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Breast Cancer Survivors with Pain: An Examination of the Relationships between Body Mass Index, Physical Activity, and Symptom Burden

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Abstract

Purpose: Overweight and obesity are common for breast cancer survivors and associated with high symptom burden (i.e., pain, fatigue, depressive symptoms). Physical activity may protect breast cancer survivors with higher body mass indexes (BMI) from increased symptoms. However, the role of physical activity in buffering the relationship between higher BMI and greater symptoms is unclear.

Methods: Baseline data from a randomized trial investigating Pain Coping Skills Training among breast cancer survivors (N=327) with pain were used to examine the relationship between self-reported BMI (kg/m2) and physical activity level (Rapid Assessment of Physical Activity; suboptimal vs. optimal) with pain (Brief Pain Inventory; severity and interference), fatigue (PROMIS Fatigue short form), and depressive symptoms (Center for Epidemiological Studies Depression Scale). Analyses were conducted in SPSS. Hayes PROCESS macro (Model 1) assessed whether physical activity moderated the relationship between BMI and symptoms.

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Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Institutional Review Board of Duke University (Pro00070823) and has been registered on Clinicaltrials.gov (NCT02791646).

Consent to participate: Written informed consent was provided by all individuals participating in this study.

Results: Lower BMI (B=.06, p<.01) and optimal physical activity (B=−.69, p<.01) were independently associated with lower pain interference. Lower BMI was also associated with lower pain severity (B=.04, p<.001). Neither BMI nor physical activity were associated with fatigue or depressive symptoms. Physical activity did not moderate the relationship between BMI and symptoms.

Conclusions: Among breast cancer survivors experiencing pain, higher BMI and being less physically active were related to greater pain (i.e., severity and/or interference). Physical activity did not buffer the relationships between BMI and pain, fatigue, and depressive symptoms, suggesting that physical activity alone may not be sufficient to influence the strength of the relationships between BMI and symptoms.

Keywords

Breast Cancer; Body Mass Index; Physical Activity; Pain; Fatigue; Depressive Symptoms

I. Introduction

There are approximately 4.1 million women with a history of breast cancer in the United States.[1] Higher body mass index (BMI) is a known risk factor for breast cancer.[2, 3] Weight gain is also common for breast cancer survivors during and following treatment,[4] with rates of overweight (BMI ≥25 to <30 kg/m^2) and obesity (BMI ≥30 kg/m^2) increasing more rapidly for breast cancer survivors than for women without a history of cancer.[2] Overweight and obesity are associated with poorer prognosis for breast cancer survivors, including increased risk of recurrence and cancer-specific and all-cause mortality.[5]

Breast cancer survivors with overweight or obesity are at greater risk for physical and emotional sequelae.[6, 7] Pain, fatigue, and emotional distress (e.g., depressive symptoms), in particular, are common and often persistent symptoms for breast cancer survivors that may be exacerbated by overweight or obesity.[6–13] For example, overweight and obesity can place added stress on joints leading to increased pain. Breast cancer survivors with obesity endorse more joint symptoms (e.g., arthralgias) and greater endocrine therapy-related joint pain and stiffness.[14] The secretion of inflammatory markers (e.g., pro-inflammatory cytokines) by adipose tissue (i.e., body fat) has been hypothesized as one contributing factor and common pathway in the development and persistence of both pain and fatigue among breast cancer survivors with overweight or obesity.[13, 15]

When compared to women without a cancer history, breast cancer survivors also experience higher rates of depressive symptoms,[16] and breast cancer survivors with obesity may be at even greater risk for depressive symptoms.[6, 7] Obesity has been associated with brain regions linked to emotion regulation among breast cancer survivors [17], which has been hypothesized to contribute to the relationship between obesity and depressive symptoms.[18] As with pain and fatigue, obesity-related inflammation may also promote depressive symptoms.[19] Factors that are particularly salient for breast cancer survivors with overweight or obesity, like weight gain, changes in body image, and changes in functional status resulting from treatment-related physical symptoms (e.g., pain, fatigue) may further contribute to emotional distress.[20, 21] Though the relationships between BMI

and pain, fatigue, and depressive symptoms are complex, overweight and obesity have been consistently linked to greater symptom burden for breast cancer survivors.

Physical activity may play an important role in the management of patients' symptoms. It is recommended that all adults, including cancer survivors, engage in ≥150 minutes/week of moderate activity or ≥75 minutes/week of vigorous activity, as well as two or more days per week of muscle strengthening activity, and limit time spent sedentary.[22] Breast cancer survivors' levels of physical activity may decrease following diagnosis,[23] with research suggesting that survivors' rates of adherence to recommended physical activity guidelines are lower than women without a cancer history.[24] Overweight and obesity may further challenge breast cancer survivors' abilities to be physically active.[25] Greater time spent sedentary is associated with greater pain, fatigue and depressive symptoms, particularly among breast cancer survivors who are less physically activity.[26, 27] Conversely, breast cancer survivors engaging in greater intensity and/or duration of physical activity have been found to experience less pain[32] and fatigue[28] and fewer depressive symptoms.[26, 29]; however, much of this work has been conducted among women with lower BMIs (i.e., average BMI<27 kg/m^2).[26, 29] Less is known, though, about the impact of physical activity for managing symptom burden among breast cancer survivors with overweight or obesity.

Physical activity is also a key weight management behavior. In a recent study of breast cancer survivors, those engaging in physical activity and caloric restriction experienced greater weight loss than those engaging in caloric restriction alone.[30] Physical activity is particularly important for maintaining weight loss and preventing weight gain.[31] Breast cancer survivors often struggle with weight gain.[4] This may be due to a variety of factors, including metabolic changes associated with cancer treatments (e.g., chemotherapy, endocrine therapies)[32] and menopausal status at the time of diagnosis[33–35] as well as increased sedentary behavior and decreased physical activity resulting from increased physical (e.g., pain, fatigue) and emotional symptoms.[27, 32, 36] While physical activity is often encouraged among breast cancer survivors, the impact of excess weight on survivors' abilities to be physically active is less often discussed and addressed.

Taken together, prior research suggests that breast cancer survivors with higher BMIs may be more vulnerable to pain, fatigue, and depressive symptoms, and this may be particularly relevant if they are less physically active. Using baseline data from a randomized trial[37], this secondary analysis examines the relationship between women's BMI (kg/m^2) and physical activity level with pain (i.e., severity and interference), fatigue, and depressive symptoms. It was hypothesized that greater physical (i.e., pain severity and interference, fatigue) and emotional (i.e., depressive symptoms) symptom burden would be experienced by women with higher BMIs, and greater physical and emotional symptom burden would be experienced by women who were less physically active. A secondary study aim was to examine the moderating role of physical activity in the relationship between BMI and pain, fatigue, and depressive symptoms. It was hypothesized that physical activity would buffer the association between BMI and physical and emotional symptom burden.

II. Methods

a. Procedures

Study procedures for the parent trial received institutional review board approval (Pro00070823), have been registered on Clinicaltrials.gov (NCT02791646), and have been reported in detail previously.[37] Study staff reviewed electronic medical records to assess for initial eligibility. If the initial inclusion criterion was met (i.e., breast cancer diagnosis within the past two years), a potential participant was mailed a recruitment letter signed by their oncologist and the principal investigator. The letter informed the patient that they may qualify for a randomized trial examining the use of Pain Coping Skills Training[37] and provided them with a phone number for opting out of further contact. Patients who did not opt out were scheduled for a phone call appointment with a staff member to receive additional study information. If still interested, patients completed eligibility screening (i.e., worst pain score in the past week) and informed consent. As part of the parent trial, participants completed a baseline assessment via Qualtrics consisting of self-report questionnaires measuring demographic and medical characteristics, physical activity, pain (i.e., severity and interference), fatigue, and depressive symptoms. Participants received $30 for completing the baseline assessment.

b. Participants

Women with breast cancer (N=327) were recruited from 2017-2020 into the parent trial. Eligibility criteria for the parent trial included: 1) diagnosis of stage I-IIIC breast cancer within the past two years; 2) ≥18 years of age; 3) life expectancy of ≥12 months, confirmed by oncologist; and 4) self-reported worst pain severity rating in the past week of ≥5 out of 10 at the time of screening, consistent with moderate-to-severe pain.[38] Patients were excluded from the parent trial if they reported (verified by medical chart review): 1) cognitive impairment; 2) severe psychiatric condition (e.g., psychotic disorder or episode) or suicidal intent that would contraindicate safe participation in the parent trial; and/or 3) current or past (<6 months) engagement in Pain Coping Skills Training (PCST) for cancer pain.

c. Measures

Demographic and Medical Characteristics.—Demographic (i.e., age, race, ethnicity, education, partner status) and medical (i.e.., BMI [current weight in kg/height in m^2], cancer stage, surgeries and treatments received, use of antidepressant and/or pain medication, medical comorbidities) characteristics were collected by participant self-report at the baseline assessment. Medical comorbidities included rheumatoid arthritis, osteoarthritis, sciatica, hypertension, heart disease, diabetes, chronic obstructive pulmonary disease (COPD), depression, and anxiety. Medical characteristics were confirmed via electronic medical record review at the time of the baseline assessment.

Physical Activity.—Physical activity was assessed with the nine-item Rapid Assessment of Physical Activity (RAPA).[39] This measure assesses aerobic physical activity, strength, and flexibility. Seven aerobic exercise items ask participants whether they have, in the past week, engaged in varying levels of physical activity (yes/no). Items gradually increase in

exertion level, starting with 1 (I rarely or never do any physical activities), 2 (I do some light or moderate physical activities, but not every week), 3 (I do some light physical activity every week), 4 (I do moderate physical activities every week, but less than 20 minutes a day or 5 days a week), 5 (I do vigorous physical activities every week, but less than 20 minutes a day or 3 days a week), 6 (I do 30 minutes or more a day of moderate physical activities, 3 or more days a week), and 7 (I do 20 minutes or more a day of vigorous physical activity 3 or more days per week). Following scoring guidelines [39], values 1 through 5 were categorized as suboptimal physical activity while values 6 and 7 were categorized as optimal physical activity. The RAPA has been previously used in medical populations experiencing pain (e.g., cancer, cardiovascular disease).[40, 41]

Physical Symptom Burden.—Pain was assessed with the Brief Pain Inventory (BPI).[42] Four pain severity items asked participants to rate their pain at its worst, least, and average over the past week as well as their current pain. Response options ranged from 0 (no pain) to 10 (worst pain imaginable). Severity items were averaged for a composite score (Cronbach's α=.86). Seven pain interference items asked participants to rate the degree to which, over the past week, pain interfered with daily activities (i.e., general activity, mood, walking ability, normal work [including housework], relations with others, sleep, and enjoyment of life). Response options ranged from 0 (does not interfere) to 10 (completely interferes). Pain interference items were averaged for a composite score and demonstrated good reliability (Cronbach's α=.91). The BPI is recommended for use in clinical trials assessing pain and is frequently used in cancer samples.[43]

Fatigue was assessed utilizing the seven item Patient-Reported Outcome Measurement Information System-Fatigue (PROMIS-Fatigue) scale.[44] Participants were asked to identify the number of times during the past week they experienced tiredness, extreme exhaustion, lack of energy, and limitations in performing work (including housework) due to fatigue, as well as how many times during the past week they felt too tired to think clearly, bathe/shower, and whether they had enough energy to exercise strenuously. Response options ranged from 1 (never) to 5 (always). As recommended by the PROMIS scoring guidelines, items were summed, and the raw summed scores were then converted to T-scores.[45] Higher T-scores indicated higher levels of fatigue. The PROMIS-Fatigue scale is commonly used in cancer samples[44] and demonstrated adequate reliability in the present sample (Cronbach's α=.78).

Emotional Symptom Burden.—Depressive symptoms were assessed utilizing the 20-item Center for Epidemiological Studies Depression Scale (CES-D).[46] Participants were asked to rate the number of times during the previous week they experienced depressive symptoms (e.g., low mood, anhedonia, difficulty concentrating). Response options ranged from 0 (rarely or none of the time) to 3 (all of the time). These items were summed to obtain a total score with higher scores indicating higher levels of depressive symptoms. The CES-D is frequently used to assess depressive symptoms among breast cancer survivors[47] and demonstrated excellent reliability in the present sample (Cronbach's α=.90).

d. Analytic Strategy

Preliminary descriptive analyses were conducted using Statistical Package for the Social Sciences Version 27 (SPSS 27). All variables of interest were screened for outliers, and distributions were inspected for skewness, kurtosis, and multivariate assumptions of normality. One extreme outlier (71.01 kg/ m^2) was removed from the BMI distribution. Linear regression analyses were conducted to examine separate associations between BMI (continuous) and physical activity (dichotomous; 0=suboptimal physical activity vs. 1=optimal physical activity) with continuous outcome variables (i.e., pain severity, pain interference, fatigue, depressive symptoms). Sensitivity analyses using binary logistic regressions were also conducted to assess the likelihood of membership to clinical categories of outcome variables (i.e., pain severity, pain interference, fatigue, depressive symptoms)[38, 48–50] given membership to categories of predictor variables (i.e., BMI, physical activity). [39] Significance level for all regressions was $p<.05$.

Model 1 of the Hayes PROCESS macro (Version 2.16.2)[51] was used to assess moderation, with physical activity serving as a dichotomous moderator (0=suboptimal physical activity vs. 1=optimal physical activity) of the relationships between BMI (continuous) and continuous outcome variables (i.e., pain severity, pain interference, fatigue, depressive symptoms). Moderation was confirmed if the interaction term (BMI x Physical Activity) was significant ($p<.05$).[51] Significant interaction terms were examined further to assess conditional effects of the predictor (BMI) at different levels of the moderator (i.e., suboptimal vs. optimal physical activity).[51]

Demographic (i.e., age, race, education) and medical (i.e., cancer stage, receipt of breast cancer treatment [i.e., chemotherapy, radiation, or surgery] during the week before baseline assessment, receipt of endocrine therapy during the week before baseline assessment, and diagnosis with pain-related conditions [e.g., rheumatoid arthritis, osteoarthritis, and/or sciatica]) variables known to be associated outcome variables in prior literature[6, 52–59] were considered for inclusion as covariates; only those significantly associated with each particular outcome variable were retained in the corresponding regression and moderation models (see Notes for Tables 3 and 4 and Supplemental Table 1).

III. Results

a. Participant Characteristics

The average age of women in this study was 57.19 (*SD*=11.87) years old. More than one-third (35.6%) of the sample identified as a racial minority. Most participants reported a college education, with 31.2% obtaining a bachelor's degree. Just over half of women (58.4%) reported being married (Table 1).

At enrollment, mean time since diagnosis was approximately 10 months (*SD*=6.21). For most women (97.2%), this was their first diagnosis of breast cancer. Over half the sample reported stage I disease (56.0%). Breast conserving surgery was common, with 56.9% of the sample having undergone lumpectomy, quadrantectomy, partial mastectomy, or segmental mastectomy. Only 8.3% (*n*=27) reported receipt of chemotherapy during the week before the baseline assessment, and 10.8% (*n*= 35) reported receipt of radiation during that same time

frame. At the time of the baseline assessment, 15.1% endorsed receipt of endocrine therapy. Additional medical characteristics are reported in Table 1.

Descriptive statistics for the primary study variables are reported in Table 2. Women in the current sample had an average BMI of 30.79 kg/m^2 (*SD*=7.43), with 27.7% with overweight (≥25 to <30 kg/m2) and 48.6% with obesity (≥30 kg/m^2). In terms of physical activity, 54.9% (*n*=179) of women endorsed suboptimal levels of physical activity.[39] Average pain severity (*M*=4.04, *SD*=1.73) was mild, with just under 30% (*n*=95) of the sample endorsing moderate or severe pain at the time of baseline assessment.[38] Average pain interference (*M*=4.07, *SD*=2.43) was moderate, though 70 participants (21.5%) endorsed severe pain interference.[50] Women reported mild fatigue on average (T-score *M*=56.01, *SD*=7.11), with the majority of the sample (72.4%) falling in the below average to mild category.[49] Approximately half of the sample (50.6%) obtained a CES-D score (*M*=17.60, *SD*=10.30) at or above the established cut-off (≥16) indicating risk for clinical symptoms of depression[48].

b. Association between BMI and Physical Activity with Primary Study Variables

In unadjusted linear regression analyses (Table 3), higher BMI was significantly associated with higher pain severity (*B*=.06, 95% CI [.03,.08], *p*<.001) and pain interference (*B*=.08, 95% CI [.04,.11], *p*<.001). BMI was not significantly related to fatigue (*B*=.04, 95% CI [−.07,.14], *p*=.47) or depressive symptoms (*B*=.04, 95% CI [−.11,.19], *p*=.60,). After adjusting for covariates, BMI remained significantly associated with pain severity (*B*=.04, 95% CI [.02,.07], *p*<.001) and pain interference (*B*=.06, 95% CI [.03,.10], *p*<.01) such that for each 1 unit increase in BMI, there was a .04 and .06 increase in pain severity and interference, respectively. BMI was not significantly related to fatigue (*B*=.06, 95% CI [−.04,.16], *p*=.26) or depressive symptoms (*B*=.07, 95% CI [−.08,.22], *p*=.37) in adjusted regression models (Table 3). Sensitivity analyses using binary logistic regressions showed that BMI category (i.e., normal vs. overweight; normal vs. obese) was not associated with clinical categories for pain severity, pain interference, fatigue, or depressive symptoms (Supplemental Table 1).

In unadjusted regressions analyses (Table 3), report of physical activity in the optimal range was significantly related to lower pain interference (*B*=−.76, 95% CI [−1.29,−.23], *p*=.005). Physical activity was not significantly related to pain severity (*B*=−.28, 95% CI [−.66,.10], *p*=.15), fatigue (*B*=−.50, 95% CI [−2.06,1.05], *p*=.53), and depressive symptoms (*B*=−1.97, 95% CI [−4.22,.28], *p*=.09) in unadjusted regression models. Physical activity falling in the optimal range remained significantly associated with lower pain interference once covariates were added to the regression model (*B*=−.69, 95% CI [−1.21,−.17], *p*=.009). In adjusted regression models, physical activity was not significantly associated with pain severity (*B*=−.19, 95% CI [−.55,.17], *p*=.31), fatigue (*B*=−.41, 95% CI [−1.95,1.13], *p*=.60), or depressive symptoms (*B*=−1.78, 95% CI [−3.99,.43], *p*=.11). In line with linear regression models, sensitivity analyses using binary logistic regressions showed that after adjusting for covariates (Supplemental Table 1), women falling into the optimal category of physical activity were less likely to fall into the severe category of pain interference (*Exp(B)*=.44, 95% CI[.24,.80], *p*=.007). Category of physical activity was not associated with clinical

categories for pain severity, fatigue, or depressive symptoms in adjusted models (see Supplemental Table 1).

Physical Activity as a Moderator—Physical activity was assessed as a moderator of the relationships between BMI and pain severity, pain interference, fatigue, and depressive symptoms. Covariates were included in all moderation models. Main effects linking higher BMI with higher pain severity (B=.05, 95% CI [.02,.08], p=.002) and pain interference (B=.05, 95% CI [.003,.09], p=.04) were retained; physical activity was marginally associated with pain interference (B=−.53, 95% CI [−1.05,.00], p=.05). All interaction terms were not significant, suggesting that physical activity did not moderate the relationships between BMI and pain severity (B=−.02, 95% CI [−.07,.04], p=.57), pain interference (B=.02, 95% CI [−.06,.09], p=.67), fatigue (B=.06, 95% CI [−.16,.29], p=.58), and depressive symptoms (B=.05, 95% CI [−.17,.28], p=.65) in this sample. In other words, the relationship between BMI and symptoms did not differ based on level (i.e., suboptimal vs. optimal) of physical activity. Unstandardized parameter estimates for fully adjusted moderation models are presented in Table 4.

IV. Discussion

This study examined the relationships between BMI and level of physical activity with women's physical (i.e., pain, fatigue) and emotional (i.e., depressive symptoms) symptom burden in a large, diverse sample of breast cancer survivors with pain. The selection of breast cancer survivors self-reporting at least moderate pain at screening (vs. breast cancer survivors with minimal pain) yields a sample for whom BMI and physical activity may be especially relevant. Rates of overweight and obesity in the present sample were high, with more than 75% of survivors having a BMI ≥25. Indeed, the percentage of participants with overweight or obesity was higher than rates (57% to 66%) noted in a recent systematic review of breast cancer survivors in the US.[60] Rates found in the present study may have been impacted by the parent study's recruitment of survivors with at least moderate pain, and could suggest that breast cancer survivors with overweight or obesity may be more vulnerable to pain, as has been suggested in prior research.[15] In fact, in the present study, BMI was independently and positively associated with pain severity and pain interference.

The majority of breast cancer survivors in the present study endorsed suboptimal levels of physical activity. Low levels of physical activity seen in the present sample may be a function of survivors' moderate to severe levels of self-reported pain at screening, as well as moderate levels of pain interference. Physical activity in the suboptimal range was significantly associated with greater pain interference, but not pain severity, both on a continuous scale as well as when assessed categorically. That is, women who fell in the optimal level of physical activity were less likely to fall into the severe category of pain interference. This aligns with prior research showing that high levels of sedentary behavior are linked to greater physical disability in breast cancer survivors.[61] Perhaps paradoxically though, physical activity is one of the most effective ways to reduce disability and the interference of symptoms (i.e., pain) on daily functioning.[61–64] Similarly, physical activity has been consistently associated with lower depressive symptoms among breast cancer survivors [59]. Results here hint at such a relationship with women who endorsed

physical activity in the optimal range reporting fewer depressive symptoms, although this association was only marginally significant. Likewise, when assessed categorically, women who fell in the optimal level of physical activity were less likely to fall into the clinical category for depressive symptoms; however, this relationship did not hold once covariates were added to the model. More nuanced measurement of physical activity (e.g., minutes of activity, type of physical activity) may better elucidate this relationship in future work.

Neither BMI nor physical activity were significantly associated with fatigue when assessed both continuously and categorically in the present study. Participants were on average 10 months from their diagnosis, and most women had completed primary cancer treatments. Cancer-related fatigue, though persistent for many, often decreases over time, especially following treatment completion.[52] The risk for severe fatigue, in particular, has been found to decrease in the first 6 months following treatment.[52] The average fatigue score for participants in this study was approximately one-half standard deviation above the mean of the general US population.[44, 45, 65] Though elevated, the average fatigue score fell in the mild range.[45, 65] The milder reports of fatigue in the present sample may be one possible factor contributing to the lack of associations between BMI and physical activity with fatigue.

Alternative explanations should also be considered; for example, it is possible that, in the current sample, other variables are more strongly related to fatigue (e.g., age, cancer stage). In linear regression models, age and cancer stage covariates were associated with fatigue, such that younger breast cancer survivors and those with higher stage disease reported higher fatigue. In this sample, fatigue may be more prevalent and persistent for breast cancer survivors with higher stage and younger age for a variety of reasons, including the need for more aggressive treatments or having more competing demands (e.g., work, childcare responsibilities).[52, 66–69] In a recent study, the relationship between adherence to physical activity guidelines and lower levels of fatigue was stronger for breast cancer survivors aged <50 when compared to older survivors.[68] Additional research is necessary to better understand our finding in the population under study – breast cancer survivors with a recent history of moderate to severe pain.

In moderation models, physical activity did not buffer the association between BMI and pain, fatigue or depressive symptoms. It is possible that the high rate of overweight and obesity seen in the present study may have restricted women’s abilities to engage in physical activity in a way that would result in improved symptoms. A prior study of endometrial cancer survivors similarly did not find physical activity to impact the strength of the relationship between body weight and quality of life domains.[70] A second study of endometrial cancer survivors found the influence of physical activity on fatigue to be greatest for survivors in the normal BMI range.[71] Although our null result does not confirm our hypothesis, it is still informative. Specifically, our finding suggests that, in the current sample, being more physically active alone may not influence the strength of the relationship between BMI and symptoms. This result should be considered preliminary though, and more work using larger and longitudinal datasets is needed to better assess whether physical activity might moderate the relationship between BMI and physical and emotional symptoms.

Supportive care interventions targeting pain during breast cancer survivorship should assist women with maintaining a healthy weight due to the relationship between BMI, pain, and pain interference. Additionally, these interventions may also benefit from assisting women with increasing physical activity in the service of pain management and maintenance of weight loss. Our group's prior work[72, 73] developing combined behavioral weight and symptom management interventions for individuals with both chronic pain (i.e., patients with osteo- or rheumatoid arthritis) and overweight or obesity has incorporated strategies to improve diet and increase physical activity along with behavioral strategies to address symptoms that interfere with healthy lifestyle behaviors (e.g., changing dietary patterns, caloric restriction) necessary for weight management. Results suggest that the combined interventions produce symptom reductions while also assisting patients with weight loss and control. Combined behavioral weight and symptom management interventions are beneficial for breast cancer survivors,[74] though randomized trials are needed to examine the efficacy of these interventions for breast cancer survivors with overweight or obesity and comorbid pain.

Limitations should be noted. The sample was primarily well-educated and older, which may limit generalizability. The cross-sectional study design limits our ability to make causal inferences in the relationships examined in this study. The relationship between overweight and obesity and physical and emotional symptom burden is likely reciprocal over time such that weight gain is associated with increased symptom burden *and* increased symptom burden may influence factors (e.g., dietary behaviors) associated with weight gain.[75, 76] Future longitudinal research is necessary to better understand the direction and nature of the relationships between BMI and physical activity with pain, fatigue, and depressive symptoms. Additionally, our sample size was relatively modest, likely limiting our ability to robustly assess for moderation. Finally, participants provided a subjective rating of their physical activity in the past week. Future research should consider using objective measures of physical activity, like actigraphy or wearable fitness trackers, to better understand the role of physical activity, activity type, and activity intensity on cancer symptoms, like depression and fatigue.

The results presented have meaningful clinical implications for cancer survivorship care. Physical activity alone may not be sufficient for symptom management among breast cancer survivors with moderate-to-severe pain and higher BMIs. Results underscore the importance of addressing factors contributing to higher BMI, as higher BMI was associated with worse pain severity and interference. BMI and physical activity may represent two potentially synergistic targets for interventions aimed at reducing pain experienced by breast cancer survivors. Behavioral interventions combining strategies to improve diet and eating behavior, increase physical activity, and address pain may be necessary. Consistent assessment of behavioral factors contributing to higher BMI and physical inactivity throughout breast cancer survivorship may result in earlier and more targeted interventions to address excess weight, sedentary lifestyles, and symptom burden.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic and Medical Characteristics (N=327)

	N (%)	*M* (*SD*)[a]
Age (years)		57.19 (11.87)
Race		
White/Caucasian	203 (62.1%)	
Racial Minority	116 (35.6%)	
Black/African American	97 (29.7%)	
Two or More Races	9 (2.8%)	
Asian	9 (2.8%)	
American Indian or Alaskan Native	1 (0.3%)	
Other	3 (0.9%)	
Not Reported/Declined	5 (1.5%)	
Ethnicity		
Non-Hispanic	311 (95.1%)	
Hispanic or Latino	5 (1.5%)	
Hispanic Mexican	2 (0.6%)	
Hispanic Cuban	3 (0.9%)	
Hispanic Puerto Rican	2 (0.6%)	
Hispanic Other	4 (1.2%)	
Education		
Less than High School Diploma	7 (2.1%)	
High School Diploma	41 (12.5%)	
Some College	106 (32.4%)	
Bachelor's Degree	102 (31.2%)	
Graduate Degree	71 (21.7%)	
Partner Status		
Single	40 (12.2%)	
Married	191 (58.4%)	
Divorced	62 (19.0%)	
Separated	6 (1.8%)	
Widowed	24 (7.3%)	
Life-/Long-term Partner	4 (1.2%)	
Cancer Diagnosis [b]		
First/Initial	317 (97.2%)	
Recurrence	9 (2.8%)	
Months Since Diagnosis		10.11 (6.21)
Stage		
I	183 (56.0%)	
II	113 (34.6%)	
III	31 (9.5%)	
Breast Surgery History[c] (% yes)		

	N (%)	*M* (*SD*)[a]
Mastectomy – one breast	54 (16.7%)	
Mastectomy – two breasts	65 (20.1%)	
Breast Conserving Surgery[d]	185 (56.9%)	
Lymph Node Removal	286 (88.3%)	
Reconstruction	73 (22.5%)	
Received Chemotherapy[e] (% yes)	27 (8.3%)	
Received Radiation[e] (% yes)	35 (10.8%)	
Received Surgery[e] (% yes)	22 (6.7%)	
Received Endocrine Therapy[e] (% yes)	49 (15.1%)	
Antidepressant Medication Use (% yes)	123 (37.7%)	
Pain Medication Use (% yes)	212 (64.8%)	
Rheumatoid Arthritis (% yes)	29 (9.0%)	
Osteoarthritis (% yes)	77 (23.8%)	

Note:

[a] *M*=mean, *SD*=standard deviation;

[b] *n*=326 due to missing data;

[c] As women may have received more than one type of breast surgery, results do not add up to 100% and instead reflect the number (%) of women reporting having had each surgical procedure;

[d] Breast Conserving Surgery includes lumpectomy, quadrantectomy, partial mastectomy, segmental mastectomy;

[e] Received Chemotherapy, Radiation, Surgery, and Endocrine Therapy is for week before baseline assessment.

Table 2.

Descriptive Statistics for Primary Study Variables

Variable	N	Range	M (SD)[a]	Categories	
					n (%)
BMI [b]	325[c]	16.76 – 62.55	30.79 (7.43)	Normal <25	77 (23.7)
				Overweight (25 – 30)	90 (27.7)
				Obesity (≥30)	158 (48.6)
Physical Activity	326	-	-	Suboptimal	179 (54.9)
				Optimal	147 (45.1)
Pain Severity	325	.00 – 9.75	4.04 (1.73)	Mild (<5)	230 (70.8)
				Moderate + Severe (≥5)	95 (29.2)
Pain Interference	325	.00 – 10.00	4.07 (2.43)	Mild + Moderate (<6)	255 (78.5)
				Severe (≥6)	70 (21.5)
Fatigue	326	29.40 – 77.10	56.01 (7.11)	Below Average + Mild (<60)	236 (72.4)
				Moderate + Severe (≥60)	90 (27.6)
Depressive Symptoms	326	.00 – 45.00	17.60 (10.30)	Subclinical <16	161 (49.4)
				Clinical ≥16	165 (50.6)

Note:

[a] *M*=mean, *SD*=standard deviation;

[b] BMI=body mass index;

[c] Sample size for primary study variables ranged from *n*=325 to *n*=326 due to missing data.

Table 3.

Unadjusted and Adjusted Linear Regression Parameters

	Pain Severity[e]		Pain Interference[f]		Fatigue[g]		Depressive Symptoms[h]	
	B [a]	*95% CI* [b]	*B*	*95% CI*	*B*	*95% CI*	*B*	*95% CI*
Unadjusted Models [c]								
BMI	.06***	[.03,.08]	.08***	[.04,.11]	.04	[−.07,.14]	.04	[−.11,.19]
Physical Activity	−.28	[−.66,−.10]	−.76**	[−1.29,−.23]	−.50	[−2.06,1.05]	−1.97	[−4.22,.28]
Adjusted Models [d]								
BMI	.04***	[.02,.07]	.06**	[.03,.10]	.06	[−.04,.16]	.07	[−.08,.22]
Physical Activity	−.19	[−.55,.17]	−.69**	[−1.21,−.17]	−.41	[−1.95,1.13]	−1.78	[−3.99,.43]

Note:

[a] unstandardized beta;

[b] 95% confidence interval for unstandardized parameter estimate;

[c] unadjusted for covariates;

[d] adjusted for covariates;

[e] covariates for pain severity model: race (0=White vs. 1=Non-White), education (0=high school diploma or less vs. 1=some college or more), and cancer stage (0=stage I vs. 1=stage II & III);

[f] covariates for pain interference model: race (0=White vs. 1=Non-White), education (0=high school diploma or less vs. 1=some college or more), and receipt of endocrine therapy in past week (0=no vs. 1=yes);

[g] covariates for fatigue model: age and cancer stage (0=stage I vs. 1=stage II & III);

[h] covariates for depressive symptoms model: age; ;

* $p<.05$;

** $p<.01$;

*** $p<.001$.

Table 4.

Adjusted Moderation Model Parameters

	Pain Severity[c]			Pain Interference[d]			Fatigue[e]			Depressive Symptoms[f]		
	B [a]	*p*	*95% CI* [b]	*B*	*p*	*95% CI*	*B*	*p*	*95% CI*	*B*	*p*	*95% CI*
BMI	.05**	.002	[.02,.08]	.05*	.04	[.003,.09]	.03	.64	[−.10,.16]	.03	.68	[−.11,.16]
Physical Activity	−.05	.78	[−.42,.32]	−.53	.05	[−1.05,.00]	−.25	.75	[−1.84,1.34]	−.30	.72	[−1.90,1.30]
BMI x Physical Activity	−.02	.57	[−.07,.04]	.02	.67	[−.06,.09]	.06	.58	[−.16,.29]	.05	.65	[−.17,.28]

Note:

[a] unstandardized beta;

[b] 95% confidence interval for unstandardized parameter estimate; Moderation models shown are adjusted for covariates;

[c] covariates for pain severity model: race (0=White vs. 1=Non-White), education (0=high school diploma or less vs. 1=some college or more), and cancer stage (0=stage I vs. 1=stage II & III);

[d] covariates for pain interference model: race (0=White vs. 1=Non-White), education (0=high school diploma or less vs. 1=some college or more), and receipt of endocrine therapy in past week (0=no vs. 1=yes);

[e] covariates for fatigue model: age and cancer stage (0=stage I vs. 1=stage II & III);

[f] covariates for depressive symptoms model: age;

* $p<.05$;

** $p<.01$.