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How changes in physical activity relate to fatigue interference, mood, and quality of life during treatment for non-metastatic breast cancer

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ABSTRACT

Objective: Physical activity (PA) following surgery for breast cancer may improve depressive symptoms and quality of life (QoL) via reduction in fatigue-related daily interference (FRDI). Less is known about how change in PA may relate to these psychosocial factors throughout the course of treatment. In a secondary analysis of a previous psychosocial intervention trial, we examined relationships between change in PA, depressive symptoms, and functional QoL, as mediated by change in FRDI, and whether naturally occurring change in PA provided benefit independent of the intervention.

Method: Women ($N = 240$) with non-metastatic stage 0–III breast cancer were randomized to cognitive-behavioral stress management (CBSM) or a control 2–10 weeks post-surgery. PA, FRDI, clinician-rated depressive symptoms, self-reported depressed mood, and functional QoL were assessed at baseline and three months post-intervention.

Results: Increased PA was associated with reductions in clinician-rated depressive symptoms, depressed mood, and improved QoL, mediated by a reduction in FRDI. This was above and beyond the effect of CBSM.

Conclusions: Increased PA may mitigate FRDI and improve depressive symptoms and functional QoL for women undergoing breast cancer treatment, beyond effects of a psychosocial intervention. Benefits of an integrated PA and psychosocial approach should be investigated further.

1. Introduction

Fatigue, depressive symptoms, and diminished quality of life (QoL) are among the serious breast cancer treatment-related side effects [1]. Physical activity may mitigate the severity of physical and psychological sequelae associated with a breast cancer diagnosis and treatment [2–4]; women with breast cancer who engage in physical activity have less fatigue [5,6], depressive symptoms [6], and better quality of life (QoL) [5–7]. The process by which physical activity reduces these symptoms is less understood [8]. Previously, women with non-metastatic breast cancer reported greater physical activity and had less concurrent perceived daily interference due to fatigue, less clinician- and self-rated depressive symptoms, and better functional QoL following surgery [9]. Moreover, fatigue interference served an intermediary role; greater physical activity was related to less depressive

symptoms and better functional QoL via reduced fatigue interference [9]. While these findings suggest a potential mechanism relating physical activity to mood outcomes, the relationships must be examined longitudinally for better understanding.

Despite potential benefits, most women with breast cancer do not meet the American College of Sports Medicine (ACSM) physical activity recommendations, which encourage patients to engage in at least 150 min of moderate or 75 min of vigorous intensity activity each week during treatment [10]. Unfortunately, physical activity often decreases after diagnosis, especially among women undergoing radiation or chemotherapy [11]. Given previous evidence of the concurrent relationships between physical activity, fatigue interference, depressive symptoms, and QoL post-surgically [9], understanding how changes in physical activity may influence these outcomes over time is relevant as women manage treatment-related symptoms.

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In addition to physical activity, psychosocial interventions involving cognitive-behavioral, relaxation, and mindfulness techniques have shown efficacy in improving fatigue, depressive symptoms, and QoL in breast cancer [12–14]. Group-based cognitive-behavioral stress management (CBSM) has been particularly efficacious in reducing fatigue interference and depressed mood and improving QoL for women during breast cancer treatment [15–17]. As such, researchers have investigated whether an integrative approach combining physical activity and cognitive-behavioral techniques may attenuate treatment-related symptoms for women with non-metastatic breast cancer [18]. However, whether increased physical activity may be additionally beneficial for women who participate in CBSM has not been explored. Support for the additive effect of increased physical activity on psychosocial adjustment may encourage consistent promotion of physical activity among breast cancer patients.

The current study was a secondary analysis that aimed to (1) examine whether the relationships between physical activity and physical and psychosocial factors in the previously reported post-surgical cross-sectional study [9] are observed longitudinally during treatment, such that change in physical activity from pre- to post-intervention predicts changes in fatigue interference, clinician- and self-rated depressive symptoms, and functional QoL; (2) assess whether the influence of modified physical activity involvement on changes in depressive symptoms and functional QoL is mediated by change in fatigue interference; and (3) explore whether change in physical activity contributes additional benefit above and beyond CBSM. We hypothesized that an increase in physical activity would be associated with a reduction in fatigue interference, clinician- and self-rated depressive symptoms, and an increase in functional QoL, that the effect of increased physical activity on mood outcomes would be mediated by reduced fatigue interference, and that an increase in physical activity would be independently related to reduction in FRDI and improved QoL outcomes, above and beyond the effect of CBSM.

2. Methods

2.1. Participants

Participants were part of a larger, single center, single blind, randomized, parallel assignment efficacy trial, testing a CBSM intervention. A detailed description of the original study design is available elsewhere [16,17]. Study approval was granted by the University of Miami's Institutional Review Board (National Institutes of Health Clinical Trial NCT01422551). Women diagnosed with non-metastatic stage 0-IIIb breast cancer were recruited through physician referrals and community advertising. Participants were required to have had surgery for primary breast cancer in the 2–10 weeks prior to enrollment (lumpectomy, mastectomy, or bilateral mastectomy). Exclusion criteria included: (1) diagnosis of stage IV breast cancer or prior cancer (except minor skin cancers such as squamous or basal cell carcinomas); (2) ongoing neoadjuvant or post-surgical adjuvant treatment; (3) a major medical condition other than cancer; (4) < 21 or > 75 years of age; (5) non-fluency in English; (6) previous hospitalization for psychiatric conditions; and (7) current psychosis, substance use disorder, suicidality, major depressive disorder, or panic disorder.

2.2. Procedures

Eligible women who were interested in participating gave informed consent and were enrolled. Following the baseline assessment, participants were randomized to CBSM or a 1-day psychoeducational control group. Randomization and assessments were completed by blinded study coordinators. Initial assessments took place at approximately 2–10 weeks post-surgery and prior to adjuvant cancer treatment (chemotherapy and/or radiation). Women were reassessed 3 months post-intervention. Assessments included blood and saliva samples, patient-

reported psychosocial questionnaires, and a clinician-administered measure.

2.3. CBSM intervention

Women randomized to the CBSM intervention met 2 h per week for ten consecutive weeks. CBSM is a structured, manualized psychosocial intervention that combines relaxation (e.g., muscle relaxation and imagery) and cognitive behavioral therapy (e.g., cognitive restructuring, coping effectiveness training, assertiveness, and anger management skills) [19]. CBSM aims to attenuate muscle tension and increase relaxation, replace negative cognitions pertaining to breast cancer and treatment, improve coping strategies, and build and maintain social support networks. Interventionists were trained in the protocol, and sessions were videotaped and monitored weekly for fidelity by two clinical psychologists.

2.4. Control

Participants assigned to the 1-day psycho-educational control seminar received an abbreviated dose (i.e., 5–6 h) of information about CBSM, which was delivered in a classroom lecture format. This seminar took place one weekend during the corresponding 10-week CBSM intervention. Women primarily received information related to breast cancer and its treatment. The seminar did not involve any in-session or at-home practice of CBSM techniques and was designed to emulate an informational self-help seminar.

2.5. Measures

2.5.1. Demographic and medical characteristics

Women self-reported demographics, medical condition, and cancer-treatment at baseline and follow-up assessment. Characteristics included age, ethnicity, employment status, marital status, income, education, stage of disease, type of surgery, days elapsed from surgery to baseline assessment, and type of adjuvant treatment. Self-reported information was verified with medical record review.

2.5.2. Physical activity

Intensity, frequency, and duration of physical activity were measured using a brief version of the Seven-Day Physical Activity Recall Questionnaire [20]. This measure is widely utilized in cancer populations [21]. Participants recorded the time engaged in vigorous and/or moderate activity each day of the previous week. Vigorous intensity activities require substantial energy expenditure and increased heart rate (e.g., jogging, running, sustained swimming). Moderate intensity activities increase heart rate, yet conversation is possible (e.g., yard work, heavy housecleaning, brisk walking). Since moderately to vigorously intense activity is most beneficial for health outcomes [22], minutes of moderate and vigorous activity per week were combined. The reliability in the current sample was strong ($\alpha = 0.90$).

2.5.3. Fatigue-related daily interference

The 7-item Perceived Interference subscale of the 12-item Fatigue Symptom Inventory (FSI) was used to measure the extent to which respondents perceive that fatigue interferes with daily life, roles, and responsibilities, hereinafter referred to as fatigue-related daily interference (FRDI). The FSI was developed and validated for cancer populations [23]. Items (e.g., “Rate how much, in the past week, fatigue has interfered with your normal work activity”) are rated on a Likert-type scale from 1 (no interference) to 9 (extreme interference). Items are averaged to obtain a total FRDI score ranging from 1 to 9, with higher scores indicating greater FRDI. The reliability for the FRDI subscale within the current sample was strong ($\alpha = 0.93$).

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