Published in final edited form as:

Psychol Health. 2009 October ; 24(8): 965–980. doi:10.1080/08870440802110831.

Fatigued Breast Cancer Survivors: The Role of Sleep Quality, Depressed Mood, Stage, and Age

Rajni Banthia, Ph.D.,

SDSU/UCSD Joint Doctoral Program in Clinical Psychology

Vanessa L. Malcarne, Ph.D.,

San Diego State University, Rebecca and John Moores University of California, San Diego Cancer Center

Celine M. Ko, Ph.D.,

SDSU/UCSD Joint Doctoral Program in Clinical Psychology

James W. Varni, Ph.D., and

Texas A&M University, College Station

Georgia Robins Sadler, BSN, MBA, Ph.D.

Rebecca and John Moores University of California, San Diego Cancer Center, Department of Surgery, UCSD School of Medicine

Abstract

Cancer-related fatigue is associated with lower health-related quality of life and the majority of breast cancer survivors experience persistent fatigue after finishing treatment. The present study examined age, cancer stage, sleep quality, and depressed mood as predictors of five dimensions of fatigue in seventy fatigued breast cancer survivors who no longer evidenced any signs of cancer and were finished with treatment. Discriminant function analyses were used to predict fatigue subgroup membership (higher, lower) from age, stage, mood, and sleep for five subtypes: General, Mental, Emotional, and Physical Fatigue, and Vigor. Significant discriminant functions were found for all subtypes. Findings suggest that age, staging, mood, and sleep are all important predictors, but there are differential relationships when subtypes of fatigue are considered. Given current limitations in treating fatigue directly, interventions targeting mood and sleep should be considered as alternate approaches to reduce fatigue.

Keywords

Fatigue; Breast Cancer; Sleep Quality; Depressed Mood

Sixty to ninety-six percent of women with breast cancer experience fatigue following diagnosis and treatment (Jacobsen et al., 1999; Longman, Braden, & Mishel, 1999; Portenoy & Itri, 1999; Shimozuma et al., 1999; Stone et al., 2000). Often the first and last symptom

experienced during the course of cancer (Longman et al.; Portenoy & Itri; Stone et al.; Walsh, Donnelly, & Rybicki), cancer-related fatigue (CRF) is reported more frequently than other side effects and can be more disruptive (Wagner & Cella, 2004). Time since the end of treatment does not relate consistently to decreases in CRF, suggesting CRF can persist for an indeterminate duration (Mast, 1998).

CRF can be especially disruptive for survivors of breast cancer, as it detracts from one's ability to return to work and/or resume taking care of family, roles that women often are expected to return to following the end of treatment (Levine et al., 1988). Women in treatment can hold onto the hope that fatigue will disappear once they complete treatment, but this hope can be shattered in the post-treatment phase if fatigue persists (Ashbury et al., 1998). During the post-treatment phase, women are unlikely to see their health care providers as regularly as they did while on treatment, and thus their fatigue may go unaddressed. They may also receive less support from friends and family who expect cancer-related problems to cease once the disease has been cured (Escalante et al., 2001).

There is controversy regarding whether CRF is best conceptualized as a symptom, side-effect, syndrome, or disorder (Ahsberg & Furst, 2001), and there are different approaches to measuring fatigue. Due to its broad conceptualization, it is useful to approach measurement of CRF in a general/global fashion (Lai, Crane, & Cella, 2006), and also to assess opposite constructs such as vigor or energy (Stein et al., 1998). To capture the extent of its impact, a thorough assessment also should include attention to various aspects of fatigue (Smets et al., 1995). Cella et al. (1998) have identified three primary dimensions of CRF. The psychological/ emotional dimension is characterized by mood disturbance, anhedonia, and decreased motivation. The cognitive/ mental aspect is noted by diminished concentration and capacity to direct attention, as well as memory problems. The behavioral/ physical dimension is marked by weakness and difficulty initiating activity or completing tasks.

More needs to be learned about the etiology of CRF in breast cancer survivors (Knowles, Borthwick, McNamara, Miller, & Leggot, 2000), and potential predictors and closely related correlates should be measured carefully (Bennett et al., 2004). Among the many possibilities, comorbid medical conditions, enduring side effects, and deconditioning due to decreased activity may contribute to CRF (Wagner & Cella, 2004). Biological markers have been examined in survivors (Collado-Hidalgo et al., 2006), but do not account for all CRF cases. In addition, demographic variables such as cancer stage and age, as well as psychosocial factors such as sleep quality and depressed mood, have been posited to influence CRF in breast cancer survivors (Bleiker, Pouwer, van de Ploeg, Leer, & Ader, 2000; Bower et al., 2000).

Age and fatigue

Younger breast cancer patients tend to report more severe CRF than their older counterparts (Glaus, 1998). Younger women are diagnosed with breast cancer less often than older women yet are more likely to present advanced disease and/or undergo aggressive treatment regimens, both of which can lead to severe fatigue (Cimprich, Ronis, & Martinez-Ramos, 2002). In addition, young women may have greater social and environmental demands (e.g.,

work, young children), which can further contribute to fatigue (Cimprich et al.). Moreover, CRF may present more drastic changes for younger women who have not yet experienced fatigue in response to aging, leading them to make more pronounced reports of fatigue (Cimprich et al.). Fatigue perception is subjective and influenced by past experiences and expectations for the future; hence, personal standards for tolerating fatigue may vary by age (Visser et al., 2000).

Cancer stage and fatigue

Disease stage is associated with CRF in cancer patients (Cella et al., 1998). One plausible explanation for this relationship is that advanced stage patients tend to receive more aggressive cancer therapy, which has been linked with greater presentation of side effects such as CRF (Fairclough et al., 1999). Consistently, survivors who were diagnosed with later-stage disease are less likely to have their energy levels return to baseline following treatment (Andrykowski et al., 1998).

Sleep quality and fatigue

Approximately 51% of breast cancer survivors report sleep-related difficulties (Savard et al., 2005), and the most common complaints are insomnia, restlessness, and excessive sleepiness (Davidson, Mac Lean, Brundage, & Schulze, 2002). CRF is distinguished from ordinary tiredness in that it is not alleviated by rest and may be attributable to poor sleep quality (Ancoli-Israel, Moore, & Jones, 2001). In survivors, both CRF and sleep are affected by stress, medication, and negative affect (Andrykowski et al., 1998). In other breast cancer survivor studies that found significant relationships between CRF and sleep, poor sleep quality and daytime drowsiness were associated with fatigue severity (Bower et al., 2000; Servaes et al., 2002), and efforts to improve sleep quality were associated with reductions in drowsiness as well as CRF (Broeckel et al., 1998).

Depressed mood and fatigue

Much of the survivor literature has reported a positive association between CRF and depression (Andrykowski et al., 1998; Bower et al., 2000; Broeckel et al., 1998; Hann et al., 1998; Servaes et al., 2002; Shimozuma et al., 1999). However, many studies have confounded assessment of depression and CRF by using measures of fatigue that include items with considerable construct overlap with depression. Broeckel et al. (1998) assessed whether participants met diagnostic criteria for depression rather than measuring symptom severity. Use of a continuous (rather than categorical) measure of mood could better distinguish depression from CRF by increasing the specificity of assessment, and subsequently allow for examination of subtle relationships with depression.

Present study

The present study examined relationships of five dimensions of CRF (general, physical, mental, and emotional fatigue plus vigor) in breast cancer survivors with cancer stage, age, sleep, and depressed mood. Specifically, we identified higher and lower fatigue subgroups of breast cancer survivors for each of the fatigue dimensions, and compared differences

between those subgroups using discriminant function analysis. Following what has been learned from the existing literature, younger age, higher stage of cancer at diagnosis, poorer sleep quality, and more depressed mood were hypothesized to be associated with reports of greater fatigue and less vigor.

METHODS

Sample

Seventy breast cancer survivors (all women) participated in this study. Demographic information including age, ethnicity, education, marital status, occupation, and income was collected (Table 1). For descriptive purposes, the following cancer-related statistics were obtained: stage of cancer at diagnosis, type of treatment, length of treatment, and months since termination of treatment (Table 1). Breast cancer diagnosis and self-reported medical information were verified by women's health care providers upon obtaining written release of these data. A phone screening was administered to each potential participant prior to enrollment to determine eligibility.

To be included in this study, participants had to score a minimum of 5 on the MFSI General fatigue scale (this value represents the mean of a noncancer sample obtained in the measure's validation study); the resulting sample's mean General fatigue score was 13.79 ($SD = 5.6$) with a range of 5-24. Women who scored less than 5 were excluded because the objective was to study a sample that reported above average levels of fatigue. In addition, survivors had to be off-treatment for breast cancer for at least one month but no more than three years (with the exception of Tamoxifen), be fluent in English, and reside in San Diego County. Survivors with a history of any stage of cancer (including in-situ or stage 0) were included as the objective was to recruit a broad range of fatigued survivors; however, no women with in-situ cancer volunteered for participation. Similarly, patients with a history of metastatic or recurrent disease were not excluded.

Procedures

Participants were recruited to take part in this study from medical centers, support groups, media coverage, and community organizations over a one year period. Potential participants learned about the study from distributed flyers, presentation forums, or health care providers (who were informed about the study during meetings with research assistants). Effort was made to recruit a sample that was demographically heterogeneous and representative of the population of breast cancer survivors experiencing clinically significant fatigue in San Diego. It was not possible to document the total number of women that were approached for participation as proxy and passive methods of recruitment were employed to respect patient confidentiality in compliance with Institutional Review Board requirements. Approximately 18% of women who called about the study were ineligible and approximately 9% of eligible callers opted not to participate. Data were not collected on nonparticipants due to absence of written consent. Following the phone screening and informed consent process, eligible women were enrolled. Trained and supervised pre- and post-doctoral level research assistants conducted assessments in survivors' homes. All 70 participants completed the study and received \$100 for their involvement.

Measures

The 30-item Multidimensional Fatigue Symptom Inventory- Short Form (MFSI-SF; Stein et al., 1998) was designed for use with cancer patients and survivors. The MFSI-SF has five factor-analytically-derived subscales (General (e.g. “I feel run down.”), Emotional (e.g. “I am distressed.”), Physical (e.g. “My body feels heavy all over.”), and Mental (e.g. “I am confused.”) fatigue, and Vigor (e.g. “I feel energetic.”)). Respondents are asked to use a five-point rating scale (0 = not at all; 4 = extremely) to rate each statement based on the extent to which it was true for them during the past week. Scores are computed by summing individual response ratings within each domain; there is no total score. Reliability and validity in cancer patient samples have been well established. In terms of overlap with other constructs assessed in this study, the MFSI-SF contains no items that directly address sleep quality. As for depressed mood, this measure does have an Emotional fatigue subscale, but items on this subscale are not included in the calculation of other subscale scores.

The Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989) is a 19-item measure of sleep quality over the prior month (e.g. “How would you rate your sleep quality overall?”). It yields seven subscales: Latency, Duration, Efficiency, Disturbance, Use of Sleep Medication, Daytime Sleep Dysfunction, and Subjective Sleep Quality. The global sleep quality score (range: 0-21) reflects the summation of the seven component scores, with higher scores (above five) indicating poorer sleep quality. The PSQI has been used extensively in research with cancer populations and is deemed valid and reliable. In terms of overlap, the PSQI contains no items that directly address fatigue, mood symptoms, or depression.

The 20-item Center for Epidemiological Studies- Depression Scale (CES-D; Radloff, 1977) assesses depressive symptomatology over the week prior to administration. Total scores range from 0 to 60, with higher scores representing more severe symptoms, weighted by frequency of presentation. While the goal of this measure is not diagnostic, the clinical cut-off score is 16. Respondents indicate how often they have experienced symptoms (e.g. “I was bothered by things that usually don't bother me”) on a four-point scale (0 = rarely or none of the time to 3 = most of the time). The CES-D is considered particularly appropriate for use with medical populations since its focus is on cognitive, motivational, and affective, rather than somatic, symptoms of depression. It has been validated for use with cancer patients (Beeber, Shea, & McCorkle, 1998), and has excellent reliability. In terms of overlap, the CES-D contains no items that directly address fatigue or somatic symptoms and only one item that inquires about sleep quality.

RESULTS

Descriptive statistics for participants' scores on each of the study measures, including the mean, range, standard deviation, kurtosis, skewness, and coefficient alpha, are presented in Table 2. On average, the present sample reported being greatly fatigued on all five dimensions. Participants were selected based on elevated General fatigue scores and it was expected that scores on the remaining four MFSI-SF dimensions would also be elevated.

As expected, this sample also reported suffering from depressed symptomatology and having poor sleep quality. The Radloff (1977) validation study of the CES-D included a normative sample of breast cancer patients, and the CES-D mean score found in the present study was almost one standard deviation higher than the mean found in the validation study. The mean score also was slightly greater than the cut-off score for clinical levels of depression (Radloff). The Buysse et al. (1989) validation study of the PSQI included a normative sample of cancer patients, and the average PSQI global score found in the present study was approximately one standard deviation higher than the mean reported in the validation study. The mean score was one-half standard deviation greater than the cut-off score for clinical levels of sleep disturbance (Buysse et al.).

Simple bivariate relationships of the four predictors (age, cancer stage, CES-D, and PSQI) to the five fatigue dimensions are reported in Table 3. The CES-D total score was significantly correlated with all MFSI-SF subscales. The correlations of the greatest magnitude were with Emotional (.81) and Physical (.42) fatigue and Vigor (−.47). The PSQI global score was significantly correlated with the CES-D total score, as well as with all MFSI-SF subscales except Mental fatigue. The correlations of the greatest magnitude were with General (.44) and Physical (.42) fatigue.

Discriminant function analysis was used to identify significant predictors of higher/ lower-scoring subgroups for each of the five fatigue dimensions. Two fatigue subgroups at extreme ends of the distributions of each of the MFSI-SF subscale scores were created by selecting subjects whose scores were either at least one-half standard deviation above (higher fatigue) or below (lower fatigue) the mean score for each subscale, using the standard deviations from the present sample. The score ranges for these subgroups are found in Table 4. There was sufficient power to examine four predictor variables using discriminant function analysis according to the guideline that the sample size should equal at least ten times the number of predictors (Tabachnik & Fidell, 2001). The four predictor variables (age, stage of cancer, CES-D, and PSQI) were combined into one linear discriminant function (LDF) in an attempt to discriminate each pair of fatigue groups based on differences in the predictors and provide the best discrimination between higher- and lower-fatigue subgroups.

Significant LDFs were found for all five fatigue subscales. A summary of the following statistics is presented in Table 4: percentage of variance accounted for by the LDF (Eigenvalue transformed), Wilks' Lambda, Chi-square, group centroids, and predicted classification values. Standardized canonical discriminant function coefficients were used to describe the unique contribution each individual predictor added to the LDF (Table 4). Variables that had coefficients above an absolute value of .33 (shared variance greater than 10%) were interpreted as strong predictors (Tabachnik & Fidell, 2001). Higher scores on the CES-D predicted membership in the higher fatigue group for all subtypes, as well as the lower Vigor group. Higher scores on the PSQI predicted membership in the higher fatigue group for General and Physical Fatigue, as well as the lower Vigor group. Lower stage of cancer predicted membership in the higher fatigue group for Mental Fatigue, as well as the lower Vigor group. Younger age predicted membership in the higher fatigue group for Mental and Emotional Fatigue, as well as the lower Vigor group.

Results also can be considered in terms of variables on which the higher and lower fatigue subgroups differed. For the General and Physical fatigue subscales, the higher fatigue group reported higher scores on the CES-D and PSQI relative to the lower fatigue group. For Mental fatigue, the higher fatigue group was on average younger and had a lower stage of cancer as well as higher CES-D scores than the lower fatigue group. For Emotional fatigue, the higher fatigue group was on average younger and had higher values on the CES-D relative to the lower fatigue group. For Vigor, the lower group was on average younger, had a lower stage of cancer, and had higher CES-D and PSQI scores than the higher group.

DISCUSSION

Although this sample was selected on the basis of general fatigue, the breast cancer survivors in our study reported CRF across all five dimensions. The mean scores of all subscales were elevated above normative mean values of both cancer and noncancer samples. The highest mean reported was for general fatigue, where the average per-item response on a five-point scale corresponded to reports that survivors were “somewhat” to “moderately” fatigued. Average per-item responses for the other four dimensions were in the “a little” to “somewhat” fatigued range. Endorsement of general fatigue subscale items may have been highest because they are the most broadly worded items and may be the easiest with which to identify. The strongest intercorrelations within the subscales were between general and physical fatigue (.67), and general fatigue and vigor (−.52). In contrast, general fatigue was not significantly correlated with physical and mental fatigue, suggesting relative independence of these subscales.

Age, cancer stage, and fatigue

The literature suggests an association between age and CRF in cancer survivors, but in the present sample only mental and emotional fatigue varied with age (not physical or general fatigue or vigor). Using discriminant function analyses, younger age predicted higher fatigue group membership for mental and emotional fatigue, and lower vigor group membership. Older women in this study reported less mental and emotional fatigue than younger women. Advanced disease stage at diagnosis was hypothesized to be associated with greater CRF. In contrast, less severe stage of cancer predicted higher fatigue group membership for mental fatigue, and lower vigor group membership, but was not associated with any other study variables including depressed mood and sleep quality. This counterintuitive finding may be attributable to the skewed distribution for disease stage, which included few participants with stage III or IV disease.

These findings are consistent with the literature that suggests that breast cancer and its sequelae may be especially burdensome for younger survivors (Cimprich et al., 2002; Glaus, 1998). Being sick may feel incongruent with being younger because of age-related expectancies and peer comparisons. There was no relationship between age and general or physical fatigue, suggesting that the more somatic aspects of CRF may be less affected by age. Younger women may be more strongly affected by CRF in cognitive and emotional domains because of age-related demands (e.g., employment, young children) and expectancies (e.g., not anticipating serious illness and being unaccustomed to sickness).

Interestingly, age was not significantly related to sleep quality or depressed mood. Another study of breast cancer survivors also did not find an association between age and depression but did report a positive correlation between number of children at home and psychological distress (Deshields et al., 2006). The authors attributed this effect to greater fear of death, exposure to toxic treatments, responsibilities that require physical labor, and concern for impact on children. Future studies should explore age-related findings, examining specific age-related experiences and role changes in relation to fatigue, rather than simply years of life.

The role of depressed mood and sleep quality

Depressed mood was significantly correlated with all fatigue subscales, vigor, and sleep quality. Sleep quality was significantly correlated with general, emotional, and physical fatigue. These direct effects are consistent with existing literature on breast cancer survivors (Andrykowski et al., 1998; Bower et al., 2000; Broeckel et al., 1998; Hann et al., 1998; Shimozuma et al., 1999) showing that sleep and mood are salient concerns for those who experience higher levels of CRF. Due to overlapping diagnostic criteria and symptom presentation, the orthogonality of fatigue, sleep, and depressed mood is often questioned. CRF is often mislabeled or dismissed as depression or sleep disturbance. While the correlations between these variables were statistically significant, the magnitude of the relationships were only low to moderate (r 's = .24-.47) and accounted for relatively little shared variance (R^2 = 6-22%). The only correlation that did not fall in this range was between emotional fatigue and depressed mood (r = .81; R^2 = 64%). These findings suggest substantial independence of most aspects of CRF from depressed mood and sleep disturbance with the exception of emotional fatigue, which demonstrated substantial overlap with depression.

It has been proposed that difficulty in distinguishing CRF from depression may present because many items on measures of fatigue are similar to items found on measures of depressed mood, as is true for the MFSI-SF Emotional fatigue subscale. However, Jacobsen et al. (2003) found that correlations between depression and CRF remained high following removal of overlapping assessment items. Alternatively, keeping overlapping items but categorizing them into separate subscales, similar to the approach taken with the MFSI-SF Emotional fatigue subscale, which essentially measures the subset of fatigue that is associated with depressed mood, may be a better solution. The five dimensional format allows for measurement of each subtype specifically, without presuming them to be the same or collapsing them into a total score.

The current study suggests that depressed mood is a robust enough factor to discriminate higher and lower fatigue on multiple dimensions. Bower et al. (2000) also found that presence of depressed mood was a distinguishing factor between fatigued and non-fatigued breast cancer survivors, when fatigue was measured unidimensionally. Although not all fatigued women in our study were depressed, findings suggest that depressed mood may be a risk factor for post-treatment fatigue or vice-versa. History of depression has been associated with greater vulnerability for CRF, possibly as a conditioned response, following

onset of illness (Morrow et al., 2002). Longitudinal studies will need to tease out the causal direction of this relationship.

The relationships between sleep disturbance and elevated fatigue in the current study are consistent with findings in the existing literature on breast cancer survivors (Andrykowski et al., 1998; Bower et al., 2000; Servaes et al., 2002). Broeckel et al. (1998) found that poor sleep quality was a predictor of CRF severity, and the present study supported those findings through discriminant function analyses that showed fatigue subgroup membership was associated with sleep quality. While not all fatigued women in our study were severely sleep disturbed, improving the sleep quality of breast cancer survivors may be an avenue of intervention for post-treatment fatigue. The lack of association between sleep and mental fatigue was surprising, and this relationship could be mediated via stress or other forms of psychological distress.

Significance and implications

Although fatigue is the symptom reported most commonly by breast cancer survivors, its significance or even presence has been under recognized and under appreciated by health care providers (Hann et al., 1998). Little systematic attention is directed towards fatigue during cancer follow-up visits (Ashbury et al., 1998). Some clinicians believe that survivors tend to over report minor aches and pains (Mast, 1998), or that CRF is a psychological construct lacking true physiological underpinnings (Broeckel et al., 1998). Conversely, some physicians and survivors believe that CRF is an inevitable, unpreventable, and untreatable accompaniment of the breast cancer experience, also leading them to ignore it (Ashbury et al.).

Further study is needed to expand knowledge of the etiology, prevalence, and management of CRF (Winningham et al., 1994). CRF has affective, cognitive, behavioral, physiological, economic, and social sequelae (Portenoy & Itri, 1999; Curt et al., 2000); and more work is needed to develop its conceptualization. This study suggests that survivor fatigue is a HRQOL factor of considerable magnitude, and one that often is associated with depressed mood and poor sleep quality. Given clear evidence of the far-reaching impact, more attention needs to be devoted to post-treatment CRF and its associated problems. This study evidenced differential relationships between the subdimensions of fatigue and other constructs that are worthy of future investigation.

Limitations

The present study is limited by its cross-sectional design and conclusions about causality or prediction cannot be drawn. A longitudinal study following participants from diagnosis through treatment and survivorship would allow tracking of CRF patterns, course, and progression over time. Further, as the sample was entirely comprised of off-treatment cancer survivors, the present data cannot inform distinctions between pre-, peri-, and post-treatment fatigue, or between cancer-related and noncancer related fatigue. Physiological data (e.g., Hemoglobin or Estrogen levels) were not obtained; in addition, assessment was retrospective and self-reported and there was no account of other life events or family history of breast cancer and fatigue. Collateral reports from family members may have

increased the overall precision and context of scores. Lastly, history of depression or sleep disorders was not assessed.

The sample was homogeneous demographically, which might limit the external validity and generalizability of these findings. Proportionately, however, the sample is representative of San Diego County residents on ethnicity. Self-selection bias might also limit the representativeness of this convenience sample, as the most fatigued breast cancer survivors may not have volunteered due to the perceived demands that were associated with participation in the study. Also, breast cancer survivors not experiencing above average levels of fatigue (i.e. general fatigue scores below 5) were not enrolled in the study, limiting variability on study outcomes. In addition, results may not be applicable to survivors of chronic illnesses other than breast cancer, or men as gender may affect symptom presentation (Walsh et al., 2000). A larger sample size might have created the power to detect additional or more pronounced effects.

Future directions

More research is needed with breast cancer survivors who have finished treatment but continue to experience adverse effects such as fatigue, depressed mood, and compromised sleep quality. Varied types of data should be collected from diverse samples of chronic illness survivors. While an experimental study of CRF may not be feasible ethically, structural equation modeling with a larger sample size and more power might provide grounds for drawing conclusions about the causality of post-treatment fatigue.

Future studies that obtain regular and frequent reports from survivors longitudinally following treatment may further explain the persistence of post-treatment fatigue. Given the challenges associated with assessing CRF, Ecological Momentary Assessment (EMA; Shiffman & Stone, 1998) is a valuable tool for achieving more precise measurement with decreased risk of retrospective report bias. In terms of contribution to the breast CRF literature, this present-oriented recording approach could add to the understanding of the post-treatment fatigue experience by detailing patterns that present throughout the day. Another emerging strategy is computerized adaptive testing of CRF, which can provide a precise assessment without administering a large number of questions (Lai et al., 2005).

Clinical implications

Comprehensive cancer care, including ongoing HRQOL evaluation and assessment of CRF, is needed for survivors after their formal treatment regimen concludes. Sleep disturbance and depressed mood (past and current) should be screened along with fatigue as part of routine follow-up of cancer survivors. Preliminary efforts suggest the need for tailored clinical practice guidelines and standards of care for breast cancer survivors (Ferrell et al., 1998) although no standardized psychosocial, pharmacological, or preventive interventions exist for CRF (Gallagher & Buchsel, 1998). The initiation of intervention studies with patients who are still receiving treatment (e.g. Mock et al., 1997) has increased hope for eventual amelioration of CRF. Before prevention and treatment strategies can be developed further, the predictors, correlates, and nature of CRF must be better understood (Hann et al., 1998).

Given current limitations in treating CRF, the identification of potentially modifiable variables that account for the relationship between cancer/treatment and fatigue may provide targets for intervention (Michael, Berkman, Colditz, Holmes, & Kawachi, 2002). It has been difficult to treat physical symptoms of CRF directly, especially when they are without identifiable physiological basis. Due to their demonstrated association with post-treatment fatigue, sleep quality and depressed mood may serve as more proximal points of intervention. Treating depressed mood and poor sleep quality, variables for which efficacious therapies have been developed, subsequently may decrease CRF levels (Fawzy et al., 1995). Furthermore, addressing mood and sleep needs early may prevent the onset of CRF, or at least minimize it, and matching patients to particular types of therapies may increase the efficacy of fatigue treatment (Stasi et al., 2003). Treatment outcome studies and randomized-controlled clinical trials are needed to test the efficacy and eventual effectiveness of therapies for CRF.

Finally, despite its detrimental effects, fatigue may be a somewhat adaptive response to cancer that is retained as a coping strategy during survivorship (Morrow et al., 2002). Through its association with sleep and depressed mood, fatigue may justify increased rest, reduced energy consumption, and withdrawal from unnecessary or tiring activities, which can be adaptive during the cancer experience. In future investigations of fatigue responses, implications should be explored from multiple perspectives. It is imperative to continue studying survivors to advance understanding of cancer's lasting association with fatigue, depressed mood, and sleep disturbance. Future studies also should investigate potential mediating factors such as stress and other related cognitive or behavioral factors such as catastrophizing or physical activity (Jacobsen & Stein, 1999).

Acknowledgments

Funded by the Moores UCSD Cancer Center Foundation Grant 05397A and R25 CA 65745.

REFERENCES

- Ahsberg E, Furst CJ. Dimensions of fatigue during radiotherapy: An application of the Swedish Occupational Fatigue Inventory (SOFI) on cancer patients. *Acta Oncologica*. 2001; 40(1):37–43. [PubMed: 11321658]
- Ancoli-Israel S, Moore PJ, Jones V. The relationship between fatigue and sleep in cancer patients: A review. *European Journal of Cancer Care*. 2001; 10:245–255. [PubMed: 11806675]
- Andrykowski MA, Curran SL, Lightner R. Off-treatment fatigue in breast cancer survivors: A controlled comparison. *Journal of Behavioral Medicine*. 1998; 21(1):1–18. [PubMed: 9547419]
- Ashbury FD, Findlay H, Reynolds B, McKerracher K. A Canadian survey of cancer patients' experiences: Are their needs being met? *Journal of Pain and Symptom Management*. 1998; 16(5): 298–306. [PubMed: 9846024]
- Beeber LS, Shea J, McCorkle R. The Center for Epidemiological Studies Depression Scale as a measure of depressive symptoms in newly diagnosed patients. *Journal of Psychosocial Oncology*. 1998; 16:1–20.
- Bennett B, Goldstein D, Lloyd A, Davenport T, Hickie I. Fatigue and psychological distress-exploring the relationship in women treated for breast cancer. *European Journal of Cancer*. 2004; 40:1689–95. [PubMed: 15251158]

- Bleiker EMA, Pouwer F, van der Ploeg HM, Leer JWH, Adèr HJ. Psychological distress two years after diagnosis of breast cancer: Frequency and prediction. *Patient Education and Counseling*. 2000; 40:209–217. [PubMed: 10838000]
- Bower JE, Ganz PA, Desmond KA, Rowland JH, Meyerowitz BE, Belin TR. Fatigue in breast cancer survivors: Occurrence, correlates and impact on quality of life. *Journal of Clinical Oncology*. 2000; 18(4):743–755. [PubMed: 10673515]
- Broeckel JA, Jacobsen PB, Horton J, Balducci L, Lyman GH. Characteristics and correlates of fatigue after adjuvant chemotherapy for breast cancer. *Journal of Clinical Oncology*. 1998; 16(5):1689–1696. [PubMed: 9586880]
- Buyse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research*. 1989; 28:193–213. [PubMed: 2748771]
- Cella D, Peterman A, Passik S, Jacobsen P, Breitbart W. Progress toward guidelines for the management of fatigue. *Oncology*. 1998; 12:369–377. [PubMed: 10028520]
- Cimprich B, Ronis DL, Martinez-Ramos G. Age at diagnosis and quality of life in breast cancer survivors. *Cancer Practice*. 2002; 10(2):85–93. [PubMed: 11903273]
- Collado-Hidalgo A, Bower JE, Ganz PA, Cole SW, Irwin M. Inflammation markers identify fatigue in breast cancer survivors. *Clinical Cancer Research*. 2006; 12:2759–2766. [PubMed: 16675568]
- Curt GA, Breitbart W, Cella D, Groopman JE, Horning SJ, Itri LM, Johnson DH, Miaskowski C, Scherr SL, Portenoy RK, Vogelzang NJ. Impact of cancer-related fatigue on the lives of patients: new findings from the fatigue coalition. *The Oncologist*. 2000; 5(5):353–360. [PubMed: 11040270]
- Davidson JR, MacLean AW, Brundage MD, Schulze K. Sleep disturbance in cancer patients. *Social Science and Medicine*. 2002; 54:1309–1321. [PubMed: 12058848]
- Deshields T, Tibbs T, Fan MY, Taylor M. Differences in patterns of depression after treatment for breast cancer. *Psychooncology*. 2006 in press.
- Escalante CP, Grover T, Johnson BA, Harle M, Guo H, Mendoza TR, Rivera E, Ho V, Lee EL, Cleeland CS. A fatigue clinic in a comprehensive cancer center: Design and experiences. *Cancer*. 2001; 92(6):1708–1713. [PubMed: 11598891]
- Fairclough DL, Fetting JH, Cella D, Wonson W, Moinpour CM. Quality of life and quality adjusted survival for breast cancer patients receiving adjuvant therapy. *Quality of Life Research*. 1999; 8:723–731. [PubMed: 10855346]
- Fawzy FI, Fawzy NW, Arndt LA, Pasnow RV. Critical review of psychosocial interventions in cancer care. *Archives of General Psychiatry*. 1995; 52:100–113. [PubMed: 7848046]
- Ferrell BR, Grant MM, Funk BM, Otis-Green SA, Garcia NJ. Quality of life in breast cancer survivors: Implications for developing support services. *Oncology Nursing Forum*. 1998; 25(5): 887–95. [PubMed: 9644705]
- Gallagher EM, Buchsel PC. Breast cancer and fatigue: How to help women with breast cancer live with treatment-related fatigue. *American Journal of Nursing*. 1998; (Supplement):17–20. [PubMed: 9584354]
- Glaus A. Fatigue in patients with cancer: Analysis and Assessment. *Recent Results in Cancer Research*. 1998; 145:1–172.
- Gutstein HB. The biologic basis of fatigue. *Cancer*. 2001; 92(6):1678–1683. [PubMed: 11598886]
- Hann DM, Jacobsen PB, Azzarello LM, Martin SC, Curran SL, Fields KK, Greenberg H, Lyman G. Measurement of fatigue in cancer patients: Development and validation of the Fatigue Symptom Inventory. *Quality of Life Research*. 1998; 7:301–310. [PubMed: 9610214]
- Jacobsen PB, Stein K. Is fatigue a long-term side effect of breast cancer treatment? *Cancer Control*. 1999; 6:256–263. [PubMed: 10758555]
- Jacobsen PB, Donovan KA, Weitzner MA. Distinguishing fatigue and depression in patients with cancer. *Seminars in Clinical Neuropsychiatry*. 2003; 8(4):229–40. [PubMed: 14613050]
- Jacobsen PB, Hann DM, Azzarello LM, Horton J, Balducci L, Lyman GH. Fatigue in women receiving adjuvant chemotherapy for breast cancer: Characteristics, course and correlates. *Journal of Pain and Symptom Management*. 1999; 18(4):233–242. [PubMed: 10534963]

- Knowles G, Borthwick D, McNamara S, Miller M, Leggot L. Survey of nurses' assessment of cancer-related fatigue. *European Journal of Cancer Care*. 2000; 9:105–113. [PubMed: 11261011]
- Lai JS, Cella D, Dineen K, Bode R, Von Roenn J, Gershon RC, Shevrin D. An item bank was created to improve the measurement of cancer-related fatigue. *Journal of Clinical Epidemiology*. 2005; 58(2):190–7. [PubMed: 15680754]
- Lai JS, Crane PK, Cella D. Factor analysis techniques for assessing sufficient unidimensionality of cancer related fatigue. *Quality of Life Research*. 2006; 15:1179–1190. [PubMed: 17001438]
- Levine M, Guyatt G, Gent M, DePauw S, Goodyear MD, Hryniuk WM, Arnold A, Findlay B, Skillings JR, Bramwell VH, Levin L, Bush H, Abu-Zahra H, Kotalik J. Quality of life in Stage II breast cancer: An instrument for clinical trials. *Journal of Clinical Oncology*. 1988; 6:1798–1810. [PubMed: 3058874]
- Longman AJ, Braden CJ, Mishel MH. Side-effects burden, psychological adjustment, and life quality in women with breast cancer: Pattern of association over time. *Oncology Nursing Forum*. 1999; 26(5):909–915. [PubMed: 10382190]
- Mast ME. Correlates of fatigue in survivors of breast cancer. *Cancer Nursing*. 1998; 21(2):136–142. [PubMed: 9556940]
- Mishel MH. The measurement of uncertainty in illness. *Nursing Research*. 1981; 30:258–263. [PubMed: 6912987]
- McNair, DM.; Lorr, M.; Droppleman, L. Manual for the Profile of Mood States-Revised 1992. Educational and Industrial Testing Service; San Diego, CA: 1992.
- Michael YL, Berkman LF, Colditz GA, Holmes MD, Kawachi I. *Journal of Psychosomatic Research*. 2002; 52:285–293. [PubMed: 12023125]
- Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, Quitasol W, Mitchell S, Chakravarthy A, Gage I. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. *Oncology Nursing Forum*. 1997; 24(6):991–1000. [PubMed: 9243585]
- Morrow GR, Andrews PLR, Hickok JT, Roscoe JA, Matteson S. Fatigue associated with cancer and its treatment. *Supportive Care in Cancer*. 2002; 10:389–398. [PubMed: 12136222]
- Pinto BM, Maruyama NC. Exercise in the rehabilitation of Breast Cancer Survivors. *Psychooncology*. 1999; 8:191–206. [PubMed: 10390732]
- Porock D, Kristjanson LJ, Tinnelly K, Duke T, Blight J. An exercise intervention for advanced cancer patients experiencing fatigue: A pilot study. *Journal of Palliative Care*. 2000; 16(3):30–36. [PubMed: 11019505]
- Portenoy RK, Itri LM. Cancer-related fatigue: Guidelines for evaluation and management. *The Oncologist*. 1999; 4:1–10. [PubMed: 10337366]
- Radloff LS. The Center for Epidemiological Studies- Depression Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*. 1977; 1(3):385–401.
- Savard J, Simard S, Ivers H, Morin CM. Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: Sleep and psychological effects. *Journal of Clinical Oncology*. 2005; 23:6083–96. [PubMed: 16135475]
- Servaes P, Prins J, Verhagen S, Bleijenberg G. Fatigue after breast cancer and in chronic fatigue syndrome: Similarities and differences. *Journal of Psychosomatic Research*. 2002; 52(6):453–459. [PubMed: 12069869]
- Shiffman, SM.; Stone, AA. Ecological momentary assessment: A new tool for behavioral medicine research.. In: Krantz, DS.; Baum, A., editors. *Technology and Methods in Behavioral Medicine*. Lawrence Erlbaum Associates, Inc.; Mahwah, NJ: 1998. p. 117-131.
- Shimozuma K, Ganz PA, Peterson L, Hirji K. Quality of life in the first year after breast cancer surgery: Rehabilitation needs and patterns of recovery. *Breast Cancer Research and Treatment*. 1999; 56:45–57. [PubMed: 10517342]
- Shimozuma K, Ganz PA, Peterson L, Hirji K. Quality of life in the first year after breast cancer surgery: Rehabilitation needs and patterns of recovery. *Breast Cancer Research and Treatment*. 1999; 56:45–57. [PubMed: 10517342]

- Smets EMA, Garssen B, Bonke B, De Haes JCJM. The multidimensional fatigue inventory (MFI): Psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*. 1995; 39(5):315–325. [PubMed: 7636775]
- Stasi R, Abriani L, Beccaglia P, Terzoli E, Amadori S. Cancer-related fatigue: Evolving concepts in evaluation and treatment. *Cancer*. 2003; 98(9):1786–801. [PubMed: 14584059]
- Stein KD, Martin SC, Hann DM, Jacobsen PB. A multidimensional measure of fatigue for use with cancer patients. *Cancer Practice*. 1998; 6(3):143–152. [PubMed: 9652245]
- Stone P, Richardson A, Ream E, Smith AG, Kerr DJ, Kearney N. Cancer-related fatigue: Inevitable, unimportant, and untreatable? Results of a multi-centre patient survey. *Annals of Oncology*. 2000; 11:971–975. [PubMed: 11038033]
- Tabachnik, BG.; Fidell, LS. *Using Multivariate Statistics*. 4th Edition.. Allyn & Bacon Publishers; Needham Heights, MA: 2001.
- Visser MRM, Smets EMA, Sprangers MAG, de Haes HJCJM. How response shift may affect the measurement of change in fatigue. *Journal of Pain and Symptom Management*. 2000; 20(1):12–18. [PubMed: 10946164]
- Wagner LI, Cella D. Fatigue and cancer: causes, prevalence and treatment approaches. *British Journal of Cancer*. 2004; 91(5):822–8. [PubMed: 15238987]
- Walsh D, Donnely S, Rybicki L. The symptoms of advanced cancer: Relationship to age, gender, and performance status in 1,000 patients. *Supportive Care in Cancer*. 2000; 8:175–179. [PubMed: 10789956]
- Winningham ML, Nail LM, Burke MB, Brophy L, Cimprich B, Jones LS, Pickard-Holley S, Rhodes V, St. Pierre B, Beck S, Glass EC, Mock VL, Mooney KH, Piper B. Fatigue and the cancer experience: The state of the knowledge. *Oncology Nursing Forum*. 1994; 21(1):23–36. [PubMed: 8139999]

Table 1

Sample demographic and clinical data

<i>Age</i>	<i>Months since termination of treatment</i>	<i>Hours per night of sleep</i>
M=52.5	M= 11.3	M=7.2
SD=12.2	SD=10.3	SD=1.5
Range=32-83	Range=1-36	Range=4-10.5
<i>Length of treatment in months</i>	<i>Marital status</i>	<i>Education</i>
M=6.6	Never married	< Grade school
SD=4.6	Married	High school graduate
Range=1-24	Separated	Some college
	Divorced	College graduate
	Widowed	Graduate school
<i>Stage of breast cancer</i>	<i>Treatment</i>	
	Surgery	97.1%
Stage I	Hormone therapy	25.7%
Stage II	Breast reconstruction	34.3%
Stage III	Chemotherapy	71.4%
Stage IV	Immunotherapy	2.9%
Unknown	Radiation	71.4%
	Watchful waiting	5.7%
<i>Ethnicity</i>	<i>Living situation</i>	<i>Relationship status</i>
White/Caucasian	Alone	Living with a spouse
Black/African American	Family(kids and spouse)	In significant relationship
Asian/Pacific Islander	Children only	Not in a relationship
Hispanic/Mexican American	Spouse/partner only	
Other	Roommate	
<i>Work Status</i>	<i>Household income</i>	<i>Therapeutic alternatives</i>
Homemaker	Less than \$10,000	Relaxation therapy
Full-time	\$10,000 - \$19,999	Hypnosis

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Part-time paid	14.3%	\$20,000 - \$29,999	10.0%	Guided imagery	7.1%
Retired	21.4%	\$30,000 - \$39,999	8.6%	Spiritual healing	18.6%
Disabled	14.3%	\$40,000 - \$49,999	14.3%	Meditation	18.6%
Volunteer	20.0%	\$50,000 - \$59,999	10.0%	Self-help groups	22.9%
Student	4.3%	\$60,000 - \$69,999	5.7%	Energy healing	2.9%
Not working, looking for a job	4.3%	Greater than \$70,000	27.1%	Biofeedback	0.0%
Sick leave from job	4.3%	Unknown	11.4%	Other	28.6%

* Had option of choosing multiple selections

Sample descriptive data

Table 2

	Study Data				
	M	SD	Range	Alpha	Skewness Kurtosis
<i>MFSI-SF</i> **					
General fatigue	13.79	5.60	5-24	.96	-.02 -.96
Physical fatigue	7.70	5.38	0-23	.86	.58 -.33
Mental fatigue	10.00	4.63	0-21	.86	.05 -.73
Emotional fatigue	8.01	4.91	0-20	.88	.33 -.21
Vigor	10.72	4.71	1-23	.92	.49 .21
<i>CES-D</i>					
Total score	18.51	10.61	3-47	.78	.65 -.28
<i>PSQI</i> *					
Sleep latency	1.31	0.99	0-3		.45 -.77
Sleep duration	0.89	0.88	0-3		.89 .29
Habitual sleep efficiency	0.77	1.00	0-3		1.12 .12
Sleep disturbance	1.89	0.58	1-3		.01 -.01
Daytime dysfunction	1.50	0.74	0-3		.45 -.23
Sleep quality	1.36	0.83	0-3		.16 -.46
Use of sleep medications	0.91	1.25	0-3		.86 -1.04
Global score	8.63	4.09	2-19	.76	.60 -.01

* Normative values are based on cancer patients (all types).

** Normative values are based on female breast cancer patients.

Table 3

Correlations of study variables

	1	2	3	4	5	6	7	8	9	10	11
1. Age	1.00	-.206	.118	-.219	-.039	-.076	-.245 [*]	-.345 [*]	.216	-.114	-.122
2. Length of treatment	-	1.00	.024	-.055	.170	.049	.074	-.110	-.149	.193	.211
3. Months since end of treatment	-	-	1.00	-.059	-.013	-.009	.071	-.157	.041	-.072	.086
4. CES-D Total score	-	-	-	1.00	.378 ^{**}	.417 ^{**}	.365 ^{**}	.809 ^{**}	-.466 ^{**}	.283 [*]	-.116
5. MFSI-SF General fatigue	-	-	-	-	1.00	.666 ^{**}	.223	.155	-.524 ^{**}	.438 ^{**}	-.147
6. MFSI-SF Physical fatigue	-	-	-	-	-	1.00	.299 [*]	.291 [*]	-.346 ^{**}	.417 ^{**}	-.071
7. MFSI-SF Mental fatigue	-	-	-	-	-	-	1.00	.395 ^{**}	-.245 [*]	.151	-.162
8. MFSI-SF Emotional fatigue	-	-	-	-	-	-	-	1.00	-.380 ^{**}	.240 [*]	-.078
9. MFSI-SF Vigor	-	-	-	-	-	-	-	-	1.00	-.308 ^{**}	.247 [*]
10. PSQI Global score	-	-	-	-	-	-	-	-	-	1.00	.022
11. Stage of cancer at diagnosis	-	-	-	-	-	-	-	-	-	-	1.00

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Table 4

Discriminant function analyses statistics for higher and lower fatigue groups

MFSI-SF subscale	General	Physical	Emotional	Mental	Vigor
Higher fatigue group (n)	24	21	21	23	18
Scoring range for higher fatigue group	16.59	10.39	10.47	12.32	13.08
Lower fatigue group (n)	19	28	20	24	22
Scoring range for lower fatigue group	10.99	5.01	5.56	7.68	8.37
% variance accounted for by LDF	100	100	100	100	100
Wilks' Lambda	.643	.645	.331	.691	.368
Chi-Square	17.2	19.8	40.9	15.9	36.0
Df	4	4	4	4	4
Significance <i>p</i>	.002	.001	<.0005	.003	<.0005
Group centroid for higher group	.647	.839	1.35	-.668	1.41
Group centroid for lower group	-.818	-.630	-1.42	.640	-1.16
% correctly classified into higher group	70.8	71.4	85.7	78.3	100
% correctly classified into lower group	89.5	85.7	95.0	79.2	81.8
% correctly classified overall	79.1	79.6	90.2	78.7	90.0
Standardized canonical discriminant function coefficients					
Age	.12	.30	-.43	.51	.76
Stage of breast cancer	-.31	-.03	-.07	.41	.56
CES-D total score	.58	.50	.99	-.72	-.70
PSQI global score	.75	.88	-.21	-.10	-.59