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ORIGINAL ARTICLE

Effect of progressive resistance training on health-related quality of life in the first year after breast cancer surgery – results from a randomized controlled trial

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ABSTRACT

Aims: To examine the effect of progressive resistance training (PRT) on health related quality of life and a predefined symptom cluster of pain–sleep–fatigue.

Methods: This study was a planned secondary analysis of a randomized controlled trial examining the effect of PRT on prevention of arm lymphedema in a population of women between 18 and 75 years undergoing breast cancer surgery with axillary lymph node dissection. Participants were allocated by computer randomization to usual care control or a PRT intervention in a 1:1 ratio. The intervention, initiated in the third post-operative week, consisted of three times PRT per week, supervised in groups in the first 20 weeks, and self-administered in the following 30 weeks. Questionnaire assessments were made at baseline, 20 weeks and 12 months, with the European Organization for Research and Treatment in Cancer Core questionnaire (EORTC QLQ C30) and the Functional Assessment of Chronic Illness Therapy-(FACIT) fatigue questionnaire. The symptom cluster of pain–sleep–fatigue was measured with a constructed score adding EORTC C30 subscales of insomnia, pain, and fatigue. Data were treated as repeated measurements and analyzed with mixed models.

Results: Among 158 recruited participants, we found a clinically relevant increased emotional functioning with nine points at both follow-ups ($p = .02$), and 16 and 11 points at 20 weeks and 12 months respectively ($p = .04$) in social functioning. Furthermore, in the subgroup of women with the symptom cluster pain–sleep–fatigue present at baseline, a significant effect was found for global health status ($p = .01$) and social functioning ($p = .02$).

Conclusion: To our knowledge, this is the first study to report clinically relevant effects of PRT on social and emotional functioning in the first postoperative year after breast cancer surgery. Furthermore, a subgroup of women with the pain–sleep–fatigue symptom cluster had particular benefit from PRT on global health status and social functioning.

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Introduction

Diagnosis and treatment for breast cancer (BC) have consistently been linked with impaired Health Related Quality of Life (HRQoL) [1]. In several systematic reviews and meta-analyses, exercise and physical activity have been shown to significantly address this association [2–4], both during adjuvant chemotherapy [5], during radiotherapy [6], and after finalizing systemic treatment [2]. However, the individual trials have tested mostly supervised multimodal exercise interventions with short follow-up in populations smaller than 100 women with BC, and they have often reported small effect sizes. Based on these studies, the grading of the evidence has reached the level of 'a possible effect' of exercise on HRQoL in patients with BC, due to the low or very low quality of the evidence [2–4,6].

Pathways through which exercise act on HRQoL can be biological (e.g., improving fitness), psychological (e.g., reducing anxiety and depression), psychosocial (e.g., improving self-efficacy and sense of accomplishment), and through reducing symptoms (e.g., fatigue and pain) [7]. Although these pathways have been associated with exercise in general, the separate effect of resistance exercise after surgery

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Supplemental data for this article can be be available here.

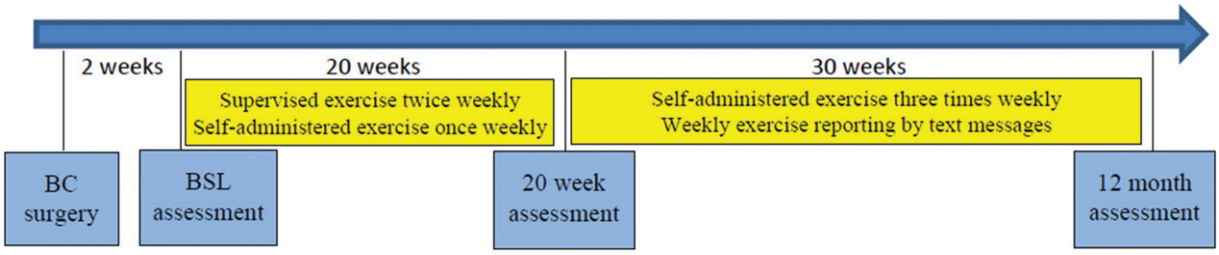

Figure 1. Timeline and overview of the 1-year intervention for 158 women treated for primary breast cancer with axillary lymph node dissection, LYCA study, East Denmark, 2015–2018. BC: breast cancer; BSL: baseline.

for BC involving axillary lymph node dissection has not received much attention, possibly due to fear of inflicting an increased risk of lymphedema and pain. However, evidence now supports the safety of progressive resistance training (PRT) in this population [8], making way for the effect on HRQoL to be examined in more depth.

Besides HRQoL, a frequent target for exercise studies has been to reduce fatigue, and even though findings show benefits from exercise, the small effect sizes are rarely sufficient to be clinically relevant [5,6,9]. However, in the last decade, research in this area has advanced through the investigation of symptom clusters [10]. A symptom cluster can be defined as two or more co-occurring symptoms that are somehow related to one another [11]. In BC, fatigue together with sleeplessness and pain has frequently been seen to form such a cluster [12–14]. One mechanistic pathway linking these three symptoms is chronic low-grade inflammation, which impacts all three symptoms individually, and through behavioral mechanisms the symptoms have the potential to further reinforce each other [14,15]. So far, mostly psychoeducational interventions have been tested in treating symptom clusters, yielding only limited evidence of an effect [16].

In secondary analyses of a randomized controlled trial, we examined the effect of supervised and self-administered PRT in the first year after surgery on global health status, functional domains of HRQoL, fatigue, and also on the symptom cluster pain–sleep–fatigue. Furthermore, in a priori subgroup analyses, we assessed if the presence of this symptom cluster at baseline influenced the effect of the intervention on global health status and functional domains of HRQoL.

Method

Setting and participants

In LYCA (ethical approval ID, H-15002714; clinicaltrials.gov, NCT02518477) we recruited from three hospitals covering eastern Denmark, a population of 2.7 million, where 2200 new breast cancer cases are found per year [17]. Between August 2015 and January 2017, 643 patients were screened for eligibility, and among the 466 eligible patients identified, 158 accepted participation. The last follow-up took place in January 2018. The primary aim of the study was to test the effect of PRT on arm lymphedema development in the first year after breast cancer surgery, with HRQoL as a secondary outcome. Eligibility criteria included women aged 18–75, diagnosed with primary unilateral BC in whom surgery included axillary lymph node dissection, and with no known distant metastases. The study design, intervention and main results of the RCT have been described in detail elsewhere [18,19]. In brief, recruitment took place on the day of surgery with collection of final consent and baseline testing 2 weeks post-surgery. Participants were then allocated to intervention or control in a 1:1 ratio by computer randomization stratified by BMI (>/< 30) and one of three recruitment sites in blocks of 6. The group allocation was concealed for the testers and data collectors throughout the study period.

Intervention

The intervention group received usual care and an especially developed program with PRT, commencing within 1 week of baseline testing. In the first 20 weeks of the intervention, participants were offered twice-weekly supervised group exercise and once-weekly self-administered exercise with dumbbells and resistance exercise bands provided. In the following 30 weeks, exercise was self-administered and prescribed to be carried out three times weekly (Figure 1), only prompted by weekly mobile phone text messages for exercise reporting. The exercise program was progressive, and included a gradual increase in intensity from low to moderate and involved exercises for upper limb, lower limb and core [18,19].

The control group received usual care, where information after surgery included advice not to lift heavy objects or engage in strenuous and prolonged physical activity involving the upper limb. All patients were referred to municipality based physiotherapy, with heterogeneous offers of manual therapy and mobility/remedial exercises. Resistance training was generally not offered in this setting.

Outcome assessment

Patient reported outcomes and socio-demographics were assessed by paper-based questionnaires collected at baseline, 20 weeks (end of supervised exercise), and at the final assessment 12 months after date of surgery.

For assessment of HRQOL, two patient reported outcome measures were used; the European Organization for Research and Treatment of Cancer, Core questionnaire (QLQ C-30 version 3) [20], and the Functional Assessment of Chronic Illness Therapy – fatigue scale (FACIT-f) [21].

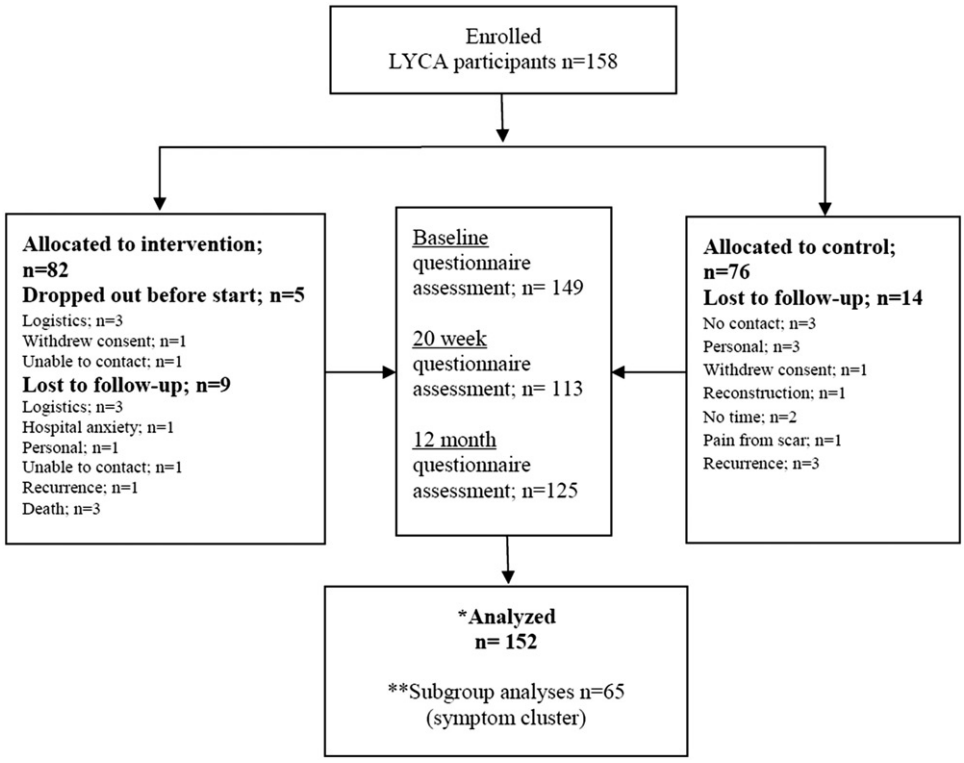

Figure 2. Recruitment and follow-up with questionnaire assessments of 158 women treated for breast cancer surgery with axillary lymph node dissection, LYCA study, East Denmark, 2015–2018. *152 participants provided data at a minimum of one assessment point. **Subgroup analysis included 65 participants with the symptom cluster pain-fatigue-sleep at baseline.

The QLQ C-30 scale consists of a 2-item scale for global health status, five function scales (physical-, role-, emotional-, cognitive- and social function) and nine symptom scales (Fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). We used the summed item score for the global health status scale and each of the function scales, and converted them to mean scores out of 100. A higher score on function scales means better functional status.

The FACIT-f scale is a 13-item self-assessment questionnaire, designed to stand alone and capture fatigue and its possible influence on activities of daily life and functioning in several chronic conditions [22]. The maximum score is 52, and a high score indicates a low level of fatigue.

Prior to data analysis, one symptom cluster was identified in the literature, that has consistently been found to affect the lives of women with BC through survivorship; pain–sleep–fatigue [23]. To measure the severity of this cluster, we created a continuous score by extracting the individual scores from the pain, insomnia and fatigue symptom scales from the EORTC QLQ-C30, and converted the sum to a total mean score out of 100, weighting the three scales equally. We also created a dichotomous score (yes/no) for symptom cluster presence, categorizing the cluster to be present if the score was above 34 on each of the three individual scales. This would be equal to reporting a minimum of 'some' when asked to the presence of the symptom.

For detailed medical information and tumor characteristics, we linked the personal identification number of each patient to data from the Danish Breast Cancer Group register and further used access to medical records to complete missing data.

Statistical analyses

The study was primarily powered to detect a minimal relevant difference in lymphedema incidence of 20%, expecting 30% in the control group and 10% in the intervention group. With $\alpha = 0.05$ and a power of 0.90, allowing a 15% loss to follow-up, the estimated sample size was determined to be 158 women.

Data were treated as repeated measurements with assessments at baseline, 20-week follow-up, and 12-month follow-up. For the continuous scores of outcomes, we used intention-to-treat tobit mixed models, assuming no difference between groups at baseline and an interaction between group and assessment at the two follow-up assessments allowing different intervention effects at each assessment. The correlation between observations from the same individual was taken into account with a random subject effect. The assumptions underlying the models were checked with residual plots. The pre-defined subgroup analyses assessing the effect in those with/without the symptom cluster present were carried out by adding an interaction between study group and the presence of symptom cluster (yes/no) to the initial model. Due to the amount of missing data, we checked in sensitivity analyses if a model using multiple imputations would change the estimates or the precision of the estimates. To improve the multiple imputations we used age and living with a partner yes/no as auxiliary variables, as

Table 1. Baseline characteristics of 158 women treated for primary breast cancer with axillary lymph node dissection, LYCA, East Denmark, 2015–2018.

Characteristic	Controls ($n = 76$)	Intervention ($n = 82$)
Sociodemographic and physical profile		
Age (years), mean (range)	52 (30–74)	53 (33–73)
Living with partner, *n* (%)	48 (63)	65 (80)
Living alone	20 (26)	15 (18)
Data missing	8 (11)	2 (2)
Education, *n* (%)		
Short or medium	10 (13)	13 (15)
Long	47 (62)	49 (60)
Other	11 (14)	17 (21)
Data missing	8 (11)	3 (4)
Employment	53 (70)	63 (77)
Full or part-time at diagnosis, *n* (%)		
Not employed, pensioned, sick leave, other	15 (20)	17 (21)
Data missing	8 (10)	2 (2)
Disease and treatment information[a]		
Histologic stage of malignancy, *n* (%)		
1	16 (21)	12 (15)
2	35 (46)	48 (59)
3	18 (24)	15 (18)
Data missing	7 (9)	7 (9)
Number of positive lymph nodes, mean (SD)	3.0 (3)	2.9 (4)
Tumor diameter (mm), mean (SD)	23 (12)	22 (12)
Data missing, *n* (%)	27 (36)	22 (27)
Chemotherapy[a]		
Adjuvant, *n* (%)	45 (59)	48 (59)
Neoadjuvant, *n* (%)	21 (28)	25 (30)
Hormone treatment, *n* (%)	51 (67)	64 (78)
Data missing, *n* (%)	2 (3)	0
Estrogen receptor status positive, *n* (%)	52 (68)	69 (84)
Data missing, *n* (%)	2 (3)	1 (1)
Health behavior		
Physical activity before diagnosis, *n* (%)		
Inactive	4 (6)	0
$<$30 min daily	22 (32)	30 (38)
Active $\geq$30 min daily	22 (32)	32 (40)
Active $>$30 min daily + high intensity more than twice weekly	20 (29)	18 (23)
Smoking, *n* (%)		
Current smoker	5 (9)	4 (5)
Ex-smoker	34 (52)	34 (42)
Never smoked	26 (39)	43 (53)
Alcohol consumption		
No, of units per week, mean (sd)	3.6 (4.1)	5.1 (5.7)
None, *n* (%)	22 (29)	22 (27)
Data missing, *n* (%)	11 (14)	9 (11)

[a]All participants had surgery including axillary lymph node dissection with either lumpectomy or mastectomy, all received radiotheraoy, and all chemotherapy was taxane based. 10 and 9 participants in the control and intervention groups respectively, were not prescribed chemotherapy.

they were somewhat correlated to the outcomes. Both the mixed models and the multiple imputations assume data is missing at random. All statistical analyses were carried out using Stata version 14.2 (SPSS, Chicago, IL).

Results

Out of the 158 women randomized, 76 were allocated to the control condition and 82 to the intervention program. Figure 2 shows the flow of participants through the study and the questionnaire response. Analyses of the effect of the intervention were based on questionnaire information from 152 participants. The equally distributed baseline characteristics (Table 1) indicate a well-balanced randomization. The mean age at diagnosis was 52 years (range 30–74), and mean body mass index was 26 (range 18–50). Three quarters of participants had at least college education, and in the control group 63% lived with a partner, whereas in the intervention group the proportion was 80%. The Appendix Table A shows all known characteristics of those with missing data compared to those with complete data.

The estimated scores for functioning scales (EORTC C30), fatigue and the symptom cluster pain–sleep–fatigue as presented in Table 2 and Appendix Figure A, show that the intervention had a significantly favorable effect on emotional and social functioning. In change from baseline to both follow-up assessments, the intervention group scored nine points higher (95% confidence interval (CI) 1; 16) on emotional functioning ($p = .02$). For social functioning the intervention group scored 16 points higher (CI 2; 31) in change from baseline to first follow-up and 11 points (CI −3; 25) to second follow-up with an overall p value of .04. The effect estimates for global health status, physical-, role-, cognitive functioning, or the symptom cluster of pain–sleep–fatigue with EORTC data did not reach statistical significance, but tended to favor the intervention group.

For fatigue measured with FACIT-fatigue, the intervention group scored 3 and 2 points higher (better) than the control

Table 2. Effect of progressive resistance training on Health Related Quality of Life and Fatigue in 152 women treated for primary breast cancer with axillary lymph node dissection, LYCA, East Denmark, 2015–2018.

		Observed data			
Outcome		Estimate	95% CI	*p*	Overall *p*
Global health scale					
20 weeks	Exercise	1.5	(−5.5; 8.5)	.678	.245
	Control	0	Reference		
12 months	Exercise	5.8	(−1.0; 12.6)	.094	
	Control	0	Reference		
Physical functioning					
20 weeks	Exercise	3.6	(−2.7; 10.0)	.257	.436
	Control	0	Reference		
12 months	Exercise	2.8	(−3.2; 8.9)	.359	
	Control	0	Reference		
Role functioning					
20 weeks	Exercise	0.9	(−12.5; 14.4)	.892	.357
	Control	0	Reference		
12 months	Exercise	9.7	(−3.7; 23.1)	.157	
	Control	0	Reference		
Emotional functioning					
20 weeks	Exercise	8.9	(1.2; 16.6)	.024	.020
	Control	0	Reference		
12 months	Exercise	8.6	(1.2; 16.1)	.023	
	Control	0	Reference		
Cognitive functioning					
20 weeks	Exercise	4.8	(−6.2; 15.9)	.392	.101
	Control	0	Reference		
12 months	Exercise	11.9	(1.0; 22.8)	.033	
	Control	0	Reference		
Social functioning					
20 weeks	Exercise	16.4	(2.3; 30.6)	.023	.042
	Control	0	Reference		
12 months	Exercise	11.3	(−2.7; 25.2)	.113	
	Control	0	Reference		
FACIT-fatigue scale					
20 weeks	Exercise	2.71	(−0.1; 5.5)	.058	.081
	Control	0	Reference		
12 months	Exercise	2.43	(−0.3; 5.2)	.080	
	Control	0	Reference		
Symptom cluster					
20 weeks	Exercise	−5.3	(−12.0; 1.3)	.117	.275
	Control	0	Reference		
12 months	Exercise	−2.7	(−9.1; 3.7)	.414	
	Control	0	Reference		

20 weeks = 20-week assessment. 12 month = 12-month assessment. Exercise = exercise intervention group. Control = usual care control group. Symptom cluster is a combination of pain, fatigue and insomnia symptom scales in QLQ-C30, score 0–100. 95% CI: 95% confidence interval.

group at 5 and 12 months, respectively, but results were not statistically significant ($p = .08$).

Results of the interaction analyses (Table 3) showed that for global health status, the participants in the intervention group with the symptom cluster present at baseline had a significant 8 points higher change-score from baseline to the 20-week assessment, and 13 points higher change score from baseline to the 12-month assessment compared to the control group (p for interaction =.01). Furthermore, for social functioning, the intervention group had a significant 29 points higher change score from baseline to the 20-week assessment and 23 points higher at the 12-month assessment (p for interaction =.02). Although the same tendency was found for the other function scales, estimates did not reach statistical significance.

Sensitivity analyses using multiple imputations did not considerably change the estimates of the intervention outcomes (data not shown).

Discussion

This study shows that a program with early PRT, supervised in the first 20 weeks and self-administered in the following 30 weeks after BC, had significant effects on emotional and social functioning. Furthermore, in a subgroup of women who reported having the symptom cluster of pain–sleep–fatigue at baseline, the intervention had an even greater impact on these two outcomes.

Previous studies examining the unimodal effect of PRT after breast cancer have found no effect on global scores for HRQoL, as illustrated in the literature review by Cheema et al. reviewing seven studies [8]. In sensitivity analysis, findings showed a small but significant effect when analyses were restricted to trials after and not during adjuvant chemotherapy (standardized mean difference =0.30 (95% CI 0.04–0.55, I^2 = 37.0%). A more recent literature review and meta-analysis of 71 randomized controlled trials, which examined the effect of various modes of exercise after all cancers on general quality of life/global health and physical functioning, found a significant, although small clinical benefit from exercise interventions (Hedges' $g = 0.15$, 95% CI 0.10; 0.20) [24]. The authors reported that no difference was observed when comparing exercise modes, but that supervised exercise was more effective than unsupervised. The results of our study therefore have novelty in terms of the clinically relevant effect, defined as >5 points increased on function scales [25], from supervised and unsupervised PRT on social and emotional functioning during adjuvant therapy and through the first year after surgery.

In trying to understand why we see a statistically significant effect on social and emotional functioning in particular, we considered if the psychosocial aspects of group-based supervised exercise bringing social interactions, improved self-efficacy, and attention from a trainer, could be relevant [26]. The LYCA intervention included a high level of support from physiotherapists due to the need for close monitoring of lymphedema and pain associated with training, and thus this explanation is plausible. Our results are largely comparable to those found for group-based supervised aerobic and combined aerobic/strength exercise interventions [24], we speculate that the effect is less dependent on the mode of exercise and more on the setting and level of support during exercise for this particular population of women at high risk for adverse effects from treatment.

We did not find an effect on fatigue measured by the FACIT-fatigue score. When looking at the baseline level of fatigue in our study population, the mean score was 40–41 (data not shown) which corresponds to the norm score observed in the background population [22], and we note with interest that the mean score stayed within the normal range throughout the study period. It might be, that the lack of potential for improvement explains why we do not see an effect. However, the evidence base for comparison of our results is sparse, with only one study having tested the effect of PRT on fatigue in 65 older post-menopausal women with BC, finding no effect of the intervention [27].

Symptom clusters in BC survivorship have proven to be persistent for years after diagnosis, and have so far been

Table 3. Effect of progressive resistance training on global health and functioning (Health-Related Quality of Life domains) according to subgroups of participants with/without presence of symptom cluster at baseline in 152 women treated for primary breast cancer with axillary lymph node dissection, LYCA, East Denmark, 2015–2018.

		No cluster at baseline				Cluster at baseline				
Outcome		β	95% CI	p	Overall p	β	95% CI	p	Overall p	p for interaction
Global health										
20 w	Exercise	−3.0	(−10.6; 4.7)	.451	.555	8.2	(−0.1; 16.6)	.054	.009	.008
	Control	0	Reference			0	Reference			
12 m	Exercise	1.5	(−5.9; 9.0)	.684		12.7	(4.5; 21.0)	.002		
	Control	0	Reference			0	reference			
Physical functioning										
20 w	Exercise	0.2	(−6.8; 7.3)	.947	.998	6.9	(−0.14; 16.6)	.072	.121	.081
	Control	0	Reference			0	Reference			
12 m	Exercise	0.0	−6.8; 6.8)	.995		6.7	(−0.7; 14.1)	.077		
	Control	0	reference			0	reference			
Role functioning										
20 w	Exercise	−3.5	(−18.6; 11.5)	.647	.515	6.3	(−9.5; 22.0)	.435	.145	.222
	Control	0	Reference			0	Reference			
12 m	Exercise	6.9	(−9.0; 20.9)	.436		15.7	(0.0; 31.4)	.050		
	Control	0	reference			0	reference			
Emotional functioning										
20 w	Exercise	5.7	(−2.8; 14.2)	.186	.294	14.2	(5.1; 23.4)	.002	.002	.066
	Control	0	Reference			0	Reference			
12 m	Exercise	5.6	(−2.6; 13.9)	.183		14.1	(5.1; 23.1)	.002		
	Control	0	reference			0	reference			
Cognitive functioning										
20 w	Exercise	−0.3	(−12.6; 12.1)	.967	.474	11.9	(−1.2; 24.9)	.074	.016	.073
	Control	0	reference			0	Reference			
12 m	Exercise	6.6	−5.7; 18.9)	.291		18.8	(5.9; 31.6)	.004		
	Control	0	reference			0	reference			
Social functioning										
20 w	Exercise	8.6	(−6.9; 24.1)	.278	.553	28.5	(11.7; 45.4)	.001	.002	.020
	Control	0	Reference			0	Reference			
12 m	Exercise	2.6	(−12.8; 17.9)	.745		22.5	(5.7; 39.2)	.008		
	Control	0	reference			0	reference			

20 w = 20-week assessment. 12 m = 12-month assessment. Exercise = exercise intervention group; Control = usual care control group. β: estimate. 95%CI: 95% confidence interval. Cluster/no cluster at baseline: the subgroup of participants with presence/absence of self-reported pain, fatigue and sleeplessness combined at first assessment.

rather treatment resistant [11,16,28]. As PRT has not been tested for this effect [16], we approached the problem from a mechanistic angle, and used PRT to target the potential chronic low-grade inflammation [29], which is also a mechanistic component with a dose–response relationship involved in pain, fatigue and sleep [30]. Contrary to our hypothesis, we did not find a significant effect of PRT on the symptom cluster severity. An explanation for the lacking effect could lie in the appropriateness of the target population, as a different and positive effect on global health status and social functioning was found for the subgroup reporting the pain–sleep–fatigue cluster at baseline. In light of this finding, it is possible that only in those with higher symptom scores at baseline, there is potential for substantial improvement and statistically significant effects.

Strengths of this study include the randomized design testing a unimodal PRT intervention offered in group sessions, where exercise evolved from supervised to self-administered through the phases of adjuvant treatment and through the first year after surgery. The clinical setting, within which the intervention was offered, is highly translatable to a community setting and would require minimal training of physiotherapists to act as supervisors. Further strengths are the validated scales for HRQoL and fatigue with relevant questions for the target group. Moreover, the study population has a high risk of developing late effects with extensive surgery and treatment, and is therefore an important target for interventions that could alleviate adverse effects on HRQoL. Further, the focus on the pain–sleep–fatigue symptom cluster reveals a particularly challenged group of patients that could have more benefit from interventions in the first year after breast cancer surgery. To our knowledge, this subgroup has not been the focus of a randomized controlled PRT trial before.

Among limitations of this study is that HRQoL was a secondary outcome, and, therefore, it is unknown whether the sample size was sufficient to detect a difference in effect. Furthermore, we do not know the psychometric properties of our measurement for the symptom cluster pain–sleep–fatigue, although the individual subscales in EORTC QLQ C30 have been thoroughly validated. Moreover, there is some missing data in this study, which we addressed by robust statistical mixed model analyses using all available data, and tested in sensitivity analyses with multiple imputations whether the missing data was likely to have skewed the results. As is often the case in exercise interventions, the risk

of selection into the study exists. More women of higher socioeconomic position and who were particularly interested in exercising might have signed up to participate, partly demonstrated in this study by the high proportion of women with a minimum of a college education. With this comes a possibility for reduced generalizability of the results. The risk of contamination also exists, with the participants in the control group being more spurred on to resistance exercise from the information material used in the recruitment procedure, potentially reducing the difference between the groups. Finally, there is a risk of a low differentiation between the study groups because both resistance exercise and aerobic exercise have an effect on chronic low-grade inflammation [31], and usual care after breast cancer surgery often contains an element of aerobic and remedial exercise offered for a limited number of weeks. However, generally we would expect participants in the intervention group to have had a higher dose and volume of exercise in the study period.

Conclusion

In summary, in this randomized controlled trial testing an early intervention with PRT through the first year of BC survivorship, we found a significant clinically relevant effect of the intervention on social and emotional functioning after 1 year of follow-up. Among participants identified post-operatively with a symptom cluster including pain, sleeplessness and fatigue, the intervention significantly improved global health status and social functioning. Our results are relevant for future research and clinical practice, as we have illustrated how screening for symptoms after surgery may help target PRT interventions among BC survivors to a relevant sub-group. However, future studies primarily aimed at exploring the benefits after BC surgery on HRQoL in populations where the symptom burden is substantial and predicts a need for intervention are necessary. Evidence in the area of symptom cluster research is still evolving and the development and testing of interventions with a mechanistic rationale would be of high value and could bring this field of research to the next level.

Disclosure statement

No potential conflict of interest was reported by the authors.

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