Victoria Mock, DNSc, AOCN
Mary Pickett, PhD, RN
Mary E. Ropka, PhD, RN, FAAN
Esther Muscari Lin, RN, MSN, ACNP, CS, AOCN
Kerry J. Stewart, EdD, FAACVPR, FACSM, FCGC
Verna A. Rhodes, EdS, FAAN
Roxanne McDaniel, PhD, RN
Patricia M. Grimm, PhD, RN, CS
Sharon Krumm, PhD, RN
Ruth McCorkle, PhD, FAAN

Fatigue and Quality of Life Outcomes of Exercise During Cancer Treatment

PURPOSE: Despite the recognition of fatigue as a common and distressing symptom during cancer treatment, there are few evidence-based interventions available to manage such fatigue. The purpose of this multi-institutional pilot study was to explore the effects of a home-based moderate walking exercise intervention on fatigue, physical functioning, emotional distress, and quality of life (QOL) during breast cancer treatment.

DESCRIPTION OF STUDY: Fifty-two women were recruited from five university hospital outpatient departments for this pilot study with an experimental design. Subjects were randomly assigned to the walking program or to usual care during adjuvant chemotherapy or radiation therapy for breast cancer. Symptoms, physical functioning, and QOL were measured at baseline, midtreatment, and at the end of treatment.

RESULTS: Women who exercised at least 90 minutes per week on 3 or more days reported significantly less fatigue and emotional distress as well as higher functional ability and QOL than women who were less active during treatment.

CLINICAL IMPLICATIONS: A home-based walking exercise program is a potentially effective, low-cost, and safe intervention to manage fatigue and to improve QOL during adjuvant chemotherapy or radiation therapy for breast cancer. This health-promoting self-care activity needs further testing in large randomized clinical trials.

KEY TERMS: Breast cancer; Emotional distress; Exercise; Fatigue; Physical functioning; Quality of life

Fatigue is the most common unmanaged symptom of patients with cancer who are receiving radiation therapy, chemotherapy, or biotherapies.[1–4] Despite widespread acknowledgment of the problems associated with fatigue, there are relatively few evidence-based interven-

Victoria Mock, DNSc, AOCN, Associate Professor, The Johns Hopkins University School of Nursing, Baltimore, Maryland.

Mary Pickett, PhD, RN, Research Assistant Professor, University of Pennsylvania School of Nursing, Philadelphia, Pennsylvania.

Mary E. Ropka, PhD, RN, FAAN, Associate Professor, University of Virginia School of Medicine, Charlottesville, Virginia.

Esther Muscari Lin, RN, MSN, ACNP, CS, AOCN, Formerly Advanced Practice Oncology Nurse/Clinician 5, University of Virginia Hospital, Charlottesville, Virginia.

Kerry J. Stewart, EdD, FAACVPR, FACSM, FCGC, Director, Cardiac Rehabilitation and Prevention, Johns Hopkins Bayview Medical Center, Baltimore, Maryland.

Verna A. Rhodes, EdS, FAAN, Associate Professor, University of Missouri—Columbia School of Nursing, Columbia, Missouri.

Roxanne McDaniel, PhD, RN, Associate Professor, University of Missouri—Columbia School of Nursing, Columbia, Missouri.

Patricia M. Grimm, PhD, RN, CS, Formerly Associate Professor, The Johns Hopkins University School of Nursing, Baltimore, Maryland.

Sharon Krumm, PhD, RN, Administrative Director of Clinical Services, Johns Hopkins Comprehensive Cancer Center, Baltimore, Maryland.

Ruth McCorkle, PhD, FAAN, Professor, Yale University School of Nursing, New Haven, Connecticut.

This research was funded by a Fatigue Initiative in Research and Education Grant (phase I) awarded by the Oncology Nursing Society Foundation through a donation from Ortho Biotech Inc.

Address for correspondence: Victoria Mock, DNSc, AOCN, The Johns Hopkins University School of Nursing, P.O. Box 50250, Baltimore, MD 21211-4250.

tions available to address this symptom.[5] In addition to the discomfort associated with the symptom, fatigue often leads to a decrease in daily activity level during cancer treatment, resulting in a lower tolerance for exercise.[2] As patients with cancer become too tired to participate fully in the roles and activities that make life meaningful, the most important impact of fatigue may be in the realm of quality of life (QOL).[6]

Exercise is effective in decreasing fatigue and improving activity tolerance in healthy individuals[7] as well as those with cardiovascular,[8] chronic respiratory,[9] and chronic renal diseases.[10] Early studies of exercise in patients with cancer indicated that exercise could increase functional capacity during chemotherapy,[11] improve marrow recovery and decrease complications during peripheral blood stem cell transplantation (PBSCT),[12] and decrease fatigue and other symptoms during radiation therapy (RT) and chemotherapy.[2,13] Research designed to test the effects of exercise interventions in patients with cancer is relatively new, and the previously published studies have limitations related to sample sizes and methods. Additional limitations include the lack of a clear, universally accepted definition of fatigue and the dearth of valid, reliable instruments to measure fatigue.

This multi-institutional randomized pilot study, the first of its kind related to fatigue, was conducted to determine the feasibility of and to explore the effects of a home-based exercise intervention on fatigue, physical functioning, emotional distress, and QOL in women receiving RT or adjuvant cytotoxic chemotherapy (CT) after breast cancer surgery. An additional aim was to examine the relationships among fatigue, physical functioning, emotional distress, and QOL.

Literature Review

Published research related to fatigue experienced by patients with cancer has increased significantly since 1991 when fatigue was identified as a research priority by the Oncology Nursing Society.[14] The majority of fatigue studies have employed descriptive and correlational research designs. Research using experimental designs to determine the efficacy or effectiveness of interventions to prevent or manage cancer treatment-related fatigue is noticeably absent.[5] To compound the problem, there is a lack of practice theories to guide intervention research. Research designed to test the effects of exercise on fatigue in samples of patients with cancer can be classified into two phases: during cancer treatment and post-treatment.

Managing Fatigue During Cancer Treatment

Only a few published studies tested exercise interventions to manage fatigue during cancer treatment.[2,13,15-17] The types of exercise being evaluated were home-based walking programs,[2,13] exercise cycles in the laboratory or hospital,[15,16] and one study in which subjects selected the type of aerobic exercise.[17] The programs have varied in length from 6 weeks during RT[2] through high-dose chemotherapy and PBSCT.[15] All of these studies demonstrated significantly lower levels of fatigue in patients who exercised during treatment. The studies were limited by small sample sizes that ranged from 14 to 59 (mean 32), with approximately half of those in the exercise arm of the study. In addition, most of these studies have consisted of samples of patients with breast cancer. While limiting the samples to one cancer diagnosis has distinct advantages at this stage of research, it may also limit the generalizability of the data to other populations at this time.[2,13,16,17]

Other studies of exercise during cancer treatment, while not focused on fatigue as an outcome, have demonstrated positive findings related to physical function during cancer treatment. A 10-week program of laboratory bicycle exercise for 45 patients with stage II breast cancer who were receiving adjuvant CT revealed a mean 40% increase in functional capacity.[11] Exercising subjects also had less nausea[18] and a reduced rate of gain in body fat[19] during treatment. In a study of 70 patients with cancer who were undergoing high-dose chemotherapy and autologous PBSCT, use of a bed exercise bicycle for 30 minutes daily resulted in increased physical performance, decreased duration of neutropenia and thrombocytopenia, and decreased length of hospitalization when compared with a control group.[12] Fatigue was not an outcome reported in this study. These studies of patients with cancer receiving active treatment suggest that exercise can be a safe and effective intervention to achieve physical and psychological benefits, including reductions in fatigue, for individuals with select cancer diagnoses and cancer treatments.

Managing Fatigue in Cancer Survivors

Studies testing exercise interventions to mitigate the adverse side effects experienced by cancer survivors after the completion of cancer therapy also have shown beneficial outcomes.[20-22] These outcomes have included decreased fatigue and increased performance,[20,21] as well as decreased anxiety and depression.[21,22] Further research on exercise in patients with cancer is needed to determine appropriate guidelines during various types of cancer treatment and to extend the preliminary work begun in this field.

Theoretical Framework

This study is guided by the Levine conservation model, an adaptation model that portrays the maintenance of life by conserving individual integrity.[23] The following four conservation principles underlie the model: conservation of energy; structural integrity; personal integrity; and social integrity.[24] Cancer diagnoses and treatments are viewed as physical and psychosocial challenges for women living with breast cancer. The walking exercise program is conceptualized as an intervention that may support the conservation of energy and structural integrity by increasing functional capacity and decreasing energy expenditure during physical activity. Conservation of personal integrity is demon-

strated when patients with breast cancer report low levels of emotional distress and high levels of QOL. Conservation of social integrity is represented by the maintenance of social functioning. Figure 1 displays the Levine model concepts, major study variables, and instruments to measure related study outcomes.

Methods

This pilot study employed a prospective, controlled, randomized design stratified by cancer treatment of adjuvant CT or RT. Subjects were randomly assigned to the investigational walking exercise intervention or to usual-care treatment groups. This stratified design was used to control for potentially confounding variables of length and type of cancer treatment program. Fatigue, physical functioning, emotional distress, and QOL outcomes were evaluated before initiation of CT or RT and at the end of treatment by study personnel who received periodic training to maximize consistency across study sites.

Setting and Sample

The five study sites were all university teaching hospital cancer centers in the Eastern United States that had high volumes of patients with breast cancer. The sites were selected to provide diversity in terms of geographic (urban/rural), socioeconomic, and ethnic (African American/White) variables to control for differences in their potential impact on acceptance of or adherence to the home-based walking exercise intervention. Differential effects of exercise on study outcomes were not expected based on geographic, socioeconomic, or ethnic variables.

A convenience sample of female subjects was recruited from outpatient cancer treatment sites based on the following inclusion criteria: 1) recently were treated for stage I, II, or IIIa breast cancer by definitive surgery; and 2) were scheduled to receive outpatient adjuvant RT or CT. A patient was ineligible if she had a concurrent major health problem that would contraindicate an exercise program.

Sample Accrual and Attrition

Fifty-two women met the inclusion criteria for study enrollment and signed informed consent forms to participate in the study. Two study subjects withdrew shortly after cancer therapy was initiated because they were "overwhelmed" by their cancer diagnosis and treatment and could not manage study participation. One subject was withdrawn after significant medical treatment comorbidities. One subject did not return for post-test measurement at the completion of cancer treatment. Statistical analyses were performed on data obtained from the remaining 48 participants. Data tables indicate when less than 48 subjects are included in the statistical analyses because of random missing data that occurred over the course of this longitudinal study.

The sample included women who were 28 to 75 years of age (mean 48 years), predominantly were married (70%), employed (66%), White (86%), and college educated (mean 15 years of education). The average body weight of the study subjects was 156 lb and the average body mass index was 25.66, which is less than the level for obesity designated at ≥ 30.[25] The majority of the women had received a state I (54%) or stage II (40%) breast cancer diagnosis. Sixty-four percent of the women were receiving RT during the study period; the remaining 36% were receiving CT. Radiation therapy protocols consisted of outpatient external beam treatments scheduled on 5 days per week for 6 weeks plus a booster dose for a total of 60 to 64 Gy. Of the 19 patients who received CT, 58% received four cycles of doxorubicin and cyclophosphamide; 37% received six cycles of cyclophosphamide, methotrexate, and fluorouracil; and 5% (one patient) received cyclophosphamide, doxorubicin, and fluorouracil (Table 1).

Walking Exercise Intervention

The walking exercise intervention, which was taught individually to subjects by trained study staff, began concurrently with adjuvant CT or RT and continued for the duration of the initial cancer treatment: 6 weeks of RT and

Conceptual Framework Concepts	Conservation of Energy	Conservation of Structural Integrity	Conservation of Personal Integrity	Conservation of Social Integrity
Study Variables:	Subjective Fatigue	Physical Functioning	Emotional Distress and QOL	Social Functioning
Study Instruments:	• Piper Fatigue Scale • 0–10 Scale Daily Diary	• MOS-Physical • Activity Level Rating Scale • Walk Test	• MOS—Emotional • Profile of Mood States	• MOS-Social

Adapted from Mock et al., 1998.[35] Used with permission of Oncology Nursing Society.

Figure 1 The Levine conservation model as it guided the study.

Table 1. ***Participant Characteristics by Exercise Intensity at Study Entry***

Characteristic	*Total Sample (n = 50)*	*Low Walker (n = 22)*	*High Walker (n = 28)*
Age (yr)			
Range	28–75	31–75	28–75
Mean	47.98	47.14	48.64
SD	11.06	11.72	10.69
Education (yr)			
Range	8–20	11–19	8–20
Mean	14.76	14.73	14.79
SD	2.54	2.45	2.66
Height (in)			
Range	59–70	59–70	61–70
Mean	65.38	65.18	65.54
SD	2.55	2.68	2.47
Weight (lb)			
Range	106–230	113–230	106–201
Mean	155.74	168.59	145.64
SD	31.30	35.10	24.07
Body mass index			
Range	18–36	19–36	18–29
Mean	25.66	27.95	23.86
SD	5.28	5.94	3.94
Ethnicity			
White	43 (86)	18 (90)	19 (83)
African American	6 (12)	2 (10)	3 (13)
Hispanic	1 (2)	0 (0)	1 (4)
Marital status			
Married/partnered	35 (70)	15 (68)	20 (71)
Unpartnered	15 (30)	7 (32)	8 (29)
Employment			
Full-time	24 (48)	12 (55)	12 (43)
Part-time	9 (18)	2 (9)	7 (25)
Unemployed	17 (34)	8 (36)	9 (37)
Breast cancer stage			
I	27 (54)	11 (50)	6 (57)
II	20 (40)	10 (45)	10 (36)
III	3 (6)	1 (5)	2 (7)
Treatment			
RT	32 (64)	14 (64)	18 (64)
CT	18 (36)	8 (36)	10 (36)
Surgical procedure			
Lumpectomy	31 (62)	15 (68)	16 (57)
Mastectomy	19 (38)	7 (32)	12 (43)

*Values given as No. (%), unless otherwise indicated.

4 to 6 months of CT. The program was described in detail in a booklet given to each subject in the intervention group. The exercise prescription was individualized for subjects based on age, level of physical fitness as determined by the baseline walk test, and type of cancer treatment.[25] Most exercise prescriptions began at 10 to 15 minutes per session and five to six sessions per week using guidelines developed with an exercise physiologist. Subjects were advanced to 30 minutes per session, five to six daily sessions per week, as their tolerance to exercise and responses to cancer treatment permitted. Instruction regarding the exercise intervention took place at the clinical site, but the program was actually implemented by the subjects at home or at another setting of their choice (eg, shopping malls during bad weather). Issues of safety were emphasized in the instruction. Adherence to the intervention was encouraged by suggesting that women walk with a partner and record exercise data in a diary to measure progress. In addition, study staff contacted subjects by phone or during clinic visits every 2 weeks to assess exercise progress and advance exercise prescriptions, monitor for safety, and provide encouragement.[26] All subjects in the exercise group kept diaries on forms especially formatted to record daily exercise activity, pulse rates, perceived exertion, and other comments they wished to volunteer about how they felt. These were mailed to study staff weekly.

Usual care for the control group consisted of whatever was standard practice in the cancer center outpatient department at each site. The investigational group received usual care in addition to the home-based walking intervention. At the time of the study, exercise was not routinely included or emphasized as a part of standard care during cancer treatment. Subjects in the usual-care group recorded fatigue levels and general physical activities as well as voluntary comments in their weekly diaries. To provide control subjects for staff attention and support, members of the usual-care group were contacted by study staff every 2 weeks to inquire about their responses to treatment.

Study Measures

Fatigue was defined as a pervasive subjective feeling of weariness, tiredness, or lack of energy that varied in occurrence and impact on functional ability and life quality. Fatigue was measured by the modified Piper fatigue scale (PFS), a 22-item, 10-point self-report scale that measures overall fatigue and four fatigue dimensions: temporal, severity, affective, and sensory.[27] Scores of 0 to 3 represent no or mild fatigue levels; scores of 4 to 6 represent moderate levels; and scores of 7 to 10 represent high levels of fatigue. The PFS has demonstrated validity and reliability in a number of other studies of patients with cancer. Internal consistency reliability (Cronbach α) ranged from .94 to .97 for the PFS in this sample. Fatigue levels also were reported in the daily diary on a 0-to-10 scale from "no fatigue" to "a great deal of fatigue." The mean daily diary fatigue levels were highly correlated ($r = .75$; $P = .00$) with the total score on the PFS.

Physical functioning, defined as the ability to ambulate and to perform normal activities of daily living, was measured by the 12-minute walk test,[28] the activity level rating scale, and the Medical Outcomes Study Short Health Form (MOS SF-36) physical functioning subscale.[29] In the 12-minute walk test, the subject is instructed to walk as far as possible on a level surface in 12 minutes and to keep going continuously, if possible, but to slow down or stop to rest at any time discomfort occurs. The distance walked, measured in feet, constitutes the measure of functional ability.[30]

The activity level rating scale assesses the level of participation in exercise or physical activity over the last month in terms of the type of activity, the frequency, and the duration. Scores are reported on a 10-point scale according to the number of minutes exercised per week. The instrument has been used with cancer patients in previous exercise studies.[2,13]

Emotional distress was measured by the Profile of Moods States (POMS). The shortened 30-item POMS measures a subject's mental/psychological status by subscales that assess the following six emotional dimensions: 1) tension-anxiety; 2) depression-dejection; 3) anger-hostility; 4) vigor-activity; 5) fatigue-inertia; and 6) confusion-bewilderment.[31] Adjectives are rated by the respondent on a 5-point scale, ranging from "not at all" (0) to "extremely" (4) during the past week. All six subscale scores are summed (the vigor score is weighted negatively) to yield a total mood disturbance (TMD) score. Higher scores reflect greater mood disturbance. Cronbach α reliability coefficients for this study were .91 to .94 for the POMS.

Quality of life was measured by the MOS SF-36 (distributed by RAND, Santa Monica, CA), a multi-item scale that includes the following eight health concepts: 1) physical functioning; 2) social functioning; 3) role functioning-physical limitations; 4) role functioning-emotional limitations; 5) bodily pain; 6) general mental health; 7) vitality; and 8) general health perceptions.[29] Higher scores (possible 0 to 100) indicate higher QOL. Internal consistency reliability estimates for the MOS SF-36 have been reported with an α coefficient of .83.[29] In the current study, internal consistency by Cronbach α ranged from .91 to .95 on the two administrations of the instrument.

Procedures

After approval for the protection of human subjects from each institution's institutional review board, potential subjects were recruited using a number of strategies: regular contact with RT and breast cancer clinic staff; attendance at breast cancer conferences; and study recruitment pamphlets placed in cancer center waiting rooms. Eligible consenting subjects were enrolled and randomized to treatment groups using assignments generated by the operations center at the principal investigator's institution, were stored in sealed envelopes for use in sequential order, and were retained at the study sites. Data management and analysis was performed using appropriate software (SPSS-PC, version 10.0, SPSS, Chicago, IL).

Results

Data Analysis

A review of RT and CT protocols received by subjects in the usual-care and exercise groups demonstrated group equivalence, that is, cancer treatment protocols were similar between the two groups and there were similar numbers of subjects receiving each of the two cancer treatments. Data analysis for the study was planned as an "intention-to-treat" model of group comparisons, whereby subjects are analyzed in the group to which they are assigned, regardless of their compliance to the treatment planned for that group.[32] However, an initial analysis of data on the activity level rating scale revealed that 50% of the subjects in the usual-care group were, in fact, actively exercising during the study period. This unexpected finding was validated by a review of subjects' study diaries, which included self-reported activities. In addition, almost one third of the women who had been randomly assigned to the exercise group did not maintain a regular exercise program as prescribed according to the study protocol as a minimum of 90 minutes per week in three or more daily sessions. It is reasonable to assume that this "diffusion of treatment" effect contributed to the resulting inability to detect statistically significant differences at post-test between the usual-care and exercise groups mean scores when compared by "intention to treat."

The data analysis plan then was changed to consider a dose-response perspective in an explanatory cohort compliance model[32] with subjects separated into "high walk" and "low walk" groups to determine the effects of exercise during treatment on study outcomes. Based on post-test data from the activity level rating scale, subjects were classified as low walk if they walked less than 90 minutes per week and high walk if they walked for greater amounts of time per week. Although an adherence perspective is appropriate in data analyses of exercise studies, inherent in this model is an obvious threat to validity.

Selection bias may be represented in this study in the following manner. Women who lived more active lifestyles or had higher levels of physical fitness may have elected to exercise regularly, while women who lived more sedentary lifestyles or had lower levels of physical fitness may have had more difficulty exercising regularly during the study period (Table 1). In fact, at baseline the low-walk group had significantly higher body mass index scores and significantly lower self-reported levels of physical activity than did the high-walk group. There were no other significant differences between the groups at baseline. Additional evidence of bias resulted from a comparison of the baseline pretest scores between low-walk and high-walk groups for physical function, mood disturbance, and fatigue. Women in the low-walk group demonstrated lower levels of physical function (12-minute walk test), higher levels of mood disturbance (POMS), and higher levels of fatigue (PFS) than did women in the high-walk group. Although these were not statistically significant differences, the analysis plan was expanded to include pre- to post-test mean change scores for each group (high walk and low walk) as well as the planned between-group comparisons.

Fatigue

Mean fatigue scores for the entire sample on the PFS began at low levels and increased over the course of both RT and CT. Fatigue scores were slightly higher for the low-walk group at pretest and became significantly higher at post-test (Fig. 2). Total fatigue scores on the PFS at post-test

were higher for patients receiving CT (mean [± SD] 3.61 ± 2.17) than for those receiving RT (mean 3.32 ± 2.07).

The diary completed by patients included a daily fatigue rating on a 0-to-10 scale. Mean fatigue scores on the daily diaries were 4.34 (± 1.82) for the low-walk group and 2.31 (± 1.48) for the high-walk group (t = 4.05, P = .00). Mean scores for patients receiving CT were consistently higher than scores of patients receiving RT (3.96 ± 1.78 vs 2.64 ± 1.85, respectively; t = −2.34, P = .01).

Fatigue also was measured by the fatigue subscale of the POMS scale. On this instrument, mean fatigue subscale scores decreased for patients in the high-walk group from 5.04 (± 5.20) to 4.35 (± 4.54) during treatment, while scores increased for patients in the low-walk group from 7.18 (± 4.82) to 9.81 (± 5.91), resulting in a significant difference between groups at post-test (P = .00).

Physical Functioning

Physical functioning was subjectively rated by patient self-report on the activity level rating scale and on the physical functioning subscale of the MOS-SF 36 as well as by an objective test of exercise tolerance, the 12-minute walk test. Subjects in the low-walk group decreased their physical activity, as measured by the activity level rating scale, over the course of cancer treatment, while subjects in the high-walk group increased their activity, resulting in a significant difference (P = .00) between the two groups at post-test (Table 2). Physical functioning scores on the MOS SF 36 decreased for both groups, but much more dramatically for the low-walk group (Fig. 3). The 12-minute walk test scores reflected an increased functional capacity for subjects in the high-walk group during treatment, as indicated by a mean increase of 175 feet from pretest to post-test (Table 2). The low-walk group performance was essentially unchanged from pretest to post-test. Comparison of groups by change-score means relevant significant differences.

Emotional Distress

Women in both the high-walk and low-walk groups reported high levels of mood disturbance on the POMS before the initiation of adjuvant therapy after breast cancer surgery. Baseline equivalence for the groups was assessed by computing t-tests for independent samples on the pretest mean scores of the POMS. Group equivalence was supported when no statistically significant differences resulted from analysis of the pretest TMD score and all subscales of the instrument. Analyses of the post-test mean scores revealed decreased levels of mood disturbance reported by the total study sample at the post-test evaluation. Moreover, there were significant differences between the mean post-test scores for the high-walk and low-walk groups for TMD (P = .00), as well as for two of the subscales, vigor and fatigue (P = .00). Women in the high-walk group reported significantly higher mean levels of vigor (13.77 vs 8.57, respectively) and lower levels of both fatigue (4.35 vs 9.81, respectively) and general mood disturbance (−1.00 vs 18.52, respectively) than did women who were identified as members of the low-walk group.

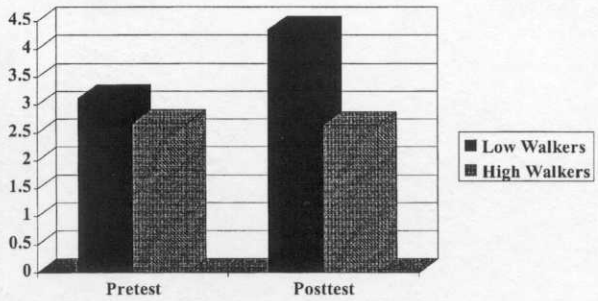

Figure 2 Comparison of mean Piper Fatigue Scale scores from pretest to posttest for low and high walkers.

To detect any significant changes in mood over the course of the study, change scores were computed on the pretreatment and post-treatment mean POMS subscale scores for both groups (high walk and low walk). Results of the analyses for the high-walk group revealed significant decreases in anxiety (t = 3.32, P = .00) and depression (t = 2.00, P = .03). Results of the analyses for the low-walk group demonstrated a significant decrease in vigor (t = 2.34, P = .02). It is notable that over the course of the study, TMD scores for the high-walk group decreased significantly (P = .00) compared with no change in the low-walk group. The only mood state score that increased from baseline to the completion of the study was the level of fatigue reported by the low-walk group.

Quality of Life

Scores on the MOS SF-36 varied among the subscales for the two groups of subjects over the course of cancer treatment (Fig. 3). With higher scores reflecting higher QOL values, baseline physical functioning scores were equivalent and moderately high for the two groups. By the end-of-treatment post-test, scores for the low-walk group had decreased 48% (P = .00), while high-walk group scores

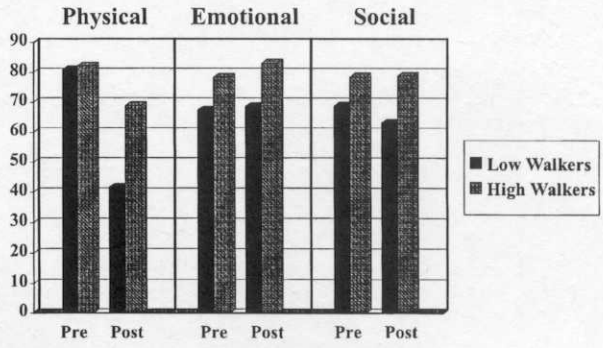

Figure 3 Mean physical, emotional, and social subscale scores on the MOS SF-36 for low and high walkers.

Table 2. ***Physical Functioning by Group Activity Level****

	Pretest Mean (SD)	*Post-test Mean (SD)*	*Difference Mean (SD)*	*P* Value
Activity level rating scale†				
Low walker (n = 20)	1.38 (2.36)	.89 (1.24)	−.53	.00
High walker (n = 24)	4.54 (2.83)	6.46 (2.17)	+1.75	
12-minute walk test (ft)				
Low walker (n = 20)	3014.48 (490.75)	3004.00 (469.79)	−10.48	.01
High walker (n = 23)	3137.00 (490.23)	3311.96 (545.60)	+174.96	

*Total n [low and high walkers] < 50 due to missing posttest values for walk data.
†Scale of 0 to 9.

decreased only 16% (P = .02). Emotional well-being subscale mean scores increased for both groups by the end of treatment, while social functioning scores increased for the high-walk group and decreased for the low-walk group.

Correlations

As indicated in Table 3, at post-test there was a strong positive Pearson correlation between the symptoms of fatigue and emotional distress experienced by the subjects. There were moderately negative correlations between physical functioning/activity level and both fatigue and emotional distress.

Discussion

The results of this study suggest that a home-based moderate walking exercise program during 6 weeks of RT or during 4 to 6 months of adjuvant CT can decrease fatigue and emotional distress while improving physical functioning and QOL during treatment for breast cancer. Higher levels of fatigue were observed for women receiving CT than for those receiving RT. A diffusion-of-treatment effect was a threat to the internal validity of the study, because 30% of subjects in the exercise group did not establish or maintain the level of exercise prescribed by the program and 50% of the subjects in the usual-care group began or continued a personal exercise program during their cancer treatment. Therefore, to compare exercisers to those who exercised little or not at all, the subjects were subsequently divided into high-walk and low-walk groups based on their level of exercise during the study.

Analysis of the diaries and other study data indicate that patients are eager to adopt potentially health-promoting self-care activities and that lack of adherence to an exercise prescription is usually related to illness or complications during cancer treatment. On the other hand, many subjects are disappointed not to be assigned to an intervention group testing a health-promoting activity and will avail themselves of the intervention on their own initiative. In fact, the prestudy exercise level was highly correlated in this study with exercise during the study, regardless of group assignment. Seventy-three percent of the high-walk group subjects exercised at baseline for greater than 90 minutes per week, while only 10% of the low-walk group subjects exercised at this level. Having previously established the habit of exercise (and experienced the beneficial effects) clearly promoted the maintenance of exercise during cancer treatment.

The results of this study agree with those of previous studies in that exercise during cancer treatment increased functional capacity,[11,12] decreased fatigue,[2,13,15,17,33] and improved QOL.[34] Levels of adherence were similar to those reported by Schwartz[17] in a home-based exercise program in which 60% of the study sample of 27 women successfully adhered to their prescribed exercise regimen. In a more recent report of the exercise study with 78 subjects,[33] 52% of the women who were not regular exercisers at study

Table 3. ***Correlation Matrix of Post-test Symptoms and Physical Functioning***

	*Fatigue**	*Emotional Distress†*	*Physical Functioning‡*	*Activity Level Rating Scale§*
Fatigue	1.00			
Emotional distress	.83	1.00§		
Physical functioning	−.65§	−.64§	1.00	
Activity level	−.31‖	−.42§	.33‖	1.00

*PFS total score.
†POMS TMD.
‡MOS SF-36.
§$P \leq .01$.
‖$P \leq .05$.

entry adhered to the program, while 75% of the women who were regular exercisers at baseline adhered.

The study results provide support for the theoretical framework, the Levine conservation model, with regard to each of its four conservation principles. High-walk subjects conserved energy as reflected in the lower fatigue levels compared with low-walk subjects. The conservation of structural integrity for high-walk subjects was demonstrated by increased functional capacity on the 12-minute walk test. The conservation of personal integrity was reflected in lower mood distress scores on the POMS and higher QOL scores on the MOS-SF 36 for the high-walk subjects. The conservation of social integrity was represented by increased pretest to post-test scores on the social functioning subscale of the MOS-SF 36 for high-walk subjects, while scores for low-walk subjects decreased over the course of their breast cancer treatment.

Limitations

Although this multi-institutional study accrued a diverse sample, the results of the study should be generalized with caution to other women being treated for breast cancer because of the convenience sampling. In addition, the sample size of 48 women in this pilot project limited the statistical approaches available for data analysis and the power to see differences between groups. Issues related to the cancer treatment were also problematic. Not all the women were treatment-naive; that is, some came with symptoms from a prior treatment. In addition, 50% of the subjects in the usual-care group were actively exercising during study participation, while 30% of the subjects in the exercise group were not able to maintain a regular exercise program. This diffusion of treatment resulted in a lack of significant differences between groups and led to a change from the intention-to-treat model of group comparison to the explanatory compliance cohort model that was described.

Additional limitations of the study are related to the use of the self-administered intervention and self-report of activity and outcomes. The use of a self-administered intervention requires the stringent use of follow-up contacts by research assistants to facilitate the standardization and implementation of the intervention. This approach is currently being used in an expanded multi-institutional project based on the feasibility and clinical outcomes of the reported study.[35] In the expanded project, eligibility criteria require that patients be sedentary at study entry as well as treatment-naive. In addition, techniques to increase adherence to exercise have been included in the expanded project.

The limitations of self-report measures of outcomes are well known. An approach to managing these concerns would be the identification and measurement of significant outcome variables by more objective approaches such as the use of activity meters, worn by the participant, or treadmill testing to ensure a more definitive measure of function and exertion.

Clinical and Research Implications

Results suggest that study design is very important when testing an exercise intervention during cancer treatment. Prestudy exercisers will likely continue exercising regardless of group assignment and may not need the structured program. Symptoms are related to the type of treatment, so stratification or blocking by treatment is necessary. Also, subjects should be treatment-naive because recent treatment causes higher levels of symptoms on baseline tests and difficulty measuring the effects of the intervention.

The intervention itself, a low-cost, low-risk walking exercise program, can be taught easily and monitored by clinicians. This health-promoting self-care activity holds potential as an intervention to help manage fatigue and emotional distress during cancer treatment while maintaining the physical ability to engage in usual activities. The exercise program is a positive, wellness-focused therapy that emphasizes hopefulness and a sense of strength and control during cancer treatment.

The authors recommend that a walking intervention be further tested in larger samples of nonexercising patients with cancers that represent diverse cancer sites. Also, further research is needed to develop effective strategies that help patients to decrease barriers to exercise and to increase adherence to an exercise program. Finally, future studies of the effects of exercise in combination with other treatment modalities (eg, biologic response modifier therapy) and at other points in the survival trajectory are needed.

Acknowledgments

The authors thank the participating institutions and staff for their help and support, with special thanks to John H. Fetting, MD, Associate Director for Clinical Practice at The Johns Hopkins Cancer Center, who served as medical consultant to the project.

References

1. Longman AL, Braden CJ, Mishel MH. Side effects burden in women with breast cancer. *Cancer Pract.* 1996;4:274-280.
2. Mock V, Dow KH, Meares C, et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncol Nurs Forum.* 1997; 24:991-1000.
3. Robinson KD, Posner JD. Patterns of self-care needs and interventions related to biologic response modifier therapy: fatigue as a model. *Semin Oncol Nurs.* 1992;8(suppl):17-22.
4. Sitzia J, Huggins L. Side effects of cyclophosphamide, methotrexate, 5-fluorouracil (CMF) chemotherapy for breast cancer. *Cancer Pract.* 1998;6:13-21.
5. Ream E, Richardson A. From theory to practice: designing interventions to reduce fatigue in patients with cancer. *Oncol Nurs Forum.* 1999;26:1295-1303.
6. Nail LM, Jones LS. Fatigue as a side effect of cancer treatment: impact on quality of life. *Qual Life Nurs Challenge.* 1995;4: 8-13.

7. Pollock ML, Gaesser GA, Butcher JD. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exerc.* 1998;30:975-991.
8. Bittner V, Oberman A. Efficacy studies in coronary rehabilitation. *Exer Test Cardiac Rehabil.* 1993;11:333-347.
9. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med.* 1995;122:823-832.
10. Painter PL, Nelson-Worel JN, Hill MM, et al. Effects of exercise training during hemodialysis. *Nephron.* 1986;43:87-92.
11. MacVicar MG, Winningham ML, Nickel JL. Effects of aerobic interval training on cancer patients' functional capacity. *Nurs Res.* 1989;38:348-351.
12. Dimeo F, Fetscher S, Lange W, Mertelsmann R, Keul J. Effects of aerobic exercise on the physical performance and incidence of treatment-related complications after high-dose chemotherapy. *Blood.* 1997;90:3390-3394.
13. Mock V, Burke MB, Sheehan PK, et al. A nursing rehabilitation program for women with breast cancer receiving adjuvant chemotherapy. *Oncol Nurs Forum.* 1994;21:899-908.
14. Mooney KH, Ferrell BR, Nail LM, Benedict SC, Haberman MR. Oncology Nursing Society research priorities survey. *Oncol Nurs Forum.* 1991;18:1381-1388.
15. Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer.* 1999;85: 2273-2277.
16. MacVicar MG, Winningham ML. Promoting the functional capacity of cancer patients. *Cancer Bull.* 1986;38:235-239.
17. Schwartz AL. Daily fatigue patterns and effect of exercise in women with breast cancer. *Cancer Pract.* 2000;8:16-24.
18. Winningham ML, MacVicar MG. The effects of aerobic exercise on patient reports of nausea. *Oncol Nurs Forum.* 1988; 15:447-450.
19. Winningham ML, MacVicar MG, Bondoc M, Anderson JI, Minton JP. Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. *Oncol Nurs Forum.* 1989;16:683-688.
20. Dimeo FC, Tilmann MHM, Bertz H, Kanz L, Mertelsmann R, Keul J. Aerobic exercise in the rehabilitation of cancer patients after high dose chemotherapy and autologous peripheral stem cell transplantation. *Cancer.* 1997;79:1717-1722.
21. Dimeo F, Rumberger BG, Keul J. Aerobic exercise as therapy for cancer fatigue. *Med Sci Sports Exerc.* 1998;30:475-478.
22. Segar ML, Katch VL, Roth RS, et al. The effect of aerobic exercise on self-esteem and depressive and anxiety symptoms among breast cancer survivors. *Oncol Nurs Forum.* 1998;25: 107-113.
23. Fawcett J. *Analysis and Evaluation of Conceptual Models of Nursing.* Philadelphia, Pa: FA Davis Co; 1994.
24. Levine ME. The conservation principles of nursing: twenty years later. In: Riehl-Sisca J, ed. *Conceptual Models for Nursing Practice.* Norwalk, Conn: Appleton-Lange; 1989.
25. American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription.* Sixth ed. Baltimore, Md: Williams & Wilkins; 2000.
26. Ruiz M, Dibble E, Gilliss N, Gortner S. Coaching by telephone using self-efficacy theory. *Appl Nurs Res.* 1992;17:154-162.
27. Piper BF, Dibble S, Dodd MJ, Weiss MC, Slaughter R, Paul S. Revised Piper Fatigue Scale: psychometric evaluation in women with breast cancer. *Oncol Nurs Forum.* 1998;25: 677-684.
28. Larson JL, Covey MK, Vitalo CA, Alex CG, Patel M, Kim MJ. Reliability and validity of the 12-minute distance walk in patients with chronic obstructive pulmonary disease. *Nurs Res.* 1996;45:203-210.
29. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. *Med Care.* 1992;30:473-483.
30. Jones NL, Campbell EJM. *Clinical Exercise Testing.* Philadelphia, Pa: WB Saunders; 1982.
31. Shacham S. A shortened version of the profile of mood states. *J Pers Assess.* 1983;47:305-306.
32. Piantadosi S. *Clinical Trials: A Methodologic Perspective.* New York, NY: John Wiley & Sons; 1997:175-177.
33. Schwartz AL. Exercise and weight gain in breast cancer patients receiving chemotherapy. *Cancer Pract.* 2000;8:231-237.
34. Schwartz AL. Fatigue mediates the effects of exercise on quality of life. *Qual Life Res.* 1999;8:529-538.
35. Mock V, Ropka M, Rhodes V, et al. Establishing mechanisms to conduct multisite research: fatigue in cancer patients; an exercise intervention. *Oncol Nurs Forum.* 1998;25:1391-1397.