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Subjective and Objective Measures of Sleep Quality in Advanced Cancer: A Possible Clinical Marker for Depression

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Abstract

Purpose: It is estimated that between 30 and 75% of patients with cancer experience depression, poor nocturnal sleep, and daytime sleepiness. Research designed to specifically examine associations of depression with subjective and objective sleep measures is lacking. Thus the purpose of these analyses was to compare relationships among depression, subjective and polysomnographic measures of sleep.

Methods: Secondary data analysis design was used to assess sleep quality, and self-rated depression of patients with advanced cancer recruited from a university-based medical system. Responses to the Beck Depression Inventory-II (BDI-II), Pittsburgh Sleep Questionnaire Index (PSQI), and the Epworth Sleepiness Scale (ESS), and polysomnography data were analyzed using descriptive, correlation, and regression statistics.

Results: A total of 114 patients with advanced cancer completed the study. PSQI and ESS scores were positively correlated with BDI-II scores. Total nocturnal sleep time and a prolonged REM latency were also positively related to BDI-II scores. When controlling for selected demographic and clinical features, the relationships between polysomnographic variables and depression were no longer significant.

Conclusions: Depression was related to subjective sleep quality and daytime sleepiness suggesting that these problems occur together. In addition, higher levels of depression were associated with nocturnal sleep time and prolonged REM latency.

Keywords: Sleep quality; Pittsburgh Sleep Questionnaire Index; Epworth Sleepiness Scale; Depression, advanced cancer

Introduction

The relationship between sleep disturbances and depression is a well-recognized problem. It is estimated that 30% to 75% of patients with cancer will experience these symptoms during the course of the disease [1,2]. Sleep problems in particular have been associated with decreased quality of life and work productivity, fatigue, psychological distress, pain, impaired cognitive function, and disruptions in social interactions [3-8]. Poor sleep can also contribute to immunosuppression, which can have significant effects on the cancer process [9]. In advanced cancer populations problems with sleep have been linked to a person's desire for a hastened death, while depression has been found to be an independent predictor of early death [10,11].

Sleep disturbances in cancer patients are characterized by difficulty falling asleep, problems maintaining sleep, poor sleep efficiency, early awakening, and excessive daytime sleepiness [2,12,13]. It has been suggested that poor sleep in this population is associated with the biochemical changes occurring during neoplastic growth and the use of anticancer treatments [2,12,14]. Further research has shown that opioids used to treat cancer related pain can also affect a patients sleep quality and diurnal wakefulness [15,16]. Identified risk factors of sleep disturbances in individuals with cancer include: younger age, a general lack of energy, higher anxiety levels, and previous post-traumatic experience [17-19].

There is a distorted circadian rhythm in patients with advanced cancer, which was associated with complaints of poor sleep quality, fatigue, and insomnia [20]. Recent studies have shown that the more disrupted the daily sleep/wake circadian rhythm, the worse the depression [21,22]. Historically, sleep disturbances were viewed as a secondary condition that was caused by, or associated with, primary depression [23]. Current thinking suggests that these conditions have a bi-directional relation and can be considered comorbid disorders or symptom clusters [12,23-27].

The two-process model of sleep regulation has been widely used in both clinical practice and research of sleep in a variety of populations [28-30]. According to this model, there are two major processes that underlie sleep and waking, process S and process C. Process S, or the drive to sleep, is determined by prior sleep and waking and rises during wakefulness and declines during sleep. Slow wave sleep (EEG power - 0.75 to 4.5 Hz range) is a key indicator of process S. In depression, process S is deficient, which is reflected by a diminution of delta activity and slow wave sleep [31]. Sleep deprivation due to prolonged periods of wakefulness tends to enhance the deficiencies of process S associated with depression. Process C, or sleep propensity, determines the thresholds for sleep onset and termination, and is regulated by the master circadian oscillator, the suprachiasmatic nucleus (SCN). Depressed individuals experience a wide range of circadian rhythm disturbances, causing disruptions in process C, characterized by changes in sleep architecture, early morning waking and hypersomnia [32-34].

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Although sleep disturbances and depression are prevalent, these conditions are often underrecognized, and undermanaged in patients with advanced cancer [35]. Sleep disturbances in particular, can be assessed both objectively and subjectively, but the objective and subjective measurements do not always correlate [12,36]. Patients with advanced cancer frequently complained of poor sleep despite having good sleep efficiency revealed through actigraphy [37]. Objective measures of sleep are not frequently used in cancer research, as investigators tend to rely more on subjective screening tools [38,39]. Diagnosing depression in cancer can be just as challenging due to the number of somatic symptoms frequently attributed to the cancer itself or anticancer treatments [40-43]. However, a factor analysis study of an oncology sample conducted by Passik and colleagues found that diurnal variation and insomnia did not cluster with somatic symptoms of depression, suggesting that sleep-related symptoms might be a unique clinical marker [44]. Thus, the purpose of this study was to compare and contrast relationships among depression, subjective measures of nocturnal sleep and daytime sleepiness, and polysomnographic measures of nocturnal and diurnal sleep.

Methods

A descriptive, correlational design was used to conduct a secondary data analysis of data obtained from a larger study examining sleep/wake patterns in patients with advanced cancer. The institutional review board approved the study. The purpose of the larger study was to describe the sleep/wake patterns of patients with advanced cancer using continuous ambulatory polysomnography (PSG) and to explore relationships with selected demographic and clinical variables [13]. All participants underwent continuous ambulatory PSG over a 42-hour period of time in their home setting and completed a sleep diary in which day and night were determined by participant reported "lights on" and "lights off" [13].

Sample

Patients were eligible for the study if they (a) had a diagnosis of advanced solid tumor malignancy (stages III and IV); (b) had no significant history of neurological disorders, alcohol/substance abuse, previous sleep apnea, or cerebral metastasis; and (c) had a Karnofsky Performance Score (KPS) equal to, or greater than 50. Patients were excluded from the study is they (a) had a recent hospital discharge; or (b) were unable to schedule in-home PSG until at least 5 days subsequent to the most recent chemotherapy and/or radiotherapy or 1 week after hospitalization.

The sample included 114 well-characterized patients with advanced solid tumor cancer (mean age 55.2 ± 9.0 years; 49% female) screened from medical oncology clinics within a large university health care system. Table 1 shows the demographic features of the sample. The majority of the sample was diagnosed with lung cancer (31.6%) followed by breast cancer (28.9%). The mean KPS was 76.3 (± 11.0). About 89% of the participants had been treated with chemotherapy, while only 39.5% of the sample received radiotherapy treatment. The clinical features of the sample can be found in Table 2.

Measures

Demographic and clinical data, medications, and laboratory information were obtained from medical record screening by the project manager, a registered nurse, in the original study. Depression was measured using the self-administered Beck Depression Inventory-II (BDI-II) prior to the first 24 hours of PSG. The BDI-II is the revised version of the Beck Depression Inventory, which has been updated to correspond with diagnostic criteria of depressive episodes from the Diagnostic and Statistical Manual of Mental Disorders IV-TR [45,46]. The BDI-II is comprised of 21 items, each consisting of four self-evaluative statements describing the intensity of depression symptom severity. The scores for each rating on the 21 items are then summed to yield a total value ranging from 0 to 63. According to the BDI-II manual, a total values score can be interpreted as minimal (0 to 13), mild (14 to 19), moderate (20 to 28), and severe (29 to 63) depression [46].

Objective measurement of nocturnal and daytime sleep was obtained using PSG recordings (Embla Systems, Broomfield, CO)

Variable	*n*	%
Age	114	100.0
Mean 55.2 ± 9.0 years		
Range (33 – 73 years)		
Gender		
Male	58	50.9
Female	56	49.1
Race		
White/Caucasian	45	39.5
African American	64	56.1
Other	5	4.4
Marital Status		
Married	50	43.9
Unmarried	64	56.1
Living Situation		
Lives alone	21	18.4
Lives with other	93	86.1
Employment Status		
Employed	17	14.9
Not employed	97	85.2
Disabled	59	51.8
Education		
High school of less	49	43.0
Above high school	65	57.0

Table 1: Demographic Features of the Sample.

Variable	*n*	%
Diagnosis		
Breast	33	28.9
Colon	18	15.8
Head & neck	12	10.5
Lung	36	31.6
Other	33	28.9
ECOG Scores		
0	21	18.4
1	71	62.3
2	22	19.3
Chemotherapy		
No	13	11.4
Yes	101	88.6
Radiotherapy		
No	69	60.5
Yes	45	39.5
Surgery		
No	113	99.1
Yes	1	0.9
Opioids		
No	30	26.3
Yes	84	73.7
Antidepressants		
No	78	68.4
Yes	36	31.6
Steroids		
No	109	95.6
Yes	5	4.4
Sedative/Hypnotics		
No	93	81.6
Yes	21	18.4

Note. ECOG = Eastern Cooperative Oncology Group

Table 2: Clinical Features of the Sample.

over a continuous 42 hours period of time with all recordings starting before 1800 hours on their first night and ending between 1200 hours and 1400 hours the day after the second night. Subjective measure of sleep quality was obtained using participant recorded sleep diaries and the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a self-rated questionnaire, which assess sleep quality and disturbances over a one-month interval of time [47]. The questionnaire is comprised of nineteen individual items generating seven component scores (sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction), which are summed to yield one global score [47]. Subjective measure of daytime sleepiness was obtained using the Epworth Sleepiness Scale (ESS). The ESS is a self-administered questionnaire, which provides a measure of the subject's general level of daytime sleepiness [48]. Subjects are asked to rate their level of sleepiness on a scale of 0-3 in eight different proposed situations to be summed together to provide a total score over the whole range of daytime sleepiness [48]. Both the PSQI and ESS were self-administered prior to the first 24 hours of PSG. The details of the design and methods of the larger study have been published elsewhere [13].

Data Analysis

Descriptive statistics were used to summarize the data. There were no significant differences between nocturnal PSG variables for the first and second nights, so the data were pooled together. Nocturnal PSG measures calculated included: Total Sleep Time (TST); sleep efficiency; percentage of TST spent in stages 1,2,3, and 4, and Rapid Eye Movement Sleep (REM); latency to the first 60 seconds of continuous sleep; and the latency to the first epoch of REM sleep. Daytime PSG sleep measures calculated included: TST; percentage of time spent in sleep stages; and an index of awakenings lasting at least 60 seconds. Nonparametric analysis was used because most variables did not meet the assumptions of parametric procedures. The spearman rho (r_s) and partial (r_p) correlation procedures were used to detect significant relationships between BDI-II scores, and sample characteristics, subjective measures of nocturnal sleep and daytime sleepiness, and PSG measures of nocturnal and diurnal sleep. Although parametric assumptions were not met, according to the central limit theorem the sample size in this study permitted the use of hierarchical linear regression analyses to further explore the relationship between depression (BDI-II scores) and significantly correlated predictor variables. SPSS (SPSS Inc, Chicago, IL) was the statistical package used. The level of significance was set at $\alpha = 0.05$.

Results

Depression measures

The mean total score for the BDI-II (n = 114) was 13.0 ± 8.0 (SD). 60.5% of the participants scored in the minimal range (0-13), 22.8% scored in the mild range (14-19), 12.3% scored in the moderate range (20-28), and 4.4% scored in the severe range (29-63).

The relationship between various demographic, clinical characteristics and depression was examined using correlation statistics. The variable of age was found to have a significant correlation ($r_s = -0.23$; $p < 0.02$) with total BDI-II scores suggesting that younger age was associated with higher levels of depression. The analysis of the association between categorical variables and depression found that female patients reported significantly more depression ($r_s = 0.20$, $p < 0.05$) than male patients. When controlling for age and gender, patients taking opioid ($r_p = 0.21$, $p < 0.04$) and antidepressants ($r_p = 0.31$, $p < 0.01$) experienced statistically significantly more depression compared to those patients not taking these medications.

Nocturnal and daytime sleep/waking measures

The mean total score for the PSQI (n = 114) was 7.0 ± 3.3 (SD). The nocturnal PSG sleep measures appear in Table 3. The sample averaged approximately 6.4 hours of sleep per night. The majority of nocturnal sleep occurred in non-rapid eye movement (NREM) stage 2 (73.8%) followed by NREM stage 1 (10.9%). An absence of NREM stages 3 and 4 was noted in most participants. Nocturnal sleep latency was within normal limits (<30 minutes) but the REM latency was prolonged at 129.0 minutes ± 97.4 minutes, which is suggestive of nocturnal sleep fragmentation.

The mean total score for the ESS (n = 114) was 7.7 ± 4.3 (SD). The daytime PSG sleep measures appear in Table 4. During the daytime, participants slept on average 89.3 minutes ± 94.2 minutes. The majority of daytime sleep occurred in NREM stage 2 (59.9%) followed by NREM stage 3 (20.1%), while a minority of sleep occurred in REM (4.2%). An absence of NREM stages 3 and 4 was noted in all participants.

Nocturnal and daytime sleep/waking measures and depression

Table 5 shows the relationships between sleep measures with BDI-II. Increasing depression was positively correlated to worse subjective sleep quality ($r_s = 0.51$; $p < 0.01$) but not worse sleep efficiency as would be normally expected. Level of depression severity also was not an indicator of nocturnal sleep onset latency. Once participants fell asleep, those with higher levels of depression took longer time to reach first onset of REM sleep ($r_s = 0.23$; $p < 0.02$) but this relationship was no longer significant when controlling for antidepressant and opioid medication use. During the nocturnal sleep period, participants with higher levels of depression tended to have longer periods of total sleep time ($r_s = 0.19$; $p < 0.05$). Neither, the amount of time spent in different stages of nocturnal sleep nor the number of arousals occurring throughout the night were not found to be associated with level of

Variable	Mean (SD)	Normal*
	382.3(96.5)	340–466
Total Sleep Time (min)	29.7(41.7)	< 30
Sleep Latency (min) to first 60 seconds of sleep		
Sleep Efficiency (%) referred to sleep period	77.2(12.8)	86–100
NREM (%)		
Stage 1		
Stage 2	10.9(5.9)	3–12
Stage 3	73.8(8.4)	51–72
Stage 4	0.3(1.0)	0-17
REM (%)	0.0	0-17
REM Latency (min)	15.0(7.8)	17-25
Arousal Index (events/hour)	129.0(97.4)	65-104
	63.9(18.0)	Not available

Note. min = minutes; sec = seconds; REM = rapid eye movement; NREM = non-REM; * According to Williams et al., 1974

Table 3: Nocturnal Sleep Parameters (Two nights pooled).

Variable	Mean (SD)
Total Sleep Time (min)	89.3(94.2)
NREM (%)	
Stage 1	20.1(18.8)
Stage 2	59.9(30.4)
Stage 3	0.0
Stage 4	0.0
REM (%)	4.2(7.7)

Note. min = minutes; REM = rapid eye movement; NREM = non-REM

Table 4: Daytime Sleep Parameters.

Dependent: BDI-II	Spearman's	P-value
Total ESS score	0.23	0.02
Global PSQI score	0.51	0.00
Nocturnal Total Sleep Time (min)	0.19	0.05
Nocturnal REM Latency (min)	0.23	0.01

Note. BDI-II = Beck Depression Inventory-II; ESS = Epworth Sleepiness Scale; PSQI = Pittsburgh Sleep Questionnaire Index; min = minutes; REM = rapid eye movement

Table 5: Significant Correlations Between Sleep Variables with BDI-II.

depression severity. During the day, those participants with higher levels of depression reported higher levels of general daytime sleepiness ($r_s = 0.23$; $p < 0.03$). However, this relationship could not be confirmed through PSG as none of the daytime objective sleep measures were significantly correlated with the BDI-II.

In order to further examine the relationship between depression and sleep/wake measures, total BDI-II scores was hierarchically regressed with variables entered in three blocks. Significantly correlated demographic and clinical characteristics including age, gender, and use of antidepressant and opioid medications, were entered in the first block and accounted for 20.8% of the variance ($p < 0.01$). The subjective sleep measures, total PSQI and ESS scores, were entered in the second block and accounted for an additional 12.1% of the variance ($R^2 = 0.329$, $p < 0.01$). The objective sleep measures of nocturnal REM latency and average nocturnal total sleep time were entered in the third block and only accounted for 0.9% of the variance and was not significantly different from the second block. Overall the regression model accounted for 33.8% of the variance in depression but found that the selected polysomnographic sleep variables were not significant predictors of depression.

Discussion

The American Psychiatric Association has developed the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-V), with assistance of DSM-V sleep-wake nosology. The primary purpose of the DSM-V sleep-wake nosology is to improve the recognition of sleep disorders that are associated with other health conditions by incorporating quantitative physiologic measures (polysomnographic and neurobiologic) into the diagnostic classification system, and dimensional measures of severity [49]. This is the first study to our knowledge to employ both subjective and continuous PSG quantitative measures to examine the relationship between sleep/waking and depression in a sample of patients with cancer.

Similar to previous reports, the sleep/wake pattern in our sample was characterized by poor sleep maintenance, reduced quality of sleep, and difficulty with the ability to initiate and maintain sleep states [1,2,4-6,8,12,14-16,21,27,37,38]. Overall 39.5% of our sample reported mild to severe symptoms of depression, contrary to other studies that found a higher prevalence of depression symptoms [11,17].

Sleep disturbances are a common complaint for most depressed patients and belong to the core symptoms of depressive disorders [31]. Our study found that subjective complaints of poor sleep quality and excessive daytime sleepiness were significantly related to the severity of depression. Although this finding was congruent with previous results the measure of sleep disturbance cannot be encapsulated by subjective assessments alone [11,16,17,32,37]. Previous research examining both subjective and objective sleep measures using actigraphy in depressed patients with cancer have produced mixed results [12,36,37]. Similar to results reported by Gibbins and colleagues [37], our study found that depression was positively correlated to poor subjective sleep quality but was not correlated to the objective measure of sleep efficiency. However, our study did find that increased levels of depression were associated with longer periods of total nocturnal sleep time and a prolonged REM latency after sleep.

Although this study did not attempt to infer causal effects of sleep/wake variables on depression, the descriptive results obtained can be applied to the conceptual context of the two-process model of sleep regulation [28-30]. Process S refers to the homeostatic process of sleep regulation, which is a dependent function of prior sleep and waking duration. Process S was derived from studies examining slow wave sleep activity and reflects that the need for sleep builds throughout the day and dissipates during the night. Most participants in our study were unable to attain slow wave sleep activity. This result was expected, as patients with depression tend to have a diminution of slow wave sleep [31]. Though, it was surprising that the absence of time spent in slow wave sleep was not significantly correlated with the severity of depression. This observation might be explained by the potential confounding factors in the sample including medication use, age, and pain levels. Participant perception of excessive daytime sleepiness was significantly related to higher levels of depression. It is unclear whether daytime sleepiness is predictor of depression or whether it is the reverse. The lack of slow wave sleep can prevent the dissipation of sleep need and increase daytime sleep tendency. The relationship between the lack of slow wave sleep and severity of depression might have been mediated by daytime sleepiness.

Process C refers to the circadian process of sleep regulation, which determines the thresholds for sleep onset and termination, and is regulated by the SCN. REM sleep is markedly influenced by process C, as the incidence of REM sleep has been used as a phase indicator of circadian oscillation [28-30]. In normal sleep, there is a decreasing trend of REM sleep propensity during the daytime hours while during the night it is the reverse [30]. In our study, there was a small percentage of REM sleep that occurred during the day, which typically does not occur in healthy individuals. We also found that prolonged REM latency after sleep onset was correlated with higher levels of depression. This result is incongruent with previous psychobiological research that has shown that a shorter REM latency period is typically associated with depression [31]. This difference was probably related to the use of antidepressants, especially selective serotonin reuptake inhibitor medications, by many of the participants in our sample. It has also been generally assumed that total sleep time is determined to a large extent by circadian factors [29,30]. Although the mean total sleep time in this sample was noted to be within a normal range, it should be noted that participants with longer periods of nocturnal total sleep time had significantly higher levels of depression. This result was also probably related to the use of antidepressant and opioid medications in our sample.

The findings of this study suggest that the interaction between Process S and Process C is altered in advanced cancer patients with depression. The almost total absence of slow wave sleep and prolonged REM latency may have contributed to the poor sleep quality, and daytime sleepiness in the sample. This increase in daytime sleepiness and poor sleep quality suggest that the homeostatic need for sleep was not dissipated at night, and/or the circadian ability to decrease sleep propensity during the day and increase sleep propensity during the night was attenuated.

The question of which comes first, depression or sleep disturbance remains unknown. Healthcare professionals need to be aware of the

presence of symptom clusters when evaluating sleep and depression in patients with cancer [50]. Symptom clusters suggest that sleep disturbances might be part of multiple interrelated symptoms including depression, which have a synergistic adverse effect on quality of life [7,12,50]. A major limitation of this study was that the secondary data analysis design bounded our analyses to the variables collected by the original investigators. This restricted our ability to examine other variables usually found in cancer symptom clusters, which may have contributed to depression severity and/or sleep disturbances. The concept of depression was also restricted to a cross-sectional measure of the BDI-II, prohibiting the ability to draw inferences concerning subtypes or longitudinal course of depression in the sample. Our regression analysis suggests that younger age and poor subjective sleep quality were significant predictors of depression but we were unable to determine causal, mediating, or moderating relationships. Due to our relatively small sample size (n = 114) the use of path analysis or structural equation modeling techniques to further examine these relationships would not be appropriate. Future research using larger sample sizes is needed to estimate possible causal relations between the variables found in cancer symptom clusters. Research is also needed to determine if subjective sleep appraisals are predicted by certain psychological factors in patients with advanced cancer [51].

Conculsions

To our knowledge, the results of this exploratory study provide the first comprehensive description of the relationship between sleep/wake state and depression of patients with advanced cancer using both subjective and polysomnographic measures. The results suggest that subjective sleep quality and daytime sleepiness, increased total nocturnal sleep time, and prolonged REM latency have a profound impact on depression severity, highlighting the need for careful screening of both subjective and objective measures of sleep. The clinical significance of these results should be interpreted with caution due to confounding sample characteristics and further work is needed to identify the underlying mechanisms of sleep regulatory processes associated with depression in advanced cancer.

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References

1. Clark J, Cunningham M, McMillan S, Vena C, Parker K (2004) Sleep-wake disturbances in people with cancer part II: evaluating the evidence for clinical decision making. Oncol Nurs Forum 31: 747-771.
2. Lee K, Cho M, Miaskowski C, Dodd M (2004) Impaired sleep and rhythms in persons with cancer. Sleep Med Rev 8: 199-212.
3. Anderson KO, Getto CJ, Mendoza TR, Palmer SN, Wang XS, et al. (2003) Fatigue and sleep disturbance in patients with cancer, patients with clinical depression, and community-dwelling adults. J Pain Symptom Manage 25: 307-318.
4. Chen ML, Yu CT, Yang CH (2008) Sleep disturbances and quality of life in lung cancer patients undergoing chemotherapy. Lung Cancer 62: 391-400.
5. Dirksen SR, Epstein DR, Hoyt MA (2009) Insomnia, depression, and distress among outpatients with prostate cancer. Appl Nurs Res 22: 154-158.
6. Shuman AG, Duffy SA, Ronis DL, Garetz SL, McLean SA, et al. (2010) Predictors of poor sleep quality among head and neck cancer patients. Laryngoscope 120: 1166-1172.
7. Stepanski EJ, Walker MS, Schwartzberg LS, Blakely LJ, Ong JC, et al. (2009) The relation of trouble sleeping, depressed mood, pain, and fatigue in patients with cancer. J Clin Sleep Med 5: 132-136.
8. Vargas S, Wohlgemuth WK, Antoni MH, Lechner SC, Holley HA, et al. (2010) Sleep dysfunction and psychosocial adaptation among women undergoing treatment for non-metastatic breast cancer. Psychooncology 19: 669-673.
9. O'Donnell JF (2004) Insomnia in cancer patients. Clinical Cornerstone 6: S6-S14.
10. Lloyd-Williams M, Shiels C, Taylor F, Dennis M (2009) Depression--an independent predictor of early death in patients with advanced cancer. J Affect Disord 113: 127-132.
11. Mystakidou K, Parpa E, Tsilika E, Pathiaki M, Galanos A, et al. (2007) Depression, hopelessness, and sleep in cancer patients' desire for death. Int J Psychiatry Med 37: 201-211.
12. Berger AM, Parker KP, Young-McCaughan S, Mallory GA, Barsevick AM, et al. (2005) Sleep wake disturbances in people with cancer and their caregivers: state of the science. Oncol Nurs Forum 32: E98-126.
13. Parker KP, Bliwise DL, Ribeiro M, Jain SR, Vena CI, et al. (2008) Sleep/Wake patterns of individuals with advanced cancer measured by ambulatory polysomnography. J Clin Oncol 26: 2464-2472.
14. Roscoe JA, Kaufman ME, Matteson-Rusby SE, Palesh OG, Ryan JL, et al. (2007) Cancer-related fatigue and sleep disorders. Oncologist 12 Suppl 1: 35-42.
15. Mercadante S, Girelli D, Casuccio A (2004) Sleep disorders in advanced cancer patients: prevalence and factors associated. Support Care Cancer 12: 355-359.
16. Mystakidou K, Parpa E, Tsilika E, Pathiaki M, Patiraki E, et al. (2007) Sleep quality in advanced cancer patients. J Psychosom Res 62: 527-533.
17. Mystakidou K, Parpa E, Tsilika E, Gennatas C, Galanos A, et al. (2009) How is sleep quality affected by the psychological and symptom distress of advanced cancer patients? Palliat Med 23: 46-53.
18. Price MA, Zachariae R, Butow PN, deFazio A, Chauhan D, et al. (2009) Prevalence and predictors of insomnia in women with invasive ovarian cancer: anxiety a major factor. Eur J Cancer 45: 3262-3270.
19. Rogers LQ, Courneya KS, Robbins KT, Rao K, Malone J, et al. (2008) Factors associated with fatigue, sleep, and cognitive function among patients with head and neck cancer. Head Neck 30: 1310-1317.
20. Levin RD, Daehler MA, Grutsch JF, Quiton J, Lis CG, et al. (2005) Circadian function in patients with advanced non-small-cell lung cancer. Br J Cancer 93: 1202-1208.
21. Du-Quiton J, Wood PA, Burch JB, Grutsch, JF, Gupta D, et al. (2010). Actigraphic assessment of daily sleep-activity pattern abnormalities reflects self-assessed depression and anxiety in outpatients with advanced non-small cell lung cancer. Psycho-Oncology 19: 180-190.
22. Palesh OG, Collie K, Batiuchok D, Tilston J, Koopman C, et al. (2007) A longitudinal study of depression, pain, and stress as predictors of sleep disturbance among women with metastatic breast cancer. Biol Psychol 75: 37-44.
23. Weinberger T, Forrester A, Markov D, Chism K, Kunkel EJ (2010) Women at a dangerous intersection: diagnosis and treatment of depression and related disorders in patients with breast cancer. Psychiatr Clin North Am 33: 409-422.
24. Donovan KA, Jacobsen PB (2007) Fatigue, depression, and insomnia: evidence for a symptom cluster in cancer. Semin Oncol Nurs 23: 127-135.
25. Hoyt MA, Thomas KS, Epstein DR, Dirksen SR (2009) Coping style and sleep quality in men with cancer. Ann Behav Med 37: 88-93.
26. McMillan SC, Tofthagen C, Morgan MA (2008) Relationships among pain, sleep disturbances, and depressive symptoms in outpatients from a comprehensive cancer center. Oncol Nurs Forum 35: 603-611.
27. Sateia MJ, Lang BJ (2008) Sleep and cancer: recent developments. Curr Oncol Rep 10: 309-318.
28. Borbély AA (1982) A two process model of sleep regulation. Hum Neurobiol 1: 195-204.
29. Borbély AA, Achermann P (1999) Sleep homeostasis and models of sleep regulation. J Biol Rhythms 14: 557-568.
30. Daan S, Beersma DG, Borbély AA (1984) Timing of human sleep: recovery process gated by a circadian pacemaker. Am J Physiol 246: R161-183.
31. Riemann D, Berger M, Voderholzer U (2001) Sleep and depression--results from psychobiological studies: an overview. Biol Psychol 57: 67-103.

32. Boyce P, Barriball E (2010) Circadian rhythms and depression. Aust Fam Physician 39: 307-310.

33. Gorwood P (2010) Restoring circadian rhythms: a new way to successfully manage depression. J Psychopharmacol 24: 15-19.

34. Gouin JP, Connors J, Kiecolt-Glaser JK, Glaser R, Malarkey WB, et al. (2010) Altered expression of circadian rhythm genes among individuals with a history of depression. J Affect Disord 126: 161-166.

35. Palesh OG, Roscoe JA, Mustian KM, Roth T, Savard J, et al. (2010) Prevalence, demographics, and psychological associations of sleep disruption in patients with cancer: University of Rochester cancer center-community clinical oncology program. J Clin Oncol 28: 292-298.

36. Young-McCaughan S, Mays MZ, Arzola SM, Yoder LH, Dramig SA, et al. (2003) Research and commentary: Change in exercise tolerence, activity and sleep patterns, and quality of life in patients with cancer participating in a structured exercise program. Oncology Nursing Forum 30: 441-454.

37. Gibbins J, McCoubrie R, Kendrick AH, Senior-Smith G, Davies AN, et al. (2009) Sleep-wake disturbances in patients with advanced cancer and their family carers. J Pain Symptom Manage 38: 860-870.

38. Ancoli-Israel S, Moore PJ, Jones V (2001) The relationship between fatigue and sleep in cancer patients: a review. Eur J Cancer Care (Engl) 10: 245-255.

39. Passik SD, Whitcomb LA, Kirsh KL, Theobald DE (2003) An unsuccessful attempt to develop a single-item screen for insomnia in cancer patients. J Pain Symptom Manage 25: 284-287.

40. Akechi T, Nakano T, Akizuki N, Okamura M, Sakuma K, et al. (2003) Somatic symptoms for diagnosing major depression in cancer patients. Psychosomatics 44: 244-248.

41. Cathcart F (2006) Psychological distress in patients with advanced cancer. Clin Med 6: 148-150.

42. McDaniel JS, Musselman DL, Porter MR, Reed DA, Nemeroff CB (1995) Depression in patients with cancer. Diagnosis, biology, and treatment. Arch Gen Psychiatry 52: 89-99.

43. Rao A, Cohen HJ (2004) Symptom management in the elderly cancer patient: fatigue, pain, and depression. J Natl Cancer Inst Monogr : 150-157.

44. Passik SD, Lundberg JC, Rosenfeld B, Kirsh KL, Donaghy K, et al. (2000) Factor analysis of the Zung Self-Rating Depression Scale in a large ambulatory oncology sample. Psychosomatics 41: 121-127.

45. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders (4th ed.). Washington, DC.

46. Beck AT, Steer RA, Brown GK (1996) Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation.

47. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28: 193-213.

48. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14: 540-545.

49. Reynolds III CF, Redline S (2010) The DSM-V sleep-wake disorders nosology: An update and an invitation to the sleep community. J Clin Sleep Med 6: 9-10.

50. Dodd MJ, Miaskowski C, Paul SM (2001) Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum 28: 465-470.

51. Williams RL, Karacan I, Hursch CJ (1974). EEG of human sleep: Clinical applications. New York, NY: John Wiley & Sons.