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# Fatigue After Treatment for Early Stage Breast Cancer:

## A Controlled Comparison

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## Abstract

**BACKGROUND—**Evidence suggests that fatigue may be a greater problem for cancer survivors than people without cancer. The present study sought to determine whether fatigue was greater in women who had completed treatment for early-stage breast cancer relative to a demographically matched comparison group of women with no cancer history.

**METHODS—**As part of a larger study, women with stage 0-II breast cancer were recruited before the start of chemotherapy and radiotherapy (n = 100) or radiotherapy only (n = 121). Fatigue was assessed at the end of treatment and 2, 4, and 6 months later. An age- and geographically matched sample of women with no history of cancer was recruited and assessed for comparison purposes.

**RESULTS—**Relative to comparison subjects, breast cancer survivors reported more days of fatigue in the past week at all 4 study assessments ($P < .05$). These differences appeared to be clinically meaningful in that a greater percentage of patients than nonpatients earned scores in the abnormal range on this measure at each assessment ($P < .05$). Additional analyses indicated that differences in fatigue between patients and comparison subjects were attributable primarily to heightened fatigue in women who received both chemotherapy and radiotherapy.

**CONCLUSIONS—**Findings suggest that fatigue is a greater problem for breast cancer survivors in the 6 months after completion of chemotherapy than for women with no cancer history. Future research should include longer-term follow-up to determine the persistence of fatigue in this population of survivors.

### Keywords

fatigue; breast cancer; adjuvant therapy; survivorship

Evidence suggests that fatigue is among the most common problems experienced by adult cancer survivors.[1-3] For example, a survey of adults who had been diagnosed with cancer approximately 1 year previously found that 67% reported a problem with fatigue.[2] Although frequently reported, questions arise about whether fatigue is a greater problem for cancer survivors than for people without cancer. The issue reflects the finding that fatigue is also common in the general population.[4,5]

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One useful approach to determining whether fatigue is a greater problem for cancer survivors is to compare survivors with individuals who have no history of cancer. Consideration should be given to matching the samples on demographic characteristics associated with fatigue, such as age,[4-6] because differences in these characteristics could confound interpretation of results. Consideration should also be given to recruiting samples of cancer survivors with similar disease and treatment histories because variability in these characteristics is likely to contribute to variability in fatigue.[7-9]

Comparisons of the type proposed have been conducted primarily with breast cancer patients treated with adjuvant therapy. In 1 study,[10] 88 women with stage 0-IIIa breast cancer were compared with an age-matched sample of 88 women who had benign breast problems but no history of breast cancer. Patients had completed treatment an average of 25 months previously (range, 2-54 months), with the majority (67%) having received adjuvant therapy (chemotherapy and/or radiotherapy). Findings showed that survivors reported greater fatigue on the Piper Fatigue Scale and the Medical Outcomes Study (MOS) Vitality Scale.

In another study,[11] 61 women with stage I-III breast cancer were compared with an age-matched sample of 59 women with no cancer history nominated by the patients. All the patients had received chemotherapy and 48% also received radiotherapy. The average time since chemotherapy completion was 471 days (range, 108-875 days). Findings showed that survivors reported greater fatigue on the Profile of Mood States Fatigue Scale (POMS-F), the Multidimensional Fatigue Symptom Inventory (MFSI), and measures of current fatigue and fatigue interference from the Fatigue Symptom Inventory (FSI).

In a study using a similar design,[12] 45 women with stage 0-III breast cancer were compared with an age-matched sample of 44 women with no cancer history nominated by the patients. All the patients had received radiotherapy and had completed treatment an average of 22 months previously (range, 5-88 months). No significant ($P < .05$) differences were found on any of the fatigue measures administered (POMS-F, MFSI, and FSI).

In a study limited to individuals age 70 year and older,[13] 127 women who had been diagnosed with breast cancer at least 1 year previously were compared with 87 women without cancer participating in a longitudinal study of aging. Patients had been diagnosed an average of 5.1 years previously (range, 1-15 years), with 65% having received chemotherapy and 17% having received radiotherapy. Findings showed that survivors reported more severe fatigue on the MOS Vitality Scale and more frequent fatigue on the FSI.

In 1 other study of this type,[14] 164 women with stage I-III breast cancer were compared with an ageand race-matched sample of 164 women with no history of cancer recruited using the neighborhood control method.[15] The patients had all been diagnosed 5½ years previously and treated with chemotherapy. There was no significant ($P < .05$) difference on the 1 fatigue measure for which results were reported (MOS Vitality Scale). A subsequent report derived from the same study compared 267 disease-free survivors with 187 controls.[16] There were no significant ($P < .05$) differences between patients and controls on the MOS Vitality Scale or the General and Physical Fatigue Scales of the MFSI. However, patients who had not previously received an educational intervention[17] scored significantly higher on the MFSI Mental Fatigue Scale than both patients who had received the intervention and controls.

The lack of consistent findings across studies can be attributed, in part, to differences in methodology. These include differences in fatigue measures administered and differences in the average time since treatment completion. Beyond this, several of the studies have methodological features that limit the conclusions that can be drawn. First, only 2 studies recruited comparison subjects without cancer directly from the community.[13,14] The possibility that women with benign breast problems[10] and women nominated by breast cancer

patients[11,12] may have problems with fatigue that could lead to biased findings cannot be ruled out. Second, only 1 study recruited patients who were all at a similar timepoint from the end of treatment.[14] The wide intervals in time since treatment completion in the other studies[10-12] preclude generalizability of the results to a specific timepoint in the survivorship period. Third, only 2 studies[12,14] limited participation to breast cancer patients treated with the same adjuvant therapy modality. The other studies did not conduct analyses comparing the treatment subgroups with their respective matches, possibly because of small sample sizes. Consequently, it is unknown whether results from these studies are generalizable to all the different treatment modalities represented in the samples.

The present study was designed to further an understanding of fatigue after treatment for early stage breast cancer by addressing several limitations of previous research. To this end, the study used an age- and geographically matched comparison sample recruited from the community to limit potential biases in reports of fatigue. The patient sample included only women with nonmetastatic breast cancer who received adjuvant therapy (radiotherapy alone or chemotherapy plus radiotherapy) to limit variability in disease and treatment status. Sufficient numbers of patients were recruited to permit meaningful comparisons of each treatment subgroup with their respective matched controls. Finally, all post-treatment assessments were conducted in the 6 months after completion of radiotherapy to provide information about fatigue at specific timepoints early in the course of cancer survivorship. These data were used to test the hypothesis that breast cancer survivors would report greater fatigue than women with no history of cancer. Differences between patients and comparison subjects were expected to be greatest at the initial patient assessment, diminishing over the 6-month follow-up period. Consistent with prior research directly comparing treatment subgroups,[18,19] we also predicted that women treated with both chemotherapy and radiotherapy would report greater fatigue relative to comparison subjects than women treated with radiotherapy alone.

## METHODS

### Participant Selection and Recruitment

Patients were eligible if they: 1) were at least 18 years of age; 2) had no documented or observable psychiatric or neurological disorders that would interfere with participation; 3) were able to speak and read English; 4) were women diagnosed with stage 0-II breast cancer; 5) had no other history of cancer besides basal cell skin carcinoma; 6) had been treated surgically for breast cancer; 7) were scheduled to receive chemotherapy followed by radiotherapy (CT + RT group) or radiotherapy only (RT group) at the Moffitt Cancer Center (MCC; Tampa, Fla) or the Lucille Parker Markey Cancer Center (LPMCC; Lexington, Ky); 8) had no prior history of chemotherapy or radiotherapy; and 9) reported no history of conditions in which fatigue is a prominent symptom (ie, AIDS, multiple sclerosis, rheumatoid arthritis, fibromyalgia, or chronic fatigue syndrome). As part of a larger study investigating quality of life, patients were screened for eligibility and asked to provide written informed consent during an outpatient visit before the start of chemotherapy (CT + RT group) or radiotherapy (RT group). Assessments relevant to the current report were conducted at the end of treatment (just before the last radiotherapy treatment), and 2, 4, and 6 months after treatment. Every patient who completed the 6-month assessment was matched with a nonpatient participant using procedures described below. Of 317 patients enrolled in the study, 221 (70%) completed the 6-month assessment (MCC n = 113; LPMCC n = 108) and were included in the present analysis. Compared with patients who completed the 6-month assessment, noncompleters were significantly ($P < .05$) more likely to have received chemotherapy and radiation and to have greater body mass index, less education, and less income.

Eligibility criteria for nonpatients were that they must: 1) be women; 2) be within 5 years of the age of the patient to whom they would be matched; 3) reside within the same zip code as their patient match; 4) have no discernable psychiatric or neurological disorders that would interfere with study participation; 5) be able to speak and read English; 6) report no history of cancer (other than basal cell skin carcinoma) or other potentially life-threatening diseases; and 7) report no history of conditions in which fatigue is a prominent symptom (as described above). Potential nonpatient participants were identified using a database maintained by Marketing Systems Group (Fort Washington, Pa) that draws from all listed telephone households in the US and is estimated to include demographic and contact information for approximately two-thirds of the US population. For each patient who completed the 6-month assessment, up to 25 women who resided in the same zip code and were within 5 years of the patient's age were selected randomly from the database. One of these women was randomly selected and sent a letter of introduction. If this woman did not opt out by calling a toll-free telephone number (MCC) or did return a postcard expressing interest (LPMCC), telephone contact was initiated to further determine eligibility. If she met all eligibility criteria and verbally agreed to participate, an appointment was set up to obtain written consent and conduct an assessment. If the first woman selected could not be reached, was ineligible, refused to participate, or did not keep the appointment, another woman on the list was selected randomly until a woman matched to the patient was recruited and completed the assessment.

## Measures

**Demographic and clinical data—**Age, race/ethnicity, marital status, annual household income, educational level, height, weight, and menopausal status were assessed in all participants via self-report. Disease stage, type of breast surgery, chemotherapy agents (CT + RT group only), cumulative radiation doses, and hormone therapy status were assessed in patients via chart review.

**Fatigue—**The Fatigue Symptom Inventory[20] (FSI) is a 14-item measure that assesses the frequency and severity of fatigue and its perceived disruptiveness. Analyses focused on participants' ratings of fatigue severity (0 = not at all fatigued, 10 = as fatigued as I could be) on the day they felt most fatigued in the past week (FSI most), on average in the past week (FSI average), and right now (FSI current). Analyses were also conducted using ratings of the number of days fatigued in the past week (0 to 7) (FSI days) and the average rating of the degree (0 = no interference, 10 = extreme interference) to which fatigue interfered with general activity, ability to bathe and dress, normal work activity, ability to concentrate, relations with others, enjoyment of life, and mood (FSI interference). Previous research has demonstrated the reliability and validity of the FSI in women diagnosed with breast cancer.[11,12,20] Participants also completed the 7-item Profile of Mood States (POMS) Fatigue Scale,[21] on which they rated the degree to which they felt fatigued in the past week (0 = not at all, 4 = extremely). A total score was calculated (possible range = 0 to 28), with higher scores indicating greater fatigue.

## Statistical Analysis

Preliminary analyses were conducted to identify possible differences in demographic characteristics between patient and nonpatient participants. Chi-square analyses were conducted on categorical variables (eg, marital status) and *t*-test were conducted on continuous variables (eg, age).

In the main analysis, general linear models were used to compare data on fatigue collected from patients at the 4 assessment points with data collected from their nonpatient matches at their 1 assessment. Additional general linear model analyses were conducted to determine whether differences observed in the main analyses were attributable to differences between

CT + RT patients and their respective matches and/or RT patients and their respective matches. Analyses were also conducted to evaluate the meaningfulness of statistically significant differences in fatigue between patients and non-patients. In these analyses, participants' fatigue ratings were classified as "abnormal" if they were more than 1 standard deviation (1 SD) above the mean of the nonpatient group on the measure being evaluated. A similar threshold has been recommended for identifying abnormal (ie, impaired) performance on measures of cognitive abilities.[22] Scores of this magnitude would be expected in normally distributed variables to occur in fewer than 16% of individuals. A mean difference on a measure was considered to be clinically meaningful if chi-square analyses indicated that the percentages of patients and nonpatients with scores in the abnormal range differed significantly.

Sporadic missing data on fatigue for 32 of the 442 participants (7%) were estimated using multiple imputation techniques.[23] A $P \leq .05$ probability level (2-tailed) was used in all analyses to evaluate statistical significance. Analyses were conducted using SAS statistical software (SAS Institute, Cary, NC). With sample sizes of 221 individuals per group for the main analyses, statistical power was adequate (>.80) to detect small to medium size differences (d = .3) in fatigue levels.

## RESULTS

### Characteristics of Patients and Nonpatients

Demographic characteristics of the patient and nonpatient samples appear in Table 1. Although age was used as a matching variable, the nonpatient sample was older than the patient sample by 2.44 years ($P > .006$). Differences on all other demographic variables were not significant ($P > .05$). On the basis of these results, age was included as a covariate in subsequent comparisons of patients with nonpatients. Clinical characteristics of CT + RT patients and RT patients appear in Table 2.

### Comparison of Fatigue Between Patients at the End of Treatment Assessment and Nonpatients

Significant differences were evident between patients at the end of treatment assessment and nonpatients on all 6 fatigue measures (see Table 3). In each instance, patients reported greater fatigue than nonpatients ($P \leq .008$). The observed mean differences appeared to be clinically meaningful in that a greater percentage of patients than nonpatients scored in the abnormal range on each measure ($P \leq .001$, see Table 4). Additional analyses indicated that CT + RT patients reported greater fatigue than their matches on 5 of the 6 measures ($P \leq .02$, see Table 5). RT patients reported greater fatigue than their matches on all 6 measures ($P \leq .02$, see Table 6).

### Comparison of Fatigue Between Patients at the 2-Month Assessment and Nonpatients

Significant differences were evident between patients at the 2-month assessment and nonpatients in ratings of the number of days fatigued (see Table 3). Similar to the end of treatment assessment, patients reported more days of fatigue ($P = .009$). The observed mean difference appeared to be clinically meaningful in that a greater percentage of patients than nonpatients scored in the abnormal range ($P = .006$, see Table 4). Additional analyses indicated that CT + RT patients ($P = .001$), but not RT patients ($P = .48$), reported more days of fatigue than their matches (see Tables 5 and 6).

Significant differences were also evident between patients at the 2-month assessment and nonpatients in ratings of current fatigue (see Table 3). Similar to the end of treatment assessment, patients provided higher ratings of current fatigue ($P = .007$). The observed mean difference appeared to be clinically meaningful in that a greater percentage of patients than

nonpatients scored in the abnormal range ($P = .02$, see Table 4). Additional analyses indicated that CT + RT patients ($P = .02$), but not RT patients ($P = .10$), reported greater current fatigue than their matches (see Tables 5 and 6).

Significant differences were also evident between patients at the 2-month assessment and nonpatients in POMS-F scores (see Table 3). Similar to the end of treatment assessment, patients scored higher on the POMS-F ($P = .05$). The observed mean difference did not appear to be clinically meaningful in that the percentages of patients and nonpatients scoring in the abnormal range did not differ ($P = .30$, see Table 4). Additional analyses indicated that CT + RT patients ($P = .05$), but not RT patients ($P = .36$), scored higher on the POMS-F than their matches (see Tables 5 and 6).

### Comparison of Fatigue Between Patients at the 4-Month Assessment and Nonpatients

Significant differences were evident between patients at the 4-month assessment and nonpatients in ratings of the number of days fatigued (see Table 3). Similar to the end of treatment and 2-month assessments, patients reported more days of fatigue ($P = .01$). The observed mean difference appeared to be clinically meaningful in that a greater percentage of patients than nonpatients scored in the abnormal range ($P = .01$, see Table 4). Additional analyses indicated that CT + RT patients ($P = .003$), but not RT patients ($P = .43$), reported more days of fatigue than their matches (see Tables 5 and 6).

Significant differences were evident between patients at the 4-month assessment and nonpatients in ratings of the current fatigue (see Table 3). Similar to the end of treatment and 2-month assessments, patients provided higher ratings of current fatigue ($P = .04$). Although there was a mean difference, there was no difference ($P = .07$) in the percentages of patients and nonpatients scoring in the abnormal range (see Table 4). Additional analyses did not reveal significant differences between CT + RT patients and their matches ($P = .11$) or RT patients and their matches ($P = .15$) on this measure (see Tables 5 and 6).

Significant differences were also evident between patients at the 4-month assessment and nonpatients in ratings of most fatigue (see Table 3). Contrary to predictions, patients provided lower ratings than nonpatients of their level of fatigue on the day they felt most fatigued in the past week ($P = .05$). Although there was a mean difference in most fatigue, there was no difference ($P = 1.00$) in the percentages of patients and nonpatients scoring in the abnormal range on this measure (see Table 4). Additional analyses did not reveal significant differences between CT + RT patients and their matches ($P = .31$) or RT patients and respective matches ($P = .10$) on this measure (see Tables 5 and 6).

### Comparison of Fatigue Between Patients at the 6-Month Assessment and Nonpatients

Significant differences were evident between patients at the 6-month assessment and nonpatients in ratings of the number of days fatigued (see Table 3). Similar to all 3 previous assessments, patients reported more days of fatigue ($P = .04$). The observed mean difference appeared to be clinically meaningful in that a greater percentage of patients than nonpatients scored in the abnormal range on this measure ($P = .04$, see Table 4). Additional analyses indicated that CT + RT patients ($P = .03$), but not RT patients ($P = .41$), reported more days of fatigue than their respective matches (see Tables 5 and 6).

Significant differences were also evident between patients at the 6-month assessment and nonpatients in ratings of most fatigue (see Table 3). Similar to the 4-month assessment, patients provided lower ratings than nonpatients of their level of fatigue on the day they felt most fatigued in the past week ($P = .01$). Although there was a mean difference in most fatigue, there was no difference ($P = 1.00$) in the percentages of patients and nonpatients scoring in the

abnormal range on this measure (see Table 4). Additional analyses indicated that RT patients ($P$ = .05), but not CT + RT patients ($P$ = .13), provided lower ratings of most fatigue than their respective matches (see Tables 5 and 6).

## DISCUSSION

The present study yielded 3 major findings. First, the results clearly showed that the degree of fatigue experienced by patients at the completion of adjuvant therapy was greater than that experienced by women with no history of cancer. These differences were present for both treatment subgroups and appeared to be clinically meaningful. Second, results showed that the differences between patients and comparison subjects evident at the end of treatment tended to diminish over time. However, even at the 6-month follow-up assessment a statistically significant and clinically meaningful group difference in fatigue duration was still evident. Third, the results consistently showed that the diminishment in fatigue over time varied as a function of treatment subgroup, with greater fatigue evident only among women treated with both chemotherapy and radiotherapy relative to comparison subjects. These latter findings are consistent with several previous studies showing that, among women with breast cancer, posttreatment fatigue is greater in those treated with adjuvant chemotherapy than in those not treated with adjuvant chemotherapy.[18,19]

Contrary to expectations, nonpatients' ratings of most fatigue in the past week were greater than patients' ratings at the 4-month and 6-month assessments. It should be noted, however, that neither difference appeared to be clinically meaningful. One possible explanation for this pattern is that a “response shift” occurred in patients' perceptions of fatigue. Response shift has been defined as a change in internal standards brought about by a change in health status.[24] In the context of cancer treatment, response shift may represent an adaptive response to aversive symptoms.[25] As patients try to deal with treatment side effects, changes in internal standards may occur such that perceptions of symptom severity are attenuated. Evidence for response shift includes 2 previous studies that demonstrated changes in internal standards for fatigue among breast cancer patients treated with radiotherapy.[26,27] With regard to the current study, the results suggest that patients' recalibrated their standards for the most fatigue they had ever experienced upward as a consequence of undergoing cancer treatment. This recalibration would explain why their ratings of greatest fatigue in the posttreatment period were generally lower than those of individuals who had never experienced cancer-related fatigue.

The reasons why differences were consistently evident in the posttreatment period on a measure of fatigue duration and not on measures of fatigue severity or interference are not entirely clear. One possibility mentioned already in another context is that certain methods of assessing fatigue may be more susceptible to response shift than others. Specifically, measures rated along highly subjective dimensions (ie, perceived severity and perceived interference) may be more susceptible to changes over time in internal standards than measures rated along less subjective dimensions (ie, estimating number of days fatigued). Regardless of the explanation, the present study demonstrates the value of conducting a multidimensional assessment of fatigue given the differential pattern of results.

Although the present study addressed several methodological shortcomings of prior studies, several limitations were still present. First, attrition among patients was related to several demographic factors and to receipt of chemotherapy plus radiation. The potential exists that the current results could be biased by this selective attrition. Second, despite matching procedures, the survivor sample was significantly younger than the noncancer sample. Inclusion of age as a covariate in comparisons of the 2 samples was used to address this limitation. Third, the study included patients who received 2 different forms of adjuvant

treatment. However, sufficient numbers of participants were enrolled to allow meaningful statistical comparisons of each treatment subgroup with their respective matches. Indeed, these comparisons revealed interesting findings showing persistence of fatigue in 1 treatment subgroup and not the other. Fourth, the samples reflected little racial diversity. Accordingly, the results may not be generalizable to minority women with breast cancer. Fifth, patients were followed for only 6 months after treatment completion. The possibility that fatigue present at the 6-month assessment would still be evident at later points in time is unknown.

Finally, the present study did not address the issue of why patients treated with both chemotherapy and radiotherapy were still experiencing more days of fatigue 6 months after completing treatment relative to a noncancer comparison group. Other lines of research suggest that behavioral and/or biological mechanisms may be responsible. With regard to behavioral mechanisms, there is evidence that breast cancer patients exercising less and engaging in more catastrophic coping about fatigue at the end of treatment are more likely to report heightened fatigue over the next 6 months.[28] Additional evidence for the role of exercise includes research demonstrating the benefits of exercise in improving fatigue among breast cancer survivors.[29] With regard to biological mechanisms, there is evidence that, among breast cancer survivors who were at least 1 year post-diagnosis and had completed adjuvant therapy, those who were fatigued show higher levels of proinflammatory cytokine activity than those who were not fatigued.[30,31] Findings from the current study suggest that future research focus on breast cancer patients experiencing heightened fatigue during adjuvant chemotherapy and explore whether interventions administered during or at the end of treatment are effective in preventing or limiting fatigue in the posttreatment period. Future research should also examine how intervention efforts could be targeted based on the identification of behavioral and biological risk factors for persistent fatigue in the posttreatment period.

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**TABLE 1**

Demographic Characteristics of Patients and Controls

| | Patients (N = 221) | Controls (N = 221) | P |
|---|---|---|---|
| Age, mean ± SD | 54.60 ± 9.53 | 57.04 ± 9.01 | .006 |
| Body mass index, mean ± SD | 27.10 ± 5.91 | 27.86 ± 6.20 | .19 |
| Household income | | | .13 |
| ≥$40,000 per y | 71% | 63% | |
| ≤$40,000 per y | 29% | 37% | |
| Race | | | 1.00 |
| White | 92% | 93% | |
| Nonwhite | 8% | 7% | |
| Menopausal status | | | 1.00 |
| Premenopausal | 71% | 71% | |
| Peri- or postmenopausal | 29% | 29% | |
| Marital status | | | .18 |
| Married | 73% | 67% | |
| Not married | 27% | 33% | |
| Education | | | .25 |
| College degree | 42% | 48% | |
| <College degree | 58% | 52% | |

**TABLE 2**

Clinical Characteristics of Patients

| | CT + RT patients (N = 100) | RT patients (N = 121) |
|---|---|---|
| Surgery | | |
| Lumpectomy | 91% | 100% |
| Mastectomy | 9% | 0% |
| Stage | | |
| 0 | 2% | 16% |
| I | 24% | 77% |
| II | 74% | 7% |
| Hormonal therapy | | |
| Yes | 53% | 83% |
| No | 47% | 17% |
| Radiation dose in cGy | | |
| Mean (SD) | 6065 (587) | 6045 (683) |
| No. of chemotherapy cycles | | |
| 4 | 61% | - |
| 6 | 14% | - |
| 8 | 24% | - |
| 9 | 1% | - |
| Chemotherapy regimens | | |
| Anthracycline, cyclophosphamide | 55% | - |
| Anthracycline, cyclophosphamide, taxane | 29% | - |
| Cyclophosphamide, methotrexate, fluorouracil | 13% | - |
| Anthracycline, taxane | 1% | - |
| Anthracycline, cyclophosphamide, fluorouracil | 1% | - |
| Anthracycline, cyclophosphamide, fluorouracil, taxane | 1% | - |

**TABLE 3**

Fatigue Levels in Patients and Controls

| | Controls M (SD) | Patients end of treatment M (SD) *P* | Patients 2-mo follow-up M (SD) *P* | Patients 4-mo follow-up M (SD) *P* | Patients 6-mo follow-up M (SD) *P* |
|---|---|---|---|---|---|
| POMS-F | 4.51 (5.40) | 7.57 (6.54) <.0001 | 5.52 (5.55) .05 | 5.01 (5.19) .24 | 5.08 (5.57) .24 |
| FSI most | 3.80 (2.60) | 4.54 (2.99) .008 | 3.41 (2.89) .16 | 3.28 (2.82) .05 | 3.14 (2.85) 01 |
| FSI average | 2.38 (2.05) | 3.11 (2.41) .0009 | 2.25 (2.18) .63 | 2.19 (2.08) .43 | 2.12 (2.23) .24 |
| FSI current | 1.53 (1.94) | 2.79 (2.74) <.0001 | 2.07 (2.40) .007 | 1.92 (2.31) .04 | 1.76 (2.26) .21 |
| FSI days | 2.50 (2.13) | 4.28 (2.62) <.0001 | 3.05 (2.57) .009 | 3.01 (2.62) .01 | 2.92 (2.61) .04 |
| FSI interference | 1.15 (1.55) | 1.74 (2.02) .0007 | 1.23 (1.67) .52 | 1.15 (1.61) .79 | 1.20 (1.76) .67 |

POMS-F indicates Profile of Mood States Fatigue Scale; FSI, Fatigue Symptom Inventory.

**TABLE 4**

Rates of Abnormal Fatigue in Patients and Controls

| | Cutoff score* | % Controls | Patients end of treatment %*P* | Patients 2-mo follow-up %*P* | Patients 4-mo follow-up %*P* | Patients 6-mo follow-up %*P* |
|---|---|---|---|---|---|---|
| POMS-F | 10 | 14 | 28 .0005 | 18 .30 | 16 .69 | 15 .79 |
| FSI most | 7 | 18 | 31 .001 | 17 1.00 | 18 1.00 | 18 1.00 |
| FSI average | 5 | 14 | 28 .0005 | 18 .36 | 19 .25 | 17 .51 |
| FSI current | 4 | 15 | 35 <.0001 | 24.02 | 23 .07 | 21 .14 |
| FSI days | 5 | 19 | 52 <.0001 | 31 .006 | 30 .01 | 28 .04 |
| FSI interference | 3 | 13 | 25 .001 | 17 .29 | 15 .58 | 17 .23 |

POMS-F indicates Profile of Mood States Fatigue Scale; FSI, Fatigue Symptom Inventory.

*Based on 1 standard deviation criterion.

**TABLE 5**

Fatigue Levels in Chemotherapy Plus Radiotherapy (CT + RT) Patients and Controls

| | Controls M (SD) | CT + RT patients end of teatment M (SD) *P* | CT + RT patients 2-mo follow-up M (SD) *P* | CT + RT patients 4-mo follow-up M (SD) *P* | CT + RT patients 6-mo follow-up M (SD) *P* |
|---|---|---|---|---|---|
| POMS-F | 4.32 (5.10) | 7.43 (5.81) <.0001 | 5.62 (5.45) .05 | 5.16 (5.10) .14 | 5.06 (5.62) .27 |
| FSI most | 3.85 (2.55) | 4.41 (2.72) .20 | 3.51 (2.77) .36 | 3.43 (2.70) .31 | 3.23 (2.82) .13 |
| FSI average | 2.40 (1.90) | 3.10 (2.16) .02 | 2.37 (2.11) .99 | 2.33 (2.04) .97 | 2.11 (2.24) .39 |
| FSI current | 1.55 (1.99) | 2.65 (2.51) .0008 | 2.20 (2.33) .02 | 1.94 (2.18) .11 | 1.80 (2.30) .34 |
| FSI days | 2.40 (1.85) | 4.47 (2.50) <.0001 | 3.39 (2.57) .001 | 3.27 (2.65) .003 | 3.05 (2.59) .03 |
| FSI interference | 1.06 (1.33) | 1.62 (1.71) .01 | 1.32 (1.67) .18 | 1.12 (1.40) .47 | 1.14 (1.59) .60 |

POMS-F indicates Profile of Mood States Fatigue Scale; FSI, Fatigue Symptom Inventory.

**TABLE 6**

Fatigue Levels in Radiotherapy (RT) Patients and Controls

| | Controls M (SD) | RT patients end of treatment M (SD) *P* | RT patients 2-mo follow-up M (SD) *P* | RT patients 4-mo follow-up M (SD) *P* | RT patients 6-mo follow-up M (SD) *P* |
|---|---|---|---|---|---|
| POMS-F | 4.67 (5.64) | 7.68 (7.09) .0003 | 5.24 (5.63) .36 | 4.89 (5.26) .72 | 5.11 (5.52) .53 |
| FSI most | 3.76 (2.64) | 4.65 (3.19) .02 | 3.33 (2.98) .28 | 3.16 (2.92) .10 | 3.06 (2.87) .05 |
| FSI average | 2.37 (2.17) | 3.12 (2.61) .02 | 2.16 (2.23) .55 | 2.08 (2.12) .34 | 2.12 (2.23) .43 |
| FSI current | 1.52 (1.90) | 2.90 (2.91) <.0001 | 1.96 (2.45) .10 | 1.90 (2.42) .15 | 1.73 (2.24) .40 |
| FSI days | 2.59 (2.34) | 4.12 (2.71) <.0001 | 2.77 (2.54) .48 | 2.80 (2.57) .43 | 2.82 (2.63) .41 |
| FSI interference | 1.23 (1.72) | 1.85 (2.25) .02 | 1.51 (1.67) .81 | 1.18 (1.77) .90 | 1.25 (1.88) .90 |

POMS-F indicates Profile of Mood States Fatigue Scale; FSI, Fatigue Symptom Inventory.