Online Exclusive Article

Fatigue and Other Variables During Adjuvant Chemotherapy for Colon and Rectal Cancer

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Purpose/Objectives: To examine patterns of fatigue and other variables (sleep quality, sleep-wake variables, activity and rest, circadian rhythms, quality of life [QOL], blood counts, and demographic and medical variables) during colon and rectal cancer adjuvant chemotherapy, as well as feasibility of the study.

Design: Longitudinal, descriptive feasibility study.

Setting: Two oncology clinics in the midwestern region of the United States.

Sample: From April 2006–December 2008, 27% of screened subjects (n = 21) enrolled and 14 completed the study. Participants were middle aged, partnered, and employed and had postsecondary education.

Methods: Measurements completed during the first week of three two-week cycles (chemotherapy 1–3) and at six weeks (before chemotherapy 4) were the Piper Fatigue Scale, Pittsburgh Sleep Quality Index, wrist actigraphy, Functional Assessment of Cancer Therapy–Colon, blood counts, and demographic and medical data form. Analysis included descriptive statistics and repeated-measures analysis of variance.

Main Research Variables: Fatigue, sleep quality, sleep-wake variables, activity-rest, circadian activity rhythms, and QOL.

Findings: Fatigue was mild at baseline and rose to moderate levels during chemotherapy 1–3. Sleep quality was poor the months prior to chemotherapy 1 and chemotherapy 4. Actigraphy data revealed disturbed sleep, low daytime activity, and impaired circadian activity rhythms during the first week after chemotherapy 1–3. QOL ratings were similar to those in other cancer populations. Fatigue increased, and white blood cell counts decreased significantly over time.

Conclusions: During adjuvant chemotherapy, patients reported moderate fatigue and poor sleep quality; actigraphs confirmed problems with sleep maintenance as well as low daytime activity and disturbed circadian rhythms. Multiple barriers were encountered during the study.

Implications for Nursing: Clinicians should screen for fatigue and sleep-wake variables and use guidelines to select interventions.

Colon and rectal cancer are the fourth most commonly diagnosed and the second most frequent cause of cancer deaths in the United States (American Cancer Society, 2010). By the time of diagnosis, the cancer often has spread to regional or distant sites. In stages IIA–C, five-year survival rates are about 72%–85%, and in stages IIIA–B, 44%–83% (American Cancer Society, 2010). In addition to surgery, chemotherapy and radiation therapy are prescribed to improve survival and quality of life (QOL) (Cera & Wexner, 2005; Shelton, 2002). Chemotherapy regimens most commonly prescribed for locally advanced colon and rectal cancer include fluorouracil (5-FU), leucovorin, and oxaliplatin (FOLFOX); irinotecan may be substituted for oxaliplatin (FOLFIRI) (Engstrom et al., 2009a, 2009b; Grenon & Chan, 2009). Patients with rectal cancer often receive neoadjuvant 5-FU concurrent with radiation therapy. Oxaliplatin is more likely to produce peripheral neuropathy, and irinotecan may create more gastrointestinal toxicity and hair loss (Saltz et al., 2008). Both regimens are associated with dose-related clusters of symptoms, including fatigue, anorexia, weight loss, pain, fever, and dehydration, which affect functioning and QOL, but sleep-wake variables have not been described (Aprile, Ramoni, Keefe, & Sonis, 2008; Morse, 2006). Cancer-related fatigue has been reported as the most frequent and distressing toxicity of colon and rectal chemotherapy (Aprile et al., 2008).

Literature Review

Fatigue is defined as a distressing, persistent, subjective sense of physical, emotional, and cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning (National Comprehensive

Cancer Network, 2010). Using open-ended–response questions and the Functional Assessment of Cancer Therapy–General instrument, a large sample (N = 534) ranked fatigue as the number one concern in 10 of 11 types of cancers (Ward et al., 1999). Patients with colon or rectal cancer (62%, n = 50) reported fatigue as their primary concern, followed by QOL issues (Butt et al., 2008). Patients with varying cancers (N = 400; colorectal n = 150) at different stages and receiving various treatments ranked fatigue as highly important (Osoba et al., 2006).

Little is known about fatigue and QOL in patients with colon or rectal cancer who are receiving adjuvant chemotherapy. One qualitative study identified the common theme of "salvaging their normal lives" from patients' experiences with the recent diagnosis and treatment of colon or rectal cancer (Houldin & Lewis, 2006). A study of Canadian patients with colon or rectal cancer found that better general health and perceived quality of care predicted higher health-related QOL about nine months after diagnosis (Yost, Hahn, Zaslavsky, Ayanian, & West, 2008). Patients with advanced rectal cancer who received neoadjuvant chemotherapy and radiotherapy reported at the first postoperative visit that the most noted changes were in physical functioning and fatigue (Arraras Urdaniz, Arias de la Vega, et al., 2006). Another sample of patients with advanced rectal cancer, who received standard chemotherapy, reported improved fatigue, insomnia, and QOL (Arraras Urdaniz, Vera Garcia, et al., 2006).

Most patients receiving adjuvant chemotherapy for colon or rectal cancer are older than 50 years and are at risk for sleep-wake variables, but sleep in this population has been understudied (Vena, Parker, Cunningham, Clark, & McMillan, 2004). Some studies have reported circadian activity rhythms (see Table 1) determined by actigraphs without including information about objective sleep or daytime activity-rest or subjective sleep quality. Two-year survival of patients with metastatic colon or rectal cancer (N = 200) was higher when patients had discernible circadian activity rhythms versus impaired rhythms (Mormont et al., 2000). Patients with better circadian activity rhythms reported higher QOL or lower fatigue (Mormont et al., 2000, 2002; Rich et al., 2005).

The only study that compared circadian activity rhythms in healthy adults (n = 15; median age = 24 years) with rhythms in patients with colon or rectal cancer (n = 10; median age = 61 years) found similar mean mesor of 145 movements per minute for the young, healthy adults and 148 movements per minute for the patients with cancer. Acrophase (hours) in the healthy adults was 17:00 versus 15:24 in the patients with cancer. The median 24-hour autocorrelation coefficient (r24) was similar at 0.57 in both groups (Chevalier, Mormont, Cure, & Chollet, 2003).

Rich et al. (2005) reported mean mesor in patients with colorectal cancer; values were 84 movements per minute in patients with impaired rhythms and 107.5 movements per minute in those with stronger rhythms. Median r24 values in patients with metastatic colorectal cancer ranged from 0.22 in those with impaired rhythms to 0.58 in those with stronger rhythms (Rich et al., 2005). Median r24 values obtained from 72 hours of actigraphy monitoring before chemotherapy in two other samples of patients with metastatic colorectal cancer with good performance status were 0.41 (Mormont et al., 2002) and 0.42 (Mormont et al., 2000). Those studies were limited by a lack of comparisons with case-controlled healthy adults.

A meta-analysis of sleep studies published in peer-reviewed journals from 1960–2003 concluded that older adults' objective sleep significantly declined across the

Table 1. Circadian Activity Rhythm Variables Obtained by Actigraphs

Circadian Variable	Definition	Values in Healthy Young Adults
Mesor	24-hour rhythm adjusted mean of the activity counts; higher values signify more robust activity (Lentz, 1990).	Movements per minute: 138.2 (8.4) (Farr & Boen, 1996); 150.3 (17.7) (Brown et al., 1990)
Amplitude	Peak (or trough) value of the cosine curve minus the mesor; denotes the rhythmic change of an individual's activity during the 24-hour period (Lentz, 1990)	Movements per minute: 112.4 (4.9) (Farr & Boen, 1996); 109.0 (23.4) (Brown et al., 1990)
Acrophase	The peak amplitude actual clock time (Lentz, 1990)	Early afternoon (14:00–15:00) (Brown et al., 1990)
Circadian quotient	Strength of the circadian rhythm; determined by dividing the amplitude by the mesor; higher values represent an estimation of degree of activity and sleep consolidation throughout each day (Levin et al., 2005).	Ratio: closer to 1 (Levin et al., 2005)
24-hour autocorrelation (r24)	Comparison of the regularity and consistency of the rhythm one day to the next (Chevalier et al., 2003)	Ratio: range = –1 to +1; optimal range = +1 (Rich et al., 2005)

adult lifespan (Ohayon, Carskadon, Guilleminault, & Vitiello, 2004). Total sleep time was consistently reported to range from 6–6.5 hours per night and sleep efficiency (SE) to range from 77%–82% in healthy older adults (Buysse et al., 1991; Ohayon et al., 2004; Yoon, Kripke, Youngstedt, & Elliott, 2003). However, sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI), was reported as 4.4 (2.8) in older adult men and 5.1 (3.2) in older women; mean scores less than or equal to 5 indicate good sleep. Mean minutes awake after sleep onset (wake after sleep onset, WASO), reflecting problems with sleep maintenance, were reported as ranging from 55 minutes (Ohayon et al., 2004) to 84 minutes per night in healthy older adults; normal is less than 30 minutes, or less than 10% of total time in bed (Evans & Rogers, 1994). One report of mean time awake during the day (15.1 hours) and mean nap time (68 minutes) was found in healthy older adults (Evans & Rogers, 1994).

Healthcare providers try to maximize QOL in patients with colon or rectal cancer who are receiving chemotherapy. The researchers of the current study targeted such patients during the first six weeks of adjuvant or neoadjuvant chemotherapy, with or without concomitant radiation therapy, to examine patterns of fatigue and other variables. Specific aims during the first week of three two-week cycles of adjuvant chemotherapy and at six weeks were to

- Examine patterns of fatigue, sleep quality, sleep-wake variables, activity and rest, circadian rhythms, QOL, blood counts, and demographic and medical variables.
- Determine the feasibility of conducting the pilot study.

Methods

Conceptual Framework

The researchers used a longitudinal, descriptive design for this feasibility study. Piper's Integrated Fatigue Model guided the study (Piper, Lindsey, & Dodd, 1987). Activity and rest, changes in regulation transmission, and sleep-wake patterns were selected from the model because they have been found to influence fatigue in patients with cancer.

Setting and Sample

From April 2006–December 2008, the researchers recruited participants from a medical center and a community medical oncology clinic in the midwestern region of the United States. Participants were enrolled before the first chemotherapy treatment for colon or rectal cancer. Inclusion criteria were (a) aged 19 years and older; (b) diagnosed for the first time with stage II–III colon or rectal cancer and, if diagnosed with rectal cancer, scheduled to begin IV adjuvant chemotherapy with or without radiation therapy; (c) English-speaking and able to complete the research instruments; and (d) Eastern Cooperative Oncology Group (ECOG) performance status of 2 or better. Eligibility criteria were broadened in mid-2008 to include patients with stage IV disease with good performance status who were prescribed the same chemotherapy regimens used for stage II–III disease.

Exclusion criteria included self-reported history of diagnosed sleep disorders (e.g., obstructive sleep apnea, restless leg syndrome, periodic limb movement disorder, chronic insomnia), comorbidities associated with poor sleep quality and fatigue (e.g., chronic fatigue syndrome, fibromyalgia, unstable congestive heart failure, chronic obstructive pulmonary disease, neuromuscular disease, depression, untreated hypo- or hyperthyroidism, treatment with steroid therapy), or a job with rotating or permanent night shifts.

Procedures

The institutional review boards at both clinical sites approved the study. Oncology clinicians identified eligible patients and invited them to participate. A research nurse contacted interested potential participants in person or, with their permission, by telephone to provide information and screen for eligibility. The research nurse arranged to meet the eligible patients before the first chemotherapy treatment in a private room in the oncology clinic. The nurse obtained written informed consent and gave instructions on completing instruments and wearing the actigraph. The researchers scheduled data collection times (see Table 2) to coincide with the participants' chemotherapy every two weeks. They kept the time to complete instruments brief to reduce subject burden.

Instruments

Demographic and medical data: To collect data at baseline before the first chemotherapy treatment, the researchers used a form previously developed and tested. Among the data requested were age, ethnic and racial background, education, marital status, surgical procedure, cancer stage, and blood counts.

Fatigue: The **Piper Fatigue Scale (PFS)** measures present fatigue in four dimensions: behavioral severity (six items), sensory (five items), cognitive and mood (six items), and affective and meaning (five items) (Piper et al., 1998). Each item is anchored by two words, and a respondent selects the number from 1–10 that best describes the fatigue that he or she is experiencing; higher scores reflect more severe fatigue. Internal consistency reliability of the scale and four subscales ranges from 0.9–0.99 across studies and was 0.97–0.99 in this study.

Sleep quality: The **PSQI** measures subjective sleep quality and daytime sleepiness during the previous month (Buysse, Reynolds, Monk, Berman, & Kupfer,

Table 2. Timeline of Data Collection

Variable	Measurement	Baseline	Chemotherapy 1	Chemotherapy 2	Chemotherapy 3	Chemotherapy 4
Demographic and medical	Questionnaire	X	–	–	–	–
Fatigue	PFS	X	Day 3	Day 3	Day 3	–
Sleep quality	PSQI	X	–	–	–	X
Objective sleep-wake disturbances	Actigraphy	–	7 days and nights, continuous	7 days and nights, continuous	7 days and nights, continuous	–
Quality of life	FACT-C	X	–	–	Day 1	–
Blood counts	Hgb, WBC	X	–	Day 15	Day 29	–

FACT-C—Functional Assessment of Cancer Therapy–Colorectal (Ward et al., 1999); Hgb—hemoglobin; PFS—Piper Fatigue Scale (Piper et al., 1998); PSQI—Pittsburgh Sleep Quality Index (Buysse et al., 1989); WBC—white blood count

Note. Chemotherapy 1 was days 1–7; chemotherapy 2 was days 15–22; chemotherapy 3 was days 29–36; chemotherapy 4 was day 42 (six weeks).

1989). Responses to 19 items result in a total score and seven component scores that are weighted equally on a 0–3 scale, yielding a global score ranging from 0–21; higher scores indicate poorer sleep quality. Cronbach alpha for global PSQI was 0.69–0.72 in the current study. A PSQI score greater than 5 has a sensitivity of 89.6% and a specificity of 86.5% in identifying poor sleepers.

Sleep-wake disturbances, activity and rest, and circadian rhythms: The study used octagonal **Motionlogger® actigraph** (Ambulatory Monitoring, Inc.). Actigraphs offer a useful, noninvasive method of objectively quantifying actual movement and are an important index of sleep-wake variables and activity and rest in field studies (Brown, Smolensky, D'Alonzo, & Redman, 1990; Kripke, Mullaney, Messin, & Wyborney, 1978). Actigraphy is used to evaluate insomnia and is a valuable and valid addition to diary information (Hauri & Wisbey, 1992). Calibrations of the actigraph with polysomnography have been reported to be plus or minus 10% (Brown et al., 1990).

Participants wore the actigraph securely on the nondominant wrist in their usual environments the first week of each two-week cycle. They were taught to avoid getting the actigraph wet and to push a marker when turning the "lights off" and getting "out of bed" in the morning. Participants recorded the times they pushed the marker on the **Morin Sleep Diary** (Morin, 1993) each morning. The actigraphs recorded activity counts in one-minute epochs (intervals) per guidelines (Littner et al., 2003). Night sleep-wake variables included number of awakenings, wake after sleep onset in minutes (WASO-M) and percentage (WASO-P), percentage of time asleep after sleep onset, and total sleep time (minutes). Participants' minutes to sleep onset, referred to as sleep latency, were not included in this report because sleep onset is difficult to determine in uncontrolled settings (Lichstein et al., 2006). Daytime activity and rest variables included mean daytime activity, total sleep and wake time (minutes), percentage of time awake, and percentage of time asleep. The circadian rhythm variables included mesor, amplitude, acrophase, circadian quotient, and r24. The researchers used values from healthy midlife adults (Farr & Boen, 1996) and older adults (Evans & Rogers, 1994) for comparison.

Quality of life: The **Functional Assessment of Cancer Therapy–Colorectal (FACT-C)** is a 36-item Likert-scale questionnaire that assesses QOL in patients with colon and rectal cancer over the prior seven days; higher scores reflect better QOL. The FACT-C combines specific concerns related to colon and rectal cancer with concerns common to all patients with cancer and is sensitive to changes in functional status (Ward et al., 1999). Concurrent validity and internal consistency reliability have been established and were 0.93–0.99 in this study. Subscales include physical well-being (seven items), functional well-being (seven items), social and family well-being (seven items), and emotional well-being (six items), as well as the colorectal cancer subscale (nine items).

Data Analysis

The researchers downloaded the actigraph files and used Action4 (Action4 Procedure Manual, Ambulatory Monitoring, Inc.) to determine the epochs demonstrating sleep or activity. They followed established procedures to edit raw data, delete missing data, and handle naps prior to bedtime (Berger et al., 2008). Results were downloaded into a spreadsheet program.

Several preliminary analyses were performed on all variables with SPSS® [version 16.0] for Windows®, including frequency distributions to look for outliers

and violation of normality of distributions. Missing data were minimal and random and accounted for by scale score calculation procedures. Instruments that had greater than 10% missing data were excluded from the analysis. Descriptive statistics (means, standard deviations, standard errors of the means, and frequency distributions and percentages) were performed for each variable. Repeated-measures analyses of variance (RM-ANOVA) were run to examine changes over time in fatigue and other variables.

Results

Most enrolled participants (N = 21) who completed baseline data (n = 19) were middle aged, partnered, and employed and had some postsecondary education (see Table 3). One participant met the broadened eligibility criteria; the reserachers found that retaining that participant's data made no difference in the study results. Most participants had colon cancer (68%) and had a colectomy (53%) prior to chemotherapy.

Patterns of Fatigue

Mean fatigue (PFS) scores (see Table 4) reflected mild (range = 0–3.99) levels at baseline that rose to moderate levels (range = 4–6.99) on day 3 after chemotherapy 1. Fatigue remained moderately intense after chemotherapy 2 and lowered slightly after chemotherapy 3. The most intense fatigue was in the sensory dimension, reflecting fatigue in specific (e.g., tired eyes and shoulders) and generalized areas (e.g., feeling drained, weak, or exhausted). Total fatigue, analyzed with RM-ANOVA, increased significantly over time ($F = 2.89$; $p = 0.049$).

Sleep Quality

Mean perceived sleep quality (PSQI) scores reflected poor sleep during the months prior to chemotherapy 1 and chemotherapy 4 (see Table 5). The "sleep disturbances" subscale was highest at both times. That subscale reflects sleep maintenance and includes waking up in the middle of the night or early morning for several reasons (e.g., to use the bathroom, too hot).

Actigraphy: Sleep-Wake

Means for sleep-wake variables obtained by wrist actigraphy during the first week after each chemotherapy session were close to values from older adults but reflected problems with sleep maintenance when compared to healthy young adults (see Table 6). The number of awakenings was higher than in healthy young and older adults, as were WASO-M and WASO-P. The percentage of time asleep after first onset ranged from 76%–82% and was lower than values from healthy young adults (85% or greater). Only total sleep time was close to the norm of 6.5 hours per night in older adults. Improvements occurred in nighttime sleep-wake values between chemotherapy 1 and chemotherapy 3, but no changes occurred over time.

Table 3. Demographic Characteristics

Characteristic	n	%
Age (years)		
$\bar{X}$ = 65	–	–
Range = 47–82	–	–
Gender		
Female	7	37
Male	12	63
Living arrangements		
Alone	3	16
Not alone	16	84
Employment status		
Working	11	58
Not working	6	32
Not available	2	11
Educational level		
High school graduate	6	32
Some college	7	37
College graduate	2	11
Postcollege graduate	4	21
Level of activity		
Physical (on feet most of time)	5	26
Moderate (some sitting and some activity)	11	58
Sedentary (sitting most of the time)	3	16
Household income ($)		
Less than 20,000	1	5
20,000–40,000	5	26
More than 40,000	10	53
Does not wish to provide	3	16
Type of cancer		
Colon	13	68
Rectal	4	21
Both	2	11
Surgical procedure		
Colectomy	10	53
Resection of the rectum	3	16
Other	1	5
None	5	26
Cancer stage		
IIA or IIB	3	16
IIIA, IIIB, or IIIC	15	79
IV	1	5
Lymph node status		
Positive	15	79
Negative	4	21
Chemotherapy protocol		
5-fluorouracil (5-FU) and leucovorin	9	47
FOLFOX (leucovorin, 5-FU, and oxaliplatin)	6	32
Continuous 5-FU	4	21
Radiation treatment planned		
Yes, concurrent	4	21
Yes, after chemotherapy	1	5
No	14	74
Eastern Cooperative Oncology Group status		
0	8	42
1	5	26
2	6	32

N = 19

Note. Because of rounding, not all percentages total 100.

Table 4. Fatigue According to Piper Fatigue Scale (PFS) at Various Time Points in Patients With Colon or Rectal Cancer Receiving Chemotherapy

Variable	Baseline	Chemotherapy 1	Chemotherapy 2	Chemotherapy 3
PFS total				
$\bar{X}$	2.87	4.26	5.23	4.52
SD	1.95	2.65	2.44	2.59
n	18	17	16	15
Behavioral severity				
$\bar{X}$	2.13	4.21	4.63	3.67
SD	1.89	3.24	2.44	2.47
n	19	18	16	15
Sensory				
$\bar{X}$	3.49	5.08	5.66	4.89
SD	2.25	3.03	2.62	2.69
n	19	18	16	15
Cognitive and mood				
$\bar{X}$	3.11	3.66	4.63	4.07
SD	2.22	2.2	2.42	2.14
n	19	17	16	15
Affective and emotional				
$\bar{X}$	2.54	4.07	5.2	4.75
SD	2.21	2.84	2.57	2.91
n	18	17	16	15

Note. PFS measurements were taken 48 hours after chemotherapy 1–3.

Actigraphy: Activity-Rest

Daytime activity and rest variable values all were at the low end of the range for healthy young adults. Total wake time was 12%–15% lower than in healthy adults. Mean daytime total sleep time, indicating naps, was three to four times higher than normal and increased over time from 1.75–2.3 hours, or 11%–15% of the day.

Actigraphy: Circadian Activity Rhythms

Acrophase was the only circadian variable within normal limits. Twenty-four-hour activity rhythm measures were 78%–83% (mesor) and 66%–72% (amplitude) of values obtained in healthy young adults. Rhythm consistency from day to day (r24) was 0.33–034 during the first week after chemotherapy 1–3.

Quality of Life

Means and standard deviations for total and subscale QOL scores (see Table 7) were consistent with normal performance status ratings for the seven days before chemotherapy 1 and chemotherapy 3 (Cella et al., 1993). QOL scores were close to previous reports from general populations and from patients with colon or rectal cancer and were stable over time. Although no separate measure of emotional well-being (EWB) was included in the current study, the FACT-C EWB scores were consistent with norms from patients with cancer and improved slightly between measurements.

Blood Counts

Means for hemoglobin (12.3 [1.4]; n = 19) and white blood counts (7.4 [2.6]; n = 19) were within normal limits at baseline. Hemoglobin was stable (11.8 [1.7]; n = 15) prior to chemotherapy 2 (12.3 [1.5]; n = 15) and prior to chemotherapy 3. White blood count decreased over time ($F = 19.22$; $p < 0.001$); values were low (5.2 [1.7]; n = 15) prior to chemotherapy 2 and lower prior to chemotherapy 3 (4.7 [1.4]; n = 15).

Feasibility

The desired sample was 24 participants. Of those screened (n = 79), 30 (38%) did not meet inclusion criteria, 28 (35%) chose not to participate, 21 (27%) were enrolled, 19 (24%) provided baseline data, 14 (67%) of those enrolled completed the study, and 13 provided actigraph data. A barrier was the low number of patients who started adjuvant chemotherapy for stage II or III colon or rectal cancer during the study period. After 30 months of recruitment, the institutional review boards approved the expansion of study eligibility to include patients with stage IV disease with ECOG status of 2 or higher and similar chemotherapy regimens. One patient with stage IV disease enrolled. The study was designed to collect salivary and blood samples to test for acute-phase reactants and cytokines. However, patients forgot to collect the salivary samples at home and problems occurred with obtaining the extra blood samples in the clinic. Therefore, that part of the study was dropped.

Discussion

To the authors' knowledge, this is the first study to examine patterns of fatigue with a multidimensional scale and other variables during adjuvant chemotherapy for colon and rectal cancer. Fatigue has been ranked as the most prevalent and distressing symptom associated with chemotherapy for colon and rectal cancer, yet few studies have focused on the topic. The participants in this study reported mild fatigue at baseline even though nearly half the sample had had recent surgery. Participants were not anemic, which could have partially explained the mild fatigue reported. Fatigue increased over time and

remained moderately intense during chemotherapy 1–3. The researchers encountered numerous barriers.

This is the first report of sleep quality that used a multidimensional tool in this population at baseline and the first six weeks of chemotherapy. The patients reported poor-quality sleep during the months prior to chemotherapy 1 and chemotherapy 4; scores reflected that sleep quality was poorer than that reported by healthy young and older adults (Buysse et al., 1989, 1991). Although sleep quantity has been found to decrease across the adult lifespan (Ohayon et al., 2004), healthy older adults have reported scores reflecting good sleep quality (Buysse et al., 1991). Perceptions of poor sleep may have been caused by the patients' recent diagnoses of cancer, the physical effects of recent surgery, current chemotherapy or radiation therapy, comorbid conditions, medications, and other symptoms (Vena et al., 2004).

In this study, sleep measured by actigraphy coincided with subjective reports of poor sleep. Most of the sample was adherent in wearing the actigraph and had minimal missing data. Results showed problems with sleep maintenance, but total sleep time was similar to that in healthy older adults (Evans & Rogers, 1994; Ohayon et al., 2004; Yoon et al., 2003). Percentage of time asleep during the first week after chemotherapy 1–3 was lower than, but close to, the 79%–82% sleep efficiency reported in healthy older adults. Percentage of time asleep reflects sleep after first onset and does not include minutes of latency, about 5% of the night included in sleep efficiency calculations. Sleep efficiency is lower because sleep latency is included in the calculation.

Total sleep time was similar to that in healthy older adults, but the current sample spent more time in bed to obtain that amount of sleep. Participants spent only 12–13 hours per day out of bed during the first week after chemotherapy. Daytime activity levels measured by wrist actigraphy were borderline low, indicating clinically relevant findings because participants were early in chemotherapy. Excess time in bed and low activity during cancer chemotherapy may lead to complications, including lower physical functioning, falls, and loss of independence. The relatively older age of the participants predisposed them to normal age-related changes in body composition, including increased fat mass, sarcopenia, and declines in lean body mass, flexibility, muscle strength, and bone density (Courneya et al., 2004; Dutta, 1997; Hurley & Roth, 2000; Suh & Lyles, 2003). A meta-analysis by Schmitz et al. (2005) examined the effect of controlled physical activity in cancer survivors and determined that inactivity during and after cancer chemotherapy can have ill effects on cardiorespiratory functioning. Thus, time in bed beyond the recommended seven to nine hours per night may be a risk factor for several complications.

The mean r24 was lower than median values reported previously in patients with metastatic colon or rectal cancer (Chevalier et al., 2003; Mormont et al., 2000, 2002; Rich et al., 2005). Lower r24 values have been associated with lower QOL, higher fatigue, and shorter two-year survival in patients with metastatic colon or rectal cancer (Mormont et al., 2000, 2002; Rich et al., 2005). Values were higher than in previous reports of patients with impaired rhythms (Rich et al., 2005).

In the current sample, QOL in the week before chemotherapy 1 and chemotherapy 3 was consistent with adults with normal performance status receiving chemotherapy (Cella et al., 1993). Participants reported

Table 5. Pittsburgh Sleep Quality Index (PSQI) Scores in Patients With Colon or Rectal Cancer Receiving Chemotherapy

		Baseline (N = 19)		Chemotherapy 4[a] (N = 13)	
Subscale	Possible Range	$\bar{X}$	SD	$\bar{X}$	SD
Total score	0–21	9.78	4.75	7.15	4.14
Sleep quality	0–3	1.11	0.99	1.11	0.99
Sleep latency	0–3	1.37	1.16	1	0.88
Sleep duration	0–3	1.53	1.26	0.93	0.92
Habitual sleep efficiency	0–3	1.58	1.39	0.77	1.01
Sleep disturbances	0–3	1.63	0.68	1.63	0.68
Use of sleeping medications	0–3	1.26	1.33	0.71	1.14
Daytime dysfunction	0–3	1	0.77	1.36	1.08

[a] Chemotherapy 4 was six weeks after chemotherapy 1.

Note. PSQI reported sleep quality during the previous month. Measurement was taken on either day 1 or 3 of chemotherapy cycle 4.

Table 6. Actigraph[a] Sleep Variables at Chemotherapy Treatments[b]

Variable	Values in Healthy Young Adults	Chemotherapy 1			Chemotherapy 2			Chemotherapy 3		
		n	$\bar{X}$	SD	n	$\bar{X}$	SD	n	$\bar{X}$	SD
Nighttime Sleep-Wake										
Number of awakenings	2–6 times per night[c]	12	12.37	5.30	12	12.24	7.12	12	11.11	5.66
Mean time awake after sleep onset (WASO) (minutes)	30 or less than 10% of time in bed[c]	12	96.59	71.22	12	110.81	95.72	12	78.11	77.85
WASO-P (percentage)	10% or less[c]	12	19.97	15.46	12	21.77	18.82	12	15.81	14.25
Percentage of time asleep	85% or higher[c]	12	76.82	16.31	12	76.23	18.82	12	82.12	14.36
Total sleep time per night	8–9 hours or 420–540 minutes[c]	12	392.28	96.61	12	379.8	106.01	12	404.26	81.3
Daytime Activity and Rest										
Mean daytime activity	155–265 movements per minute[d]	14	161.68	22.11	13	151.76	27.12	13	152.4	27.24
Total wake time (minutes)	900–1020[d, e]	13	813.78	61.07	12	786.78	84.06	12	783.71	65.49
Percentage of time awake	90% of the day[e]	13	88.61	5.37	12	85.28	6.69	12	85.13	8.53
Percentage of time asleep	10% of the day[e]	13	11.39	5.37	12	14.72	6.69	12	14.87	8.53
Total sleep time per day (minutes)	30[e]	13	106.47	53.69	12	133.92	63.39	12	140.4	88.24
Circadian Activity Rhythms										
Mesor	138.2 (8.4)[f] 150.3 (17.7)[d]	13	115.27	17.4	13	108.54	19.51	13	107.6	18.2
Amplitude	112.4 (4.9)[f] 109 (23.4)[d]	13	81.11	14.06	13	74.34	23.26	13	74.53	17.93
Acrophase	Early afternoon (14:00–15:00)[d]	13	14:26	–	13	14:06	–	13	14:19	–
Circadian quotient	Closer to 1[g]	13	0.72	0.15	13	0.69	0.18	13	0.7	0.15
24-hour autocorrelation (r24)	Range = –1 to +1 optimal = +1[h]	13	0.34	0.08	13	0.33	0.15	13	0.34	0.13

[a] Actigraph (Ambulatory Monitoring, Inc.); [b] Mean of seven nights after chemotherapy 1–3; [c] Berger et al., 2005; [d] Brown et al., 1990; [e] Evans & Rogers, 1994; [f] Farr & Boen, 1996; [g] Levin et al., 2005; [h] Rich et al., 2005

Note. No significant difference on any variable over time

no change in total and subscale QOL scores over time despite poor sleep, low daytime activity, and impaired circadian activity rhythms during the first week after each chemotherapy. The results may be related to the lack of sensitivity of the FACT-C measurement, participants' good performance status before chemotherapy, or insufficient time for dose-related and cumulative chemotherapy effects to occur. Participants may have been attempting to "grin and bear it" and salvage their normal lives (Houldin & Lewis, 2006) to avoid treatment delays or dose reductions.

Fatigue increased and white blood cell counts decreased from chemotherapy 1 to chemotherapy 3; no other blood count variables changed over time. Sleep variables trended in a positive direction, but daytime activity and circadian rhythms became more disrupted and may have led to lower QOL later.

Strengths of the study include the focus on a neglected area, the longitudinal design, the use of subjective and actigraph measurements, and the use of tools with established reliability and validity. Limitations include the small sample and the refusal and withdrawal rates. Those who declined or withdrew may have had a different experience than those who participated. The researchers were unable to determine whether poor sleep already was present or changed as a result of cancer

Table 7. Functional Assessment of Cancer Therapy–Colorectal Cancer (FACT-C) in Patients With Colon or Rectal Cancer Receiving Chemotherapy

Variable	Baseline	Chemotherapy 3[a]
FACT-C		
$\bar{X}$	111.91	112.04
SD	15.61	19.83
n	18	15
Colon and rectal cancer–specific		
$\bar{X}$	18.58	18.5
SD	4.05	4.33
n	18	15
FACT-General		
$\bar{X}$	93.33	93.54
SD	12.75	16.43
n	18	15
Social and family well-being		
$\bar{X}$	16.54	16.84
SD	6.12	2.58
n	18	15
Emotional well-being		
$\bar{X}$	16.87	19
SD	4.6	3.89
n	18	15
Functional well-being		
$\bar{X}$	18.51	18.47
SD	5.1	5.66
n	18	15
Physical well-being		
$\bar{X}$	22.84	20.73
SD	3.8	5.12
n	18	15

[a] Chemotherapy 3 was four weeks after chemotherapy 1.

Note. No significant changes occurred in total or subscale scores over time.

diagnosis and surgery. They were unable to examine those who received radiation separately because of the small sample. Timing of measurement completion may have influenced results. Lack of information regarding comorbid conditions and medications and problems obtaining salivary cortisol levels also are limitations.

Implications for Nursing

Patients with colon or rectal cancer need to be screened at baseline and at regular intervals for the frequent and distressing symptoms of fatigue and sleep-wake disturbances. For fatigue, clinicians should use the tool recommended by the National Comprehensive Cancer Network (2010): "How would you rate your fatigue on a scale of 0–10 over the past seven days?" For sleep disturbances, the Oncology Nursing Society's Putting Evidence Into Practice project suggested the Insomnia Severity Index (Eaton & Tipton, 2009). When a fatigue screen is positive, further assessment is indicated. Patients need to be educated on interventions that are recommended for practice or likely to be effective in relieving their fatigue and sleep-wake disturbances. When sleep disorders are suspected, patients need to be evaluated by their primary physicians and referred to an accredited sleep center.

Research implications include a need to replicate this study in a larger, more diverse sample for a longer time. Findings also support the need to collect data from healthy controls matched for age, sex, and comorbid conditions. Future studies should overcome the high refusal and withdrawal rates. Interventions should be designed for patients with colon and rectal cancer receiving chemotherapy with moderate to severe fatigue and sleep-wake disturbances. The topic is important because the American Cancer Society (2010) estimated more than 140,000 newly diagnosed patients with colon and rectal cancer and nearly 50,000 deaths in 2008 from the combined cancers.

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