12-2012

The Effect of Exercise on Cancer-related Fatigue in Women Receiving Treatment for Non-metastatic Breast Cancer: Evidence-based Practice Literature Review

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December 13th, 2012

Abstract

The purpose of this integrative literature review is to determine if an exercise program has an effect on reducing cancer-related fatigue in women receiving treatment for non-metastatic breast cancer. Key words used in the database search parameters of nursing (CINAHL) and medical (PubMed) literature (published 2002 to 2012) included “breast cancer,” “exercise,” and “fatigue.” Data analysis and findings of the studies demonstrated that both supervised and home-based exercise programs are safe and effective in reducing cancer-related fatigue in the non-metastatic breast cancer patient population. However, additional studies need to be completed before definitive conclusions can be made, especially in regards to the specific type, duration, and intensity of exercise prescription needed for each patient. Findings of these studies can be applied to the clinical practice of an advanced practice registered nurse by providing evidence on the importance of screening for and providing recommendations to treat cancer-related fatigue in women treated for non-metastatic breast cancer.

Word count: 154

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Nearly twelve-percent of women in the United States will be diagnosed with invasive breast cancer throughout their lifetime (American Cancer Society [ACS], 2012). With the large number of women diagnosed and receiving treatment for non-metastatic breast cancer, it is important that providers understand specific side effects related to the diagnosis and associated therapies and how they affect each patient. One of the most debilitating side effects of battling breast cancer and further receiving adjuvant therapies such as chemotherapy and radiation therapy to treat the cancer is cancer-related fatigue (CRF) (Hsieh, Sprod, Hydock, Carter, Hayward, & Schneider, 2008). According to the National Comprehensive Cancer Network (NCCN) (2011), "cancer-related fatigue is a distressing persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning" (p. FT-1). CRF significantly affects patients' quality of life (QoL) by making patients too tired to participate in activities they enjoyed prior to their cancer diagnosis and treatment experience (NCCN, 2011).

Cancer-related fatigue is not related to rest and is often worse for patients who are actively receiving treatment for their cancer (Silver, 2006). CRF is estimated to be experienced by nearly 80% of women who receive chemotherapy and/or radiation therapy (NCCN, 2011) and is often reported as more debilitating than pain, nausea or constipation—all conditions which are treatable with medications (NCCN, 2011). CRF is a cumulative symptom which directly affects patients' QoL and can last for weeks, months or even years during and after treatment has subsided (Silver, 2006). This makes it incredibly important for oncology providers to assess for and provide interventions to help reduce or eliminate this debilitating symptom.

Cancer-related fatigue often presents as a combination of symptoms and may be due to side effects from chemotherapy and radiation therapy, direct effect from the tumor, decreased nutritional intake, and lack of sleep, to name a few (NCCN, 2011; Silver, 2006). Also, many symptoms such as pain, distress, and anemia occur simultaneously with fatigue and may be the contributing factor(s) of women developing CRF during their cancer treatment (NCCN, 2011). Treatments such as chemotherapy and radiation therapy are often incorporated as adjuvant therapies—additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back—with the intent to eliminate microscopic cancer cells not removed during surgery and to lower the risk of reoccurrence of the woman's breast cancer (National Cancer Institute, n.d.; Hsieh et al., 2008). However, these therapies do not come without significant side effects.

Cancer treatments such as chemotherapy and radiation therapy cause CRF in a variety of ways. "Radiation therapy has been implicated in the occurrence of interstitial myocardial fibrosis and coronary and carotid artery arteriosclerosis" (Hsieh et al., 2008, p. 910) leading to CRF. Radiation therapy causes CRF through a cumulative effect; patients receiving adjuvant radiation therapy often do not feel the effects of treatment until 2-3 weeks after therapy has ceased (Silver, 2006). Chemotherapy medications not only target the malignant, cancer-causing cells; they also target the body's healthy, non-cancerous cells. The amount of energy that is required to heal the damage which has been done to healthy tissues can lead to extreme feelings of fatigue (Silver, 2006). Side effects of chemotherapy, such as nausea, mouth sores, taste changes, diarrhea and heartburn can alter one's ability and desire to consume adequate nutrition needed to maintain an appropriate amount of energy to fight the breast cancer (Silver, 2006). Chemotherapy can lead to a reduction in blood counts required to carry oxygen to tissues, which consequently leads to development of anemia and a significant amount of fatigue. It is estimated that 70 percent of patients develop anemia during chemotherapy treatment (Cleveland Clinic, 2011). One of the only ways to combat this type of fatigue without discontinuing treatment is by recognizing and treating the anemia with pharmacologic intervention, such as erythropoietin injection (NCCN, 2011).

When a patient receiving treatment for non-metastatic breast cancer complains of fatigue, it is essential for oncology providers to screen for multiple symptoms to determine the cause or offending symptom(s) of fatigue to aid them in potentially eliminating the patient's symptoms (NCCN, 2011). If any treatable contributing factors, such as nutritional abnormalities or anemia are discovered during a provider's assessment of CRF, those conditions need to be treated to help reduce the patient's reported fatigue (NCCN, 2011). However, often CRF is not due to a pharmacologically-treated condition and consequently, a provider should be aware of non-pharmacologic therapies that help reduce extremely distressing CRF. A non-pharmacologic therapy researched recently is the prescription of an exercise program, either home-based or supervised to treat cancer-related fatigue. The rationale for using exercise to treat cancer-related fatigue, according to Mock, Frangakis, Davidson, Ropka, Pickett, Poniatowski, Stewart, Cameron, Zawacki, Podewils, Cohen, & McCorkle (2005):

> The combined effects of toxic treatments plus decreased levels of activity during treatment reduce the capacity for physical performance. A reduced functional capacity means that the cancer patient expends greater effort relative to maximal ability to perform usual activities, thus leading to higher levels of fatigue.

> Exercise training attenuates the loss and even increases functional capacity, resulting in reduced effort and decreased fatigue at any level of work. (p. 465)

The American College of Sports Medicine (ACSM) (2012) recommends that all Americans partake in at least 150 minutes of moderate-intensity exercise each week to maintain a healthy lifestyle. According to the Centers for Disease Control and Prevention (CDC), moderate-intensity physical activity is when "a person's target heart rate [is] 50 to 70% of his or her maximum heart rate" (CDC, 2011b, para. 2). A person's maximum heart rate (MHR) is determined by subtracting his/her age from 220. To determine the percentage of MHR, one would multiply his/her MHR by the percentage that he/she is interested in calculating (for example, multiply by 0.50 to determine 50% of MHR) (CDC, 2011b). Examples of moderate-intensity exercise include walking briskly, water aerobics, riding a bicycle slower than 10 miles per hour, or partaking in general gardening (CDC, 2011a). The CDC recommends that people use the "talk test" to determine the level of exercise intensity that they are doing at the present time. According to the CDC, "as a rule of thumb, if you're doing moderate-intensity activity you can talk, but not sing, during the activity" (CDC, 2011a, para. 3). The U.S. Department of Health & Human Services (2008) maintains a similar stance to the CDC and ACSM; they recommend obtaining 150 to 300 hours of moderate-intensity exercise per week, noting that this intensity of exercise provides substantial amounts of health benefits for both the healthy and oncology patient populations.

Research Question

The research question addressed in this integrative review is: In women with non-metastatic breast cancer receiving adjuvant chemotherapy and/or radiation therapy, does the prescription of a home-based or supervised exercise program versus usual care decrease the severity of cancer-related fatigue?

Critical Appraisal of the Evidence

Theoretical Background of Exercise as a Cancer-Related Fatigue Intervention

Fernando Carlos Dimeo (2001) expanded on research conducted in 1983 by Mary Winningham by exploring the physiologic and pathologic causes of cancer-related fatigue and further suggested that exercise may serve as an effective intervention to treat this debilitating side effect in patients with non-metastatic breast cancer. Dimeo noted that when fatigue occurs during daily activities, is not resolved with rest, occurs for a prolonged duration of time and greatly affects patient's normal activities of daily living, it is therefore classified as pathologic and requires provider's interventions. The effects of chemotherapy and radiation therapy on the delivery of oxygen and energy production throughout the body significantly contribute to the cause of cancer-related fatigue. In past years, physicians' recommendation for fatigue was to rest; this resulted in a negative outcome of muscle wasting and loss of fitness ability, further increasing a patient's fatigue. Dimeo noted previous research findings on positive effects of exercise on cancer-related fatigue in patients with peripheral stem cell transplantation and further suggested research focus on the effect of exercise on cancer-related fatigue in patients with breast cancer.

Data Analysis

A thorough database search was conducted looking at both nursing (CINAHL) and medical (PubMed) literature published between the years of 2002 to 2012. Key words used in the database search parameters were "breast cancer," "exercise," and "fatigue." Articles were initially included if the title and abstract included the words “cancer,” exercise,” and “fatigue,” and a total of twenty-two articles were initially selected that fit within the stated parameters. Each study was reviewed for further inclusion criteria, specifically the participants having a primary breast cancer diagnosis and receiving current adjuvant treatment. It is important to note that both meta-analyses (Cramp, 2010; Velthius, Agasi-Idenburg, Aufdemkampe, & Wittink, 2010) in this review researched patients with various types of cancer—not just breast cancer—experiencing cancer-related fatigue; however, in both reviews, a majority of the studies analyzed were completed on women with non-metastatic breast cancer. It was personal clinical knowledge that the NCCN (2011) maintained a published guideline on cancer-related fatigue; as a result, this guideline was analyzed and referenced as supportive material for this literature review.

The Johns Hopkins Nursing Evidence-Based Practice (JHNEBP) evidence rating scales (Newhouse, Dearholt, Poe, Pugh, & White, 2005) were used to analyze the included studies and meta-analyses in this integrative review. The JHNEBP rating scales systematically analyze the article’s strength of study design, research strategies, results, conclusions and if the study’s findings will affect clinical practice (Newhouse et al., 2005). A total of six articles were determined to be most inclusive for this literature review. All of the included articles were published between the years of 2005 to 2011. The research was completed on populations residing in a diverse population of countries, including Taiwan, Canada, the United States, and countries throughout Europe. The sample sizes in all of the articles reviewed varied from 8 to 377 total participants.

The five quantitative studies in this review all had a similar purpose of exploring the effect of exercise on cancer-related fatigue in women with non-metastatic breast cancer (Wang, Boekmke, Wu, Dickerson, & Fisher, 2011; Mock et al., 2005; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010). There was a noticeable pattern of results between all five studies; they all found that exercise (either home-based or supervised) programs have a significant effect on reducing CRF (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010; Ingram, Wessel, & Courneya, 2010). The analyzed studies and meta-analyses in this review were all quantitative in design except for one study, which was qualitative and purposely selected to demonstrate patient perspective of participating in an exercise program during cancer treatment (Ingram et al., 2010).

The research designs—randomized controlled trials, experimental, quasi-experimental and meta-analyses—were appropriate for the research problems and hypotheses being studied (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010). All of the research studies included an intervention group consisting of an exercise program and a control group, which was typically usual care. The experimental, longitudinal study by Wang et al. (2011) was unique in that it measured women's levels of fatigue at four predetermined time points and that it followed patients prior to their initial surgery to remove the breast cancer. The sampling of the studies and demographics of the participants were included in all of the analyzed studies, noting the mean age of the women and often the education level for the participants (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010). The research studies by Mock et al. (2005), Hsieh et al. (2008), Ingram et al. (2010), Cramp (2008), and Velthius et al. (2010) did not note the race or socioeconomic status of the participants. Consequently, it could be argued that it is difficult to generalize the data to a more diverse, multicultural patient population. The experimental, longitudinal study by Wang et al. (2011), however, was conducted on a Taiwanese breast cancer population, and the results of this study are important for this review because they demonstrate the application of this research on a diverse population.

The participants in all of the experimental studies were first screened for exclusion criteria, including conditions or symptoms which contradicted exercise and would place the patients at further harm if they were to participate in the studies (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010). Also, many of the studies included frequent interactions between the researchers and participants (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008) and the modification of the exercise programs if the patients' health conditions changed throughout the studies, further implying that the researchers did not want to cause the participants harm during the study periods (Mock et al., 2005; Hsieh et al., 2008). The primary means of data collection in all of the studies included the use of questionnaires, interviews, self-journals, and scales, which furthermore did not place the participants at harm (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010).

Research-Based Evidence

Experimental and quasi-experimental studies: Mock et al. (2005) conducted the first multi-institutional prospective, randomized controlled trial exploring the effects of a moderate-intensity home-based walking exercise program on fatigue levels in women with non-metastatic breast cancer while receiving adjuvant chemotherapy or radiation therapy. The stratified assignment of participants to groups defined by their first adjuvant treatment and then further randomization to intervention or control groups supported the strength of the study's design, one that was similar to a clinical trial design. Mock et al.'s study was conducted at four university teaching hospitals and four community cancer centers located on the East coast of the United

States. The sample size was large with a total of 119 women, including 57% who received radiation and 42% who received chemotherapy. As previously mentioned, the participants were randomized to intervention and control groups, but the researchers were not blind to who was in either group, which was noted by the researchers as a potential limitation of the study. The researchers attempted to control this by having the participants self-administer questionnaires and by using numbers, not names, on all of the data forms (Mock et al., 2005).

The primary outcome of the study was fatigue, measured both pre-therapy and post-therapy using the Piper Fatigue Scale (Mock et al., 2005). The researchers also studied the physical functioning and activity levels of the participants, using the 12-minute Walk Test, the Medical Outcomes Study Short Health Form, and the Physical Activity Questionnaire as measurement tools. The p value, set to define statistical significance, was a strength of the study with $p = 0.03$. The statistical analysis of data included looking at the "intent-to-treat effect" and the "effect of actually exercising", measured by the method of "instrumental variables with principle stratification (IV/PS)" (Mock et al., 2005, p. 467). This method estimates each participant's adherence to her assigned group and further assigns each participant to a principal strata group: never-taker; always-taker; full-complier; or defier. This method helps to more accurately analyze the data as some participants' data, specifically the never-takers and always-takers, will not accurately reflect their randomization group due to their principal strata. This principle is also known as "complier-average-causal effect (CACE);" it only focuses on the data of the full-compliers (the participants who fully follow the intervention or control to which they are assigned) (Mock et al., 2005, p. 468).

The mean fatigue scores (Piper Fatigue Scale) for all participants at the beginning of the study was 2.42 (SD = 2.46) and increased to 2.20 (SD = 2.52) to 3.75 (SD = 2.41) for patients receiving radiation therapy and 2.77 (SD = 2.34) to 3.46 (SD = 2.60) for patients receiving chemotherapy (Mock et al., 2005). For full-compliers assigned to the usual care group, the estimated change in fatigue score from baseline was 1.17; and the change in fatigue score for the full-compliers in the exercise group was -0.86. Through applying the principle of CACE, the difference in mean fatigue outcomes was -2.03, which demonstrates statistical significance of using exercise to combat cancer-related fatigue. Using the JHNEBP evidence rating scales, this prospective, randomized controlled trial has a *strength of evidence rating of I* and a *quality rating of A/high* (Newhouse et al., 2005).

Wang et al. (2011) completed an experimental, longitudinal research study using a walking program for Taiwanese women with early-stage breast cancer. This was the first study of this kind in Taiwan, and was unique because the study was started prior to the women completing their initial surgery and adjuvant chemotherapy treatments. The study looked at various outcomes, including QoL, fatigue and sleep disturbance. The sample for this study was medium in size (N=72) and included an exercise group (N=35) and control group (N=37). The participants were recruited by convenience sampling with randomization to exercise and control groups. The use of convenience sampling is a limitation of Wang et al.'s study; however, the use of randomization to both an intervention and control group was a noted strength of the study. The completion rate for the study was 80.6%; and the compliance rate for the exercise group was 93.8%, with both rates notably higher than the study's comparison literature review and with both rates supporting the validity of the study.

The Functional Assessment of Chronic Illness Treatment – Fatigue (FACIT-F) instrument was used to measure the occurrence of the outcome variable of fatigue (Wang et al., 2011). Repeated-measure analysis of variance (RMANOVA) was ultimately used to analyze the data of the study due to the hierarchical linear model (HLM), which was the main analysis method to measure change of the clinical outcomes over a 6-week time period, not serving as an appropriate means for measuring change of fatigue over the study period. The results of the study indicated that "subjects in the exercise group had less fatigue than those in the usual-care group and supported findings of most exercise interventional studies" (Wang et al., 2011, p. E10). Significant differences in fatigue between the exercise and usual care groups was noted at nadir time (time 3 = 8.52, $P < .001$) and at the end of the exercise program (time 4 = 5.78, $P < .001$). It is important to note that the change in fatigue levels was greater for the exercise group; however, the results were not statistically significant ($F_{1,60} = 9.74$, $P = .003$) (Wang et al., 2011). Using the JHNEBP evidence rating scales, this experimental, longitudinal study has a *strength of evidence rating of I* and a *quality rating of B/good* (Newhouse et al., 2005).

Hsieh et al. (2008) researched the effects of moderate-intensity, individually-prescribed, supervised exercise on cancer-related fatigue and cardiopulmonary function in women with breast cancer immediately following treatment completion. The participants of this quasi-experimental study were selected through convenience sampling at the Rocky Mountain Cancer Rehabilitation Institute, which is a noted by the researchers to be a limitation of the study. The rather large sample (N=96) was divided into four non-randomized groups: surgery alone; surgery and chemotherapy; surgery and radiation; and surgery, chemotherapy and radiation. The revised Piper Fatigue Scale was used to assess the participants' cancer-related fatigue. One-way analysis of variance (ANOVA) was used to analyze the study's data and statistical significance was set at $P \leq 0.05$. In addition to studying the effect of exercise on fatigue, the researchers also looked at the effect of exercise on cardiopulmonary function; results of those outcomes will not be discussed in this review.

The results of the study indicated that moderate-intensity, individualized, prescribed exercise reduces fatigue in breast cancer patients who are monitored immediately after completing adjuvant therapy (Hsieh et al., 2008). The exercise intervention resulted in significant reductions ($P < 0.05$) in fatigue in multiple categories—behavioral fatigue; affective fatigue; sensory fatigue; cognitive and mood fatigue; and total fatigue—for the surgery/chemotherapy, surgery/radiation therapy, and surgery/chemotherapy/radiation therapy groups. The surgery and radiation therapy group had the greatest reduction in behavioral (-51.05% change), affective (-36.36% change), sensory (-46.03% change), and total fatigue (-39.47% change). The researchers noted that the inclusion of a non-exercise, control group would have strengthened the study's results (Hsieh et al., 2008). Using the JHNEBP evidence rating scales, this study quasi-experimental, study has a *strength of evidence rating of II* and a *quality rating of B/good* (Newhouse et al., 2005).

Meta Analyses of Randomized Controlled Trials

Cramp (2008) completed a meta-analysis which was included in the Cochrane Database of Systematic Reviews of twenty-eight randomized controlled trials (RCTs) (N = 2083 participants) evaluating the effect of exercise on cancer-related fatigue both during and after cancer treatment. Cramp's review looked at patients with various types of cancer; however, the majority of the studies (N = 16 studies; N = 1172 participants) researched patients with breast cancer. Cramp searched all relevant databases (a total of eight), oncology journals and reference lists for additional articles not found in the initial database searches. The mode and intensity of exercise, including both home-based and supervised exercise programs, varied among the reviewed studies. There were other outcome variables that were researched in the RCTs analyzed by Cramp, including aerobic capacity, QoL, anxiety, depression, self-efficacy, and other long-term outcomes of exercise.

Cramp (2008) used a meta-analysis to look at both *post-test means* and *change data* between the exercise intervention groups and control groups. For the *post-test means* results, a total of 920 participants' data was analyzed for the exercise intervention and 742 participants' data was analyzed for the control group. Cramp determined that the intervention of exercise was statistically more significant than the control group on the outcome of fatigue (SMD -0.23, 95% CIs -0.33 to -0.13). A total of 454 participants received the exercise intervention and 399 participants were part of the control group in the *change data* analysis. Cramp noted, "at the end of the intervention periods exercise was statistically more effective than the control intervention (SMD -0.23, 95% CIs -0.36 to -0.09)" (p. 7). Cramp determined through this meta-analysis that exercise intervention has a statistically significant impact on CRF both during adjuvant therapy and post-therapy.

Cramp (2008) noted that limitations of the review included, but were not limited to: a diverse range of studies with small numbers of participants; lack of statistical heterogeneity in RCTs completed during clinical treatment; the publishing of studies in only the English language which may reflect selective publication with statistically significant data only; and the possibility of the previous researchers selectively reporting only statistically significant data. The exercise intervention in only nine of the 28 reviewed RCTs was in congruence with the ACSM recommendation for 30 minutes of moderate-intensity exercise, 5 days per week. This finding may be suggestive that the ACSM guidelines are not appropriate for recommendation specifically to cancer patients and that the development of new cancer-specific exercise recommendations may be necessary in the future (Cramp, 2008). Using the JHNEBP evidence rating scales, this meta-analysis review has a *strength of evidence rating of I* and a *quality rating of A/high,* making the results of this review very pertinent and applicable to clinical practice (Newhouse et al., 2005).

Velthius et al. (2010) completed a meta-analysis of 18 randomized controlled trials that were conducted to determine the short- and long-term effectiveness of different exercise prescriptions on cancer-related fatigue experienced during treatment. Of the 18 total analyzed studies, 12 studies were conducted on breast cancer patients while receiving treatment. The exercise intervention in these studies ranged from home-based aerobic and/or resistance exercise to supervised aerobic and/or resistance exercise. All of the 12 studies had a control usual care group, except one study's control group consisted of a placebo stretching protocol. The main outcome variable was patient-reported fatigue which was measured by various questionnaires and scales, including the Piper Fatigue Scale and revised Piper Fatigue Scale; the Functional Assessment Cancer Therapy-Fatigue and Anemia scales, Profile of Mood States, Functional Assessment of Cancer Therapy-Fatigue, Brief Fatigue Inventory, and the Symptom Assessment Scale. The methodological quality of the study (0.7 with standard error of 0.06) was determined by the researchers with the use of the PEDro scale. Six of the twelve RCTs in breast cancer patients had a methodological total score of >5 (total score possible = 8) (Velthius et al., 2010).

This meta-analysis used multiple subgroup analyses of pooled data from high-quality studies to determine if there were significant results to draw conclusions on the different exercise programs (Velthius et al., 2010). The researchers completed a subgroup analysis on three high-quality studies looking at supervised, aerobic exercise; these three studies included a total of 340 patients and demonstrated a medium-sized and significant reduction in CRF (SMD 0.30, 95% confidence interval 0.09 to 0.51). In another subgroup analysis of two high-quality studies (total of 128 patients) looking at a home-based exercise program, the researchers determined a small, non-significant reduction in CRF (SMD 0.10, 95% confidence interval -0.25 to 0.45). Consequently, the researchers concluded that supervised, aerobic exercise programs were more effective in reducing CRF than home-based exercise programs. They further stated that supervised exercise programs may be more effective in the short-term period surrounding adjuvant treatment, possibly due to the individual not being able to effectively judge the intensity or adherence to the exercise program that is necessary to achieve positive physiologic results (Velthius et al., 2010).

Velthius et al. (2010) state that the general exercise prescription for breast cancer patients currently receiving or just recently completed adjuvant therapy is “low to moderate intensity, regular frequency (three to five times a week) for at least 20 minutes per session, involving aerobic, resistance, or mixed exercise types” (p. 219). Because there were very few adverse effects associated with both the home-based and supervised exercise programs (total of eight, or 0.72%) and because of the participants’ moderate to excellent adherence in the reviewed studies, the researchers state that these programs are safe and do not pose any health risks to patients with non-metastatic breast cancer who are receiving adjuvant treatment (Velthius et al., 2010). Using the JHNEBP evidence rating scales, this meta-analysis review has a *strength of evidence rating of I* and a *quality rating of A/high,* making the results of this review very pertinent and applicable to clinical practice (Newhouse et al., 2005).

Additional Evidence

Qualitative study: Ingram, Wessel, & Courneya (2010) researched women’s “perceptions of participating in a structured, home-based exercise program while receiving adjuvant chemotherapy for breast cancer, including perceptions of facilitators of and challenges to exercise" (p. 239). The Participant Evaluation of Feasibility and Acceptability was used to collect both qualitative and quantitative data to for the study. The participants maintained personal exercise logs and were contacted every-other-week by research assistants who inquired about the participants' progress and modified their exercise prescriptions as necessary. The most common *exercise challenge* encountered by the participants in Ingram et al.'s study was fatigue, specifically after receiving a chemotherapy dose.

The researchers of this study recognized that because the study was qualitative in nature and the sample size was small, it may be difficult to apply the results to a larger, more generalized population (Ingram et al., 2010). However, the frequent contacts between the researchers and participants, in addition to the data being consistent that women with breast cancer receiving adjuvant chemotherapy "valued exercise and implemented a variety of strategies to maintain the exercise program" (Ingram et al., 2010, p. 241), the researchers do believe that the results may serve as a useful guide for oncology providers prescribing exercise as an intervention for cancer-related fatigue in women with non-metastatic breast cancer who are receiving adjuvant chemotherapy. Using the JHNEBP evidence rating scales, this qualitative study has a *strength of evidence rating of III* and a *quality rating of B/good* (Newhouse et al., 2005).

Implications for Clinical Nursing Practice

The findings of this integrative review are consistent and help support the research question of "In women with non-metastatic breast cancer receiving adjuvant chemotherapy and/or radiation therapy, does the prescription of a home-based or supervised exercise program versus usual care decrease the severity of cancer-related fatigue?" Findings of this integrative review support the most recent recommendations by the National Comprehensive Cancer Network (2011) that screening for cancer-related fatigue should occur in every provider interaction with patients receiving treatment for non-metastatic breast cancer, and when CRF is identified, the incorporation of exercise in breast cancer patients' treatment plans is an appropriate intervention to reduce this CRF. The prescription of either a home-based or supervised exercise program that integrates low to moderate-intensity aerobic exercise in a regular frequency—at least 20 to 30 minutes per session, approximately three to five times per week—has shown to be effective in reducing CRF in breast cancer patients (Mock et al., 2005; Wang et al., 2011; Hsieh et al., 2008; Cramp, 2008; Velthius et al., 2010) and is an appropriate intervention for oncology providers to offer.

The incorporation of physical activity is an inexpensive, effective and low-risk intervention to combat CRF in patients with breast cancer (Velthius et al., 2010; Wang et al., 2011). The prescription of a home-based aerobic exercise program is a "widely applicable, feasible and acceptable" (Mock et al., 2005, p. 475) intervention for treating CRF in the breast cancer patient population. Women participating in a home-based exercise program are able to scale back the intensity of their exercise or perform their full exercise program in multiple, shorter sessions if they are experiencing negative side effects of treatment, however, this may result in the exercise not be physically beneficial if the exercise intensity is too low (Velthius et al., 2010; Ingram et al., 2010). Nonetheless, the incorporation of some exercise versus none poses benefits for patients during active cancer treatment as inactivity can lead to further muscle and cardiorespiratory decline (Velthius et al., 2010; Dimeo, 2001).

Supervised exercise programs provide an opportunity for women to complete safe, monitored exercise and have their programs individualized and tailored if they experience side effects secondary to their cancer treatment (Hseih et al., 2008). Breast cancer patients' adherence to the exercise program is significantly higher when the exercise is supervised by physical therapists specialized in cancer exercise therapy (Hseih et al., 2008; NCCN, 2011). Specific patient situations which should trigger a referral to physical therapy to assist in exercise prescription include, but are not limited to: patients with comorbidities that affect cardiopulmonary function; patients in the immediate post-operative period; or patients who begin adjuvant treatment in a baseline deconditioned state (NCCN, 2011).

Women with breast cancer are often open to any and all suggested interventions to help them feel as best they can during active treatment; as a result, the inclusion of an exercise intervention is often well-received by breast cancer patients (Wang et al., 2011). In addition to helping the patients feel better, participants in Wang et al.'s (2011) study noted that physical activity became a primary coping mechanism for the women's cancer journey. The results of Ingram et al.'s (2010) study also support this concept; when breast cancer patients are educated on the potential side effects associated with treatment and how to adjust their exercise program accordingly, they are more prepared for stressors of cancer treatment and how to cope with these stressors using an exercise program as a coping mechanism. For the implementation of the exercise program to be effective, NCI (2012) recommends for providers to suggest the incorporation of activities that patients enjoy and specify implementation strategies for the patient so the exercise program can be realistically incorporated into the patients' daily routine. In addition to prescribing exercise as an intervention for CRF, providing further non-pharmacologic resources, such as participating in support groups, may provide beneficial effects for the women receiving active treatment for breast cancer (NCCN, 2011). This information is important for advanced practice registered nurses (APRNs) because our care is tailored to meet the holistic needs of our patients by providing interventions that have both physical and psychological effects.

The implementation of an exercise program into care of the patient receiving adjuvant treatment for non-metastatic breast cancer is dependent on the education of oncology providers by APRNs on the positive effect of exercise on reducing CRF (Santa Mina, Alibhai, Matthew, Guglietti, Steele, Trachtenberg, & Ritvo, 2012). APRNs who are experienced and knowledgeable of this topic can present continuing education courses to educate oncology support staff and providers on the importance of incorporating of exercise into cancer care in addition to various implementation strategies to utilize in practice (Santa Mina et al., 2012). The screening for CRF in this patient population should be encouraged with each provider interaction. It is essential for an APRN to develop a policy and documentation procedure that notes the severity of CRF that all breast cancer patients report. If moderate to severe CRF is present, a provider should have the knowledge and resources to determine the appropriate prescription of moderate-intensity exercise for the patient. Patient education materials must be developed by APRNs who are experienced in prescribing exercise for CRF to assist their colleagues with communicating with their patients the importance of exercise to reduce the severity of CRF and other symptoms associated with a cancer diagnosis and treatment regimen (Santa Mina et al., 2012). Finally, APRNs and oncology providers should seek to develop relationships with physical therapists and local, community-health facilities to provide opportunities for referrals to develop individualized exercise programs and provide a location for supervised group exercise classes for breast cancer patients (Santa Mina et al., 2012).

Summary and Recommendations

Findings of the six studies included in this integrative review support that APRNs ought to actively screen for cancer-related fatigue and when identified, prescribe appropriate, individualized exercise interventions and associated education on the effects of exercise on CRF. Further research should be completed to determine the most effective and least time-consuming method to screen for CRF in the outpatient setting so all patients with non-metastatic breast cancer can receive an intervention if they suffer from feelings of CRF (Velthius et al., 2010). Additional RCTs must be completed before definitive conclusions can be made, especially in regards to developing oncology-specific guidelines regarding intensity, duration and type of exercise therapy for the patient receiving active cancer treatment (Velthius et al., 2010; NCCN, 2011).

Further research should be conducted to determine more specific types of exercise, such as the inclusion of resistance exercises and more specialized exercise programs that focus on both the mind and body, for example, yoga practice, and their effects on CRF (NCI, 2012). Additional recommendations on which patients are most appropriate for supervised exercise programs and when to refer patients to supervised exercise programs would be beneficial for the APRN in oncology practice. The studies analyzed in this review included sample populations from various areas of the world; however, additional research conducted in the United States of more diverse, marginalized patient populations would provide evidence for APRNs to develop culturally-competent recommendations for exercise prescriptions to treat cancer-related fatigue in the non-metastatic breast cancer patient.

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