



Changes in and predictors of severity of fatigue in women with breast cancer: A longitudinal study



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ABSTRACT

Background: Fatigue is the most common symptom experienced by cancer patients. However, longitudinal studies of changes in the severity and predictors of fatigue are limited.

Objectives: The purposes of this study were to evaluate changes in fatigue severity in women with breast cancer prior to and for twelve months after surgery. Factors that affected the severity and the trajectory of fatigue were identified.

Design, settings, participants: This observational prospective study approached 334 women who were scheduled for breast cancer surgery in a medical center located in northern Taiwan. Among the 334 women, 239 met the inclusion/exclusion criteria. The final sample size used for the data analysis was 200.

Methods: Fatigue, depressive symptom, and symptom distress were evaluated in women prior to and at 1, 2, 3, 4, 5, 6, 8, 10, and 12 months after surgery for breast cancer. Hierarchical linear modeling (HLM) was applied where level-1 data consisted of repeated observations of study variables within each subject and level-2 data consisted of static characteristics of individual subject.

Results: The fatigue levels ranged from 1.92 to 3.09. Changes in fatigue severity demonstrated a quadratic trajectory that increased and reached the peak at the second month after the surgery, followed by a gradual decrease. After adjusting for the effect of receipt of chemotherapy, symptom distress, and depressive symptom, the quadratic change pattern for fatigue became imperceptible. Women who had a partial mastectomy ($P = 0.028$), had a higher educational level ($P = 0.048$), were married ($P = 0.043$), and had poorer functional performance at diagnosis ($P = 0.043$) had higher levels of fatigue.

Conclusions: Patients who underwent surgery for breast cancer reported mild to moderate levels of fatigue over a period of 12 months. Fatigue levels fluctuated with patients' level of depressive symptoms, symptom distress, and receipt of chemotherapy.

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What is already known about the topic?

- Fatigue has been recognized as one of the most common symptoms in patients who receive therapy for breast cancer.
- Fatigue may persist long after the treatment being completed and can have a negative impact on the quality of life.

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- Other symptoms, such as depression, sleep disturbances, and menopausal symptoms, are associated with fatigue.

What this paper adds

- Fatigue severity reached the peak at the 2nd month after the surgery. At the 6th month, it decreased to the preoperative levels and down to the lowest point at the 12th month.
- Fatigue levels not only fluctuated with patients' level of depressive symptoms and overall symptom distress, but also depended on whether patients were receiving chemotherapy at that time.
- The differences between fatigue severity experienced by women who do and do not receive chemotherapy suggest that fatigue caused by the last chemotherapy cycle may not totally diminished before the next chemotherapy cycle.

1. Introduction

Fatigue is the most common symptom reported by patients who receive therapy for breast cancer (Arnold et al., 2001; Jereczek-Fossa et al., 2002). It may persist long after treatment is completed (Fan et al., 2005) and can have a negative impact on quality of life (QOL) (Bower et al., 2000; Byar et al., 2006). Moreover, study has shown that high level of fatigue independently predicted shorter recurrence-free and overall survival in breast cancer patients (Groenvold et al., 2007). Since fatigue may persist long after treatment has ended, researchers need to pay more attention to fluctuations in and trajectories of fatigue from the beginning of treatment to some time after treatment (Minton and Stone, 2008).

In general, the results from longitudinal studies with breast cancer patients suggested that fatigue worsened during chemotherapy and radiotherapy (Byar et al., 2006; Goldstein et al., 2012; Irvine et al., 1998; Schmidt et al., 2011), but improved after completion of adjuvant treatment (Byar et al., 2006; Goldstein et al., 2012; Irvine et al., 1998). For studies examined fatigue during chemotherapy cycles, findings were not consistent. Berger (1998) found that fatigue was higher at 48 h after each treatment and lower at cycle midpoints. However, de Jong et al. (2006) reported that fatigue was highest at the third day after chemotherapy and may have another peak at the 11th day for the 28-days-interval treatment regimen. In a recent study, Liu et al. (2012) reported that compared to baseline, fatigue level was significantly worse during both cycle 1 and cycle 4 and seem to be highest at the first week. When the observation of fatigue was extended to time after adjuvant therapy, an improvement of fatigue was often found. For example, in a study with 25 breast cancer patients receiving doxorubin-based chemotherapy (Byar et al., 2006), fatigue levels were found to be moderately intense during treatment and decreased significantly over time. In a recent larger prospective cohort study of women with breast cancer (Goldstein et al., 2012), fatigue became persistent in only 11% and 6% of breast cancer women at 6 months and 12 months, respectively, after the end of adjuvant treatment. However, one study measuring

fatigue at before, during, and after adjuvant therapy failed to find significant changes in fatigue over time (Von Ah et al., 2008). Another small study evaluating fatigue at pre-radiation therapy, 2 months and 2.5 years after radiation therapy found that some dimensions of fatigue at 2.5 years after radiation therapy were even higher than that at pre-radiation or 2 months after radiation while other dimensions did not show significant change over time (Geinitz et al., 2004). In those studies that used a longitudinal design to study fatigue in breast cancer patients (Berger and Walker, 2001; Byar et al., 2006; de Jong et al., 2006; Geinitz et al., 2004; Schmidt et al., 2011; Von Ah et al., 2008), some were limited by small sample sizes ranging from 25 to 54 (Byar et al., 2006; Geinitz et al., 2004; Von Ah et al., 2008), others were either had a short observation period covering only 2–4 cycles of chemotherapy, or had long intervals between measurements (Geinitz et al., 2004; Von Ah et al., 2008), or asked patients to retrospectively rate their fatigue at different stages of disease/treatment trajectories (Schmidt et al., 2011). No study has taken all types of adjuvant treatments into account.

In addition to fatigue, patients with breast cancer also experience a variety of other symptoms. Among these symptoms, depression was most frequently found to be link with fatigue (Bower et al., 2000; Geinitz et al., 2004; Liu et al., 2009). The relationship between fatigue and depression is not unexpected since fatigue is one of the indicators of depression, and chronic fatigue may also result in depression (de Jong et al., 2002). Other symptoms associated with fatigue in breast cancer patients include pain (Bower et al., 2000; Matthews et al., 2012), sleep disturbances (Bower et al., 2000; Liu et al., 2009; Matthews et al., 2012), menopausal symptoms (Glaus et al., 2006), and overall symptom distress (Berger and Walker, 2001; Byar et al., 2006). As covariate symptoms may also change over time, it is not clear whether fatigue levels fluctuate with the changes of these symptoms.

In summary, findings from studies exploring the change patterns of fatigue in breast cancer patients are inconsistent, and many of the studies were limited with methodological shortcomings such as small sample size, short observation period, or long interval between assessments. In addition, no study has considered all types of adjuvant treatment in one study and no study has measured pre-surgery level of fatigue. Depressive symptom and symptom distress have been consistently found to correlate with fatigue in breast cancer patients. However, no study has considered whether the change in these covariate symptoms affect the change of fatigue. This longitudinal study was designed to model the trajectory of fatigue from pretreatment to posttreatment (i.e., 12 months) in women with breast cancer while controlling for both time-independent and time-dependent covariates. The specific purposes of this study were to (1) explore the trajectory of fatigue over 1 year after surgery in women with breast cancer; (2) determine whether change over time in the severity of fatigue fluctuated with levels of depressive symptoms and overall symptom distress; and (3) identify factors that influenced the severity and pattern of change in fatigue after controlling for the influence of depressive symptoms and overall symptom distress.

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