

The Effects of Pain, Gender, and Age on Sleep/Wake and Circadian Rhythm Parameters in Oncology Patients at the Initiation of Radiation Therapy

David Buffum,^{*} Theresa Koetters,^{*} Maria Cho,^{*} Liz Macera,^{*} Steven M. Paul,^{*} Claudia West,^{*} Bradley Aouizerat,^{*} Laura Dunn,[†] Marilyn Dodd,^{*} Kathryn Lee,^{*} Bruce Cooper,^{*} William Wara,[‡] Patrick Swift,[§] and Christine Miaskowski^{*}

^{*}School of Nursing, University of California, San Francisco, California.

[†]School of Medicine, University of California, San Francisco, California.

[‡]Kaiser Permanente, San Francisco, California.

[§]Alta Bates Comprehensive Cancer Center, Berkeley, California.

Abstract: To date, no studies have evaluated for differences in subjective and objective measures of sleep disturbance in oncology outpatients with and without pain. This descriptive study, recruited 182 patients from 2 radiation therapy (RT) departments at the time of the patient's simulation visit. Approximately 38% of the sample reported moderate to severe pain (ie, worst pain intensity of 6.2 ± 2.4). After controlling for age, patients in pain reported worse sleep quality and more sleep disturbance using the Pittsburgh Sleep Quality Index. With the General Sleep Disturbance Scale, patients in pain reported poorer sleep quality, increased use of sleep medications, and more daytime sleepiness. In addition using an objective measure of sleep disturbance (ie, actigraphy), significant gender \times pain interactions were found for sleep onset latency, percentage of time awake at night, wake duration, total sleep time, and sleep efficiency. While no differences were found in female patients, males in pain had worse scores than males without pain. Findings from this study suggest that pain and sleep disturbance are prevalent in oncology outpatients and that a patient's age and gender need to be considered in any evaluation of the relationship between pain and sleep.

Perspective: The effects of pain on subjective and objective sleep parameters appear to be influenced by both patients' age and gender.

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Key words: Pain, cancer, sleep disturbance, sleep, wakefulness, gender, insomnia, circadian rhythm, radiation therapy, actigraphy.

Pain occurs in 50% of oncology outpatients and has negative effects on patients' mood, functional status, and quality of life (QOL).^{16,45} More recent evidence suggests that sleep disturbance occurs in 33%

to 40% of oncology outpatients, twice the prevalence rate of sleep problems in the general population.^{7,22,59} A poor night's sleep can decrease daytime wakefulness, cognition, functional ability, and QOL,^{19,46} and, while controversial, may result in decreased survival.^{36,56}

Given the high prevalence of both pain and sleep disturbance, the co-occurrence of these 2 symptoms should not be surprising. However, only 6 studies have evaluated the impact of pain on sleep disturbances in oncology patients.^{5,29,44,46,53,57} In a prospective study of 1,635 patients with primarily gastrointestinal and genitourinary cancers referred to a pain clinic,²⁹ 59% of patients experienced both insomnia and pain. In a cross-sectional study of 91 outpatients with pain from lung and colon cancer,⁵⁷ 56% reported sleep disturbances from their pain. In a third study of 22 oncology outpatients receiving radiation therapy (RT) for painful bone metastasis,⁴⁶ patients reported moderate levels of

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Address reprint requests to: Christine Miaskowski, RN, PhD, FAAN, Professor and Associate Dean for Academic Affairs, Sharon A. Lamb Endowed Chair, American Cancer Society Clinical Research Professor, Department of Physiological Nursing, University of California, 2 Koret Way – Box 0610, San Francisco, CA 94143-0610. E-mail: chris.miaskowski@nursing.ucsf.edu

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pain and had a mean sleep efficiency of only 70.7%. In a cross-sectional study of 84 patients with a variety of cancer diagnoses that evaluated whether sleep disturbance mediates the effects of pain on fatigue, Beck et al⁵ found that pain influenced fatigue directly as well as indirectly by its effects on sleep. The authors concluded that patients who are in pain experience sleep disturbance and report more fatigue. In a longitudinal study of 93 women with metastatic breast cancer,⁵³ increases in pain over a 12-month period were associated with increased levels of sleep disturbance. Finally, in a study of 85 outpatients with cancer pain,⁴⁴ over 60% reported sleep disturbance. In addition, pain's level of interference with sleep measured by the Brief Pain Inventory (BPI) was positively correlated with both sleep disturbance intensity and distress.

While findings are inconsistent across primarily population based studies, 2 demographic characteristics that may influence subjective and objective evaluations of sleep disturbance are age (for reviews, see^{1,51}) and gender (for reviews, see^{20,37,55}). As noted by Neikrug and Ancoli-Israel,⁵¹ older adults complain more about sleep disturbance. However, while studies have found that over 50% of older adults complain of chronic insomnia, chronic sleep disturbances are primarily associated with poorer health and chronic comorbid conditions in the elderly. In studies that excluded individuals with comorbid conditions, disturbed sleep was a rare occurrence in healthy, older adults. In terms of gender differences in sleep disturbance, a number of reviews noted that when measured objectively, healthy women appear to have better sleep quality than men. However, women of all age groups report more sleep problems including inadequate sleep time and insomnia than men.^{20,37,55}

Taken together, findings from the 6 studies cited above^{5,29,44,46,53,57} suggest that cancer pain is associated with sleep disturbance. However, the majority of these studies are limited by relatively small sample sizes and the use of single items to assess sleep disturbance. To date, no study has compared differences in subjective and objective sleep disturbance parameters between oncology patients with and without pain. Given the paucity of research on the effects of pain on sleep in oncology patients, the purposes of this study were to determine, after controlling for age and gender, if there were differences in subjective reports of sleep disturbance and objective reports of nocturnal sleep/rest, daytime wake/activity, and circadian activity rhythm parameters between oncology patients with and without pain at the initiation of radiation therapy (RT).

Methods

Patients and Settings

This descriptive, correlational study is part of a larger, longitudinal study that evaluated multiple symptoms in patients who underwent primary or adjuvant RT.^{3,23,47} Patients were recruited from 2 RT departments located in a Comprehensive Cancer Center and a community-

based oncology program at the time of the patient's simulation visit.

Patients were eligible to participate if they: were ≥ 18 years of age; were scheduled to receive primary or adjuvant RT for 1 of 4 cancer diagnoses (ie, breast, prostate, lung, brain); were able to read, write, and understand English; gave written informed consent; and had a Karnofsky Performance Status (KPS) score of ≥ 60 . Patients were excluded if they had: metastatic disease; more than 1 cancer diagnosis; or a diagnosed sleep disorder.

Instruments

The study instruments included a demographic questionnaire, the KPS scale,³⁵ the Pittsburgh Sleep Quality Index (PSQI),^{13,15} and the General Sleep Disturbance Scale (GSDS).³⁸ Pain was evaluated using a modified version of the Brief Pain Inventory (BPI).²¹ Objective data on sleep-wake circadian activity rhythms were obtained by continuous noninvasive monitoring of activity over 48 hours using a wrist motion sensor (Mini Motionlogger Actigraph; Ambulatory Monitoring, Inc., Ardsley, NY).^{2,12,50} A minimum of 36 hours of continuous data is necessary to have sufficient data to calculate circadian activity rhythm parameters for a 24-hour period length.¹⁰

The demographic questionnaire obtained information on age, gender, marital status, education, ethnicity, employment status, children at home, living alone, and the presence of a number of comorbid conditions. Patient's functional status was assessed using the KPS scale which ranges from 30 (I feel severely disabled and need to be hospitalized) to 100 (I feel normal; I have no complaints or symptoms). The KPS has well established validity and reliability.^{34,35}

Multiple dimensions of pain were evaluated using a modified version of the BPI.²¹ Patients who responded yes to the question of having pain other than every day kinds of pain were asked to rate its intensity (ie, now, average, worst, and least), in the past week, using 0 (no pain) to 10 (pain as intense as you can imagine) numeric rating scales (NRSs).³³ In addition, patients were asked to complete a body map of pain locations, to indicate the number of hours per day and days per week that they were in significant pain, the amount of pain relief they were experiencing (0% = no relief to 100% = complete relief), and to rate pain's level of interference with function (0 = does not interfere to 10 = completely interferes).

The PSQI consists of 19 items designed to assess the quality of sleep in the past month. The global PSQI score is the sum of the 7 component scores (ie, subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, daytime dysfunction). Each component score ranges from 0 to 3 and the global PSQI score ranges from 0 to 21. Higher global and component scores indicate more severe complaints and a higher level of sleep disturbance. A global PSQI score of >5 provides a sensitive and specific measure of poor sleep quality.¹⁵ A cutoff score of 8 was found to discriminate poor sleep quality in oncology patients.¹⁷ The PSQI has established internal

Table 1. Definitions of Sleep/Wake, Activity/Rest, and Circadian Rhythm Parameters Obtained with Actigraphy

VARIABLE	DEFINITION
Sleep onset latency (SOL)	Number of minutes between when someone lays down to sleep and actually goes to sleep (measure of sleep initiation)
Percent wake at night	Percentage of time awake after sleep onset during a sleep period (measure of sleep maintenance)
Number of awakenings	Total number of awakenings during a sleep period
Wake duration	Number of minutes per awakening
Total sleep time	Total sleep time while in bed; number of minutes of sleep while in bed
Sleep period time	Total number of minutes in bed
Sleep efficiency (SE)	The number of minutes of sleep divided by the total number of minutes in bed, multiplied by 100
Total sleep time/day	Number of minutes asleep during the day from 9:00 to 20:59
Total wake time/day	Number of minutes awake during the day from 9:00 to 20:59
Sleep percent of day	Percentage of time asleep during the day from 9:00 to 20:59
Wake percent of day	Percentage of time awake during the day from 9:00 to 20:59
Mesor	24 hour rhythm adjusted mean of activity counts; higher values represent more robust activity
Amplitude	Peak (or trough) value of the cosine curve minus the mesor; represents the rhythmic change of an individual activity during the 24-hour period
Peak activity	Sum of the mesor and amplitude values; it represents more robust circadian activity rhythms
Acrophase	Actual clock time of the peak amplitude
Circadian quotient	Strength of the circadian rhythm, calculated by dividing the amplitude by the mesor
Autocorrelation	Comparison of the regularity and consistency of the rhythm from one day to the next day

consistency, test-retest reliability, and construct validity.^{6,15,17} In this study, the Cronbach's alpha for the global PSQI score was .72.

The GSIDS consists of 21 items designed to assess the quality of sleep in the past week. Each item was rated on a 0 (never) to 7 (everyday) NRS. The GSIDS total score is the sum of the 7 subscale scores (ie, quality of sleep, quantity of sleep, sleep onset latency, midsleep awakenings, early awakenings, medications for sleep, excessive daytime sleepiness) that can range from 0 (*no disturbance*) to 147 (*extreme sleep disturbance*). Each mean subscale score can range from 0 to 7. Because each of the GSIDS items are rated on a scale of 0 (never) to 7 (everyday), the subscale scores provide an estimation of the number of days per week that a patient experiences a particular problem. Higher total and subscale scores indicated higher levels of sleep disturbance. Subscale mean scores of ≥ 3 and a GSIDS total score of ≥ 43 indicate a significant level of sleep disturbance.²⁶ The GSIDS has well-established validity and reliability in shift workers, pregnant women, and patients with cancer and HIV.³⁸⁻⁴¹ In the current study, the Cronbach's alpha for the GSIDS total score was .84.

Objective data on sleep-wake circadian activity rhythms were obtained by continuous noninvasive monitoring of activity over 48 hours using wrist actigraphy (Ambulatory Monitoring Inc, Ardsley, NY). Seven nocturnal sleep/rest, 4 daytime wake/activity, and 6 circadian activity rhythm parameters were selected that were identified by a National Cancer Institute sponsored conference,⁹ an expert panel that recommended a standard set of research assessments in insomnia,¹⁴ and recently published studies.^{8,11} The definitions for each of these parameters are listed in Table 1.

Wrist actigraphy is validated with EEG measures of sleep and awakenings in men and women with both healthy and disturbed sleep patterns.^{2,14} It provides

continuous motion data using a battery-operated wristwatch-size microprocessor that senses motion with a piezo-electric beam and detects movement in all 3 axes. The accompanying Action 4® software (Ambulatory Monitoring Inc, Ardsley, NY) allows analysis of activity and nonactivity as well as automatic scoring of sleep and wake in 1-minute intervals.

Patients were asked to use the event marker on the wrist actigraph to indicate "lights out" and "lights on" time. Patients reported no difficulties wearing the wrist actigraph. Since the actual time is important in the calculation of the amount of sleep obtained in the amount of time designated for sleep, having an additional source of information about nap times, bed times, and wake times is important. This information was recorded by patients in a 2-day diary. Upon awakening, the patients used the diary to indicate the number of awakenings during the night.

Study Procedures

The study was approved by the Committee on Human Research at the University of California, San Francisco and at the second site. At the time of the simulation visit (ie, approximately 1 week prior to the initiation of RT), patients were approached by a research nurse to discuss participation in the study. After obtaining written informed consent, patients completed the demographic questionnaire, KPS scale,³⁵ BPI,²¹ PSQI,¹⁵ and GSIDS,³⁸ and height and weight were obtained. Medical records were reviewed for disease and treatment information.

In addition, patients wore the wrist actigraph to monitor sleep and activity continuously for 2 consecutive days and nights. They completed the 2-day diary that included sleep and wake times, naps, meal times, and level of physical activity during the day. Patients were asked to return the questionnaires and actigraphs to the research

Table 2. Differences in Demographic and Clinical Characteristics Between Oncology Patients With (n = 69) and Without Pain (n = 113)

CHARACTERISTIC	PAIN MEAN (SD)	NO PAIN MEAN (SD)	STATISTICS (t test, P VALUE)
Age (years)	58.1 (12.6)	61.8 (11.5)	t = -2.06, P = .041
Education (years)	16.1 (2.8)	16.0 (3.0)	t = .17, P = .867
Karnofsky Performance Status score	87.1 (12.6)	92.8 (10.6)	t = -3.20, P = .002
Weight (pounds)	183.3 (46.8)	179.1 (36.2)	t = .64, P = .527
Number of comorbidities	5.8 (2.2)	4.2 (2.5)	t = 4.20, P < .0001
Time since diagnosis (months)	5.9 (6.2)	7.3 (10.9)	t = -1.00, P = .320
	%	%	Fisher's Exact Test P value
Gender			
Female	60.9	39.8	.006
Male	39.1	60.2	
Lives alone			
Yes	26.1	31.9	.504
No	73.9	68.1	
Ethnicity			
White	71.6	72.6	1.00
Non-White	28.4	27.4	
Marital status			
Married/partnered	50.7	60.7	.214
Other	49.3	39.3	
Employed			
Yes	37.9	49.1	.162
No	62.1	50.9	
Have children at home			
Yes	21.3	16.2	.409
No	78.7	83.8	
Diagnosis			
Breast cancer	55.2	33.7	$\chi^2 = 14.30$, P = .003
Prostate cancer	30.4	54.0	
Brain cancer	4.3	8.8	
Lung cancer	10.1	3.5	

nurse in the RT department at the completion of the 2 days of data collection.

Data Analysis

Data were analyzed using SPSS v.18 (SPSS Inc, Chicago, IL). Descriptive statistics and frequency distributions were generated for the sample characteristics and symptom data. Actigraphy files, programmed in zero-crossing mode with 30-second intervals, were analyzed using the Cole-Kripke algorithm in the Action 4® software (Ambulatory Monitoring Inc, Ardsley, NY) by 2 of the researchers (KL and CW). The file was first scanned for missing data. If more than 4 hours of day data or 2 hours of night data were missing, that day's or night's data were not used in the analyses. Time limits were set for the 48-hour period. The file was reviewed and intervals

were individually set for each day and night period using, in order of priority as decision guides: the event marker, diary data, channel data, and cascading movement data. Cosinor analysis fit a cosine and sine wave to the wrist actigraphy data using a least-squares cosinor regression model to determine circadian activity rhythms. The mesor (24-hour adjusted mean value or y-intercept), amplitude, and acrophase (time of day for peak activity) were the circadian activity rhythm parameters obtained from the regression model.⁴² The auto-correlation coefficient for a 24-hour rhythm was obtained from the Action 4® software program.

Based on the patient's response to the question about having pain other than every day kinds of pain, patients were categorized into pain (n = 69) and no pain (n = 113) groups. Independent sample t tests and Chi square or Fisher's Exact test analyses were used to evaluate for differences in demographic and clinical characteristics between patients with and without pain. Based on these initial analyses of demographic characteristics, significant age and gender differences were found between the two groups. Because of reported age^{28,52} and gender^{32,37,54} differences in sleep disturbance, age (as a continuous variable) was entered as a covariate and gender (a dichotomous variable) was entered as a fixed factor in the univariate analysis of variance that evaluated for differences in subjective and objective sleep parameters between patients with and without pain. In addition, gender × pain group interactions were evaluated.

All calculations used actual values. Adjustments were not made for missing data or for multiple testing.⁵⁸ Therefore, the cohort for each analysis was dependent on the largest set of available data across groups. A P value of < .05 is considered statistically significant.

Results

Differences in Demographic and Clinical Characteristics Between Patients With and Without Pain

As shown in Table 2, no differences were found between the 2 pain groups in most demographic or clinical characteristics except age, gender, KPS scores, number of comorbidities, and diagnoses. Patients in pain were significantly younger (P = .041), more likely to be female (P = .006), have a lower KPS score (P = .002), and a higher number of comorbidities (P < .0001). In terms of cancer diagnosis, post hoc contrasts demonstrated that the pain group had a larger proportion of breast cancer patients than the no pain group (55.2 versus 33.7%, P = .005) and the no pain group had a larger proportion of prostate cancer patients than the pain group (54.0 versus 30.4%, P = .003).

Pain Characteristics

The pain characteristics of the patients are summarized in Table 3. At the time of the simulation visit, approximately 38% of the sample (n = 69) reported pain. In terms of causes of pain, 34.3% of the patients attributed their pain to their cancer or its treatment, 49.3% to another

Table 3. Pain Characteristics (n = 69)

CHARACTERISTIC	MEAN (SD)
Pain intensity (0–10)	
Pain now	2.5 (2.5)
Average pain	3.4 (1.9)
Worst pain	6.2 (2.4)
Least pain	1.3 (1.4)
Hours per day in significant pain	7.1 (8.0)
Days per week in significant pain	3.3 (3.0)
Number of pain locations	6.1 (5.8)
Percentage of pain relief (%)	56.9 (31.3)
Pain interference (0–10)	
General activity	3.1 (3.0)
Mood	2.8 (2.7)
Walking ability	3.4 (3.3)
Normal work	4.0 (2.9)
Relations with other people	1.9 (2.6)
Sleep	3.7 (3.1)
Enjoyment of life	3.6 (3.1)
Sexual activity	2.4 (3.4)
Total interference score	3.1 (2.3)

Abbreviation: SD, standard deviation.

medical condition, and 16.4% to both their cancer and another medical condition. The mean worst pain intensity score was 6.2 (SD = 2.4). The mean pain relief score from the current analgesic regimen was 56.9% (SD = 31.3) and the mean total pain interference score was 3.1 (SD = 2.3). On average, patients checked 6.1 (SD = 5.8) painful locations on the body map. The most common painful sites (ie, frequency >30%) were the calf, thigh, low back, chest, upper arm, and shoulder.

Differences in Subjective Reports of Sleep Disturbance Between Patients With and Without Pain

Table 4 summarizes the differences in PSQI and GSDS scores between patients with and without pain. In terms of PSQI subscale and total scores, after controlling for age, only daytime dysfunction exhibited a significant pain group \times gender interaction. Simple effect contrasts demonstrated that while no differences in daytime dysfunction scores were found between females who did and did not experience pain, males in pain reported significantly higher daytime dysfunction scores than males without pain. Significant main effects of pain group were found for the PSQI subscales of quality and disturbance, as well as the global PSQI score with patients in pain reporting higher scores than patients without pain. In addition, significant main effects of gender (the gender means are not reported in Tables) were found for the PSQI subscales of latency (1.22 [standard error (SE) = .10] versus .85 [SE = .11]), use of sleep medications (1.04 [SE = .13] versus .56 [SE = .14]), and global PSQI score (7.54 [SE = .41] versus 6.17 [SD = .43]), with females reporting higher scores than males.

In terms of GSDS subscale and total scores, after controlling for age, no significant pain group \times gender interactions were found. Significant main effects of

pain group were found for the GSDS subscales of quality, medications, and daytime sleepiness, as well as the total GSDS score with patients in pain reporting higher scores than patients without pain. In addition, a significant main effect of gender was found for the GSDS subscale of onset latency (2.20 [SE = .23] versus 1.32 [SE = .24]), with females reporting higher scores than males.

Differences in Objective Reports of Nocturnal Sleep/Rest, Daytime Wake/Activity, and Circadian Activity Rhythm Parameters Between Patients With and Without Pain

Table 5 summarizes the differences in nocturnal sleep/rest, daytime wake/activity, and circadian activity rhythm parameters between patients with and without pain. In terms of the sleep/wake parameters, after controlling for age, sleep onset latency, percent awake at night, wake duration, total sleep time, and sleep efficiency exhibited significant pain group \times gender interactions. Simple effect contrasts demonstrated that while no differences in any of these sleep/wake parameters were found between females who did and did not experience pain, males in pain reported significantly worse scores than males without pain. Significant main effects of gender were found for sleep period time (498.34 [SE = 8.51] versus 471.88 [SE = 8.71]) with females having better scores than males.

After controlling for age, no significant interaction or main effects were found for any wake/activity parameters or circadian activity rhythm parameters. Significant main effects of pain group were found for the mesor with patients in pain having a higher mesor than patients without pain.

Discussion

This study is the first to evaluate the effects of cancer pain on sleep disturbance in a relatively large sample of oncology outpatients using both subjective and objective measures of sleep/wake and circadian rhythm parameters. While both groups of patients experienced significant amounts of sleep disturbance, findings from this study suggest that in addition to pain, age and gender are important patient characteristics that need to be considered in any evaluation of sleep disturbance in oncology patients.

Main Effects of Pain

While no studies have used both the PSQI or GSDS to evaluate subjective ratings of sleep disturbance in oncology patients with pain, consistent with previous reports,^{29,44,46,53,57} patients with pain reported significantly higher levels of sleep disturbance (ie, higher global PSQI and total GSDS scores) than patients without pain. For both subjective measures, the mean total scores were above the cutpoints for clinically significant levels of sleep disturbance.^{15,17,26} In addition, the global PSQI scores for patients with and without pain were

Table 4. Differences in Subjective Sleep Measures Between Oncology Patients With (n = 69) and Without (n = 113) Pain

PITTSBURGH SLEEP QUALITY INDEX																
PARAMETER	AGE		GENDER		PAIN GROUP		GROUP × GENDER		NO PAIN* N = 113	PAIN* N = 68	NO PAIN MALES* N = 68	PAIN MALES* N = 27	CONTRAST P	NO PAIN FEMALES* N = 45	PAIN FEMALES* N = 41	CONTRAST P
	F	P	F	P	F	P	F	P								
Quality	4.20	.04	.36	.55	5.90	.02	.23	.63	.88 ± .07	1.15 ± .09	.94 ± .09	1.17 ± .14	NS	.81 ± .11	1.14 ± .12	NS
Latency	8.66	.004	5.35	.02	2.35	.13	.54	.46	.93 ± .09	1.14 ± .11	.80 ± .11	.91 ± .17	NS	1.06 ± .14	1.38 ± .15	NS
Duration	3.95	.048	.04	.84	.50	.48	.05	.82	.92 ± .09	1.03 ± .12	.96 ± .12	1.03 ± .18	NS	.89 ± .14	1.03 ± .15	NS
Sleep efficiency	.17	.69	2.70	.10	.30	.58	.23	.64	.66 ± .09	.74 ± .12	.55 ± .13	.56 ± .19	NS	.76 ± .15	.92 ± .16	NS
Disturbance	.03	.87	3.66	.06	19.5	<.001	.01	.93	1.31 ± .05	1.68 ± .07	1.22 ± .07	1.59 ± .10	NS	1.40 ± .08	1.76 ± .09	NS
Use of sleep meds	.38	.54	5.51	.02	3.69	.06	.34	.56	.62 ± .11	.97 ± .14	.33 ± .15	.78 ± .23	NS	.91 ± .18	1.16 ± .19	NS
Daytime dysfunction	1.89	.17	1.62	.20	3.48	.06	6.02	.02	.79 ± .06	.98 ± .08	.58 ± .09	1.03 ± .13	.004	.99 ± .10	.928 ± .11	.68
Global score	2.62	.11	4.75	.03	7.92	.005	.02	.90	6.07 ± .34	7.64 ± .44	5.35 ± .45	6.99 ± .69	NS	6.79 ± .54	8.29 ± .58	NS
GENERAL SLEEP DISTURBANCE SCALE																
Quality	8.41	.004	.07	.80	4.46	.04	.06	.81	2.24 ± .18	2.86 ± .23	2.16 ± .24	2.85 ± .37	NS	2.32 ± .29	2.86 ± .30	NS
Quantity	1.86	.17	1.45	.23	3.75	.06	1.05	.31	4.28 ± .12	4.65 ± .15	4.05 ± .16	4.62 ± .24	NS	4.51 ± .19	4.68 ± .20	NS
Onset latency	3.75	.06	6.15	.01	3.44	.07	.80	.37	1.47 ± .19	2.05 ± .25	1.18 ± .25	1.47 ± .39	NS	1.77 ± .30	2.63 ± .33	NS
Mid-sleep awakenings	.97	.33	.01	.91	2.57	.11	.36	.55	4.42 ± .25	5.06 ± .32	4.32 ± .33	5.20 ± .50	NS	4.51 ± .40	4.91 ± .42	NS
Early awakenings	1.41	.24	1.55	.22	.96	.33	.18	.67	2.31 ± .22	2.66 ± .28	2.14 ± .29	2.34 ± .44	NS	2.50 ± .35	2.98 ± .37	NS
Medications	.03	.87	.28	.60	7.22	.008	.53	.47	.24 ± .06	.48 ± .07	.18 ± .07	.49 ± .12	NS	.30 ± .09	.48 ± .10	NS
Daytime sleepiness	.13	.72	2.82	.10	5.07	.03	1.57	.21	1.77 ± .13	2.24 ± .17	1.44 ± .17	2.17 ± .26	NS	2.10 ± .21	2.31 ± .22	NS
Total score	2.10	.15	2.15	.14	9.57	.002	.93	.34	37.20 ± 1.79	46.27 ± 2.32	33.37 ± 2.39	45.25 ± 3.65	NS	41.04 ± 2.86	47.30 ± 3.07	NS

Abbreviation: NS, not significant.

*Values are age-adjusted means ± standard errors of the mean.

Table 5. Differences in Nocturnal Sleep/Rest, Daytime Wake/Activity, and Circadian Activity Rhythm Parameters Between Oncology Patients With (n = 69) and Without (n = 113) Pain

NOCTURNAL SLEEP/REST																
PARAMETER	AGE		GENDER		PAIN GROUP		GROUP × GENDER		No PAIN* N = 107	PAIN* N = 63	No PAIN MALES* N = 65	PAIN MALES* N = 25	CONTRAST P	No PAIN FEMALES* N = 42	PAIN FEMALES* N = 38	CONTRAST P
	F	P	F	P	F	P	F	P								
Sleep onset latency	0.42	.52	4.02	.047	7.43	.007	4.46	.04	13.46 ± 2.25	23.54 ± 2.93	13.82 ± 3.00	31.71 ± 4.65	.01	13.10 ± 3.65	15.37 ± 3.90	.39
% wake at night	.01	.95	17.76	<.001	11.57	.001	10.50	.001	12.36 ± 1.15	18.78 ± 1.50	13.88 ± 1.53	26.40 ± 2.37	<.001	10.85 ± 1.86	11.16 ± 1.99	.89
Number of awakenings	4.47	.04	.12	.73	.71	.40	2.6	.11	16.76 ± .83	15.61 ± 1.08	18.13 ± 1.11	14.78 ± 1.72	NS	15.38 ± 1.35	16.44 ± 1.44	NS
Wake duration	3.53	.06	13.63	<.001	11.50	.001	11.80	.001	3.44 ± .51	6.26 ± .66	3.77 ± .67	9.45 ± 1.05	<.001	3.10 ± .82	3.06 ± .88	.99
Total sleep time (TST)	1.76	.19	18.53	<.001	5.68	.02	7.55	.007	406.47 ± 7.85	375.74 ± 10.23	392.27 ± 10.45	326.13 ± 16.21	.002	420.66 ± 12.71	425.35 ± 13.61	.78
Sleep period time	4.58	.03	4.15	.04	.04	.84	.56	.46	483.99 ± 6.88	486.24 ± 8.97	474.98 ± 9.16	468.78 ± 14.21	NS	492.99 ± 11.14	503.69 ± 11.93	NS
Sleep efficiency	.00	.97	17.25	<.001	11.61	.001	8.64	.004	84.02 ± 1.25	77.02 ± 1.63	82.13 ± 1.67	69.09 ± 2.58	.001	85.91 ± 2.03	84.94 ± 2.17	.64
DAYTIME WAKE/ACTIVITY																
TST (day)	.25	.62	.05	.82	.52	.47	2.42	.12	53.69 ± 9.77	42.39 ± 12.20	67.92 ± 13.05	32.34 ± 19.19	NS	39.47 ± 16.09	52.44 ± 16.54	NS
Total wake time (day)	.25	.62	.05	.82	.52	.47	2.42	.12	666.31 ± 9.77	677.61 ± 12.20	652.09 ± 13.05	687.66 ± 19.19	NS	680.53 ± 16.09	667.56 ± 16.54	NS
Sleep percent (day)	.25	.62	.05	.82	.52	.47	2.42	.12	7.46 ± 1.36	5.89 ± 1.69	9.43 ± 1.81	4.49 ± 2.66	NS	5.48 ± 2.24	7.28 ± 2.30	NS
Wake percent (day)	.25	.62	.05	.82	.52	.47	2.42	.12	92.54 ± 1.36	94.11 ± 1.69	90.57 ± 1.81	95.51 ± 2.66	NS	94.52 ± 2.24	92.72 ± 2.30	NS

Abbreviation: NS, not significant.

*Values are age adjusted means ± standard errors of the mean.

comparable to those reported for patients receiving cancer chemotherapy.^{4,6}

An evaluation of disturbances in various sleep parameters in the past month using the PSQI found that patients in pain reported worse sleep quality and higher levels of sleep disturbance than pain-free patients. Using a 1-week recall with the GSDS, poorer sleep quality was confirmed and more frequent use of sleep medications and higher levels of daytime sleepiness were identified in the pain group. These findings suggest that pain has negative effects on specific subjective sleep parameters. Because the individual GSDS items are rated on a scale of 0 (never) to 7 (everyday), the subscale scores provide an estimation of the number of days per week that a patient experiences a particular problem. An examination of each of the GSDS subscale scores suggests that these oncology patients with pain experienced disturbances in most of the sleep parameters on 2 to 5 days per week.

An examination of the effects of pain on nocturnal sleep/rest parameters demonstrated its deleterious effects on every parameter except number of awakenings and the amount of time patients spent in bed. As with the subjective measures, for both patients with and without pain, all of the nocturnal sleep/rest parameters were worse than healthy adult values.^{8,18}

Pain Group \times Gender Interactions

A number of significant pain group \times gender interactions were found for both subjective and objective sleep parameters. Of note, while no differences were found between female patients with and without pain, male patients with pain reported significantly higher levels of daytime dysfunction, as well as significantly longer sleep onset latency, a higher percentage of time awake at night, a longer duration of time for each awakening, and less sleep time per night. On average, men in pain slept 5.4 hours per night compared to 6.5 hours for men not in pain. The high levels of sleep disturbance in both groups of men may be partially explained by the high percentage of patients with prostate cancer as compared to lung and brain cancer in the sample. In a small number of studies, men with prostate cancer reported significant amounts of sleep disturbances as a result of urinary frequency problems and hot flashes associated with hormonal therapy.^{24,25,31,60} Findings from this study suggest that pain exacerbates the sleep disturbances of men with prostate cancer at the initiation of RT. These findings warrant confirmation in future studies.

Main Effects of Gender

A number of significant gender effects were found for both subjective and objective sleep parameters. Compared to male patients, females reported longer sleep onset latency, more frequent use of sleep medications, and higher global scores on the PSQI as well as longer sleep onset latency on the GSDS. These findings are consistent with previous reports that women's subjective ratings of sleep disturbance, including inadequate sleep time and insomnia, are higher than men's reports. In

addition, objective data on nocturnal sleep/rest parameters were consistent with previous studies^{13,65} in that female patients, regardless of pain status, spent more time in bed than male patients.

While additional research on gender differences in various sleep/wake parameters in cancer patients is warranted, 1 study of 80 newly diagnosed lung cancer patients found no relationships among gender, pain, fatigue, and insomnia.³⁰ In another study of 86 adults with insomnia and 86 healthy controls,⁶⁴ no significant gender differences were found in polysomnographic measures of sleep duration or sleep efficiency or in subjective estimates of sleep quality, using the PSQI. In contrast, findings from several studies suggest that complaints of insomnia are more frequent among women with peri- and post-menopausal symptoms^{48,49,63} and may be associated with higher rates of depression and anxiety.^{61,62} It is interesting to note, that the subjective and objective sleep parameters of men in pain were similar to those of women with and without pain. The impact of pain on gender differences in sleep disturbance warrants additional investigation in future studies.

Effects of Age

Consistent with large population-based studies,^{27,28} several subjective and objective sleep parameters were associated with age. Our study findings confirm that compared to younger adults, older adults reported less sleep disturbance, but had poorer sleep when the parameters are measured objectively using actigraphy or polysomnography. In this study, many of the self-reported PSQI and GSDS sleep scores were lower in the older patients (ie, better sleep quality, shorter sleep onset latency, longer sleep duration). Conversely, objective data revealed that increasing age was associated with more awakenings and a weaker 24-hour rhythm (ie, autocorrelation). However, these results need to be interpreted with caution, because while significant, the correlations were relatively modest (ie, .22 to -.33). While every parameter was not examined, a recent meta-analysis of objective sleep parameters in otherwise healthy individuals across the lifespan⁵² showed decreases in total sleep time and sleep efficiency particularly in persons over 60 years of age.

Several study limitations need to be acknowledged. While the sample size was relatively large, findings from this study warrant confirmation with a larger sample. Because the sample was primarily Caucasian, the findings from this study cannot be generalized to diverse racial or ethnic groups. In this study, actigraphy was measured for 48 hours rather than for at least the recommended 72 hours to minimize respondent burden in this sample of patients. Therefore, the circadian activity rhythm parameters warrant replication with larger samples who are evaluated for longer periods of time.^{12,43} Finally, while the number of comorbidities was different in the patients with and without pain, this variable was not included as a covariate in the analyses. Future studies

with larger samples need to evaluate the influence of comorbidities, in addition to age and gender, on sleep disturbances in oncology patients.

In summary, findings from this study suggest that cancer pain has deleterious effects on patients' subjective reports of sleep disturbances, as well as on most objective measures of nocturnal sleep/rest, daytime wake/activity, and circadian activity rhythm parameters at the initiation of RT. The use of actigraphy supplemented by subjective measures is practical and provides a useful estimate of sleep-wake and circadian activity rhythm disturbances. The results of this study suggest that the relationships between pain and sleep

disturbance are more complicated than simply saying that pain has negative effects on sleep. The effects of pain on sleep need to be examined within the context of age and gender. Future studies need to evaluate all of these parameters in larger samples of oncology patients. In addition, additional research is warranted to confirm the specific relationships between pain and sleep-wake disturbances; clarify the mechanisms by which sleep is disturbed; improve the consensus among research with standardization of measurement tools; and determine the best interventions that can be used to decrease pain and improve sleep in oncology patients.

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