Nonpharmacologic Supportive Strategies
to Promote Quality of Life in Patients
Experiencing Cancer-Related Fatigue:
A Systematic Review

Ausanee Wanchai, RN, MSN, Jane M. Armer, RN, PhD, FAAN, and Bob R. Stewart, EdD

Cancer-related fatigue (CRF) is a distressing symptom that affects the quality of life (QOL) of patients with breast cancer and their families. The effectiveness of pharmacologic therapies alone has not been sufficient in the management of CRF; therefore, a combination of pharmacologic and nonpharmacologic approaches is justified. The purpose of this article is to critically review the literature related to nonpharmacologic supportive strategies in enhancing QOL among patients with breast cancer experiencing CRF. The results show that exercises (e.g., home-based exercise, supervised exercise), education and counseling, sleep therapy, and complementary therapy are feasible as effective nonpharmacologic supportive interventions to improve QOL in patients with breast cancer suffering from CRF. Therefore, nurses may consider these nonpharmacologic supportive strategies as adjunctive interventions to pharmacologic interventions in enhancing QOL for patients with breast cancer experiencing CRF. However, because previous studies had some methodologic limitations, such as small sample size, lack of objective measures, or predominantly Caucasian sample, future research to further explore nonpharmacologic interventions in this area is warranted.

At a Glance

- About 26%–90% of patients with breast cancer suffer from cancer-related fatigue (CRF) during cancer treatment and they can experience CRF up to 10 years after treatment ends.
- The majority of studies have reported that exercise was a feasible and effective intervention to ameliorate CRF for patients with breast cancer.
- Oncology nurses must be aware of CRF and use an appropriate instrument to assess this symptom in patients with breast cancer.

With advances in early detection and treatment, the five-year relative survival rate for women with breast cancer has improved from 63% in the early 1960s to 90% in 2010 (American Cancer Society, 2010). However, side effects of cancer treatments, such as chemotherapy, radiation therapy, surgery, and hormone therapy, may contribute to symptoms that affect quality of life (QOL) for these patients (Mustian et al., 2007; Stone, Richards, A’Hern, & Hardy, 2001). Among potential side effects, cancer-related fatigue (CRF) was considered to be the most distressing cancer symptom and side effect of treatment, and it may persist for months or years after completion of breast cancer treatment (Bower et al., 2000; Patrick et al., 2004). Byar, Berger, Bakken, and Cetak (2006) asserted that CRF experience is a subjective and multidimensional concept that cannot be explained by only the physiologic aspect; physical, psychological, social, and spiritual aspects all are associated with CRF. From patients’ perspectives, fatigue is more than just being tired in a way that they had not expected (Wu & McSweeney, 2007). Compared with typical fatigue, CRF is more rapid in onset, more
energy draining, more intense, longer lasting, more severe, and more unrelenting (Holley, 2000).

A study by Goedendorp, Gielissen, Verhagen, Peter, and Bleijenberg (2008) showed that patients with breast cancer reported higher severe fatigue than patients with prostate cancer. Previous studies reported prevalence rates of CRF ranging from 26%–90% for patients with breast cancer who were undergoing adjuvant chemotherapy (Andrykowski, Schmidt, Salsman, Beacham, & Jacobsen, 2005; Downie, Mar Fan, Houédé-Tchen, Yi, & Tannock, 2006; Goldstein et al., 2006). In addition, although CRF was found to be a moderately intense symptom during chemotherapy treatments that decreased significantly over time, it was not resolved for all women (Byar et al., 2006). Previous studies showed that one-third of breast cancer survivors reported more severe fatigue (Alexander, Minton, Andrews, & Stone, 2009; Bower et al., 2000), and some breast cancer survivors still experienced CRF 2–10 years after completing treatment (Bower et al., 2006; Mehnert et al., 2007; Servaes, Gielissen, Verhagen, & Bleijenberg, 2007).

CRF is the symptom with the highest impact on QOL and daily living of patients with breast cancer (Díaz et al., 2008; Gupta, Lis, & Grutsch, 2007; Janz et al., 2007). Patients with breast cancer perceive CRF as the most debilitating and pervasive symptom because it interferes with all aspects of their lives, including emotional and physical well-being, interpersonal and family relationships, and employment (Downie et al., 2006). A study by Byar et al. (2006) found that higher fatigue was associated with lower QOL among patients with breast cancer. In another study, Kim et al. (2008) showed that fatigue was negatively associated with breast cancer survivors’ health-related QOL. According to Morrow (2007), CRF had a greater impact on QOL than other cancer-related symptoms such as pain, depression, and nausea, as perceived by patients with cancer. Similarly, Arndt, Stegmaier, Ziegler, and Brenner (2006) found that CRF was the strongest predictor of impaired QOL in patients with breast cancer.

CRF not only impacts the patients, but it also adversely affects their entire support system, particularly caregivers. Curt et al. (2000) reported that 65% of patients with cancer indicated that their fatigue resulted in their primary caregivers taking at least one day off work in a typical month. In another study, Passik and Kirsh (2005) reported that CRF was correlated to spousal caregivers’ depression and strain, which led to less engagement in their jobs and social activity. Therefore, nurses should acknowledge and understand CRF and provide interventions to reduce or treat this condition. The optimal goal is improving the patient’s QOL (Miller & Kearney, 2002; Wells & Fredric, 2001).

The National Comprehensive Cancer Network ([NCCN], 2010) proposed useful guidelines to managing CRF that emphasize screening and management of contributing factors, including pain, emotional distress, sleep disturbance, anemia, nutrition, activity level, medication side-effects profiles, and other comorbidities. For a pharmacologic approach, Carroll, Kohli, Mustian, Roscoe, and Morrow (2007) conducted a literature review of clinical trials that assessed pharmacologic agents for the treatment of CRF and found that several studies have shown the efficacy of epoetin alfa and darbepoetin alfa in treating CRF for patients with anemia. However, other types of medications, such as psychostimulants and central nervous system stimulants, showed promise in open-label prospective designs, but evidence is lacking from placebo-controlled, randomized trials. Therefore, because effectiveness of pharmacologic therapies alone has not been sufficient in managing CRF, a combination of pharmacologic and nonpharmacologic supportive approaches may be necessary. A need exists to examine nonpharmacologic methods (Dimeo, 2001; NCCN, 2010). The purpose of this article was to review the literature related to nonpharmacologic supportive strategies that enhance QOL among patients with breast cancer experiencing CRF. This article will identify knowledge gaps that will provide suggestions for future nonpharmacologic supportive strategies to ameliorate CRF and, in turn, enhance QOL for patients with breast cancer.

Literature Review

A literature review from 2000–2010 was performed using the MEDLINE® and CINAHL® databases and the following key words: breast cancer patient, oncology patient, fatigue, cancer-related fatigue, quality of life, health-related quality of life (HRQOL), physical activity, and exercise. Initial studies were screened for inclusion based on abstracts. The search was limited to English-language literature. Inclusion criteria were articles of randomized, controlled trials and quasi-experimental studies concerning the nonpharmacologic supportive strategies that may enhance or promote the QOL in patients with breast cancer suffering from CRF. Studies had to have CRF and/or QOL as outcomes of interest. Eighty-nine articles were identified, 28 of which met the criteria and were selected for review (see Table 1).

The majority of the research studies included (75%) were randomized, controlled trials, and seven studies (25%) used quasi-experimental designs. Of the 28 studies, 19 (68%) focused on patients with breast cancer during treatment and 9 (32%) focused on breast cancer survivors after treatment completion. With regard to nonpharmacologic supportive interventions used in the studies, 17 (61%) evaluated effect of exercise intervention on reducing CRF in women with breast cancer, followed by education and counseling (18%), sleep therapy (11%), and complementary therapies (11%). The studies within these four major areas are evaluated in more detail throughout this article.

Exercise

Pooling the data from 17 reviewed studies that investigated the effectiveness of exercise on reducing CRF in patients with breast cancer, the author concluded that exercise was beneficial for those suffering from CRF during and after treatment. Past empirical studies have reported a variety of exercise programs that could ameliorate CRF and improve QOL for patients with breast cancer, including supervised exercise, home-based exercise, and other strategies (e.g., use of print materials, trained volunteers) to promote exercise in women with breast cancer.

Regarding supervised exercise, eight studies employed supervised exercise interventions to reduce CRF and improve QOL in patients with breast cancer (Campbell, Mutrie, White, McGuire, & Kearney, 2005; Courneya, Segal, Gelmon, et al., 2007; Courneya, Segal, Mackey, et al., 2007; Daley et al., 2007; Drouin et al., 2005; Heim, v.d. Malsburg, & Niklas, 2007; Hwang et al., 2008; Milne, Wallman, Gordon, & Courneya, 2008). However, the studies produced inconsistent findings regarding the effectiveness of supervised exercise in
Table 1. Nonpharmacologic Supportive Strategies to Promote QOL in Patients With Breast Cancer Experiencing CRF

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<tr>
<th>STUDY</th>
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<td><strong>SUPERVISED EXERCISE</strong></td>
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<td>Campbell et al., 2005</td>
<td>22 patients with breast cancer receiving adjuvant treatment</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>Revised PFS</td>
<td>Supervised exercise program for 12 weeks</td>
<td>Women in intervention group reported significantly higher levels of physical functioning and QOL than CON. No significant differences were reported in fatigue and satisfaction with life between groups.</td>
</tr>
<tr>
<td>Courneya, Segal, Gelmon et al., 2007</td>
<td>242 patients with breast cancer receiving cancer chemotherapy</td>
<td>Three-armed, randomized, controlled trial: UC, RET, and AET</td>
<td>FACT-Anemia</td>
<td>Supervised exercise training at 1–2 weeks after first chemotherapy administration and ending three weeks after final chemotherapy administration</td>
<td>At six-month follow-up, RET group reported significantly higher self-esteem than UC group, and AET group reported significantly lower anxiety than UC group. In addition, compared with participants reporting no regular exercise, those reporting regular aerobic and resistance exercise reported significantly better patient-rated outcomes, including QOL and CRF.</td>
</tr>
<tr>
<td>Courneya, Segal, Mackey et al., 2007</td>
<td>242 patients with breast cancer receiving adjuvant chemotherapy</td>
<td>Three-armed, randomized, controlled trial: UC group, supervised RE, and supervised AE</td>
<td>FACT-Anemia</td>
<td>Supervised exercise training included delays, beginning 1–2 weeks after starting chemotherapy and ending three weeks after chemotherapy.</td>
<td>AE was significantly superior to UC for improving self-esteem and aerobic fitness. RE was significantly superior to UC for improving self-esteem, muscular strength, lean body mass, and chemotherapy completion rate. Changes in cancer-specific QOL, fatigue, depression, and anxiety favored the exercise groups but did not reach statistical significance.</td>
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<tr>
<td>Daley et al., 2007</td>
<td>108 breast cancer survivors 12–36 months after treatment completion</td>
<td>Three-armed, randomized, controlled trial: UC group, exercise-placebo, and exercise therapy group</td>
<td>Revised PFS</td>
<td>Supervised AE with an exercise specialist three times per week for eight weeks</td>
<td>Supervised AE therapy intervention reported significantly improved QOL compared to UC. Exercise therapy and exercise-placebo reported a higher physical self-worth score than UC. No difference was reported for fatigue among exercise therapy and UC groups.</td>
</tr>
<tr>
<td>Drouin et al., 2005</td>
<td>20 patients with breast cancer receiving radiation</td>
<td>Two groups, pretest/post-test design: AE group versus placebo-stretching group</td>
<td>Revised PFS</td>
<td>Moderate-intensity AE 3–5 times per week for seven weeks</td>
<td>AE group had significantly improved peak aerobic capacity, fatigue, and psychological factors (anger-hostility and depression-dejection).</td>
</tr>
<tr>
<td>Heim et al., 2007</td>
<td>63 patients with breast cancer at the beginning of in patient rehabilitation</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>MFI</td>
<td>Structured physical training program and additional muscle strength and AE adjusted to the special needs of the patients</td>
<td>Scores for global QOL, physical well-being, and functionality increased from baseline to the end of rehabilitation, but additional improvement three months later was found only in the intervention group. CRF was significantly reduced in the intervention group, but not in the CON group.</td>
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</table>

ABMT—autologous bone marrow or peripheral blood stem cell transplantation; AE—aerobic exercise; AET—aerobic exercise therapy; BFI—Brief Fatigue Inventory; CCSP—comprehensive coping strategy program; CON—control; CRF—cancer-related fatigue; DE—delayed exercise; FACT—Functional Assessment of Cancer Therapy; HRQOL—health-related quality of life; IE—immediate exercise; MFI—Multidimensional Fatigue Inventory; PFS—Piper Fatigue Scale; PT—polarity therapy; QOL—quality of life; RE—resistance exercise; RET—resistance exercise training; ROM—range of motion; TIP-C—telephone interpersonal counseling; UC—usual care; VAS-F—Visual Analogue Scale for Fatigue

(Continued on the next page)
Table 1. Nonpharmacologic Supportive Strategies to Promote QOL in Patients With Breast Cancer Experiencing CRF (Continued)

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<td><strong>SUPERVISED EXERCISE (continued)</strong></td>
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<td>Hwang et al., 2008</td>
<td>40 patients with breast cancer receiving radiotherapy</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>BFI</td>
<td>Supervised moderate-intensity exercise therapy for 50 minutes three times per week for five weeks</td>
<td>Significant differences existed in the changes in QOL, CRF, shoulder ROM, and pain score between the groups. In the intervention group, researchers observed an increase in QOL and shoulder ROM and a decrease in CRF and pain scores. In contrast, the CON group showed a decrease in QOL and shoulder ROM and an increase in CRF and pain scores.</td>
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<tr>
<td>Milne et al., 2008</td>
<td>58 breast cancer survivors within two years of completing adjuvant therapy</td>
<td>Randomized, controlled trial: IE group versus DE group</td>
<td>Schwartz Cancer Fatigue Scale</td>
<td>12 weeks of supervised AE and RE, three times per week</td>
<td>QOL significantly increased in the IE group from baseline to 12 weeks and from 12–24 weeks compared to the DE group.</td>
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<td><strong>HOME-BASED EXERCISE</strong></td>
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<tr>
<td>Headley et al., 2004</td>
<td>32 women with advanced breast cancer who were beginning outpatient chemotherapy</td>
<td>Randomized, controlled, longitudinal trial: intervention group versus CON group</td>
<td>Functional Assessment of Chronic Illness Therapy–Fatigue, version IV</td>
<td>Seated exercise program using home videotapes three times per week for four cycles of chemotherapy</td>
<td>The intervention group showed significantly less increase in fatigue and slower decrease in physical QOL than the CON group.</td>
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<tr>
<td>Mock et al., 2001</td>
<td>52 patients with breast cancer receiving radiotherapy or chemotherapy</td>
<td>Multi-institutional randomized, controlled trial: intervention group versus CON group</td>
<td>PFS</td>
<td>Home-based exercise intervention (six weeks of radiotherapy and 4–6 months of chemotherapy) at least 10–30 minutes per session, with 5–6 sessions per week</td>
<td>Women who exercised at least 90 minutes per week over the course of three or more days reported significantly less fatigue and emotional distress and higher functional ability and QOL than women who were less active during treatment.</td>
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<tr>
<td>Mock et al., 2005</td>
<td>119 patients with breast cancer receiving adjuvant chemotherapy or radiotherapy</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>PFS</td>
<td>Home-based, moderate-intensity walking exercise program 5–6 times per week during cancer treatment</td>
<td>Of participants randomized to exercise, 72% adhered to the exercise; 61% of the CON group adhered. A significant decrease was reported in fatigue for intervention group.</td>
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<tr>
<td>Pinto et al., 2005</td>
<td>86 patients with breast cancer who had completed treatment</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>Linear analog scale for fatigue</td>
<td>Home-based physical activity intervention for 12 weeks, with at least 10–30 minutes per day for at least 2–5 days per week</td>
<td>Significant improvements were observed in vigor in the intervention group, in addition to a reduction in fatigue. A positive trend existed in the intervention’s effects on overall mood and body esteem.</td>
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<td>Schwartz et al., 2001</td>
<td>72 patients with breast cancer receiving adjuvant chemotherapy</td>
<td>Pretest and posttest, single-group design</td>
<td>VAS-F</td>
<td>Home-based, moderate-intensity exercise intervention for 15–30 minutes, 3–4 days per week for eight weeks</td>
<td>Exercise significantly reduced levels of fatigue.</td>
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ABMT—autologous bone marrow or peripheral blood stem cell transplantation; AE—aerobic exercise; AET—aerobic exercise therapy; BFI—Brief Fatigue Inventory; CCSP—comprehensive coping strategy program; CON—control; CRF—cancer-related fatigue; DE—delayed exercise; FACT—Functional Assessment of Cancer Therapy; HRQOL—health-related quality of life; IE—immediate exercise; MFI—Multidimensional Fatigue Inventory; PFS—Piper Fatigue Scale; PT—polarity therapy; QOL—quality of life; RE—resistance exercise; RET—resistance exercise training; ROM—range of motion; TIP-C—telephone interpersonal counseling; UC—usual care; VAS-F—Visual Analogue Scale for Fatigue
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<td>Yuen &amp; Sword, 2007</td>
<td>22 breast cancer survivors who completed treatment</td>
<td>Three-armed, randomized, controlled trial: AE, RE, and UC</td>
<td>PFS</td>
<td>Home-based exercise three times per week for 12 weeks</td>
<td>Significantly reduced fatigue levels were observed in AE group, as well as improved six-minute walk test scores for RE group. No significant changes in fatigue or functional status were found in UC group.</td>
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<td><strong>OTHER STRATEGIES TO PROMOTE EXERCISE</strong></td>
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<tr>
<td>Pinto et al., 2008</td>
<td>25 breast cancer survivors who completed treatment at least three months earlier</td>
<td>Pretest and post-test, single-group design</td>
<td>FACT-Fatigue</td>
<td>Telephone-based intervention to encourage participants to adopt moderate-intensity physical activity, followed up 12 weeks later</td>
<td>At 12 weeks, significant increases were found in participants’ physical activity and improvements in fatigue, QOL, and vigor.</td>
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<td>Vallance et al., 2007</td>
<td>377 breast cancer survivors who completed adjuvant therapy</td>
<td>Three-armed, randomized, controlled trial: a standard public health recommendation for physical activity, a step pedometer, and a combination of breast-cancer-specific print materials and step pedometers</td>
<td>FACT-Anemia</td>
<td>Print materials and step pedometers, followed over 12 weeks</td>
<td>The combined group reported significantly improved QOL and reduced fatigue compared with the standard recommendation group.</td>
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<td>Badger et al., 2005</td>
<td>48 patients with breast cancer receiving treatment</td>
<td>Repeated-measures experimental design of intervention and CON group</td>
<td>MFI</td>
<td>TIP-C for six weeks</td>
<td>Only an increase in positive affect and a decrease in stress were found to be statistically significant. Trends were found for decreases over time in depression, negative affect, and fatigue for the TIP-C group.</td>
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<td>Fillion et al., 2008</td>
<td>87 breast cancer survivors who completed treatment</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>MFI</td>
<td>Brief group intervention combined stress management psycho-education and physical activity intervention over four weeks</td>
<td>The intervention group showed greater improvement in fatigue, energy level, and emotional distress at a three-month follow-up, and physical QOL at post-intervention, compared with the CON group.</td>
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<tr>
<td>Gaston-Johansson et al., 2000</td>
<td>110 patients with breast cancer who underwent ABMT</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>VAS-F, a 100 mm vertical VAS</td>
<td>CCSP composed of preparatory information, cognitive restructuring, and relaxation with guided imagery taught to patients two weeks before hospital admission</td>
<td>CCSP was found to be effective in significantly reducing nausea and nausea with fatigue seven days after ABMT.</td>
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ABMT—autologous bone marrow or peripheral blood stem cell transplantation; AE—aerobic exercise; AET—aerobic exercise therapy; BFI—Brief Fatigue Inventory; CCSP—comprehensive coping strategy program; CON—control; CRF—cancer-related fatigue; DE—delayed exercise; FACT—Functional Assessment of Cancer Therapy; HRQOL—health-related quality of life; IE—immediate exercise; MFI—Multidimensional Fatigue Inventory; PFS—Piper Fatigue Scale; PT—polarity therapy; QOL—quality of life; RE—resistance exercise; RET—resistance exercise training; ROM—range of motion; TIP-C—telephone interpersonal counseling; UC—usual care; VAS-F—Visual Analogue Scale for Fatigue.
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<td>Molassiotis et al., 2009</td>
<td>54 patients with breast cancer and 110 patients with colorectal cancer receiving oral chemotherapy</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>National Cancer Institute’s Common Toxicity Criteria</td>
<td>Homecare program by a nurse for 18 weeks</td>
<td>The homecare group reported significant improvement in fatigue, oral mucositis, diarrhea, constipation, nausea, pain, and insomnia in the first four cycles of chemotherapy.</td>
</tr>
<tr>
<td>Yates et al., 2005</td>
<td>109 patients with breast cancer receiving adjuvant chemotherapy</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>Revised PFS, FACT-Fatigue, and 11-point numeric rating scales</td>
<td>Individualized fatigue education and support program delivered in the clinic and by phone over 10–20 minute sessions one week apart</td>
<td>The increases between baseline and immediate postintervention fatigue scores were significantly greater for the CON group when compared with the intervention group. No significant effect was observed on cancer self-efficacy, QOL, and psychological well-being.</td>
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<td><strong>SLEEP THERAPY</strong></td>
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<td>Berger, Kuhn, Farr, Von Essen et al., 2009</td>
<td>219 patients with breast cancer receiving breast cancer adjuvant chemotherapy treatment</td>
<td>Randomized, controlled trial: behavior therapy group versus healthy-eating CON group</td>
<td>PFS</td>
<td>Behavior therapy plan two days before each chemotherapy treatment and 30, 60, and 90 days after the last treatment</td>
<td>The behavior therapy group experienced significant improvement on global sleep quality but not on objective sleep or fatigue outcomes more than one year after treatment.</td>
</tr>
<tr>
<td>Dirksen &amp; Epstein, 2008</td>
<td>72 patients with breast cancer after first treatment</td>
<td>Randomized, experimental design with two groups and pretest/post-test</td>
<td>Profile of Mood States fatigue-inertia subscale</td>
<td>Cognitive-behavior therapy for 10 weeks</td>
<td>Women receiving cognitive-behavior therapy had significant improvements in fatigue, trait anxiety, depression, and QOL.</td>
</tr>
<tr>
<td>Savard et al., 2005</td>
<td>57 women with chronic insomnia secondary to breast cancer</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>MFI</td>
<td>Cognitive-behavior therapy for eight weeks</td>
<td>Women receiving insomnia treatment intervention had significantly greater global QOL than those in the CON group. A significant difference was observed between pre- and post-treatment fatigue scores in intervention group.</td>
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<td><strong>COMPLEMENTARY THERAPIES</strong></td>
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<td>Danhauer et al., 2009</td>
<td>44 patients with breast cancer undergoing cancer treatment</td>
<td>Randomized, controlled trial: intervention group versus CON group</td>
<td>FACT-Fatigue</td>
<td>Restorative yoga for 10 weekly, 75-minute classes</td>
<td>The yoga group reported significant improvement in fatigue; no significant difference was found for the CON group.</td>
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<tr>
<td>Galantino et al., 2003</td>
<td>11 breast cancer survivors who had undergone adjuvant therapy in past year</td>
<td>Pilot study with two intervention groups</td>
<td>BFI</td>
<td>Tai chi and walking program for one hour, three times per week for six weeks</td>
<td>Although both interventions fostered a trend toward decreased fatigue, they did not reach statistical significance.</td>
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<tr>
<td>Roscoe et al., 2005</td>
<td>15 patients with breast cancer undergoing radiation therapy</td>
<td>Pilot study of three groups: received standard care, received PT at week 1, and received PT week 1 and week 2</td>
<td>Functional Assessment of Chronic Illness Therapy–Fatigue, version IV</td>
<td>PT was given to patients one or two times during treatment.</td>
<td>A significant improvement was observed in both CRF and HRQOL in the 10 patients who received PT compared to the five CON patients.</td>
</tr>
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</table>

ABMT—autologous bone marrow or peripheral blood stem cell transplantation; AE—aerobic exercise; AET—aerobic exercise therapy; BFI—Brief Fatigue Inventory; CCSP—comprehensive coping strategy program; CON—control; CRF—cancer-related fatigue; DE—delayed exercise; FACT—Functional Assessment of Cancer Therapy; HRQOL—health-related quality of life; IE—immediate exercise; MFI—Multidimensional Fatigue Inventory; PFS—Piper Fatigue Scale; PT—polarity therapy; QOL—quality of life; RE—resistance exercise; RET—resistance exercise training; ROM—range of motion; TIP-C—telephone interpersonal counseling; UC—usual care; VAS-F—Visual Analogue Scale for Fatigue.
reducing CRF and improving QOL in patients with breast cancer. Of the eight studies, four showed that supervised exercise significantly improved QOL and reduced CRF in women with breast cancer (Courneya, Segal, Gelmon, et al., 2007; Heim et al., 2007; Hwang et al., 2008; Milne et al., 2008). Two studies reported that supervised exercise was effective only in significant improvement of QOL, not CRF (Campbell et al., 2005; Daley et al., 2007). In one, Daley et al. (2007) noted some limitations that might affect the study results, reporting that some intervention contamination occurred in the exercise-placebo and usual care groups because the placebo group believed they had been assigned to an active exercise arm. As a result, participants in the placebo group increased their activity outside of placebo intervention sessions. In addition, a type I error may have occurred because of multiple statistical testing. A study conducted by Campbell et al. (2005) also had a limitation to the generalizability of the study because of the small sample size (N = 22). Therefore, future research is warranted to confirm the results of these studies.

In addition to the six studies, a study conducted by Drouin et al. (2005) showed that women with breast cancer who were supervised in performing moderate-intensity aerobic exercise significantly improved peak aerobic capacity, fatigue, and mood subscale factors of anger-hostility, depression-dejection, and tension-anxiety. Unfortunately, the study did not examine whether aerobic exercise training would be effective in improving QOL among patients with breast cancer. Finally, a large multicenter, randomized, controlled trial conducted by Courneya, Segal, Mackey, et al. (2007) showed that supervised aerobic exercise was effective in improving self-esteem, muscular strength, lean body mass, aerobic fitness, and body fat percentage. However, changes in QOL, fatigue, depression, and anxiety did not reach statistical significance, although a trend toward improvement in the exercise groups was observed. The authors realize that some limitations exist in the study, including the 70% adherence rate and a homogenous sample of well-educated survivors. Therefore, one may conclude that, despite some inconsistency in findings and some limitations in the previous studies, the research evidence is sufficient for clinical nurses to encourage patients with breast cancer to maintain an optimal level of supervised exercise as it is beneficial in physical (e.g., muscular strength, aerobic capacity) and psychological aspects (e.g., depression, anxiety) related to CRF and QOL of patients with breast cancer. No deleterious effects were reported.

A home-based exercise program likely is a feasible and effective intervention to manage CRF for patients with breast cancer. All seven studies produced consistent findings regarding the effectiveness of home-based exercise to reduce CRF in patients with breast cancer (Headley, Owny, & John, 2004; Mock et al., 2001, 2005; Pinto, Frierson, Rabin, Trunzo, & Marcus, 2005; Schwartz, 2000; Schwartz, Mori, Gao, Nail, & King, 2001; Yuen & Sword, 2007). Unfortunately, only two previous studies (Headley et al., 2004; Mock et al., 2001) investigated QOL as an outcome variable. First, Mock et al. (2001) reported that women with breast cancer who exercised three or more days per week for at least 90 minutes total reported significantly less fatigue, emotional distress, and higher functional ability and QOL than women who were less active during treatment. The study had strength because it was a randomized, controlled trial conducted in multiple institutions, but the small sample size (N = 52) was a limitation.

Similarly, Headley et al. (2004) reported that women with advanced breast cancer who performed seated exercise using home videotapes three times per week for four cycles of chemotherapy had a slower decline in total and physical QOL and lower fatigue scores than women in the control group. The authors noted that the interpretation of the study must be cautious because of the small sample size (N = 38) and the differences in marital status between participants in the intervention group and the control group that might affect outcomes such as fatigue and QOL. Accordingly, these limitations should be considered for further research. Therefore, based on the available studies in the literature, one may conclude that home-based exercise during and after cancer treatment should be recommended for patients with breast cancer along the treatment continuum as it may reduce CRF and improve QOL.

Two strategies have been used to promote exercise that could reduce CRF and increase QOL for patients with breast cancer: use of print materials combined with step pedometers and use of trained volunteers. With regard to breast cancer-specific physical activity print materials and step pedometers, Vallance, Courneya, Plotnikoff, Yasui, and Mackey (2007) conducted a large randomized, controlled trial to investigate the effects of these methods on physical activity and QOL in 377 breast cancer survivors. The results showed that participants in the combined group who received breast cancer-specific print materials and step pedometers reported significantly improved QOL and reduced fatigue compared to those who received the standard recommendation for physical activity. The strengths of this study included a large sample size and minimal number lost to follow-up, but the study was limited by the self-report of physical activity, failure to blind survivors from their pedometer step count during baseline and postintervention testing, and multiple statistical testing.

In terms of trained volunteers, a pilot study by Pinto, Rabin, Abdow, and Papandonatos (2008) demonstrated that trained volunteers could feasibly deliver telephone-based physical activity interventions to breast cancer survivors. After receiving 12 weekly calls from trained volunteers to encourage participants to adopt moderate-intensity physical activity, significant increases occurred in participants’ physical activity and improvements in fatigue, QOL, and vigor were noted. Effects also were maintained at 24 weeks. The limitations of this study were the small sample size (N = 25) and the use of a single-group design. However, one may conclude that although only two studies exist that examined strategies to promote exercise, which could reduce CRF and increase QOL for patients with breast cancer, the preliminary evidence gives clinical nurses techniques that may be useful in encouraging patients with breast cancer to engage in physical activity.

**Education and Counseling**

Education and counseling about CRF, its adverse effects, and strategies to deal with it have been reported to greatly benefit...
patients with breast cancer in coping with CRF, particularly those beginning potentially fatigue-inducing treatments (NCCN, 2010). Five reviewed studies employed educational and counseling interventions to reduce CRF and/or improve QOL in patients with breast cancer (Badger et al., 2005; Fillion et al., 2008; Gaston-Johansson et al., 2000; Molassiotis et al., 2009; Yates et al., 2005). These studies used a variety of educational and counseling intervention methods.

Telephone counseling is one effective method of providing CRF education. A preliminary study by Badger et al. (2005) showed that patients with breast cancer who received six-week telephone interpersonal counseling reported decreased fatigue, stress, and depression, as well as increased positive affect over time. They hypothesized that fatigue might be reduced through psychological aspects, such as decreasing depression and stress. However, future research is needed to explain that hypothesis because the study was conducted with a small sample size (N = 48). In addition, because the telephone counseling intervention was offered for only six weeks, the authors suggested future research to investigate whether an increased number of sessions would be more beneficial to the patients for symptom management and QOL.

A combined stress management, psychoeducation, and physical activity intervention is another feasible and effective strategy to improve QOL and reduce CRF in breast cancer survivors. A randomized, controlled trial by Fillion et al. (2008) showed that participants who received a brief psychoeducational group intervention focusing on active coping strategies and physical activity reported greater improvement in fatigue, energy level, and emotional distress at the three-month follow-up, and physical QOL at postintervention compared to participants in the control group. The authors noted that the generalizability of the findings was limited because of a majority of well-educated participants, a small sample size (N = 87), and the multilevel aspect of the intervention in terms of the psychoeducative versus exercise component. Additional research should be conducted to close those gaps. For instance, conducting research in low-educated samples, increasing sample size, and examining the effect of psychoeducative programs on exercise would be helpful.

Yates et al. (2005) conducted a randomized, controlled trial of an educational intervention for managing fatigue in 109 women receiving adjuvant chemotherapy for early-stage breast cancer. The results showed that preparatory education and support resulted in short-term benefits (one to two weeks after completion of the intervention) in terms of reducing intensity of CRF and its impact on daily life. Compared to the control group, patients in the intervention group reported a significantly greater mean increase in the number of fatigue-management actions recommended by healthcare providers. Unfortunately, the effectiveness of this intervention in the long-term period was not found. The authors realized that issues such as accuracy and quality in delivering interventions, the appropriateness of the strategies used for the problem, the dose or intensity of the intervention, the use of subjective rather than objective measures of CRF, and measurement error might affect the study results. Therefore, future research is needed to overcome those gaps and to evaluate whether the educational and support intervention is effective in reducing CRF among patients with breast cancer over a long-term period.

Another form of education to improve QOL in patients with breast cancer with CRF is a home care nursing program, which includes symptom assessment, patient education, and/or treatment on the basis of agreed-upon protocols through a standard home visit and phone call during cancer treatment. A randomized, controlled trial by Molassiotis et al. (2009) showed that a home care program by a nurse during treatment cycles (18 weeks) was able to assist patients with breast or colorectal cancer in managing their treatment’s adverse effects (e.g., fatigue, oral mucositis, diarrhea, constipation, nausea, pain, insomnia) better than standard care, particularly during the first few weeks of treatment. However, the QOL scores measured by the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire—Core 30 were not different between the two groups, except for the financial outcome, which was statistically significantly improved in the home care group (p < 0.05). The authors explained that this finding might be related to the instrument used in the study, because of lack of sensitivity of the instrument, lack of relevant content to the individual patient, and inappropriate timing of the assessment. Therefore, future studies may consider using other instruments that may be more specific and appropriate to measure HRQOL and also consider a more appropriate assessment time.

Finally, a randomized, controlled trial conducted by Gaston-Johansson et al. (2000) showed that the comprehensive coping strategy program, composed of preparatory information, cognitive restructuring, and relaxation with guided imagery, was effective in reducing fatigue and nausea in patients with breast cancer who underwent autologous bone marrow transplantation. However, the study did not investigate whether the comprehensive coping strategy program was effective in improving QOL. In addition, because the sample in the study was predominantly Caucasian, married, well-educated, and affluent, the generalizability of the findings is limited to other races or ethnicities and lower income or education levels. Accordingly, future research should use a more diverse sample in terms of sociodemographics.

Although the previous studies regarding education and counseling strategies require further work because of various limitations, telephone counseling; a combined stress management, psychoeducation, and physical activity intervention; home care nursing programs; and comprehensive coping strategy programs all are potentially beneficial nonpharmacologic supportive strategies that may be applied in clinical practices for patients with breast cancer suffering from CRF.

Sleep Therapy

Although CRF and cancer-related sleep disorders are distinct, previous studies provided evidence supporting a strong correlation between CRF and sleep disorders in patients with breast cancer (Ancoli-Israel et al., 2006; Bower et al., 2000; Okuyama et al., 2000; Servaes, Verhagen, & Bleijenberg, 2002). The possibility of a reciprocal relationship underscores potential strategies to reduce CRF by improving sleep quality (Roscoe et al., 2007). One approach of nonpharmacologic supportive interventions to optimize sleep quality and also decrease CRF in patients with breast cancer is cognitive-behavior therapy intervention. In two randomized, controlled trials, behavior therapy was effective in improving sleep, CRF, and QOL in women with breast cancer (Dirksken & Epstein, 2008; Savard, Simard, Ivers, & Morin, 2005).
However, the small sample size and lack of variance in population (participants were predominantly Caucasian, well-educated, and affluent), limit the generalizability of study findings to diverse populations, such as those in Hispanic or Asian ethnic groups and lower education or income levels.

Berger, Kuhn, Farr, Von Essen, et al. (2009) reported that the behavior therapy sleep intervention, which included stimulus control, modified sleep restriction, relaxation insomnia, and sleep hygiene counseling, resulted in improvements in global sleep quality, but not fatigue, in women with breast cancer more than one year after adjuvant chemotherapy treatment. The authors explained that the potential impact of the behavior therapy sleep intervention might be reduced by the lack of variance because participants reported lower fatigue and better sleep at baseline than expected. Therefore, additional research is needed to explore the impact of this intervention with patients who reported moderate-to-severe insomnia and high fatigue prior to and during breast cancer treatment. In terms of clinical practices, nurses also can combine a cognitive-behavior intervention with other strategies in helping patients with breast cancer suffering from CRF because sleep disorder seems to be related to CRF in this population (Servaes et al., 2002).

Complementary Therapies

Three reviewed studies investigated the effects of complementary therapies on reducing CRF and improving QOL in patients with breast cancer (Danhauser et al., 2009; Galantino et al., 2003; Roscoe, Matteson, Mustian, Padmanaban, & Morrow, 2005). The complementary therapies used were tai chi, restorative yoga, and polarity therapy. First, Galantino et al. (2003) conducted a pilot study with 11 breast cancer survivors undergoing adjuvant therapy to examine the effect of tai chi and walking on CRF. The results showed no significant reduction in fatigue in either group, which the authors explained might be related to small sample size. The study did not investigate whether tai chi would be effective in improving QOL in patients with breast cancer; therefore, additional research is needed to examine the effects of tai chi on reducing CRF and improving QOL in patients with breast cancer.

Another type of complementary therapy used to reduce CRF in patients with breast cancer was restorative yoga. A pilot study with pretest and post-test design conducted by Danhauer et al. (2009) showed that patients with breast cancer who attended a yoga group reported a significant improvement in fatigue, whereas no significant difference was found in the control group. The results also showed that women who started with higher negative affect and lower emotional well-being derived greater benefit from the restorative yoga intervention compared to the control group. However, HRQOL and fatigue were not significantly different between the two groups. The major limitations of the study were small sample size (N = 44) and multiple statistical comparisons. Therefore, future research should involve large randomized, controlled trials to confirm the results of this study.

Polarity therapy is another complementary therapy used to enhance QOL for patients with breast cancer suffering from CRF. Polarity therapy is an energy therapy that uses gentle human touch to balance energy fields of living organisms and re-store a state of well-being (Roscoe et al., 2005). A randomized, controlled trial by Roscoe et al. (2005) showed a statistically significant improvement in both CRF and HRQOL in patients with breast cancer undergoing radiotherapy who received a polarity therapy compared to those in the control group. The study finding suggests that energy therapy such as the polarity approach may have positive benefits on improving CRF and HRQOL for patients with breast cancer. However, this is the only published study to investigate the efficacy of polarity therapy in patients with breast cancer with CRF. Importantly, because the study was conducted with a small sample size (N = 15), further research is needed to establish a sufficient scientific evidence base regarding the efficacy of polarity therapy on CRF and HRQOL among patients with breast cancer (Mustian et al., 2007).

Despite some benefits of complementary therapy in reducing CRF and improving QOL for patients with breast cancer, few studies exist researching these nonpharmacologic supportive strategies. Many types of complementary therapies (e.g., acupuncture, therapeutic touch, Reiki) are frequently used by patients with breast cancer to reduce distress from side effects of cancer treatment (Wanchai, Armer, & Stewart, 2010). Therefore, additional research still is needed regarding these particular strategies.

Implications for Nursing

This review highlights several implications for healthcare providers who work with patients with breast cancer experiencing CRF. In terms of CRF assessment, two subcategories of instruments used for CRF assessment appeared in the reviewed studies: (a) unidimensional scales, such as the Profile of Mood States fatigue-inertia subscale (Dirksen & Epstein, 2008), the linear analog scale (Pinto et al., 2005), and a verbal rating scale as applied in the National Cancer Institute’s Common Toxicity Criteria (NCI-CTC); and (b) multidimensional assessment tools, such as the Piper Fatigue Scale (Berger et al., 2009; Mock 2001, 2005; Yuen & Sword, 2007), the Functional Assessment of Cancer Therapy-Anemia (Courneya, Segal, Gelmon, et al., 2007; Courneya, Segal, Mackey, et al., 2007; Vallance et al., 2007), and the Multidimensional Fatigue Inventory (Badger et al., 2005; Fillion et al., 2008; Heim et al., 2007; Savard et al., 2005). These instruments address CRF in different ways. For instance, the Piper Fatigue Scale addresses the severity, distress, and impact of fatigue, whereas the verbal rating scale in the NCI-CTC measures severity of fatigue (Portenoy & Itri, 1999). In the context of clinical practices, nurses should consider the details of each tool and select one that is appropriate for the patient situation and clinical research questions.

In terms of nonpharmacologic supportive strategies, previous studies have shown consistent support for exercise interventions in reducing CRF and enhancing QOL in patients with breast cancer both during and after treatment. Therefore, motivating and encouraging patients with breast cancer to engage in exercise would be beneficial. Based on this literature review, home-based exercise, supervised exercise, and other strategies to promote exercise could reduce CRF and improve QOL for patients with breast cancer. However, because of small sample sizes in previous studies, application should be
carefully considered. According to Lucía, Earnest, and Pérez (2003) and NCCN (2010), exercise prescriptions should be individualized given the many factors that can influence exercise tolerance of each person (e.g., severity of disease, age, gender, chemotherapy dose). To obtain the most benefits of exercise, patients with cancer should exercise in at least 15- to 20-minute sessions of low-to-moderate aerobic activity three to five days a week, with a maximum heart rate from 55%–85% (Drouin et al., 2005; Hwang et al., 2008; Lucía et al., 2003).

Education and counseling also were likely to be effective in reducing CRF and enhancing QOL in patients with breast cancer. Healthcare providers should consider these nonpharmacologic supportive strategies as adjunctive interventions to pharmacologic intervention in ameliorating CRF in this population. At a minimum, preparing information on CRF and its management for patients with breast cancer before starting cancer treatments that may contribute to CRF may be helpful (Yates et al., 2005). A variety of educational methods such as telephone support, comprehensive coping strategy, combined stress management and physical activity, or even nurse-in-home visits can be used to inform patients on self-management of CRF (Badger et al., 2005; Fillion et al., 2008; Gaston-Johansson et al., 2000; Molassiotis et al., 2009; Yates et al., 2005). However, because few studies examined the effects of educational methods on reducing CRF and enhancing QOL, the authors cannot determine which method was most effective. Therefore, additional research to determine which method is best or most appropriate in practice is needed.

Previous studies have shown that sleep therapy was effective not only in reducing CRF by improving sleep quality but also in improving other psychosocial symptoms related to CRF (e.g., anxiety, depression). Therefore, assessing sleep quality and potentially intervening with sleep therapy when patients with breast cancer report CRF is imperative (Berger, Kuhn, Farr, Lynch, et al., 2009; Berger, Kuhn, Farr, Von Essen, et al., 2009; Dirksen & Epstein, 2008). Healthcare providers may apply three components of behavior therapy (stimulus control, sleep restriction, and sleep hygiene) to optimize sleep quality for patients with breast cancer because poor sleep quality can increase CRF.

With regard to stimulus control, the following suggestions should be provided to patients with breast cancer: going to bed at the same time each night or when sleepy, maintaining a regular rising time each day, and getting out of bed after 20 minutes if unable to fall sleep. For the sleep restriction principle, healthcare providers should inform patients with breast cancer to avoid afternoon naps and limit total time in bed. Finally, the sleep hygiene principle can be used by educating patients with breast cancer to avoid caffeine in the afternoon and also to establish an environment that can promote sleep, such as preparing a dark, quiet, and comfortable bedroom (NCCN, 2010).

Combining behavior therapy with complementary therapies such as tai chi, restorative yoga, and polarity therapy also may be considered as they could help the patients relax (Danhauser et al., 2009; Galantino et al., 2003; Roscoe et al., 2005). However, because only three pilot studies reported the efficacy of the complementary therapies in reducing CRF and improving QOL among patients with breast cancer, future research to confirm these findings is warranted.

Although the reviewed studies are promising—as the majority were randomized, controlled trials—the findings need to be treated with caution because of methodologic limitations. For example, many studies were conducted with a small sample size and lacked power size calculations. Consequently, more work with larger randomized, controlled trials is required. In addition, future research to investigate the interventions that can reduce CRF and improve QOL in the long-term is required because studies have shown that breast cancer survivors can experience CRF up to 10 years after treatment (Bower et al., 2000; Yates et al., 2005). Based on this literature review, although one study considered women with advanced disease experiencing CRF (Headley et al., 2004), no study has examined the efficacy of nonpharmacologic supportive interventions for patients with breast cancer experiencing CRF at the end of life. Therefore, additional research should be considered for this particular area. Finally, because the samples in these studies were predominantly highly educated Caucasian women from higher income levels, additional research in diverse populations such as Asians or African Americans and people with lower education or income levels is warranted.

**Conclusion**

CRF is a pervasive issue in patients with breast cancer during and after treatment, and healthcare providers should be concerned with CRF symptoms experienced by these patients. Based on data currently available, exercise, education and counseling, sleep therapy, and complementary therapy appear to be helpful methods in improving QOL in patients with breast cancer experiencing CRF. However, because of the methodologic limitations of previous studies, further research using randomized, controlled trials is needed to confirm the effectiveness of these strategies.

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