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Research article

The added value of supervised hydrotherapy sessions to a 12-week exercise program after breast cancer treatment: a three-arm pseudo-randomized pilot study

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Abstract: Sufficient physical activity after breast cancer treatment is crucial for improvement of a wide range of health-related outcomes and survival. The first aim of this pilot study was to explore whether adding supervised hydrotherapy sessions to a standard 12-week exercise program consisting of already two supervised sessions of land-based exercises has beneficial effects on physical and mental functioning and quality of life in breast cancer survivors. As a secondary aim, the added value of a third supervised training session with land-based exercises to the same standard exercise program was investigated. Breast cancer patients who finished primary cancer treatment were allocated to one of the three 12-week exercise programs, i.e. a standard exercise program with two supervised land-based exercise sessions per week (control group) or the same standard program with an additional weekly supervised hydrotherapy session (hydrotherapy-group) or land-based exercise session (land-based exercise group). The efficacy of the three programs was tested by comparing changes in physical and mental functioning and quality of life from pre- until post-intervention. Twenty-six (41%) patients were allocated to the control group, 21 (33%) to the hydrotherapy-group and 16 (26%) to the land-based exercise group. The results show no differences in any outcome between the three groups. Comparing the two exercise programs with three supervised sessions, results show a significantly larger improvement in the self-reported moderate (median (IQR) +1240 (412;3330) vs. +50(-1088;1125);p=0.020) and total physical activity level (+2982 (878;5457) vs. +370(-576;1718);p=0.008) in the hydrotherapy-group compared to the land-based exercise group. The opposite was found for the outcome 'physical symptoms', a subscale from the health-related quality of life questionnaire with a larger improvement in the land-based exercise group compared to the hydrotherapy-group (+3(0.6;4.8) vs. +0.6(-0.8;2.1); p=0.008). In conclusion, the results of this pilot study indicate that adding a third weekly supervised session to a 12-week exercise program consisting of already two weekly supervised sessions had no added value for the improvement of physical and mental functioning and quality of life after breast cancer treatment. If a third supervised session is organized, hydrotherapy may be a valuable exercise modality since moderate and total physical activity levels seem to improve more compared to an exercise program with three supervised land-based exercise sessions. For self-reported physical symptoms

although, a land-based exercise program seems more beneficial. Because of the limited sample size and pilot study design all obtained findings need to be interpreted with caution.

Keywords: Exercise, cancer survivors, hydrotherapie

1. Introduction

Breast cancer is the most common type of cancer in women in the world. In 2021, the estimation of new patients was 2.2 million (or 24.5% of all female cancers) worldwide [1]. The burden of cancer continues to grow worldwide, placing enormous physical, financial and emotional strains on individuals, their families, the health system and communities [1].

During and after breast cancer treatment, patients can experience a wide range of side effects. The most frequently reported symptom is fatigue [2]. This side effect may persist for many years after completion of therapy [2]. These patients also have poor health related quality of life (HRQoL), difficulty with returning to work and independent living in comparison with non-fatigued women [2]. Although less frequent, other physical consequences of breast cancer treatment are lymphedema, pain, decreased upper limb function and general physical deconditioning [3-5]. During and after active cancer treatment, breast cancer survivors also often experience mental health problems, such as depression, anxiety and fear about their prognosis, sexual dysfunctions, and changes in body image [6, 7].

There is overwhelming evidence to conclude that specific doses of aerobic training combined with resistance training can improve cancer-related health outcomes, including fatigue, physical functioning, anxiety, depressive symptoms and HRQoL, described above [8-10]. Moreover, all levels of physical activity post-diagnosis help to reduce breast cancer and all-cause mortality by 30% and 41%, respectively [8-10]. The guideline for cancer-survivors to achieve these beneficial effects include '150 minutes of aerobic physical activity of moderate-intensity exercises and 2 to 3 strength training sessions per week, focusing on stretching and balance exercises, for at least 12 weeks and supervised' [8-10]. No specific recommendations on the exercise modality are given. In addition, many breast cancer patients experience a lack of motivation to exercise after their cancer treatment because of low confidence in the benefits of exercise and other practical barriers, leading to low adherence [11-13]. Providing supervision and choosing an exercise modality preferred by the patient may improve adherence and outcomes of the exercise program [8-10].

A preferred exercise modality by many breast cancer patients is hydrotherapy [14, 15]. However, so far, evidence for the clinical benefits of hydrotherapy is not yet robust. Two studies observed that hydrotherapy resulted in a significant reduction in arm volume compared to floor exercises [16, 17]. Other studies show that a hydrotherapy program effectively reduces neck and shoulder pain, reduces the presence of tender muscle points in the shoulder-neck region, decreases fatigue, improves emotional well-being and improves HRQoL compared to patients who received a land-based exercise training [16, 18-20] However, as highlighted by two recent systematic reviews on hydrotherapy, the content (duration, intensity, frequency) of the hydrotherapy program differs greatly between these studies. Also, within a study, the intensity between the hydrotherapy and comparison intervention often differs as well, making it even more difficult to draw conclusions on the effectiveness of hydrotherapy [14, 15]. Last, these systematic reviews had to conclude that the overall risk of bias of the available studies was moderate to critical with in particular issue in the randomisation process, deviations from intended interventions and selection of the reported results [14, 15].

In conclusion, further research is needed to establish the role of hydrotherapy as part of an exercise program after breast cancer treatment. Therefore, the first aim of this pilot study is to investigate whether adding a supervised hydrotherapy session to a standard 12-week exercise program consisting of already two weekly supervised sessions of land-based exercises has beneficial effects on physical and mental functioning in breast cancer survivors. As a secondary aim, the added value of a third training session with land-based exercises to the same standard exercise program will be investigated.

2. Methods

This study applies the principles established in the Declaration of Helsinki and was reported according to the CONSORT guidelines, extended for pilot studies [1]. The study was approved by the ethical committee of the University Hospitals Leuven (s63338) and registered at clinicaltrials.gov (NCT05455385). The study was funded by the Department of Physical Medicine and Rehabilitation and the Multidisciplinary Breast Center of the University Hospital Leuven and the Department of Rehabilitation Sciences of KU Leuven.

2.1. Procedure

This study is a three-arm, pseudo-randomized pilot trial conducted in a sample of women after breast cancer treatment participating in a 12-week exercise program with two land-based exercise training sessions at the University Hospital of Leuven, Belgium. Each month, before the start of a new exercise program, all eligible participants were contacted by phone and informed about the possibility to participate in the pilot study. After signing informed consent, participants were allocated to one of the three groups: a group receiving 1) the standard exercise program alone (i.e. **control group**); 2) the standard exercise program and one additional supervised hydrotherapy training session (i.e. **hydrotherapy group**) or 3) the standard program and one additional supervised land-based training session (i.e. **land-based exercise group**). Allocation was randomized based on the availability (due to COVID-19 restrictions) of the pool for the upcoming 12 weeks. If the pool was available, participants were randomized to one out of the three groups. If the pool was not available, participants were randomized to the control group or the land-based exercise group. All participants are assessed before and after their exercise program. Recruitment, allocation and assessments were carried out by two master's students in Physiotherapy and Rehabilitation Sciences.

2.2. Participants

Participants are recruited at the University Hospital of Leuven, department of Physical Medicine and Rehabilitation within the standard 12-week exercise program after breast cancer treatment organized by this department. The inclusion criteria are men and women after surgery for breast cancer (mastectomy/breast-conserving and/or axillary lymph node dissection /sentinel node biopsy), possible (neo)adjuvant chemotherapy and radiotherapy have been completed, hormone and/or targeted therapy may still be ongoing. Patients are excluded if they have comorbidities or other reasons that make hydrotherapy impossible, i.e. open wounds or allergy to chlorine, severe physical disabilities, severe mental disabilities and pregnancy.

2.3. Interventions

The standard exercise program consists of one session in a fitness room and one session in an aerobics room, supervised by an experienced physical therapist with a master's degree (A.G). A session takes 90-minutes and consists of 30 minutes of cardio-training, 40 minutes of strength exercises (for arms, legs, core-stability) and 20 minutes of balance exercises and stretching/relaxation. For the session in the fitness room, patients follow an individualized program based on a cardiopulmonary exercise test (CPET). The intensity

of the exercise program is guided by heart rate, i.e. moderate-to-vigorous intensity with a heart rate between 60% and 80% (according to the Karvonen formula) of the maximum heart rate [2]. The treadmill is used for a personalised interval training and the bicycle ergometer for an endurance training. Fitness apparatus are used for strength training including the hip abductor, hip adductor and squat press for the legs and back pull, butterfly and pull down for the arms. Intensity of the strength training is determined by self-perceived exertion. In the aerobics room, own body weight, small weights, steps, fitness balls and elastic bands are used. As prescribed in the guidelines [2], the training sessions are first increased in the number of repetitions and then in the intensity of the exercises, based on the individual progression.

In addition to these two supervised land-based training sessions, participants in the **control group** are expected to carry out at least one additional training session of moderate-to-vigorous intensity at home in order meet the guidelines for exercise after cancer treatment [2]. Participants allocated to the **hydrotherapy-group** received one additional supervised session of 1.5 hours in a swimming pool. Similar as for the land-based training session, a session consists of 30 minutes of cardio-training (e.g. walking, running and jumping), 40 minutes of strength exercises (for arms, legs, core-stability with small exercise materials) and 20 minutes of balance exercises and stretching/relaxation. At last, participants allocated to the **land-based exercise-group**, received a third supervised session of 1.5 hours in the aerobics room. The content of this session was similar to the content of the session in the aerobics room as part of the standard exercise program.

2.4. Outcome measures

All participants were assessed before and after the 12-week exercise program. The assessments were performed on the day of their first training session at the Department of Physical Medicine and Rehabilitation of the University Hospitals Leuven, campus Pellenberg. All participants had to perform five clinical tests (duration of 30 minutes) and completed seven questionnaires (duration of 40 minutes) related to their mental and physical functioning and HrQoL. A detailed overview of the outcome measures is given in Table 1. In addition to the clinical and self-reported outcomes, attendance (i.e. how often the patient attended the supervised training sessions) was registered. Demographics (including age, body mass index, time since surgery and cancer-treatment related factors) were collected from the patient's medical file.

Table 1 Overview of the outcome measures and assessment methods

Physical functioning	
Shoulder mobility using an inclinometer (°)	Shoulder Range of Motion (ROM) is measured with a Dr. Rippstein Plurimeter-V analogue inclinometer [3]. The inclinometer is placed perpendicular to the humeral axis, just below the tuberositas deltoidea. The subject, standing upright, is instructed to perform an arm abduction movement in the coronal plane and a forward arm movement in the frontal plane with full elbow extension and neutral wrist flexion/extension. The assessor corrects the patient for compensation. The maximum shoulder ROM of both movements was recorded.
Relative arm volume by perimetry (%)	Arm circumference measurements are performed bilaterally using a perimeter, a flexible stainless-steel rod with a measuring tape attached every 4 cm and a 20 g weight at the end. Arm circumference is measured at the level of the olecranon and at 4, 8, 12, 16 and 20 cm proximal and distal to the olecranon. The volume of the arm is calculated using a formula for a truncated cone and is corrected for arm dominance. The relatively excessive arm volume is then

	calculated as follows: (volume of operated limb - volume of non-operated limb) / volume of non-operated limb) x 100 [4].
Muscle power by handgrip strength (kg)	Handgrip strength is measured with the Jamar Handheld Dynamometer [5]. The participant stands straight and holds the arm next to him or her at a 90-degree angle to the elbow. Two measurements are taken on each hand and the average of the values is calculated.
Flexibility by the sit-and-reach test (cm)	The Sit and reach test is a linear flexibility tests which helps to measure the extensibility of the hamstrings and lower back [6]. The test subject sits with feet flat against a box/wall and legs stretched out. With arms and fingers stretched out, the test subject pushes the measuring slide as far forward as possible and holds this position for a while. The participant pushes with the fingertips of both hands simultaneously. The legs must remain stretched out.
Exercise capacity by the 6-minute walk test (m)	The 6-minute walking test is used to assess patients' gait pattern, walking speed and cardiorespiratory endurance [7]. It measures the maximum distance the patient can maximally cover in 6 minutes. The patient is allowed to use walking aids and/or prosthesis(s) during the test.
Pain burden by the Brief Pain Inventory (BPI)	The BPI measures the severity of pain symptoms and interference with daily functioning using an 11-point scale [8]. First, average pain intensity (0-10, with higher scores meaning higher pain intensity) during the past 24 hours is recorded. Second, the pain-interference index is calculated from 7 items on pain-related functioning (general physical activity, mood, ability to walk, work and household tasks, relationships with others, sleep, vitality) by averaging the different items (0-10). A higher score indicates a higher interference.
Physical functioning by the Patient-Reported Outcomes Measurement Information System (PROMIS)	PROMIS Physical Function Short Form (PROMIS-PF-SF) [9] is a 10-item tool measuring physical function of upper extremity, lower extremity, central region and activities of daily living. Item scores range between 1 (unable) and 5 (no problem). Responses are transformed to standardized T-scores using the PROMIS conversion table, with 50 representing the general population mean and SD of 10. Higher scores indicate better perceived function.
Physical activity level by the International Physical Activity Questionnaire (IPAQ) – Long form	The IPAQ-long form measures self-reported physical activity levels in adults [10]. A total score of MET-min/week is calculated for total, work, household, leisure-time and transportation physical activity.
Mental functioning	
Body image by the Body Image Scale (BIS)	The BIS is a patient-reported outcome measure to evaluate body image during and after cancer treatment [11]. The BIS consists of 10 items and measures cognitive, affective and behavioural symptoms of body image. It uses a 4-point scale, where 0 = not at all and 3 = very much. The total score ranges from 0 to 30 and can be calculated by summing the 10 items together. The higher the score, the higher the level of body image disturbance.

Fatigue by the Functional Assessment of Chronic Illness Therapy - Fatigue Scale (FACIT-F)	The FACIT-F measures the impact of fatigue caused by the treatment of chronic diseases [12]. It consists of 13 items, with a total score between 13 and 65. A higher score on the scale indicates more fatigue.
Anxiety and depression by the Hospital Anxiety and Depression Scale (HADS-A and HADS-D)	The HADS measures core symptoms of anxiety and depression without including physical symptoms [13]. It consists of an anxiety scale and a depression scale, both containing 7 items with a total score from 0-21 where the higher the score, the more complaints.
Quality of life	
Quality of life by the McGill Quality of Life questionnaire	The McGill quality of life questionnaire (MQoL)[14] is a 16-item questionnaire on overall quality of life over the past two days. Each item is scored on a Likert scale (0 and 10) with opposites at each end. The subscale 'general quality of life' contains one item with scores ranging from 0 to 10. 'Health-related quality of life' is divided in 5 subscales: physical symptoms (3 items), physical well-being (1 item), psychological symptoms (4 items), existential well-being (6 items) and social support (2 items). The total score for health-related quality of life is the mean of the scores of the subscales. Higher scores indicate better well-being of the particular component of quality of life being measured.

2.5. Statistical analyses

Because most of the data was not normally distributed the median and interquartile ranges were reported and nonparametric tests were used. Taking into account the baseline assessment of the participant, the change in scores from before to after the training program were compared between the three groups by the Kruskal-Wallis test. The level of significance was set at $\alpha = 0.05$. In case of an overall significant difference in this change between the 3 groups, a posthoc pairwise comparison test was performed with the Mann-Whitney-U test. For the posthoc test, p-values are corrected for multiple testing by a Bonferroni correction, setting the critical p-value at p=0.05/3. Statistical analyses were performed with IBM SPSS Statistics, version 28 (SPSS Inc., USA).

3. Results

From April 2021 until March 2022, 81 participants met the inclusion criteria and were contacted by phone. Sixty-three subjects agreed to participate in the pilot study and were allocated to one of the three exercise programs. Twenty-six (41%) patients were allocated to the control group, 21 (33%) to the hydrotherapy-group and 16 (26%) to the land-based exercise group. Two participants dropped out from the control group and two from the land-based exercise group, all because of difficulties in combining the training program with work resumption. A flow of the participants is given in Figure 1.

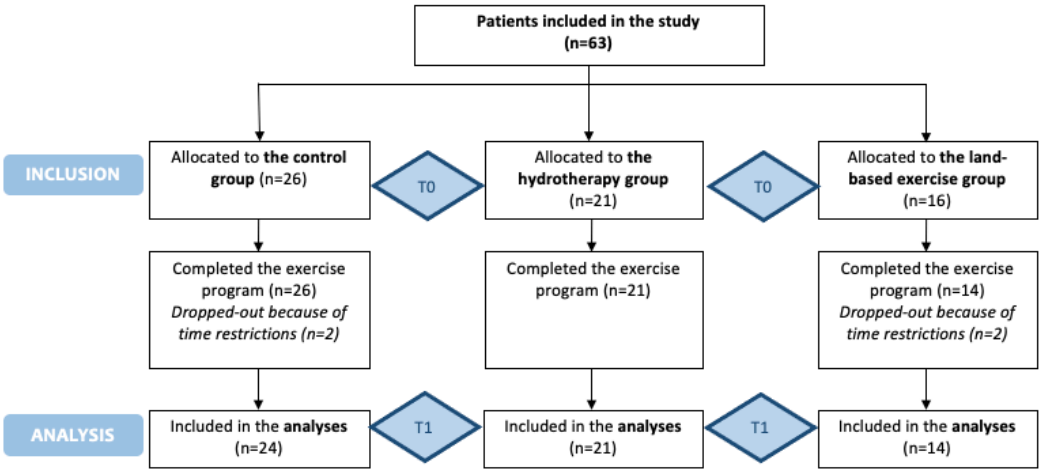

Figure 1 Flow of the participants; T0=baseline, pre-intervention; T1=3 months, post-intervention

The patient's characteristics are given in Table 2. The median age of all participants is 50 years and the median BMI is 25 kg/m^2.

Table 2. Patients' characteristics (n=63). Figures are numbers (percentages) and median (interquartile range).

	Total (n=63)	**Control group** (n=26)	**Hydrotherapy group** (n=21)	**Land-based exercise group** (n=16)
Age (years)	49 (43 – 57)	49 (43 – 57)	46 (38 – 57)	49 (40 – 55)
Body Mass Index (kg/m^3)	25 (22 – 28)	25 (23 – 26)	25 (22 – 29)	25 (22 – 29)
Time after surgery (years)	0.7 (0.4 – 1)	0.6 (0.3 – 1)	0.7 (0.4 – 1)	1 (0.5 – 1.6)
Surgery at dominant side	39 (62%)	15 (58%)	14 (67%)	10 (63%)
Radiotherapy	53 (84%)	23 (89%)	17 (81%)	13 (81%)
Chemotherapy	32 (51%)	11 (42%)	10 (48%)	10 (63%)
Hormone therapy	51 (81%)	22 (85%)	16 (76%)	13 (81%)
Targeted therapy	14 (22%)	10 (39%)	2 (10%)	2 (13%)
Type of breast surgery Mastectomy Breast conserving	 27 (43%) 36 (57%)	 16 (62%) 10 (38%)	 11 (52%) 10 (48%)	 6 (38%) 10 (62%)
Type of axillary surgery ALND SLNB		 13 (50%) 13 (50%)	 12 (57%) 9 (43%)	 10 (62%) 6 (38%)
Attendance (% of scheduled training sessions)	96 (86 – 100)	96 (87 – 100)	91 (84 – 97)	97 (80 – 100)

ALND= Axillary Lymph Node Dissection, SLNB= Sentinel Lymph Node Biopsy

Table 3 provides an overview of the efficacy estimates of all outcomes. In table 4, the results of the posthoc analyses of the efficacy outcomes with a significant overall difference in change from baseline to post-intervention between groups are portrayed. A significant overall difference between groups was found for self-reported moderate physical activity level, total physical activity level and physical symptoms, as part of health-related quality of life (Table 3). The posthoc analyses revealed that the improvements in moderate and total physical activity levels were significantly larger in the hydrotherapy group compared to the land-based exercise group (Table 4). However, after correction for multiple testing, the critical p-value for moderate physical activity was not reached. For 'physical symptoms', the improvement from before until after the exercise program was significantly larger in the land-based exercise group compared to the hydrotherapy group. For all other outcomes, no statistically significant differences were found between groups.

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Table 3. Overview of the outcomes evaluated pre- and post-intervention. Median (interquartile range) is given.

	Control group (n=26)		**Hydrotherapy group (n=21)**		**Land-based exercise group (n=16)**		Overall p-value for difference in change between groups*
	PRE	POST	PRE	POST	PRE	POST	
Clinical outcome measures							
Abduction ROM (°)	138 (120; 149)	142 (130; 160)	130 (118; 141)	138 (128; 155)	143 (114; 1550	147 (126; 160)	0.369
Forward flexion ROM (°)	150 (139; 160)	150 (140; 160)	142 (137; 151)	152 (140; 161)	145 (130; 162)	154 (135; 161)	0.110
Relative arm volume (%)	-0.5 (-2.4; 4.5)	-0.5 (-3.1; 2.4)	-0.4 (-5.4; 4.2)	-0.7 (-2.6; 3.4)	-0.4 (-2.2; 4.6)	-1.4 (-5.7; 2.9)	0.578
Handgrip strength (kg)	23.8 (19.9; 27.1)	22.5 (20.5; 26.5)	26 (21.3; 29)	26 (24; 30)	24 (20; 32)	27 (21; 32)	0.524
Flexibility (cm)	17.8 (14.3; 27.6)	23.2 (15.2; 31.4)	16.3 (9.2; 25)	24.4 (15.3; 28.8)	18.9 (9.8; 27.2)	24.0 (14.6; 29.3)	0.289
Exercise capacity (m)	581 (524; 625)	658 (629; 720)	544 (507; 625)	603 (575; 715)	600 (552; 645)	663 (633; 722)	0.702
Self-reported physical functioning							
Pain intensity (0-10)	3.5 (1.0; 6.3)	3.0 (1.0; 5.0)	4.0 (1.5; 6.0)	4.0 (0.0; 5.0)	4.5 (2.0; 5.8)	1.5 (0.0; 3.3)	0.596
Pain interference (0-10)	2.8 (1.4; 5.1)	1.8 (1.3; 4.8)	3.3 (0.9; 4.1)	2.2 (0.0; 5.0)	3.4 (1.9; 4.7)	1.3 (0.0; 2.0)	0.084
Physical functioning (13.8-61.3 t-score)	41.4 (36.5; 45.7)	46.0 (42.0; 52.0)	41.2 (36.6; 45.7)	43.8 (40.5; 46.2)	42.0 (36.1; 45.5)	46.0 (41.5; 50.0)	0.229
Moderate PA level (MET-min/week)	875 (60; 1635)	1860 (1020; 3960)	1200 (240; 2430)	2580 (1070; 4660)	2090 (1080; 4927)	2018 (1170; 4463)	**0.049***
Vigorous PA level (MET-min/week)	0 (0;0)	960 (240; 1440)	0 (0; 180)	1440 (480; 1928)	0 (0; 0)	720 (180; 1620)	0.960
Total PA level (MET-min/week)	2476 (1135; 4585)	4160 (3110; 6036)	2340 (865; 4367)	5217 (2921; 8857)	3675 (1887; 6954)	4217 (2268; 7615)	**0.020***
Self-reported mental functioning							
Body image (0-30)	14 (11; 20)	8 (5; 13)	14 (6; 20)	10 (5; 18)	17 (6; 22)	7 (2; 14)	0.069
Fatigue (13-65)	21 (16; 31)	18 (15; 21)	23 (19; 32)	21 (16; 24)	24 (17; 32)	16 (13; 20)	0.414
Anxiety (0-21)	8 (4; 11)	5 (4; 7)	8 (6; 11)	7 (5; 9)	8 (4; 13)	4 (2; 6)	0.420

Depression (0-21)	6 (2; 9)	2 (1; 5)	4 (3; 9)	4 (2; 5)	5 (2; 9)	2 (0; 4)	0.355
Quality of life							
General quality of life (0-10)	7.0 (6.0; 8.0)	8.0 (7.0; 8.0)	6.0 (5.0; 8.0)	7.0 (5.0; 8.0)	7.0 (5.0; 8.0)	8.0 (7.8; 9.0)	0.657
Health-related quality of life (0-10)	6.1 (4.9; 7.4)	7.7 (5.7; 8.1)	6.0 (4.6; 7.1)	5.7 (5.0; 7.8)	6.0 (5.3; 7.0)	7.6 (7.1; 9.2)	0.119
Physical symptoms (0-10)	3.5 (2.6; 4.6)	6.0 (3.0; 8.0)	3.7 (2.5; 5.0)	4.3 (2.5; 5.8)	3.7 (2.3; 6.2)	7.5 (5.8; 10.0)	**0.029***
Physical well-being (0-10)	6 (4.8; 7.0)	8.0 (6.0; 8.0)	6.0 (5.0; 7.5)	7.0 (5.5; 8.0)	6.5 (4.0; 7.0)	8.0 (7.8; 9.0)	0.520
Psychological symptoms)0-10)	6.6 (4.5; 7.9)	7.3 (5.5; 8.8)	5.3 (4.4; 7.9)	6.0 (5.3; 7.8)	6.5 (5.0; 8.1)	8.9 (5.8; 9.3)	0.909
Existential well-being (0-10)	6.9 (6.0; 7.9)	7.7 (6.5; 8.3)	6.8 (5.3; 7.8)	7.0 (5.0; 7.9)	6.9 (5.4; 8.0)	8.1 (7.8; 9.1)	0.209
Social support (0-10)	7.8 (6.0; 9.0)	7.5 (6.5; 9.0)	8.0 (5.3; 9.0)	7.0 (6.0; 9.3)	8.0 (7.1; 8.4)	8.3 (7.8; 9.0)	0.657

ROM=Range of Motion; kg=kilogram; cm=centimeter; m=meter; PA=Physical Activity; MET-min=Metabolic Equivalent; *Overall between groups testing was performed with the Kruskall-Walis test; the critical p-value was set at p=0.05.

Table 4. Results of the posthoc analyses of the efficacy outcomes with a significant overall between groups difference. Median (interquartile range) is given.

	Change from pre- until post-intervention			**P-value for pairwise comparison***		
Outcome measure	**Control group (n=23)**	**Hydrotherapy group (n=21)**	**Land-based exercise (n=14)**	**Control vs. hydrotherapy**	**Control vs. land-based**	**Hydrotherapy vs. land-based**
Health-related quality of life - Physical symptoms (0-10)	+1.6 (0; 4.3)	+0.6 (-0.8; 2.1)	+3 (0.6; 4.8)	0.132	0.172	**0.008**
Moderate PA level (MET-min/week)	+510 (-180; 1830)	+1240 (412; 3330)	+50 (-1088; 1125)	0.250	0.100	0.020
Total PA level (MET-min/week)	+1189 (-89; 3256)	+2982 (878; 5457)	+370 (-576; 1718)	0.590	0.234	**0.008**

PA=Physical activity; *Pairwise comparison was performed with the Mann-Whitney-U test; the critical p-value was set at p=0.05/3 (or =0.017).

4. Discussion

The first aim of this pilot study was to explore whether adding a supervised hydrotherapy session every week to a standard 12-week exercise program consisting of already two supervised sessions of land-based exercises per week has beneficial effects on physical and mental functioning and quality of life in breast cancer survivors. As a secondary aim, the added value of a third weekly supervised training session with land-based exercises to the same standard exercise program was investigated. Regarding both aims, the results show no statistical differences in any outcome between the standard exercise program with two supervised sessions and the other two programs with three supervised sessions. Comparing the two exercise programs with three supervised sessions, results show a significantly larger improvement in the self-reported total and moderate physical activity level in the hydrotherapy-group compared to the land-based exercise group. For the outcome 'physical symptoms', a subscale from the health-related quality of life questionnaire, a larger improvement was found in the land-based exercise group compared to the hydrotherapy-group. Although limited statistically significant results, probably due to the pilot study design, a clinically relevant improvement was found for certain outcomes within a specific training group.

Increasing physical activity levels after (breast) cancer treatment is very important to improve a wide range of health-related outcome measures [2,15,16]. As recommended in international guidelines, programs for cancer survivors should contain *'150 minutes of aerobic physical activity of moderate-intensity exercises and 2 to 3 strength training sessions per week, for 12 weeks'* [2,15,16]. One hundred-fifty minutes of moderate-intensity aerobic exercise each week corresponds with about 500 MET minutes per week [17]. The results of this pilot study show a median increase in at least 500 MET minutes/week of moderate and total physical activity in the control group and hydrotherapy-group as well from pre- until post-intervention, pointing towards an important and clinically relevant improvement [17]. In the land-based exercise group, the increase in physical activity levels did not reach this threshold. This result is remarkable since they also had three supervised sessions. A possible explanation may be the use of the short-form of the International Physical Activity Questionnaire (IPAQ-SF) to evaluate physical activity levels. This questionnaire was chosen because it is a short and easy-to-complete questionnaire. However, it is well described that, in line with other self-reported physical activity measures, the IPAQ-SF typically overestimates physical activity as measured by objective criteria [18]. On the other hand, reliability studies indicate that the IPAQ-SF can be used in repeated measures studies, although the true magnitude of the change over time, if any, may not be accurate [18]. Using objective measures of physical activity such as accelerometry is warranted in future studies.

Based on this specific result and the overall non-significant difference in any of the outcomes between the group with only two supervised sessions versus the groups with three supervised sessions, the need for supervision should be discussed. In general, evidence shows overall greater beneficial effects of exercise programs on health-related outcomes when supervision is provided [2,15,16]. It is however not clear whether this can be attributed to the setting (e.g. more attention from a healthcare provider, reinforcement) or because a higher dose of exercise may be better achieved with supervised training [2]. In the present pilot study, the supervised sessions of the exercise programs were carefully designed following the evidence-based prescriptions for frequency, intensity, time and type (FITT). For the home-based program, participants were encouraged to have a third training session at home. However, no concrete advice according to the FITT principles was provided for this, nor this was monitored with e.g. a diary or wearable. Doing this in future studies may give better insight into the need for supervision of a third session and its effect on health-related outcomes.

Although improvements in physical activity levels in the control- and hydrotherapy-group were considerable larger compared to the land-based exercise group, the only significant improvement in one of the health-outcomes was seen in the land-based exercise-group, namely self-reported physical symptoms as part of health-related quality of life. This contradictory result may be explained again by the design of this pilot study with in particular a small sample size. Also, as discussed above, self-reported physical activity levels should be interpreted with caution. In particular for this outcome 'physical symptoms', it has to be noted that, although the questionnaire used, i.e. McGill Quality of Life questionnaire, was validated in the breast cancer population [14], patients had to choose three physical symptoms themselves and score their burden. Details on which symptoms were reported is not available but high variability in this may affect the interpretation of this outcome. Overall, for most physical functioning outcomes, we do see small improvements in all groups pointing towards the general beneficial effects of all three exercise programs. For the mental functioning outcomes, all outcomes did improve in all three groups with the most remarkable improvements in 'body image' and 'fatigue' in the land-based exercise program'. For 'body image' in particular, this result is encouraging since low self-esteem and distorted body image are common psychological symptoms after breast cancer [19]. Up to now, studies focused on mind-body and educational interventions and cosmetic and beauty treatments to improve these symptoms. Further research should explore the beneficial effects of exercise programs.

Regarding feasibility of the different exercise programs, attendence rates were high for all three programs. Two drop-outs were noted in the control- and land-based-exercise program. This indicates that adding a third supervised sessions seems not to affect the feasibility to complete the exercise programs.

To our knowledge, this is the first study comparing three exercise programs with different exercise modalities and a different number of supervised sessions. This novel set-up provides insights into the need of supervision and the value of different exercise modalities. Another strength of the study was the set-up of the exercise programs themselves according to the FITT principles with a combination of aerobic and strength exercises. However, some limitations of the design of this pilot study should be mentioned and considered when interpreting the results. First, no a priori sample size calculation was performed given the exploratory character of this study. However, based on feasibility, it was anticipated to recruit 62 participants in total. This number was reached with 63 inclusions. Second, due to COVID-19 restrictions, the swimming pool was not available during the entire duration of the study, and capacity was limited to 4 people. This resulted in pseudo-randomization and unequal group numbers. When setting up a large well-powered randomized three-arm controlled trial in the future, these strengths and limitations should be considered. In addition to this controlled trial, cost-effectiveness analyses and a process evaluation [20] are required to prepare for implementation in daily care.

Based on the results of this pilot study and available international guidelines, at this moment we recommend **for clinical practice** to provide 12-week exercise programs with two supervised exercise sessions. Patients should be encouraged to be physically activity at home as well to reach the overall guideline. If possible and preferred by the patient, a third supervised session may be offered. Concerning the exercise modality, no convincing evidence is available to recommend hydrotherapy over land-based exercises. Both are safe [21,22], and, again, to make physical activity enjoyable and sustainable, the needs and preferences of the patients for a certain exercise modality should be considered. The ultimate goal is indeed to make patients engage in the recommended types and levels of exercise over their lifetime [2]. For future research, this pilot study demonstrates that the design with three supervised sessions is feasible, as well as the administering of this set of clinical and self-reported outcome measures (70 minutes in total). However, form a

clinical and cost-effectiveness perspective, the minimal required number of supervised exercise sessions to have beneficial effects should be studied. We recommend doing an a priori sample size calculation with self-reported physical functioning (e.g. Physical symptoms subscale of the McGill Quality of Life questionnaire) as primary outcome as this matters the most to patients. As key secondary outcomes, we recommend a clinical measure of exercise capacity (e.g. 6-minutes walking test) and an objective measure (e.g. wearable) for physical activity levels as this seems more reliable than self-reported physical activity levels. Further, better monitoring of physical activity at home with a diary or wearable is warranted together with a longer follow-up period of at least 6 months.

5. Conclusions

The results of this pilot study indicate that adding a third weekly supervised session to a 12-week exercise program consisting of already two supervised sessions had no added value for the improvement of physical and mental functioning and quality of life after breast cancer treatment. If a third supervised session is organized, hydrotherapy may be a valuable exercise modality since moderate and total physical activity levels seem to improve more compared to an exercise program with three supervised land-based exercise sessions. For self-reported physical symptoms although, a completely land-based exercise program may be more beneficial. Because of the limited sample size and pilot study design, all obtained findings need to be interpreted with caution.

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