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ORIGINAL ARTICLE

Adherence to a long-term progressive resistance training program, combining supervised and home-based exercise for breast cancer patients during adjuvant treatment

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ABSTRACT

Background: The purpose of the study was to examine adherence and identify patient- and treatment-related factors associated with adherence to a 20-week combined supervised and home-based progressive resistance training program in women treated for breast cancer.

Methodology: The study population consisted of the intervention group in a randomized clinical trial examining the effect of resistance exercise on lymphoedema prevention ($n = 82$). The full program lasted 50 weeks, with an initial 20 weeks combined supervised and home-based exercise followed by 30 weeks self-administered exercise. Information about attendance rates (supervised exercise) and exercise dairies (home-based exercise) in the first 20 weeks was available for 74 and 62 participants, respectively. Adherence was measured as numbers of exercise sessions performed divided by expected number of exercise sessions with >2/3 categorized as high adherence. Age-adjusted odds ratios (OR) were used to assess the associations between patient- and treatment-related factors with adherence.

Results: The number of participants with high adherence to supervised exercise decreased in the late period (from week 11 onward) compared to the early period (65% vs. 48%) whereas the proportion of participants with high adherence to home-based exercise remained close to 55%. The most prominent factor associated with high adherence to supervised exercise was neoadjuvant chemotherapy [OR 7.09; 95% confidence interval (CI), 1.12–44.62]. For home-based exercise, lower adherence was seen in obese participants (OR 0.16; 95% CI, 0.04–0.65) and in participants with average or below average lower body muscle strength at baseline (OR 0.12; 95% CI, 0.03–0.46).

Conclusion: The results of this study offer valuable information on factors associated with adherence to a program of supervised and home-based exercise. Interventions may be adapted to ensure higher adherence rates through supportive efforts targeted to women who are obese, have low muscle strength and who receive no or adjuvant chemotherapy (as opposed to neoadjuvant chemotherapy) during exercise.

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Introduction

Improvements in quality of life and symptoms like fatigue and physical functioning have repeatedly been documented as benefits of exercise during adjuvant cancer treatment [1–4]. However, adherence to regular exercise for women undergoing treatment for breast cancer can be challenging due to psychosocial factors related to the diagnosis and physical side effects from the treatment [5]. Women treated for breast cancer have traditionally been advised to avoid strenuous activities of the affected arm, including progressive resistance training (PRT), due to fear that overload could trigger lymphedema [6,7]. Although the existing literature does not support this [8], it may add yet another dimension to barriers for exercise.

High adherence is paramount in exercise trials as it impacts the outcome and ultimately the internal validity, but achieving this is a well-documented challenge [9,10]. Knowledge of factors associated with adherence could be useful in finding adherence-promoting strategies, but unfortunately the body of evidence in this area is incoherent due to heterogeneity in settings and circumstances of the particular intervention. A systematic review of 18 randomized clinical trials (RCTs) in mixed cancer survivors (including nine studies on breast cancer) showed moderate evidence of a positive association between exercise history and adherence to exercise during and after cancer treatment, while findings were inconsistent for all other factors reviewed [10]. Specifically in women with breast cancer [2,11–14], the most

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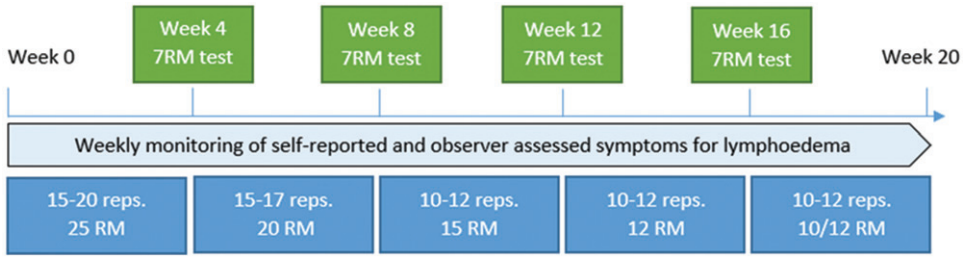

Figure 1. Outline of timeline and the progressive resistance training program with testing and monitoring in LYCA, phase 1 (week 1–approximately week 20).

consistent factor associated with adherence to exercise was body mass index (BMI) with an inverse association observed for supervised and home-based exercise both during and after chemotherapy [11,14].

Previous studies of adherence to exercise among breast cancer patients have primarily been conducted for supervised, medium-length exercise interventions (12–17 weeks) during or after chemotherapy [2,12–14]. To our knowledge, no studies have examined factors associated with exercise adherence to longer-lasting PRT interventions combining supervised and home-based exercise during adjuvant therapy in women at substantial risk of developing lymphedema. Detailed knowledge on factors important for adherence provide an opportunity to apply early strategies supporting participants at risk of low adherence.

The aim of this study was to examine adherence to an intervention combining supervised and home-based exercise during adjuvant therapy for women with breast cancer participating in a RCT [15].

Material and methods

Setting and participants

Preventive intervention against LYmphoedema after breast CAncer (LYCA) was a multi-center, single-blind RCT. In brief, women aged 18–75 undergoing breast cancer surgery with axillary lymph node dissection were recruited postoperatively from August 2015 to January 2017 from three breast surgery clinics covering East Denmark. All participants signed informed consent before entering the study. Computer randomization allocated participants to intervention (in addition to usual care) or control group (usual care), stratified by recruiting hospital and BMI (cut point: 30 kg/m^2). The intervention comprised two phases; phase 1 covered the first 20 weeks combining supervised and home-based exercise while building exercise tolerance and increasing load, and phase 2 covered the following 30 weeks with self-administered exercise. Adherence in phase 1 and phase 2 were analyzed separately, as exercise mode and exercise reports between the phases were unassociated. This paper concerns adherence to exercise in phase 1, as data for phase 2 were not yet available. For further details of setting, participants and the exercise program we refer to a previous paper [15].

Exercise intervention

In Phase 1, participants started exercising at first opportunity after baseline testing, which took place two weeks post-surgery. Group sessions with up to 15 participants were supervised by physiotherapists at three locations associated with each of the recruiting hospitals. Sessions of 1-hour duration were scheduled in afternoons/evenings on two weekdays with one day in between. Participants were instructed to attend twice a week and to follow a home-based program once a week resembling the supervised program for which weights and resistance bands were provided. The intervention covered major muscle groups and ensured individualized progression from low to moderate intensity, and a continuous adaptation of load to the individual's muscle strength (Figure 1).

The duration of phase 1 exercise was extended if participants for various reasons (e.g., pain or swelling) could not progress to moderate exercise load within the 20-week period, with maximum length of phase 1 lasting up to 30 weeks. If participants were challenged with regards to time and resources, supervised sessions could be replaced by home-based exercise. If a participant did not show up for two consecutive supervised sessions without notification, she was contacted by phone by the study coordinator in order to motivate return to the program.

Assessment of outcomes and covariates

Exercise adherence rates were obtained via attendance rates to supervised exercise recorded by the instructors and exercise diaries for home-based exercise kept by the participants. Missing data in the diaries was interpreted as though no home-based exercise was done for that week. If the participant never showed up or no exercise diaries were provided, they were not included in the analysis of home-based exercise. Furthermore, for some of the participants who provided no diaries, we collected information by an interview about the home-based exercise at the end of phase 1.

Sociodemographic, lifestyle and symptom information were retrieved from paper-based questionnaires filled in at baseline. We grouped cohabitation into living with a partner (married or cohabiting) or living alone, and education into short (basic school, 7–9 years), medium (high school or vocational, 9–12 years) or long (higher education, $>$12 years). Employment status was measured as employed, not employed or retired. We categorized smoking into current, former or never smoker while alcohol intake was categorized as high-risk intake ($\geq$14 units per week), no high-risk intake or no alcohol intake based on current national guidelines. Physical activity was dichotomized into meeting national

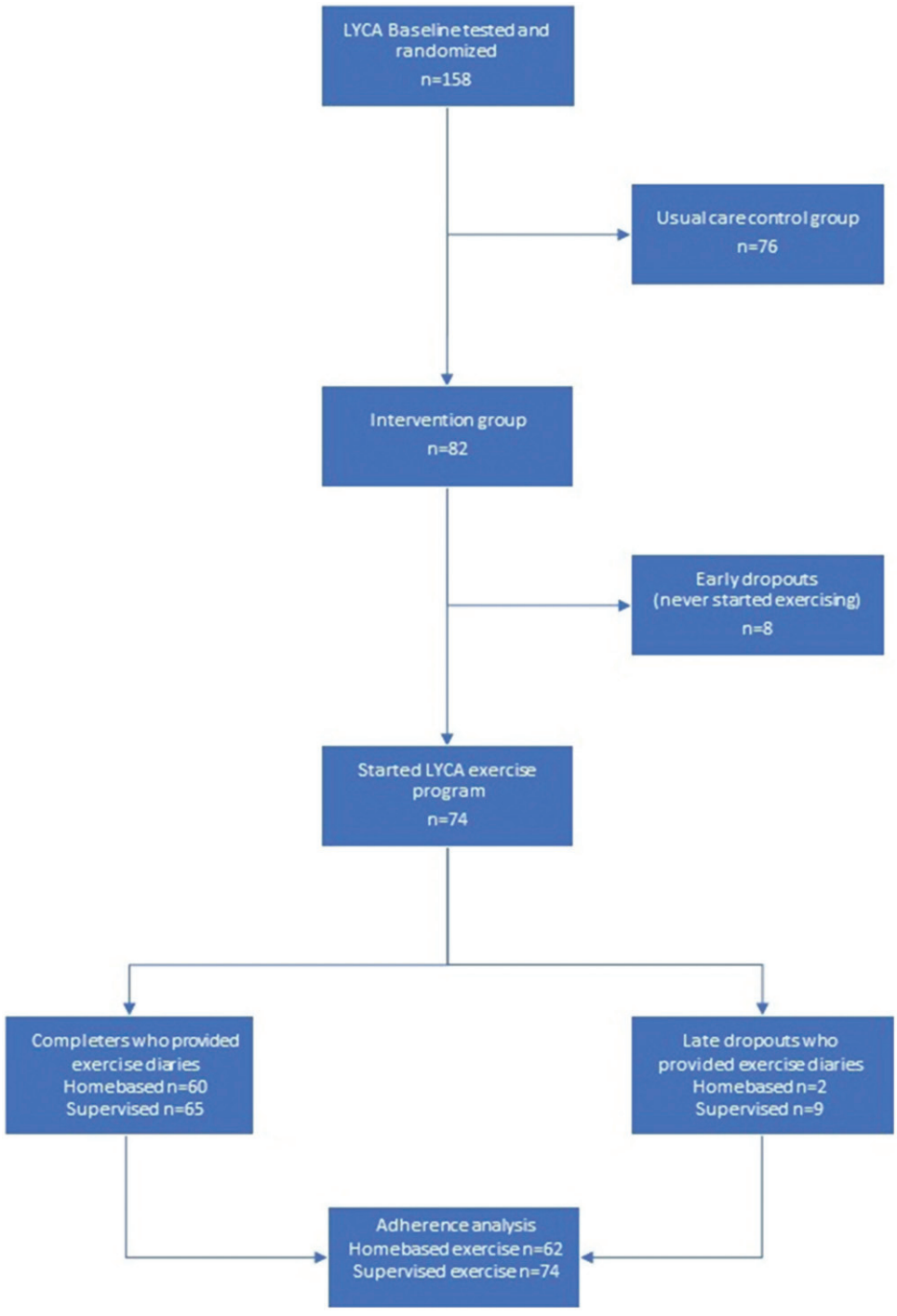

Figure 2. Flowchart illustrating the passage through the intervention group in LYCA, phase 1 (week 1–approximately week 20).

guidelines with 30 daily minutes of physical exercise including 20 minutes of high-intensity physical activity at least twice a week or not.

Fatigue was measured by the FACIT-fatigue questionnaire and dichotomized as recommended into high and low-to-moderate level of fatigue [16]. BMI was calculated from self-reported height and measured weight and was grouped into normal weight ($<25\ kg/m^2$), overweight ($25–29.9\ kg/m^2$) and obese ($\geq 30\ kg/m^2$).

Participants muscle strength was tested at baseline, including isometric handgrip test and 7RM (repetition maximum) leg press test. Values were standardized according to age and sex. Handgrip strength was dichotomized into 'fair to excellent' or 'needs improvement' [17] and leg press into 'above average' or 'average or below' [17].

At the end of the intervention program, information about chemotherapy was collected from medical records and classified into neoadjuvant, adjuvant or no chemotherapy. Distance to exercise facility from home was measured by an online map (www.krak.dk) and dichotomized using a cut point at 5 km. Furthermore, exercise location was included as a covariate.

Exercise adherence

We used the World Health Organization's definition of adherence 'the extent to which a person's behavior corresponds with the agreed recommendation from a healthcare provider' [18]. Adherence was estimated as the number of exercise sessions attended in percent of the expected number of sessions. The expected number was determined by the individuals' phase 1 duration subtracting sessions where supervised exercise was not offered (due to sick instructors and public holidays). Adherence was dichotomized into 'low to medium' and 'high' using a cut point of 2 sessions per week (67%) based on findings from meta-analyses on resistance exercise in a healthy population [19–21]. To allow for comparison with existing literature, we made additional analyses using a cut point of 80% as high adherence. We investigated overall program adherence (supervised and home-based exercise combined throughout the whole period), adherence to supervised exercise, and adherence to home-based exercise separately and in two different time periods; the first 10 weeks (early) and from 11 weeks until the end of phase 1 (late).

Statistical analyses

The associations between adherence (low/medium, high) and the described covariates were studied in cross tables using Fisher's exact test to evaluate statistical significance. The analyses were performed by exercise type and period. *p*-values lower than .05 were considered statistically significant. Logistic regression models (high adherence vs. low/medium) adjusted for age in four categories were fitted for descriptive purposes. The results of the logistic regression analyses are given in odds ratios (OR) with corresponding 95% confidence intervals (CI) adjusted for age. All statistical analyses were carried out using STATA version 14.

Results

In total, 82 participants were allocated to the LYCA intervention group. We obtained complete data including attendance lists and diaries from 74 and 62 participants for supervised and home-based exercise sessions respectively. Eight participants (10%) never showed up for the intervention and were categorized 'early dropouts'. Another 11 participants (15%) dropped out from supervised exercise or both the supervised and home-based exercise between week 1 and 12 (mean 7.2 weeks) and were categorized as 'late dropouts' (Figure 2). The primary reason for late dropout was logistics.

Patient- and disease-related characteristics as well as physical measures of the early dropouts were not significantly different from late dropouts or participants who completed the program (data not shown). Early dropouts were excluded from further analysis.

Overall program adherence

Out of the 62 participants who provided information on both supervised and home-based exercise, 73% achieved high adherence (≥67% of sessions) to the overall phase 1 program (Table 1), while 56% achieved ≥80% adherence (data not shown).

Adherence to supervised exercise in the early period of phase 1 was high for 65% of participants, and 48% in the late period. The proportion of participants with high adherence to home-based exercise was unchanged throughout both periods (55% vs. 56%) (Figure 3).

The majority of the 62 completing participants was aged 55–64 years, had long education, was employed, had normal weight, did not smoke or have high-risk alcohol intake. Further, most exercised less than the recommended level and scored low on muscle strength (Table 1). Most were assigned to adjuvant chemotherapy and had high levels of fatigue.

Adherence rates only differed between participants with below/average or above average muscle strength with high adherence rates for 24% and 57% respectively ($p = .02$, Table 1). However, in age-adjusted regression analysis we did not find a statistically significant association (age-adjusted OR 0.28; 95% CI, 0.07–1.04, data not shown).

Adherence to supervised exercise

In the early period, smoking was more frequent among participants with low/medium compared to high adherence ($p = .02$); failing to reach statistical significance in logistic regression (age-adjusted OR, 0.62; 95% CI, 0.21–1.83 for former smokers versus never smokers). In the late period, more participants with high adherence had received neoadjuvant therapy compared to participants with low/medium adherence ($p = .01$; Table 2) corresponding to an age-adjusted OR of 7.09 (95% CI, 1.12–44.62) compared to no chemotherapy. Women who received adjuvant therapy had a non-significant age-adjusted OR for high adherence of 1.37 (95% CI, 0.27–6.92; data not shown).

Adherence to home-based exercise

In regard to home-based exercise, being normal weight ($p = .04$; Table 2) was more common among participants with high adherence in the late period, corresponding to age-adjusted OR's of 0.47; 95% CI, 0.12–1.88 and 0.16 (95% CI, 0.04–0.65) for overweight and obese participants, respectively compared to normal weight participants. Consistent with findings for overall program adherence, having above average lower body muscle strength was more common among participants with high adherence in the late period ($p = .01$, Table 2) with an age-adjusted OR of 0.12 (95% CI, .03–.46) compared to less than average strength (data not shown).

Discussion

In this study of adherence to exercise in the first 20-week period of a 50-week intervention of individualized PRT among women who received axillary lymph node dissection for breast cancer, we found high adherence to supervised

Table 1. Overall program adherence to supervised and home-based exercise combined for the whole period for all participants starting exercise and providing information about home-based exercise.

	Low/Medium Adherence ($N = 17$), N (%)	High Adherence ($N = 45$), N (%)	p
Age (Years)			.43
<45	2 (12%)	7 (16%)	
45–54	6 (35%)	19 (42%)	
55–64	7 (41%)	9 (20%)	
65–74	2 (12%)	10 (22%)	
Living with partner			.71
Yes	13 (81%)	38 (84%)	
No	3 (19%)	7 (16%)	
Education			1.00
Short + Medium	3 (19%)	8 (18%)	
Long	13 (81%)	37 (82%)	
Employment status			.81
Employed	13 (81%)	31 (74%)	
Not employed	0 (0%)	1 (2%)	
Retired	3 (19%)	10 (24%)	
BMI			.24
Normal weight	7 (41%)	24 (5%)	
Overweight	3 (18%)	12 (27%)	
Obese	7 (41%)	9 (20%)	
Smoking habits			.56
Current smoker	0 (0%)	1 (2%)	
Former smoker	9 (56%)	19 (42%)	
Never smoker	7 (44%)	25 (56%)	
Alcohol habits			.66
High-risk intake	1 (6%)	7 (17%)	
No high-risk intake	10 (63%)	23 (55%)	
Never drinking alcohol	5 (31%)	12 (29%)	
Physical activity beforediagnosis			.31
Meeting recommendations	2 (13%)	13 (29%)	
Below recommendations	13 (87%)	32 (71%)	
Fatigue			.67
High	14 (93%)	39 (86%)	
Low–Moderate	1 (7%)	6 (13%)	
Upper body muscle strength			.18
Excellent–Fair	0 (0%)	6 (14%)	
Needs Improvement	16 (100%)	37 (86%)	
Lower body muscle stregth			.02
Above average	4 (24%)	25 (57%)	
Average or below average	13 (76%)	19 (43%)	
Chemotherapy			.69
Neoadjuvant	5 (29%)	13 (29%)	
Adjuvant	10 (59%)	22 (49%)	
None	2 (12%)	10 (22%)	
Distance to exercise facility			.48
≤5 KM	2 (12%)	10 (22%)	
>5 KM	15 (88%)	35 (78%)	
Exercise facility			.33
Herlev hospital	9 (53%)	31 (69%)	
Naestved hospital	5 (29%)	6 (13%)	
Rigshospitalet	3 (18%)	8 (18%)	

Total number does not always ad up to 62 due to missing values. Low/medium adherence is <67% of training sessions; high adherence ≥67% of training sessions. p-values are based on Fischer's exact test.

exercise in the first ten weeks which decreased in the next up to 10 weeks with approximately half of the participants maintaining exercise rates classified as 'high' meaning 'acceptable' from a clinical perspective. Participants who had received neoadjuvant chemotherapy were more likely to achieve high adherence to supervised exercise compared to women who received adjuvant or no chemotherapy, while high BMI and low muscle strength in the lower body at baseline were associated with low adherence to home-based exercise.

When examining overall program adherence (supervised and home-based exercise combined) almost 80% of the participants adhered to two out of three weekly sessions. When using 80% as threshold for high adherence, slightly more than half of participants achieved high adherence which remains comparable to findings in other intervention studies in breast cancer patients. Noted, none of the previous studies involved interventions of 20-week supervised and home-based PRT concurrently with adjuvant treatment [2,11–14]. Our findings indicate that adherence is challenged over time and therefore, long-term programs may need extra resources to keep acceptable adherence rates. A similar trend was found in two other studies ($n = 37$ and $n = 78$) where the exercise interventions lasted 6 months and 12 weeks respectively [11,12].

The acceptable adherence observed in LYCA may partially be attributed to the consistent contact with the physiotherapist keeping participants motivated. The combination of the

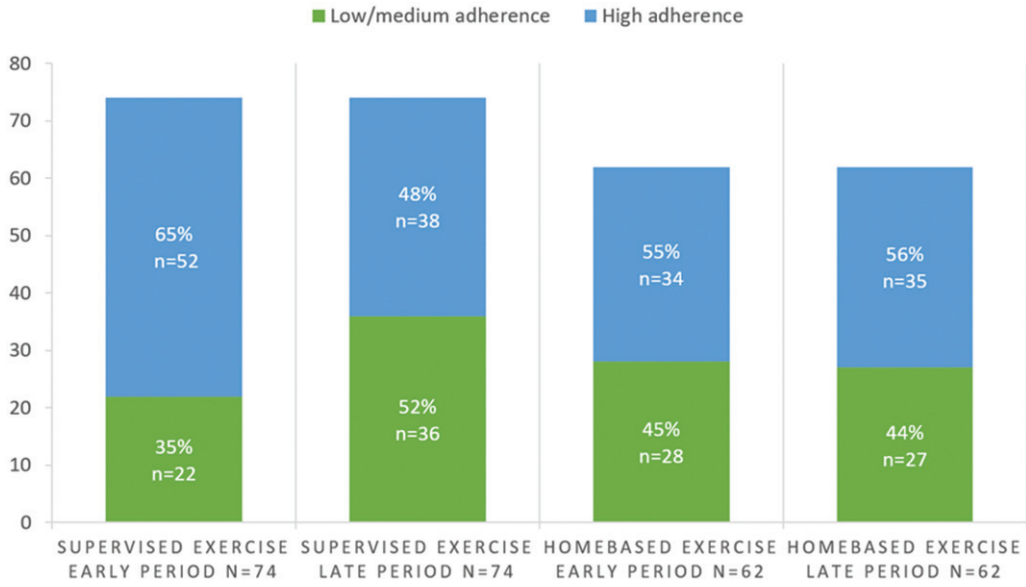

Figure 3. Distribution of low/medium and high adherence in the two types of exercise in the early (week 1–10) and late (week 11–approximately week 20) period for the participants who exercised in LYCA.

two types of exercise settings allowed for flexibility while still providing the necessary monitoring and guidance by the instructor. This flexibility can be crucial when the intervention takes place during adjuvant therapy, where the participants have several other medical appointments and often a high burden of side effects. The participants possibly also benefitted from the social support from the other participants in the group [22] and the fact that the intervention began close to the time of diagnosis and surgery, as it may represent a period with high motivation for behavioral change [23].

In LYCA, all women in the program received adjuvant radiotherapy and most received chemotherapy. Compared to the women who received chemotherapy after surgery, participants who received neoadjuvant chemotherapy and were beyond the initial side effects from treatment at intervention start, may not have been as challenged with participation in supervised exercise in the longer term (beyond 10 weeks) as reflected in the sevenfold likelihood of high adherence among these women. Another study of exercise adherence during adjuvant treatment in breast cancer [14], likewise found that a short chemotherapy protocol was associated with high adherence. This is further supported by a study of a supervised exercise intervention, where side effects or treatment-related factors were the reasons given for half of all canceled sessions [24].

In our study, obesity was associated with lower adherence to home-based exercise, in line with previous exercise studies [11,14]. Furthermore, adherence to home-based exercise was lower for participants who had below/average lower body muscle strength at baseline. We would expect, that participants characterized by obesity and/or low levels of lower body muscle strength did not exercise regularly before the diagnosis. Previous studies have found a positive association between exercise history and adherence to exercise [10]. Surprisingly, we did not find any association between self-reported physical activity before diagnosis and adherence but this might be explained by reporting bias or residual confounding by our dichotomization of the variable.

Not without relevance, a large proportion of participants had high levels of fatigue just after surgery, but this was not associated with lower adherence during the 20-week program, indicating that exercise may also hold potential for interventions targeting fatigue at this point in the treatment trajectory.

Strengths and limitations

A strength of this study is that we have information on both supervised and home-based exercise. The two types of exercise appeal differently to women and each exercise type have distinct advantages and disadvantages in terms of guidance and expenses. Being able to examine the two types separately and combined provides more detailed information about exercise adherence and characteristics associated with adherence.

A further strength is that we examine adherence to a relatively long intervention component and look at associated factors in the early and late periods separately. This provides a perspective on exercise adherence that projects into the phase where cancer treatments and their side effects accumulate and collide with challenges of daily life. We examined a number of factors potentially associated with participation in an exercise program, using both patient-reported and assessor-measured variables on sociodemographic, lifestyle, wellbeing and physical constitution. Furthermore, a strength is the translatable setting and the readily available exercise form. If this program was to be implemented in primary care settings, a similar adherence rate is likely.

A well-known challenge in clinical exercise studies is that participation in the study may appeal more to patients used to physical activity and exercise. This limits the generalizability of our results. The lack of systematic registration of the reasons for not exercising or canceling a session is a limitation. This information could have provided knowledge

Table 2. Adherence to supervised and home-based exercise, respectively, among participants who exercised in phase 1 in LYCA by early (week 1–10) and late (week 11–approximately week 20) period.

	Supervised exercise ($N = 74$)				Home-based exercise ($N = 62$)			
	Early period		Late period		Early period		Late period	
	Low/Med adherence $N = 22$ (%)	High adherence $N = 52$ (%)	Low/Med adherence $N = 35$ (%)	High adherence $N = 38$ (%)	Low/Med adherence $N = 28$ (%)	High adherence $N = 34$ (%)	Low/Med adherence $N = 27$ (%)	High adherence $N = 33$ (%)
Age (years)								
<45	18	15	20	13	18	12	15	12
45–54	45	38	34	47	43	38	33	45
55–64	18	29	29	24	25	26	37	18
65–74	18	17	17	16	14	24	15	24
	$p = .82$		$p = .72$		$p = .76$		$p = .36$	
Living with partner								
Yes	75	85	79	84	81	85	81	85
No	25	15	21	16	19	15	19	15
	$p = .49$		$p = .76$		$p = .74$		$p = .74$	
Education								
Short + medium	5	19	12	18	22	15	27	12
Long	95	81	88	82	78	85	73	88
	$p = .27$		$p = .53$		$p = .51$		$p = .19$	
Employment status								
Employed	81	75	70	86	85	68	73	77
Not employed	5	2	3	3	4	0	4	0
Retired	14	23	27	11	11	32	23	23
	$p = .57$		$p = .20$		$p = .09$		$p = .87$	
BMI								
Normal weight	50	50	49	53	43	56	33	64
Overweight	23	25	17	29	21	26	26	21
Obese	27	25	34	18	36	18	41	15
	$p = 1.00$		$p = .26$		$p = .29$		**$p = .04$**	
Smoking habits								
Current smoker	14	0	3	5	0	3	0	3
Former smoker	45	41	46	38	48	44	54	39
Never smoker	41	59	51	57	52	53	46	58
	$p = .02$		$p = .72$		$p = 1.00$		$p = .50$	
Alcohol habits								
High-risk intake	14	15	15	12	4	22	8	19
No high-risk intake	62	56	62	56	54	59	62	52
No alcohol intake	24	29	24	32	42	19	31	29
	$p = .93$		$p = .78$		$p = .06$		$p = .53$	
Physical activity								
Meeting recommendations	10	27	21	24	19	29	16	27
Below recommendation	90	73	79	76	81	71	84	73
	$p = .21$		$p = .78$		$p = .55$		$p = .36$	
Fatigue								
High	90	80	76	89	85	91	84	94
Low–moderate	10	20	24	11	15	9	16	6
	$p = .49$		$p = .21$		$p = .45$		$p = .39$	
Upper body muscle strength								
Excellent–fair	5	12	6	14	7	13	4	15
Needs improvement	95	88	94	86	93	88	96	85
	$p = .67$		$p = .43$		$p = .68$		$p = .38$	
Lower body muscle strength								
Above average	43	50	40	57	36	58	19	67
Average or below average	57	50	60	43	64	42	81	33
	$p = .62$		$p = .17$		$p = .12$		**$p = .01$**	
Chemotherapy								
Neoadjuvant	14	33	11	42	29	29	26	30
Adjuvant	68	50	66	45	61	44	52	52
None	18	17	23	13	11	26	22	18
	$p = .24$		**$p = .01$**		$p = .27$		$p = .94$	
Distance to exercise facility								
≤5 km	23	21	14	29	18	21	11	24
>5 km	77	79	86	71	82	79	89	76
	$p = 1.00$		$p = .16$		$p = 1.00$		$p = .32$	
Exercise facility								
Herlev Hospital	86	58	66	66	57	71	63	67
Naestved Hospital	9	17	14	16	25	12	26	12
Rigshospitalet	5	25	20	18	18	18	11	21
	$p = .06$		$p = 1.00$		$p = .36$		$p = .28$	

Proportions do not always ad up to 100% due to missing values. Low/medium adherence is <67% of training sessions; high adherence ≥67% of training sessions. *p*-values are based on Fischer's exact tests. *p*-values below level of significance (.05) are given in bold.

concerning reasons for low adherence and valuable inputs to how a more optimal exercise program should be designed. We did not assess motivational factors such as interest in exercise, perceived importance of exercise and self-efficacy. These factors have inconsistently been found associated with adherence in some studies [2,12].

The self-reported registration of home-based exercise and pre-diagnosis physical activity confer a risk of reporting bias. The missing exercise diaries and the retrospective diaries obtained after the supervised program ended introduce a risk of attrition bias, and to minimize this we interpreted the information in the most conservative manner. The most

important limitation is the small sample size, which increases the risk of type 2 error, that is, not detecting a difference where one actually exists. Furthermore, the many statistical tests performed raise the possibility that some of the associations found may be due to chance. If we had used Bonferroni correction, all results would have lost statistical significance. However, it could be argued that using Bonferroni would be overcorrecting in such an exploratory analysis not primarily powered to study adherence [25].

This study shows that acceptable adherence is viable during the first phase of an exercise program for women exposed to adverse effects to previous and ongoing cancer treatment, bearing in mind that adherence to the second phase of the 1-year exercise program was not addressed here.

In summary, we found high adherence to supervised exercise in the first 10 weeks of the 20-week PRT program in women with breast cancer at high risk for lymphedema, although it decreased somewhat over the last 10-week period. Home-based exercise adherence was lower than adherence to supervised exercise, and it remained unchanged through the 20-week period. Our results suggest that in order to promote high adherence to exercise in the adjuvant treatment setting after breast cancer, it may be favorable to offer support during chemotherapy, in home-based exercise, to those with below/average lower body muscle strength and those who are obese.

Ethical approval

The LYCA trial was approved by the participating hospitals and the Regional Ethical Committee System [H-15002714].

Disclosure statement

The authors report no conflicts of interest.

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