

Physical Activity and the Risk of Breast Cancer Recurrence: A Literature Review

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With 191,410 cases diagnosed in 2006, breast cancer is the most common form of cancer among women (U.S. Cancer Statistics Working Group, 2010). Physical activity may complement current therapies to increase the odds of curing breast cancer in patients. Observational studies suggest that regular engagement in physical activity may reduce the risk of breast cancer recurrence and breast cancer-related mortality (Ibrahim & Al-Homaidh, 2011). However, before effective physical activity interventions can be developed for women with breast cancer, a better understanding is needed of the factors that influence physical activity behavior in this population.

This article evaluates research literature pertaining to the effects that physical activity has on decreasing the recurrence of and mortality from breast cancer in women with curatively treated localized breast cancer. In addition, the article describes factors related to physical activity behavior to help develop and implement effective physical activity interventions for women with breast cancer, and reviews the evidence that attempts to identify barriers and facilitators for regular physical activity participation among women with a breast cancer diagnosis.

Methods

An extensive review of the epidemiologic literature on the effect of physical activity on breast cancer recurrence and mortality was conducted using PubMed articles up to December 2010, using the following key words: *physical activity*, *exercise*, *breast cancer*, *breast cancer recurrence*, and *breast cancer mortality*. To examine the association between physical activity and breast cancer recurrence and mortality, the researchers only included studies if breast cancer recurrence or mortality served as the dependent variable; physical activity served as the independent variable; and a measure of association between physical activity, breast cancer recurrence, or breast cancer mortality was reported.

Purpose/Objectives: To examine the association between physical activity and breast cancer mortality and recurrence, and to provide an overview of factors related to physical activity behavior in women with breast cancer.

Data Sources: An extensive review of the epidemiologic literature on the effect of physical activity on breast cancer recurrence and mortality was conducted using PubMed up to December 2010, involving the following key words: physical activity, exercise, breast cancer, breast cancer recurrence, and breast cancer mortality.

Data Synthesis: For breast cancer recurrence and breast cancer-related mortality, studies were included if physical activity served as the independent variable and a measure of association was reported. To examine determinants of physical activity, studies were included if a hypothesized factor served as the independent variable and a measure of association was reported.

Conclusions: Of the six studies that examined the influence of physical activity on breast cancer mortality, four (67%) reported a protective effect (i.e., inverse association), two examined the influence of physical activity on breast cancer recurrence and reported a nonsignificant risk reduction. Few studies have examined factors that influence physical activity behavior in women with breast cancer, and findings suggest that psychosocial factors play an important role in influencing the activity patterns of breast cancer survivors. Future longitudinal studies are needed to confirm those findings.

Implications for Nursing: To prevent breast cancer recurrence and breast cancer-related mortality, nurses should encourage breast cancer survivors to engage in regular exercise.

To identify studies that examined factors influential to physical activity behavior in women diagnosed with breast cancer, the current study's researchers conducted a PubMed search using the following key words: *exercise*, *breast cancer*, *psychosocial*, and *environment*. A study was included if physical activity served as the dependent variable, a hypothesized factor served as the independent variable, and a measure of association between physical activity and the hypothesized factor was reported. Manual searches of the reference lists from the

retrieved articles also were performed. Only English-language articles were included. The effect of physical activity on breast cancer risk, recurrence, and mortality was categorized using the following coding scheme: (a) protective effect, if a significant inverse association was reported; (b) nonsignificant inverse association, if a reduction in risk was reported with a nonsignificant trend or nonsignificant confidence interval; and (c) no effect, if a nonsignificant positive association existed.

Physical Activity and Breast Cancer Recurrence and Mortality

Numerous studies have examined the influence of physical activity on breast cancer risk; however, the literature on the relationship among physical activity and breast cancer recurrence and mortality is less developed. Only six studies have examined the influence of physical activity on mortality from breast cancer (Abrahamson et al., 2006; Friedenreich, Gregory, Kopciuk, Mackey, & Courenya, 2009; Holick et al., 2008; Holmes, Chen, Feskanich, Kroenke, & Colditz, 2005; Irwin et al., 2008; Pierce et al., 2007); two of the studies also investigated the influence of physical activity on breast cancer recurrence (Friedenreich et al., 2009; Holmes et al., 2005). Of the six studies, four (67%) found that physical activity had a protective effect on breast cancer mortality (Friedenreich et al., 2009; Holick et al., 2008; Holmes et al., 2005; Pierce et al., 2007); two studies (33%), however, reported that physical activity had a nonsignificant risk reduction on breast cancer mortality (Abrahamson et al., 2006; Irwin et al., 2008). The four studies demonstrating a reduction in breast cancer mortality had a hazard ratio (HR) ranging from 0.51–0.78. The two studies examining the influence of physical activity on breast cancer recurrence reported a nonsignificant trend, with relative risks ranging from 0.74–0.76 (Friedenreich et al., 2009; Holmes et al., 2005).

In a prospective observational study of 2,987 RNs with a history of breast cancer, Holmes et al. (2005) showed that women who walked three to five hours per week were 43% less likely to develop recurrent breast cancer and 50% less likely to die from breast cancer than women who engaged in less than one hour of physical activity per week. Similarly, in a cohort of 1,231 women diagnosed with breast cancer, Friedenreich et al. (2009) showed that, after adjustments for confounders, women in the highest (greater than 19 metabolic equivalent [MET] hours/week) quartiles of recreational physical activity were 46% less likely to die from breast cancer than women in the lowest quartile (less than or equal to 5 MET hours/week). MET refers to measuring the energy cost of specific physical activities compared to the energy cost during rest (Ainsworth, 2000). Moderate (HR = 0.56, 95%

confidence interval [CI] [0.38, 0.82]) and vigorous intensity recreational activity (HR = 0.74, 95% CI [0.48, 0.98]) also decreased the risk of breast cancer death. In addition, those in the highest quartile of physical activity (HR = 0.76, 95% CI [0.55, 1.03]) were 34% less likely to develop recurrent breast cancer. In support of those studies, Pierce et al. (2007) showed that among 1,490 women diagnosed with breast cancer, those exercising 1,320–6,420 MET minutes per week (Cox hazard = 0.58; $p = 0.02$) were 42% less likely to die from breast cancer compared to women exercising less than 226 MET minutes per week.

In examining the association between physical activity and breast cancer survival, Holick et al. (2008) showed a dose-response relationship between physical activity and breast cancer-related mortality among 4,482 women with breast cancer. Women who engaged in more than 21 MET hours per week of physical activity (HR = 0.51, 95% CI [0.29, 0.89]) had a lower risk of dying from breast cancer compared to women exercising less than 2.8 MET hours per week.

Irwin et al. (2008) reported a nonsignificant inverse association between physical activity and breast cancer mortality among 983 women in the Health, Eating, Activity, and Lifestyle study. When physical activity was assessed a year before diagnosis, women who exercised nine or more MET-hours per week or more (HR = 0.83, 95% CI [0.49, 1.38]) were 17% less likely to die from breast cancer compared to women who exercised 0 MET hours per week. When physical activity was assessed two years after diagnosis, more active women (HR = 0.65, 95% CI [0.23, 1.87]) were 35% less likely to die from breast cancer. Also reporting a nonsignificant inverse association, Abrahamson et al. (2006) showed that women exercising 75.6–98 MET hours per week (HR = 0.78, 95% CI [0.56, 1.08]) were 22% less likely to die from breast cancer compared to women exercising 1.6–21.5 MET hours per week.

Although too few studies have been conducted to draw strong conclusions, the six studies suggest that, to minimize breast cancer recurrence and mortality, breast cancer survivors should engage in at least 180–240 minutes of moderate-intensity physical activity per week, which is higher than the current recommendation of 150-minutes of at least moderate-intensity physical activity for U.S. adults (U.S. Department of Health and Human Services, 2008). Given that all six studies provided observational evidence only, randomized, controlled trials are needed to confirm the protective effect of exercise on breast cancer recurrence and mortality.

Factors Influencing Physical Activity in Women With Breast Cancer

Despite the benefits of physical activity on the reduction of breast cancer recurrence and mortality, a

significant percentage of women with breast cancer do not engage in regular physical activity. A prospective study of leisure-time exercise in 231 women with early-stage breast cancer showed that prior to breast cancer diagnosis, 70% of women met current physical activity guidelines (Andrykowski, Beacham, & Jacobsen, 2007). However, after the first course of adjuvant therapy, the percentage of women meeting guidelines dropped to 39%. After the second course of cancer treatment, the percentage dropped to 15%. Individuals continued to be insufficiently active, failing to meet physical activity guidelines two months (41%) and six months (37%) after completing treatment. Similarly, Harrison, Hayes, and Newman (2009) showed that among 287 patients with breast cancer, 33%, 35%, and 33% met current physical activity guidelines at 6, 12, and 18 months, respectively, following diagnosis.

Given the increasing evidence that physical activity benefits women diagnosed with breast cancer, the demand for physical activity programs for breast cancer survivors should increase. To maximize the success of the programs, the factors that influence physical activity participation among women must be understood. Researchers have examined (a) predictors of exercise behavior prior to a randomized, controlled exercise intervention (Hong et al., 2007), (b) factors that predict exercise adherence during an exercise intervention (Courneya et al., 2008; Pinto, Rabin, & Dunsiger, 2009), (c) predictors of follow-up exercise behavior after a randomized, controlled exercise intervention (Courneya et al., 2009), and (d) determinants of exercise behavior in breast cancer survivors (Milne, Wallman, Guilfoyle, Gordon, & Corneya, 2008; Pinto et al., 2002).

Predictors of Exercise Behavior Before the Intervention

Prior to the randomization of the Women's Healthy Eating and Living exercise intervention study, Hong et al. (2007) examined the demographics, as well as clinical, physical health, psychosocial, and lifestyle behaviors, that influenced self-reported physical activity among 2,819 women with breast cancer (post-treatment). Results showed that among evaluated demographic variables, which included age, education, race, marital status, and body mass index (BMI), only education ($p \leq 0.001$), ethnicity ($p \leq 0.001$), and BMI ($r = -0.27$, $p \leq 0.001$) were significantly related to physical activity levels. Among the clinical variables (cancer stage, time since diagnosis, and treatment), only current stage at diagnosis ($r = -0.05$, $p < 0.01$) and treatment type ($F = 3.92$, $p \leq 0.001$) were significantly associated with activity behavior. The physical health factors examined included physical functioning, role limits because of physical health problems, pain, and general health. Of those, only physical functioning ($r = 0.29$, $p \leq$

0.001) and general health ($r = 0.23$, $p \leq 0.001$) were significant. An assessment of mental health included measuring role limitations resulting from emotional problems, vitality, emotional well-being, social functioning, and depression. Among the mental health factors, vitality ($r = 0.33$, $p \leq 0.001$) and depression ($r = -0.11$, $p \leq 0.001$) were significantly related to physical activity behavior. Health behaviors included alcohol intake ($r = 0.1$, $p \leq 0.001$), current smoking ($p \leq 0.001$), and dietary composition ($r = 0.26$, $p \leq 0.001$), and were related to physical activity participation. However, after controlling all of the variables in a multiple regression analysis, education (beta = -0.055), BMI (beta = -0.175), a composite of physical and mental health factors (beta = 0.162), alcohol intake (beta = 0.048), and dietary intake (beta = 0.195) emerged as significant independent predictors of physical activity.

Predictors of Exercise Adherence During Intervention

The Theory of Planned Behavior (TPB) (Ajzen, 1991) indicates that behavioral intention is the most important predictor of behavior, with factors that influence behavioral intention including an individual's attitude, their subjective norm (i.e., belief about whether most people approve or disapprove of the behavior), and their perceptions of whether they have control over the behavior. Courneya et al. (2008) used the TPB to examine the influence of its constructs in predicting six-month adherence to a supervised aerobic versus resistance-training program for women with breast cancer during chemotherapy ($N = 242$). Adherence to the exercise training was 70%. Surprisingly, none of the key constructs from TPB, including intention, perceived control, instrumental attitude, affective attitude, or subjective norm, significantly predicted adherence to aerobic or resistance exercise. Rather, location (beta = 0.28 , $p = 0.001$), peak oxygen uptake (VO_{2peak}) (beta = 0.19 , $p = 0.016$), disease stage (beta = 0.18 , $p = 0.015$), and depression (beta = -0.16) remained significant and explained 21% of the variance in exercise adherence.

In a randomized, controlled trial of home-based exercise adherence in recently treated breast cancer survivors ($N = 43$), Pinto et al. (2009) assessed the influence of demographic and medical variables as well as constructs from the Transtheoretical Model (TTM). The TTM is a model of behavior change that involves progressing through five distinct stages of behavioral change, including precontemplation, contemplation, preparation, action, and maintenance. In the home-based program, women received weekly exercise counseling from research staff via telephone, with the counseling sessions based on TTM and Social Cognitive Theory. The variables assessed included age, education, marital status, stage of cancer, time since diagnosis,

history of exercise, baseline activity levels, and some of the constructs from the TTM (i.e., stage of change, self-efficacy, decisional balance). Exercise adherence was assessed by evaluating minutes of exercise participation per week, number of physical steps taken during planned exercise per week, and whether the participant met her weekly exercise goal. With respect to predicting mean minutes of weekly exercise, only self-efficacy emerged as a significant predictor ($\beta = 19.46$, $p = 0.004$), with cons for exercise approaching significance ($\beta = -16.93$, $p = 0.07$). Similar results were found when predicting mean steps per week and percentage of success in meeting weekly exercise goals.

The divergent results from the two studies likely are attributable to the time period in which the exercise intervention occurred. Although speculative, psychosocial and motivational factors may be more instrumental in influencing exercise adherence once a certain amount of time has elapsed since adjuvant chemotherapy. During adjuvant chemotherapy, patients' psychosocial perceptions toward physical activity are elevated acutely; consequently, the ceiling effect may attenuate the associations toward the null. The assertion is supported by the baseline data in the study by Courneya et al. (2008).

Predictors of Follow-Up Exercise Behavior After Intervention

Courneya et al. (2009) reported the predictors of self-reported exercise behavior six months after a randomized exercise trial (aerobic versus resistance training) in patients with breast cancer ($N = 242$). Predictor variables assessed included various demographic characteristics (i.e., location, age, marital status, education, income, and employment status), psychosocial constructs (i.e., quality of life, self-esteem, fatigue, anxiety, depression, motivation, perceived control, instrumental attitude, affective attitude, and subjective norms), medical information (i.e., disease stage, lumpectomy versus mastectomy, nontaxane chemotherapy versus taxane chemotherapy, relative dose intensity less than 85% versus relative dose intensity greater than or equal to 85%), four cycles of chemotherapy versus six or more), behavioral variables (i.e., smoking status, pretrial exercise status, trial adherence, and intervention arm), and physical fitness or body composition variables (i.e., VO_{2peak} , strength, BMI, body fat percentage, and lean body mass).

Among the demographic variables, only age was significantly related to follow-up exercise behavior ($p = 0.03$). Of the psychosocial constructs, postintervention fatigue ($p = 0.03$), change in fatigue ($p = 0.03$), aerobic-exercise motivation ($p = 0.03$), resistance-exercise motivation ($p = 0.004$), resistance-exercise perceived control ($p = 0.008$), aerobic-exercise instrumental at-

titude ($p = 0.002$), resistance-exercise instrumental attitude ($p = 0.006$), and aerobic-exercise subjective norms ($p = 0.04$) were significantly associated with follow-up exercise behavior. Regarding medical information, lumpectomy versus mastectomy ($p = 0.02$) and nontaxane chemotherapy versus taxane chemotherapy ($p = 0.01$) were significantly related to follow-up exercise behavior. For the behavioral variables, only pretrial exercise ($p < 0.001$) was related to follow-up exercise behavior. For the physical fitness and body composition variables, postintervention VO_{2peak} ($p < 0.01$), postintervention strength ($p = 0.01$), change in strength ($p = 0.04$), postintervention BMI ($p = 0.03$), and postintervention body fat percentage ($p = 0.03$) were significantly related to follow-up exercise behavior. The results suggest that demographic, medical, behavioral, fitness, psychosocial, and motivational variables play important roles in exercise participation six months after an exercise intervention among women with breast cancer.

Determinants of Exercise Behavior in Breast Cancer Survivors

In a sample of 558 breast cancer survivors not undergoing cancer therapy, Milne et al. (2008) used the Self-Determination Theory (SDT) to explain survivors' exercise behavior. In addition to measuring key constructs from SDT (e.g., extrinsic motivation, introjected regulation, identified regulation, intrinsic motivation, perceived competence, autonomy support), demographic variables (i.e., age, marital status, education, income, employment status, and location of residence) and medical variables (i.e., diagnosis, cancer stage, menopausal status, treatments received, and date of treatments) were assessed. Results showed that the absence of lymphedema ($p < 0.01$) and a higher income ($p < 0.01$) were associated with meeting physical activity guidelines. In addition, breast cancer survivors who met physical activity guidelines reported more identified regulations and intrinsic motivation ($p < 0.01$), autonomy support ($p < 0.01$), and competence ($p < 0.01$) than survivors who did not meet guidelines. Hierarchical regression showed that the SDT constructs explained 20% ($p < 0.01$) of the variance in physical activity.

Pinto et al. (2002) conducted a cross-sectional study to examine motivators of health behaviors (e.g., physical activity and dietary fat intake) among 86 women diagnosed with breast cancer who were not currently undergoing any cancer-related treatments. In addition to assessing physical activity and dietary fat intake, participants completed a questionnaire assessing overweight or obesity status, motivational readiness for exercise and weight loss, and some (i.e., stage of change, decisional balance, and self-

efficacy) of the constructs from the TTM. Results showed that those in the higher stages of motivational readiness (e.g., maintenance) engaged in more moderate-to-vigorous physical activity than those in lower stages (e.g., precontemplation, contemplation). In addition, compared to women who were considered unhealthy (dietary fat greater than or equal to 30% fat and not in the action or maintenance stage of change for exercise), women who were considered healthy (i.e., low-fat diet and exercising at recommended levels) reported significantly higher self-efficacy for exercise ($\bar{X} = 3.27$ versus 2.26, $p \leq 0.001$). In addition, compared to healthy-weight women, overweight and obese women were more likely to be in the early stages of motivational readiness for weight loss ($p = 0.01$) and reported significantly lower exercise self-efficacy ($\bar{X} = 2.71$ versus 3.18, $p = 0.01$).

Discussion

Although additional studies are needed, the results support that psychosocial factors can predict physical activity behavior among breast cancer survivors. Future studies should continue to use a theoretical framework for studying exercise motivation among women with breast cancer (Wood, 2008). Theoretical predictors of physical activity will allow for a better understanding of the key determinants of physical activity behaviors that can be targeted with interventions. Such information may be helpful for increasing the activity levels of women with breast cancer. Studies, although limited, suggest that the TTM is a useful framework for explaining exercise behavior among women with breast cancer (Pinto et al., 2002), as well as individuals with other diseases and disabilities (Cardinal, Kosma, & McCubbin, 2004; Garner & Page, 2005). In a meta-analysis by Marshall and Biddle (2001), only three of the 71 studies included all of the TTM constructs, and most studies were cross-sectional. Therefore, when applying the TTM, future studies, particularly longitudinal designs, should use all the key constructs of the TTM. Specifically, future longitudinal studies using the TTM to explain exercise behavior among women with breast cancer should include an assessment of processes of change, as the TTM construct remains relatively unexamined in that population. Processes of change are not only important in describing strategies individuals use to change exercise behavior, but they are highly important for informing intervention programs.

Conclusion

Evidence suggests that regular participation in physical activity appears to reduce the risk of breast cancer (Friedenreich et al., 2009) and that regular engagement

in physical activity after breast cancer diagnosis can help protect against breast cancer recurrence and breast cancer-related mortality. Studies indicate that psychosocial factors play an important role in influencing the activity patterns of breast cancer survivors; however, future longitudinal studies are needed to confirm those findings.

Implications for Nursing

Nurses are viewed as highly respectable sources of health information (Hesse et al., 2005). Therefore, nurses can help to influence the physical activity behaviors of women with breast cancer. The evidence that physical activity can reduce breast cancer recurrence and mortality suggests that, when feasible, nurses should encourage breast cancer survivors to participate in physical activity on a regular basis by engaging them in a conversation about physical activity, which involves reflective listening, as opposed to strictly directing or providing traditional advice. Nurses should encourage survivors who have undergone recent surgery for breast cancer to resume their normal daily activities and begin exercising as soon as possible (Irwin, George, & Matthews, 2010). During chemotherapy and radiation, breast cancer survivors should continue their normal daily activities and exercise as much as possible, with the exercise routine being adjusted based on the effects of the treatment. After initial treatment ends, striving to meet recommended levels of physical activity (a minimum of 150 minutes of moderate-intensity physical activity per week) is suggested; although, some evidence suggests that at least 180 minutes of moderate-intensity physical activity per week is needed to reduce breast cancer recurrence (Holmes et al., 2005). However, women with metastatic breast cancer may be at increased risk for bone fractures and should employ a gradual progression of exercise. Nurses are in a unique position to improve the survival rates of breast cancer survivors and can do so through the promotion of physical activity.

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