoker	9/29 (31)	7/18 (39)	11/24 (46)	
Never smoked	17/29 (59)	11/18 (61)	12/24 (50)	
Missing	0	17	0	
Other physical activity†				
Never	1/29 (3)	0/30 (0)	1/23 (4)	0.637
Once a month	3/29 (10)	2/30 (7)	4/23 (17)	
Once a week	14/29 (48)	17/30 (57)	13/23 (57)	
Every day	11/29 (38)	11/30 (37)	5/23 (22)	
Missing	0	5	1	
BMI ‡, kg/m²				
Mean [±SD]	28.5 [±4.1]	28.1 [±6.1]	28.5 [±5.4]	
<18.5	0/29 (0)	0/29 (0)	0/24 (0)	0.579
18.5-25	6/29 (21)	10/29 (34)	6/24 (25)	
25-30	13/29 (45)	8/29 (28)	11/24 (46)	
≥30	10/29 (34)	11/29 (38)	7/24 (29)	
Missing	0	6	0	

* Fisher's exact test
† i.e., walking, jogging, strength-training, bicycling.
‡ Body Mass Index<18.5= underweight, 18.5-25 = normal weight, 25-30= overweight, ≥30 = obesity

HOOS scores, body-image, and well-being are shown with median and inter-quartile range. We compared DASH and HOOS scores at baseline and after the study-period within each group with the Wilcoxon's signed-rank test. Median change during the study period for these variables was compared in-between the groups with the Kruskal-Wallis test.

TABLE 2
Demographics Versus Limb Volume

	Land Exercise N=29 (%)	Water Exercise N=35 (%)	Standard Care N=24 (%)	Difference between groups, p-value*
Arm lymphedema	28/29 (97)	25/35 (71)	21/24 (88)	
Leg lymphedema	1/29 (3)	10/35 (29)	3/24 (13)	0.021
Breast cancer n=69				
Lymph node dissection Yes	26/27 (96)	18/18 (100)	20/20 (100)	1.000
Lymph node dissection No	1/27 (4)	0/18 (0)	0/20 (0)	
Missing	0	2	2	
Sentinel node Yes	10/17 (59)	6/15 (40)	4/10 (40)	0.574
Sentinel node No	7/17 (41)	9/15 (60)	6/10 (60)	
Missing	10	5	12	
External Beam Radiation Yes	23/27 (85)	19/20 (95)	21/21 (100)	0.141
External Beam Radiation No	4/27 (15)	1/20 (5)	0/21 (0)	
Missing	0	0	1	
Gynaecological cancer n=14				
Lymph node dissection Yes	1/2 (50)	5/7 (71)	0/1 (0)	0.667
Lymph node dissection No	1/2 (50)	2/7 (29)	1/1 (100)	
Missing	0	3	1	
External Beam Radiation Yes	2/2 (100)	7/9 (78)	1/1 (100)	1.000
External Beam Radiation No	0/2 (0)	2/9 (22)	0/1 (0)	
Missing	0	1	1	
Years since cancer treatment				
0-4 y	11/28 (39)	13/30 (43)	7/21 (33)	0.966
5-10 y	9/28 (32)	9/30 (30)	7/21 (33)	
≥11 y	8/28 (29)	8/30 (27)	7/21 (33)	
Missing	1	5	3	
Time between treatment and occurrence of lymphedema				
In relation to cancer treatment	7/28 (25)	12/28 (43)	6/21 (29)	0.450
Within 1 year	17/28 (61)	10/28 (36)	11/21 (52)	
> 1 year after cancer treatment	4/28 (14)	6/28 (21)	4/21 (19)	
Missing	1	7	3	
Duration of lymphedema				
<1 year	4/29 (14)	2/29 (7)	8/22 (36)	0.191
1-5years	11/29 (38)	12/29 (41)	5/22 (23)	
5-10 years	5/29 (17)	8/29 (28)	3/22 (14)	
>10 years	9/29 (31)	7/29 (24)	6/22 (27)	
Missing	0	6	2	
Earlier treatment				
Compression Yes	27/29 (93)	29/30 (97)	18/24 (75)	0.049
Compression No	2/29 (7)	1/30 (3)	6/24 (25)	
Missing	0	5	0	
Manual lymph drainage Yes	23/29 (79)	23/30 (77)	22/24 (92)	0.353
Manual lymph drainage No	6/29 (21)	7/30 (23)	2/24 (8)	
Missing	0	5	0	
Water exercise Yes	8/29 (28)	18/30 (60)	13/24 (54)	0.033
Water exercise No	21/29 (72)	12/30 (40)	11/24 (46)	
Missing	0	5	0	
Land exercise Yes	4/29 (14)	4/30 (13)	7/24 (29)	0.250
Land exercise No	25/29 (86)	26/30 (87)	17/24 (71)	
Missing	0	5	0	
Instruction in self-care Yes	26/29 (90)	24/30 (80)	18/24 (75)	0.422
Instruction in self-care No	3/29 (10)	6/30 (20)	6/24 (25)	
Missing	0	5	0	

Co-morbidity				
Hypertension Yes	13/29 (45)	8/30 (27)	9/24 (38)	0.356
Hypertension No	16/29 (55)	22/30 (73)	15/24 (63)	
Missing	0	5	0	
Cardio vascular disease Yes	3/29 (10)	4/30 (13)	3/24 (13)	1.000
Cardio vascular disease No	26/29 (90)	26/30 (87)	21/24 (88)	
Missing	0	5	0	
Thrombo embolic disease Yes	3/29 (10)	5/30 (17)	0/24 (0)	0.124
Thrombo embolic disease No	26/29 (90)	25/30 (83)	24/24 (100)	
Missing	0	5	0	
Varicose veins Yes	6/29 (21)	5/30 (17)	2/24 (8)	0.446
Varicose veins No	23/29 (79)	25/30 (83)	22/24 (92)	
Missing	0	5	0	
Erysipelas Yes	14/29 (48)	11/30 (37)	9/24 (38)	0.616
Erysipelas No	15/29 (52)	19/30 (63)	15/24 (63)	
Missing	0	5	0	
Medication				
Diuretics Yes	4/29 (14)	2/29 (7)	4/22 (18)	0.487
Diuretics No	25/29 (86)	27/29 (93)	18/22 (82)	
Missing	0	6	2	
Anti-hypertensive medication Yes	15/29 (52)	8/29 (28)	7/22 (32)	0.134
Anti-hypertensive medication No	14/29 (48)	21/29 (72)	15/22 (68)	
Missing	0	6	2	
Anti coagulates Yes	5/29 (17)	5/29 (17)	3/22 (14)	1.000
Anti coagulates No	24/29 (83)	24/29 (83)	19/22 (86)	
Missing	0	6	2	
Frequency manual lymph drainage				
Never	6/27 (22)	6/26 (23)	2/21 (10)	0.024
1-10 times per year	10/27 (37)	7/26 (27)	2/21 (10)	
1-2 times per month	9/27 (33)	10/26 (38)	7/21 (33)	
1-3 times per week	2/27 (7)	3/26 (12)	10/21 (48)	
Missing	2	9	3	

* Fisher's exact test

The body-image and well-being outcomes after the study period were compared to the baseline outcomes using the sign test. For all outcomes, the number (n) and percentage (%) of participants who had a decrease or increase (at least one step) in outcome ratings between the before and after measurements were presented, as well as those with no change (tied). For all outcomes, we used Fisher's exact test to compare the numbers that decreased or increased, excluding ties between the measurements.

Sample size calculation was performed, according to the primary outcome lymphedema volume, as: Given that data was collected from 160 exercising participants (water based and land based exercise) and that the spread in volume (standard deviation) was 220 ml for both groups, the study would have 80% power to detect a mean difference between water and land exercise groups of 101 ml (a clinically relevant difference) at 5% significance level.

RESULTS

During the study period, 88 female cancer survivors participated in the study (*Fig. 1*). Of the 35 in the water exercise group, 30 (86%) complied with ≥7 exercise sessions compared with 19 (66%) of the 29 in the land exercise group, and were thus included in the analyses. A total of 19 subjects were not included in the analyses. Six in the land exercise group dropped out because the exercises were too strenuous and four were

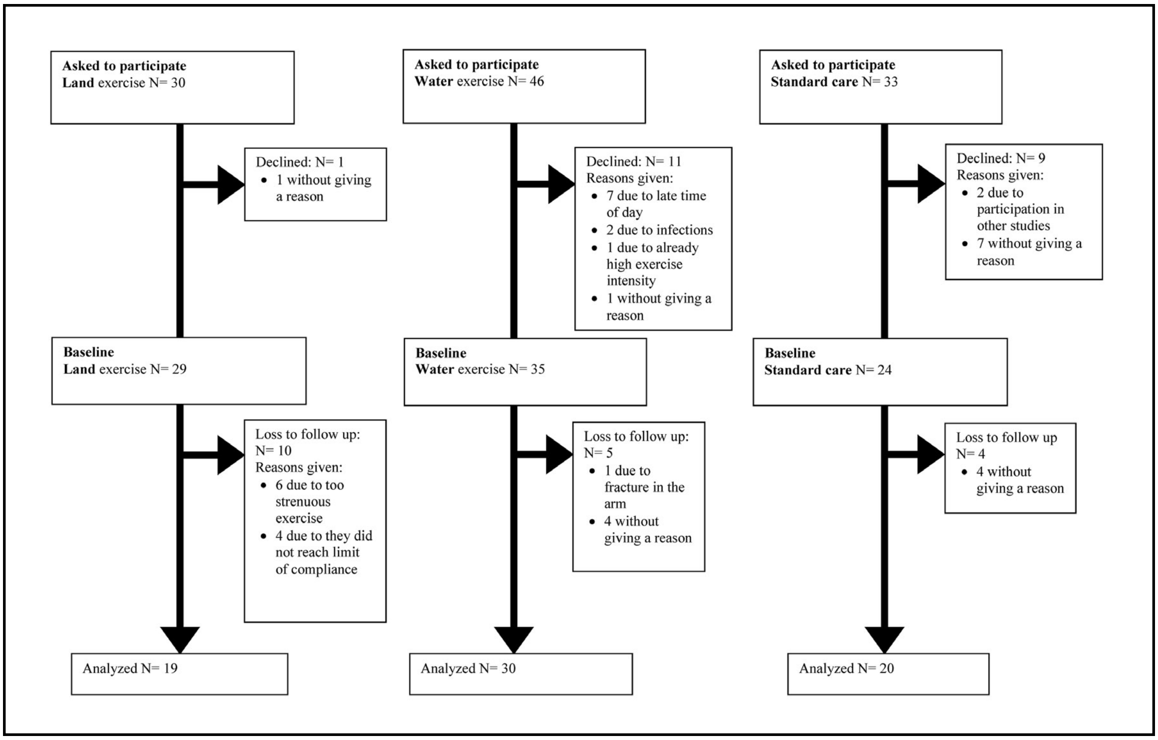

Fig. 1. Flow chart of study design

not included due to not reaching the compliance level. In the water exercise group, four dropped out for no stated reasons and one due to an arm fracture not related to the exercise (*Fig. 1*). There was almost full adherence to wearing compression garments during the interventions.

Characteristics Related to Limb Volume in the Study Groups

The subjects in the water exercise group were somewhat younger than the women in the land exercise and standard care groups, and were also professionally active to a higher extent than subjects in the other groups. A high proportion of the subjects in all groups were overweight or obese at baseline. Limb volume increased with age. Elementary school only, and other ethnicity than Swedish (n=14), also appeared related to larger limb volumes (*Table 1*).

Clinical Data and Earlier Treatment Related to Limb Volume

At baseline, the mean volume difference between the edematous and healthy limb was 277 ml in subjects with arm lymphedema (n=41) and 1,057 ml in subjects with leg lymphedema (n=8). On average, it was approximately eight years since the women in all three groups had been treated for cancer. The start of lymphedema or swelling developed in relation to cancer treatment or within one year in most of the women but the time since diagnosis was widespread from under one year up to over ten years, with no differences between the groups. There was a higher prevalence of a history of erysipelas in the land exercise compared to the water exercise group and compared to the standard care group. Compression therapy (sleeves or bandaging) was less common in the standard care group compared to the two intervention groups (75%, versus 97% and 93%, respectively). Previous manual lymph drainage was most common in the standard care group and most frequently presently performed in the same group (48%, versus 11% and 7%, respectively). Previous instructions in self-care were more common in the land exercise group compared to the other groups. Larger limb volumes were seen in women who had had erysipelas and who had hypertension. Subjects who had been treated with diuretics and hypertensive medication also had larger edemas (*Table 2*).

Reduction in Limb Volume, Swelling, and BMI

A higher proportion of subjects in the water exercise group compared to subjects in the land exercise group reduced their arm lymphedema volume (p=0.029). There was no statistically significant difference in the size of the reduction of limb volume between the exercise groups after (compared to before) intervention. The women with arm lymphedema in the water exercise group had reduced their lymphedema volume (p=0.046) after (compared to before) intervention (*Table 2*), and this was not seen in the other groups. In leg lymphedema, no differences in limb volume in the groups after (compared to before) intervention were found (*Table 3*). In the water exercise group, the subjects reported a lower frequency of limb swelling after (compared to before) intervention (p=0.031), while neither the land exercise group nor the standard care group reported a decrease (*Table 4*). There was a significant reduction in BMI (p=0.047) in the water exercise group after intervention but not in the other groups. The size of BMI reduction did not differ statistically significantly between the groups after (compared to before) intervention (p=0.812) (*Table 3*).

Range of Motion (ROM) and Increased Physical Function

After intervention with land exercise, subjects improved their external rotation in the shoulder (p=0.012). Elevation in the shoulder was significantly decreased but this was not clinically significant. There were no other improvements in range of motion in or between the groups. After intervention, subjects with arm lymphedema in the land exercise group had improved DASH scores (p=0.049).There were no changes in DASH scores in the other two groups after the interventions. Among subjects with leg lymphedema, neither the proportion improving joint movement or HOOS scores, nor the size of the improvements were found to differ between the groups after (compared to before) the study period (*Table 3*).

Changes in Well-Being and Body Image

Overall well-being was high at baseline in all three groups, and stayed at these levels during the study period without statistically significant differences between the groups (*Table 4*).

DISCUSSION

We found that more female cancer survivors decreased their secondary lymphedema volume after water exercise compared to land exercise. However, the size of the limb volume reduction did not differ between the types of exercise. Further, larger studies are needed to examine these results. The water exercise group also reduced their BMI and self-reported frequency of swelling after intervention. However, improvements were shown in daily shoulder function, measured with DASH and in external rotation of the shoulder after intervention in the land group.

The land exercise group did not change in limb volume, BMI, and self-reported swelling. Water training has hypothetical benefits: In water, the hydrostatic pressure (33) can be similar to wearing a compression sleeve or hosiery on land (34), which is the most common treatment for secondary lymphedema and could, theoretically,

TABLE 3
Results for Limb Volume, BMI, Joint Movement and Daily Function

	Land Exercise				Water Exercise				Standard Care				Differences between groups- Mean difference; P-value of Increased/ Decreased
	Before N=19 Mean (SD)	After N=19 Mean (SD)	Diff Mean (CI) P-value	n (%) Decreased Equal Increased	Before N=19 Mean (SD)	After N=19 Mean (SD)	Diff Mean (CI) P-value	n (%) Decreased Equal Increased	Before N=20 Mean (SD)	After N=20 Mean (SD)	Diff Mean (CI) P-value	n (%) Decreased Equal Increased	
Arm volume edematous limb, ml	2611 (571)	2600 (574)	-10 (-65-44) 0.697	6 (33) 0 (0) 12 (67)	2856 (520)	2793 (530)	**-63 (-125--1) 0.046**	10 (77) 0 (0) 3 (23)	NA‡‡	NA	NA	NA	0.185 0.029
Leg volume Edematous limb, ml	NA	NA	NA	NA	10645 (2190)	10819 (2395)	173 (-172-518) 0.265	1(14.3) 0 (0) 6 (86)	NA	NA	NA	NA	0.872 1.000
Body mass index[1], kg/m²	28.8 (3.9)	28.7 (4.1)	-0.1 (-0.5-0.4) 0.674	8 (47) 4 (24) 5 (29)	27.4 (4.8)	27.1 (4.8)	-0.3 (-0.5-0.0) 0.047	12 (52) 4 (17) 7 (30)	29.0 (5.5)	28.9 (6.0)	-0.1 (-0.9-0.7) 0.861	10 (53) 4 (21) 5 (26)	0.812 1.000
Elevation, shoulder, 0-180 degrees	159.4 (10.6)	155.3 (11.2)	-4.2 (-7.5-0.8) 0.017	9 (50) 8 (44) 1 (6)	157.5 (18.9)	161.0 (16.8)	3.5 (-1.4-8.4) 0.132	0 (0) 5 (63) 3 (38)	NA	NA	NA	NA	0.010 0.014
Abduction shoulder, 90-180 degrees	153.6 (22.9)	154.7 (17.3)	1.1 (-2.8-5.1) 0.56	6 (33) 6 (33) 6 (33)	143.1 (40.3)	147.5 (37.6)	4.4 (-0.8-9.6) 0.088	0 (0) 5 (63) 3 (38)	NA	NA	NA	NA	0.316 0.229
External rotation shoulder, 0-90 degrees	55.6 (15.3)	62.2 (13.0)	6.7 (1.7-11.6) 0.012	4 (22) 4 (22) 10 (56)	67.9 (11.5)	70.8 (10.8)	2.9 (-0.6-6.4) 0.093	0 (0) 5 (63) 3 (38)	NA	NA	NA	NA	0.316 0.541
Flexion hip, 0-120 degrees	NA	NA	NA	NA	112.9 (12.9)	114.3 (13.1)	1.4 (-0.8-3.7) 0.172	0 (0) 5 (71) 2 (29)	NA	NA	NA	NA	0.220 1.000

Flexion knee, 0-135 degrees	NA	NA	NA	NA	128.6 (14.9)	127.9 (14.7)	-0.7 (-2.5-1.0) 0.356	1 (14) 6 (86) 0 (0)	NA	NA	NA	NA	0.078 1.000
Daily life physical function	**Before N=19 Median (IQR)[3]**	**After N=19 Median (IQR)[3]**	**P-value**	**n (%) Increased Equal Decreased**	**Before N=22 Median (IQR)[3]**	**After N=22 Median (IQR)[3]**	**P- value**	**n (%) Increased Equal Decreased**	**Before N=16 Median (IQR)[3]**	**Before N=16 Median (IQR)[3]**	**P- value**	**n (%) Increased Equal Decreased**	**Differences between groups, Median difference P-value Increased/ Decreased P-value**
DASH-score[2]	24 (6-32)	15 (6-23)	0.049	12 (67) 1 (6) 5 (28)	15 (11-22)	15 (8-22)	0.772	8 (57) 0 (0) 6 (43)	30 (12-37)	29 (14-34)	0.734	7 (44) 0 (0) 9 (56)	0.174 0.303
HOOS-score[2]	NA	NA	NA	NA	87 (51-100)	91 (64-100)	0.438	3 (38) 2 (25) 3 (38)	NA	NA	NA	NA	0.120 1.000

NA= Not applicable. [1] <18.5 =underweight, 18.5-25=normal weight, 26-30=overweight, >30=obesity. [2] DASH - Disability of Arm Shoulder and Hand, points 1-100, 1 =excellent. HOOS - Hip dysfunction and Osteoarthritis Outcome Score, points 1-100, 100 =excellent. [3] Inter Quartile Range

influence the limb volume together with the exercise itself. Even if this is a small study, this can be a new hypothesis to explore in lymphedema research.

The self-reported frequency of swelling decreased in the water exercise group. The decreased frequency of swelling after water exercise has not been noted before in studies as an important variable to examine. Our results indicate that swelling is not constant every day, and there can be improvements in self-reported frequency regarding water exercise.

Self-reported BMI was reduced in the water exercise group. One risk factor for developing or worsening lymphedema is a BMI over 30 (18,35), and it can be a particularly important issue to find exercise forms that can affect the women's weight as we know that physical exercise can. The reduction of BMI in our study is not in line with one other study comparing the two training forms, where reduction of BMI was instead shown in land exercise (18). Perhaps the colder water (<29°C) made it possible to use more intensive training, which could be the explanation for the reduced BMI in our study. BMI was self-reported, and there could be a hidden bias in the reduced BMI. However, we think that the risk for bias is small because comparison of objective and subjective BMI in the exercise groups before the final analysis showed the same results. Self-reported BMI was also used for all participants in all groups.

The land exercise group improved their daily physical shoulder function and joint mobility. This contradicts another study (18), where this improvement was a result of water

TABLE 4
Results for Well-Being, Body-Image and Frequency of Swelling

	Lane Exercise			Water Exercise			Standard Care			Differences between groups, P-value Increased/ Decreased
	Before Median (IQR)*	After Median (IQR)*	P-value n (%) Decreased Equal Increased	Before Median (IQR)*	After Median (IQR)*	P-value n (%) Decreased Equal Increased	Before Median (IQR)*	After Median (IQR)*	P-value n (%) Decreased Equal Increased	
Frequency of arm/leg swelling (1-6)[1]	5 (5-6)	5 (3-6)	0.180 7 (41) 8 (47) 2 (12)	6 (6-6)	6 (5-6)	0.031 6 (27) 16 (73) 0 (0)	6 (5-6)	5 (5-6)	0.453 5 (29) 10 (59) 2 (12)	0.509
n	17	17		22	22		17	17		
Overall well-being (1-7)[2]	6 (4-6)	5 (5-6)	0.453 2 (11) 12 (63) 5 (26)	5 (4-6)	5 (4.5-6)	1.000 6 (25) 11 (46) 7 (29)	5 (4-6)	5 (4-6)	0.344 7 (39) 8 (44) 3 (17)	0.265
n	19	19		24	24		18	18		
Physical health (1-7)[2]	5 (3-6)	5 (4-6)	0.581 5 (28) 5 (28) 8 (44)	5 (4-5)	5 (4-6)	1.000 4 (18) 14 (64) 4 (18)	4.5 (3.5-5)	5 (3.5-5)	1.000 3 (19) 9 (56) 4 (25)	0.889
n	18	18		22	22		16	16		
Cannot trust my body anymore (1-4)[3]	2 (1-3)	2 (1-2)	0.289 6 (32) 11 (58) 2 (11)	2 (1-3)	2 (2-3)	1.000 2 (13) 10 (67) 3 (20)	2 (1-3)	2 (1-3)	0.289 2 (11) 10 (56) 6 (33)	0.161
n	19	19		15	15		18	18		
My body feels damaged (1-4)[3]	2 (1-3)	2 (1-3)	0.227 8 (42) 8 (42) 3 (16	2 (1-2)	2 (1-2)	1.000 3 (20) 10 (67) 2 (13)	2 (2-3)	2 (2-3)	0.727 5 (28) 10 (56) 3 (17)	1.000
n	19	19		15	15		18	18		

*IQR Inter Quartile Range
[1] 1-6 (1.Never, 2.About once per quarter, 3.A couple of times per month, 4.A couple of times per week, 5. Almost every day, 6. Constantly)
[2] Visual Digital Scale 1-7
[3] 1-4 (1. Not at all, 2. A little, 3. Moderately, 4. Much)

exercise. The DASH questionnaire includes questions mostly about daily movements above 90° in the shoulder joint. One can speculate that land exercise is more effective in influencing certain movements compared to the water exercise where the arms are held in line with the water surface. Elevation in the shoulder decreased after land exercise, and we can perhaps declare that from an error of 4-5 degrees with regard to clinical relevance (36,37).

Well-being did not differ in or between the groups in this study. The term "well-being" used in our study may be compared to studies that use inventories or questionnaires measuring "quality-of-life" (QOL). Well-being is perhaps a more direct and intuitive concept than QOL that individuals can respond to directly, instead of summary scores of QOL issues constructed by the health care system. In our study, well-being was scored high from the start in all groups, and therefore it is not reasonable to expect any improvements in any of the groups or in-between the groups. Significant improvements of QOL after interventions have been shown in other studies on secondary lymphedema (17,19).

Body-image did not show any significant differences in or between the groups. We know from earlier studies (38) that lymphedema often has a negative influence on body-image and that a long period of physical activity intervention can improve body-image (39). In this context, the intervention in this study might have been too short to really influence the body-image outcome.

In order to reduce objective and self-reported swelling, female cancer survivors with lymphedema may be offered water exercise training. To improve daily shoulder function, one may speculate that movements above the water surface may affect specific functions and in the future additional shoulder elements in exercise programs could be included.

Our study showed that physical exercise did not worsen the lymphedema, a result in line with other studies (13-17). Individuals with lymphedema should no longer be afraid to perform physical exercise but we should be aware that certain individuals may be at risk. For example, it has been reported that weight lifting exercises can trigger erysipelas in lower leg lymphedema (40). More detailed research needs to be carried out on the risks and predictors for developing lymphedema with regards to physical exercise. On the other hand, cancer survivors also very often suffer from fatigue, and physical exercise in water is one way to reduce this (41).

It can be an advantage that the participants performed exercises in colder water (<29°C) because warmer water is tiring and would have made the participants slow down against more intense training. Warmer water of 33-34°C is the most commonly used temperature for individuals with lymphedema treated in physiotherapy. Such programs have been used for many years but to our knowledge no one has studied if water training can improve lymphedema limb volume. The purpose of exercising in warmer water is often to increase mobility and give the patient with functional disability the possibility of training. Tidhar used warmer water (33°C) in her study about Aqua Lymphatic Therapy (19). The intervention in that study was slow motions and massage under water, which cannot be compared to our study. We know from other studies that aerobic exercise preferably should be done at least twice a week to obtain any influence on physical changes and that the changes can persist after three months (18). Unfortunately, we had no practical ability to perform exercises twice a week. In future exercise studies, it may be important to have a second follow-up a couple of months after the intervention to see if the results in limb volume and BMI are maintained. Also, there is a need to systematically increase and study the exercise demands placed upon the body with increased exercise intensity, total repetitions, and repetition speed. In group training we do not have the possibility to reach this progressive overload in the same way as we do when instructing patients individually (42).

Limb volume was measured with either circumference or water displacement depending on local facilities. We think this had a small risk for influence on the primary outcome since the methods are well correlated (20).

The female cancer survivors with leg lymphedema in the study were too few to draw conclusions from and the HOOS function questionnaire is not fully applicable to these patients. The questionnaire includes many questions on symptoms from the hip, and the participants did not recognize themselves in these particular questions. Future intervention studies including physical function in the lower extremities may utilize some other function questionnaire for women with leg lymphedema. On the other hand, DASH was well suited for the arm lymphedema sufferers in this study. In the study we developed, a new study-specific questionnaire focusing on the specific aspects of lymphedema and exercise, function, well-being and body-image in lymphedema sufferers. It is based on patients' own experiences, extensive literature searches and the authors' long clinical experience in lymphedema treatment, and developed in a well thought out and well-used epidemiological manner (28-31), which is a strength of the study.

This intervention study was controlled, but not randomized, and three different cities were chosen for practical reasons, which may have introduced a risk of confounding. Comparability in demographics in the groups and that the groups were studied under comparable time periods strengthens the study's internal validity. Our sample size calculation from the beginning was detected on a larger group than we succeeded in including in the final study. Intervention studies are complex and the number of participants who agreed to participate was reduced because of practical and medical issues. Practical issues were that the colder pool and gymnastic hall were too far away from the participants' home destinations and that the time in the evening did not suit them. The survivors were asked by the physiotherapeutic clinics if they wanted to take part in the study. We may have chosen the most well motivated women, which may have had an effect on internal validity, so called self-selection bias. The drop-out rate from baseline was 19%, so we think there is a small risk that the number of participants in the study has influenced the validity of our results. Six women in the land exercise group dropped out because the training was too strenuous. These women were the somewhat elderly women (over eighty years). Perhaps elderly women could preferably be proposed water instead of land exercise if aerobic training is chosen. Four women in the land exercise group were excluded from the final analysis because they did not reach our pre-study determined criteria for the compliance rate (participation seven times). Compared with the higher compliance in the water exercise group, this may be a confounder, influencing the validity of the results, but may also be an indication that water exercise is better tolerated in individuals with physical impairments.

In conclusion, we found that after participation in water exercise, a higher proportion of female cancer survivors with lymphedema reduced their lymphedema, compared to women who participated in land exercise. However, there was no difference in the size of the reduction of arm lymphedema limb volume between the groups. Participants in the water exercise group reduced limb volume, BMI, as well as self-reported frequency of swelling after the intervention, whereas no reduction was seen among participants in the land exercise group. On the other hand, participants in the land exercise group reported an improved daily shoulder function measured with DASH and increased shoulder outer rotation after the intervention. To guide future female cancer survivors with lymphedema to effective exercise, resulting in reduced limb volume and improved function, adequate evidence-based programs are needed.

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