The Effect of Seated Exercise on Fatigue and Quality of Life in Women With Advanced Breast Cancer

Judith A. Headley, RN, PhD, AOCN®, CCRP,
Kristin K. Ownby, RN, PhD, ACRN, AOCN®, CHPN, and Lauri D. John, PhD, RN, CNS

Purpose/Objectives: To examine the effects of a seated exercise program on fatigue and quality of life (QOL) in women with metastatic breast cancer.

Design: Randomized, controlled, longitudinal trial.

Setting: Outpatient clinic of a comprehensive cancer center.

Sample: Convenience sample of 38 women who were beginning outpatient chemotherapy.

Methods: Subjects were randomized to a control or intervention group; the intervention was performance of a seated exercise program using home videotape three times per week for four cycles of chemotherapy. All subjects completed the Functional Assessment of Chronic Illness Therapy–Fatigue Version IV (FACIT–F) at baseline and at the time of the next three cycles. Subjects were asked to document the frequency, duration, and intensity of all exercise participation on monthly calendars.

Main Research Variables: Exercise, fatigue, and QOL.

Findings: 32 subjects, 16 per group, completed the study follow-up. With a mixed modeling approach, total FACIT–F scores for the entire sample declined at a significant rate ($p = 0.003$) beginning with cycle 3 but at a slower rate for the experimental group ($p = 0.02$). Fatigue scores indicated less increase and physical well-being subscale scores showed less decline for the experimental group ($p = 0.008$ and $p = 0.02$, respectively).

Conclusions: Women with advanced breast cancer randomized to the seated exercise intervention had a slower decline in total and physical well-being and less increase in fatigue scores starting with the third cycle of chemotherapy.

Implications for Nursing: Seated exercise may be a feasible exercise program for women with advanced cancer for controlling fatigue and improving physical well-being.

Key Points . . .

- Fatigue is a debilitating and complex symptom in patients with advanced cancer and has been understudied in this population in the literature.
- This study suggests that participation in low- to moderate-intensity exercise such as seated exercise may mitigate the increase in fatigue over time that commonly occurs with chemotherapy treatment.
- Adherence is a factor that must be addressed when investigating exercise interventions for fatigue in patients with cancer and needs further study.

More than three-fourths of patients with cancer have debilitating fatigue, and almost one-third report fatigue on a daily basis. Literature has shown that fatigue is experienced by 75%–99% of patients with cancer receiving chemotherapy (Nail & Jones, 1995) and that it increases with each cycle of treatment (Headley, 1997; Woo, Dibble, Piper, Keating, & Weiss, 1998). The presence of fatigue has been associated with chemotherapy dose limitation or discontinuation of therapy (Skalla & Rieger, 1995; Whedon, Stearns, & Mills, 1995; Winningham et al., 1994).

About 50% of patients with cancer have reported a preference for nonpharmacologic interventions to manage fatigue (National Comprehensive Cancer Network [NCCN], 2001). Research studies have demonstrated that exercise is the nonpharmacologic intervention with the strongest evidence of therapeutic benefit for managing fatigue (Dimeo, 2001; NCCN). Findings of studies that tested the intensity levels of aerobic exercise indicated that exercise of low to moderate intensity has beneficial effects on physical fitness and selected psychological parameters, such as coping ability (Dimeo, Tilmann, et al., 1997; Winningham, 1991).

Research studies have shown that walking exercise programs decrease fatigue and improve quality of life (QOL) in patients with breast cancer receiving treatment for local or regional disease (Mock et al., 1994, 1997; Sitzia & Huggins, 1998). Although the significance of fatigue in patients with metastatic disease has been well documented, little research has explored exercise interventions for fatigue in women with advanced breast cancer (Courneya & Friedenreich, 1999; Messias, Yeager, Dibble, & Dodd, 1997). The purposes of this pilot study were to (a) examine perceptions of fatigue and the effects of a seated exercise program over time on fatigue and QOL in patients with breast cancer receiving chemotherapy for distant metastases and (b) determine the feasibility of a larger study.

At the time this article was written, Judith A. Headley, RN, PhD, AOCN®, CCRP, was an associate professor of clinical nursing in the Houston School of Nursing at the University of Texas Health Science Center; she currently is the oncology nurse specialist at CorSolutions, Inc., in Rosemont, IL. Kristin K. Ownby, RN, PhD, ACRN, AOCN®, CHPN, is an assistant professor of clinical nursing in the Houston School of Nursing at the University of Texas Health Science Center, and Lauri D. John, PhD, RN, CNS, is an assistant professor of clinical nursing in the Austin School of Nursing at the University of Texas. *This study was funded by the 1999 Hoechst Marion Roussel, Inc., Research Grant from the ONS Foundation and the University of Texas Health Science Center in the Houston School of Nursing. (Submitted June 2003. Accepted for publication October 31, 2003.)*

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Background and Literature Review

Fatigue can continue for years after the completion of cancer therapy, especially chemotherapy. Treatment-related fatigue is chronic, persistent, profound, and usually unrelieved by rest (Nail & Jones, 1995). The prevalence of severe fatigue is lower in patients with newly diagnosed breast cancer (15%) and increases as the cancer becomes more advanced (78%) (Stone, Richards, A'Hern, & Hardy, 2000). Surveys of patients with metastatic disease have shown that the prevalence of fatigue ranges from 60%–90% (Barnes & Bruera, 2002; Cella, Davis, Breitbart, & Curt, 2001; Portenoy et al., 1994).

Patients with cancer have identified fatigue as the longest lasting and most disruptive symptom experienced during and after cancer treatment (Curt et al., 2000). Fatigue has been found to negatively affect QOL (Ashbury, Findlay, Reynolds, & McKerracher, 1998), pain tolerance (Cella, Peterman, Passik, Jacobsen, & Breitbart, 1998; Dodd et al., 2001), cognition (Valentine & Meyers, 2001), mood (Woo et al., 1998), and sleep (Berger & Higginbotham, 2000). Fatigue also has been associated with increased caregiver hours (Jensen & Given, 1993).

Fatigue has been related to inactivity that resulted in loss of muscle mass and reduced cardiac output, leaving patients with cancer in a deconditioned state (Barnes & Bruera, 2002). Winningham et al. (1994) found that a cycle of decreasing activity and increasing fatigue led to accelerated deterioration and deconditioning that resulted in patients fatiguing more quickly when they participated in activity. Researchers have found an inverse relationship between physical activity and fatigue during cancer treatment (Berger, 1998; Berger & Farr, 1999; Hickok, Roscoe, Morrow, & Bushunow, 1998). A positive relationship has been found between fatigue and restless sleep at night in patients with cancer that was associated with decreased activity levels during the day (Mormont et al., 2000). Chronic fatigue has led to decreased tolerance for performing activities of daily living (Nail, Jones, Greene, Schipper, & Jensen, 1991), which has gained increased importance with the current trend toward outpatient treatment.

Physical exercise after cancer diagnosis consistently has been found to have a positive effect on QOL parameters, including physical, functional, psychological, and emotional well-being (Schwartz, Mori, Gao, Nail, & King, 2001). Exercise has improved sleep quality and decreased fatigue (Dimeo, Tilmann, et al., 1997; Mock, 2003; Mock et al., 1997), decreased pain (Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997), and decreased depression (Segar et al., 1998). An integrated literature review indicated that lower levels of fatigue were reported by participants who exercised, regardless of type or length of cancer or treatment (Mock, 2001). Other outcomes related to exercise included decreased depression and anxiety, improved QOL, and increased performance (Mock, 2003).

Patients with advanced cancer have not been included in published exercise studies. Although fatigue has been documented in patients with metastatic disease (Messias et al., 1997; Sarna, 1993), little research has been reported on interventions for fatigue in patients with advanced disease. Courneya and Friedenreich (1999) reviewed studies that used exercise as an intervention to improve QOL variables. They noted the importance of conducting exercise research in patients with later-stage cancer and the need for studies that use repeated assessments of the main variables of interest to understand the timing of QOL changes that occur with physical exercise.

Although studies to date have suggested that exercise may be beneficial in relieving fatigue (Berger, 1998; Dimeo, Rumberger, & Keul, 1998; Schwartz, 1998), Portenoy and Itri (1999) noted that no data exist to delineate the most appropriate exercise program for patients with cancer. Exercise interventions for combating fatigue and improving QOL in patients with cancer have focused on cycling and walking regimens; however, no published research exists regarding the use of seated exercise programs in this population. Disability resulting from metastatic disease, influence of climate, and safety concerns have been found to interfere with participation in outdoor aerobic activity for many patients with cancer (Schwartz). Seated exercise provides an alternative to other exercises.

Stevenson and Topp (1990) conducted a study evaluating the effects of moderate- and low-intensity long-term exercise by 72 older adults. They found that a low-intensity exercise regimen, which may be safer and more feasible over time, improved fitness levels and independent functioning and promoted positive perceptions of well-being. Tate and Petruzzello (1995) studied the impact of varying intensity levels of aerobic exercise on mood in healthy volunteers. They found that both moderate- and high-intensity exercise decreased anxiety and improved affect. Findings from these studies indicate that a moderate-intensity exercise program, such as seated exercise, can have a positive impact on physiologic, functional, and psychological well-being of individuals. Nicholson, Czernwicz, Mandilas, Rudolph, and Greyling (1997) studied 40 older patients with hip fractures to determine whether a six-week chair exercise program decreased depression and improved selected physiologic parameters. Findings suggested that a six-week period of moderate-intensity exercise was adequate to stimulate cardiovascular adaptations (e.g., decreased systolic blood pressure and heart rate) and improve mood.

The literature reviewed makes apparent that fatigue is a highly prevalent symptom among patients with cancer that has a negative impact on their QOL. Exercise has been shown to be effective in relieving fatigue and improving QOL, but the majority of this research has been done with patients with early-stage breast cancer, using walking as an intervention. This pilot study aimed to examine the effects of a low- to moderate-intensity seated exercise intervention on fatigue and QOL in patients with advanced breast cancer for whom walking programs may be too intense.

Conceptual Framework

The conceptual framework that guided this research study was Roy's Adaptation Model (Roy, 1986; Roy & Andrews, 1991). The model depicts the individual as a biopsychosocial being who is able to adapt to environmental stimuli categorized as focal, contextual, or residual. In this study, the chemotherapy regimen was viewed as a focal stimulus, which leads to ineffective responses (fatigue and decreased QOL) for women with stage IV breast cancer. The researchers hypothesized that the intervention of a seated exercise program would alter subjects' coping mechanisms aimed at the focal stimulus, which would result in adaptive responses (decreased fatigue and improved QOL).

Methods

Sample and Setting

This quasi-experimental pilot study was conducted at a major comprehensive cancer center in the southwestern United States. The study was approved by the institutional review boards of the cancer center and the investigators' affiliated university. Using nonprobability consecutive sampling, the researchers invited eligible subjects waiting in the outpatient chemotherapy treatment area to participate in the study and obtained written informed consent. Participants were assigned randomly to either the control or intervention group by computer.

Participants considered for inclusion in the study included English-literate women who were at least 18 years of age, diagnosed with stage IV breast cancer, and scheduled to initiate outpatient chemotherapy. Additional inclusion criteria were having a performance status of two or less on the Zubrod scale (Stanley, 1980), being able to sit in a straight-backed chair for at least 30 minutes, and having access to a television and video cassette player. Women who had received radiation therapy during the prior two months, would be receiving high-dose chemotherapy for the purpose of bone marrow or stem cell transplantation, or would be receiving hormonal therapy as a single treatment modality were excluded. Additional exclusion criteria were serum hemoglobin level less than or equal to 8.0 g/dl, resting pain level more than 2 on a 0–10 pain scale, and symptomatic bone metastases. Using nonprobability consecutive sampling, the researchers determined that a sample size of 10 per measurement would be adequate to identify problems in design, procedure, or use of the instruments (Roscoe, 1975) for a projected sample size of 40.

Study Intervention

Those who were randomized to the intervention group were asked to participate in a 30-minute seated exercise program three times a week with at least a one-day break between sessions. The intervention involved using a commercially available video called *Armchair Fitness: Gentle Exercise* (Bernstein, 1994). The program includes a five-minute warm-up, 20 minutes of moderate-intensity repetitive motion exercises, and a five-minute cooldown. Participants sit in a straight-backed chair while performing stretching and repeated flexion and extension of the arms, head, upper torso, and legs. The video has no activities for strength or resistance training; no equipment is used. Control group participants did not engage in the seated exercise program but were permitted to continue any usual physical activity. Subjects in both groups were asked to document on monthly calendar logs the dates, times, intensity, types, and lengths of any activities, including seated exercise, if applicable, performed for the intent of physical exercise.

Instruments

Subjects completed a data form at the beginning of the study period that asked for demographic information. The form also asked for a description of exercise routines in which the subject had engaged during the previous week as well as the preceding two months. Fatigue and QOL were assessed using the **Functional Assessment of Chronic Illness Therapy–Fatigue Version IV (FACIT–F)**, which was administered at baseline and at the beginning of each course of chemotherapy for 12 weeks for a total of four measurements. The FACIT–F is a 40-item questionnaire that measures fatigue and the physical, social, emotional, and functional aspects of QOL (Cella & Webster, 1997). The instrument has had good stability ($r = 0.87$) and strong internal consistency reliability ($a = 0.95$). Convergent and divergent validity testing of the fatigue subscale have revealed a significant positive relationship with other fatigue measures, a significant negative relationship with vigor, and a lack of relationship with social desirability (Cella, 1997, 1998).

Other data collected with each cycle of chemotherapy included treatment information, cycle number, weight, height, performance status, location of metastatic disease, tumor response to treatment, current pain rating on a 0–10 scale, and current medications. Subjects were asked to document the intensity of exercise on monthly calendar logs using the **Rating of Perceived Exertion (RPE)** scale (Borg, 1970), a one-item, 12-point scale ranging from "nothing at all" to "very, very heavy." The RPE scale has been used extensively by exercise physiologists and has demonstrated strong correlation with physiologic measures of exercise intensity, including heart rate (Eston & Thompson, 1997).

Data Analysis

Descriptive statistics were used to examine all demographic data and measures of central tendency for interval level variables, including FACIT–F scores. Chi square, Fisher exact, and analysis of variance tests were performed to assess differences between groups on demographic data. To analyze the effect of the intervention, a mixed models multilevel approach similar to growth curve analysis was used. The nature of change over time for total FACIT–F scores and subscale scores was determined by examining variability in the intercept and slope. Internal consistency reliability was determined for the FACIT–F and subscales.

The data were analyzed for reliability as well as for other univariate analyses using SPSS® software (SPSS Inc., Chicago, IL). Statistical Analysis System for mixed modeling was used to analyze the effect of the intervention (Littell, Milliken, Stroup, &Wolfinger, 1996).

Results

The convenience sample consisted of 38 participants, 6 of whom did not complete the study because of disease progression, initiation of radiation therapy, or decrease in performance status, rendering them ineligible to continue. The average age of participants was 51 years (range = 37–73 years, SD = 9.43). Fisher exact test and analysis of variance were used to compare the control and experimental groups on demographic data (see Table 1). Subjects in the control group were more educated than those in the experimental group ($\overline{X} = 14.4$ years, $SD = 3.12$ versus $\overline{X} = 12.6$ years, $SD = 2.5$, respectively; $p = 0.08$) and significantly more likely to be unmarried (44% versus 6%, $p = 0.04$) than the experimental group. No significant differences existed in age, weight, or tumor response to treatment over time between the two groups. At the time of study enrollment, 12 participants (38%) documented regular exercise regimens performed at least twice weekly for a minimum of 20 minutes; eight of these women were randomized to the control group.

Table 1. Sample Demographics

Variable	Control	Intervention
$\bar{X}$ age (SD)	50.0 (7.10)	52.25 (11.43)
$\bar{X}$ education (SD)	14.4 (3.12)	12.60 (2.50)
	n	n
Marital status*		
Single	4	–
Married	9	15
Divorced or widowed	3	1
Ethnicity		
Caucasian	12	15
African American	4	1
Employment status		
Not employed	7	10
Full-time	8	6
Part-time	1	–

N = 32

* $p \leq 0.05$

Thirty-two participants completed the FACIT–F at baseline assessment, 28 at the time of the second cycle of chemotherapy, 30 at the time of the third cycle, and 24 at the time of the fourth cycle. FACIT–F scores for the entire sample decreased over time for the total scale and the physical and functional well-being subscales. However, social well-being scores remained fairly stable, and scores for the emotional well-being subscale increased slightly before returning to baseline. Fatigue scores steadily decreased over time, indicating higher levels of fatigue (see Table 2). A mixed models approach similar to growth curve analysis was used to analyze changes in scores over time in and among subjects and to analyze the effect of the intervention. This is a multilevel analysis, with the observations being the first level and individuals the second. Specifically, the time in days of each assessment was determined relative to the initial assessment. Responses then were modeled as a function of the time since baseline assessment. With the mixed modeling approach, an intercept, slope, and curvature parameters were estimated for each subject. To determine the effect of the intervention on the level and rate of change of the FACIT–F scales, the time scale was centered at 60 days after baseline, or about halfway through the assessments. This allows time for the intervention to take place and also minimizes multicollinearity with linear and quadratic terms in the model.

The total FACIT–F scores for the entire sample were examined first. Examination of the means indicated that at 60 days postbaseline, the average total score was 112.13, or about 72% of maximum. However, the slope was negative (–0.38; t[30] = –4.76; p < 0.0001), indicating that scores were declining at a rate of about one-third of a point per day, or about 2.7 points per week. The curvature also was negative (–0.0042; t[30] = –3.23; p = 0.003), indicating that this rate of decline was accelerating; thus, perception of QOL was decreasing at a significant rate for all participants, regardless of group.

The next model included group, intervention versus control, at the second level to examine its power to explain the variability in intercept and slope. The results of the model indicated that, although no difference was found in the level of total scores at 60 days postbaseline, the experimental group was declining in total well-being at a slower rate than the control group (t[49] = 2.31; p = 0.0254). No difference was found in the curvature parameter. Figure 1 shows the actual and expected values by group.

The same analyses were run for each of the subscales using the same procedures. For the fatigue subscale, a significant difference was found in the decline of scores with time (t[49] = 2.78; p = 0.0078), with the intervention group having less decline. This is represented in Figure 2. The intervention group also showed less decline over time on physical well-being (t[49] = 2.31; p = 0.0252). In addition, a tendency existed for the intervention group to show less acceleration in the downward trend (t[49] = 1.84; p = 0.0721). These results are shown in Figure 3.

Although both groups demonstrated increases in fatigue and decreases in physical well-being, the intervention group experienced significantly less increase in fatigue and less decrease in physical well-being. No significant differences existed between groups for the social, functional, or emotional well-being subscale scores at any of the time points.

Effect sizes for significant scale changes were calculated on the basis of differences in slope and ranged from 1.41 for the total FACIT–F scores to 1.75 for the fatigue subscale scores. Future recommendations for power analyses and sample size calculations for mixed models are difficult because estimators

Table 2. Total FACIT–F and Subscale Scores According to Cycle of Chemotherapy

	Baseline (n = 32)			Cycle 2 (n = 28)			Cycle 3 (n = 30)			Cycle 4 (n = 24)		
	$\bar{X}$	SD	% Maximum[a]	$\bar{X}$	SD	% Maximum[a]	$\bar{X}$	SD	% Maximum[a]	$\bar{X}$	SD	% Maximum[a]
Physical well-being	23.84	4.82	85	23.25	5.10	83	20.90	6.37	75	16.92	8.45	60
Social well-being	20.88	5.07	75	20.64	4.82	74	20.77	4.80	74	20.88	4.59	75
Emotional well-being	15.39	5.27	64	16.50	5.53	69	17.90	4.45	75	15.08	5.78	63
Functional well-being	20.50	5.12	73	19.12	6.38	68	19.33	6.62	69	17.46	7.38	62
Fatigue[b]	40.00	10.95	77	38.54	11.22	74	35.93	11.45	69	29.33	14.76	56
Total FACIT–F	120.61	22.87	81	118.04	23.53	80	114.83	26.89	78	99.66	29.59	67

[a] % maximum is the percentage of subjects who achieved the maximum (best possible) score.

[b] Lower scores on the fatigue subscale indicate more fatigue.

FACIT–F—Functional Assessment of Chronic Illness Therapy–Fatigue Version IV

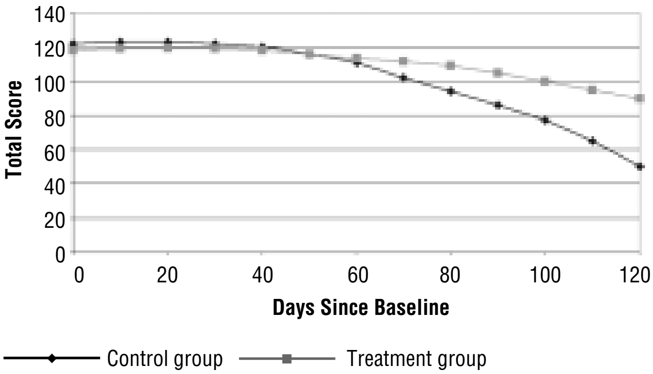

Figure 1. Total Functional Assessment of Chronic Illness Therapy–Fatigue Scores Over Time According to Group

do not have closed form solutions, and the structure of the variance-covariance matrix needs to be specified (Paul Swank, personal communication, October 31, 2002). Cronbach alpha coefficients for the subscales ranged from 0.80–0.96, indicating strong reliability for the instrument in this administration.

Discussion

This pilot study was unique in that most intervention studies involving exercise have not enrolled people with advanced cancer nor have studies examined the use of seated exercise to lessen fatigue in patients with cancer. The findings from this pilot study indicated that fatigue increases in women with metastatic breast cancer as they progress through their cycles of chemotherapy. This is not an unexpected finding and is consistent with other studies that have documented progressive fatigue as patients with cancer undergo treatment (Headley, 1997; Woo et al., 1998). Participants in the intervention group experienced less increase in fatigue and slower decrease in physical QOL than those in the control group, suggesting that exercise may be beneficial for women receiving treatment for advanced breast cancer. These findings must be interpreted with caution, however, because participants in the intervention group were significantly more likely to be married than those in the control group; spousal support may have had an impact on fatigue and QOL, thus confounding the results of the intervention. These findings support the need for further study to identify the optimal combination of frequency and intensity of seated exercise to yield maximal impact on fatigue.

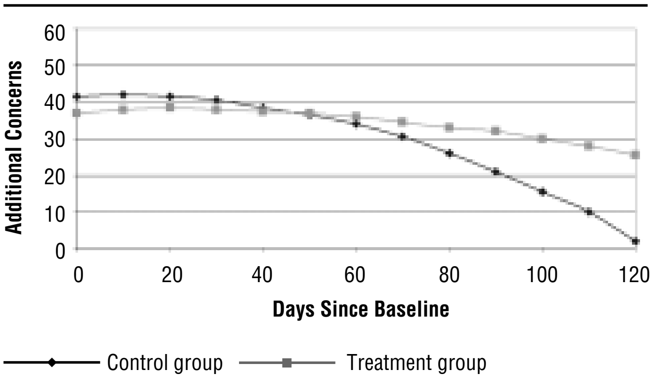

Figure 2. Fatigue Subscale Scores Over Time According to Group

The attrition rate for the study was 16% (n = 6), which was attributed to events unrelated to the exercise intervention such as need for palliative care or radiation therapy. Complete data through cycle four were available for only 75% of the initial sample because some subjects elected to receive their chemotherapy closer to home or were lost to follow-up. However, no significant difference was found in total FACIT–F or subscale scores at baseline between the subjects who dropped by cycle 4 and those who did not. No adverse events were related to participation in the exercise intervention. The exercise intervention seemed to be feasible and safe for women with metastatic breast cancer in this study.

Several women in the experimental group stated that the seated exercise video was not physically challenging. A common complaint was that the participants in the video were older, some wheelchair bound, who did not appear to be as vigorous as the subjects perceived themselves to be. The researchers found interesting that one-third of the women had routine exercise regimens prior to entry into the study, despite living with advanced breast cancer. Based on this anecdotal evidence, the researchers recommend the identification and testing of a different seated exercise video that is somewhat more physically challenging and includes younger performers.

Adherence to the exercise intervention declined over the three-month period; however, the overall adherence rate was 75%, which was comparable to the adherence rate of 72% that was found by Mock et al. (2001) in a study of women with early-stage breast cancer. One-third of the women in that study experienced progression of their disease; however, no significant change occurred in adherence between the women who had progression of their disease and those who had stable or remitting disease. Adherence to an exercise program was the focus of a study by Pickett et al. (2002), who found that some subjects had a decline in adherence to physical activity over time, but no relationship existed between decline and the symptoms of the disease or side effects of treatment. Adherence may not be related to disease or treatment side effects, but to other causes that need to be explored in further research.

The subjects in this pilot study were asked to document the types, duration, and levels of exercise intensity for each activity by noting RPE on monthly calendars; however, insufficient data were recorded to address these elements of exercise participation. The subjects were especially inconsistent in their documentation of RPE. The researchers had anticipated that the calendar data would provide information needed to support the interpretation of the data; however, many subjects did not record calendar data other than documenting that the seated intervention was performed. The authors suggest that a future study should include the use of a diary format. Further recommendations include having a research assistant make weekly telephone calls and monthly home visits to promote data entry. These contacts also could be useful in supporting active video participation in the intervention. The researchers recognize that calendar entries may not provide sufficient contextual information regarding symptom or exercise experiences; therefore, they recommend incorporating a qualitative inquiry component to future studies to understand issues related to motivation.

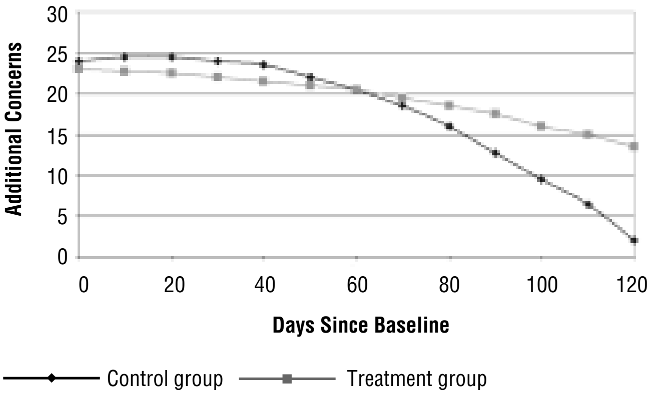

Figure 3. Physical Well-Being Subscale Scores Over Time According to Group

The FACIT–F seemed to perform well in this feasibility study, with very good reliability and little missing data. The instrument measures multiple dimensions of QOL in addition to fatigue, is relatively short (40 items), and is easy to complete. It is an appropriate choice for future studies that are aimed at examining patients' perceptions of fatigue as well as multidimensional QOL.

The strengths of the study include the application of a modified form of exercise in women with advanced breast cancer. Such women may benefit from exercise that can be performed in a chair in the safety and comfort of the home setting. Another strength is the use of mixed modeling analysis that allowed trends to be identified and scores to be predicted over time. Additionally, the study was largely feasible with minor alterations in procedures. The QOL instrument was reliable in this study. Limitations of the study include subject attrition and somewhat low adherence rates. The researchers suggest that future studies address alternate ways of measuring exercise intensity, closer subject follow-up and monitoring, and factors that relate to adherence to exercise programs. Also, despite random assignment to groups, the participants in the intervention group were significantly more likely to be married, and effects of spousal support may have obscured intervention effects.

Women with metastatic breast cancer often have existing exercise regimens. Participation in some form of exercise can reduce fatigue associated with chemotherapy treatment. The role of nurses in assessment and implementation of care is crucial to addressing patients' exercise preferences and tolerance and potential effects on symptom control.

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Author Contact: Judith A. Headley, RN, PhD, AOCN®, CCRP, can be reached at judy@jheadley.com, with copy to editor at rose_mary @earthlink.net.

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- Breast Cancer Research
  http://breast-cancer-research.com
- National Breast Cancer Coalition
  www.natlbcc.org
- MedlinePlus: Breast Cancer
  www.nlm.nih.gov/medlineplus/breastcancer.html

Links can be found at www.ons.org.