

This material is protected by U.S. copyright law. To purchase quantity reprints, e-mail reprints@ons.org. For permission to reproduce multiple copies, e-mail pubpermissions@ons.org.

Fatigue, Pain, and Functional Status During Outpatient Chemotherapy

Mary Lou Siefert, DNSc, AOCN®

Approximately 1.44 million new cases of cancer were diagnosed in the United States in 2007 (Jemal et al., 2009). Incidence rates from 1995 for men and 1999 for women through 2004 have remained fairly constant, whereas mortality rates have decreased continually since the early 1990s; thus, more people are living with cancer and experiencing the consequences of active treatment. Cancer treatments may result in better survival outcomes, which are certainly desirable; however, treatments may negatively affect quality of life, with increased symptoms impacting functional status. Symptoms that are particularly prevalent and bothersome are fatigue and pain.

Nursing care for cancer-related fatigue includes three major interventions: monitoring and assessing patients, taking actions to facilitate rest and conserving energy, and teaching patients and family members self-management strategies (Mitchell, Beck, Hood, Moore, & Tanner, 2007). However, interventions and strategies often are not very effective (Yurtsever, 2007) or well defined, and gaps exist in the knowledge regarding the management of fatigue and the relationships of fatigue and pain with changes in functional status over time during chemotherapy treatment (Mitchell et al., 2007). Original work by Mishel (1988) established that lack of information regarding expected treatment effects on symptoms and how to interpret and manage persistent or new symptoms can contribute to uncertainty and distress. Clinical and informational or educational interventions need to be based on well-defined problems and the patterns of their occurrence and timed to occur before fatigue and pain levels are distressful and functional status is impaired (National Comprehensive Cancer Network, 2008). Maximal benefit will be gained from interventions that are tailored specifically to the patients' relationships of the symptoms of fatigue, pain, and functional status. Given, Given, Azzouz, Stommel, and Kozachik (2000) suggested that the synergistic effect of multiple symptoms is unknown, and the coexistence of symptoms may have more than an additive effect on functional status (Lenz, Pugh, Milligan, Gift,

Purpose/Objectives: To examine the relationship of fatigue and pain with functional status and the pattern of the two symptoms' occurrence over time in individuals with cancer who were receiving outpatient chemotherapy. The aims were to describe the levels of fatigue and pain with functional status and the inter-relationships with each other and with demographic and clinical variables over time.

Design: Descriptive, correlational.

Setting: Outpatient chemotherapy clinic in the New England region of the United States.

Sample: Total available population of 70 consecutive adult patients with breast cancer (n = 9), colorectal cancer (n = 21), lung cancer (n = 21), or lymphoma (n = 19).

Methods: Retrospective data were extracted from the medical records; descriptive, correlational, and mixed-modeling methods were used to describe the sample and to examine the relationships of the symptoms and functional status.

Main Research Variables: Fatigue, pain, functional status, and demographic and clinical factors.

Findings: Fatigue was the most frequently reported symptom; pain was rarely and almost exclusively reported by patients with lung cancer or lymphoma during their early treatments. Fatigue and functional status impairment were highly associated with each other and had similar relationships with the other variables.

Conclusions: The patterns and relationships of fatigue and functional status reported by this fairly healthy sample provide useful information to help guide early assessments and nursing interventions for people receiving outpatient chemotherapy.

Implications for Nursing: The patterns and severity of symptoms and functional status impairment in people with colorectal cancer or lymphoma warrant further investigation. Targeted exercise interventions for specific outpatient populations should be developed and tested to address specific patterns of symptoms and functional status impairment in individuals with cancer.

& Suppe, 1997). Examining the relationships of multiple symptoms is important to effectively treat concurrent symptoms (Miaskowski, Dodd, & Lee, 2004; Given et al., 2000).

Purpose

The purpose of this study was to examine the relationships of fatigue and pain with functional status and the pattern of the two symptoms' occurrence over time in individuals with cancer who were receiving outpatient chemotherapy. The specific aims were to (a) describe the levels of fatigue and pain recorded by nurses in the outpatient records of individuals with breast cancer, colorectal cancer, lung cancer, or lymphoma who were receiving outpatient chemotherapy; (b) describe the level of functional status recorded for those same individuals; and (c) explore the relationship of fatigue, pain, and level of functional status with each other and with demographic and clinical variables over time.

Symptom Experiences and Types of Cancers

The symptom experiences related to breast cancer (Berger & Higginbotham, 2000; Carpenter, Johnson, Wagner, & Andrykowski, 2002; Knopf, 2001; Kurtz, Kurtz, Stommel, Given, & Given, 1999; Leddy, 1997; Thompson, 2007) and lung cancer (Cooley, 2000; Cooley, Short, & Moriarty, 2003; Given et al., 2000; Kozachick, Mock, & Bandeen-Roche, 2007; McCorkle & Quint-Benoliel, 1983; Weisman & Worden, 1976–1977) are well represented in the literature. Very little has been published related to the symptom experience of those with colorectal cancer, the third most common cancer in men and women in the United States (Jemal et al., 2009). Lymphoma, a much less frequently occurring malignancy than breast, colorectal, or lung cancer (Jemal et al., 2009), has been discussed rarely in literature on symptom experience.

A search of the recent literature on symptom experience, excluding chemotherapy-induced peripheral neuropathy, revealed few studies in which individuals with colorectal cancer were included (Barsevick, Pasacreta, & Orsi, 1995; Galloway & Graydon, 1996; Given et al., 2000; Kozachik et al., 2007; Yurtsever, 2007). Depressive symptoms in individuals after colorectal surgery were predictors of impaired functional status (Barsevick et al., 1995), and symptoms and distress in relation to diagnosis and prognosis have been reported, but not the experience of symptoms during treatment (Fernandez, Porta, Malats, Belloc, & Gallen, 2002; Hansen, Morsel-Carlsen, & Bulow, 1997). In early studies conducted by Weisman and Worden (1976–1977), people with lung cancer were found to have more symptoms and existential distress than people with other types of cancer, and increased distress was associated with more symptoms. People with lung cancer have consistently reported the highest levels of distress related to pain and fatigue (Degner & Sloan, 1995; Given et al., 2000; McCorkle & Quint-Benoliel, 1983) and higher levels of symptom distress than people with other types of

cancer (Degner & Sloan, 1995) or illnesses (McCorkle & Quint-Benoliel, 1983). Women with breast cancer have reported that functionality is affected by symptoms related to menopause and chemotherapy treatments and has a negative effect on quality of life (Boehmke, 2004; Ganz, Rowland, Meyerowitz, & Desmond, 1998; Graf & Geller, 2003; Knopf, 2001, 2002; Schover, 1991). Age and symptom severity have been predictors of fatigue and functionality (Berger & Higginbotham, 2000; Kurtz et al., 1999), and gender may or may not be a predictor of symptom distress (Cooley et al., 2003; Degner & Sloan, 1995; Kopeck et al., 2007). Some evidence suggests that fatigue associated with chemotherapy and hematopoietic stem cell transplantation, a common treatment for lymphoma, plays a significant role in unplanned hospital admissions (Coleman, Coon, Mattox, & O'Sullivan, 2002) and is associated with decreased physical functioning (Hacker et al., 2006).

A gap exists in the knowledge and research examining the relationships of concurrent symptoms over time and their relationships with functional status in people across cancer diagnoses and in the ambulatory treatment population. Whether patterns of prevalence exist is unknown, as are the effects of concurrent fatigue and pain over time among patients with certain types of cancer being treated with chemotherapy.

Psychobiologic Entropy Model

The Winningham (1999) Psychobiological Entropy model guided the study and proposes a complex inter-relationship among sources of energy, symptoms, treatments, disease factors, and activity with fatigue, described as a primary or secondary symptom. The model's propositions related to energy sources, fatigue, and functional status also are supported by the literature, which reports that exercise programs for people with cancer receiving treatment and post-treatment are beneficial in mitigating fatigue and maintaining and improving functional status (Dimeo, 2001; Mock et al., 2001; Stricker, Drake, Hoyer, & Mock, 2004).

Methods

A retrospective, descriptive, correlational study was conducted to address the research aims (Polit & Hungler, 1999b).

Sample and Setting

A consistent staff member at a community hospital outpatient clinic in the New England region of the United States identified records of 165 patients who had breast, colorectal, or lung cancer or lymphoma and were treated with chemotherapy during a four-year period. Inclusion criteria also were having made at least two outpatient visits for chemotherapy treatment and

having had approximately five months elapse between the first and last treatments. Ninety-five records were excluded for the following reasons.

- No outpatient chemotherapy treatment (n = 77)
- Two or more treatments but on consecutive days with no elapsed time between treatments (n = 11)
- Only one treatment recorded (n = 6)
- A duplicate record (n = 1)

The final sample included records of 70 patients with 341 encounters for outpatient chemotherapy treatment.

Data Collection and Instruments

Prior to data collection, approval was obtained from the data collection site's review board. All data were extracted from the patients' records (chemotherapy flow sheets, physician orders, physician progress notes, and demographic data sheets) and recorded on a data collection form constructed for the purposes of this study and pilot tested with two patients' records. The data collection related to the key variables is described in the "Study Variables" section. Reliability of extracted data was ensured with staggered data checks by a consistent staff member who compared the extracted data to the original patients' records. Inter-rater reliability between the two coders was 95% or greater.

All data from consecutive treatment time points were extracted to cover a time span of five months per patient record. To capture all patients treated and to examine the fatigue, pain, and functional status over time of treatment, records with greater than five encounters (n = 16, 23%) and some with fewer than five (n = 22, 31%) were included. As many as eight encounters were included in the final analysis; the approximate five-month elapsed time was consistent over all encounters. Twelve encounters were eliminated from six patients who received 9–11 treatments. Of those six patients, two with colorectal cancer had 9 treatments each, three with lung cancer had 10 treatments each, and one with lung cancer had 11 treatments. Because the intervals between treatments were not the same elapsed time for patients overall or within a given diagnosis, each observation was given a value reflecting the treatment number, and another variable was created to reflect the elapsed time between successive treatments. All analyses were conducted with SAS® v.8 (SAS Institute, Inc.) software.

Study Variables

The three main descriptive variables of fatigue, pain, and functional status were single-item self-reported scores and were recorded by the clinic nurses in pre-defined areas on the chemotherapy flow sheets each time a patient was in the chemotherapy clinic for treatment. Standardized definitions for each of the three self-report scales were printed on the chemotherapy treatment flow sheets. The use of a single-item self-

reported score to measure the intensity of an individual symptom has been recommended for clinical practice (Hinds, Schum, & Srivastava, 2002; Mock et al., 2000). The experience, severity, and distress of symptoms and functional status are best measured by reports from the patients who are experiencing them (Cleeland, 2001; McCorkle, 1987; Mock et al., 2000; Winningham, 1999). Fatigue and pain were scored on 11-point analog scales (0–10); 0 reflected absence of the symptom, and 10 was the worse possible experience of the symptom. The functional status analog scale (0–4) was a self-reported score of actual performance of activities compared to usual performance; 0 reflected a functional status equivalent to predisease performance without restriction, and 4 represented a severely diminished functional status of complete disability to the point that the patient was confined to a bed or chair and was not able to carry out any self-care. Specific definitions for each functional status score (0–4) were printed on the flow sheet. Other clinical variables that were analyzed in relation to fatigue, pain, and functional status were the diagnosis, number of treatments, number of chemotherapy agents, and number of comorbidities. Demographic variables included age, gender, ethnicity, marital status, employment, and insurance status.

Data Analysis

Descriptive and correlational statistics for the analysis included frequencies, chi-square and Fischer's exact tests, and Pearson and Spearman correlations. Correlations were defined as very small or slight (< 0.1), small (0.1–0.29), moderate (> 0.29–0.59), and large or high (> 0.59) based on typically small coefficients (Polit, 1996; Polit & Beck, 2008). Fatigue, pain, and functional status were analyzed as continuous variables. T tests, analysis of variance (ANOVA), and mixed modeling were used to analyze and compare the sample demographically and clinically by gender and by diagnosis, as well as to examine the relationships and associations of the demographic and clinical variables with fatigue, pain, and functional status over time of treatment. The Kruskal-Wallis test was used because normality of the data remained questionable even with the log transformed variables at baseline and the last treatment. Repeated-measures analysis with a spatial power covariance structure to account for unequally spaced time points was used to examine the relationships of fatigue and functional status with each other and the other variables over the time of treatment.

Fatigue, Pain, and Functional Status

Analyses were conducted with ANOVA to compare the means, standard deviations, and differences among diagnoses. Chi-square and Fischer's exact results were used to describe fatigue and pain frequencies at each

treatment. Homogeneity of variance and normality of the data were checked; when either was questioned, residual analysis with log transformations of fatigue and functional status was performed.

Relationships Among Fatigue, Pain, and Functional Status and With Demographic and Clinical Variables

The concurrent existence and relationships of fatigue, pain, and functional status at each treatment for all diagnoses combined and at each treatment by diagnosis and number of comorbidities were explored with chi-square and Fisher's exact tests and correlation procedures. Because pain occurred so infrequently (15 [4%] of the 341 encounters), further exploration was not pursued. The associations between fatigue and functional status scores also were analyzed with treatment number and number of days over the course of treatment with mixed-modeling procedures. The relationships and associations of fatigue and functional status with demographic and clinical variables were explored over time of treatment with repeated-measures analysis, and correlation procedures were used at each treatment time point.

Because the time periods between treatments were not spaced equally, a repeated-measures analysis was employed, assuming smaller correlations of the repeated measurements for observations that were further apart in time, using a spatial power covariance structure (Littell, Milliken, Stroup, & Wolfinger, 1996). Even though the spatial power covariance structure does not require equally spaced data as the autoregressive covariance structure does, all analyses using the spatial power covariance structure also were conducted with the autoregressive structure comparing the statistics and Akaike's Information Criterion (AIC) scores between the two models. The significance levels of all variables included in the models were similar, and although the AIC scores were always just slightly lower with the autoregressive covariance structure, the spatial covariance structure was selected for the analysis because it was the more appropriate model given the unequally spaced time data.

The relationships of gender, age, marital status, diagnosis, and number of comorbidities and chemotherapy drugs with either fatigue or functional status were explored at each treatment with t tests, Fisher's exact tests, correlation procedures, and ANOVA and over the course of all treatments with a repeated-measures analysis with the spatial power covariance structure.

Results

Sample

Table 1 reports demographic information; 70 patients, 47 women (67%) and 23 men (33%) with a mean age

Table 1. Sociodemographic and Clinical Description of the Sample

Variable	Total (N = 70)	Male (n = 23)	Female (n = 47)	p
Age (years)				0.91
$\bar{X}$	62.1	61.8	62.2	
SD	12.8	12.3	13.2	
Variable	n	n	n	p
Age (years)				0.85
49 or younger	15	4	11	
50–64	23	8	15	
65 or older	32	11	21	
Ethnicity				0.93
Caucasian	56	18	38	
Hispanic	7	3	4	
African American	6	2	4	
Asian	1	—	1	
Employment				0.37
Employed	27	7	20	
Unemployed	13	3	10	
Retired	24	11	13	
Disabled	2	—	2	
Missing	4	2	2	
Insurance				0.94
Private	33	10	23	
Medicare	29	10	19	
Medicaid	6	2	4	
Missing	2	1	1	
Marital status				0.01
Married	41	17	24	
Widowed	11	—	11	
Single	8	2	6	
Divorced	8	2	6	
Missing	2	2	—	
Diagnosis				0.07*
Breast cancer	9	—	9	
Colon cancer	21	12	9	
Lung cancer	21	5	16	
Lymphoma	19	6	13	
Comorbidities				0.28
None	19	7	12	
One	32	8	24	
Two	15	5	10	
Three	3	2	1	
More than three	1	1	—	
Baseline chemotherapy drugs				0.12
One	15	3	12	
Two	36	12	24	
Three	7	5	2	
Four	12	3	9	
Last treatment chemotherapy drugs				0.52
One	21	5	16	
Two	32	11	21	
Three	5	3	2	
Four	12	4	8	

* p value excludes breast cancer; p = 0.01 with breast cancer included.

of 62.1 ($\pm$ 12.8) years, were included. Men and women did not differ on demographic variables except marital status; men were significantly more likely to be married (p = 0.01). Eighty percent (n = 56) of the sample was

Caucasian, most of the patients were retired or unemployed (n = 37, 53%) and had either private or Medicare healthcare insurance (n = 62, 89%).

The sample was described clinically by gender (see Table 2) and diagnosis (see Tables 3 and 4) at the first and last treatments. By diagnosis, the sample consisted of those with breast cancer (n = 9, 46 encounters), colorectal cancer (n = 21, 111 encounters), lung cancer (n = 21, 102 encounters), and lymphoma (n = 19, 82 encounters). A significant difference was found in diagnosis by gender (p = 0.01); however, when breast cancer was excluded, no significant difference existed (p = 0.07). Women with breast cancer were significantly younger (p = 0.03) than patients with the other three diagnoses.

The number of treatments per patient ranged from 2–8; those with breast cancer received 5–6 treatments, and those with colorectal cancer, lung cancer, or lymphoma received 2–8 treatments. The total elapsed time between the first treatment and the last treatment varied from 4–157 days, with no significant difference (p = 0.88) by diagnosis in the mean number of days (71.9, SD = 35.3) from first to last treatment for all diagnoses combined. Nearly half of the patients (n = 32, 46%) had one comorbidity, more than a quarter of the sample had none (n = 19, 27%), and no significant differences existed in number of comorbidities by diagnosis or gender.

Aims A and B

Fatigue did not differ by diagnosis at treatments and was reported in 142 (42%) of the 341 encounters (mean scores ranged from 0–3.6; median scores ranged from 0–2 by treatment). Pain also did not differ by diagnosis at treatments and was reported in only 15 (4%) of the 341 encounters (mean scores 0–0.9; a median of 0 by treatment). But a significant difference was found in pain when controlling for treatment number; the first two treatments accounted for 11 (73%) of the 15 encounters, and those with lung cancer (6 encounters) or lymphoma (7 encounters) accounted for 13 (87%) of the 15 encounters. Functional status impairment did not differ by treatment or diagnosis at treatments and was

reported in 115 (34%) of the 341 encounters (mean scores ranged from 0–1; median scores ranged from 0–1). But a significant difference existed in functional status when treatment number was controlled; the highest reported score, 3, was reported twice, once by a patient with lung cancer at treatment one and once by a patient with lymphoma at treatment two.

Aim C

Concurrent fatigue and pain: Patients reported concurrent fatigue and pain in 14 (4%) of the 341 observations; in 93% of all observations where pain was reported, fatigue also was reported. Patients with lung cancer (5 encounters) or lymphoma (7 encounters) accounted for 12 of the 14 encounters (79%), and 11 of those 12 reports were within the first two treatments. The largest correlation between fatigue and pain occurred at the first treatment (r = 0.3, p = 0.04).

Concurrent fatigue and functional status impairment: Patients reported concurrent fatigue and functional status impairment in 69 (20%) of 341 encounters. In 49% of the encounters where fatigue existed, functional status also was impaired. Patients with lung cancer and lymphoma accounted for 52 (75%) of the 69 encounters for concurrent fatigue and functional status impairment. For all diagnoses combined and at all treatments, fatigue and functional status had positive correlations; the correlations ranged from small to large and were larger in the later treatments.

In the repeated-measures analysis, evidence existed that functional status scores had a highly significant effect on fatigue scores (F = 9.59, p = < 0.0001) and that fatigue scores had a highly significant effect on functional status scores (F = 4.62, p = < 0.0001) over time. No significant difference was found in fatigue scores at different treatments (F = 0.47, p = 0.86), no evidence was found of change over time (F = 0.18, p = 0.67), and no association was found with the interaction of the number of treatments and level of functional status (F = 0.67, p = 0.78). The level of functional status differed significantly over time (F = 6.04, p = 0.01); a significant

Table 2. Fatigue, Pain, and Functional Status by Gender at Baseline and Last Treatment

	Total (N = 70)		Men (n = 23)		Women (n = 47)		
Variable	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	p
Baseline treatment							
Fatigue	1.77	2.4	1.24	2.2	2.05	2.5	0.22
Pain	0.53	1.7	0.39	1.7	0.59	1.7	0.68
Functional status	0.46	0.7	0.26	0.5	0.56	0.7	0.09
Last treatment							
Fatigue	1.8	2	1.9	1.9	1.7	2	0.72
Pain	0.3	1.2	0.1	0.5	0.3	1.5	0.5
Functional status	0.5	0.7	0.2	0.4	0.7	0.7	0.002

Table 3. Age and Clinical Description by Diagnosis

Variable	Total (N = 70)	Breast (n = 9)	Colorectal (n = 21)	Lung (n = 21)	Lymphoma (n = 19)	p
Age (years)						0.03
$\bar{X}$	62.03	50.89	64.95	63.95	61.95	
SD	12.8	12.7	11.8	10.8	4	
Variable	n	n	n	n	n	
Age (years)						0.08
49 or younger	15	6	2	3	4	
50–64	23	1	9	7	6	
65 or older	32	2	10	11	9	
Comorbidities						0.21
None	19	6	6	4	3	
One	32	3	7	11	11	
Two	15	–	5	5	5	
Three	3	–	2	1	–	
More than three	1	–	1	–	–	
Baseline chemotherapy drugs						< 0.0001
One	15	2	5	5	3	
Two	36	7	12	15	2	
Three	7	–	2	1	4	
Four	12	–	2	–	10	
Last treatment chemotherapy drugs						< 0.0001
One	21	6	5	7	3	
Two	32	3	12	14	3	
Three	5	–	1	–	4	
Four	12	–	3	–	9	

tional status impairment at 9 of the 11 encounters (82%) and 7 of the 11 observations (64% of the time), respectively. A total of 9 of the 11 (82%) encounters where fatigue, pain, and functional status impairment existed were reported by patients with lung cancer (5 observations) or lymphoma (4 observations), and 6 of the 9 (67%) encounters occurred during the first treatment. All but one of the patients who reported the concurrent existence of fatigue, pain, and functional status impairment had at least one comorbidity.

Relationship of fatigue and functional status impairment with demographic and clinical variables: No effect of age on fatigue or functional status score was found over time or at different treatments. The repeated-measures analysis revealed a significant effect of marital status on fatigue scores ($F = 3.26$, $p = 0.01$); widows reported higher fatigue scores in the earlier treatments. Gender had a significant effect over time on functional status scores ($F = 9.06$, $p = 0.003$) but not on fatigue scores; women reported worse functional status scores at all treatments and had significantly worse scores at two treatments ($t = -2.8$, $p = 0.007$; $t = -2.05$, $p = 0.046$).

Including only the effects of length of treatment time (days) and the number of treatments, no effect was found on the level of fatigue, but a significant effect was found on the reported level of functional status over time ($F = 7.22$, $p = 0.008$) that did not differ at different treatments. No effect by diagnosis was found with fatigue over time; although not significant, patients with lymphoma reported the highest mean levels of fatigue at most treatments. Over time, a significant effect by diagnosis occurred ($F = 4.32$, $p = 0.005$) with functional status; the effect changed over time ($F = 3.92$, $p = 0.05$) and did not differ at different treatments ($F = 0.53$, $p = 0.81$) or with the interaction effect of diagnosis and treatment number ($F = 0.42$, $p = 0.99$). Patients with breast cancer had better functional status (lower scores) overall compared to patients with the other three diagnoses; those with lung cancer and lymphoma reported the highest mean functional status scores. Patients with colorectal or lung cancer reported their worst functional status at

interaction effect of fatigue with number of treatments occurred ($F = 1.91$, $p = 0.003$), but the effect was not significantly different ($F = 1.22$, $p = 0.29$) at different treatments. Lower fatigue scores had a more significant effect earlier, with higher fatigue scores having more effect later on functional status scores.

Concurrent pain and functional status: Patients reported concurrent pain and functional status impairment in 13 (4%) of the 341 encounters; in 87% of the encounters where pain existed, functional status also was impaired. Patients with lung cancer and lymphoma accounted for 85% (11 encounters) of all observations where pain and functional status impairment occurred concurrently, and the majority of those encounters (10, or 91%) occurred at the first and second treatments. Pain and functional status had small to moderate correlations for all diagnoses combined, and the largest correlation was at the first treatment ($r = 0.53$, $p = < 0.0001$).

Concurrent fatigue, pain, and functional status: The concurrent existence of fatigue, pain, and functional status impairment was reported at 11 (3%) of the 341 encounters and was limited by the number of encounters (13 times) of concurrent pain and functional status impairment. Women and older patients (aged 65 years or older) reported concurrent fatigue, pain, and func-

Table 4. Fatigue, Pain, and Functional Status by Diagnosis at Baseline and Last Treatment

	Total (N = 70)		Breast (n = 9)		Colorectal (n = 21)		Lung (n = 21)		Lymphoma (n = 19)		
Variable	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	$\bar{X}$	SD	p
Baseline treatment											
Fatigue	1.8	2.4	0	—	1.9	2.2	1.7	2.2	2.3	3.2	0.14
Pain	0.5	1.7	0	—	0	—	0.9	2	0.9	2.4	0.12
Functional status	0.5	0.7	0.11	0.3	0.4	0.5	0.7	0.8	0.4	0.8	0.18
Last treatment											
Fatigue	1.8	2.0	0.4	0.9	1.8	2.1	2.1	1.8	2.3	2.7	0.08
Pain	0.3	1.2	0.3	1	0.1	0.5	0.1	0.3	0.6	2.1	0.97
Functional status	0.5	0.7	0.1	0.4	0.3	0.5	0.6	0.6	0.8	0.9	0.06

Note. All p values are Kruskal-Wallis (nonparametric).

treatment 1, whereas those with lymphoma reported worse functional status scores in the later treatments.

Most correlations between fatigue and the number of comorbidities were small. In the repeated-measures analysis, the number of comorbidities had a significant effect ($F = 4.5$, $p = 0.002$) on fatigue; it was not different over time and did not change at different treatments or with the interaction effect of comorbidities and treatment number. Patients with two comorbidities reported the highest levels of fatigue at most treatments when compared to patients with either fewer or more than two comorbidities. Patients without comorbidities did not report significantly lower fatigue scores. The number of comorbidities had very small to moderate positive correlations with functional status scores at each treatment. Over time, the number of comorbidities had a significant effect ($F = 4.55$, $p = 0.001$) on the level of functional status; the effect changed significantly over time ($F = 5.52$, $p = 0.02$) but was not changed at different treatments or with the interaction effect of comorbidities and treatment number. The effect was largest for one or two comorbidities; those without comorbidities tended to report better functional status scores at later treatments.

A significant difference by diagnosis was found in the number of chemotherapy agents received at the first five of the eight treatments. Patients with breast cancer received the fewest number of agents, a maximum of two agents at any treatment; those with colorectal cancer as many as four agents, those with lung cancer as many as three agents, and most with lymphoma as many as four agents at each treatment.

A significant difference in fatigue ($F = 3.49$, $p = 0.03$) and functional status ($F = 3.97$, $p = 0.01$) was found by the number of agents received only at treatment 5; patients who received four agents reported higher scores than those receiving fewer agents. Most correlations between the number of agents received and fatigue or functional status scores were small or moderate and positive. Over time, the number of agents administered did not have a significant effect on fatigue or functional

status scores. However, the effect by the number of agents on functional status changed significantly over time ($F = 7.40$, $p = 0.007$), although it, too, was not different at different treatments ($F = 1.03$, $p = 0.41$) or by the interaction effect of the number of agents and treatment number ($F = 0.69$, $p = 0.83$).

Discussion

Fatigue was the most frequently reported symptom, consistent with previous reports in the literature (Fieler, 1997; Irvine, Vincent, Graydon, Bubela, & Thompson, 1994; King, Nail, Kremer, Strohl, & Johnson, 1985; Kozachick et al., 2007; Nail, 1993; National Comprehensive Cancer Network, 2008; Richardson, 1995; Yurtsever, 2007), although the incidence and levels were lower in this study. Fatigue was reported most frequently by older patients, women, and those who had lung cancer or lymphoma. Patients with colorectal cancer reported fatigue at treatment one and again at later treatments. Pain was reported with very low incidence, mostly at the early treatments, and almost all those who reported pain also reported concurrent fatigue and functional status impairment. The functional status scores tended to be low (less impairment), and the patterns of occurrence paralleled fatigue; fatigue and functional status correlated with each other, consistent with the literature and the model used to guide this study (Anderson et al., 2003; Curt et al., 2000; Flechtner & Bottomley, 2003; Hacker et al., 2006; Irvine et al., 1994; Sadler et al., 2002; Sarna, 1993; Tanaka, Akechi, Okuyama, Nishiwaki, & Uchitomi, 2002; Winningham, 2001). Patients with breast cancer overall reported low levels and incidence of symptoms, those with colorectal cancer had a unique pattern of occurrence, and those with lung cancer or lymphoma reported most of the concurrent symptoms and higher levels of fatigue, pain, and functional status impairment.

This was a fairly healthy outpatient sample, with most patients having only one comorbidity and access to health care as evidenced by 97% of the sample having

either private or public healthcare insurance. The low number of comorbidities also helps to explain the overall low level of functional status impairment. The associations of fatigue and functional status with the number of chemotherapy agents also may be a proxy for the diagnosis, or the drugs associated with each diagnosis may have had an effect on the symptoms experienced in this population. The patients in this study represent a population in a setting that is amenable to a moderate walking exercise intervention targeting fatigue and functional status during and after treatment (Stricker et al., 2004). Nurses should encourage patients to participate in a moderate walking exercise program and make referrals to physical therapy as needed to help them maintain optimal functional status and mitigate fatigue (Mock et al., 2001, 2005; Stricker et al., 2004).

Limitations

Data on stage of disease were not available and may have helped to explain some of the findings, specifically the overall low incidence of symptoms in women with breast cancer. The external validity of the findings is limited based on the sample size and the demographic and clinical characteristics of the sample. A secondary analysis of data, despite the efficiency of its use (Hearst, Grady, Barron, & Kerlikowske, 2001; Polit & Hungler, 1999a), has limitations related to lack of control over the original data (Hearst et al., 2001). The researcher attempted to mitigate this limitation by including analysis of the data related to the treatments, demographics, and clinical information over time in four different diagnoses and with men and women. Gender was represented equally, and with maintenance of both the internal and statistical conclusion validity and future replication, the findings can be generalized with more confidence to a similar population of patients.

Implications for Nursing Practice

Implications for future research include conducting prospective studies with larger samples to examine the patterns, incidence, and severity of symptoms and functional status impairment in those with colorectal cancer and lymphoma. The examination of symptoms and functional status related to gender and age differ-

ences also should be confirmed. Furthermore, the sample was homogenous in terms of socioeconomic and ethnic groups; although it did represent the larger geographic population from which the sample was drawn, future studies should target those with less access to health care and from different ethnic groups. Future replication of the study in different samples would help to validate the findings for a larger target population.

The recognition of the prevalence of fatigue and the association with functional status impairment has important clinical implications. The more significant effect of fatigue on functional status earlier in the treatment course suggests the need for early interventions such as moderate exercise to help maintain functional status and mitigate fatigue (Mock et al., 2005; National Comprehensive Cancer Network, 2008; Stricker et al., 2004). Oncology nurses should recognize the need for early and well-timed assessments of patients' symptoms and related functional status to identify those who are at risk. Well-timed and targeted interventions should be developed and tested. Evidence-based standards of care, including standardized assessments at each contact, should be developed, tested, implemented, and continually evaluated for specific populations. By targeting populations with specific needs related to symptom distress and functional status, and by using systematic and structured assessments early in treatment courses, healthcare professionals could increase the efficiency with which we use ever-more-expensive and limited healthcare resources. Fatigue, related symptoms, and functional status impairment must be identified early and treated at the appropriate time; patients and their caregivers need information for monitoring and managing symptoms and maintaining functional status, including encouragement of exercise.

The author gratefully acknowledges Ruth McCorkle, PhD, FAAN, for her mentorship and assistance with this work.

Mary Lou Siefert, DNSc, AOCN®, is an assistant professor in the William F. Connell School of Nursing at Boston College in Chestnut Hill, MA. This research was partially supported by funding from the Delta Mu Chapter of Sigma Theta Tau. Siefert can be reached at mlsiefert@aya.yale.edu, with copy to editor at ONFEditor@ons.org. (Submitted December 2008. Accepted for publication May 24, 2009.)

Digital Object Identifier: 10.1188/10.ONF.114-123

References

- Anderson, K.O., Getto, C.J., Mendoza, T.R., Palmer, S.N., Wang, X.S., Reyes-Gibby, C.C., & Cleeland, C.S. (2003). Fatigue and sleep disturbance in patients with cancer, patients with clinical depression, and community-dwelling adults. *Journal of Pain and Symptom Management*, 25, 307–318. doi: 10.1016/S0885-3924(02)00682-6
- Barsevick, A.M., Pasacreta, J., & Orsi, A. (1995). Psychological distress and functional dependency in colorectal cancer patients. *Cancer Practice*, 3, 105–110.
- Berger, A.M., & Higginbotham, P. (2000). Correlates of fatigue during and following adjuvant breast cancer chemotherapy: A pilot study. *Oncology Nursing Forum*, 27, 1443–1448.
- Boehmke, M.M. (2004). Measurement of symptom distress in women with early-stage breast cancer. *Cancer Nursing*, 27, 144–152.
- Carpenter, J.S., Johnson, D.H., Wagner, L.J., & Andrykowski, M.A. (2002). Hot flashes and related outcomes in breast cancer survivors and matched comparison women [Online exclusive]. *Oncology Nursing Forum*, 29, E16–E25. doi: 10.1188/02.ONF.E16-E25
- Cleeland, C.S. (2001). Cancer-related fatigue: New directions for

- research. Introduction. *Cancer*, 92(6, Suppl.), 1657–1661. doi: 10.1002/1097-0142(20010915)92:6<1657::AID-CNCR1492>3.0.CO;2-7
- Coleman, E.A., Coon, S.K., Mattox, S.G., & O'Sullivan, P. (2002). Symptom management and successful outpatient transplantation for patients with multiple myeloma. *Cancer Nursing*, 25, 452–460.
- Cooley, M.E. (2000). Symptoms in adults with lung cancer. A systematic research review. *Journal of Pain and Symptom Management*, 19, 137–153.
- Cooley, M.E., Short, T.H., & Moriarty, H.J. (2003). Symptom prevalence, distress, and change over time in adults receiving treatment for lung cancer. *Psycho-Oncology*, 12, 694–708. doi: 10.1002/pon.694
- Curt, G.A., Breitbart, W., Cella, D., Groopman, J.E., Horning, S.J., Itri, L.M., . . . Vogelzang, N.J. (2000). Impact of cancer-related fatigue on the lives of patients: New findings from the Fatigue Coalition. *Oncologist*, 5, 353–360. Retrieved from <http://theoncologist.alphamedpress.org/cgi/content/full/5/5/353>
- Degner, L.F., & Sloan, J.A. (1995). Symptom distress in newly diagnosed ambulatory cancer patients and as a predictor of survival in lung cancer. *Journal of Pain and Symptom Management*, 10, 423–431.
- Dimeo, F.C. (2001). Effects of exercise on cancer-related fatigue. *Cancer*, 92(6, Suppl.), 1689–1693. doi: 10.1002/1097-0142(20010915)92:6<1689::AID-CNCR1498>3.0.CO;2-H
- Fernandez, E., Porta, M., Malats, N., Belloc, J., & Gallen, M. (2002). Symptom-to-diagnosis interval and survival in cancers of the digestive tract. *Digestive Diseases and Sciences*, 47, 2434–2440. doi: 10.1023/A:1020535304670
- Fieler, V.K. (1997). Side effects and quality of life in patients receiving high-dose rate brachytherapy. *Oncology Nursing Forum*, 24, 545–553.
- Flechner, H., & Bottomley, A. (2003). Fatigue and quality of life: Lessons from the real world. *Oncologist*, 8(Suppl.), 5–9. Retrieved from http://theoncologist.alphamedpress.org/cgi/content/full/8/suppl_1/5
- Galloway, S.C., & Graydon, J.E. (1996). Uncertainty, symptom distress, and information needs after surgery for cancer of the colon. *Cancer Nursing*, 19, 112–117.
- Ganz, P.A., Rowland, J.H., Meyerowitz, B.E., & Desmond, K.A. (1998). Impact of different adjuvant therapy strategies on quality of life in breast cancer survivors. *Recent Results in Cancer Research*, 152, 396–411.
- Given, C.W., Given, B., Azzouz, F., Stommel, M., & Kozachik, S. (2000). Comparison of changes in physical functioning of elderly patients with new diagnoses of cancer. *Medical Care*, 38, 482–493.
- Graf, M.C., & Geller, P.A. (2003). Treating hot flashes in breast cancer survivors: A review of alternative treatments to hormone replacement therapy. *Clinical Journal of Oncology Nursing*, 7, 637–640. doi: 10.1188/03.CJON.637-640
- Hacker, E.D., Ferrans, C., Verlen, E., Ravandi, F., van Besien, K., Gelms, J., & Dieterle, N. (2006). Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncology Nursing Forum*, 3, 614–624. doi: 10.1188/06.ONF.614-624
- Hansen, H.J., Morsel-Carlson, L., & Bulow, S. (1997). [Patients' perception of symptoms in colorectal cancer. A cause of delay in diagnosis and treatment.] *Ugeskrift for Laeger*, 159, 1941–1944.
- Hearst, N., Grady, D., Barron, H.V., & Kerlikowske, K. (2001). Research using existing data: Secondary data analysis, ancillary studies, and systematic reviews. In S.B. Hulley, S.R. Cummings, W.S. Browner, D. Grady, N. Hearst, & T.B. Newman (Eds.), *Designing clinical research* (2nd ed., pp. 195–212). Philadelphia, PA: Lippincott Williams and Wilkins.
- Hinds, P.S., Schum, L., & Srivastava, D.K. (2002). Is clinical relevance sometimes lost in summative scores? *Western Journal of Nursing Research*, 24, 345–353. doi: 10.1177/019394590202400404
- Irvine, D., Vincent, L., Graydon, J.E., Bubela, N., & Thompson, L. (1994). The prevalence and correlates of fatigue in patients receiving treatment with chemotherapy and radiotherapy. A comparison with the fatigue experienced by healthy individuals. *Cancer Nursing*, 17, 367–378.
- Jemal, A., Siegel, R., Ward, W., Hao, Y., Xu, J., & Thun, M.J. (2009). Cancer statistics, 2009. *CA: A Cancer Journal for Clinicians*, 59, 225–249. doi:10.3322/caac.20006
- King, K.B., Nail, L.M., Kreamer, K., Strohl, R.A., & Johnson, J.E. (1985). Patients' descriptions of the experience of receiving radiation therapy. *Oncology Nursing Forum*, 12(4), 55–61.
- Knobf, M.T. (2001). The menopausal symptom experience in young mid-life women with breast cancer. *Cancer Nursing*, 24, 201–211.
- Knobf, M.T. (2002). Carrying on: The experience of premature menopause in women with early stage breast cancer. *Nursing Research*, 51, 9–17.
- Kopec, J.A., Yothers, G., Ganz, P.A., Land, S.R., Cecchini, R.S., Wieand, H.S., . . . Wolmark, N. (2007). Quality of life in operable colon cancer patients receiving oral compared with intravenous chemotherapy: Results from National Surgical Adjuvant Breast and Bowel Project Trial C-06. *Journal of Clinical Oncology*, 25, 424–430. doi: 10.1200/JCO.2005.05.2597
- Kozachik, S., Mock, V., & Bandeen-Roche, K. (2007). Symptom clusters in elderly cancer patients: A longitudinal, comparative perspective [Abstract 104]. *Oncology Nursing Forum*, 34, 208.
- Kurtz, M.E., Kurtz, J.C., Stommel, M., Given, C.W., & Given, B. (1999). The influence of symptoms, age, comorbidity and cancer site on physical functioning and mental health of geriatric women patients. *Women and Health*, 29(3), 1–12.
- Leddy, S.K. (1997). Healthiness, fatigue, and symptom experience in women with and without breast cancer. *Holistic Nursing Practice*, 12, 48–53.
- Lenz, E.R., Pugh, L.C., Milligan, R.A., Gift, A., & Suppe, F. (1997). The Middle-Range Theory of Unpleasant Symptoms: An update. *Advances in Nursing Science*, 19(3), 14–27.
- Littell, R.C., Milliken, G.A., Stroup, W.W., & Wolfinger, R.D. (1996). *SAS system for mixed models*. Cary, NC: SAS.
- McCorkle, R. (1987). The measurement of symptom distress. *Seminars in Oncology Nursing*, 3, 248–256.
- McCorkle, R., & Quint-Benoliel, J. (1983). Symptom distress, current concerns and mood disturbance after diagnosis of life-threatening disease. *Social Science and Medicine*, 17, 431–438.
- Miaskowski, C., Dodd, M., & Lee, K. (2004). Symptom clusters: The new frontier in symptom management research. *Journal of the National Cancer Institute. Monographs*, 32, 17–21. doi: 10.1093/jncimonographs/lgh023
- Mishel, M.H. (1988). Uncertainty in illness. *Image—The Journal of Nursing Scholarship*, 20, 225–232.
- Mitchell, S.A., Beck, S.L., Hood, L.E., Moore, K., & Tanner, E.R. (2007). Putting Evidence Into Practice: Evidence-based interventions for fatigue during and following cancer and its treatment. *Clinical Journal of Oncology Nursing*, 11, 99–113. doi: 10.1188/07.CJON.99-113
- Mock, V., Atkinson, A., Barsevick, A., Cella, D., Cimprich, B., Cleeland, C., . . . Stahl, C. (2000). NCCN practice guidelines for cancer-related fatigue. *Oncology*, 14(11A), 151–161.
- Mock, V., Frangakis, C., Davidson, N.E., Ropka, M.E., Pickett, M., Poniatowski, B., . . . McCorkle, R. (2005). Exercise manages fatigue during breast cancer treatment: A randomized controlled trial. *Psycho-Oncology*, 14, 464–477. doi: 10.1002/pon.863
- Mock, V., Pickett, M., Ropka, M.E., Muscari Lin, E., Stewart, K.J., Rhodes, V.A., . . . McCorkle, R. (2001). Fatigue and quality of life outcomes of exercise during cancer treatment. *Cancer Practice*, 9, 119–127. doi: 10.1046/j.1523-5394.2001.009003119.x
- Nail, L. (1993). Coping with intracavitary radiation treatment for gynecological cancer. *Cancer Practice*, 1, 218–224.
- National Comprehensive Cancer Network. (2008). *NCCN Clinical Practice Guidelines in Oncology™: Cancer-related fatigue* [v.2008.1]. Retrieved from http://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf
- Polit, D. (1996). Bivariate description. In *Data analysis and statistics for nursing research* (pp. 69–89). Stamford, CT: Appleton and Lange.
- Polit, D.F., & Beck, C.T. (2008). Describing data through statistics. In *Nursing research: Generating and assessing evidence for nursing practice* (8th ed., pp. 556–582). Philadelphia, PA: Wolters Kluwer, Lippincott Williams and Wilkins.
- Polit, D.F., & Hungler, B.P. (1999a). Quantitative analysis: Descriptive statistics. In *Nursing research: Principles and methods* (pp. 439–468). Philadelphia, PA: Lippincott.

- Polit, D.F., & Hungler, B.P. (1999b). Research designs for quantitative studies. In *Nursing research: Principles and methods* (6th ed., pp. 193–218). Philadelphia, PA: Lippincott.
- Richardson, A. (1995). The pattern of fatigue in patients receiving chemotherapy. In A. Richardson & J. Wilson-Barnett (Eds.), *Nursing research in cancer care* (pp. 225–245). London, United Kingdom: Scutari Press.
- Sadler, I.J., Jacobsen, P.B., Booth-Jones, M., Belanger, H., Weitzner, M.A., & Fields, K.K. (2002). Preliminary evaluation of a clinical syndrome approach to assessing cancer-related fatigue. *Journal of Pain and Symptom Management*, 23, 406–416.
- Sarna, L. (1993). Correlates of symptom distress in women with lung cancer. *Cancer Practice*, 1, 21–28.
- Schover, L.R. (1991). The impact of breast cancer on sexuality, body image, and intimate relationships. *CA: A Cancer Journal for Clinicians*, 41, 112–120. doi: 10.3322/canjclin.41.2.112
- Stricker, C.T., Drake, D., Hoyer, K.A., & Mock, V. (2004). Evidence-based practice for fatigue management in adults with cancer: Exercise as an intervention. *Oncology Nursing Forum*, 31, 963–976. doi: 10.1188/04.ONF.963-976
- Tanaka, K., Akechi, T., Okuyama, T., Nishiwaki, Y., & Uchitomi, Y. (2002). Impact of dyspnea, pain, and fatigue on daily life activities in ambulatory patients with advanced lung cancer. *Journal of Pain and Symptom Management*, 23, 417–423. doi:10.1016/S0885-3924(02)00376-7
- Thompson, P. (2007). The relationship of fatigue and meaning in life in breast cancer survivors. *Oncology Nursing Forum*, 34, 653–660. doi: 10.1188/07.ONF.653-660
- Weisman, A.D., & Worden, J.W. (1976–1977). The existential plight in cancer: Significance of the first 100 days. *International Journal of Psychiatry in Medicine*, 7, 1–15.
- Winningham, M. (1999). Fatigue. In C.H. Yarbrow, M.H. Frogge, & M. Goodman (Eds.), *Cancer symptom management* (pp. 58–76). Boston, MA: Jones and Bartlett.
- Winningham, M.L. (2001). Strategies for managing cancer-related fatigue syndrome: A rehabilitation approach. *Cancer*, 92(4, Suppl.), 988–997. doi: 10.1002/1097-0142(20010815)92:4+<988::AID-CNCR1411>3.0.CO;2-O
- Yurtsever, S. (2007). The experience of fatigue in Turkish patients receiving chemotherapy. *Oncology Nursing Forum*, 34, 721–728. doi: 10.1188/07.ONF.721-728