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Combined Aerobic and Resistance Training in Breast Cancer Survivors: A Randomized, Controlled Pilot Trial

Abstract

The purpose of this pilot study was to examine the effects of a combined cardiorespiratory and resistance exercise training program of short duration on the cardiorespiratory fitness, strength endurance, task specific functional muscle capacity, body composition and quality of life (QOL) in women breast cancer survivors. Sixteen subjects were randomly assigned to either a training ($n = 8$; age: 50 ± 5 yrs) or control non-exercising group ($n = 8$; age: 51 ± 10 yrs). The training group followed an 8-week exercise program consisting of 3 weekly sessions of 90-min duration, supervised by an experienced investigator and divided into resistance exercises and aerobic training. Before and after the intervention period, all of the subjects performed a cardiorespiratory test to measure peak oxygen uptake ($\dot{V}O_{2peak}$), a dynamic strength endurance test (maximum number of repetitions for chest and leg press exercise at 30–35% and 100–110% of body mass, respectively) and a sit-stand test. Quality of life was assessed using the European Organization for Research and Treatment of Cancer QLQ-C30 (EORTC-C30) questionnaire. In response to training, QOL, $\dot{V}O_{2peak}$ (mean 3.9 ml/kg/min; 95% CI, 0.93, 6.90) performance in leg press (17.9 kg; 95% CI, 12.8, 22.4) and sit-stand test (– 0.67 s; 95% CI, – 0.52, – 1.2) improved ($p \leq 0.05$). We observed no significant changes in the control group. Combined cardiorespiratory and resistance training, even of very brief duration, improves the QOL and the overall physical fitness of women breast cancer survivors.

Key words
$\dot{V}O_{2peak}$ · exercise · disease · resistance · quality of life · sit-stand test

Introduction

Previous research has assessed the effects of cardiorespiratory exercise training engaging large muscle groups (treadmill or outdoor walking, leg pedalling exercise) on the physical work capacity and tolerance to physical fatigue of cancer patients and survivors (e.g., see refs. [6] and [23] for a comprehensive review). Results from these studies consistently show a significant improvement in functional capacity after training. Due to the high incidence and improved survival rate of breast cancer, compared with other types of cancer (which has considerably increased the necessity of improving patients' quality of life (QOL) during and after treatment against this type of tumour), most investigations in the field have evaluated breast cancer patients and survivors [6].

Considerably less research [2,12,13,19,29,31], especially using a randomized control design [29,35] has been conducted on the

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effects of resistance training on the physical work capacity of cancer patients or survivors. Resistance exercise should, however, be an integral component of any exercise training program [15], as it attenuates the muscle atrophy induced by both treatment and sedentary living habits in cancer patients/survivors and also contributes to improved overall physical capacity [23]. Indeed, increased muscle mass and strength induced by resistance training result in an attenuated cardiovascular stress response to any given load because the load now represents a lower percentage of the maximal voluntary contraction [28]. Only a few, non-controlled reports [2,12,13,31] have assessed the effects of concurrent resistance and aerobic training in cancer patients. Training-induced improvements in QOL usually paralleled strength gains in patients with various types of cancer, e.g., an overall increase of 43% in dynamic muscle strength was accompanied by a 21% improvement in one of the main QOL outcomes (patient's rating of functional living index) after 10 weeks of both aerobic and resistance training in patients with various types of cancer [12].

One of the best direct indicators of cardiorespiratory fitness is peak oxygen uptake ($\dot{V}O_{2peak}$). This variable is an excellent indicator of health status and an independent predictor of mortality in both healthy and unhealthy humans [5,30], but except in some cases (e.g., [7,19,24,36]), it has not usually been directly measured in studies with cancer patients/survivors. In this population, training improvements in maximal cardiorespiratory capacity are commonly estimated through indirect variables, such as maximal walking velocity or distance covered during a treadmill test (e.g., [9,10,34]). To our knowledge, only one (non-controlled) study has used an integrative approach to measure the effects of a total fitness program (aerobic *and* resistance) exercise training on the QOL and overall physical capacity (muscle strength and indirectly estimated $\dot{V}O_{2peak}$) of cancer patients [2]. No similar investigation has been conducted in cancer survivors. Lastly, studies on the effects of exercise training on the physical capacity of cancer patients/survivors have used both short (≤ 10 weeks) (e.g., [9,10,12,24,29,35,36]), or longer term (≥ 3–4 months) programs (e.g., [7,35]). Although both short and longer term training studies add important, complementary information to the body of knowledge in the field, short-term studies have a practical advantage. By reporting the early benefits of exercise, they indeed support the rationale for cancer sufferers to enter into training programs as soon as possible. The finding that even a few weeks of regular exercise might be sufficient to start helping patients and survivors cope with the anti-cancer treatment and its long lasting, deleterious side effects is a promising finding for this subpopulation. Accordingly, the purpose of this pilot study was to examine the effects of a relatively brief (8 weeks) concurrent cardiorespiratory and resistance training program on the cardiorespiratory fitness, lower and upper body dynamic strength endurance, task specific functional muscle capacity (evaluated with a specific strength task test), body composition (% body fat and muscle mass) and QOL in breast cancer survivors. We hypothesized that cardiorespiratory fitness, dynamic strength endurance, functional capacity, muscle mass and QOL would increase after training and remain unchanged in the control group, whereas muscle mass would tend to increase with training.

Methods

Subjects

Before entering the study, informed consent was obtained from each participant and the study was approved by the local Human Investigations Committee. A preliminary screening for subject selection was performed in the medical database of the Oncology Department of Hospital Comarcal Santiago Apóstol (Miranda de Ebro, Spain). A total of 37 subjects were contacted by telephone (November – December 2003) and a preliminary medical examination and the completion of a lifestyle history questionnaire were performed prior to the start of the study (December – January 2003). After the corresponding oncologist provided consent, subjects were deemed eligible for the study if they met each of the following conditions: 1) post-menopausal women surviving breast cancer (2 to 5 years post-treatment; age range: 40–60 years), 2) physical activity level: walking less than a total of 30–60 · min^{-1} three days · $week^{-1}$ and performing no strenuous exercise such as running, cycling, swimming or resistance training, and 3) previous anti-cancer treatment consisting of surgery with axillary lymphadenectomy and both post-surgery radiotherapy and chemotherapy. Women were excluded from the study if they had cardiac disease (New York Heart Association II or greater), uncontrolled hypertension (blood pressure > 160/90 mm Hg), uncontrolled pain, or any other condition that contraindicated exercise training in cancer patients or survivors [23], e.g., increased risk of bone fractures, severe anaemia (< 8 g/dL) or platelet count lower than $50 \cdot 10^9$/µL. Women with lymphedema were also excluded.

Twenty women of the 37 who had been contacted met all the above mentioned eligibility criteria and were randomly assigned to either a training (n = 10) or control group (n = 10). Two subjects from each group did not complete the study and thus the final number of subjects evaluated was n = 8 in each group.

All the 16 women who completed the study were survivors of stage I–II ductal breast carcinoma (Table **1**). The time elapsed after treatment was similar in both groups (training: 36 ± 13 months; control: 35 ± 12 months). The mean age, body mass and body mass index of each groups at the start of the study was: 50 ± 5 yrs (training) and 51 ± 10 yrs (control); 66.7 ± 10.5 kg (training) and 67.7 ± 8.9 kg (controls); and 24.0 ± 3.2 kg · m^{-2} (training) and 25.1 ± 3.5 kg · m^{-2} (control), respectively.

Study design

This pilot study utilized a single blind design. The treatment allocation system was set up so that the researcher who was in charge of enrolling participants did not know in advance which treatment the next person would get, i.e., a process termed "allocation concealment" [32,33]. Allocation concealment prevents researchers from (unconsciously or otherwise) influencing which participants are assigned to a given intervention group. Research assistants (exercise physiologists) with no knowledge of group assignment were designated to measure the outcome variables (questionnaires of QOL, anthropometrical evaluation, and cardiorespiratory and dynamic strength endurance tests).

Table **1** Stage of disease and treatment protocol (with respect to surgery and chemotherapy) of the 16 study subjects

Group	*Stage of disease*	*Type of surgery*	*Chemo-therapy protocol*	*Time post-treatment (months)*
Training				
1	I	lumpectomy	CFM	24
2	I	lumpectomy	CFM	30
3	I	lumpectomy	CFM	58
4	II	lumpectomy	CFM	36
5	II	MRM	A + CFM	50
6	II	MRM	CFM	24
7	II	RM	CFM	24
8	II	RM	CFM	45
Control				
1	I	lumpectomy	CFM	24
2	II	lumpectomy	CFM	31
3	I	lumpectomy	CFM	36
4	I	lumpectomy	CFM	60
5	I	lumpectomy	CFM	33
6	II	MRM	A + CFM	24
7	II	MRM	A + CFM	30
8	II	RM	A + CFM	45

All the subjects received radiotherapy. Abbrevations: MRM (modified radical mastectomy), MR (radical mastectomy), CFM (cyclophosphamide, methotrexate and 5-fluorouracil), A (adriamycin)

Intervention: training program

Subjects in the intervention group followed an 8-week training program (February – March 2004). During the 8-week period, subjects in the control group followed their usual sedentary lifestyle (physical activity level < walking for a total of 30 – 60 · min^{-1} three days · $week^{-1}$ and performing no strenuous exercise such as running, cycling, swimming or resistance training). All of the subjects from both groups were assessed before and after the 8-week period (end of January and early April, respectively).

The 8-week exercise training program consisted of 3 weekly sessions of 90-min duration each. All sessions were performed in the same community fitness club (Miranda de Ebro, Spain) and supervised by the same experienced investigator. Each session started and ended with a 10-min warm-up and cool-down period, consisting of cycle-ergometer pedalling at very light workloads and stretching exercises for all major muscle groups. The 70-min core portion of the training session was divided into resistance and aerobic training. Resistance training included 11 exercises engaging the major muscle groups (chest press, shoulder press, leg extension, leg curl, leg press, leg calf rise, abdominal crunch, low back extension, arm curl, arm extension, and lateral pull-down). All exercises were performed through the full range of motion normally associated with correct technique for each exercise. Stretching of the muscles involved in an exercise was performed at the end of each set of resistance exercise. During the first 4 weeks, subjects performed two and one set of exercises for large (e.g., leg press) and small muscle groups (e.g., arm extension), respectively, and all sets were performed at a resistance that allowed 12 – 15 repetitions (12 – 15 repetition maximum, RM). Thereafter, the resistance used was individually adjusted to allow the completion of 8 – 10 repetitions for three sets of the large muscle group exercises and two sets of the small muscle group exercises. The resistance used for each exercise was increased by 5 – 10% when the subject could perform the prescribed maximum number of repetitions per set. After an increase in resistance, the repetitions per set typically decreased to the low end of the prescribed repetition range (12 or 8 repetitions). Abdominal and lower back exercises were performed in a 15 – 20 repetition maximum zone. At the beginning of the program, aerobic training consisted of pedalling on a cycle-ergometer for 20 min at 70% of the maximal heart rate (HR_{max}) observed during the pre-training cardiorespiratory test. The duration and intensity of the sessions was gradually increased during the 8-week period so that the subjects completed 30 min of continuous pedalling at 80% of HR_{max} by the end of the training program. For subjects in the poorest physical condition, it was sometimes necessary to divide the first sessions into shorter time intervals to complete the total 20-min target duration (e. g., 2 bouts of 10 min). Blood total creatine kinase levels were measured every week to ensure that the training program did not induce excessive muscle damage, i. e., levels < 167 IU · l^{-1} [11].

Testing procedures before and after the 8-week period

On the same day as the cardiorespiratory tests, QOL was measured using the questionnaire developed by the European Organization for Research and Treatment of Cancer (EORTC): the EORTC QLQ-C30 [1,14]. We used the third version (3.0), which has been shown to be valid and reliable when applied to Spanish cancer patients [3]. This questionnaire includes 30 items relating to physical, role, social, emotional, cognitive and functioning and a global scale of QOL (maximum score of 100). For simplicity, we reported the results of the global scale and the main variable related to exercise training, i. e., physical functioning. Before the cardiorespiratory test, blood samples were obtained from an antecubital vein (between 8 : 30 a. m. and 9 : 00 a. m.) to determine haematocrit and haemoglobin levels using a Sysmex NE-1500 haematology analyzer.

All cardiorespiratory tests were performed in the same community sports medicine unit (Gabinete Médico-Deportivo, Miranda de Ebro, Spain) at the same time of the day (10 : 00 a.m. – 14 : 00 p.m.) under similar environmental conditions (temperature, ~ 20 °C; relative humidity, 45 – 55 %; barometric pressure, ~ 720 mm Hg) on an electrically braked cycle-ergometer (Variobike 600, Marquette Hellige, Freiburg, Germany). Subjects refrained from performing physical activity during the 24 h period before the tests. After a warm-up period of 5-min with no load, power output was increased from an initial value of 20 W by 10 W · min^{-1}. Subjects maintained pedal cadence within the range of 60 – 70 rev · min^{-1}. A cadence monitor was placed in view of the subject during each test and a designated investigator insured that they maintained the required pedalling cadence throughout the duration of the test. The tests were terminated upon volitional exhaustion of the subjects and/or when cadence could not be maintained at a minimum of 60 rev · min^{-1}. Respiratory gas-exchange data were measured *breath-by-breath* using open circuit spirometry (Oxycon Delta, Jaeger, Viasys Healthcare, Hoechberg, Germany). Peak oxygen uptake ($\dot{V}O_{2peak}$) and ventilation ($\dot{V}E_{peak}$) and peak values of ventilatory equivalent for oxygen ($\dot{V}E \cdot \dot{V}O_2^{-1}$) and carbon dioxide ($\dot{V}E \cdot \dot{V}CO_2^{-1}$) and respiratory exchange ratio (RER) were recorded as the highest average values obtained for any continuous 20-second period. The peak power output (PPO) was computed as follows [21]:

$$PPO = PO_f + ([t/60 \cdot 10])$$

where PO_f is the power output (W) of the last completed workload, t is the time (in s) the last uncompleted workload was maintained, 60 is the duration (in s) of each completed workload, and 10 is the power output difference (W) between consecutive workloads. Heart rate and blood pressure were monitored during the tests using 12-lead ECG tracings and a manual pressure cuff, respectively.

Forty-eight hours after the cardiorespiratory test, functional muscle performance was determined using a sit-stand test [18]. For this test, we used a straight-backed chair (40 cm high) and asked each subject to sit and stand, as fast as possible, five times with their arms folded across their chest. The subject was timed from the initial sitting position to the final standing position at the end of the fifth stand by using a stopwatch to the nearest 0.01 s [7]. One day after the sit-stand test, dynamic upper and lower-body muscle dynamic endurance strength were measured on a bench and leg-press machine (Salter, Barcelona, Spain), with a load of 30 – 35% and 100 – 110% of body mass, respectively. Each subject was instructed to perform each exercise to momentary muscular exhaustion. The total number of repetitions performed was recorded. Any repetitions not performed with a full range of motion were not counted. Previous research has also used endurance strength tests to assess the dynamic muscle strength of healthy women and the physiological effects of resistance training [25, 26]. A warm-up period, including aerobic and stretching exercises (~ 10 min), and warm-up sets with the aforementioned machines, preceded each test.

In an effort to eliminate anticipated learning effects and establish reliability of both sit-stand and dynamic strength endurance tests [17], before the start of the study the subjects performed: 1) three to four familiarization sessions with both types of tests over a 1-week period that were followed by 2) repeated tests showing significant ($p < 0.01$) intra-class correlation coefficients ($R = 0.983$, $R = 1.00$ and $R = 0.969$) and low coefficients of variation (– 1.6%, 0.0% and 6.0%) for sit-stand, bench and leg press tests, respectively. All sit-stand and dynamic strength endurance strength tests, as well as familiarization sessions, were performed in the abovementioned community sports medicine unit. Finally, we chose to use tests of strength endurance and the sit-stand test instead of tests of maximal strength (as the 1 RM used in other cancer studies, e. g., Adamsen et al. [2]) since improvements in maximal dynamic strength would not be of great practical relevance for cancer sufferers or survivors, as opposed to athletes in general. In the former, indeed, maximal strength is not a main determinant of their ability to perform physical activities of daily living, which are mostly submaximal-strength tasks, e. g., climbing stairs, sitting and rising from a chair, etc.

Body composition was assessed indirectly through changes in body mass and subcutaneous skinfolds. Skinfold measurements were made at three sites (triceps, abdominal, and suprailiac) to estimate percentage of body fat [20]. Total muscle mass (kg) was estimated from anthropometrical data following the prediction equation developed by Lee et al. [22], using multi-slice magnetic resonance imaging:

$$\text{Muscle mass (kg)} = \text{Height (m)} \cdot (0.00744 \cdot CAG^2 + 0.00088 \cdot CGT^2 + 0.00441 \cdot CCG^2) + 2.4 \cdot \text{gender} - 0.048 \cdot \text{age (yrs)} + 7.8$$

where CAG is corrected arm girth, CTG is corrected thigh girth, CCG is corrected calf girth, and gender equals 1 for male and 0 for female. Limb girths were corrected for subcutaneous adipose tissue thickness as follows: the skinfold caliper measurement (S) was assumed to be twice the subcutaneous adipose tissue thickness, and the corrected girths (Gm) were calculated as $Gm = \text{limb girth} - \pi \cdot S$ (in cm).

All anthropometric measurements were performed by the same researcher in the abovementioned community sports medicine unit.

Statistics

Mean values of all the variables at baseline were compared between both groups using paired *t*-tests (for parametric data) or Wilcoxon tests (for categorical data, i. e., global QOL and physical function scores). To evaluate the interactive effect of group and time, independent *t*-tests were used to compare the change in values over time (post-test minus pre-test) in training and control groups for: body composition (body mass, fat mass and muscle mass, % body fat, % muscle mass); blood (haemoglobin, haematocrit and erythrocyte count); peak cardiorespiratory values ($\dot{V}O_{2peak}$, PPO, PPO/body mass, HR, $\dot{V}E$, $\dot{V}E \cdot \dot{V}O_2^{-1}$, $\dot{V}E \cdot \dot{V}CO_2^{-1}$ and RER); and dynamic strength endurance (bench press, leg press) and sit-stand tests. Data collected for the second pre-training endurance strength and sit-stand tests were used in the analyses. The mean change over time (post-test minus pre-test) in both training and control groups for both global QOL and physical function scores was compared using the Mann Whitney U test. For parametric variables (i.e., all except global QOL and physical function), results are expressed as mean (SD), and the size of the change and its precision were provided by reporting the change in mean values and the 95% confidence intervals (95%CI) for the change, respectively. Results as median (minimum – maximum) for categorical data (i.e., global QOL and physical function scales). The level of significance was set at 0.05.

Results

The mean value of all the variables that have been studied did not differ at baseline between both groups ($p > 0.05$).

Adherence to training and possible adverse effects

Adherence to training averaged 91.1 ± 6.9% (individual values of 95.8%, 100%, 87.5%, 87.5%, 100%, 83.3%, 91.7%, and 83.3%, respectively, for each subject of the training group). No major adverse effect and no major health problem were noted in the subjects of both groups over the 8-week period. In the training group,

Table 2 Pre and post values for variables tested in the training (n = 8) and control (n = 8) groups. Parametric data are shown as mean (SD), whereas categorical data (QOL and physical function scores) are shown as median (minimum – maximum)

	Training		*Control*			
	pre	*post*	*pre*	*post*		
Categorical variables						
QOL	63 (33 – 83)	92 (67 – 100)	71 (42 – 100)	63 (33 – 83)		
Physical function	87 (73 – 100)	93 (80 – 100)	93 (87 – 100)	93 (80 – 100)		
Parametric variables					**Overall change in means**	**95 % CI for overall change in means**
Body mass (kg)	66.7 (10.5)	65.6 (8.7)	67.7 (8.9)	67.3 (8.9)	– 0.7	– 2.93 to 1.38
Fat mass (kg)	16.4 (6.6)	14.7 (4.8)	15.3 (4.8)	15.3 (4.6)	– 1.7	– 3.58 to 0.24
Muscle mass (kg)	27.3 (2.4)	28.0 (2.7)	28.6 (2.5)	28.3 (2.9)	1.0*	0.25 to 1.86
Body fat (%)	24 (6)	22 (5)	22 (5)	22 (4)	– 2.0*	– 0.3 to – 3.8
Muscle mass (%)	41 (5)	43 (4)	43 (3)	42 (3)	3*	0.1 to 3.2
Haemoglobin ($g \cdot dL^{-1}$)	14.1 (1.0)	14.0 (0.9)	14.1 (1.0)	14.0 (0.9)	0	– 0.38 to 0.18
Haematocrit (%)	42 (2)	42 (2)	42 (2)	42 (2)	0	– 3.3 to 1.5
Erythrocyte count ($\times 10^6 \cdot mm^{-3}$)	4.7 (0.3)	4.7 (0.3)	4.7 (0.3)	4.7 (0.3)	0	– 0.38 to 0.18
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	23.7 (5.8)	25.9 (4.5)	27.4 (3.9)	25.7 (3.7)	3.9*	0.93 to 6.90
PPO (W)	85 (24)	110 (16)	91 (12)	94 (12)	22*	10 to 35
PPO : body mass ($W \cdot kg^{-1}$)	1.31 (0.46)	1.71 (0.39)	1.38 (0.30)	1.41 (0.31)	0.37*	0.17 to 0.56
HR_{peak} ($b \cdot min^{-1}$)	164 (16)	161 (16)	160 (15)	156 (15)	1	– 6 to 8
$\dot{V}E_{peak}$ ($L \cdot min^{-1}$)	54 (13)	60 (9)	63 (13)	59 (13)	10*	4 to 16
$\dot{V}E_{peak} \cdot \dot{V}O_{2peak}^{-1}$	32.2 (4.8)	33.5 (3.2)	32.1 (7.5)	32.3 (6.4)	1.1	– 2.71 to 4.94
$\dot{V}E_{peak} \cdot \dot{V}CO_{2peak}$	29.0 (3.4)	30.0 (2.7)	28.5 (5.1)	29.8 (3.7)	– 0.3	– 3.92 to 3.24
RER_{peak}	1.11 (0.06)	1.12 (0.05)	1.12 (0.08)	1.11 (0.10)	0.02	– 0.06 to 0.09
Bench press (n° reps.)	0.0 (0.0)	2.0 (2.0) (n = 7)	0.3 (0.8) (n = 6)	0.5 (1.2) (n = 7)	1.8†	– 0.3 to 3.9
Leg press (n° reps.)	10.1 (6.8) (n = 7)	26.3 (6.2) (n = 7)	16.9 (5.5) (n = 7)	15.2 (4.7) (n = 6)	17.9*	12.8 to 22.4
Sit and stand test (s)	7.90 (0.8)	7.19 (0.65) (n = 6)	7.53 (0.49)	7.49 (0.55) (n = 6)	– 0.67*	– 0.52 to – 1.25

"Overall change in means" is the change (post minus pre means) for the training group minus the change (post minus pre means) for the control group. Abbrevations: QOL (quality of life), CI (confidence interval), PPO (peak power output), $\dot{V}O_{2peak}$ (peak oxygen uptake), HR_{peak} (peak heart rate), $\dot{V}E_{peak}$ (peak ventilation), $\dot{V}E_{peak} \cdot \dot{V}O_{2peak}^{-1}$ and $\dot{V}E_{peak} \cdot \dot{V}CO_{2peak}^{-1}$ (peak values of ventilatory equivalents for oxygen and carbon dioxide, respectively) and RER_{peak} (peak respiratory exchange ratio). Symbols: * significant interactive effect of group and time ($p < 0.05$); † $p = 0.08$ for the interactive effect of group and time

blood total creatine kinase consistently remained under normal levels (< 167 $IU \cdot l^{-1}$), indicating no excessive muscle damage. Although no follow-up was systematically conducted in the study participants after the second battery of tests, women in the training group were satisfied with the results of the study and reported their intention to continue the training program on their own, at least twice per week.

Quality of life

There was a significant mean change in both the global scale ($p = 0.002$) and physical function scale ($p = 0.04$) after the training program, as measured by the EORTC QLQ-C30, with the training group improving compared to the control group (Table **2**).

Body composition

We observed a significant interactive effect of group and time for the change in total muscle mass (kg), % body fat and % muscle mass, but not for body mass (kg) and fat mass (kg) (Table **2**).

Blood oxygen transport capacity

No significant interactive effect of group and time was found for the blood values tested (Table **2**).

Cardiorespiratory tests

A significant interactive effect of group and time was found for $\dot{V}O_{2peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$) and PPO ($W \cdot kg^{-1}$) (Fig. **1**) and peak ventilation ($L \cdot min^{-1}$) (Table **2**), but not for peak values of $\dot{V}E \cdot \dot{V}O_2^{-1}$, $\dot{V}E \cdot \dot{V}CO_2^{-1}$ and RER (Table **2**).

Dynamic strength endurance and functional performance

A significant interactive effect of group and time was found for leg press (Fig. **1**) and sit-stand test but not for bench press (Table **2**).

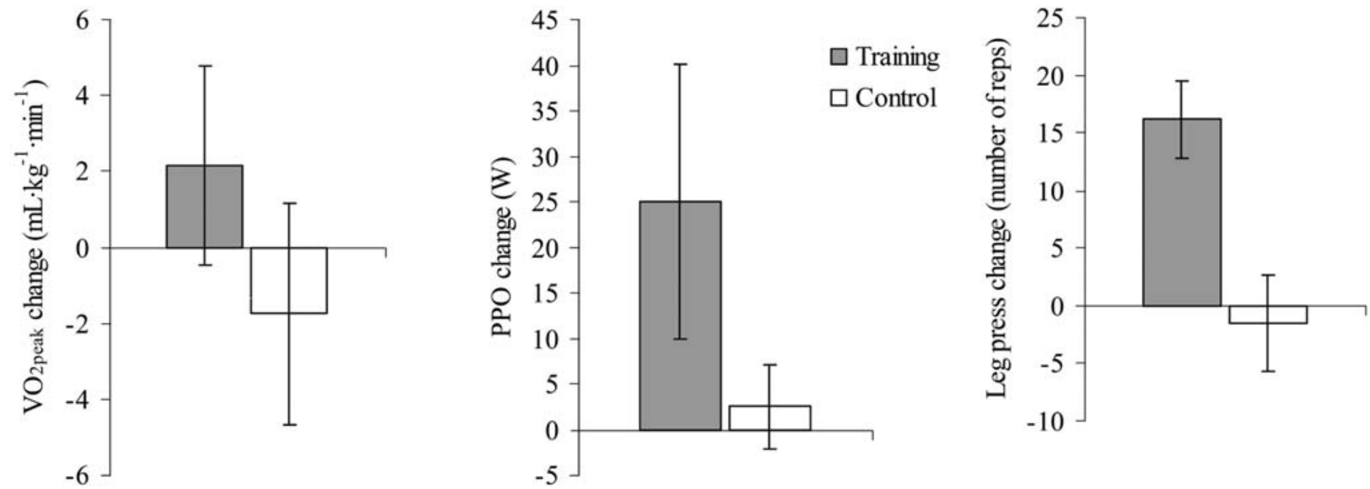

Fig. 1 Mean ± SD change in peak oxygen uptake ($\dot{V}O_{2peak}$, $mL \cdot kg^{-1} \cdot min^{-1}$), peak power (PPO, W) and leg press performance (number of repetitions) between pre and post values for training (n = 8) and control (n = 8) groups.

Discussion

Our study shows that a brief (8 week) structured supervised training program combining cardiorespiratory and resistance exercises positively effects changes in cardiorespiratory capacity, strength endurance, muscle function and QOL in breast cancer survivors. These findings are of relevance as previous research has shown that long-term fatigue (that is attributable, at least partly, to physical deconditioning) with subsequent decreases in QOL is also a serious problem for cancer survivors, as up to 30% may experience this symptom for years after termination of treatment [8,23]. For instance, Berglund and colleagues [4] showed that fatigue persisted (and was the most commonly reported symptom) in 68% of women survivors of breast cancer who were treated with adjuvant chemotherapy (same protocol as here) between two and 10 years previously and were overall healthy and recurrence-free at the time of follow-up (i.e., as were our subjects). Although previous controlled studies have demonstrated the beneficial effect of exercise programs in patients with cancer [6,23], we believe that our results uniquely demonstrate the multifaceted improvement in physical functioning and also demonstrate the efficacy of even a brief period of a formal exercise program. Specific to our findings are improvements in $\dot{V}O_{2peak}$, improved dynamic strength endurance (in the lower body), increased muscle functional capacity (evaluated with a specific test), and improved QOL and body composition after training. Especially unique was the improvement in dynamic strength endurance for the leg press. This increase in dynamic strength endurance was accompanied by an increase in estimated muscle mass. These are important findings as impaired muscle function and subsequent early fatigue are often related more to muscle wasting than to the specific organ system impacted by a disease [16]. On the other hand, our study is not without methodological limitations, such as a small number of muscle groups being evaluated during the strength endurance tests, no direct assessment of body composition and muscle cross sectional area, or lack of further follow-up of the subjects after the short-term training program. Future studies using larger population samples and overcoming the aforementioned limitations should corroborate our preliminary, yet promising findings.

Little research [2,12,13,19,29,31], especially using a randomized control design [29,35], has been conducted on the effects of resistance training on the physical work capacity of cancer patients or survivors. Segal et al. [35] reported significant improvements in upper and lower body muscle strength in a large number of men with prostate cancer (n = 82) compared to their controls (n = 73) after a 12-wk program. Unfortunately, participants did not undergo a familiarization period before performing the baseline strength tests, nor did they perform a second test to assess the reliability of the test results. We believe that a familiarization period to eliminate learning effects and assess the reliability of pre-training tests are necessary to accurately determine the effects of training on human muscle strength [17]. In addition, all training sessions in our study were directly supervised by an investigator, a procedure that has been shown to be important in causing maximal gains during strength training compared to unsupervised programs [26]. Further, we assessed the effects of exercise training on the sit-stand test, i.e., the ability to perform lower-body functional living tasks as rising from a chair that involve rapid movements. This issue has not been previously investigated in cancer patients/survivors, although important physical abilities such as balance, coordination, maximal strength and the ability to generate torque are performance determinants in the aforementioned test [17]. Performance during this type of test is indeed impaired by declined joint function (relative to hip, knee, and ankle torque) and/or decreased ability to recover balance after perturbation or to carry out time-critical actions requiring moderate-to-substantial strength [17].

McKenzie and Kalda [29] estimated the effects of an 8-week combined aerobic (arm-ergometer) and resistance exercise training program on the QOL, and arm circumference and volume of women breast cancer survivors with unilateral upper extremity lymphedema secondary to treatment. In their study, QOL (e.g., improved physical functioning) showed a similar improvement as in our subjects following training. Furthermore, lymphedema was not affected by upper-body strength training exercises. In our study women with lymphedema were excluded since we were concerned that this could have affected performance during the demanding baseline bench press tests (which included reliability assessment and familiarization periods). Taken together, the findings by McKenzie and Kalda [29] and those reported here show the lack of detrimental effects.

Some studies have attempted to assess the effects of exercise training on the $\dot{V}O_{2peak}$ of cancer patients/survivors [7,19,24, 36]. $\dot{V}O_{2peak}$ attained during a graded maximal exercise is considered the single best indicator of aerobic physical fitness [27]. When expressed relative to body mass, $\dot{V}O_{2peak}$ is also an indicator of health status and predictor of mortality [5,30]. In this regard, the mean values of $\dot{V}O_{2peak}$ reported in our subjects, that were clearly below $30\,ml \cdot kg^{-1} \cdot min^{-1}$, reflect the poor physical condition of this subpopulation and the need for breast cancer patients and survivors to engage in exercise training programs to improve their $\dot{V}O_{2peak}$ values, and thus their overall health status. Improvements in exercise capacity and $\dot{V}O_{2peak}$ following training are related to QOL, particularly in patients with exercise capacity limited by various disease processes [15]. Finally, the finding that training improved peak values for absolute power and power expressed relative to body mass is important. Improvements in the ability to perform normal day to day activities are likely to increase independence and sense of well-being, therefore a change in body composition with a concomitant increase in power output would positively influence physical function and QOL.

In conclusion, combined cardiorespiratory and resistance training under supervised training conditions improves the QOL and the overall physical fitness of breast cancer survivors following even a brief (8-week) exercise program. Our data, together with those of previous research with cancer patients/survivors, emphasize the beneficial effects of exercise programs in this population.

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