Original Article

Fatigue and Quality of Life in Breast Cancer Patients Undergoing Autologous Stem Cell Transplantation: A Longitudinal Comparative Study

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Abstract
*As more individuals are being treated for cancer with high-dose therapy and autologous stem cell rescue (ASCR), there is growing interest in treatment side effects and their impact on quality of life. The primary aim of this study was to determine if the severity of fatigue and its impact on quality of life is significantly greater in women undergoing ASCR for breast cancer than in women of similar age with no history of cancer. A group of women being treated with ASCR for breast cancer (*n = *31) and a group of women of similar age with no history of cancer (*n = *49) participated in this study. Patients completed measures of fatigue and psychosocial functioning prior to treatment, midway through treatment, and toward the end of treatment. Healthy comparison subjects completed the same measures three separate times. Breast cancer patients undergoing ASCR reported significantly more frequent fatigue and more severe fatigue than women with no cancer history. In addition, fatigue had a significantly greater impact on daily functioning and quality of life in patients than in women with no cancer history. Fatigue during ASCR for breast cancer was related to both medical factors (i.e., time since transplant) and psychosocial factors.*

During ASCR for breast cancer, women experience fatigue which is worse than what is "normally" experienced and which interferes with daily functioning and quality of life. Future research should focus on identifying the biological correlates of fatigue, psychological and physiological mechanisms by which fatigue is produced, and interventions to alleviate fatigue.
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Key Words
Fatigue, bone marrow transplantation, breast cancer, quality of life

Introduction

As an increasing number of breast cancer patients are being treated with high-dose chemotherapy and autologous stem cell rescue (ASCR), there is growing interest in the experience of side effects during ASCR and the im-

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pact of those side effects on patients' quality of life.[1] One of the most common and disruptive side effects of cancer treatment is fatigue. Several definitions of fatigue have been offered. Aistairs[2] described cancer related fatigue as ". . . a condition characterized by subjective feelings of generalized weariness, exhaustion, and lack of energy resulting from prolonged stress that is directly or indirectly attributable to the disease process". Bruera and McDonald[3] defined fatigue as "a clinical syndrome characterized by generalized weakness as well as physical and mental fatigue." Fatigue has also been defined as a subjective phenomenon characterized by ". . . tiredness, weakness, lack of energy, exhaustion, lethargy, depression, inability to concentrate, malaise, boredom, sleepiness, lack of motivation, and decreased mental status."[4] These definitions suggest that fatigue is a multidimensional, subjective phenomenon that may affect physical, cognitive, and emotional functioning. Further, in more severe cases, patients have been observed to discontinue treatment.[4] Thus, in addition to the impaired functioning, fatigue levels have also interfered with treatment and dose requirements.

While fatigue has been studied in patients undergoing more standard chemotherapy and radiotherapy treatments,[4–7] there have been only two empirical studies dedicated to the assessment of this phenomenon in patients undergoing transplantation. Andrykowski and colleagues[8] collected data on fatigue severity from patients undergoing autologous or allogeneic bone marrow transplantation (BMT) for a variety of hematological diseases. Fatigue levels were measured shortly before transplantation and one year afterward using the Profile of Mood States Fatigue Scale (POMS-F) and the Sleep, Energy and Appetite Scale (SEAS). All 28 subjects were in disease remission at the time of follow-up. Results indicated that 89% of subjects reported feeling tired both before and after transplant, and that patients who reported more severe fatigue experienced more difficulties with physical and social functioning. Although no systematic changes in levels of fatigue from pre-to post-transplant proved statistically significant, it was observed through a subgroup analysis based on age that older patients reported reduced energy relative to the younger patients ($P < 0.05$).

McQuellon and colleagues[9] studied 24 female breast cancer patients undergoing autologous BMT. Assessments were conducted prior to transplant and 100 days post-treatment, but fatigue was assessed only in the post-transplant assessment. In this sample, 17% of patients reported experiencing fatigue following transplant.

The studies reviewed above suffer from several methodological limitations that limit the conclusions that can be drawn about fatigue during transplantation. In one study there was little examination of demographic, medical, and/or treatment differences within the samples, i.e., they reported on results based on both male and female patients without addressing potential gender differences and included patients with different types of cancer and who had undergone different types of transplant without controlling for these variables.[8] Further, with only two points of comparison, pre-BMT and 1 year post-BMT, there is no way to determine the effect that the process of transplantation may have on more immediate recovery. In another study, fatigue was assessed using only an unstructured interview and no standard instrument.[9] They also only collected data at one point after transplantation and thus were not able to assess the progression or trends of any changes in fatigue. Finally, both studies did not include a control group, making it difficult to put the amount of fatigue reported by patients into a meaningful context.

The current study was designed to improve on these past studies of fatigue during transplantation. Focusing specifically on the experience of this side effect in women undergoing ASCR for breast cancer, gender, type of disease, and type of transplant were held constant. In addition, a unique feature of this study was the inclusion of a comparison group of healthy women similar in age to the ASCR patients with no history of cancer. Fatigue was assessed longitudinally (3 times) in both ASCR patients and the healthy control subjects.

There were three principal aims of this study. The first aim was to determine if the prevalence of fatigue and its impact on quality of life is significantly greater in women undergoing ASCR for breast cancer than in women of similar age with no history of cancer. The second aim was to determine if anxiety and depressive symptomatology, psychosocial factors that may be related to fatigue, were significantly greater in ASCR patients than in women with

no history of cancer. The third aim was to identify medical and psychosocial factors that may be associated with more severe fatigue during ASCR. Medical variables assessed in this study included disease-related factors (e.g., stage at time of treatment) and treatment-related factors (e.g., time between reinfusion and engraftment).

Methods

Subjects

Patients. To be eligible for the ASCR group, women had to be scheduled to undergo ASCR as treatment for breast cancer at Moffitt Cancer Center from March 1995 through June 1996. In addition, these women had to: a) be 18 years or older; b) have no known untreated or unstable major medical conditions; c) have no known major psychiatric or neurological disorders that would interfere with completion of the measures; d) be able to read English; and e) have no history of treatment for other types of cancer. Of 42 patients who were eligible to participate, 1 (2%) refused, 6 (14%) died during the procedure, and 4 (10%) withdrew from participation because they felt too ill to complete the questionnaires. Complete longitudinal data was collected from 31 (74%) patients.

Healthy control subjects. To be eligible for the healthy control group, in addition to having no history of any type of cancer, the women had to: a) be 18 years or older; b) have no known untreated or unstable major medical conditions; c) have no known major psychiatric or neurological disorders that would interfere with completion of the measures; d) be able to read English. Five (9%) eligible women refused to participate. The participants completed the questionnaires on three separate occasions (see procedures below); 14 (28%) of participants withdrew from the study after the first or second assessment (usually due to time constraints). Complete longitudinal data was collected from 49 healthy control subjects.

Procedure

Patients. Breast cancer patients scheduled to undergo ASCR who met eligibility criteria were recruited to the study during an outpatient appointment prior to their admission into the hospital for transplant. Patients were given the baseline assessment packet during this appointment, and instructed to complete the measures at home within 1 week prior to admission and bring the completed measures on the day of admission. Patients were administered a second assessment at midtreatment (i.e., on or about the day of reinfusion), and a third assessment toward the end of treatment (i.e., a few days prior to discharge). The average time between the first and second assessment was 2.5 (SD = 2.0) weeks, and between the second and third assessment was 2.6 (SD = 2.9) weeks.

Healthy control subjects. The healthy control group was made up of female friends and relatives of patients who were recruited as part of a study of fatigue following BMT for breast cancer.[10,11] Patients were asked to nominate a female friend or relative within 5 years of her age with no known history of cancer to participate in the study. Women with no history of cancer who were nominated to participate were first sent a letter of introduction to the study. They were then contacted via telephone and, if they met all eligibility criteria, were recruited to the study. Self-report questionnaires were sent to and returned by the healthy subjects via mail. In order to be able to compare fatigue over time between healthy subjects and ASCR patients, the healthy comparison subjects were mailed the Fatigue Symptom Inventory (FSI) (and other study measures) three times (with approximately 2–3 weeks between assessments). The second and third assessments were preceded by a reminder telephone contact. The average time between the first and second assessment was 2.4 (SD = 3.5) weeks, and between the second and third assessment was 2.7 (SD = 3.0) weeks.

Measures

The packet of questionnaires that was administered to all of the participants contained a demographic and medical background form, the Profile of Mood States Fatigue Scale (POMS-F),[12] the FSI,[10] the State-Trait Anxiety Inventory (STAI),[13] and the Center for Epidemiological Studies Depression Scale (CES-D).[14]

The POMS-F[12] consists of 7 items that assess feelings of weariness and low energy. Respon-

dents indicate the degree to which they have experienced each of these feelings during the previous week on 5-point intensity scales (0 = Not at all; 4 = Extremely). Scores can range from 0–28; higher scores indicate worse fatigue.

The FSI[10] is comprised of 13 items that measure levels and symptoms of fatigue. Using an 11-point rating scale (0 = Not at all fatigued; 10 = Extreme fatigue) the measure includes four items rating fatigue intensity and seven items rating fatigue disruptiveness. It also includes two items measuring fatigue frequency (0–7 days) and duration (0 = None of the day; 10 = The entire day). Higher scores on intensity, duration, and disruptiveness indicate worse fatigue. Reliability and validity of the measure have been demonstrated.[10]

The STAI[13] contains two 20-item scales that measure state (current or situational) anxiety and trait (general) anxiety. Respondents rate each item on a 4-point Likert scale (State version: 1 = Not at all; 4 = Very much so, and Trait version: 1 = Almost never; 4 = Almost always). Scores range 20–80; higher scores indicate worse anxiety. Extensive data on reliability (range 0.83 to 0.92) and validity support the utility of the test.[13]

The CES-D[14] is a 20-item measure of depressive symptomatology. Respondents rate how frequently they have experienced each depressive symptom during the past week on a 4-point rating scale (0 = Rarely or none of the time; 3 = Most or all of the time). Scores range from 0–60; higher scores indicate worse depressive symptomatology. The reliability and validity of the CES-D has been demonstrated.[14]

Statistical Analyses

Possible differences in demographic characteristics between the ASCR patients and healthy control subjects were evaluated using analyses of variance (ANOVA) and chi-square analyses. With regard to possible differences between the two groups on measures of fatigue and psychosocial variables (i.e., depressive symptomatology and anxiety), it was expected that ASCR patients would report more fatigue and worse psychosocial distress than healthy subjects. Differences between the two groups across time were evaluated using a 2 × 3 (Group × Time) repeated-measures ANOVA. Group differences were evaluated at the three assessment points using ANOVA. Finally, the relationship of demographic, medical, and psychosocial variables to individual differences in fatigue among ASCR patients was examined by performing correlational analyses.

Results

Demographic Characteristics

Information about demographic characteristics of the ASCR patients and the healthy control subjects is presented in Table 1. The ASCR patients ranged in age from 36 to 74 years (mean = 51.3; SD = 15.4). The majority of these women were white (90%) and married (84%). Sixty-eight percent of the patients had attended college and 42% were employed full- or part-time at the time the data was collected. The average time since initial breast cancer diagnosis was 18 months (range 5–80 months). At the time of transplant, 28% of the patients had Stage II disease, 21% had Stage III, 48%

Table 1
Demographic Characteristics of ASCR Patients and Healthy Control Subjects

	Patients ($N = 31$) $n(\%)$	Healthy control subjects ($N = 49$) $n(\%)$
Marital status		
Never married	1 (3)	4 (8)
Currently married	26 (83)	35 (72)
Separated	2 (7)	0 (0)
Divorced	2 (7)	9 (18)
Widowed	0 (0)	1 (2)
Race		
White	28 (90)	46 (94)
Black	2 (7)	2 (4)
Hispanic	1 (3)	1 (2)
Education		
<8th grade	1 (3)	0 (0)
Some high school	1 (3)	0 (0)
High school graduate	8 (26)	9 (18)
Some college	12 (39)	18 (37)
College graduate	6 (19)	14 (29)
Some graduate school or graduate degree	3 (10)	8 (16)
Employment status[a]		
Full time	8 (26)	31 (63)
Part time	5 (16)	8 (16)
Not employed	18 (58)	10 (21)
Income		
<10,000	2 (7)	0 (2)
10,000–19,999	1 (4)	3 (7)
20,000–39,999	16 (57)	10 (22)
40,000–59,000	4 (14)	18 (40)
60,000–100,000	5 (18)	7 (16)
>100,000	0 (0)	6 (13)

[a]Chi-square = 10.0. $P \leq 0.001$: all other comparisons were nonsignificant ($P > 0.05$).

had Stage IV, and 3% had what was called Stage V disease (i.e., inflammatory breast cancer). The healthy control subjects ranged in age from 36 to 55 years (mean = 50.6; SD = 7.9). Like the ASCR patients, these women were primarily white (96%), married (71%), and had attended college (82%). Most of the healthy control subjects (82%) were employed at the time the data was collected. There were no significant differences between the ASCR patients and healthy control subjects on age or any other demographic variables with the exception of working status: a significantly greater proportion of the healthy control subjects were employed ($P < 0.001$).

Differences on Measures of Fatigue

Scores of the ASCR patients and healthy control subjects on measures of fatigue severity (POMS-F) and fatigue duration and intensity (FSI) are presented in Table 2. There were no significant differences between the groups at the baseline assessment. Patients reported being fatigued significantly more days in the past week (FSI) and for a significantly greater amount of time each day (FSI) midway through their treatment as compared to healthy subjects. Also, patients reported fatigue toward the end of treatment which was significantly more severe (POMS-F) and had occurred significantly more often during the previous week (FSI) than fatigue reported by healthy subjects. The increase in the amount of time each day that patients experienced fatigue (FSI) was significantly greater as compared to a relatively stable level of fatigue reported by the healthy subjects [Time × Group Interaction = F (2,146) = 5.26, $P < 0.01$].

Scores of the ASCR patients and healthy comparison subjects on fatigue interference ratings are presented in Table 3. At baseline, patients reported that fatigue interfered to a significantly greater degree with their ability to work than did healthy subjects. At midtreatment, compared to healthy subjects, fatigue interfered significantly with patients' general activity level, relations with others, and mood. Fatigue in ASCR patients nearing the completion of treatment interfered to a significantly greater extent with their general activity level, ability to work, concentrate, bathe or dress, relations with others, enjoyment of life, and

Table 2
Fatigue Scores for ASCR Patients and Healthy Control Subjects Prior to Treatment, Midtreatment and Near Completion of Treatment[a]

	Prior to treatment (mean ± SD)	Midtreatment (mean ± SD)	Near treatment completion (mean ± SD)
POMS Fatigue Scale			
Patients	7.4 ± 7.3	9.3 ± 7.8	9.3 ± 7.8**
Healthy control subjects	6.4 ± 6.3	6.9 ± 5.1	4.8 ± 4.5
Fatigue duration ratings			
No. of days/past week			
Patients	3.9 ± 2.9	5.1 ± 2.2**	4.5 ± 2.8**
Healthy control subjects	2.9 ± 2.3	3.5 ± 2.3	3.0 ± 2.2
Amount of time each day			
Patients	2.6 ± 2.0	4.5 ± 3.0***	4.4 ± 3.1***
Healthy control subjects	2.5 ± 1.9	2.5 ± 1.7	2.2 ± 1.5
Fatigue intensity ratings			
Most fatigue			
Patients	5.4 ± 2.8	5.3 ± 2.8	5.8 ± 3.1
Healthy control subjects	5.2 ± 2.6	5.4 ± 2.3	4.5 ± 2.8
Least fatigue			
Patients	2.1 ± 1.9	2.3 ± 2.1	2.4 ± 2.2*
Healthy control subjects	1.4 ± 1.6	1.8 ± 1.8	1.4 ± 1.6
Average fatigue			
Patients	3.8 ± 3.0	3.9 ± 2.0	3.9 ± 2.4**
Healthy control subjects	2.8 ± 2.0	3.2 ± 1.8	2.6 ± 2.0
Current fatigue			
Patients	2.9 ± 2.7	3.5 ± 2.7	2.9 ± 2.9
Healthy control subjects	2.3 ± 2.4	2.7 ± 2.2	2.4 ± 2.5

[a]Asterisks indicate between-group differences at each of the assessment points which were significant at: *$P < 0.05$ **$P < 0.01$ ***$P < 0.001$.

Table 3
Fatigue Interference Scores for ASCR Patients and Healthy Control Subjects Prior to ASCR Treatment, Midtreatment and Near Completion of Treatment[a]

	Prior to treatment (mean ± SD)	Midtreatment (mean ± SD)	Near treatment completion (mean ± SD)
Fatigue interference ratings			
General activity			
Patients	2.3 ± 2.5	3.6 ± 3.3**	3.8 ± 3.2***
Healthy control subjects	2.1 ± 2.4	1.9 ± 2.1	1.4 ± 2.0
Work			
Patients	2.8 ± 3.2*	2.9 ± 3.2	4.5 ± 4.2***
Healthy control subjects	1.6 ± 1.9	1.9 ± 1.8	1.2 ± 1.8
Concentration			
Patients	1.5 ± 2.2	2.2 ± 2.9	3.3 ± 3.2***
Healthy control subjects	1.4 ± 1.5	1.9 ± 1.5	1.2 ± 1.3
Relations with others			
Patients	1.7 ± 2.5	2.6 ± 2.9*	2.5 ± 2.8***
Healthy control subjects	1.2 ± 1.6	1.4 ± 1.6	0.8 ± 1.3
Ability to bathe and dress			
Patients	0.6 ± 1.8	0.9 ± 2.1	0.9 ± 1.8**
Healthy control subjects	0.2 ± 0.6	0.4 ± 1.2	0.1 ± 0.4
Enjoyment of life			
Patients	2.1 ± 2.5	2.9 ± 3.5	3.3 ± 3.7***
Healthy control subjects	1.7 ± 2.2	1.8 ± 2.2	1.2 ± 1.7
Mood			
Patients	2.5 ± 2.6	2.9 ± 2.9*	2.8 ± 2.7**
Healthy control subjects	1.7 ± 2.1	1.9 ± 1.7	1.5 ± 1.4

[a]Asterisks indicate between-group differences at each of the assessment points which were significant at: *$P < 0.05$ **$P < 0.01$ ***$P < 0.001$.

mood. Comparison of patients' vs. healthy subjects' interference ratings over time revealed three significant interactions indicating that patients reported increased interference due to fatigue with general activity [F (2, 146) = 3.31, $P < 0.05$], ability to work [F (2,146) = 3.75, $P < 0.05$], and ability to concentrate [F (2,146) = 4.27, $P < 0.05$] during transplant, whereas interference ratings of the healthy subjects remained stable over time.

Differences on Psychosocial Measures

Scores of the ASCR patients and healthy control subjects on measures of depression and anxiety are presented in Table 4. The ASCR patients reported significantly worse depressive symptomatology toward the end of treatment as compared to healthy subjects. Comparison between the two groups over time revealed that depression increased in ASCR patients but remained stable in healthy subjects [time × group interaction $F(2,138) = 2.36$, $P < 0.10$].

There were no significant differences in anxiety between the ASCR patients and healthy subjects. Patients reported increased anxiety at midtreatment which had returned close to baseline levels by the end of treatment (these changes did not reach statistical significance).

Correlates of Fatigue in ASCR Patients

In order to better understand the nature of fatigue in patients undergoing ASCR for breast cancer, correlational analyses were conducted to explore the relationships of demographic, medical, and psychosocial variables to the severity of fatigue (as measured by the POMS-F) toward the end of treatment (Table 5). None of the demographic variables correlated significantly with fatigue. Among the medical variables, time since initial diagnosis, size of the original tumor, number of nodes involved, cancer stage (I–IV) at diagnosis, and cancer stage (I–IV) at the time of ASCR did not correlate significantly with fatigue. We also examined difference in fatigue according to the type of conditioning regimen patients had undergone: 61% of patients received cyclophosphamide, thio-TEPA, and carboplatin [15]; 35% received thio-TEPA, Novantrone, and Taxol [16]; and 4% received ifosfamide, carboplatin, and etoposide [17]. An ANOVA revealed that scores on the POMS-F were not different across these three conditioning regimens. In addi-

Table 4
ASCR Patients and Healthy Control Subjects Ratings on the Psychosocial Variables Prior to ASCR Treatment, Midtreatment and Near Completion of Treatment[a]

	Prior to treatment (mean ± SD)	Midtreatment (mean ± SD)	Near treatment completion (mean ± SD)
Depression ratings			
Patients	8.5 ± 9.5	12.8 ± 9.6	14.5 ± 9.4*
Healthy control subjects	7.7 ± 6.8	9.1 ± 7.7	7.0 ± 7.0
Anxiety ratings			
Patients	32.8 ± 12.6	35.9 ± 12.4	33.3 ± 10.0
Healthy control subjects	33.0 ± 10.6	33.0 ± 9.9	31.9 ± 10.8

[a]Asterisks indicate between-group differences at each of the assessment points which were significant at: $*P < 0.001$.

tion, two indicators of overall treatment course were assessed in this study: the number of days from transplantation (i.e., reinfusion of stem cells) until engraftment and the length of hospital stay. Engraftment was defined as 3 consecutive days of absolute neutrophil count greater than or equal to 500/ml. In this sample, there was an average of 12 (range = 8 to 32) days to engraftment, and patients for whom engraftment took a longer period of time reported more severe fatigue toward the end of treatment. The average length of hospital stay for this sample was 29 (range = 19 to 77) days; patients whose hospitalization lasted longer reported worse fatigue toward the end of treatment.

Finally, both psychosocial variables, depressive symptomatology and anxiety, were significantly related to fatigue. More severe fatigue toward the end of treatment was associated with more depressive symptoms and with more severe anxiety.

Table 5
Correlates of Fatigue in ASCR Patients

Variables	*r*
Demographic variables	
Age	0.09
Marital status	−0.11
Race	0.02
Working status	0.19
Medical variables	
Time since diagnosis	0.22
Tumor size	−0.17
Number of nodes	−0.10
Stage at diagnosis	0.32
Stage at transplant	0.07
Days to engraft	0.41*
Days in hospital	0.50**
Psychosocial variables	
Anxiety	0.52**
Depression	0.77***

$*P < 0.05$; $**P < 0.01$; $***P < 0.001$.

Discussion

In this study, women who were undergoing ASCR for breast cancer were compared with women of similar age with no history of cancer on demographic factors, fatigue, and psychosocial variables. In addition, the medical and psychosocial correlates of fatigue in ASCR patients were assessed. This discussion summarizes the main findings and examines the clinical significance and implications of the results. The ASCR patients and healthy comparison subjects were similar on demographic characteristics, with the exception of working status: significantly more of the healthy comparison subjects were employed outside the home. This is not surprising since most patients likely had left their jobs in preparation for their hospital admission. With regard to fatigue, the patients were somewhat (although not significantly) more fatigued than the healthy control subjects at baseline. This is likely due to the fact that prior to ASCR, the patients had undergone surgery as well as adjuvant chemotherapy and/or radiotherapy. These treatments, in conjunction with the stress associated with being prepared for ASCR, would account for the increased fatigue in the patients prior to transplant.

Over the course of treatment, patients' fatigue increased but in most cases not significantly. Compared to controls, patients remained more fatigued across the three assessments, and were significantly more fatigued at midtreatment and toward the end of treatment. Overall, the results indicate that undergoing ASCR produces considerable fatigue in breast cancer patients. In a recent study it was shown that breast cancer patients who have completed ASCR also report significantly worse fatigue than healthy women of similar age.[11] Andrykowski et al.[8]

found that 89% of ASCR patients reported symptoms of fatigue prior to ASCR and 1 year after ASCR. More longitudinal research is needed to identify the pattern and persistence of fatigue throughout the transplant process and following completion of ASCR.

With regard to psychosocial distress, patients reported worse depressive symptomatology than the healthy subjects and patients' depressive symptoms became worse over the course of treatment. Patients' anxiety level was not significantly higher than that of healthy women, nor did it change greatly during ASCR. The pattern of psychosocial distress (i.e., symptoms of depression and anxiety) experienced by cancer patients undergoing transplant has been examined by several researchers. In a study of breast cancer patients undergoing autologous BMT, symptoms of depression and anxiety were assessed prior to ASCR, at midtreatment, and shortly before hospital discharge. Psychosocial distress was most severe at midtreatment but had returned to baseline levels toward the end of treatment.[18] In other studies, psychosocial distress was assessed in cancer patients prior to ASCR and following completion of treatment. Gaston-Johansson et al.[19] reported that compared to before transplant, patients experienced worse depressive symptoms immediately following treatment but these symptoms progressively decreased during the next two weeks. Syrjala et al.[20] reported that transplant recipients experienced the same level of psychosocial distress prior to treatment, 90 days post-treatment, and 1 year post-treatment. In a recent study we found that when compared to a group of healthy women with no history of cancer, women who have completed ASCR for breast cancer report significantly worse depressive symptomatology but not significantly worse anxiety.[21]

In the breast cancer patients, severe fatigue was associated with time to engraftment and length of hospital stay, i.e., patients who required more time to recover reported worse fatigue toward the end of their hospitalization. The longer recovery time implies that these patients experienced more complications and experienced a more difficult treatment course, although this was not formally assessed in this study. Future studies should assess the impact of physical complications during transplant on fatigue and quality of life. Physiologic indices (e.g., use of medications, laboratory values) should also be included to better assess the biological nature and mechanisms of fatigue. Finally, worse fatigue during ASCR was significantly associated with increased psychosocial distress, i.e., worse depressive symptomatology and a higher level of anxiety. This finding is consistent with those of some of our other studies in which we found that fatigue following ASCR or radiotherapy for breast cancer is positively and significantly associated with increased distress.[11,21] The relationship of fatigue to psychosocial distress may mimic the relationship observed between pain and psychosocial distress in cancer patients. Reports suggest that individuals who report worse pain also generally report more symptoms of depression and anxiety.[22] However, the nature and direction of the relationship between pain or fatigue with psychosocial distress has yet to be fully explained. Perhaps psychosocial distress exacerbates existing fatigue, or perhaps the functional limitations that occur due to fatigue produce a negative mood state.

The limitations of the current study include a sample that consisted primarily of women who were Caucasian, married, well educated, and from a middle to upper socioeconomic status; generalizations to breast cancer patients with different demographic characteristics cannot be made. In addition, the 10% dropout rate due to some patients feeling too ill to complete the self-report measures may have resulted in an underreporting of fatigue. A strength of the current study was the use of a longitudinal design, but even though the breast cancer patients were initially assessed prior to ASCR, they had already undergone chemotherapy and/or radiotherapy, treatments which can cause considerable fatigue.[4] In fact, the level of fatigue reported by the patients at the first assessment was higher (although not to a statistically significant extent) than was reported by the healthy controls. These baseline differences may have limited our ability to detect significant longitudinal differences between the patients and healthy controls. Finally, although the ASCR patients reported that fatigue increased over the course of treatment, there were few significant changes due to the level of fatigue reported at the first assessment. One way to assess the patterns of fatigue which may occur during cancer treatment would be to identify patients

at the time of diagnosis and follow them throughout their entire treatment regimen.

Despite these limitations the findings of this study suggest that fatigue is an ongoing problem for patients undergoing ASCR for breast cancer. Future research should focus on the physiological and psychosocial mechanisms by which fatigue is produced and on the development of interventions to alleviate fatigue in cancer patients.

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