

**Original Article****Trajectories of Evening Fatigue in Oncology Outpatients Receiving Chemotherapy**

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**Abstract**

**Context.** Fatigue is a distressing persistent sense of physical tiredness that is not proportional to a person's recent activity. Fatigue impacts patients' treatment decisions and can limit their self-care activities. Although significant interindividual variability in fatigue severity has been noted, little is known about predictors of interindividual variability in initial levels and trajectories of evening fatigue severity in oncology patients receiving chemotherapy.

**Objectives.** To determine whether demographic, clinical, and symptom characteristics were associated with initial levels and the trajectories of evening fatigue.

**Methods.** A sample of outpatients with breast, gastrointestinal, gynecological, and lung cancer ( $N = 586$ ) completed demographic and symptom questionnaires a total of six times over two cycles of chemotherapy. Fatigue severity was evaluated using the Lee Fatigue Scale. Hierarchical linear modeling was used to answer the study objectives.

**Results.** A large amount of interindividual variability was found in the evening fatigue trajectories. A piecewise model fit the data best. Patients who were white, diagnosed with breast, gynecological, or lung cancer, and who had more years of education, childcare responsibilities, lower functional status, and higher levels of sleep disturbance and depression reported higher levels of evening fatigue at enrollment.

**Conclusion.** This study identified both nonmodifiable (e.g., ethnicity) and modifiable (e.g., childcare responsibilities, depressive symptoms, sleep disturbance) risk factors for more severe evening fatigue. Using this information, clinicians can identify patients at higher risk for more severe evening fatigue, provide individualized patient education, and tailor interventions to address the modifiable risk factors. *J Pain Symptom Manage 2015;50:163–175. © 2015 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

**Key Words**

*Evening fatigue, chemotherapy, hierarchical linear modeling, symptom trajectories, diurnal variations, symptom patterns, gastrointestinal cancer, breast cancer, gynecological cancer, lung cancer*

**Introduction**

Fatigue is the most common symptom reported by oncology patients during treatment.<sup>1</sup> More than

one-third of outpatients undergoing chemotherapy (CTX) experience clinically meaningful levels of fatigue.<sup>2</sup> Fatigue impairs patients' functional status

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and decreases their quality of life.<sup>3,4</sup> Fatigue can be so severe that it negatively impacts patients' treatment decisions and severely limits their self-care activities.<sup>5-7</sup>

Most of the longitudinal studies on fatigue in patients undergoing cancer treatment have evaluated for changes in fatigue severity over the past day,<sup>8</sup> weeks,<sup>9,10</sup> or before and after treatment.<sup>11-13</sup> A new and emerging area of research is an evaluation of diurnal variations in fatigue severity. For example, fatigue severity in healthy individuals varies over the course of the day, usually increasing in the evening.<sup>14</sup> In addition, differences in morning and evening fatigue were found in patients with rheumatoid arthritis, primary Sjögren's syndrome, systemic lupus erythematosus,<sup>15</sup> and chronic renal failure.<sup>16</sup>

Only four studies were identified that evaluated diurnal variations in fatigue in oncology patients undergoing CTX<sup>17,18</sup> or radiation therapy (RT).<sup>19,20</sup> In particular, our research team evaluated for differences in the trajectories and predictors of morning and evening fatigue in patients with breast<sup>19</sup> and prostate<sup>20</sup> cancer who underwent RT. For both morning and evening fatigue, women with breast cancer reported higher fatigue severity scores than men with prostate cancer.<sup>19,20</sup> Using hierarchical linear modeling (HLM), younger age and higher levels of sleep disturbance before RT were associated with higher levels of morning fatigue in the patients with breast cancer.<sup>19</sup> In contrast, these two characteristics predicted initial levels and changes over time in *both* morning and evening fatigue in patients with prostate cancer.<sup>20</sup> Depression predicted initial levels of evening fatigue in patients with breast cancer, whereas it predicted both initial levels and the trajectories of morning fatigue in patients with prostate cancer. Finally, being employed, having children living at home, higher trait anxiety, lower body mass index (BMI), and a higher number of chronic conditions were associated with diurnal variability in fatigue in women with breast cancer but not in men with prostate cancer.

Only two studies were found that examined diurnal variations in morning and evening fatigue in oncology patients undergoing CTX.<sup>17,18</sup> In one study of a sample of 78 patients with gynecological (GYN) cancer,<sup>18</sup> fatigue was assessed three times a day at 10 AM, 2 PM, and 6 PM for six days before and after the first three CTX cycles. Using the mean daily fatigue score, the authors reported an intraday effect of increasing fatigue severity throughout the course of the day.<sup>18</sup> Although fatigue severity was assessed across three CTX cycles, the assessments were completed on the six days before through the six days after the infusion. Therefore, variability in fatigue severity in relationship to specific time points within a CTX cycle (e.g., acute effects of

CTX, midcycle, recovery period) was not assessed. In addition, predictors of interindividual variability were not evaluated.

In the other study that evaluated 18 patients with a variety of cancer diagnoses who underwent CTX or RT,<sup>17</sup> fatigue was measured hourly during the hours patients were awake for three days. The 72 hours of data were superimposed onto one 24-hour grid and plotted to determine if diurnal trends were present. Fatigue scores were significantly lower in the morning hours compared with the afternoon and evening hours. However, diurnal variations and predictors of fatigue associated with CTX were not reported.

This limited body of research suggests that the severity of fatigue in oncology patients varies over the course of the day.<sup>17-20</sup> However, only one study reported findings for patients undergoing CTX.<sup>18</sup> To date, no study has evaluated for interindividual variability in fatigue severity across specific time points in the CTX administration cycle. In addition, predictors of interindividual variability in fatigue severity in patients receiving CTX were not evaluated.

Given the paucity of research on diurnal variations in and predictors of fatigue severity in oncology patients undergoing CTX, the purposes of this study, in a sample of outpatients with breast, gastrointestinal (GI), GYN, and lung cancer who were receiving two cycles of CTX, were to evaluate for variations in evening fatigue severity and to determine which demographic, clinical, and symptom characteristics predicted initial levels and the trajectories of evening fatigue.

## Methods

### *Theoretical Framework*

The Theory of Symptom Management (TSM) provides the theoretical framework for this study.<sup>21</sup> The three essential concepts in the TSM are symptom experience, symptom management, and symptom outcomes. The TSM posits that symptoms are dynamic, evolve over time, and interact with antecedents that include demographic (e.g., age, sex, education, ethnicity, marital status) and clinical (e.g., cancer type and stage, type of treatment, comorbidities) characteristics. Symptom experiences frame the person's perception, evaluation, and responses to symptoms and are the beginning of the symptom management process.<sup>21</sup> Increased information on the fatigue experience of oncology patients undergoing CTX will assist with the development of tailored interventions to manage fatigue. Therefore, this study will evaluate associations between a number of demographic, clinical, and symptom characteristics and evening fatigue severity reported by patients during CTX.

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