Sleep-Wake Disturbances and Quality Of Life in Patients With Advanced Lung Cancer

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Purpose/Objectives: To examine the scope and severity of subjective sleep-wake disturbances in patients with lung cancer and compare them to a group of healthy adults who were similar in age, gender, and race, and to examine the impact of sleep-wake disturbances on measures of health-related quality of life (QOL).

Design: Descriptive, comparative.

Setting: University-based and private urban ambulatory care clinics.

Sample: 43 patients with advanced non-small cell or small cell lung cancer and 36 healthy adults. All participants were cognitively intact, and none had any known neurologic disorder, polysomnographically diagnosed sleep disorder, mood or anxiety disorders, or cerebral metastasis.

Methods: Questionnaires, interview, and medical record review.

Main Research Variables: Nocturnal sleep (quality, quantity, and disturbance), daytime sleepiness, and health-related QOL (physical, mental).

Findings: Patients with lung cancer had poor perceived nocturnal sleep quality and excessive daytime sleepiness that differed significantly from the comparison group. Sleep disturbances in the group with lung cancer were characterized by breathing difficulty, cough, nocturia, and frequent awakenings. Sleep-wake disturbances were significantly associated with poorer health-related QOL after controlling for group. Excessive daytime sleepiness was associated most often with decreases in mental health, whereas poor nocturnal sleep was associated most often with decreases in physical health.

Conclusions: Findings suggest that sleep-wake disturbances are common in patients with lung cancer and that the disturbances are significantly associated with health-related QOL. Patients with lung cancer may be at risk for sleep-disordered breathing.

Implications for Nursing: The magnitude of nocturnal sleep disturbance and daytime sleepiness identified in this study reinforces the importance of ongoing screening and effective intervention for sleep-wake disturbances in patients with lung cancer.

Key Points . . .

- ➤ Nurses cannot rely on a single question of global sleep quality to screen for nocturnal sleep disturbance.
- ➤ Evaluation of daytime sleepiness should be a component of ongoing assessment for sleep-wake disturbances.
- ➤ Patients with lung cancer have many disease- and treatment-related factors that may disrupt the sleep-wake cycle.

Although sleep-wake disturbances have been described in patients with cancer (Clark, Cunningham, McMillan, Vena, & Parker, 2004), the nature and impact of the disturbances have not been well characterized, especially in site- and stage-specific cancer samples. Notably, some studies have suggested that differences in sleep-wake patterns among specific cancer groups can be found and that nocturnal sleep disturbance and daytime sleepiness may be particularly troublesome for patients with lung cancer (Davidson, Maclean, Brundage, & Schulze, 2002; Silberfarb, Hauri, Oxman, & Schnurr, 1993).

Lung cancer is a common malignant disease that exacts significant morbidity and mortality (American Cancer Society, 2006; Brown, Lipscomb, & Snyder, 2001; Malone, Harris, & Luscombe, 1994). Patients with progressive, advanced cancer of the lung experience numerous demographic, lifestyle, psychosocial, clinical, and treatment-induced changes that have the potential to generate nocturnal sleep disturbance and daytime sleepiness (Vena, Parker, Cunningham, Clark, & McMillan, 2004), such as difficulty getting to sleep, early-morning awakenings, prolonged nocturnal wakefulness, and altered sleep architecture (Davidson et al., 2002; Ginsburg, Quirt, Ginsburg, & MacKillop, 1995). In studies of subjectively and objectively measured sleep, people with lung cancer have demonstrated poorer quality of sleep than other groups with cancer as well as control groups (Davidson et al.; Silberfarb et al., 1993).

Excessive daytime sleepiness, or the inability to maintain an alert, awake state, may be an underrecognized problem for patients with cancer. Subjective reports of drowsiness, sedation, or sleepiness have been reported in patients with lung cancer (Davidson et al., 2002; Silberfarb et al., 1993). In addition, daytime napping also has been reported in this population (Davidson et al.; Silberfarb et al., 1993). Sys-

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tematic assessment of prevalence and frequency of daytime sleepiness, however, is lacking.

Adequate nocturnal sleep and daytime alertness are necessary for health, well-being, and functioning (Durmer & Dinges, 2005; Lee, Cho, Miaskowski, & Dodd, 2004). Disturbed sleep-wake patterns may have significant adverse effects on quality of life (QOL) and survival of patients with lung cancer. Sleep-wake disturbances consistently are rated among the most distressing symptoms that patients with cancer face (Degner & Sloan, 1995; Sarna, 1993). Davidson et al. (2002) described specific effects of sleep-wake disturbance on well-being and functioning as interference with emotions, the ability to cope, the ability to concentrate, and the ability to carry out usual activities. Furthermore, Degner and Sloan reported that a lower symptom distress score was predictive of longer survival time in patients with lung cancer irrespective of age and stage of diagnosis. Although no direct association between sleep and survival was made, nocturnal sleep disruption, pain, and fatigue produced the most distress in the sample.

Research on sleep-wake disturbances in diagnosis- and stage-specific groups with cancer, including lung cancer, is limited. However, data indicate that sleeping and waking are disturbed in patients with lung cancer and that the disturbances contribute to decreased QOL in this population. Therefore, the purpose of this study was to examine the scope and severity of subjective sleep-wake disturbances in patients with advanced lung cancer and compare them to a group of healthy adults similar in age, gender, and race. In addition, the study examined the association between sleep-wake disturbances and measures of health-related QOL.

Conceptual Framework

The Two-Process Model of Sleep Regulation provided a conceptual framework for the study. According to the model, homeostasis (process S) and circadian rhythmicity (process C) interact to influence sleeping and waking (Borbely, 1982). Process S (homeostatic drive for sleep) is a measure of sleep need and depends on the prior pattern of sleeping and waking. Process C (circadian control) is a sinusoidal rhythm with a time period of approximately 24 hours that is independent of sleeping or waking. Process C fluctuates across the day and night and is driven by a clock-like mechanism in the brain (suprachiasmatic nucleus). Although process S and process C are conceptually separate processes, they are not independent. Sleep propensity, sleep structure, and waking are regulated by a subtle and complex interaction between the two processes and are mediated by neuronal, neuroendocrine, and thermoregulatory functions (Dijk, 1997; Van Someren, 2000). Therefore, mechanisms or factors that oppose or enhance process S or process C can have a significant effect on the timing, duration, and structure of sleep as well as daytime functioning.

The model provided a framework for understanding how cancer, cancer treatment, and patient characteristics might affect sleeping and waking. In addition to demographic (age, gender), lifestyle (caffeine, sleep habits), and psychological (depression, anxiety) factors that affect sleep-wake patterns in general, patients with lung cancer face additional disease- and treatment-related factors that can interfere with process S or process C and disrupt the sleep-wake cycle (Vena et al., 2004). The factors are shown in Table 1. In the current study, several aspects of nocturnal sleep, including overall sleep quality, habitual sleep latency, habitual sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medications, and daytime dysfunction, were assessed (see Figure 1). Trait sleepiness also was measured.

Methods

Sample and Setting

Approval for the study was obtained from the Emory University Institutional Review Board. Informed consent was obtained prior to enrollment of participants. The sample included adults aged 21 years and older who were able to read and write English (as evidenced by an ability to read aloud the first paragraph of the consent form) and had no significant cognitive impairment (Mini Mental Status Examination score of 24 or higher). Participants with cancer had a primary diagnosis of stage IIIB or IV non-small cell lung or extensive small cell lung cancer. Comparison group participants had self-reported good health or no health condition that affected activities of daily living (Karnofsky Performance Status [KPS] score of 70 or higher) and were comparable in age, race, and gender to the group with lung cancer. Potential participants were excluded if they had the following medical conditions, which are known to affect cognition or sleep: Parkinson disease or another neurologic disorder; any polysomnographically diagnosed sleep disorder; a diagnosis of a mood, anxiety, or psychotic disorder; or known cerebral metastasis at the time of enrollment.

Participants were recruited during regular visits to five ambulatory clinics (three medical oncology and two internal medicine) in the metropolitan Atlanta, GA, area. Of 147 potentially eligible participants, 91 agreed to participate in the study (62%). Two participants were determined to be ineligible after enrollment (brain metastases), and 10 participants (three with lung cancer and seven healthy adults) did not return questionnaires, leaving a total sample size of 79 (43 patients with lung cancer and 36 healthy adults). Sample size was based on statistical tests to compare groups on sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI). The researchers planned to use nonparametric methods. Because of a lack of a recognized sample size formula for rank tests, sample size was determined for the equivalent parametric test (t test) (Norman & Streiner, 2000). In other cancer samples, PSQI global scores have ranged from 6.67–8.3 (SD = 4.0–5.3) (Beck, Schwartz, Towsley, Dudley, & Barsevick, 2004; Carpenter & Andrykowski, 1998; Fortner, Kasprowicz, Wang, Forjaz, & Stepanski, 2000; Owen, Parker, & McGuire, 1999). Because PSQI global scores above five indicate moderate-to-severe sleep disturbance, the researchers wanted to be able to determine a three-point difference between groups. Because the researchers anticipated a pattern of intermediate variability in group means, a sample size of 36 participants per group was proposed to achieve 80% power at α equal to 0.05 to detect the difference in PSQI global sleep quality scores according to procedures recommended by Cohen (1988).

Measures

Four instruments were used in the study. After giving informed consent, participants were supplied with all study

Table 1. Factors Common to Patients With Lung Cancer That May Interfere With Sleep Regulation

Factor	Mechanisms	Homeostatic Process S	Circadian Process C
Disease related			
Altered activity and rest cycles	Decreased exposure to environmental cues that reset the body's biologic clock		X
	Irregular sleeping patterns, including napping	X	
Pain	Pain produces a persistent arousal state.	X	
Fatigue	Decreased activity		X
	Daytime sleepiness may be a significant component of perceived fatigue.	X	
Altered hormone secretion	Blunted or erratic circadian patterns of cortisol secretion may indicate disruption in circadian rhythms. Cortisol levels are higher during wakefulness.	X	
	Decreased or blunted melatonin secretion may indicate disruption in circadian rhythms. Melatonin plays a role in regulation of sleep patterns.		X
Cytokine production	Some inflammatory cytokines regulate physiologic, nonrapid eye movement sleep. Increased levels of the cytokines promote sleepiness.	X	
	Inflammatory cytokines may induce fever, altering circadian temperature regulation.		X
Impaired respiratory function	Cough and dyspnea, especially when accompanied by anxiety, can produce an arousal state. Breathing may be altered by the disease process. Sleep further disrupts breathing, especially in the rapid eye movement phase.	X	
Treatment related			
Chemotherapy	Vinorelbine may transiently alter the circadian rhythm of body temperature as well as activity and rest. Taxanes have been shown to upregulate inflammatory cytokines.		X
Radiotherapy	Possible upregulation of inflammatory cytokines		X
Medications	Drugs used for supportive management (e.g., opioids, nonsteroidal anti-inflammatory drugs, antiemetics, anxiolytics, steroids, antidepressants) can alter sleep architecture or produce drowsiness.	X	X

Note. Based on information from Ancoli-Israel et al., 2001; Bartsch & Bartsch, 1999; Lee et al., 2004; Mazzoccoli et al., 2003; Silber et al., 2004; Vena et al., 2004; Vgontzas & Chrousos, 2002.

instruments. If time did not permit completion of the instruments during the clinic visit, the investigator gave each enrollee a self-addressed, stamped envelope in which to return the questionnaires. Follow-up phone calls were made to encourage participants to return questionnaires.

Subject information form: All participants were interviewed to obtain demographic and relevant clinical and treatment information. Additional clinical information was obtained from a review of medical records. Demographic variables included age, gender, race or ethnicity (self-defined), marital status, education level, employment, and household income. Clinical data included body mass index (BMI), KPS, comorbid conditions, and metastatic sites. Treatment data included current and previous cancer therapies (chemotherapy, radiotherapy, surgery, and biotherapy).

Pittsburgh Sleep Quality Index: The PSQI is a 19-item, self-rated questionnaire that assesses sleep quality and disturbances during the previous four weeks (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Habitual sleep parameters, including sleep latency, total sleep time, and sleep efficiency, are calculated from responses. In addition, seven component scores evaluate subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction, each of which is scored on a range of 0–3. The seven component scores are added to yield one global score with a range of 0–21 points, with higher scores indicating greater sleep disturbance. A global sleep quality score of five or higher indicates significant sleep disturbance.

The reliability and validity of the PSQI were assessed during an 18-month period with "good" sleepers, "poor" sleepers, and sleep-disordered patients. Internal homogeneity was 0.83 using Cronbach's α (Buysse et al., 1989). The PSQI demonstrated utility for self-administration, internal consistency reliability, and construct validity in patients with a variety of cancers (Beck et al., 2004; Carpenter & Andrykowski, 1998). Cronbach's α was 0.72 for the sample.

Epworth Sleepiness Scale: The Epworth Sleepiness Scale (ESS) is a simple, self-administered questionnaire that measures trait sleepiness or the general level of daytime sleepiness,

Daytime dysfunction: degree to which sleepiness or lack of energy interferes with daily activities

Habitual sleep duration: self-reported number of hours slept during nocturnal sleep period

Habitual sleep efficiency: self-reported ratio of total sleep time to total bedtime

Habitual sleep latency: self-reported time from turning out the lights until the onset of sleep

Sleep disturbances: factors that may disrupt nocturnal sleep, including difficulty getting to sleep, awakenings, nocturia, difficulty breathing, coughing or snoring, feeling too hot or cold, pain, and bad dreams

Sleep quality: the overall character of sleep, including quantity, frequency of disturbances, use of medication, and daytime function as measured by the Pittsburgh Sleep Quality Index

Trait sleepiness: self-reported propensity to fall asleep in selected situations as measured by the Epworth Sleepiness Scale

Figure 1. Definitions for Sleep-Related Variables

Note. Based on information from American Academy of Sleep Medicine, 2005; Kryger et al., 2005; Silber et al., 2004.

independent of short-term variations during the day and from day to day, by examining reported propensity to sleep in hypothetical situations. Total ESS scores significantly distinguished healthy subjects from patients with sleep apnea, narcolepsy, and hypersomnia (Johns, 1991). The strength of the ESS is the range of situations that participants respond to as inducing dozing, which provides a measure of subjective sleepiness during the course of daily activities. ESS scores can range from 0–24, with scores of 10 or higher indicating excessive daytime sleepiness. Internal consistency reliability for this study was 0.79.

Medical Outcomes Study Short Form-36 Version 2: The Medical Outcomes Study Short Form-36 Version 2 (SF-36) is a 36-item instrument designed to measure health-related QOL. The SF-36 has proven useful in surveys of general and specific populations for comparing the relative burden of diseases. The questionnaire yields scores for eight health domains (i.e., physical function, social function, role limitations–physical, role limitations–emotional, bodily pain, general mental health, vitality, and general health) (Ware & Sherbourne, 1992). The time frame for all items is within the previous four weeks. In addition, the questionnaire yields psychometrically based physical component summary (PCS) and mental component summary (MCS) measures. These summary measures were used as measures of health-related QOL in this study.

Reliability, content validity, and construct validity have been evaluated in numerous studies, and the SF-36 has been found to be highly reliable ($\alpha \geq 0.85$) and valid for use in diverse patient groups (McHorney, Ware, Lu, & Sherbourne, 1994; McHorney, Ware, & Raczek, 1993). Version 2.0 uses norm-based scoring algorithms (T-score transformation with a mean of 50 ± 10) (Ware, 2000). Scores below 50 indicate that health status is below average, and each point is one-tenth of a standard deviation (Ware). For the sample in the present study, internal consistency reliability (Cronbach's α) for subscales ranged from 0.83–0.94.

Data Analysis

All statistical analyses were carried out using SPSS® version 10.0 (SPSS Inc., Chicago, IL). Alpha was set at 0.05. Level of measurement, central tendency, and sample size determined the selection of statistical methods. Descriptive statistics were used to characterize the sample, the quality and nature of sleep and daytime sleepiness, and measures of health-related QOL. Because the PSQI and ESS are ordinal in nature and sample sizes were small, group differences in all variables were assessed with Mann-Whitney U or chi-square tests as appropriate.

To evaluate the magnitude of poor sleep quality in the study groups, the percentage of participants who scored above five on the PSQI was assessed. To evaluate the prevalence of daytime sleepiness in the sample, frequencies were analyzed to determine what proportion of participants scored 10 or higher on the ESS. To assess the relationship between sleep-wake disturbance and health-related QOL, the association among summary measures of health-related QOL (SF-36 PCS and MCS scores) and summary measures of nocturnal sleep (PSQI global sleep quality score) and daytime sleepiness (ESS score) was examined using hierarchical linear regression. Although PCS and MCS scores were distributed normally, significant group differences were present in the measures. In addition, the group with lung cancer differed significantly from the comparison group in functional status and medication profile. Therefore, group (patients with lung cancer or healthy adults) was entered into the equation in the first step and PSQI and ESS scores were added to group in the second step to evaluate the overall association of sleep-wake disturbance with PCS and MCS while controlling for group status. The association between sleep-wake disturbance and health-related QOL was addressed by the R^2 change for the two equations.

Results

Sample Description

A description of the sample, including demographic and clinical characteristics, is provided in Table 2 and Table 3. No significant differences were found between groups on any demographic variables with the exception of employment status. The comparison group had significantly fewer participants on disability or sick leave ($\chi^2 = 8.18$, df = 2, p = 0.02). Relevant to clinical characteristics, the groups were comparable regarding BMI and number of comorbidities. Mean BMI scores for both groups were in the National Institutes of Health's overweight category (25–30) ("Clinical Guidelines on the Identification," 1998). The mean number of cormorbidities for the sample was 1.78 (SD = 1.40, median = 2.0, range = 0–5). The comparison group (a) had higher KPS scores (z = –6.78, p < 0.0001), (b) used fewer total medications (z = –3.77, p < 0.0001), and (c) took fewer sleep-wake–impairing medications such as opioids (z = –3.58, p < 0.0001), hypnotics or sedatives (z =

Table 2. Demographic Profile of the Sample

	Lung (N = 43)		Comparison (N = 36)		
Variable	$\bar{X}$	**SD**	$\bar{X}$	**SD**	**p**
Gender					0.9
Female	20	46.5	18	50.0	
Race					0.06
White	39	90.7	27	75.0	
African American	4	9.3	9	25.0	
Marital status					0.98
Married or partnered	31	72.1	26	72.2	
Single, divorced, or widowed	12	27.9	10	27.8	
Employment					< 0.01
Working full- or part-time	14	32.6	18	50.0	
Retired	21	48.8	18	50.0	
Sick leave disability	8	18.6	–	–	
Education					0.84
Less than high school	3	7.0	1	2.8	
High school	11	25.6	6	16.7	
Some college or vocational school	14	32.6	13	36.1	
College	15	34.9	16	44.4	
Annual income ($)					0.53
0–10,000	3	7.0	2	8.6	
10,000–30,000	7	16.3	6	16.7	
30,000–50,000	15	34.9	14	38.9	
> 50,000	18	41.9	14	38.9	

Table 3. Clinical Profile of the Sample

	Lung (N = 43)		Comparison (N = 36)		
Variable	**$\bar{X}$**	**SD**	**$\bar{X}$**	**SD**	**p**
Age (years)	62.70	9.87	61.25	13.55	0.9
Body mass index	26.59	4.80	28.88	4.83	0.06
Comorbidities	1.60	1.42	2.00	1.35	0.19
Karnofsky Performance Status	81.40	8.87	96.67	5.34	< 0.0001
Medications	7.09	3.79	4.08	3.08	< 0.0001
Variable	**n**	**%**	**n**	**%**	**p**
Antidepressants	9	21	3	8	0.12
Opioids	13	30	–	–	< 0.0001
Benzodiazepines	11	26	2	6	0.02
Hypnotics or sedatives	10	23	1	3	0.01

–2.60, p = 0.01), and benzodiazepines (z = –2.38, p = 0.02). Participants with lung cancer had a mean of 1.12 metastatic sites (SD = 0.70, median = 1.0, range = 0–3), and a large percentage (93%) currently were receiving chemotherapy. Only four participants were receiving radiotherapy during the study period.

Nocturnal Sleep

Table 4 presents PSQI global sleep quality and component scores for the sample. The group with lung cancer had significantly higher global sleep quality scores (poorer sleep) than the comparison group ($\bar{X}$ = 9.26 versus 5.83, respectively). Eighty-eight percent of participants with lung cancer scored five or higher, compared to 47% of the comparison group.

Although sleep duration ($\bar{X}$ = 7 hours, SD = 1.33) was equivalent between groups, significant differences were found in habitual sleep latency and sleep efficiency and their corresponding component scores. The group with lung cancer had significantly longer sleep latencies ($\bar{X}$ = 28.02 versus 16.64 minutes, respectively). Sleep latency is considered prolonged if it is longer than 30 minutes (Berry, 2003). Twenty-six percent of patients with lung cancer but only 8% of the comparison group had habitual sleep latencies longer than 30 minutes. The group with lung cancer also had a significantly lower mean sleep efficiency (normal > 85%) than the comparison group (83% versus 89%, respectively). More than half of participants with lung cancer (56%) and 27% of the comparison participants had a habitual sleep efficiency lower than 85%.

Groups did not differ significantly in sleep quality or sleep duration component scores. However, significant differences were identified for sleep disturbance, sleeping medication, and daytime dysfunction. Participants with lung cancer reported greater use of sleeping medication, more daytime dysfunction, and more sleep disturbances. To further characterize the nature of sleep disturbances between the two groups, means for sleep disturbance scores are displayed graphically in Figure 2. Sleep interruption and nocturia were the most frequently reported habitual disturbances. Compared to healthy adults, patients with lung cancer had significantly more disturbed sleep related to breathing difficulty (z = –3.47, p = 0.001), cough (z = –2.39, p = 0.02), nocturia (z = –2.77, p = 0.01), awakenings (z = –2.89, p < 0.01), feeling too hot (z = –2.09, p = 0.04), feeling too cold (z = –2.29, p = 0.02), and pain (z = –2.02, p 0.04).

Daytime Sleepiness

Patients with lung cancer had significantly higher ESS scores than the comparison group (z = –3.71, p < 0.001). Forty-four percent of patients with lung cancer reported significant daytime sleepiness (ESS score ≥ 10), compared to 14% of healthy adults.

Quality of Life

In comparison to the healthy adults, patients with lung cancer had significantly lower SF-36 PCS (z = –5.62, p < 0.001) and MCS (z = –4.59, p < 0.001) scores. PSQI global scores were significantly correlated with PCS (r_s = –0.44, p < 0.001) and MCS (r_s = –0.52, p < 0.001), indicating that poor sleep quality was associated with poorer health-related QOL. ESS scores also were cor-

Table 4. Group Differences in Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, and Medical Outcomes Study Short Form-36 Version 2 Scores

	Lung (N = 43)			Comparison (N = 36)			
Measure	**$\bar{X}$**	**SD**	**$\bar{X}$ Rank**	**$\bar{X}$**	**SD**	**$\bar{X}$ Rank**	**p**
Pittsburgh Sleep Quality Index							
Global sleep quality	9.26	3.32	50.19	5.83	2.87	27.83	< 0.001
Component scores							
Sleep quality	0.93	0.63	43.42	0.69	0.67	35.92	0.1
Sleep latency	1.42	1.12	46.80	0.69	0.92	31.88	0.002
Sleep duration	1.12	1.14	40.43	1.03	0.94	39.49	0.85
Sleep efficiency	1.37	0.66	43.84	1.11	0.46	35.42	0.02
Sleep disturbance	1.74	0.54	48.42	1.22	0.48	29.94	< 0.001
Sleeping medication	1.53	1.37	47.29	0.56	1.05	31.29	0.001
Daytime dysfunction	1.14	0.56	48.97	0.53	0.56	29.29	< 0.001
Epworth Sleepiness Scale	9.00	4.30	48.73	5.42	3.14	29.57	< 0.001
Medical Outcomes Study Short Form-36 Version 2							
Physical component summary	35.88	10.61	26.72	50.74	8.36	55.86	< 0.001
Mental component summary	47.38	10.03	29.16	56.18	6.65	52.94	< 0.001

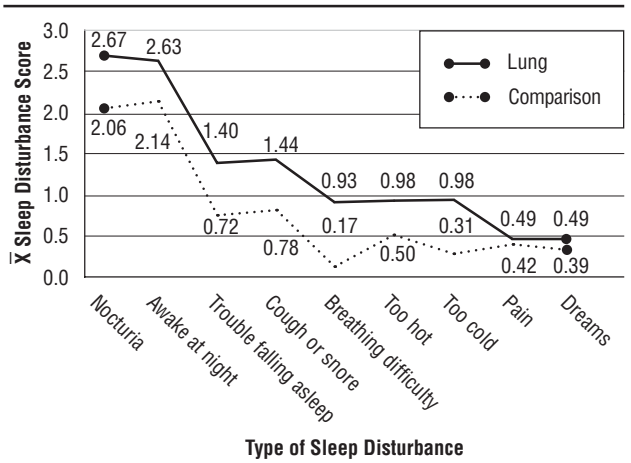

Figure 2. Sleep Disturbance Patterns in Study Groups Identified From the Pittsburgh Sleep Quality Index

related with PCS ($r_s = -0.49$, $p < 0.001$) and MCS ($r_s = -0.49$, $p = 0.03$). A higher level of daytime sleepiness was associated with poorer physical and mental health.

Hierarchical linear regressions indicated that sleep-wake disturbances were associated with decreases in QOL in addition to group designation. Regression summaries are presented in Table 5. In the first model, group accounted for 38% of the variability in PCS scores. The addition of PSQI and ESS scores to the equation accounted for a significant proportion of PCS variance after controlling for group (R^2 change = 0.12; df = 2, 75; $p < 0.001$). Although the overall model was significant, analysis of beta coefficients indicated that daytime sleepiness was most associated with decreases in PCS scores. In the second model, group accounted for 21% of the variability in MCS scores. Entry of PSQI and ESS scores to the equation also accounted for an additional proportion of MCS variance after controlling for group (R^2 change = 0.08; df = 2, 75; $p = 0.02$). However, in that case, analysis of beta coefficients indicated that nocturnal sleep quality was most associated with decreases in MCS scores.

Discussion

The nature and impact of sleep-wake disturbances in stage-specific groups with lung cancer have not been characterized fully. The present study examined the scope and severity of subjective sleep-wake disturbances in a sample of patients with late-stage lung cancer in comparison to a group of healthy adults who were similar in age, gender, and race. In addition, the study examined the impact of sleep-wake disturbances on measures of health-related QOL. Major findings were that the patients with lung cancer reported (a) disturbed nocturnal sleep quality, (b) a high prevalence of daytime sleepiness, (c) a pattern of respiratory symptoms associated with nocturnal sleep disturbance, and (d) decreases in health-related QOL that were associated with sleep-wake disturbances. The findings indicate that patients with lung cancer experience disruption in sleep regulatory mechanisms.

Participants with advanced lung cancer in the study reported poor nocturnal sleep quality, a finding that is consistent with previous reports in the literature involving similar samples (Davidson et al., 2002; Ginsburg et al., 1995; Kaye, Kaye, & Madow, 1983) and in the general population of patients with cancer (Anderson et al., 2003; Beszterczey & Lipowski, 1977; Davidson et al.; Engstrom, Strohl, Rose, Lewandowski, & Stefanek, 1999). The mean PSQI global sleep quality score for the patients with lung cancer was higher than previously reported in the literature for samples of patients with cancer and was significantly higher than the study comparison group (Beck et al., 2004; Carpenter & Andrykowski, 1998; Fortner et al., 2000; Owen et al., 1999). The findings highlight that patients with lung cancer are likely to experience severe and distressing sleep disturbances (Davidson et al.; Sarna & Brecht, 1997; Silberfarb et al., 1993; Silberfarb, Hauri, Oxman, & Lash, 1985).

Excessive daytime sleepiness was prevalent in the group with lung cancer. The findings are consistent with previous reports that suggested daytime sleepiness and daytime napping were problems for patients with lung cancer (Davidson et al., 2002; Ginsburg et al., 1995). Patients with lung cancer in the current study had significantly higher ESS scores and reported significantly higher daytime dysfunction (includ-

Table 5. Summary of Hierarchical Linear Regression Models for the Association of Sleep-Wake Disturbances With Health-Related Quality of Life

Variable	F	df	R^2	R^2 Adjusted	B	SE B	β
Model 1: physical component							
Step 1: group	46.49*	1, 77	0.38	0.37	7.43	1.09	0.61*
Step 2	24.41*	3, 75	0.49	0.47			
Group					4.95	1.20	0.41*
Pittsburgh Sleep Quality Index					−0.41	0.33	−0.13
Epworth Sleepiness Scale					0.97	0.27	−0.34*
Model 2: mental component							
Step 1: group	20.22*	1, 77	0.21	0.20	4.40	0.98	0.46*
Step 2	10.02*	3, 75	0.29	0.26			
Group					3.56	1.13	0.37*
Pittsburgh Sleep Quality Index					−0.85	0.31	−0.31*
Epworth Sleepiness Scale					0.34	0.25	0.15

β—standardized beta coefficient; B—beta coefficient; SE B—standard error of B

* $p < 0.01$

ing sleepiness and lack of energy) on the PSQI than the comparison group. Because a valid and reliable measure of trait sleepiness was used, the study was able to describe the magnitude of subjective daytime sleepiness in the sample.

Study findings suggested the possibility that sleep-disordered breathing may be a problem in the lung cancer population. Sleep-disordered breathing refers to a wide spectrum of sleep-related breathing abnormalities. Although obstructive sleep apnea is the most commonly reported form of sleep-disordered breathing, the American Academy of Sleep Medicine (2005) has identified other classifications, including central sleep apneas and sleep-related hypoventilation or hypoxemic syndromes. The premise that patients with lung cancer may be at risk for sleep-disordered breathing was based on several factors, including (a) the pattern of sleep-wake disturbances reported by patients with lung cancer in the study, (b) the disease-related threat for respiratory instability in patients with lung cancer, and (c) the normal alterations in respiration that occur during sleep.

First, the features of nocturnal sleep reported by the group with lung cancer included a longer sleep latency and lower sleep efficiency. The pattern of reported sleep disturbances included breathing difficulty, cough, nocturia, and frequent awakenings. During the diurnal period, participants with lung cancer reported significant daytime sleepiness and related daytime dysfunction. Although the symptoms may be caused by multiple factors, they are consistent with the clinical presentation of patients with sleep-disordered breathing (White, 2005).

Second, respiratory function may be compromised in patients with lung cancer as a result of both tumor- and treatment-related effects (Dudgeon, 2002; Kraut & Wozniak, 2000). Breathing is controlled by influences to the respiratory center, including chemical inputs from chemoreceptors responding to changes in oxygen, carbon dioxide, and pH levels; by mechanoreceptors in the airway, lungs, and chest wall; and by behavioral input from higher cortical centers (Caruana-Montaldo, Gleeson, & Zwillich, 2000). Respiratory control contributes significantly to maintaining homeostasis of blood gases so that metabolic functions remain normal. In patients with lung cancer, the disease process (parenchymal or pleural tumor, pleural effusion, adenopathy, airway obstruction) may result in decreased lung function and increased respiratory load (Dudgeon). Indirect sequelae of the disease and treatment such as weakness, anemia, and chemotherapy- or radiotherapy-induced lung dysfunction also render patients susceptible to additional restrictive or obstructive ventilatory deficits (Abratt & Morgan, 2002; Dudgeon; Maas et al., 2003; Miller et al., 2003).

Third, sleep is associated with a number of effects on respiration, including changes in central respiratory control, airway resistance, and muscular contractility (Morrell & Dempsey, 2002). Loss of consciousness during sleep is accompanied by a reduction in efferent neural activity to upper airway and respiratory pump muscles, leading to decreases in inspiratory muscle force and increases in resistance to airflow. This results in mild hypoventilation with small increases in $PaCO_2$ and decreases in PaO_2. Although carbon dioxide homeostasis provides the major respiratory drive during sleep, the respiratory center exhibits decreased responsiveness to hypoxia and hypercapnia. The net effect of these changes is a decreased respiratory drive compared with wakefulness. The effects are most pronounced during rapid eye movement sleep because of loss of tonic activity in the pharyngeal, laryngeal, and intercostal muscles. While awake, patients with lung cancer may be able to compensate for ventilatory deficits. However, sleep-related changes in respiratory mechanics that place additional demands on respiratory control mechanisms are clinically important for patients with lung cancer because they may elicit marked hypoxia and hypercapnia during sleep. In turn, hypercapnia, especially in the presence of hypoxia, produces an arousal from sleep (Douglas, 2005). Patients with frequent arousals may subjectively experience unrefreshing or poor quality of sleep or may complain of sleep maintenance insomnia (Flemmons & Whitelaw, 2002). Therefore, the possibility exists that patients with lung cancer at risk for compromised respiratory function caused by disease and treatment factors have an additional risk for compromised ventilation during sleep, leading to frequent awakenings, nocturnal cough, and perceived breathing difficulty. The hypothesis warrants further investigation because known interventions to stabilize breathing during sleep may provide one avenue for improving sleep quality in this population.

The marked differences between the group with lung cancer and the comparison group in QOL measures suggested that physical as well as mental aspects of QOL were significantly affected by the cancer experience. In addition to the impact of disease, nocturnal sleep-wake disturbances were significantly associated with perceived QOL. In the sample, poor nocturnal sleep quality was specifically associated with decreases in QOL related to mental health. The findings are consistent with other research that identified sleep disruption as a distressing component of the cancer experience in conjunction with well-being, functioning, and QOL (Cimprich, 1999; Davidson et al., 2002; Degner & Sloan, 1995; Redecker, Lev, & Ruggiero, 2000; Sarna, 1993). However, because of the cross-sectional design of the study, determining whether mental health state contributed to nocturnal sleep disturbance or whether sleep disturbance precipitated decreases in mental health is impossible.

This was the first study to assess the impact of daytime sleepiness on health-related QOL in patients with lung cancer. Daytime sleepiness was found to be prevalent and was significantly associated with poorer perceived QOL related to physical health. The findings suggest that daytime sleepiness may be a contributing factor of daytime dysfunction in patients with cancer, which is consistent with other research describing the negative impact of daytime sleepiness in a broad range of functional impairments in other clinical populations (Baldwin et al., 2001; Engleman & Douglas, 2004; Gooneratne et al., 2003; Parker, Bliwise, & Rye, 1999). However, decreases in physical health also may precipitate daytime sleepiness by interfering with normal circadian activity-rest patterns.

Limitations

The present study has several limitations. A convenience sample was enrolled, which limits the generalizability of the findings. Also, the data were based on subjective reports of the quality and quantity of sleep and daytime sleepiness. Although self-reports provide an understanding of an individual's perceptions of a phenomenon, they often do not reflect objective physiologic measures. Therefore,

the report of habitual sleep parameters and sleep-wake disturbances may be under- or overestimated. The cross-sectional survey design did not provide data about the course of sleep disruption or daytime sleepiness over time or in relation to temporal events (e.g., chemotherapy days). Although the data were analyzed for associations between sleep-wake disturbances and QOL, no causal or temporal associations among variables could be identified. In addition, although valid and reliable instruments were used to assess sleep-wake disturbances, evaluation is limited to the predetermined items assessed by the instruments. For example, the PSQI includes factors commonly reported to disturb nocturnal sleep. Patients with lung cancer may have numerous additional factors not assessed in the study that may contribute to disturbed sleep. Finally, because multiple comparisons using the same data set were made, the chance of type I error increased.

Implications

The general findings of the current study have implications for research and practice. The overwhelming occurrence of subjectively reported sleep-wake disturbances in the sample suggests that further research is needed to examine the nature of sleep-wake disturbances through objective as well as subjective measures. The data are necessary to increase the understanding of sleep in the lung cancer population by investigation of the prevalence of known sleep disorders, such as sleep-disordered breathing, and by identification of additional disease or treatment factors operative in patients with lung cancer that may alter sleep regulatory mechanisms. Delivery of effective interventions to promote nocturnal sleep and daytime alertness and, thus, enhance QOL in this population depends on the knowledge base.

The data reinforce the importance of ongoing assessment of nocturnal sleep and daytime sleepiness in patients with cancer in several ways. The prevalence and severity of nocturnal sleep disruptions reported by the sample emphasize the magnitude of the problem. However, on the one item on the PSQI that asks respondents to rate the overall quality of their sleep, the group with lung cancer did not rate their sleep any differently than the comparison group. This implies that nurses cannot rely on a single question to assess for sleep-wake disturbances in patients with cancer. A more comprehensive approach that includes assessment of nocturnal sleep patterns and associated behaviors, including precipitating and alleviating factors, is needed. Secondly, the prevalence of significant daytime sleepiness in the sample supports the importance of including the level of daytime sleepiness in any comprehensive evaluation for sleep-wake disturbances. Furthermore, evaluation of daytime sleepiness in conjunction with daytime function is warranted.

Nurses can be prepared to respond to the assessments by being familiar with common sleep disorders. Any indication of a primary sleep disorder warrants referral to a sleep specialist. However, poor sleep practices can complicate any disease or treatment factors that precipitate sleep-wake disturbances (Zarcone, 2000). Poor sleep habits tolerated in a healthy state may be less tolerated in the disease state. Therefore, nurses must consider evaluation of patient sleep habits and promotion of behaviors that enhance process S and process C as a first step in any plan to improve sleep and rest. Resources are available to assist nurses in developing skills in assessing and promoting sleep and rest. The American Academy of Sleep Medicine has two educational Web sites: www.sleepeducation.com and a site specifically for healthcare professionals at www.aasmnet.org/MedSleep_Resources.aspx (look under specific authors; topics written specifically for nurses are listed under Christian Guilleminault). Another helpful Web site is maintained by the National Sleep Foundation (www.sleepfoundation.org).

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