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Postsurgical Physical Activity and Fatigue-Related Daily Interference in Women with Non-Metastatic Breast Cancer

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Abstract

Purpose—Women undergoing surgery for breast cancer experience side effects such as fatigue, reduced quality of life (QOL), and depression. Physical activity (PA) is associated with improved psychological adjustment during treatment and survivorship, yet little is known about how PA relates to fatigue, depression and QOL in the period following surgery for breast cancer. The purpose of the study was to examine the relationships between these constructs in women who recently underwent surgery for breast cancer.

Methods—At two to ten weeks post-surgery, 240 women with non-metastatic breast cancer reported intensity and duration of moderate and vigorous PA (MVPA), fatigue (intensity and interference), depressed mood, clinician-rated depression, and functional QOL.

Results—In the path analysis models tested, women that reported greater weekly MVPA reported less fatigue interference, greater functional QOL, less depressed mood, and lower clinician-rated depression. Tests of indirect effects suggested that fatigue interference may be an intermediate pathway by which MVPA relates to functional QOL, clinician-rated depression, and depressed mood.

Conclusion—Women who are more physically active in the months after breast cancer surgery show greater psychological adaptation in the initial phases of their treatment.

Keywords

Breast cancer; oncology; physical activity; fatigue interference; quality of life; depression

Introduction

Fatigue and depression are among the most prevalent and debilitating side effects during breast cancer treatment (Wagner & Cella, 2004; Thornton, Andersen, & Blakely, 2010).

Physical activity (PA) may ameliorate the physical and psychological symptoms associated with cancer diagnosis and treatment (Courneya & Friedenreich, 1999; Pinto, Clark, Maruyama, & Feder, 2003; Pinto & Maruyama, 1999; Schmitz, Holtzman, Courneya, Masse, Duval, & Kane, 2005; Daley, Crank, Saxton, Mutrie, Coleman, & Roalfe, 2007). In light of this, the American College of Sports Medicine (ACSM) recommends that patients with cancer should be active for 150 minutes of moderate activity or 75 minutes of vigorous activity per week (Schmitz et al., 2010). Linkages among constructs of PA, fatigue, depressed mood, and quality of life (QOL) have been studied to varying degrees in breast cancer patients and survivors (Daley et al., 2007; Basen-Engquist, Hughes, Perkins, Shinn, & Taylor, 2008). However, few studies have examined the role of PA immediately after breast cancer surgery (Anderson et al., 2012; Cavanaugh, 2011).

Following breast cancer surgery, women have anticipatory anxiety about adjuvant treatment while emotionally and physically recovering from surgery (Carver, Lehman, & Antoni, 2003; Spencer et al., 1999; Jacobsen, Bovbjerg, & Redd, 1993). Psychological and immune function at this stressful, post-surgical time point may be associated with long-term outcomes such as disease progression, morbidity, and mortality (Blomberg et al., 2009; Carver, Smith, Antoni, Petronis, Weiss, & Derhagopian, 2005; Andersen et al., 1998). Results of a recent study suggest that beginning an exercise program within three months following surgery for breast cancer may improve recovery by increasing physical functioning (Anderson et al., 2012). Women with breast cancer who exercised according to the ACSM guidelines showed more vigor and use of adaptive coping strategies, which may be crucial for women beginning adjuvant treatment (Pinto, Maruyama, Engebretson, & Thebarge, 1998). Maintenance of PA in this timeframe may decrease the likelihood of long-term health outcomes of fatigue, depressed mood, and poor QOL. The following sections outline the specific relationships between PA and fatigue, depressed mood, and QOL.

Physical Activity and Fatigue

The severity of a woman's cancer-related fatigue influences her ability to engage in tasks and activities that may ultimately bring meaning to her daily life (Berger, 1998). Low PA is a primary contributor to cancer-related fatigue (Goedendorp, Gielissen, Verhagen, Peters, & Bleijenberg, 2008). Breast cancer survivors and women undergoing active treatment who are physically active report significant reductions in fatigue (McNeely, Campbell, Rowe, Klassen, Mackey, & Courneya, 2006; Mock et al., 2005). However little is known about whether PA is related to fatigue in the critical postsurgical recovery period. Two constructs of fatigue have been studied in breast cancer literature: self-report of fatigue intensity and fatigue interference (Donovan, Jacobsen, Small, Munster, & Andrykowski, 2008). Fatigue intensity is an individual's subjective experience of the severity of their fatigue sensations on a given day or on average. Fatigue interference is the extent to which an individual's fatigue has disrupted their functioning and activities of daily living, such as bathing, dressing, concentrating, enjoying life, going to work, and being sociable with others (Hann et al., 1998). Most research has focused on the factors influencing fatigue intensity, although measuring and relating fatigue interference to other psychosocial constructs may be equally important. For instance, a greater fatigue interference/fatigue severity ratio, where interference is greater than severity, has been shown to predict depression in cancer patients (Traeger, Braun, Greer, Temel, Cashavelly, & Pirl, 2011). In light of this, the construct of fatigue interference is examined in the present study in addition to fatigue intensity.

Physical Activity and Quality of Life

In addition to fatigue, cancer treatment also significantly affects QOL and impairs functional capacity (Courneya & Friedenreich, 1999). Further, PA may be beneficial in increasing QOL during and after treatment for breast cancer (Kirshbaum, 2007). Some studies have

found that PA interventions sustain and increase functional capacity and QOL for women undergoing active treatment (Mock et al., 2005, Holmes et al., 2005; McNeely et al., 2006). However, investigators suggest that more research is needed (Haas, 2011) as most studies were done with breast cancer survivors who had completed treatment (Penttinen et al., 2011). This highlights the need for establishing a connection between PA and QOL in the midst of treatment.

Physical Activity and Depression

Another area of research in need of more evidence is the role of PA in depression. Depression is frequently reported in women undergoing treatment for breast cancer (Mock et al., 1997) and may be characterized by symptoms such as sadness, hopelessness, and loss of interest in pleasurable activities (Mowry, 1998). While depressed breast cancer patients have worse health outcomes overall (Spiegel & Giese-Davis, 2003), physically active breast cancer survivors report significantly less depression (Daley et al., 2007) and mood disturbance (Pinto & Trunzo, 2004). Depression refers to the clinical diagnosis of major depressive disorder. However, depressed mood refers to one of the two major symptoms of clinical depression. A woman may exhibit depressed mood without meeting full criteria for major depressive disorder (Mowry, 1998). In this study, we looked at both depressed mood and depression as rated by a clinician. A Cochrane review notes the need for more research to determine the influence of PA on mood disturbances in women during treatment for breast cancer (Markes, Brockow, & Resch, 2006). Knowledge of the significance of maintaining PA during active treatment may offer clinical guidance for supportive care and may optimize recovery.

The purpose of the present study is to investigate how PA relates to functional fatigue intensity and interference, QOL, depression, and depressed mood in women recovering from breast cancer surgery during the initial phase of their treatment. This study will be the first to our knowledge to statistically model these constructs during the period of active primary treatment. The study will examine these linkages at the critical and stressful postsurgical period that has been determined to be predictive of long-term outcomes and thus, a potentially important time to intervene. The functional QOL domain was chosen as the outcome in this study because it is the QOL domain with the strongest association with overall life satisfaction (Courneya & Friedenreich, 1997). Modeling these relationships will help delineate the processes by which PA may reduce fatigue and depression and improve QOL, which could facilitate intervention development (Conn, 2010). Finally, whereas most studies on PA and breast cancer have been conducted in a predominantly Caucasian sample (Smith et al., 2009), this study sample is ethnically diverse, and therefore findings may generalize to other ethnic populations.

Ultimately, we hypothesize that the linkages among the constructs of PA, fatigue, depressed mood/depression, and functional QOL in the midst of treatment will be in line with the relationships proposed by Pinto, Clark, Maruyama, & Feder (2003) in cancer survivors. It has been proposed that (a) PA leads to a reduction in fatigue; (b) cancer patients who are less fatigued are able to participate in daily activities that make life meaningful; and, in turn, (c) have improved QOL and report less depression (Pinto et al, 2003). Conversely, research shows that individuals who are fatigued are consequently less physically active (Garber & Friedman, 2003), and we will take this into account by testing alternative models.

Method

Participants and Procedures

Participants were part of a larger study testing a cognitive-behavioral stress management intervention, as described elsewhere (Antoni et al., 2006). Ethical approval for the study was obtained by the Human Subjects Research Office of the University of Miami Institutional Review Board. Women diagnosed with non-metastatic stage 0-IIIb breast cancer who were two to ten weeks post-surgery were recruited for the parent study through physician referrals and community advertising. The women received personalized letters from their breast surgical oncologist or the American Cancer Society, which referred them to the study as an opportunity to learn stress management techniques. The post-surgery window was designed to allow enough time for postsurgical pain and swelling to be resolved and to provide time for the assessment to be conducted before adjuvant treatment began (Antoni et al., 2006). A total of 502 potential participants were referred and screened for this study. Exclusion criteria included prior cancer, prior self-reported psychiatric treatment for serious mental disorder, and a lack of fluency in English. Of the 502 women screened, 106 women did not meet inclusion criteria, and 156 women were not interested and declined participation. Enrolled participants totaled 240 women who met the inclusion criteria and had not yet begun active adjuvant treatment (chemotherapy and/or radiation).

Measures

Demographics—Information regarding demographics, socioeconomic status (i.e., income and education), medical condition, and treatment (i.e., stage of disease, type and time of surgery and type of adjuvant treatment) was collected by self-report at the baseline assessment prior to randomization.

Physical activity—Intensity, frequency, and duration of moderate to vigorous physical activity (MVPA) were measured via a brief version of the Seven Day Physical Activity Recall Questionnaire (Blair et al., 1985). This PA measure has been used extensively in prior research studies and has proven to be a valid measure of activity when compared with other measures of PA (Jacobs, Ainsworth, Hartma & Leon, 1993). The measure has been used in cancer populations (Ligibel et al., 2012) and specifically with breast cancer patients (Ottenbacher et al., 2012). In a sample of newly diagnosed breast cancer patients and prostate cancer survivors, research shows moderate agreement between weekly estimates of MVPA on the Seven Day Physical Activity Recall with objective data from an accelerometer (Sloane, Snyder, Demark-Wahnefried, Lobach, & Kraus, 2009). Participants were asked to record the total number of minutes engaged in vigorous and/or moderate activity each day of the previous week (as recalled). Participants were informed that vigorous activities are those that require substantial energy expenditure (e.g., jogging or sustained swimming). On the other hand, moderate activities are ones in which the heart rate is increased, but it is still possible to carry on a conversation (e.g., yard work or heavy housecleaning). Participants indicated about how many minutes on average they spent engaged in MVPA during each of those times. Data suggests that PA at moderate and vigorous intensity levels is beneficial for alleviating side effects and improving QOL in cancer patients (Schmitz et al., 2005; Ottenbacher et al., 2012). Therefore, reported amounts of moderate and vigorous activity were combined and analyzed together. The measure was found to have good reliability in this sample ($\alpha = .90$).

Fatigue—Fatigue (intensity and interference) was measured using the two subscales of the 14-item self-report Fatigue Symptom Inventory (FSI) (Hann et al., 1998). The 4-item intensity scale measures the severity/intensity of the individuals' fatigue over the past week, while the 7-item interference scale measures how much the fatigue has impacted ability to

function in daily roles and activities (e.g., “Rate how much, in the past week, fatigue has interfered with your normal work activity”). Possible scores range from zero to 10 on both the intensity and interference subscales. Higher scores are indicative of greater fatigue (intensity and interference). A score of three has been identified as a cutoff for clinically meaningful fatigue in a breast cancer population (Donovan et al., 2008). This measure was developed for use with cancer patients, and the psychometric properties of the scale were validated in a sample of breast cancer patients and survivors (Hann et al., 1998). The FSI has moderate test-retest reliability and has been validated against other measures of fatigue with correlations ranging from .41–.86 (Donovan & Jacobsen, 2010). In the present study, the Chronbach’s alphas for the intensity and interference subscales were .83 and .93, respectively.

Clinician-rated depression—Severity of depressive symptomatology experienced over the past week was measured using the 17-item interviewer administered Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960). This was the only measure that was not self-administered. A master’s level clinical social worker administered the HRSD in interview form to each participant. The measure uses a Likert-type scale with either three-point or five-point responses depending on the item. A final score is obtained by summing the individual item responses. Possible scores range from zero to 54, and higher scores are indicative of more severe depression. The HRSD has been used to measure depression in breast cancer patients (Hopko & Colman, 2010; Savard et al., 2006; Park, Lee, Kim, Bae, & Hahm, 2012). It has been found to be a valid and reliable measure in one study of cancer patients (Olden, Rosenfeld, Pessin, & Breitbar, 2009) and has shown good sensitivity, specificity, and predictive validity in another sample of patients with various cancer types (Hopko et al., 2007). The HRSD has strong test-retest reliability of .81 (Williams, 1988). When compared with other measures of depression such as the Beck Depression Inventory and the Minnesota Multiphasic Personality Inventory-Depression scale, it was shown to have good validity with correlations of .85 and .62, respectively (Whisman, Strosahl, Fruzzetti, Schmalzing, Jacobsen, & Miller, 1989). Clinical cutoff points for the HRSD are as follows: zero to seven = Normal; eight to 17 = Mild Depression; 18 to 24 Moderate Depression; >24 = Severe Depression (Cusin, Yang, Yeung, & Fava, 2004). The HRSD was found to have good reliability in the present sample of breast cancer patients ($\alpha = .78$).

Depressed mood—Depressed mood over the past week was measured using the depressed mood subscale of the 40-item Affect Balance Scale (ABS; Derogatis, 1975). Participants rate how often they have experienced a certain emotion on a five-point Likert-type scale. The items that comprise the depressed mood subscale are sad, hopeless, worthless, miserable, and unhappy. Possible scores range from one to five, and higher scores are indicative of greater depressed mood. The ABS has been found to be a valid and reliable measure of mood in research with breast cancer patients (Carver & Antoni, 2004; Carver et al., 2005; Grabsch et al., 2006). Test-retest reliability coefficients were between .79 and .84, and internal consistency was adequate ($\alpha = .85$) in a sample of breast cancer patients (Derogatis & Rutigliano, 1996). Reliability in the present sample was adequate ($\alpha = .80$).

Functional quality of life—The functional well-being subscale of the 44-item Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B; Brady et al., 1997) was used to assess participants’ functional QOL over the past week. There are seven items related to functional QOL that are assessed on four-point Likert type scale. Possible scores range from zero to 28, where higher scores are indicative of better functional QOL. The FACT-B was developed for use with cancer patients, validated and normed specifically for use in a breast cancer sample (Brady et al., 1997), and it is used extensively in breast cancer research examining QOL (Mandelblatt et al., 2011; Levine & Balk, 2012). The specific functional

QOL subscale has been shown to have good internal consistency ($\alpha = .86$). It is a good predictor of the extent of a patient's disease and correlates highly with the vigor subscale on the Profile of Mood States measure (Brady et al., 1997). The functional QOL subscale has good test-retest reliability at .84 (Cella et al., 1993). The FACT-B functional QOL subscale was found to have good reliability in the present sample ($\alpha = .84$).

Analytic Strategy

Prior to analyses, data were screened for outliers. One outlier for MVPA fell outside three standard deviations from the mean and was Winsorized (Wilcox, 1993) to fall within three standard deviations of the mean. Data were screened to ensure that all multivariate assumptions of normality were met. Data were checked to ensure that univariate distributions were normal, the joint distribution of any pair of variables was bivariate normal, and all bivariate scatterplots were linear and homoscedastic (Kline, 2005). Originally, the assumption of relative variances (that the ratio of the largest variance to the smallest variance is <10) was not met. Data was transformed so that MVPA was analyzed as hours per week rather than minutes per week. After transformation, the assumption of relative variances was met (Kline, 2005).

Path analysis was used to test the direct and indirect pathways by which MVPA related to fatigue (interference and intensity), functional QOL, clinician-rated depression, and depressed mood post-surgery. The full information maximum likelihood method (FIML) was implemented to estimate data values that were missing at random by estimating missing information from relations among variables in the full sample. The use of FIML, as conducted in Mplus (Muthén & Muthén, 1998–2010, Version 6.0), ensures that each participant is represented in the analyses. The sample size used in the present study was determined to be sufficient for detecting an effect based on the number of participants and the number of parameters in the model. The literature suggests that the ratio of cases to the number of model parameters would ideally be 20:1, and less ideally 10:1 (Kline, 2005). The basic model being tested in the present study estimates 12 parameters, therefore the sample size needed to detect an effect in this model is between 120–240 cases. The present sample size of 240 is well above the lower limit and sufficient to detect an effect. It is important to note, that as control variables are entered into the model, the number of parameter estimates increases. Therefore, the greater the number of control variables that exist, the less stable the estimates are.

Several indices of model fit were examined (i.e., non-significant chi-square, comparative fit index (CFI) >0.95 , a root-mean-square error of approximation (RMSEA) <0.06 , and a standardized root mean square residual (SRMR) <0.08) (Kline, 2005). The Z-statistic of the unstandardized coefficients was examined to interpret direct and indirect associations. The standardized coefficients were interpreted as measures of effect sizes and were evaluated at the following levels: 0.1 = small; 0.3 = medium; 0.5 = large (Cohen, 1988).

In the path analysis, the original model was set up to illustrate the theoretical relationships put forth by Pinto et al. (2003): to examine MVPA as an exogenous variable, fatigue as an intermediary variable, and functional QOL, depressed mood, and clinician-rated depression as outcomes. However, in model building, it is important to explore all possible directions to rule out alternative models that may better explain the data (MacKinnon, Krull, & Lockwood, 2000; MacCallum, Wegener, Uchino, & Fabrigar, 1993). It is important to test for reverse directionality of the placement of the observed variables in the path model. It is also essential to test for the influence of covariates. Demographic, socioeconomic, and cancer-specific theoretically supported control variables that may influence fatigue (interference and intensity), functional QOL, and depressed mood were examined as covariates. Two groups of covariates, cancer-specific (stage of disease, type of surgery, and

days elapsed from surgery to assessment), and demographic (age, education, and income) were entered individually into the models specified below (Ell, Xie, Wells, Nedjat-Haiem, Lee, & Vourlekis, 2008; Thornton et al., 2010). Although controlling for body mass index (BMI) would be supported theoretically, this data was not collected at the baseline assessment and is a significant limitation of the study. A total of eight models were tested and are described below.

Model 1: Fatigue intensity—In the first iteration, the model was specified with the following direct paths: 1) functional QOL, clinician-rated depression, and depressed mood regressed on fatigue intensity and 2) fatigue intensity regressed on MVPA. The following indirect paths were specified: 1) from MVPA to clinician-rated depression via fatigue intensity, 2) from MVPA to functional QOL via fatigue intensity, and 3) from MVPA to depressed mood via fatigue intensity. Paths were specified to represent associations between the three outcome variables (functional QOL, clinician-rated depression, and depressed mood). This model was tested first without control variables. See Figure 1 for an illustration of the hypothesized model.

Model 2: Fatigue intensity with covariates—In the second model iteration, control variables were entered one-by-one in a stepwise manner into Model 1 as exogenous variables relating to each of the outcome and intermediary variables.

Model 3: Fatigue interference—In the third model iteration, the model was tested identical to Model 1, except that fatigue interference replaced fatigue intensity as the intermediary variable. This model was first tested without covariates.

Model 4: Fatigue interference with covariates—The fourth model iteration tested Model 3 with the addition of cancer-specific and demographic covariates (the same as those used in Model 2).

Model 5: MVPA with covariates—The fifth model tested for the possibility of reverse directionality of the exogenous and intermediary variables in Model 4. To do this, the positions of MVPA and fatigue interference in the path analysis were switched. Therefore, in Model 5, fatigue interference was the exogenous variable, and MVPA was the intermediary variable between fatigue interference and the three outcomes (functional QOL, clinician-rated depression, and depressed mood). This model was tested with the inclusion of covariates.

Models 6, 7, and 8: Reverse directionality models—The sixth, seventh, and eighth models tested for reverse directionality of the outcome variables and the intermediary variable in Model 4. Model 6 tested functional QOL as the intermediary variable, Model 7 tested depressed mood as the intermediary variable, and Model 8 tested clinician-rated depression as the intermediary variable. In these models, fatigue interference was tested as an outcome variable. These models were tested with the inclusion of covariates.

Results

Women were between 23–70 years old with an average age of 50.3 years ($SD = 9.0$). A total of 61.3% had completed college or advanced degrees, and 36.3% were racial or ethnic minority group members (see Table 1). Women reported an average of 2.63 hours ($SD=4.75$) of moderate intensity and 0.4 hours ($SD= 2.5$) of vigorous intensity PA per week. Missing data were found to be missing completely at random (MCAR) based on Little's MCAR test, $\chi^2(88) = 86.61, p = .52$ (Little & Rubin, 2002). Additionally, only 2.7% of the

complete dataset was missing (fatigue intensity and interference = 14 (5.8%); income = 28 (11.7%); HRSD score = 9 (3.7%); ABS depressed mood subscale = 1 (0.4%); days since surgery = 9 (3.7%), stage = 2 (0.8%). Therefore, missing data was estimated with the FIML approach in the MPLUS program. This is an accepted missing data procedure for MCAR data, especially when less than five percent of the data is missing, and it is advisable for use with path analysis (Tomarken & Waller, 2005; Collins, Schafer, & Kam, 2001; Kline, 2005).

Model Testing

Model 1: Fatigue intensity—The first model iteration with fatigue intensity as the mediator was not a good fit for the data, $\chi^2(3) = 9.037, p = 0.03$, CFI = 0.97, RMSEA = 0.09, SRMR = 0.05. The direct effect from MVPA to fatigue intensity was not significant ($b = -0.04, z = -1.752, p > 0.05$).

Model 2: Fatigue intensity with covariates—In the second model iteration, control variables were added one at a time into the model. The model adjusting for all covariates was not a good fit for the data, $\chi^2(3) = 10.81, p = 0.01$, CFI = 0.96, RMSEA = 0.11, SRMR = 0.03. Again, the direct effect from MVPA to fatigue intensity was not significant ($b = -0.02, z = -0.83, p > 0.05$).

Model 3: Fatigue interference—Next, we tested whether the hypothesized model was a good fit with fatigue interference in place of fatigue intensity. This model was a good fit for the data, $\chi^2(3) = 3.65, p = 0.30$, CFI = 1.00, RMSEA = 0.03, SRMR = 0.02. The direct effect from MVPA to fatigue interference was significant ($b = -0.09, z = -3.41, p = 0.001$).

Model 4: Fatigue interference with covariates—We added covariates one by one into this model to account for the influence of demographic and treatment related covariates. The complete model with all covariates included was a good fit for the data, $\chi^2(3) = 5.60, p = 0.13$, CFI = 0.99, RMSEA = 0.06, SRMR = 0.01. The direct effect from MVPA to fatigue interference was significant ($b = -0.07, z = -2.52, p = 0.012$) such that an increase in MVPA was associated with less fatigue interference. The relationship between MVPA and fatigue interference is considered to be of a moderate effect size (0.20).

Given the good model fit and significant association between MVPA and fatigue interference, we interpreted additional direct and indirect effects. Women who had less fatigue interference reported greater functional QOL ($b = -1.67, z = -9.72, p < 0.001$) with a large effect size (0.56), less clinician-rated depression ($b = 1.047, z = 6.91, p < 0.001$) with a large effect size (0.40), and less depressed mood ($b = 0.697, z = 6.69, p < 0.001$) with a large effect size (0.42). Furthermore, the specified associations between the dependent variables were significant such that functional QOL was associated with clinician-rated depression ($b = -5.55, z = -3.62, p < 0.001$), clinician-rated depression was associated with depressed mood ($b = 3.16, z = 3.44, p < 0.01$), and depressed mood was associated with functional QOL ($b = -3.51, z = -3.75, p < 0.001$). Finally, we examined indirect effects to interpret whether fatigue interference served as a pathway by which MVPA influenced functional QOL, clinician-rated depression, and depressed mood. Results showed that the indirect path from MVPA to functional QOL via fatigue interference was significant ($b = 0.12, z = 2.44, p = 0.01$) with the indirect path accounting for 3%, and the direct effect accounting for 1.4% of the total effect. The indirect path from MVPA to clinician-rated depression via fatigue interference was significant ($b = -0.07, z = -2.33, p = 0.02$) with the indirect accounting for 29.2%, and the direct effect accounting for 5.8% of the total effect. The indirect path from MVPA to depressed mood via fatigue interference was significant ($b = -0.05, z = 2.36, p = 0.02$), with the indirect effect accounting for 21%, and the direct effect accounting for less than 1% of the total effect. This model was retained as a possible final model (see Figure 2).

Model 5: MVPA with covariates—Next, further iterations tested for reverse directionality of the model to assess the possibility that the relationship of these constructs might be different than hypothesized. Accordingly, we specified fatigue interference as the exogenous variable and MVPA as the intermediary variable. This model was not a good fit for the data (see Table 3).

Model 6, 7, and 8: Reverse directionality models—Functional QOL, clinician-rated depression, and depressed mood were each tested as the mediators with fatigue interference as an outcome. Models 7 and 8, which tested depressed mood and clinician-rated depression as putative mediators, produced models with a poor fit. However, Model 6, where functional QOL was specified as the mediator, showed a good fit for the data, $\chi^2(3) = 1.14, p = 0.77$, CFI = 1.00, RMSEA < 0.001, SRMR = 0.006. Furthermore, women who had greater MVPA reported greater functional QOL ($b = 0.27, z = 3.32, p = 0.01$). In addition, all direct, indirect, and total effects were significant (see Figure 3). As such, Model 6, with functional QOL as a pathway by which MVPA influences fatigue interference, clinician-rated depression, and depressed mood was retained as a potential final model (see Figure 3).

In sum, Model 4 (Figure 2), in which fatigue interference is the pathway by which MVPA relates to functional QOL, clinician-rated depression, and depressed mood, is in line with the literature. This model explains 85% of the variance in fatigue interference ($p < 0.05$), 38% of the variance in functional QOL ($p < 0.01$), 22% of the variance in clinician-rated depression ($p < 0.01$), and 27% of the variance in depressed mood ($p < 0.01$). The model in which functional QOL is the pathway by which MVPA relates to fatigue interference, clinician-rated depression, and depressed mood, Model 6 (Figure 3), is a plausible model as well. However, this model explains only 36% of the variance in fatigue interference ($p < 0.01$), 13% of the variance in functional QOL ($p < 0.01$), 24% of the variance in clinician-rated depression ($p < 0.01$), and 29% of the variance in depressed mood ($p < 0.01$).

Discussion

The present study characterized levels of moderate to vigorous physical activity (MVPA) reported by women in the period after surgery for breast cancer and related these levels to fatigue interference, fatigue severity, depression, depressed mood, and functional QOL. At this postsurgical time point, 82 (34.2%) of these breast cancer patients met the 150 minutes per week recommended guidelines for MVPA, while 158 (65.8%) did not. This is consistent with evidence suggesting that most breast cancer patients are inactive relative to healthy populations with levels of PA decreasing along the treatment trajectory (Ligibel, Partridge, Giobbie-Hurder, Golshan, Emmons, & Winer, 2009; Irwin et al., 2003).

Women in this study were significantly fatigued, scoring on average above the three-point cutoff on the fatigue intensity and fatigue interferences scales (Donavan et al., 2008). Furthermore, women reported functional QOL scores that were slightly lower than other breast cancer populations. In the original validation sample of breast cancer patients, the mean functional QOL score was 20.3 (Brady et al., 1997). Scores on the HRSD were in the range of other breast cancer populations with the majority of women scoring in the none-to-mild range in terms of severity (Olden et al., 2009). In another study with various cancer types ranging from recently diagnosed to survivorship (breast, lung, stomach, colon, leg, prostate, multiple myeloma, and pancreatic), the average HRSD score in non-psychiatric cancer patients was 9.3 (Hopko et al., 2007); a score comparable to that of the women in this study. Overall, these comparisons show that women in this sample reported slightly lower QOL and comparable levels of depression to other study samples.

Fatigue Interference as an Intermediary between Physical Activity and Quality of Life

While fatigue intensity was not significantly associated with MVPA with or without control variables, a significant association between MVPA and fatigue interference of a moderate effect size was observed while controlling for potential confounding factors. Prior research in women with breast cancer suggests that the variance in fatigue is largely attributed to beliefs about PA rather than actual physical fitness (Young & White, 2006). However, the previous studies (Mock et al., 2005; Kirsbaum, 2006) have not parsed out fatigue intensity from fatigue interference as was done in this study. These findings may also suggest that different processes may govern what people experience as a symptom versus what they perceive the symptom's impact to be on their lives. Practically, a person's perception of his or her symptoms may be more easily altered than the symptoms themselves. While the physical symptom of fatigue may be treatment induced and biologically based, the experience of fatigue and the daily impact of fatigue may vary amongst individuals as well as their thoughts about the fatigue. Cognitive-behavioral techniques could be explored as a path to alter perceptions about the experience of a symptom in order to maintain or improve QOL as a woman progresses through treatment (Antoni et al., 2006a; Antoni et al., 2006b). Patients could be encouraged to participate in group-based or individual interventions to learn techniques such as cognitive restructuring and time-based pacing that may be helpful in altering experience of fatigue. It is also plausible that fatigue interference is mostly attributed to a woman's attitude, beliefs, or cognitions about engaging in daily activities (Courneya, 2003), whereas fatigue intensity may be associated with actual physical fitness (Convertino, 1997). This is an important distinction, and the current study is one of only a few that examines differences in fatigue intensity and fatigue interference as they relate to other psychosocial constructs.

In addition to examining differences in fatigue intensity and interference, the study shows that physically active women reported less fatigue interference, better functional QOL, less severe depression, and lower depressed mood. These effect sizes were quite large which suggests strong relationships. We also found that less daily interference of fatigue was a pathway by which MVPA related to functional QOL, clinician-rated depression, and depressed mood, even after adjusting for demographic and medical covariates. However, it is important to note that it is not possible to test true statistical mediation in this model due to the cross-sectional nature of the data. The cross-sectional nature underscores the importance of testing reverse directionality of the model to rule out possible alternative models. It should be noted that one reverse directionality model in which functional QOL was tested as an intermediate pathway by which MVPA related to fatigue interference, clinician-rated depression, and depressed mood was a good fit for the data. Indirect and direct effects suggest it is a potential alternative model. Future longitudinal research could explore whether the directionality of this alternative model (with functional QOL as an intermediate variable) is a plausible alternative to explain these relationships. It is important to note that no other reverse directionality model (e.g., depression as the intermediate pathway) was significant in this sample. This is a strength of the study, as many studies in breast cancer patients have only examined the effects of PA on fatigue, depression, and QOL, without examining bi-directional relationships (Loprinzi & Cardinal, 2011; Basen-Engquist et al., 2008). The results of the current study are consistent with work showing that breast cancer survivors who were physically active reported fewer depressive symptoms (Yeter, Rock, Pakiz, Bardwell, Nichols, & Wilfey, 2006) and concur with a recent meta-analysis which concluded that PA is effective in improving QOL in breast cancer patients and survivors (McNeely et al., 2006).

Postoperative Clinical Relevance

These results suggest that MVPA after breast cancer surgery may be beneficial in buffering postoperative fatigue interference and impairments in mood and functional QOL. The findings are consistent with prior work examining relationships among postoperative activity, fatigue, QOL, and mood outcomes in individuals following coronary artery bypass graft (CABG) surgery (Zimmerman et al., 2007) and organ transplant (Painter et al., 1997). Research suggests that inactivity after surgery results in greater fatigue-related daily interference. Greater fatigue-related daily interference leads to less participation in meaningful activities, adversely affecting QOL, functional capacity, and mood (Christensen & Kehlet, 1993). The present findings provide preliminary support for these associations in breast cancer patients in the period shortly after surgery. It may be that physically active patients persist in daily activities and appraise their subjective fatigue as less intrusive and intense, which relates to better QOL and less negative mood (Courneya, 2003). In support of this, we did not observe associations between fatigue intensity and functional QOL outcomes. This may suggest that cognitive processes associated with fatigue interference are more powerful influencers of functional QOL and mood in the weeks after surgery for breast cancer than physical fitness.

The findings reported here suggest that it may be important to incorporate postsurgical psychoeducation on the benefits of MVPA into the patient's care regimen. Patients could be provided with examples of safe and feasible activities that would not disrupt recovery and the healing process. Clinicians should encourage women to resume MVPA as soon as possible after breast cancer surgery. Given that functional QOL is another pathway that explains the relationship between MVPA and psychological outcomes, patients may benefit from the encouragement to maintain daily routines that contribute to functional QOL. Health care providers and mental health professionals could work together to help patients establish a list of daily activities to engage in prior to surgery and a postsurgical plan to slowly resume these activities. Patients could be encouraged to keep a log of both their MVPA and functional activities for self-monitoring purposes, and this log could be reviewed with their mental health professionals at follow-up care visits. Self-monitoring of MVPA has been shown to be an effective way to increase MVPA in patients with chronic disease (Ayabe, Brubaker, Mori, Kumahara, Kiyonaga, Tanaka, & Aoki, 2010).

Furthermore, the study adds to the literature on the benefits of MVPA for women with breast cancer by illuminating processes operating in the postsurgical period. Maintaining sufficient activity during this time may be instrumental in improving recovery from surgery and may affect longer-term prognosis (Spiegel & Giese-Davis, 2003). The strengths of the study include the availability of a large sample of patients at a similar point in treatment, the application of path analysis to test direct and intermediary pathways in a theoretical model, and the use of widely accepted psychosocial indicators commonly employed in psycho-oncology research. Furthermore, the study evaluates the role of fatigue intensity separately from fatigue interference, whereas prior research has combined these constructs into one fatigue category. As seen here, these constructs operate differently. It is very important that future research measure fatigue interference and fatigue intensity as separate processes. In addition to measurement, it would be helpful to determine what other psychosocial and health outcomes are correlated with fatigue interference, and how these differ from fatigue intensity. Future research could examine the specific processes underlying fatigue interference. The study contributes to the literature by providing additional support for the relationships between MVPA and functional QOL as well as MVPA and depression. These relationships can be explored further in longitudinal designs. The ethnically diverse study sample is an additional strength, as the findings are more generalizable than those derived from predominantly Caucasian samples.

Despite the many strengths of the study, there are a number of limitations that should be considered when interpreting the results of the study. First, it is important to note that this study focuses on MVPA, rather than all PA, including mild PA. Second, there is potential bias due to self-report and retrospective recall. For instance, women may over- or underestimate the actual frequency and duration of MVPA throughout the week. An objective ecological momentary assessment measure could be used in future research to eliminate biases and recall inaccuracies from self-report data.

Another study limitation is the inability to conclude temporal or causal associations due to the cross-sectional study design. Of note, the cross-sectional nature of the data remains informative in that it suggests future research hypotheses, contributes to the literature in this area, and shows associations among constructs. Although alternative tests tended to support the most plausible relationship of the variables in our model, mediation cannot be inferred without a longitudinal study design. Furthermore, the approach to the testing of alternative models was data-driven, which in some cases may capitalize on chance or random patterns in the data. Albeit, this is an important step in model building in order to rule out a more plausible fit for the data. Another limitation is the lack of data on BMI. A woman's BMI could be a potential confounder when examining these relationships given evidence that shows that women with a lower BMI are more likely to be more physically active (Pelclova, Gaba, Tlucakova, & Pospiech, 2012).

The presence of comorbidities is a potential confounder that could play a role in the amount of MVPA, fatigue, depression, and functional QOL a woman reports, and it should be accounted for in future studies. While the sample overall is less active than the general population, this sample of women reported slightly higher duration and frequency of PA as compared to other breast cancer samples. This could potentially influence the generalizability of the results to other breast cancer populations (Ligibel et al., 2009). Furthermore, it should be noted that the age range of the sample was quite expansive and that the PA habits and side effects of treatment may be different depending on the age of the woman. Finally, the fact that these women were willing to participate in a psychosocial intervention study during breast cancer treatment may limit the generalizability of the findings. In conclusion, breast cancer patients who remain physically active minimize fatigue interference, depressed mood, and functional QOL decrements during postsurgical recovery.

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Figure 1.
The Hypothesized Model Illustrating Paths between Moderate and Vigorous Physical Activity and Fatigue Interference/Intensity, Functional Quality of Life, Clinician-Rated Depression and Depressed Mood

Figure 2. Model 4 Illustrating the Direct Paths and Related Partial Correlation Coefficients between MVPA and Fatigue Interference, Functional QOL, Clinician-Rated Depression and Depressed Mood via Fatigue Interference $^{**}p<0.01$; $^*p<0.05$

Figure 3. Model 6 Illustrating the Direct Paths and Related Partial Correlation Coefficients between MVPA and Functional QOL, Fatigue Interference, Clinician-Rated Depression and Depressed Mood via Functional QOL $^{**}p<0.01$; $^{*}p<0.05$

Table 1

Means and Standard Deviations for Study Variables at the Baseline (T1) Assessment.

Variable	Mean (SD) or Frequency (%)
Days from Surgery to Baseline (range, 14–70)	40.7 (23.19)
Age (in years)	50.55 (9.03)
Stage	
0	38 (15.8%)
I	90 (37.5%)
II	91 (37.9%)
III	19 (7.9%)
Procedure	
<i>Lumpectomy</i>	122 (50.8%)
<i>Mastectomy</i>	118 (49.2%)
Education	
<i>Did not complete High School</i>	3 (1.2%)
<i>Completed High School</i>	27 (11.3%)
<i>Post-high school</i>	63 (26.3%)
<i>Completed college</i>	87 (36.3%)
<i>Post-college</i>	60 (25%)
Income (in thousands of dollars)	79.82 (67.12)
Race/Ethnicity	
<i>White non-Hispanic</i>	152 (63.3%)
<i>Hispanic</i>	61 (25.4%)
<i>African American</i>	21 (8.8%)
<i>Asian</i>	5 (2.1%)
Moderate-Vigorous Physical Activity per week (in hours)	2.81 (4.76)
<i>Met ACSM guidelines (>150 mins per week)</i>	82 (34.2%)
<i>Did not meet ACSM guidelines (<150 mins per week)</i>	152 (65.8%)
Fatigue Interference (range, 0–10)	3.55 (1.97)
Fatigue Intensity (range, 0–10)	4.38 (1.63)
Functional Quality of Life (range, 0–28)	18.37 (5.77)
Clinician-rated Depression (range, 0–54)	7.37 (5.46)
Depressed Mood (range, 0–25)	9.87 (3.22)

Table 2

Correlations Among Study Variables

	MVPA	Fatigue Intensity	Fatigue Interference	Functional QOL	Clinician-Rated Depression	Depressed Mood
MVPA	1.000					
Fatigue Intensity	-0.11	1.000				
Fatigue Interference	-0.215	0.668	1.000			
Functional QOL	0.218	-0.386	-0.569	1.000		
Clinician-Rated						
Depression	-0.117	0.338	0.427	-0.432	1.000	
Depressed Mood	-0.105	0.304	0.47	-0.506	0.461	1.000

MVPA: Moderate-Vigorous Physical Activity
Functional QOL: Functional Quality of Life

Table 3

Structural Equation Modeling Results: Fit indices

Model Iteration	χ^2	df	p-value	CFI	RMSEA	SRMR
1	9.037	3	0.03	0.97	0.09	0.05
2	10.81	3	0.01	0.96	0.11	0.03
3*	3.65	3	0.30	1.00	0.03	0.02
4*	5.60	3	0.13	.99	0.06	0.01
5	85.67	3	<0.001	0.64	0.38	0.08
6*	1.14	3	0.77	1.00	<0.001	0.006
7	10.74	3	0.01	0.97	0.11	0.03
8	9.07	3	0.03	0.97	0.10	0.02

Abbreviations: χ^2 , Chi-square Test of Model Fit; df, Degrees of Freedom; CFI, Confidence Free Interval, RMSEA, Root Mean Square Error of Approximation; SRMR, Standardized Root Mean Square Residual

* Good Model Fit

Table 4

Unstandardized Coefficients and Standardized Correlational Effect Sizes for Direct and Indirect Effects Between Moderate-Vigorous Physical Activity and Fatigue Interference, Functional Quality of Life, Clinician-Rated Depression and Depressed Mood

MVPA and:	Direct Effect	S.E.	Effect Size	R-square
Fatigue Interference	−0.071 *	0.028	0.175	0.85 *
Fatigue Interference and:				
Functional QOL	−1.67 ***	0.172	0.423	0.382 ***
Clinician-Rated Depression	1.05 ***	0.172	0.400	0.219 ***
Depressed Mood	.700 ***	0.104	0.423	0.271 ***
	Indirect Effect	S.E.	Effect Size	R-square
MVPA and:				
Functional QOL	0.119 *	0.049	0.098	0.382 ***
Clinician-Rated Depression	−0.074 *	0.032	0.070	0.219 ***
Depressed Mood	−0.050 *	0.021	0.074	0.271 ***

*
p<.05,

**
p<.01,

p<.001

<0.10–0.30 small effect size, 0.30–0.50 medium-large effect size, >0.50 large effect size

MVPA: Moderate-Vigorous Physical Activity

Functional QOL: Functional Quality of Life