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



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

by

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Abstract

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David G. Buffum

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 cross-sectional study, recruited 182 patients with mixed types of cancer from two radiation therapy (RT) departments at the time of the patient's simulation visit. Approximately 38% of the sample reported moderate to severe pain, with a mean worst pain intensity of 6.2 (SD = 2.4) on an 11-point scale. 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. 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, significant differences in objective reports of nocturnal sleep/rest, daytime wake/activity, and circadian activity rhythm parameters between pain groups were found. These data indicate that pain is prevalent among oncology outpatients and substantially impairs sleep. Further research is warranted to describe more completely the effects of age and gender in the context of pain and sleep disturbances in oncology outpatients prior to radiation therapy.

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## Introduction

Pain occurs in 50% of oncology outpatients and has negative effects on patients' mood, functional status, and quality of life (QOL) [14, 45, 46, 60]. More recent evidence suggests that sleep disturbance occurs in 33% to 57% of oncology outpatients, twice the prevalence rate of sleep problems in the general population [5, 20, 32, 63]. A poor night's sleep can decrease daytime wakefulness, cognition, functional ability, and QOL [17, 18, 47, 53, 61], and may result in decreased survival, although this is controversial [21, 37, 58].

Only five studies have evaluated the impact of pain on sleep disturbances in oncology patients [29, 44, 47, 56, 59]. In a prospective study of 1,635 patients primarily those with gastrointestinal and genitourinary cancers referred to a pain clinic [29], 59% of patients experienced both insomnia and pain. In a cross-sectional study of outpatients with pain from lung and colon cancer (n=91) [59], 56% reported sleep disturbances from their pain. In a third descriptive correlational study of oncology outpatients receiving radiation therapy (RT) for painful bone metastasis (n=22) [47], patients reported moderate levels of pain and had a mean sleep efficiency of only 70.7%. In a longitudinal study of 93 women with metastatic breast cancer [56], increases in pain over a 12 month period were associated with increased levels of sleep disturbance. In the most recent study of 85 outpatients with cancer pain, 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 [44].

Taken together, findings from these five studies [29, 44, 47, 56, 59] 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 cancer pain on sleep, the purpose of this study was to determine 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 patients with and without cancer pain at the initiation of radiation therapy (RT).

**Methods**

Participants and Settings - This descriptive, cross-sectional study is part of a larger, longitudinal study that evaluated multiple symptoms in patients who underwent primary or adjuvant RT (NR04835; [2, 24, 25, 48]). Patients were recruited from two 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 one of four cancer diagnoses (i.e., 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 one 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], and the General Sleep Disturbance Scale (GSDS) [39]. Pain was evaluated using an modified version of the Brief Pain Inventory (BPI) [19]. 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) [1, 9, 52]. Based on previous experience, 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.

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 co-morbid conditions.

The patients' performance status was assessed using the Karnofsky Performance Status (KPS) scale [35], which was rated by the research nurse using a 0 (i.e., dead) to 100 (i.e., normal activity) scale. The KPS has a satisfactory predictive and construct validity [11] and interrater reliability [51, 65].

Multiple dimensions of pain were evaluated using a modified version of the BPI [19]. Patients who responded yes to the question of having pain other than every day kinds of pain were asked to rate its intensity (i.e., now, average, worst, and least) using 0 (no pain) to 10 (pain as intense as you can imagine) numeric

rating scales (NRSs) [34]. In addition, patients were asked to complete a body map of pain locations, to indicate the number of hours per day 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 = interfere completely).

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 seven component scores (i.e., 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 indicates a significant level of sleep disturbance [13]. A cutoff score of 8 was found to discriminate poor sleep quality in oncology patients [15]. The PSQI has established internal consistency, test-retest reliability, and construct validity [4, 13, 15]. In this study, the Cronbach's alpha for the global PSQI score was 0.72.

The GSDS consists of 21-items designed to assess the quality of sleep in the past week. Each item measures the frequency of sleep disturbance and was rated on a 0 (*never*) to 7 (*everyday*) NRS. The GSDS total score is the sum of the seven subscale scores (i.e., quality of sleep, quantity of sleep, sleep onset latency, mid-sleep 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.

Higher total and subscale scores indicated higher levels of sleep disturbance. Subscales scores of $\geq 3$ and a GSDS total score of $\geq 43$ indicates a significant level of sleep disturbance [25]. The GSDS has well-established validity and reliability in shift workers, pregnant women, and patients with cancer and HIV [39, 40, 47]. In the current study, the Cronbach's alpha for the GSDS total score was 0.84.

Objective data on sleep-wake circadian activity rhythms were obtained by continuous noninvasive monitoring of activity over 48 hours using wrist actigraphy. Seven nocturnal sleep/rest, four daytime wake/activity, and six circadian activity rhythm parameters were selected that were identified by a National Cancer Institute sponsored conference [7], an expert panel that recommended a standard set of research assessments in insomnia [12], and recently published studies [6, 8]. Wrist actigraphy is validated with EEG measures of sleep and awakenings in men and women with both healthy and disturbed sleep patterns [1, 12, 52]. 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 three axes. The accompanying Action 4® software (Ambulatory Monitoring Inc., Ardsley, NY) allows analysis of activity and non-activity as well as automatic scoring of sleep and wake in one minute intervals.

Patients were asked to use the event marker on the wrist actigraph to indicate "lights out" (when going to sleep/sleep onset) and "lights on" (when get up/wake up) 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 two 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 (i.e., approximately one 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], PSQI [13], and GSDS [39] 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 two consecutive days and nights. They completed the two 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 nurse in the RT department at the completion of the two days of data collection.

Data Analysis - Data were analyzed using SPSS version 15. 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 two of the researchers (KL and CW). The file was first scanned for missing data. If more than four hours of day data or two hours of night data were missing, that day's or night's data were not used in the analyses (based on previous experience). 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 [41]. 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 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 previously reported age [27, 55] and gender [33, 38] 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. This analysis evaluated differences in subjective and objective sleep parameters between patients with and without pain. In addition, gender x pain group interactions were evaluated.

All calculations used actual values. Adjustments were not made for missing data. Therefore, the cohort for each analysis was dependent on the largest set of available data across groups. A p-value of $<0.05$ are considered statistically significant.

**Results**

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

As shown in Table 1, no differences were found between the two pain groups in any 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 a significantly larger proportion of patients with breast cancer (55.2%) had pain compared to patients with prostate cancer (30.4%, $p = .003$).

*Pain Characteristics*

The pain characteristics of the patients are summarized in Table 2. At the time of the simulation visit, approximately 38% of the sample reported pain. Patients reported moderate to severe pain, with a mean worst pain intensity of 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 (i.e., 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 3 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 and gender, only daytime dysfunction exhibited a significant pain group x 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 (not reported in Tables) were found for the PSQI subscales of latency (1.22 (SD = .10) versus .85 (SD =.11)), use of sleep medications (1.04 (SD = .13) versus .56 (SD = .14)), and global PSQI score (7.54 (SD = .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 and gender, no significant pain group x 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 (SD = .23) versus 1.32 (SD =.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 4 and Table 5 summarize 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 and gender, sleep onset latency, percent awake at night, wake duration, total sleep time, and sleep efficiency exhibited a significant pain group x gender interaction. 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 and gender, no significant interaction or main effects were found for any wake/activity parameters or circadian activity rhythm

parameters. Significant main effects of pain 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 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 Group*

While no studies have used the PSQI or GSDS to evaluate subjective ratings of sleep disturbance in patients with cancer pain, consistent with previous reports [29, 44, 47, 56, 59], patients with cancer pain reported significantly higher levels of sleep disturbance (i.e., higher global PSQI and total GSDS scores) than patients without pain. For both subjective measures, the total scores were above the cutpoints for clinically significant levels of sleep disturbance in the patients with cancer pain [13, 15, 25]. In addition, the global PSQI scores for patients with and without pain were comparable to those reported for patients receiving cancer chemotherapy [3, 4].

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 one-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. While these findings suggest that cancer pain has negative effects on specific subjective sleep parameters, an examination of the GSDS subscale scores suggests that patients with cancer pain experienced disturbances in most of the sleep parameters on two to five days per week (i.e., subscale scores of ≥ 3).

An examination of the effects of cancer pain on nocturnal sleep/rest parameters demonstrated the deleterious effects of pain 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 [16, 28, 71].

*Pain Group X Gender Interactions*

A number of significant pain group x 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 6.54 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. A small number of studies found that men with prostate cancer reported significant amounts of sleep disturbances as a result of urinary frequency problems and hot flashes associated with hormonal therapy [22, 23, 31, 42, 54, 64, 69]. 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, consistent with previous studies [10, 72], using the objective data on nocturnal sleep/rest parameters, female patients, regardless of pain status, had greater sleep period times than male patients. While additional studies on gender differences in various sleep/wake parameters in cancer patients are warranted, one study of 80 newly diagnosed lung cancer patients found no relationships among gender, pain, fatigue, and insomnia [30]. In another study of 86 insomniacs and 86 healthy controls [70], no significant gender differences were found in objective measures of sleep continuity (i.e., sleep duration, sleep efficiency, arousal index, and percentage of time awake at

night) by polysomnography, as well as 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 [49, 50, 68] and may also be associated with higher rates of depression and anxiety [36, 62, 67].

*Main Effects of Age*

Consistent with large population-based studies [26, 27, 57, 66], 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 have poorer sleep when the parameters are measured objectively using actigraphy or polysomnography. In this study, as age increased, many of the self-reported PSQI and GSDS sleep scores decreased (i.e., better sleep quality, shorter sleep onset latency, longer sleep duration). Conversely, objective data revealed that increasing age was associated with increased number of awakenings and decreased autocorrelation. However, these results need to be interpreted with caution, because while significant, the correlations were relatively modest (i.e., .22 to -.33). While every parameter was not examined, a recent meta-analysis of objective sleep parameters in otherwise healthy individuals across the lifespan [55] showed decreases in total sleep time and sleep efficiency particularly in persons aged 60 years and older.

Several study limitations need to be acknowledged. The sample size was relatively large. Therefore, the findings from this study warrant confirmation with larger samples. Because the sample was primarily Caucasian, the findings from

this study cannot be generalized to diverse racial or ethnic groups. In this study, before RT, actigraphy was measured for 48 hours. This duration was used because it was thought the patients would not tolerate longer times due to their medical condition. Therefore, the circadian activity rhythm parameters warrant replication with larger samples who are evaluated for longer periods of time [9, 43].

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 it is more complicated than simply saying that pain had negative effects on sleep. Rather the effects of pain on sleep must be considered 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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Table 1. Differences in demographic and clinical characteristics between oncology patients with (n=69) and without pain (n=113)

| Characteristic | Pain<br>Mean (SD) | No pain<br>Mean (SD) | Statistics<br>(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 = -.10, 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 | |
| Marrital 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 | |
| Prostate cancer | 30.4 | 54.0 | $\chi^2 = 14.30$, **p = .003** |
| Brain cancer | 4.3 | 8.8 | |
| Lung cancer | 10.1 | 3.5 | |

Table 2. Pain Characteristics (n=67)

| 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) |
| 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) |

Table 3 Differences in subjective sleep measures between oncology patients with and without pain

| Parameter | Age | | Gender | | Pain Group | | Group x Gender | | No Pain* | Pain* | No Pain Males* | Pain Males* | Contrast p | No Pain Females* | Pain Females* | Contrast p |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | p | F | p | F | p | F | p | N = 113 | N = 68 | N = 68 | N = 27 | | N = 45 | N=41 | |
| **Pittsburgh Sleep Quality Index** | | | | | | | | | | | | | | | | |
| Quality | 4.20 | **.04** | 0.36 | .55 | 5.90 | **.02** | 0.23 | .63 | 0.88 ± .07 | 1.15 ± .09 | 0.94 ± .09 | 1.17 ± .14 | NS | 0.81 ± .11 | 1.14 ± .12 | NS |
| Latency | 8.66 | **.004** | 5.35 | **.02** | 2.35 | .13 | 0.54 | .46 | 0.93 ± .09 | 1.14 ± .11 | 0.80 ± .11 | 0.91 ± .17 | NS | 1.06 ± .14 | 1.38 ± .15 | NS |
| Duration | 3.95 | **.048** | 0.04 | .84 | 0.50 | .48 | 0.05 | .82 | 0.92 ± .09 | 1.03 ± .12 | 0.96 ± .12 | 1.03 ± .18 | NS | 0.89 ± .14 | 1.03 ± .15 | NS |
| Sleep efficiency | 0.17 | .69 | 2.70 | .10 | 0.30 | .58 | 0.23 | .64 | 0.66 ± .09 | 0.74 ± .12 | 0.55 ± .13 | 0.56 ± .19 | NS | 0.76 ± .15 | 0.92 ± .16 | NS |
| Disturbance | 0.03 | .87 | 3.66 | .06 | 19.5 | **<.01** | 0.01 | .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 | 0.38 | .54 | 5.51 | **.02** | 3.69 | .06 | 0.34 | .56 | 0.62 ± .11 | 0.97 ± .14 | .328 ± .15 | 0.78 ± .23 | NS | 0.91 ± .18 | 1.16 ± .19 | NS |
| Daytime dysfunction | 1.89 | .17 | 1.62 | .20 | 3.48 | .06 | 6.02 | **.02** | 0.79 ± .06 | 0.98 ± .08 | 0.58 ± .09 | 1.03 ± .13 | .004 | 0.99 ± .10 | .928 ± .11 | .68 |
| Global score | 2.62 | .11 | 4.75 | **.03** | 7.92 | **.005** | 0.02 | .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** | 0.07 | .80 | 4.46 | **.04** | 0.06 | .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 | 0.80 | .37 | 1.47 ± .19 | 2.05 ± .25 | 1.18 ± .25 | 1.47 ± .39 | NS | 1.77 ± .30 | 2.63 ± .33 | NS |
| Mid-sleep awakenings | 0.97 | .33 | 0.01 | .91 | 2.57 | .11 | 0.36 | .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 | 0.96 | .33 | 0.18 | .67 | 2.31 ± .22 | 2.66 ± .28 | 2.14 ± .29 | 2.34 ± .44 | NS | 2.50 ± .35 | 2.98 ± .37 | NS |
| Medications | 0.03 | .87 | 0.28 | .60 | 7.22 | **.008** | 0.53 | .47 | 0.24 ± .06 | 0.48 ± .07 | 0.18 ± .07 | 0.49 ± .12 | NS | 0.30 ± .09 | 0.48 ± .10 | NS |
| Daytime sleepiness | 0.13 | .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** | 0.93 | .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 |

* Values are means ± standard errors of the mean

Table 4 - Differences in nocturnal sleep/rest and daytime wake/activity parameters between oncology patients with and without pain

| Nocturnal Sleep/Rest | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parameter | Age | | Gender | | Pain Group | | Group x Gender | | No Pain* | Pain* | No Pain Males* | Pain Males* | Contrast p | No Pain Females* | Pain Females* | Contrast p |
| | F | p | F | p | F | p | F | p | N = 107 | N = 63 | N = 65 | N = 25 | | N = 42 | N = 38 | |
| 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 | 0.01 | .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** | 0.12 | .73 | 0.71 | .40 | 2.6 | .11 | 16.76 ± 0.83 | 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 ± 0.51 | 6.26 ± 0.66 | 3.77 ± 0.67 | 9.45 ± 1.05 | <.001 | 3.10 ± 0.82 | 3.06 ± 0.88 | .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** | 0.04 | .84 | 0.56 | .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 | 0.00 | .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) | 0.25 | .62 | 0.05 | .82 | 0.52 | .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) | 0.25 | .62 | 0.05 | .82 | 0.52 | .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) | 0.25 | .62 | 0.05 | .82 | 0.52 | .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) | 0.25 | .62 | 0.05 | .82 | 0.52 | .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 |

* Values are means ± standard errors of the mean

Table 5 - Differences in circadian activity rhythm parameters between oncology patients with and without pain

| Circadian Activity Rhythm | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parameter | Age | | Gender | | Pain Group | | Group x Gender | | No Pain* | Pain* | No Pain Males* | Pain Males* | Contrast p | No Pain Females* | Pain Females* | Contrast p |
| | F | p | F | p | F | p | F | p | N = 107 | N = 63 | N = 65 | N = 25 | | N = 42 | N = 38 | |
| Mesor | 2.37 | .13 | 1.43 | .23 | 3.98 | **.049** | 1.13 | .29 | 63.72 ± 1.48 | 68.53 ± 1.91 | 64.10 ± 1.88 | 71.48 ± 3.17 | NS | 63.34 ± 2.44 | 65.58 ± 2.39 | NS |
| Amplitude | 1.75 | .19 | 0.12 | .73 | 0.12 | .73 | 0.17 | .68 | 49.56 ± 1.38 | 50.34 ± 1.79 | 48.64 ± 1.76 | 50.34 ± 2.97 | NS | 50.49 ± 2.28 | 50.33 ± 2.24 | NS |
| Peak activity | 2.58 | .11 | 0.25 | .62 | 1.78 | .19 | 0.70 | .41 | 113.28 ± 2.56 | 118.87 ± 3.31 | 112.74 ± 3.25 | 121.82 ± 5.49 | NS | 113.83 ± 4.22 | 115.91 ± 4.14 | NS |
| Acrophase | 2.79 | .10 | 0.00 | .10 | 1.06 | .31 | 1.33 | .25 | 14:57 ± 18.14 | 14:87 ± 23.49 | 14:40 ± 23.07 | 15:05 ± 38.97 | NS | 14:74 ± 29.98 | 14:70 ± 29.39 | NS |
| Circadian quotient | 0.00 | .96 | 3.25 | .07 | 2.09 | .15 | 0.26 | .61 | 0.78 ± 0.02 | 0.74 ± 0.02 | 0.76 ± 0.02 | 0.71 ± 0.04 | NS | 0.81 ± 0.03 | 0.78 ± 0.03 | NS |
| Auto-correlation | 6.26 | **.01** | 0.13 | .72 | 0.08 | .78 | 0.01 | .94 | 0.46 ± 0.02 | 0.47 ± 0.03 | 0.45 ± 0.03 | 0.47 ± 0.05 | NS | 0.47 ± 0.04 | 0.48 ± 0.04 | NS |

* Values are means ± standard errors of the mean

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