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Edited by:

Sunil Sharma, MD, FAASM

Associate Professor of Medicine, Director, Pulmonary Sleep Medicine, Associate Director, Jefferson Sleep Disorders Center, Thomas Jefferson University and Hospitals, USA

Review Article

Incidence of Sleep Disturbance and Evaluation of Sleep Quality in Patients Diagnosed with Cancer

David P. Visco, MD; Michelle L. Niesley, ND, MS; Alyssa M. Hughes; Mark E. Lewis, MPH*

Eastern Regional Medical Center, Cancer Treatment Centers of America, 1331 E Wyoming Ave, Philadelphia, USA

***Corresponding author**

Mark Lewis, MPH, Eastern Regional Medical Center, Cancer Treatment Centers of America, 1331 E. Wyoming Ave, Philadelphia, PA 19124, USA, Tel: 1-215-537-7068; Fax: 1-215-537-7901; E-mail: Mark.Lewis@ctca-hope.com

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- Sleep quality, Cancer, Fatigue, Sleep disturbance, Screening

Abstract

Introduction: Sleep disorders affect 10-15% of the US population, which has significant implications for quality of life. Oncology patients often experience more prominent detrimental effects of sleep deprivation. Fatigue is one of the most debilitating symptoms, and occurs in 75% ofpatients with cancer.

Methods: Eastern Regional Medical Center implemented a process by which subjective and objective sleep screening assessment is standard practice for all patients new to the center. Patients were provided both a combined sleep questionnaire and an at-home sleep screen device. This device links the physiology of autonomic, respiratory, and mathematically captures electro cortical activity collectively referred to as cardiopulmonary coupling.

Results and Discussion: This retrospective review encompassed a total 1,207 new patients seen between March 2013 and April 2014. They were stratified into three populations having completed: subjective questionnaires, objective screening, and both measures. For the 242 patients who completed the subjective questionnaire, 65% were considered to have a likelihood of sleep disturbance, and 68% of patients reported feeling tired/fatigued/sleepy during the day. The objective screening notes 71% of patients had poor sleep quality. Interestingly for both measures, patients who had poor scores subjectively actually outperformed their counterparts on the objective sleep assessment.

Conclusion: The results of this study emphasize the importance of utilizing both subjective and objective assessments for sleep analysis. Assessing sleep with only one of these tools would not provide an accurate account of sleep disturbance. The ability to assess overall sleep quality, as well as low and high frequency coupling has proven valuable in determining further diagnostic testing or evaluations. The contradictions found between subjective, self-reported data and the objective data obtained through the Sleep Image® device suggest other factors may contribute to patients feeling sleep deprived or well rested.

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ABBREVIATIONS

PSG: Polysomnography; **EKG**: Electrocardiogram; **ERMC**: Eastern Regional Medical Center; **CPC**: Cardiopulmonary Coupling; **STOP BANG**: Snoring, Tiredness during daytime, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, Gender; **OSA**: obstructive sleep apnea; **SQI** sleep quality index; **HFC**: High Frequency Coupling; **LFC**: Low Frequency Coupling

INTRODUCTION

Dyssomnias, parasomnias, and a variety of other sleep disorders, as defined by the American Academy of Sleep Medicine's International Classification of Sleep Disorders, frequently affect quality of life in otherwise healthy populations [1]. The ill-effects of sleep deprivation are often more pronounced in oncology patients, and may become chronic problems both during and after standard oncology care. Sleep disturbances are typically unrecognized, under-reported, or overlooked in patients receiving cancer treatment due to other more problematic symptoms such as nausea, emesis, and pain. This can be attributed to the commonly held assumption that sleep disturbances 'normally' accompany a diagnosis of cancer and subsequent treatment [2-5]. It is estimated 33-50% of patients with cancer experience disturbed sleep triggered by pain, medications associated with their cancer treatment, or the psychological impact of the disease [6,7].

Fatigue in cancer patients is one of the most common disruptive symptoms not only during active cancer treatment, but well into survivorship. It negatively impacts their daily function and quality of life [8]. At the time of diagnosis, an estimated 75% of patients with cancer report having fatigue. This figure balloons to 96% in those who have received chemotherapy, and to 93% in patients who have received radiotherapy [9]. A patient's perception of their level of fatigue is multifactorial, and is influenced by daytime sleepiness. They often self-report poor sleep quality, short sleep duration, and insomnia [10].

Sleep is a required behavioral state and a natural part of life. An active yet reversible process, sleep is characterized by behavioral quiescence, as well as diminished responsiveness to external stimuli. It is regulated in the central nervous system by a complex interplay of neuronal pathways and neurotransmitters. This bimodal influence describes the interaction between naturally occurring homeostatic factors in the blood and the human circadian rhythm, to regulate the timing of sleep and wakefulness. The physiologic complexity, in conjunction with environmental and medical influences, raises grave concern as to the impact cancer can have on sleep. When assessed, patients with cancer are regularly found to have low sleep efficiency [11]. In a study by Ciccone et al., the duration of obstructive sleep apnea (OSA) was shown to contribute to the development of heart disease [12].

A person's sleep efficiency is calculated as the number of minutes of sleep divided by the total number of minutes spent in bed. A sleep efficiency of 85% or greater is considered normal. Clinically, sleep disturbances in patients with cancer may contribute to significant fatigue, decreased daytime productivity, and may affect overall response to treatment. The current understanding of excessive daytime sleepiness in cancer patients is largely based on subjective measures, such as the Epworth Sleepiness Scale. The "gold standard" objective assessment for underlying sleep disordered breathing is a diagnostic polysomnography (PSG). However, a PSG requires an overnight stay in a sleep lab, and is expensive and cumbersome to undergo for patients during active cancer treatment.

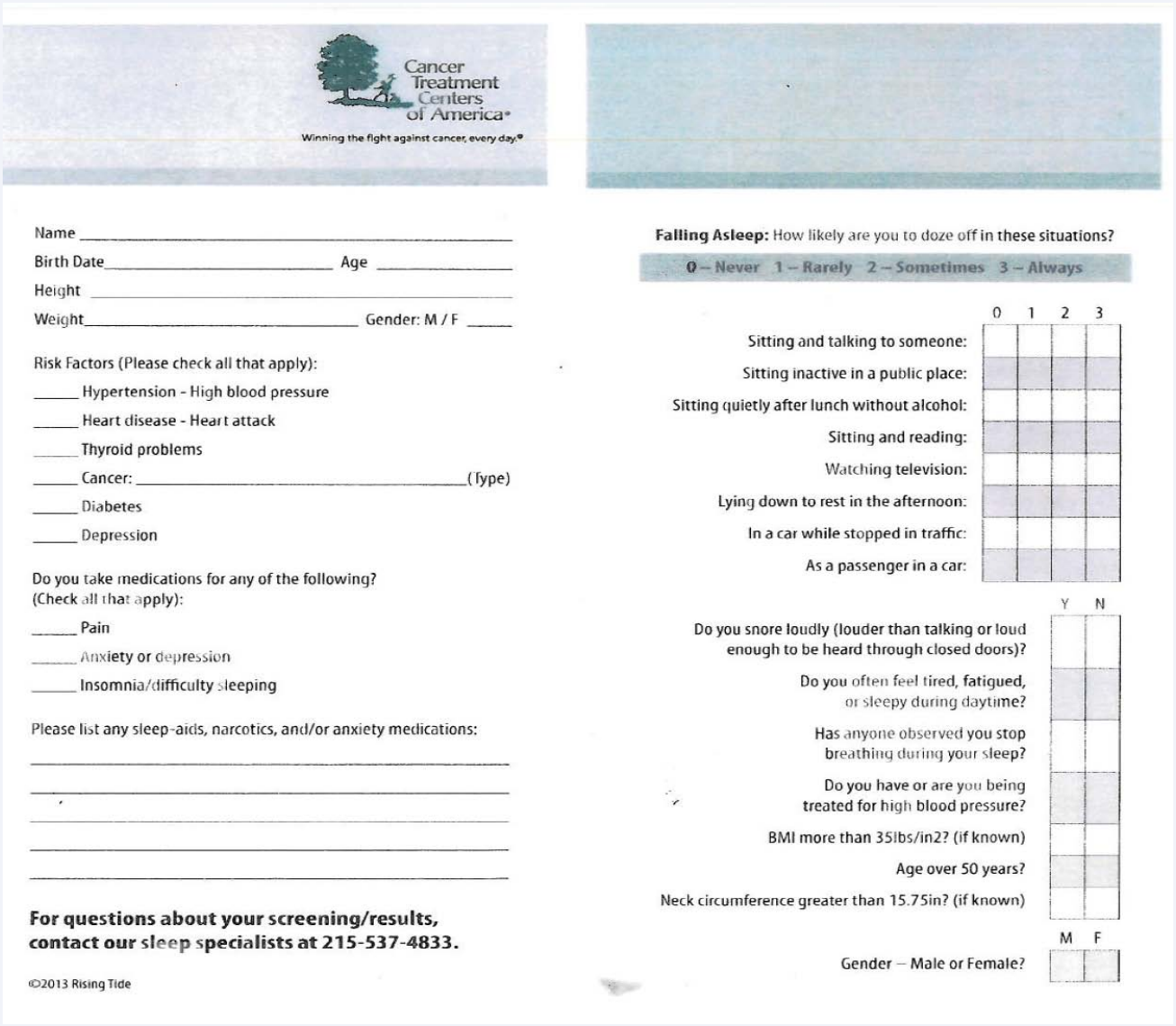
Limited information is available using non-invasive, objective physiological measures of sleep quality, such as the Sleep Image® device, in conjunction with subjective questionnaires in patients with cancer. As such, our institution piloted a program which evaluates patients via both subjective screening with Epworth Sleepiness Scale, Epworth Sleepiness Scale, STOP BANG (snoring, tiredness during daytime, observed apnea, high blood pressure, BMI, age, neck circumference, gender) Questionnaire, and focused sleep assessment combined with Sleep Image® screening which tracks the synchronization of your heart rate variability and breathing activity to provide an objective picture of your sleep quality. About the size of a deck of playing cards, this at-home screening device is also used to measure actigraphy, body position, respirations and EKG.

This retrospective study examined the prevalence of sleep disturbances and poor sleep quality in cancer patients, as these symptoms relate to overall cancer-related fatigue. We theorized patients being treated at Eastern Regional Medical Center would present with reduced sleep quality, and have a higher incidence of sleep disruptions than the general population at 10% to 15%, as noted by the National Cancer Institute at the National Institutes of Health [13].

MATERIALS AND METHODS

After receiving approval by the institutional review board, data was reviewed for patients who completed either our combined sleep questionnaire, an assessment with an at-home sleep screening device, or both. All patients sought treatment at Cancer Treatment Centers of America at Eastern Regional Medical Center (ERMC) during the period from March 2013 through April 2014. Eastern Regional Medical Center implemented a process by which subjective and objective sleep screening assessment is standard practice for all patients new to the center. The ERMC sleep questionnaire, a combination of the Epworth Sleepiness Scale and STOP BANG, was completed by patients during the first day of their three-day initial assessment. This questionnaire also asked the patients to record risk factors such as: heart disease, diabetes, depression, and existing sleep disorder; as well as to acknowledge and list any sleep-aids, narcotics, and/or anxiety medications (Figure 1). The patients were then provided with a Sleep Image® at-home sleep screening device as part of their initial overall comprehensive assessment. The patients were instructed on how to apply the device prior to retiring for the night, and time was provided to address any questions.

The at-home screening device links the physiology of autonomic, respiratory, and mathematically captures electrocortical activity, collectively referred to as cardiopulmonary coupling (CPC). The graphical output produced from the CPC analysis is referred to as a cardiopulmonary spectrogram which provides



Cancer Treatment Centers of America®
Winning the fight against cancer, every day.®

Name _____
Birth Date_____ Age _____
Height _____
Weight_____ Gender: M / F _____

Risk Factors (Please check all that apply):
_____ Hypertension - High blood pressure
_____ Heart disease - Heart attack
_____ Thyroid problems
_____ Cancer: _____(Type)
_____ Diabetes
_____ Depression

Do you take medications for any of the following?
(Check all that apply):
_____ Pain
_____ Anxiety or depression
_____ Insomnia/difficulty sleeping

Please list any sleep-aids, narcotics, and/or anxiety medications:
_____
_____
_____
_____
_____

For questions about your screening/results, contact our sleep specialists at 215-537-4833.

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Falling Asleep: How likely are you to doze off in these situations?

0 – Never 1 – Rarely 2 – Sometimes 3 – Always

	0	1	2	3
Sitting and talking to someone:				
Sitting inactive in a public place:				
Sitting quietly after lunch without alcohol:				
Sitting and reading:				
Watching television:				
Lying down to rest in the afternoon:				
In a car while stopped in traffic:				
As a passenger in a car:				

	Y	N
Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?		
Do you often feel tired, fatigued, or sleepy during daytime?		
Has anyone observed you stop breathing during your sleep?		
Do you have or are you being treated for high blood pressure?		
BMI more than 35lbs/in2? (if known)		
Age over 50 years?		
Neck circumference greater than 15.75in? (if known)		

	M	F
Gender – Male or Female?		

Figure 1 Combined Sleep Questionnaire.

a picture of sleep. Depicted are the frequency of coupling, sleep hypnogram, body position and actigraphy recorded throughout the recording. Sleep Image® defines high frequency coupling (HFC) as 0.1 to 0.4Hz and low frequency coupling (LFC) as 0.0 to 0.1Hz, which reflect stable and unstable sleep respectively. Using a proprietary algorithm, sleep quality is calculated which accounts for changes between HFC and LFC during the course of a night's sleep. It is further delineated that diseases which disrupt sleep reduce periods of HFC, and things such as pain, noise, and particular medical conditions (i.e. sleep apnea), increase LFC [14].

RESULTS AND DISCUSSION

Results

During the study timeframe, a total of 1,207 new patients were seen for an initial evaluation. Of these 1,207 patients, 279 (23%) completed a subjective sleep questionnaire, 282 (23%) completed the objective at-home Sleep Image® screening, and 89 (7%) completed both evaluations.

Subjective questionnaire: Of the unique patients who completed a subjective sleep questionnaire, thirty-seven (13%) had to be discarded due to incomplete reporting with the ERMC sleep questionnaire. The demographics of the resulting 242 (87%) patients are detailed in Table 1.

Based on the previously established standards by Johns to evaluate daytime sleepiness, patients having an Epworth sum of 10 or greater were considered high risk, with 24 being the maximum sum [15,16]. Moderate risk of daytime sleepiness was defined as an Epworth sum of 7-9, while sums of 6 or fewer were considered low risk. The STOP BANG assessment asks a series of yes/no questions (score: 2 or more), with a maximum score of eight (8) to support determining a patient's risk of OSA.

Our board certified sleep physicians assessed the patient's

Table 1: Patient Demographics.	
Age (years)	
Median Age	53
Range	20-76
Gender	
Male	96 (40%)
Female	146 (60%)
Risk Factors	
Hypertension – High BP	83 (34%)
Depression	38 (16%)
Diabetes	27 (11%)
Thyroid Problems	22 (9%)
Heart Disease – Heart Attack	15 (6%)
Cancer Types	
Breast	49 (20%)
Lung	24 (10%)
Colorectal	24 (10%)
Gynecologic Cancer	12 (5%)
Pancreatic	13 (5%)
Liver	10 (4%)
Other	110 (46%)
Medications	
Pain	96 (40%)
Anxiety or Depression	48 (20%)
Insomnia/Sleep Aids	42 (17%)
Abbreviations: BP: Blood pressure	

Epworth and STOP BANG scores in conjunction with patient sleep questionnaire demographics and risk factors to determine a patient's likelihood of sleep disturbance. Of the 242 patients having completed both portions of the questionnaire, 65% were considered to have a likelihood of sleep disturbance. Table 2 delineates the patient reported daytime sleepiness responses. Table 3 demonstrates patient responses to the STOP BANG portion of the questionnaire. Of particular interest is that 68% of patients reported feeling tired/fatigued/sleepy during the day.

Objective at-home screening: The at-home Sleep Image® device objectively ascertains a patient's sleep quality index (SQI), which typically ranges on a scale of 0 to 4+, poor to excellent respectively. The SQI is the ratio of stable sleep to unstable sleep and typically a ratio of greater than 1.67 is favorable. Variables considered for this objective Sleep Image® report include but are not limited to duration of high, low, and very low frequency coupling, total sleep time in minutes, and duration of intermittent wakefulness in minutes. Of the unique patients having completed at-home Sleep Image® screening, the average sleep quality score was 1.97, with 71% having a sleep quality of less than two, and only 17% having a sleep quality of three or greater. Table 4 demonstrates the tertile patient's sleep quality distribution.

Complete subjective and objective measures: Eighty-nine patients had a complete questionnaire and interpretable screening results, of which 56 patients were deemed likely to be sleep disturbed based on the STOP BANG and Epworth subjective questionnaires. Of these 56 patients, the mean sleep quality was 1.68, with 70% of them having a sleep quality of less than two (Table 5). However, the remaining 33 patients who did not

Table 2: Epworth Sleepiness Scale Likelihood of Dozing Off Tabulations and Percentages of Total Population.				
Question	**No. Never (%)**	**No. Rarely (%)**	**No. Sometimes (%)**	**No. Always (%)**
Sitting and talking to someone	189 (78)	30 (12)	19 (8)	3 (1)
Sitting inactive in public place	145 (60)	48 (20)	41 (17)	5 (2)
Sitting quietly after lunch w/out alcohol	111 (46)	50 (21)	63 (26)	12 (5)
Sitting and reading	71 (29)	41 (17)	82 (34)	43 (18)
Watching television	41 (17)	44 (18)	108 (45)	49 (20)
Lying down to rest in the afternoon	26 (11)	36 (15)	102 (42)	73 (30)
In a car while stopped in traffic	190 (79)	27 (11)	18 (7)	4 (2)
As a passenger in a car	89 (37)	69 (29)	58 (24)	22 (9)
Abbreviations: No. (Number)				

Table 3: STOP BANG Tabulations and Percentages of Total Population.			
Question	Yes (%)	No (%)	No Response (%)
Do you snore loudly	70 (29)	166 (69)	6 (2)
Tired/fatigued/sleepy during daytime	165 (68)	73 (30)	4 (2)
Observed stop breathing during sleep	29 (12)	210 (87)	3 (1)
High blood pressure	93 (38)	148 (61)	1 (1)
BMI more than 35lbs/in^2	23 (10)	60 (25)	159 (66)
Age over 50yrs	152 (63)	82 (34)	8 (3)
Neck circumference <15.75in	30 (12)	63 (26)	149 (62)
Abbreviations: STOP BANG (Snoring, Tiredness during daytime, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, Gender).			

Table 4: Sleep Quality Index Distribution.

Sleep Quality Rating	No. of Patients (%)	Median Rating (Range)
Poor (<1.00)	116 (41)	0.46 (0.00-0.98)
Moderate (1.00-2.00)	83 (29)	1.42 (1.00-1.98)
Good (>2.00)	83 (29)	4.63 (2.05-22.63)

Table 5: Stratification of Objective Sleep Quality by Subjectively Determined Sleep Disturbance.

Likelihood of Sleep Disturbance	No. of Patients (%)	Mean Sleep Quality Rating (Range)
Yes	56 (63)	1.68 (0.01 - 4.00)
No	33 (37)	1.52 (0.03 – 4.00)

have sleep disturbance on the self-reported assessment actually demonstrated lower sleep quality scores (mean of 1.52).

Discussion

Utilizing objective and subjective assessments, this report highlights disrupted sleep in cancer patients. The option for dual-assessment sleep screening via combined sleep screening questionnaire and the Sleep Image® device provides valuable information regarding the incidence of disrupted sleep in this patient population. Prior to the availability of the at-home sleep screening device, we obtained data on sleep quality via two mechanisms: patient reported subjective assessment via questionnaires, or sleep medicine physician consultation. Our approach was to pilot a multimodal sleep screening and assessment.

The ability to assess overall sleep quality, as well as low and high frequency coupling, has proven valuable in determining further diagnostic testing or evaluations. The patient's responses to questioning, at-home recording data, and medical history were collectively reviewed to ascertain a comprehensive assessment of their sleep. By interpreting patient responses along with objective results, we were able provide meaningful recommendations to the patient, their other treating physicians, as well as allow for the identification of sleep disturbances in addition to conventional sleep disordered breathing.

CONCLUSION

Overall, the results of this study emphasize the importance of utilizing both subjective and objective assessments for sleep analysis. Assessing sleep with only one of these tools would not provide an accurate account of sleep disturbance. While patients may subjectively report sleep disturbance on a questionnaire, objective assessment using the Sleep Image® device does not always report poor sleep quality. Similarly, subjective claims of good sleep quality are paired with objective reports of sleep disturbance. The contradictions found between subjective, self-reported data and the objective data obtained through the Sleep Image® device suggest other factors may contribute to patients feeling sleep deprived or well-rested. To obtain an accurate understanding of sleep quality for individual patients, it is important to utilize both subjective and objective assessments. Although descriptive in nature, this study demonstrated more than a four-fold prevalence of sleep disturbances and poor sleep quality in our patient population. These results suggest the need for future research to further substantiate and quantify sleep disturbance in the oncology population. As such, additional studies are currently being developed to further evaluate our sleep screening process and outcomes as related to fully diagnostic testing.

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