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Late breast cancer treatment-related symptoms and functioning: Associations with physical activity adoption and maintenance during a lifestyle intervention for rural survivors

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Abstract

Purpose—Physical activity may be difficult for survivors with poorer functioning following primary treatment. The study examined whether late symptoms of breast cancer treatment impact PA adoption (0–6 months) and maintenance (6–18 months) during a weight management intervention, and whether late symptoms influence PA when accounting for overall functioning.

Methods—Secondary analyses were conducted using a sample of survivors participating in a weight management intervention and who provided valid weight and accelerometer data at baseline and 6 months (N= 176). The Breast Cancer Prevention Trial Symptom Checklist (BCPT) assessed late treatment-related symptoms. SF-12 Physical Component Scale (PCS) and Mental Component Scale (MCS) scores assessed functioning.

Results—Change in bouted moderate to vigorous physical activity (MVPA) min/week from baseline to 6 months was not associated with BCPT scales (all p values >.05). When adding SF-12 scores to the model, change in bouted MVPA min/week was significantly associated with the PCS (p=.045). Change in MVPA min/week from 6 to 18 months was significantly associated with cognitive symptoms (p = .004), but not musculoskeletal or vasomotor symptoms (p values >.05). When adding 6-month SF-12 scores to the model, MVPA min/week was significantly associated with PCS (p= .001) and MCS (p= .028); however BCPT cognitive problems score became non-significant (p>.05)

Conclusions—Poorer physical functioning was associated with lower PA adoption, and poorer mental and physical functioning was associated with lower maintenance of PA, while late

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Ethical approval:
All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The research was approved by the University's Institution Review Board and informed consent was obtained from all participants. The study is compliant with U.S. laws for research and ethics.

Conflicts of interest:
The authors declare that they have no competing interests.

Data availability:
The dataset for the current study is available from the corresponding author on reasonable request.

symptoms generally were not. Interventionists should consider level of functioning when identifying individual PA goals during weight management interventions.

Keywords

late treatment-related symptoms; physical activity; breast cancer prevention trial symptom checklist; breast cancer survivors

Background

Physical and mental functioning has been shown to decrease following a diagnosis of breast cancer and remain lower long-term compared to individuals without a history of breast cancer [1]. The burden from late cancer treatment-related symptoms can be substantial for survivors [2] and may be an important driver in long-term physical and mental functioning [3]. Treatment associated musculoskeletal pain [4–7] and menopause symptoms [8–11] resulting from anti-hormone treatment and/or chemotherapy may affect over 50% of survivors 1–10 years post-treatment and cognitive difficulties may impair long-term cognitive functioning in up to one third of survivors [12, 13], contributing to accelerated cognitive decline in older survivors following completion of primary treatment [12]. Several studies that assessed treatment-related symptoms via the Breast Cancer Prevention Trial Symptom Checklist (BCPT) in survivors 6–24 months beyond primary treatment found that greater musculoskeletal pain, menopausal symptoms (vasomotor and vaginal discomfort), and cognitive difficulties were associated with poorer physical and mental functioning as assessed by the SF-36 [14–16].

While meeting physical activity (PA) guidelines [17] is associated with improved quality of life [18] and lower risk of cancer-specific and all-cause mortality among breast cancer survivors [19], impaired functioning and the burden of late treatment-related symptoms may make the adoption of PA and maintenance difficult. In qualitative interviews, survivors have identified difficulties related to physical and mental functioning and late treatment-related symptoms as barriers to PA following the completion of primary treatment [20], and prospective evidence supports this point. For example, in a longitudinal cohort study that followed 227 breast cancer survivors after primary treatment completion, greater declines in both physical and mental functioning as assessed by the SF-36 were associated with greater decreases in PA over the five years [21]. Specific symptoms may also directly influence PA participation. In a cross-sectional study of post-menopausal survivors, the presence of aromatase inhibitor associated musculoskeletal complaints was associated with significantly reduced self-reported PA compared to pre-treatment PA levels [22]. In a single-arm pilot exercise intervention for breast cancer survivors chronic musculoskeletal complaints (defined as lasting 6+ weeks in duration) were associated with lower PA maintenance six months post-intervention [23].

At present, little is known about the impact of three common late treatment-related symptoms; musculoskeletal, vasomotor, and cognitive difficulties, on survivors' PA adoption and maintenance. It is also not clear to what degree these late symptoms may influence PA when considering survivors' overall physical and mental functioning. The goals of the

current study were 1) to examine whether common late cancer treatment-related symptoms (musculoskeletal pain, vasomotor symptoms, and cognitive problems) impact PA adoption (0–6 months) and maintenance (6–18 months) during a weight management intervention, and 2) to investigate the degree to which these late symptoms influence PA adoption and maintenance when accounting for overall physical and mental functioning.

Methods

The main study was a randomized 18-month weight loss-maintenance trial tailored to rural breast cancer survivors that targeted decreased caloric intake and increased non-supervised PA. The study consisted of 1) a 6-month weight loss phase (0 to 6 months) where all participants received weekly group phone sessions, followed by 2) a 12-month weight loss maintenance phase (6 to 18 months) during which participants were randomized to continued group phone sessions or a newsletter condition. Study details and primary outcomes were previously reported [24, 25]. Participants (N=210) were postmenopausal female breast cancer survivors residing in rural areas of the Midwestern United States, with a BMI of 27 to 45 kg/m, and age <75 years. All participants who were followed through 18 months are reported here. The study was approved by the University's Institution Review Board and informed consent wasobtained from all participants.

Intervention

Participants attended weekly group conference calls during the weight loss phase of the program (baseline to 6 months). Sessions addressed dietary modification using a structured meal plan and gradually increasing physical activity to at least 225 min/week of moderate to vigorous physical activity (MVPA) by week 12. Instruction on PA focused on monitoring, safety, and increasing intensity, as well as problem-solving surrounding barriers to the adoption of PA. Participants submitted a weekly self-monitoring logs detailing their dietary intake, PA minutes at ≥10 minute bouts, and steps per day (goal of 10,000 steps per day). During each session, participants reported whether they met dietary and PA goals identified in the previous session. The intervention addressed exercise safety including precautions for those with lymphedema or neuropathy, and included a session on coping with menopausal symptoms specific to breast cancer survivors.

During weight loss maintenance (6 to 18 months), participants were randomized to continued bi-weekly group phone sessions or bi-weekly newsletters. Participants were encouraged to continue PA and dietary compliance, with the focus on shifting to problem solving around barriers to dietary and PA compliance.

Assessments

Participants attended in-person assessment visits at baseline, 6, 12, and 18 months. At each visit, participants were weighed in light clothing (shorts, t-shirt) in a fasting state using a calibrated digital scale accurate to 0.1 kg (Befour PS5700). PA was measured with a GT3X+ Actigraph Accelerometer (Fort Walton Beach, FL) [26, 27], which participants were instructed to wear for seven consecutive days at each point and return in a pre-stamped envelope. Accelerometer data were included if wear time exceeded10 hours per day for ≥4

days, an algorithm that has been demonstrated to validly estimate PA patterns [28]. The accelerometer outcome variable was total ≥10-minute MVPA bouted minutes per week [29]. Moderate to vigorous activity (counts ≥1952 per min) bouts [30] wherein at least 8 minutes were at/above the 1952 threshold were used to identify 10-minute MVPA bouts. Bouted MVPA minutes per valid day (≥10 hours worn) were calculated and multiplied by 7 to obtain weekly estimates.

The Breast Cancer Prevention Trial Symptom Checklist (BCPT) was used to assess the symptoms related to cancer treatment [31]. Three of the BCPT subscales: musculoskeletal (joint and muscle pain), vasomotor (hot flashes and night sweats), and cognitive difficulty (concentration) were included a priori due to the possibility of being associated with PA and weight outcomes [25]. Items are scored from 0 to 4 based on symptom bother (“not at all” to “extremely”). Global physical and mental functioning was assessed using the Medical Outcomes Study Short-Form 12 (SF-12) [32]. The Physical Component Scale and the Mental Component Scale have demonstrated strong psychometric properties among populations of women diagnosed with breast cancer [33].

Study Sample

The sample for the current analyses consisted of participants who provided valid accelerometer data at baseline and 6 months, which resulted in a final sample of 176 participants. An additional 34 participants attended the 6-month assessment but did not provide valid accelerometer data and were thus excluded from the current analyses. Participants in the current sample completed primary treatment significantly earlier (M=3.5 yrs vs 2.1 yrs, p =.027) than those who attended the 6-month visit but were excluded from the current analyses based on missing or invalid accelerometer data. However, participants in the current study did not significantly differ on any other cancer treatment-related variables, demographics, baseline BMI, percent weight loss, percent weight regain, BCPT scale scores, or SF-12 scores (all p values > .05) from those who attended the 6-month visit but were excluded from the current analyses.

Analyses

Bivariate correlations were examined among the BCPT and SF-12 variables and repeated measures t-tests were used to determine if BCPT and SF-12 variables changed from baseline to 6 months. The main outcome variable, bouted MVPA/week, was square-root transformed to correct for skewedness. We used a repeated measures ANOVA to examine the effects of BCPT musculoskeletal, vasomotor, and cognitive symptoms at baseline on change in bouted MVPA/week from baseline to 6 months. A linear mixed model using a compound symmetry correlation structure was constructed to examine the association between BCPT musculoskeletal, vasomotor, and cognitive symptoms at 6 months on change in bouted MVPA/wk during weight loss maintenance phase (6,12, and 18 months). Restricted Maximum Likelihood Estimation (REML) was used to cope with missing data at 12 and 18 months. There were no significant differences in MVPA change across randomization conditions, therefore conditions were combined.

We included the following variables as covariates in the models: treatment (antihormone therapy and chemotherapy), age, education, rurality (large rural vs. small/isolated rural [34]), and baseline body mass index (BMI). Randomization assignment was also included as a covariate in the linear mixed model.

To examine the relative effects of BCPT symptoms and overall physical and mental functioning on change in PA, we constructed two additional models identical to the ones described above that also included SF-12 Physical and Mental Component Scale scores at the corresponding time point.

Results

Table 1 presents participant demographics. Participants were a mean of 58.2 (SD =8.1) years old, 3.5 (SD =2.4) years from primary cancer treatment, 67% received chemotherapy, and 53% were on anti-hormone therapy at baseline. Mean baseline BMI was 34.1 (4.4). Participants lost a mean of 13.1% (SD = 5.7) at 6 months and regained a mean of 4.9% (SD =5.9) of their 6-month weight by 18 months. Descriptive statistics of the BCPT scales, SF-12 scales and bouted MVPA minutes are presented in Table 2. Baseline BCPT scales had small, positive associations with each other (r = .202 to .269, p values = .001); small to moderate negative correlations with the SF-12 Physical Component Scale (−.153 to −.458, p values <=.05); and the BCPT cognitive scale had a moderate negative significant correlation with SF-12 Mental Component Scale (r =−.392, p = .01; data not shown). All BCPT and SF-12 scale scores improved from baseline to 6 months (p values < .01).

Change in bouted MVPA min/week from baseline to 6 months was not associated with baseline musculoskeletal (partial eta^2= .020, p =.071), vasomotor (partial eta^2= .002, p =.580), or cognitive problems (partial eta^2= .021, p =.062). When adding SF-12 scores to the model, change in bouted MVPA min/week from baseline to 6 months was significantly associated with the SF-12 Physical Component Scale (Table 3).

Change in bouted MVPA min/week from 6 to 18 months was significantly associated with cognitive symptoms at 6 months (b= −.078, p = .004; CI = −.131, −.024), but not with musculoskeletal (b= −.044, p = .144; CI = −.104, .015) or vasomotor symptoms (b= .018, p = .549; CI = −.048, .081). When adding SF-12 scores at 6 months into the model, both the SF-12 Physical Component Scale score (b = .043, p= .001, CI = .024, .063) and Mental Component Scale score (b = .021, p= .028, CI = .002, .040) were significant, when accounting for BCPT scores and covariates (Table 4). The cognitive symptom score was non-significant when accounting for SF-12 Scales in the model.

Discussion

This study was the first to our knowledge to examine the relationship between three common, late treatment-related symptoms on the adoption and maintenance of physical activity during an 18-month weight loss maintenance intervention for breast cancer survivors. Results suggested that cognitive problems at 6 months had a small, significant association with PA maintenance from 6 to 18 months; however, no other effects were found. When we considered overall functioning, physical functioning was significantly

associated with the adoption of PA and both physical and mental functioning were significantly associated with PA maintenance, while the specific BCPT scales were not. These findings indicate that poorer physical functioning may impede the adoption of PA and poorer mental and physical functioning may hinder the maintenance of PA during a weight management intervention.

Our findings highlight a paradox in physical activity treatment research with survivors: physical activity may improve functional quality of life [18] and mortality outcomes [19], but participating in PA may be more difficult for those who already have poorer physical and mental functioning following treatment. In this regard, survivors' physical and mental functioning significantly improved during the initial 6 months of the intervention, and the magnitude of functional changes were very similar to the functional improvements reported during the Lifestyle Intervention in Adjuvant Treatment of Early Breast Cancer (LISA) Trial from baseline to 6 months (~4 points for physical functioning, ~1.7 points for mental functioning). However, despite these improvements, poorer mental and physical functioning remained a barrier to physical activity among participants in our study. Impaired functioning may restrict survivors' rate of PA change over time and our findings suggest that interventionists should consider level of functioning when identifying individual PA goals and monitoring participants' progress.

Our findings that musculoskeletal pain was not associated with adoption and maintenance of physical activity differ from other preliminary studies, including a cross-sectional study which found that musculoskeletal pain was associated with reduced retrospective self-reported PA following the initiation of an aromatase inhibitor [22] and a small pilot study where musculoskeletal pain at baseline was associated with lower self-reported maintenance of PA six months following an exercise intervention [23]. Our study methodology differed in several ways that may account for the difference in findings; we assessed physical activity using accelerometers instead of self-report questionnaires and for a longer period of time, we considered vasomotor and cognitive symptoms in addition to musculoskeletal pain, and we used a validated measure that assessed level of symptom bother, while the other two studies assessed symptom presence only. Additionally, participants in our study were on average 3.5 years beyond primary treatment completion, while the other two studies were within one year of primary treatment. It is possible that musculoskeletal pain may influence PA levels more so during the initial months of symptom onset.

This study had several limitations. First, we included individuals in analyses who provided valid accelerometer data at baseline and 6 months, and participants in the current sample were on average 1.4 years further beyond primary treatment than participants excluded due to missing or invalid accelerometer data (3.5 years vs 2.1 years). Although, time since treatment completion was not a significant covariate it is unclear whether inclusion of these participants would have substantially altered our findings. Strengths of the study included a large sample, the use of valid measures to assess treatment-related symptoms and functioning, as well as device-based measurement of physical activity.

Conclusions

Our findings suggest that poorer physical functioning was associated with lower PA adoption and poorer mental and physical functioning was associated with lower maintenance of PA, while late symptoms generally were not. Our findings suggest that interventionists should consider participants' level of functioning when identifying individual PA goals and monitoring PA change during weight management interventions.

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List of abbreviations

PA	physical activity
BCPT	Breast Cancer Prevention Trial Symptom Checklist
MVPA	moderate to vigorous physical activity
SF-12	Medical Outcomes Study Short-Form 12

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Table 1

Demographic Characteristics (N=176)

Demographic Variable	M (SD) or n (%)
Age	58.2 (8.1)
Marital Status	
Married/Cohabitating	152 (86%)
Race/Ethnicity (% Caucasian)	173 (98%)
Education	
High School/GED	41 (23%)
Some college/Associate's	69 (39%)
Bachelor's	37 (21%)
Graduate (Masters, PhD)	29 (17%)
Rurality (% small/isolated rural)	99 (56%)
Age at diagnosis	54.2 (8.3)
Stage at diagnosis[a]	
0	16 (9%)
I	71 (40%)
II	65 (37%)
III	23 (13%)
Time since treatment (years)	3.5 (2.4)
Treatment Received	
Lumpectomy	110 (63%)
Mastectomy	83 (47%)
Radiation	128 (73%)
Chemotherapy	117 (67%)
Anti-hormone Therapy (baseline)	93 (53%)
BMI	34.1 (4.4)
% weight loss at 6 months	13.1 (5.7)
% regain at 18 months	4.9 (5.9)

[a]One participant's stage at diagnosis was unknown

Table 2

Descriptive statistics for predictor and outcome variables

Predictor variables				
	Baseline	**6 months**[a]		
	Mean (SD)	**Mean (SD)**		
BCPT Musculoskeletal	3.38 (2.29)	2.68 (2.14)		
BCPT Vasomotor	2.19 (2.28)	1.58 (2.15)		
BCPT Cognitive	2.56 (2.45)	1.84 (2.41)		
SF-12 Physical	47.97 (7.68)	52.06 (7.21)		
SF-12 Mental	52.36 (7.91)	54.14 (7.88)		
Outcome variable				
	Baseline	6 months[b]	12 months	18 months[c]
	Median (IQR) (N= 176)	Median (IQR) (N =176)	Median (IQR) (N=148)	Median (IQR) (N=142)
Bouted MVPA min/week	18.19 (59.28)	55.56 (163.69)	43.0 (129.50)	38.1 (119.25)

Note: BCPT = Breast Cancer Prevention Trial Symptom Checklist

MVPA = moderate to vigorous physical activity

[a] Paired t tests indicated that all BCPT scales significantly decreased from baseline to 6 months (all p values < .01) and both SF-12 measures significantly improved (both p values =.01).

[b] Mean bouted MVPA min/wk significantly increased from baseline to 6 months (p = .001)

[c] Mean bouted MVPA min/wk significantly decreased from 6 months to 18 months (p = .001)

Table 3

Treatment-specific symptoms and general functioning predicting change in physical activity during weight loss (0–6 months)

	DV: bouted MVPA min/week[a]		
Variable	**F**	**Partial Eta squared**	**P value**
Baseline BCPT Musculoskeletal	.764	.005	.383
Baseline BCPT Vasomotor	.250	.002	.618
Baseline BCPT Cognitive	1.552	.009	.215
Baseline SF-12 Physical	4.063	.024	.045
Baseline SF-12 Mental	1.210	.007	.273

Note: Model included the following covariates: age, baseline anti-hormone therapy, chemotherapy treatment history, time since treatment completion, education, rurality, and baseline BMI.

[a]Dependent variable was square-root transformed

BCPT = Breast Cancer Prevention Trial Symptom Checklist

MVPA = moderate to vigorous physical activity

Table 4

Treatment-specific symptoms and general functioning predicting change in physical activity during weight loss maintenance (6–18 months)

	DV: bouted MVPA min/week[a]			
Variable	**Beta**	**Std. Error**	**P value**	**Confidence Interval (95%)**
6 month BCPT Musculoskeletal	.015	.032	.648	−.048, .078
6 month BCPT Vasomotor	.011	.031	.727	−.050, .071
6 month BCPT Cognitive	−.048	.029	.102	−.106, .010
6 month SF-12 Physical	.043	.010	.001	.024, .063
6 month SF-12 Mental	.021	.010	.028	.002, .040

Note: Model included the following covariates: age, anti-hormone therapy at 6-months, chemotherapy treatment history, time since treatment completion, randomization assignment, education, rurality, and baseline BMI.

Unstandardized regression coefficients are presented.

[a]Dependent variable was square-root transformed

BCPT = Breast Cancer Prevention Trial Symptom Checklist

MVPA = moderate to vigorous physical activity