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Assessing the Sleep-wake Pattern in Cancer Patients for Predicting a Short Sleep Onset Latency

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Objective: We investigated the sleep parameters and clinical factors related to short sleep onset latency (SL) in cancer patients.
Methods: We retrospectively reviewed the medical records of 235 cancer patients. Patient Health Questionnaire-9, State and Trait Anxiety Inventory (State subcategory), Insomnia Severity Index (ISI), Cancer-related Dysfunctional Beliefs about Sleep, and Fear of Progression scale scores and sleep related parameters including sleeping pill ingestion time, bedtime, sleep onset time, and wake-up time were collected. We also calculated the duration from sleeping pill ingestion to bedtime, sleep onset time, and wake-up time; duration from wake-up time to bedtime and sleep onset time; and time spent in bed over a 24 hours period.
Results: Among patients not taking sleeping pills (n = 145), early wake-up time (adjusted odds ratio [OR]: 0.39, 95% confidence interval [CI] 0.19−0.78), early sleep onset time (OR: 0.50, 95% CI 0.27−0.93), and low ISI score (OR: 0.82, 95% CI 0.71−0.93) were identified as expecting variables for SL ≤ 30 minutes. Longer duration from wake-up time to bedtime (OR: 2.49, 95% CI 1.48−4.18) predicted SL ≤ 30 minutes. Among those taking sleeping pills (n = 90), early sleep onset time (OR: 0.54, 95% CI 0.39−0.76) and short duration from pill ingestion to sleep onset time (OR: 0.05, 95% CI 0.02−0.16) predicted SL ≤ 30 minutes.
Conclusion: Cancer patients who fell asleep quickly spent less time in bed during the day. Thus, before cancer patients with insomnia are prescribed sleeping pills, their sleep parameters should be examined to improve their SL.

KEY WORDS: Sleep initiation and maintenance disorders; Sleep; Cancer; Sleep latency.

INTRODUCTION

The sleep disturbances experienced by patients with cancer are increasingly being recognized and examined [1]. Although studies on the prevalence of insomnia vary in design, type of cancer assessed, type of treatment, and phase of treatment, it is clear that 20−60% of patients with cancer suffer from insomnia and sleep disturbances. This is particularly true for female and elderly patients [2-4]. In the past, insomnia was regarded as a natural reaction to cancer and its related treatments. However, as cancer patients' survival rates have increased, improving their quality of life has become important. Insomnia is directly and indirectly related to the quality of life. Additionally, persistent insomnia is a risk factor for subsequent psychiatric disorders, such as depression, which can lead to noncompliance with cancer treatment [5,6]. Recently, both doctors and patients have expressed their interest in the awareness and treatment of insomnia.

In clinical settings, pharmacologic treatment of insomnia is preferred owing to its efficacy and simplicity. However, cancer patients with insomnia may experience maladaptive sleep behaviors or have faulty beliefs and attitudes regarding sleep, and these factors further exacerbate insomnia [3,4]. Unfortunately, pharmacologic agents do not affect the perpetuating factors of insomnia. Cognitive-behavioral therapy for insomnia (CBT-I) improves insomnia by targeting perpetuating factors, such as dysfunctional beliefs [7], and is an effective treatment for insomnia secondary to cancer [8]. CBT-I is particularly

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useful for patients with cancer as it has no associated drug-interactions or side effects [3], and patients can regain control over their sleep and effectively deal with the emotional stress caused by insomnia [9].

Approximately 60−70% of cancer patients with insomnia face difficulties in both initiating and maintaining sleep [10]. It is, therefore, important to record details of night sleep characteristics and insomnia in patients suffering from sleep disturbances. If we understand sleep parameters (e.g., sleep onset time, wake-up time, and time in bed), we can provide individualized cognitive-behavioral therapy properly in a busy clinical setting. An earlier study revealed that insomnia patients who were able to fall asleep faster usually went to bed later and had longer durations between their wake-up times and bedtimes [11]. However, whether these findings also apply to patients with cancer remains to be determined. Indeed, cancer patients with insomnia tend to adopt compensatory behaviors such as napping and going to bed earlier. They also participate in less daytime activities and spend more time in bed because of fatigue regardless of treatment [12]. Moreover, patients with cancer can experience sleep/wake disturbances. In other words, their ability to maintain sleep and waking states is affected, which may result from the dysregulation of homeostatic and circadian processes [13]. Therefore, insomnia in patients with cancer may present differently than general insomnia does. To this end, we investigated the association between sleep parameters and short sleep latency (SL $\leq$ 30 minutes) [14] and studied the differences in sleep parameters, especially time in bed during daytime (TIB/d), and the duration from wake-up time to bedtime (WTB), between cancer patients who were taking sleeping pills and those who were not.

METHODS

Subjects

This was a retrospective review of existing medical records. Patients who visited the Sleep Clinic for Cancer Patients in the Asan Medical Center between January 2017 and February 2020 were enrolled in this study. At this clinic, all patients were routinely assessed by a psychiatrist and a sleep specialist (S. Chung) for their psychiatric or sleep problems. Patients who had severe disabilities that could limit activities of daily living, organic brain diseases, cognitive dysfunction, or other primary sleep disorders including obstructive sleep apnea (snoring or repetitive apneic events during sleep) and restless legs syndrome or those who had undergone CBT-I before they visited our clinic were excluded from the final analysis. This study was approved by the Institutional Review Board of Asan Medical Center (S2020-1238-0001) and Yongin Mental Hospital (2020-16), and the requirement of written informed consent was waived for this retrospective medical records review study.

Rating Scales

Patient Health Questionnaire-9

Patient Health Questionnaire-9 (PHQ-9) is a self-rated scale used to assess the severity of depression. It consists of nine criteria, each of which can be scored from 0 to 3 for a maximum score of 27 [15].

State subcategory of State and Trait Anxiety Inventory

The State and Trait Anxiety Inventory (STAI) is a self-rated scale for measuring the traits and state of a patients anxiety. Among all 40 scoring criteria on this scale, 20 are designed to assess state anxiety and 20 to assess trait anxiety [16]. In this study, we used the Korean version of the 20 items of state anxiety, each of which can be rated from 1 to 4 [17].

Insomnia Severity Index

The Insomnia Severity Index (ISI) is a self-rated scale used to assess the severity of insomnia symptoms. It consists of seven items rated 0−4 on a Likert scale and is represented as a sum of the scores ranging from 0−28, categorized into mild (8−14), moderate (15−21), and severe insomnia (22−28) [18]. In this study, we used the Korean version of this scale [19].

Cancer-related Dysfunctional Beliefs about Sleep

The Cancer-related Dysfunctional Beliefs about Sleep (C-DBS) scale is a 2-item rating scale for assessing dysfunctional beliefs concerning sleep in patients with cancer [20]. It consists of two items: "My immune system will have serious problems if I do not go to sleep at a certain time" (question 1, immune dysfunction) and "If I do not sleep well at night, my cancer may recur or metastasize" (question 2, cancer recurrence). Each item can be rated

on a scale of 0−10.

Fear of Progression-short form

The original Fear of Progression (FoP) is a 43-item rating scale that evaluates concerns related to disease progression. In this study, we used the Korean version [21] of a 12-item short form of the original scale [22]. Each item on the FoP-short form is rated on a scale of 1−5.

Assessment of Sleep-wake Pattern, Time and Duration Variables, and Hypnotics Usage

On their first visit, patients were routinely asked the following questions: 1) "How many tablets of sleeping pills per day are you taking now?"; 2) "Are you satisfied with your sleeping pills' ability to induce sleep?"; 3) "What is the usual time at which you take sleeping pills?"; 4) "What is your usual bedtime?"; 5) "What is the usual time you fall asleep?"; 6) "What is the usual time you take to finally get out of bed in the morning?"; and 7) "What is the total number of hours you spend lying down within 24 hours, including sleeping time?" [22]. Their answers were recorded in the electronic medical records system.

Based on patient responses, we calculated the time and duration variables. The time variables, including sleeping pills ingestion time, bedtime, sleep onset time, and wake-up time, were calculated by averaging the times reported in our previous study [23]. Using the calculated time variables, duration variables, including sleep onset latency, time in bed, time in bed in 24 hours (TIB/d), durations from the ingestion of pills to bedtime (PTB), to sleep onset time (PTS), and to wake-up time (PTW), and durations from wake-up time to bedtime (WTB) and to sleep onset time (WTS) were calculated.

The number of tablets of equivalent hypnotic drugs (TEQ) was calculated using the equivalent dosage of each medication: alprazolam (0.25 mg), bromazepam (3 mg), clonazepam (0.25 mg), diazepam (5 mg), lorazepam (0.5 mg), triazolam (0.25 mg), and zolpidem (10 mg for the immediate release and 12.5 mg for the extended-release forms) [24].

Statistical Analysis

Statistical analyses were performed using the SPSS ver. 21.0 for Windows (IBM Corp., Armonk, NY, USA). The clinical characteristics were summarized as mean ± standard deviation values. The level of significance for all analyses was defined as two-tailed $p < 0.05$. Student's t test for continuous variables and a chi-square test for categorical variables were performed for between group analyses. A Spearman correlation analysis was performed to explore the association between the patients' clinical characteristics. A logistic regression analysis was used to explore the factors that may predict short SL (≤ 30 minutes) in patients with cancer.

RESULTS

Among the 255 patients, 20 were excluded owing to inadequate medical records of sleep parameters. Table 1 shows the clinical characteristics of the study subjects (n = 235). About 75% of the patients were women, with a

Table 1. Clinical characteristics of the study subjects (n = 235)

Variable	Subjects
Sex, female	175 (74.5)
Age (yr)	56.1 ± 11.2
Cancer type	
Breast	103 (43.8)
Lung	20 (8.5)
Gastro-esophageal	19 (8.1)
Pancreatic and biliary tract	17 (7.2)
Colorectal	15 (6.4)
Head and neck	14 (6.0)
Gynecologic	12 (5.1)
Hematologic	11 (4.7)
Kidney	7 (3.0)
Urinary tract	6 (2.6)
Liver	5 (2.1)
Thyroid	3 (1.3)
Others	3 (1.3)
Cancer stages[a]	
Stage 0	3 (1.4)
Stage I	52 (24.4)
Stage II	60 (28.2)
Stage III	23 (10.8)
Stage IV	66 (31.0)
Not yet confirmed	9 (4.2)
Psychiatric diagnosis	
Insomnia	153 (65.1)
Major depressive disorder	55 (23.4)
Anxiety disorder/somatic symptom disorder	12 (5.1)
Mixed anxiety and depression	5 (2.1)
Acute stress reaction/adjustment disorder	5 (2.1)
No diagnosis	3 (1.3)
Others	2 (0.9)

Values are presented as number (%) or mean ± standard deviation.
[a]Patients with cancer can be graded using the TNM staging system (n = 213).

mean age of 56.1 ± 11.2 years. The types of cancer included breast (n = 103, 43.8%), lung (n = 20, 8.5%), gastro-esophageal (n = 19, 8.1%), pancreas and biliary tract (n = 17, 7.2%), colorectal (n = 15, 6.4%), head and neck (n = 14, 6.0%), gynecologic (n = 12, 5.1%), hematologic (n = 11, 4.7%), kidney (n = 7, 3.0%), urinary tract (n = 6,

Table 2. Clinical characteristics of cancer patients who were taking sleeping pills (n = 145)

Variable	SL ≤ 30 min (n = 84)	SL > 30 min (n = 61)	*p* value
Sex, male	23 (27.4)	25 (41.0)	0.06
Age (yr)	57.5 ± 11.1	57.8 ± 10.6	0.86
Rating scales scores			
Insomnia severity index	17.9 ± 4.9	20.2 ± 4.9	0.006
Cancer-related dysfunctional beliefs about sleep	12.6 ± 5.4	12.1 ± 5.0	0.59
Fear of progression	35.0 ± 12.3	33.9 ± 11.8	0.58
Patient health questionnaire-9	11.6 ± 7.2	12.5 ± 6.6	0.42
State subcategory of state and trait anxiety Inventory	42.3 ± 10.9	41.8 ± 10.6	0.81
Time variables			
Sleeping pills ingestion time	10:42 ± 1:10 pm	10:22 ± 1:21 pm	0.13
Bedtime	10:54 ± 1:10 pm	10:30 ± 1:09 pm	0.037
Sleep onset time	11:18 ± 1:09 pm	12:07 ± 1:24 pm	< 0.01
Wake-up time	6:33 ± 1:25 am	6:59 ± 1:30 am	0.10
Duration variables			
Sleep latency (min)	22.8 ± 10.0	96.0 ± 54.0	< 0.01
Time in bed (hr)	7.6 ± 1.5	8.5 ± 1.6	< 0.01
Time in bed during 24 hr, TIB/d (hr)	9.9 ± 3.1	11.8 ± 3.7	< 0.01
Duration from pills to bedtime, PTB (min)	12.6 ± 24.6	7.2 ± 48.6	0.41
Duration from pills to sleep onset time, PTS (min)	36.0 ± 25.8	103.8 ± 61.2	< 0.01
Duration from pills to wake-up time, PTW (hr)	7.9 ± 1.5	8.6 ± 1.7	< 0.01
Duration from wake-up time to bedtime, WTB (hr)	16.4 ± 1.5	15.5 ± 1.6	< 0.01
Duration from wake-up time to sleep onset time, WTS (hr)	16.7 ± 1.5	17.1 ± 1.5	< 0.01
Number of tablets of equivalent hypnotic drugs, TEQ (tablets)	0.87 ± 0.38	1.00 ± 0.54	0.07

Values are presented as number (%) or mean ± standard deviation.
SL, sleep latency.

Table 3. Clinical characteristics of cancer patients who were not taking sleeping pills (n = 90)

Variable	SL ≤ 30 min (n = 28)	SL > 30 min (n = 62)	*p* value
Sex, male	6 (21.4)	6 (9.7)	0.12
Age (yr)	54.4 ± 9.8	53.3 ± 12.0	0.67
Rating scales scores			
Insomnia severity index	12.2 ± 6.3	17.2 ± 5.0	< 0.01
Cancer-related dysfunctional beliefs about sleep	11.3 ± 4.8	11.6 ± 5.3	0.82
Fear of progression	33.3 ± 12.4	35.8 ± 13.3	0.41
Patient health questionnaire-9	9.1 ± 6.3	11.7 ± 7.1	0.10
State subcategory of state and trait anxiety inventory	41.6 ± 15.3	42.8 ± 11.5	0.69
Time variables			
Bedtime	10:45 ± 1:16 pm	10:38 ± 1:02 pm	0.62
Sleep onset time	11:00 ± 1:15 pm	12:34 ± 1:18 pm	< 0.01
Wake-up time	6:06 ± 1:30 am	7:05 ± 1:08 am	< 0.01
Duration variables			
Sleep latency (min)	14.4 ± 14.4	115.8 ± 67.2	< 0.01
Time in bed (hr)	7.3 ± 1.7	8.5 ± 1.3	< 0.01
Time in bed during 24 hr, TIB/d (hr)	9.7 ± 3.5	11.0 ± 3.8	< 0.01
Duration from wake-up time to bedtime, WTB (hr)	16.7 ± 1.6	15.5 ± 1.4	< 0.01
Duration from wake-up time to sleep onset time, WTS (hr)	16.9 ± 1.7	17.5 ± 1.2	0.08

Values are presented as number (%) or mean ± standard deviation.
SL, sleep latency.

2.6%), liver (n = 5, 2.1%), thyroid (n = 3, 1.3%), and others (n = 3, 1.3%). The most common psychiatric diagnosis in these patients at the first visit was insomnia (153, 65.1%), followed by major depressive disorder (55, 23.4%) and anxiety disorder/somatic symptom disorder (12, 5.1%).

All 145 cancer patients were taking sleeping pills when they visited the sleep clinic for the first time. Among them, 84 showed SL ≤ 30 minutes, and 61 showed SL > 30 minutes (Table 2). There was no significant difference in sex, age, depression, anxiety, fear of disease progression, and dysfunctional beliefs about sleep. The group in which SL was > 30 minutes reported more severe insomnia symptoms, earlier bedtimes (10:30 ± 1:09 pm), and later sleep onset times (12:07 ± 1:24 pm). There was a significant difference in duration variables such as SL, time in bed, TIB/d, PTS, PTW, WTB, and WTS.

Among the 90 patients with cancer who were not taking sleeping pills at the first visit, patients with short SL (≤ 30 minutes) showed earlier sleep onset (11:00 ± 1:15 pm) and wake-up times (6:06 ± 1:30 am) (Table 3). Additionally, they showed a shorter time in bed, shorter TIB/d, and longer WTB. SL of the group that did not take sleeping pills showed significant correlations with depressive symptoms ($r = 0.23$, $p < 0.05$), sleep onset time ($r = 0.60$, $p < 0.01$), wake-up time ($r = 0.34$, $p < 0.01$), TIB/d ($r = 0.28$, $p < 0.01$), and WTB ($r = -0.38$, $p < 0.01$) (Table 4). TIB/d was correlated with clinical symptoms, including FoP score ($r = 0.23$, $p < 0.05$), depressive symptoms ($r = 0.34$, $p < 0.01$), and anxiety ($r = 0.24$, $p < 0.05$). Longer TIB/d showed significant correlations with later wake-up time ($r = 0.43$, $p < 0.01$) and earlier bedtime ($r = -0.28$, $p < 0.01$). SL of sleeping pill users showed correlations with earlier bedtime ($r = -0.22$, $p < 0.01$) and later sleep onset ($r = 0.35$, $p < 0.01$) and wake-up times ($r = 0.22$, $p < 0.01$). Among the duration variables, longer time in bed at night ($r = 0.35$, $p < 0.01$) and all day ($r = 0.37$, $p < 0.01$) showed a correlation with longer SL. Longer TIB/d showed a positive correlation with PTS ($r = 0.34$, $p < 0.01$), PTW ($r = 0.50$, $p < 0.01$), and TEQ ($r = 0.26$, $p < 0.01$).

Logistic regression analysis was conducted after adjust-

Table 4. Spearman's correlation (rho) analysis of sleep latency with the clinical characteristics of insomnia patients

Variable	Sleeping pill Non-users (n = 90)		Sleeping pill users (n = 145)	
	SL	TIB/d	SL	TIB/d
Age	−0.07	−0.03	0.01	−0.01
Rating scale scores				
Insomnia severity scale	0.33**	0.15	0.25**	0.11
Cancer-related dysfunctional beliefs about sleep	0.01	0.03	−0.05	−0.05
Fear of progression	0.16	0.23*	−0.09	0.12
Patient health questionnaire-9	0.23*	0.34**	0.05	0.17*
State subcategory of state and trait anxiety inventory	0.12	0.24*	−0.05	0.10
Time variables				
Sleeping pills ingestion time	-	-	−0.15	−0.19*
Bedtime	−0.17	−0.28**	−0.22**	−0.11
Sleep onset time	0.60**	0.002	0.35**	0.09
Wake-up time	0.34**	0.43**	0.22**	0.44**
Duration variables				
Sleep latency	-	0.28**	-	0.37**
Time in bed	0.38**	0.60**	0.35**	0.51**
Time in bed during 24 hr (TIB/d)	0.28**	-	0.37**	-
Duration from pills to bedtime (PTB)	-	-	−0.16	−0.001
Duration from pills to sleep onset time (PTS)	-	-	0.76**	0.34**
Duration from pills to wake-up time (PTW)	-	-	0.28**	0.50**
Duration from wake-up time to bedtime (WTB)	−0.38**	−0.60**	−0.35**	−0.51**
Duration from wake-up time to sleep onset time (WTS)	0.30**	−0.39**	0.14	−0.33**
Number of tablets of equivalent hypnotic drugs (TEQ)	-	-	0.08	0.26**

SL, sleep latency.
*$p < 0.05$, **$p < 0.01$.

Table 5. Logistic regression analysis to explore expecting variables for sleep latency ≤ 30 min

Expecting variable	Crude OR	95% CI	Adjusted OR	95% CI
Among subjects who are not taking sleeping pills (n = 90)[a]				
Time variables				
Insomnia severity index score	0.85	0.77−0.94	0.82	0.71−0.93
Wake-up time	0.54	0.35−0.83	0.39	0.19−0.78
Sleep onset time	0.35	0.21−0.59	0.50	0.27−0.93
Duration variables				
Insomnia severity index score	0.85	0.77−0.93	0.78	0.68−0.89
Duration from wake-up time to bedtime	1.78	1.23−2.56	2.49	1.48−4.18
Among subjects who are taking sleeping pills (n = 145)[b]				
Time variables				
Sleep onset time	0.488	1.61−2.92	0.54	0.39−0.76
Duration variables				
Duration from pills to sleep onset time	0.04	0.01−0.13	0.05	0.02−0.16

OR, odds ratio; CI, confidence interval.
[a]Adjusted for age, sex, cancer types, TNM staging, psychiatric diagnosis, and insomnia severity index score, patient health questionnaire-9 items score, fear of progression scale score, cancer-related dysfunctional beliefs about sleep scale, and state subcategory of state and trait anxiety inventory. [b]Adjusted with age, sex, cancer types, TNM staging, psychiatric diagnosis, insomnia severity index score, patient health questionnaire-9 items score, fear of progression scale score, cancer-related dysfunctional beliefs about sleep scale and state subcategory of state and trait anxiety inventory, and number of tablets of equivalent hypnotic drugs.

ing for age, sex, cancer types, Tumor-Node-Metastasis (TNM) staging, psychiatric disorder and ISI, PHQ-9, STAI, C-DBS, and FoP scores to identify predictive variables for short SL. Among patients with cancer who were not taking sleeping pills, early wake-up time (adjusted odds ratio [OR]: 0.39, 95% confidence interval [CI] 0.19−0.78) and early sleep onset time (adjusted OR: 0.50, 95% CI 0.27−0.93) from the time variables and low ISI score (adjusted OR: 0.82, 95% CI 0.71−0.93) were identified as the predictive factors for SL ≤ 30 minutes (Table 5). Longer duration of WTB (adjusted OR: 2.49, 95% CI 1.48−4.18) from the duration variables and low ISI score (adjusted OR: 0.78, 95% CI [0.68−0.89]) predicted SL ≤ 30 minutes. Among patients with cancer who were taking sleeping pills, early sleep onset time (adjusted OR: 0.54, 95% CI 0.39−0.76) from the time variables and short duration from ingestion of pills to sleep onset time (adjusted OR: 0.05, 95% CI 0.02−0.16) from the duration variables were predictive of SL ≤ 30 minutes.

DISCUSSION

In this study, we observed that early wake-up time and early sleep onset time from the time variables and longer WTB from the duration variables were predictive of short SL among patients with cancer who were not taking sleeping pills. In addition, among patients who were taking sleeping pills, early sleep onset time from the time variables and short PTS from the duration variables were predictive of short SL.

Patients with cancer who did not take sleeping pills with SL ≤ 30 minutes showed low ISI scores, which is suggestive of subthreshold insomnia. In contrast, patients with SL > 30 minutes showed moderate insomnia severity; SL has been identified as an important factor in defining insomnia [25] in all ages [26]. This suggests that recording SL is essential for evaluating the severity of insomnia in patients with cancer. Patients in the SL > 30 minutes group who did not take sleeping pills reported greater delays in sleep onset and wake-up time. They also spent more of their day and night time in bed than did the patients from SL ≤ 30 minutes group. Cancer patients had a longer daytime total nap time than cancer-free people [27]. In our study, TIB/d showed a positive correlation with FoP score, depressive symptoms, and anxiety symptoms. Thus, some of the untreated psychiatric symptoms were related to reduced awakening and probably also to reduced daytime activity. However, we found no significant differences in PHQ-9, state subcategory of STAI, FoP, and C-DBS scale scores between the SL ≤ 30 minutes and SL > 30 minutes groups in this study. Accordingly, these scale scores were excluded from the final model of logistic regression analysis.

No significant differences in PTB or duration from in-

gestion of pills to bedtime were observed between the SL $\leq$ 30 minutes and SL $>$ 30 minutes groups (Table 2). BTP was not significantly correlated with SL or TIB/d (Table 4), and as such, this index was not included as a predictive variable in the logistic regression analysis. Most patients reported that they were taking sleeping pills 30 minutes before bedtime, since this was what was typically assumed to be correct and recommended by clinicians. Previously, we reported that the PTB index was not significantly different between patients satisfied with their sleeping pills and those who were not [23]. It is plausible to consider that this result came about because most patients think they should take sleeping pills 30 minutes before bedtime.

During anticancer treatments, patients with cancer experience increased fatigue and spend more time in bed [28]. They frequently participate in less activities during the day and take frequent naps [13,29]. Additionally, cancer-related fatigue has been reciprocally associated with sleep disturbance. As mentioned above, many factors may change the sleep-wake pattern of patients during the day and night. Patients with cancer who were taking sleeping pills and had SL $\leq$ 30 minutes had later bedtimes and fell asleep faster. Similar results have been observed in patients with primary insomnia [11]. Patients typically report dissatisfaction with their hypnotic medications if they observe long intervals between the time of sleeping pill ingestion and sleep onset time [23]. Reduced sleep efficiency and dissatisfaction with sleeping pills may worsen dysfunctional beliefs of sleep and maladaptive behaviors. As sleep efficiency is likely a prognostic factor for cancer [30], it is important to find a way to improve it by reducing SL.

Moreover, patients with prior experience of using sleep aids are more likely to use hypnotic medicine during cancer treatment [31]. Taking sleeping pills during cancer treatment may raise the risk of starting or increasing hypnotic medication use. Clinicians should be concerned with the change of hypnotic medication usage pattern and periodically evaluate patient's quality of life [32].

Sleep quality can be improved by increased walking at home [33]. Longer times spent outside of bed helps to reduce the initial insomnia, and it is important to pay attention to the respiratory depression induced by sleeping pills, especially when patients have already taken sleeping pills.

Homeostatic processes interact with circadian processes and both regulate sleep patterns [34]. Homeostatic processes are determined by sleep-wake history. A longer duration of wakefulness induces increased sleep propensity [35]. As shown in our study, especially in patients with cancer, increased homeostatic drive for sleep is accompanied by decreased SL. Previous studies have shown that changes in circadian processes in patients with cancer are associated with dysfunctions in cortisol and melatonin secretion [36,37]. However, the role of the homeostatic process is still important because the two processes are compensatory. An uncontrollable biological change due to cancer actively changes cognition and behavior by increasing the homeostatic drive to sleep.

This study had some limitations. First, numerous clinical factors related to cancer itself might influence the severity of insomnia [3]. Insomnia is a persistent problem in all patients with cancer [38,39], and their maladaptive behaviors or dysfunctional beliefs about sleep might exacerbate their insomnia [3]. However, the clinical characteristics of insomnia can vary according to cancer type, stage, or treatment modality. Whilst we did not focus on a specific type of cancer, future studies should be conducted to assess insomnia in each type of cancer. Second, there were no significant differences in psychiatric symptoms such as depression, anxiety, fear of progression, or dysfunctional beliefs about sleep between the two SL groups. Many patients in this study suffered from these symptoms regardless of SL, and this should be investigated in the future. Third, other factors affecting insomnia, such as hot flushes and pain, were not evaluated because this was a retrospective review of medical records. Fourth, sleep parameters were acquired through clinician's questions instead of objective methods of actigraphy or polysomnography. Fifth, the history of cancer treatment was assessed based on yes or no questions; hence, concurrent medical treatments were not evaluated alongside psychiatric evaluations. Finally, TIB/d cannot be considered as having the same significance as activity during the day, and we did not evaluate the amount of daily activity or resting state in this study.

Despite the limitations of this study, our results may be applied in clinical practice for improving the care of patients with cancer who suffer from insomnia. First, the TIB/d index in this study was calculated to estimate the time spent lying in bed during the daytime. Classically,

the TIB index is estimated from bedtime to wake-up time. However, many patients with cancer spend their time laying down on their bed during the daytime because of fatigue. Therefore, we propose that the TIB/d index be used for estimating the daytime activity of patients with cancer in clinical settings. Second, the WTB index was included as an expecting variable for short SL in patients not taking sleeping pills. Thus, an early bedtime cannot guarantee that patients with cancer will fall asleep quickly. Our results may help to improve SL and decrease the use of sleeping pills in patients with cancer.

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■ Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

■ Author Contributions

Conceptualization: Kikyoung Yi, Seockhoon Chung. Data curation: Joohee Lee, Sungook Yeo, Kyumin Kim. Funding acquisition: Kikyoung Yi. Formal analysis: Joohee Lee, Seockhoon Chung. Methodology: Kikyoung Yi, Seockhoon Chung. Writing - original draft: Kikyoung Yi, Seockhoon Chung. Writing - review & editing: Kikyoung Yi, Joohee Lee, Sungook Yeo, Kyumin Kim, Seockhoon Chung.

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REFERENCES

1. Otte JL, Carpenter JS, Manchanda S, Rand KL, Skaar TC, Weaver M, *et al. Systematic review of sleep disorders in cancer patients: can the prevalence of sleep disorders be ascertained? Cancer Med 2015;4:183-200.*
2. Savard J, Morin CM. *Insomnia in the context of cancer: a review of a neglected problem. J Clin Oncol 2001;19:895-908.*
3. *Induru RR, Walsh D. Cancer-related insomnia. Am J Hosp Palliat Care 2014;31:777-785.*
4. Savard J, Savard MH. *Insomnia and cancer- prevalence, nature, and nonpharmacologic treatment. Sleep Med Clin 2013;8:373-387.*
5. Ford DE, Kamerow DB. *Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA 1989;262:1479-1484.*
6. DiMatteo MR, Lepper HS, Croghan TW. *Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 2000;160:2101-2107.*
7. Thakral M, Von Korff M, McCurry SM, Morin CM, Vitiello MV. *Changes in dysfunctional beliefs about sleep after cognitive behavioral therapy for insomnia: a systematic literature review and meta-analysis. Sleep Med Rev 2020;49:101230.*
8. Savard J, Simard S, Ivers H, Morin CM. *Randomized study on the efficacy of cognitive-behavioral therapy for insomnia secondary to breast cancer, part I: sleep and psychological effects. J Clin Oncol 2005;23:6083-6096.*
9. Morin CM. *Cognitive-behavioral approaches to the treatment of insomnia. J Clin Psychiatry 2004;65 Suppl 16:33-40.*
10. Sela RA, Watanabe S, Nekolaichuk CL. *Sleep disturbances in palliative cancer patients attending a pain and symptom control clinic. Palliat Support Care 2005;3:23-31.*
11. Chung S, Youn S, Kim C. *Are you asking what time did your patients go to bed?: getting the short sleep onset latency. Sleep Med Res 2018;9:58-62.*
12. Berger AM, Farr LA, Kuhn BR, Fischer P, Agrawal S. *Values of sleep/wake, activity/rest, circadian rhythms, and fatigue prior to adjuvant breast cancer chemotherapy. J Pain Symptom Manage 2007;33:398-409.*
13. Parker KP, Bliwise DL, Ribeiro M, Jain SR, Vena CI, Kohles-Baker MK, *et al. Sleep/Wake patterns of individuals with advanced cancer measured by ambulatory polysomnography. J Clin Oncol 2008;26:2464-2472.*
14. Lichstein KL, Durrence HH, Taylor DJ, Bush AJ, Riedel BW. *Quantitative criteria for insomnia. Behav Res Ther 2003;41:427-445.*
15. Kroenke K, Spitzer RL, Williams JB. *The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16:606-613.*
16. Metzger RL. *A reliability and validity study of the state-trait anxiety inventory. J Clin Psychol 1976;32:276-278.*
17. Hahn DW Lee CH, Chon KK. *Korean adaptation of Spielberger's STAI (K-STAI). Korean J Health Psychol 1996;1:1-14.*
18. Morin CM, Belleville G, Bélanger L, Ivers H. *The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep 2011;34:601-608.*
19. Cho YW, Song ML, Morin CM. *Validation of a Korean version of the insomnia severity index. J Clin Neurol 2014;10:210-215.*
20. Chung S, Youn S, Choi B. *Assessment of cancer-related dysfunctional beliefs about sleep for evaluating sleep disturbance*

in cancer patients. Sleep Med Res 2017;8:98-101.
21. Shim EJ, Shin YW, Oh DY, Hahm BJ. *Increased fear of progression in cancer patients with recurrence. Gen Hosp Psychiatry 2010;32:169-175.*
22. Mehnert A, Berg P, Henrich G, Herschbach P. *Fear of cancer progression and cancer-related intrusive cognitions in breast cancer survivors. Psychooncology 2009;18:1273-1280.*
23. Chung S, Youn S, Yi K, Park B, Lee S. *Sleeping pill administration time and patient subjective satisfaction. J Clin Sleep Med 2016;12:57-62.*
24. Benzodiazepine equivalence table [Internet]. *NRHA Drug Newsletter; 2007 Apr [cited at 2020 Jan 9]. Available from: http://www.benzo.org.uk/bzequiv.htm.*
25. Lineberger MD, Carney CE, Edinger JD, Means MK. *Defining insomnia: quantitative criteria for insomnia severity and frequency. Sleep 2006;29:479-485.*
26. Levenson JC, Troxel WM, Begley A, Hall M, Germain A, Monk TH, *et al. A quantitative approach to distinguishing older adults with insomnia from good sleeper controls. J Clin Sleep Med 2013;9:125-131.*
27. Ancoli-Israel S, Liu L, Rissling M, Natarajan L, Neikrug AB, Palmer BW, *et al. Sleep, fatigue, depression, and circadian activity rhythms in women with breast cancer before and after treatment: a 1-year longitudinal study. Support Care Cancer 2014;22:2535-2545.*
28. Roscoe JA, Kaufman ME, Matteson-Rusby SE, Palesh OG, Ryan JL, Kohli S, *et al. Cancer-related fatigue and sleep disorders. Oncologist 2007;12 Suppl 1:35-42.*
29. Mormont MC, Waterhouse J, Bleuzen P, Giacchetti S, Jami A, Bogdan A, *et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response, and longer survival in patients with metastatic colorectal cancer and good performance status. Clin Cancer Res 2000;6:3038-3045.*
30. Palesh O, Aldridge-Gerry A, Zeitzer JM, Koopman C, Neri E, Giese-Davis J, *et al. Actigraphy-measured sleep disruption as a predictor of survival among women with advanced breast cancer. Sleep 2014;37:837-842.*
31. Costantini C, Ale-Ali A, Helsten T. *Sleep aid prescribing practices during neoadjuvant or adjuvant chemotherapy for breast cancer. J Palliat Med 2011;14:563-566.*
32. Paltiel O, Marzec-Boguslawska A, Soskolne V, Massalha S, Avitzour M, Pfeffer R, *et al. Use of tranquilizers and sleeping pills among cancer patients is associated with a poorer quality of life. Qual Life Res 2004;13:1699-1706.*
33. Chen HM, Tsai CM, Wu YC, Lin KC, Lin CC. *Effect of walking on circadian rhythms and sleep quality of patients with lung cancer: a randomised controlled trial. Br J Cancer 2016;115:1304-1312.*
34. Borbély AA, Daan S, Wirz-Justice A, Deboer T. *The two-process model of sleep regulation: a reappraisal. J Sleep Res 2016;25:131-143.*
35. Kryger MH, Roth T, Dement WC. *Principles and practice of sleep medicine. 4th ed. Philadelphia:Elsevier Saunders;2005. p.419-422.*
36. Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. *Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst 2000;92:994-1000.*
37. Bartsch C, Bartsch H, Schmidt A, Ilg S, Bichler KH, Flüchter SH. *Melatonin and 6-sulfatoxymelatonin circadian rhythms in serum and urine of primary prostate cancer patients: evidence for reduced pineal activity and relevance of urinary determinations. Clin Chim Acta 1992;209:153-167.*
38. Savard J, Ivers H, Villa J, Caplette-Gingras A, Morin CM. *Natural course of insomnia comorbid with cancer: an 18-month longitudinal study. J Clin Oncol 2011;29:3580-3586.*
39. Otte JL, Carpenter JS, Russell KM, Bigatti S, Champion VL. *Prevalence, severity, and correlates of sleep-wake disturbances in long-term breast cancer survivors. J Pain Symptom Manage 2010;39:535-547.*