Sleep Disturbances In Adults With Untreated Primary Brain Tumors: Prevalence And Effect On Quality Of Life

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Abstract

Purpose: To investigate the frequency of sleep disturbances and their effects on the quality of life of adults with untreated primary benign and malignant brain tumors.

Methods: This prospective study recruited 68 and 35 patients with newly diagnosed benign and malignant brain tumors, respectively. All participants completed the Chinese versions of Athens Insomnia Scale, Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index, Hospital Anxiety and Depression Scale, and EORTC-QLQ-BN20 and the Taiwanese version of the Brief Fatigue Inventory. An actigraph was used to measure sleep parameters, namely total sleep time, sleep onset latency, wake after sleep onset, sleep efficiency, and dichotomy index ($I < 0$), for at least 3 consecutive days before treatment.

Results: The majority of the patients with benign and malignant tumors had meningioma (57.4%) and glioblastoma (40%), respectively. In patients with primary brain tumors, the prevalence of insomnia, poor sleep quality, and excessive daytime sleepiness was 59.2%, 77.7%, and 4.9%, respectively. Only 36 participants completed actigraphic assessments ($I < 0 = 95.4$), and 61.1% of them experienced circadian disruption ($I < 0 \leq 97.5$). Insomnia was the only sleep parameter that significantly affected quality of life after controlling for potential confounders ($B = 0.55$, $p = 0.02$, adjusted $R^2 = 0.60$).

Conclusion: More than 60% of the patients with primary malignant and benign brain tumors experienced insomnia, poor sleep quality, and circadian disruption. Insomnia independently correlated to quality of life before cancer-related treatment. Health-care providers can apply these findings to design effective interventions targeting sleep disturbances to improve quality of life in this population.

Introduction

Sleep disturbances (e.g., insomnia, poor sleep quality, and excessive daytime sleepiness) are common complaints reported by adults with primary brain tumors at different stages of treatment, including the postoperative stage [1–4], chemo/radiotherapy stage [5, 6], and completion and follow-up stages of chemo/radiotherapy [7–9]. Disturbed sleep profoundly affects the quality of life throughout the disease and treatment trajectories [1, 4, 5, 7–13]; however, most previous studies have focused on the post-treatment and follow-up stages [2, 3, 5, 6, 9]. A limited number of studies have been conducted on sleep patterns at the untreated stage, and hence, the effect of such sleep patterns on quality of life remains unknown. Furthermore, thus far, whether sleep disturbance manifestations differ between patients with untreated benign and malignant brain tumors remains unknown.

Circadian rhythm disturbance, one of the common sleep disturbances, has been observed in various cancer types, including breast cancer, colon cancer, and lung cancer [14–16]. Disrupted circadian rhythm results in impaired quality of life and high mortality [17]. In a recent study on benign brain tumors, nearly 60% of the patients reported experiencing circadian rhythm disruption [18]; however, circadian rhythm disruption in patients with untreated primary malignant brain tumors is unexplored.

Therefore, the aim of the current study was to investigate sleep disturbance manifestations and their effects on quality of life in adults with untreated primary benign and malignant brain tumors.

Methods

Study design and participants

This was a prospective study that used a convenience sampling method. It was approved by the institutional review boards of Taipei Medical University Hospital (No. N201901028), National Taiwan University Hospital (No. 201812054RINB), and Chang Gung Memorial Hospital (No. 202000470B0). Patients were recruited from two medical centers and one regional hospital in northern Taiwan between March 2019 and January 2020. We recruited consecutive patients who were 20–65 years old, who had received a new diagnosis of and were pathologically confirmed to have primary benign or malignant brain tumors, who had not undergone any cancer-related treatment, and who could communicate in Mandarin or Taiwanese. Participants were excluded if they were shift workers, pregnant, survivors of other cancer types, or diagnosed as having psychiatric disorders or sleep disorders before the study. Furthermore, participants who underwent surgery or certain treatments (e.g., cancer treatment) were excluded.

Instruments

Demographic and disease characteristics

An information sheet was used to collect demographic and disease characteristics, including sex, age, body mass index, education level, marital status, job status, Charlson comorbidity index, Karnofsky performance score, type(s) of benign or malignant tumor(s), and use of steroid and antiepileptic drugs. These factors have been associated with either sleep disturbances or quality of life in patients with brain tumors [10, 19].

Sleep assessments

We evaluated insomnia symptoms by using the Chinese version of the Athens Insomnia Scale (CAIS), which is a self-reported questionnaire for assessing insomnia and quantifying sleep difficulties over the past month [20]. This questionnaire comprises two components, namely nighttime and daytime symptoms (items 1–5 and 6–8, respectively), with a total score of ≥ 8 indicating suspected insomnia. Its internal consistency (Cronbach's $\alpha = 0.82$ – 0.84) and test–retest reliability ($r = 0.84$ and 0.86) were satisfactory [21].

Excessive daytime sleepiness was measured using the eight-item Chinese version of the Epworth Sleepiness Scale (CESS). Each item was scored on the basis of a 4-point Likert scale ranging from 0 to 3, resulting in a total score of 0–24. A total score of > 10 indicates daytime sleepiness. Acceptable internal consistency (Cronbach's $\alpha = 0.81$) and test–retest reliability ($r = 0.74$, $p = 0.001$) were established in a previous study [22].

The Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) was used to assess subjective sleep quality and sleep disturbances over the past month. The CPSQI comprises 19 items, with each item scored from 0 to 3 and the sum of these scores ranging from 0 to 21. A score of ≥ 5 indicates poor sleep quality [23]. The CPSQI has good internal consistency (Cronbach's $\alpha = 0.82\text{--}0.83$) and test–retest reliability ($r = 0.77\text{--}0.85$) [24]. Subjective total sleep time (TST), sleep onset latency (SOL), and sleep efficiency (SE) were obtained from the CPSQI.

The watch-like device, the Mini Motionlogger Actigraph, was used to assess objective sleep parameters, including TST, SOL, wake after sleep onset (WASO), and SE [25, 26]. The normal values for TST, SOL, WASO, and SE for healthy individuals aged 50 years are 400 mins (6.67 h), 17 min, 32 min, and 87%, respectively [27]. In addition, actigraphs are the most effective tools currently used for measuring sleep–wake rhythms in cancer survivors [15–17]. The dichotomy index ($I < 0$ value; the percentage of in-bed activity counts that are less than the median of out-of-bed counts) is an interpretable objective index ranging from 0 to 100 [28]. The $I < 0$ value of ≤ 97.5 indicates circadian rhythm disruption [29, 30]. In our study, all participants were asked to wear an actigraph unit for at least 3 consecutive days before cancer-related treatment [14]. The sleep log was coordinated with the actigraph records.

Quality of life assessment

The Chinese version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-BN20) was used to assess patients' quality of life. The EORTC-QLQ-BN20, a disease-specific supplement to the EORTC-QLQ-C30, is used to evaluate symptoms specific to brain cancer or related treatments. It consists of 20 self-reported items and is organized into four subscales that address future uncertainty (four items), visual disorder (three items), motor dysfunction (three items), and communication deficits (three items) and seven single-item scales assessing headache, seizure, drowsiness, itchy skin, hair loss, weakness of legs, and bladder control. All items are rated on a 4-point Likert-type scale, and scale scores are linearly transformed to a 0–100 scale, with high scores indicating worse quality of life. Acceptable internal consistency (Cronbach's $\alpha = 0.753\text{--}0.869$) has been established [31, 32].

Confounding factors

The Taiwanese version of the Brief Fatigue Inventory (TBFI) was used to assess fatigue severity (nine items) and its interference with daily life (six items) in the past 24 h. The first three items of fatigue severity were rated by patients at its worst, in usual scenarios, and presently within the past 24 h, with each item rated from 0 (no fatigue) to 10 (fatigue as bad as you can imagine). A score of ≥ 7 indicates “severe fatigue,” and scores of 0–6 indicate “non-severe fatigue.” The next six items describe the extent to which fatigue interferes with general activities, mood, gait, day-to-day work, interpersonal relationships, and enjoyment within the past 24 h, with each item on the scale ranging from 0 (does not interfere) to 10 (completely interferes) [33]. The TBFI yields excellent internal consistency (Cronbach's $\alpha = 0.96$ and 0.95 , respectively) and test–retest reliability (Cronbach's $\alpha = 0.89$ and 0.91 , respectively) for fatigue severity and interference [34].

The Chinese version of the Hospital Anxiety and Depression Scale is a 14-item scale, with seven items each for anxiety and depression. Each item is rated on a 4-point Likert scale (0–3), resulting in 0–21 points for each domain. A higher score indicates higher severity of depression and anxiety [35]. The scale has acceptable internal consistency (Cronbach's $\alpha \geq 0.84$) [36].

Statistical analysis

All statistical analyses were performed using SPSS for Windows (version 22.0; IBM Corporation, Armonk, NY, USA). Statistical significance was defined as $p < 0.05$. Descriptive analyses and frequency distributions were used to estimate demographic and disease characteristics. Group comparisons of demographic and disease characteristics were conducted using the independent t test and Mann–Whitney U test. A univariate linear regression model was used to identify variables related to quality of life. Variables with a p value of < 0.05 were selected for further analyses in the multivariate linear regression model to determine the association between sleep disturbances and quality of life after adjustments for possible confounders. We performed a post hoc power analysis by using G power 3.1.9.7 [37] after considering an effect size estimated from the variance explained by predictors, a two-tailed α of 0.05, and numbers of predictors.

Results

Participant characteristics

A total of 103 participants were enrolled in this study with 68 and 35 patients having benign and malignant untreated brain tumors, respectively. Only 36 patients with untreated brain tumors (26 with benign and 10 with malignant) completed the 3 consecutive days of actigraph recording before treatment. The reasons for not completing actigraph recording were tight schedule ($n = 50$), actigraph malfunction ($n = 7$), and not having the habit of wearing a wristwatch ($n = 10$). No significant difference was observed between patients who completed and did not complete actigraphy records (all $p > 0.05$, Online Appendix 1). The majority of the patients with benign and malignant tumors had meningiomas (57.4%) and glioblastomas (40%), respectively (Table 1). No significant difference was observed in demographic and clinical characteristics between the two groups, except for sex, anticonvulsant drug use, and depression level. The malignant group had a higher proportion of men, had a higher proportion of patients on anticonvulsant drugs, and had a higher level of depression than the benign group did ($p = 0.001$, 0.001 , and 0.01 , respectively).

Table 1

Demographic and clinical characteristics of patients with benign and malignant brain tumor (n = 103)

Characteristics	Benign tumor (n = 68)		Malignant tumor (n = 35)		<i>p</i>
	n	%	n	%	
Male	20	29.4	24	68.6	0.001
Age, <i>M</i> (SD)	49.2	11.1	47.8	12.5	0.55
BMI, <i>M</i> (SD)	24.7	4.3	24.2	3.9	0.57
College degree or above	32	47.1	15	42.9	0.69
Married	58	85.3	26	74.3	0.17
Employment	46	67.6	26	74.3	0.49
Newly diagnosed	65	95.6	29	82.9	0.06
Charlson comorbidity index, <i>M</i> (SD)	1.1	1.2	1	1.2	0.72
KPS score, <i>M</i> (SD)	89.9	3.2	88	6.8	0.13
Steroids use	2	2.9	2	5.7	0.60
Anticonvulsant drug use	2	2.9	11	31.4	0.001
Sedative-hypnotic use	11	16.2	3	8.6	0.37
Type of benign tumor					NA
Meningioma	39	57.4	-		
Pituitary tumor	27	39.7	-		
Others ¹	2	2.9	-		
Type of malignant tumor					NA
Glioblastoma	-		14	40	
Astrocytoma	-		7	20	
Anaplastic Oligodendroglioma	-		4	11.4	

M mean, SD standard deviation, BMI Body Mass Index, KPS Karnofsky performance scale, WHO World Health Organization, HADS Hospital Anxiety and Depression Scale, TBFI Taiwanese version of Brief Fatigue Inventory, NA Not Applicable.

Others¹: Hemangioblastoma, Schwannoma.

Others²: Anaplastic astrocytoma, Anaplastic Ependymoma, Chordoid glioma, Chondrosarcoma, Large B cell lymphoma, Neurocytoma, Oligodendroglioma, Pineal tumor.

Characteristics	Benign tumor (n = 68)		Malignant tumor (n = 35)		<i>p</i>
Others ²	-		10	28.6	
WHO Grade of brain tumor					NA
Grade 1	61	89.7	-		
Grade 2	7	10.3	13	37.1	
Grade 3	-		6	17.1	
Grade 4	-		16	45.7	
Tumor location					NA
Frontal	13	19.1	11	31.4	
Temporal	3	4.4	10	28.6	
Parietal	3	4.4	2	5.7	
Occipital	2	2.9	1	2.9	
Fronto-temporal	4	5.9	1	2.9	
Fronto-parietal	1	1.5	1	2.9	
Parieto-occipital	1	1.5	1	2.9	
Temporo-parietal	-		1	2.9	
Brain stem	3	4.4	4	11.4	
Suprasellar	31	45.6	1	2.9	
Ventricle	-		2	5.7	
Cerebellopontine angle	3	4.4	-		
Cerebral falx	2	2.9	-		
Cerebellum	1	1.5	-		
Posterior fossa	1	1.5	-		

M mean, SD standard deviation, BMI Body Mass Index, KPS Karnofsky performance scale, WHO World Health Organization, HADS Hospital Anxiety and Depression Scale, TBFI Taiwanese version of Brief Fatigue Inventory, NA Not Applicable.

Others¹: Hemangioblastoma, Schwannoma.

Others²: Anaplastic astrocytoma, Anaplastic Ependymoma, Chordoid glioma, Chondrosarcoma, Large B cell lymphoma, Neurocytoma, Oligodendroglioma, Pineal tumor.

Characteristics	Benign tumor (n = 68)		Malignant tumor (n = 35)		<i>p</i>
TBFI, <i>M</i> (SD)	1.9	1.8	2.7	2.4	0.10
HADS-Anxiety, <i>M</i> (SD)	5.7	3.4	6.1	3.8	0.55
HADS-Depression, <i>M</i> (SD)	4.6	3.6	6.5	3.6	0.01
M mean, SD standard deviation, BMI Body Mass Index, KPS Karnofsky performance scale, WHO World Health Organization, HADS Hospital Anxiety and Depression Scale, TBFI Taiwanese version of Brief Fatigue Inventory, NA Not Applicable.					
Others ¹ : Hemangioblastoma, Schwannoma.					
Others ² : Anaplastic astrocytoma, Anaplastic Ependymoma, Chordoid glioma, Chondrosarcoma, Large B cell lymphoma, Neurocytoma, Oligodendroglioma, Pineal tumor.					

Distribution of self-reported sleep disturbances

The mean scores and prevalence for self-reported sleep outcomes are presented in Table 2. We did not observe a significant difference in terms of self-reported sleep outcomes between the malignant tumor and benign tumor groups. Overall, the mean scores for the CAIS, CPSQI, and CESS were 7.8, 11.0, and 2.6, with the prevalence of insomnia, poor sleep quality, and excessive daytime sleepiness being 59.2%, 77.7%, and 4.9%, respectively, based on the cutoff points of the scales, indicating that the participants with malignant and benign tumors experienced insomnia and poor sleep quality but not excessive daytime sleepiness before treatment. Moreover, we did not observe any significant differences in the subjective sleep parameters derived from the CPSQI between the two groups (all $p > 0.05$), with mean values of 425.5 min for TST, 21.8 min for SOL, and 94.94% for SE in all patients.

Table 2
Self-reported sleep parameters in benign and malignant brain tumor patients (n = 103)

Variables	All (n = 103)		Benign (n = 68)		Malignant (n = 35)		<i>p</i>
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
CAIS, <i>M (SD)</i>	7.8	(4.7)	7.5	(4.1)	8.3	(5.7)	0.49
Insomnia (CAIS ≥ 8), <i>n (%)</i>	61.0	(59.2)	42	(61.8)	19	(54.3)	0.46
CPSQI	11.0	(5.5)	11.1	(5.3)	10.8	(6.1)	0.79
Poor sleep quality (CPSQI ≥ 5), <i>n (%)</i>	80	(77.7)	55	(80.9)	25	(71.4)	0.28
CESS	2.6	(3.6)	2.3	(3.4)	3.2	(3.9)	0.24
Excessive Daytime sleepiness (CESS > 10), <i>n (%)</i>	5	(4.9)	3	(4.4)	2	(5.7)	1.00
Total sleep time (min)	425.5	(85.8)	418.1	(77.0)	439.9	(100.4)	0.27
Sleep onset latency (min)	21.8	(17.3)	22.8	(16.8)	19.8	(18.5)	0.40
Sleep efficiency (%)	94.94	(4.21)	94.67	(4.03)	95.48	(4.54)	0.35
CAIS, Chinese version of Athens Insomnia Scale; CPSQI, Chinese version of Pittsburgh Sleep Quality Index; CESS, Chinese version of Epworth Sleepiness Scale; Total sleep time, sleep onset latency, and sleep efficiency were derived from the reports of the CPSQI.							

Distribution of objective sleep parameters

Objective sleep parameters are reported in Table 3. A total of 36 participants with brain tumors (26 benign and 10 malignant) completed the actigraphy assessment. The mean values for TST, SOL, SE, and WASO were 374.2 min, 4.4 min, 92.5%, and 31.6 min, respectively. The comparisons of the four sleep parameters did not reveal significant differences between the benign and malignant groups (all $p > 0.05$). The prevalence of circadian rhythm disruption ($I < 0$ value ≤ 97.5) was higher in the malignant group (70%) than in the benign group (57.7%); however, the difference was not statistically significant ($p = 0.71$).

Table 3
Distribution of objective sleep parameters measured by actigraphy (n = 36)

Variables	ALL (n = 36)		Benign (n = 26)		Malignant (n = 10)		<i>p</i>
	Mean	(SD)	Mean	(SD)	Mean	(SD)	
Total sleep time (min)	374.2	(124.8)	386.0	(126.8)	343.8	(120.5)	0.53
Sleep onset latency (min)	4.4	(2.6)	4.1	(2.4)	5.2	(2.9)	0.66
Sleep efficiency (%)	92.5	(4.1)	93	(3.3)	91.2	(5.7)	0.51
Wake after sleep onset (min)	31.6	(16.2)	32.1	(16.7)	30.4	(15.5)	0.86
Dichotomy I < O value	95.4	(6.1)	96	(5.3)	93.7	(7.9)	0.75
I < O ≤ 97.5, <i>n</i> (%)	22	(61.1)	15	(57.7)	7	(70.0)	0.71
Mann–Whitney U test and Chi-square tests were used to perform the analyses. I < O ≤ 97.5 indicates having circadian disruption.							

Association between sleep disturbances and quality of life

The distribution of quality of life scores in patients with untreated benign and malignant brain tumors is shown in Online Appendix 2. Headache and future uncertainty were the most common complaints in both groups. Overall, the global score in the malignant group was significantly higher than in the benign group (18.4 vs. 10.3, $p = 0.004$), indicating that quality of life is more impaired in patients with malignant brain tumors than in those with benign brain tumors.

The univariate linear regression model suggested that steroid use, brain tumor type (malignant), physical performance status, insomnia, excessive daytime sleepiness, poor sleep quality, fatigue, anxiety, and depression were associated with quality of life (all $p < 0.05$) and were sequentially entered into a multivariate linear regression model (Table 4). With consideration of other confounding factors, patients with untreated malignant brain tumors had poorer quality of life than did those with untreated benign tumors ($p = 0.01$). Insomnia ($B = 0.55$, $p = 0.02$) was the only sleep variable independently correlated with quality of life in patients with untreated benign and malignant brain tumor after adjusting for potential confounders (adjusted $R^2 = 0.60$).

Table 4
The univariate and multivariate linear regression models of quality of life (n = 103)

Variables	Univariate				Multivariate			
	<i>B</i>	SE	95% CI	<i>p</i>	<i>B</i>	SE	95% CI	<i>p</i>
Female	-2.90	2.26	-7.38 to 1.59	0.20				
College degree or above	-1.69	2.26	-6.17 to 2.78	0.46				
Married	-1.72	2.90	-7.48 to 4.03	0.55				
Employment	-2.44	2.44	-7.29 to 2.41	0.32				
Recurrent	-1.66	3.99	-9.56 to 6.25	0.68				
Steroids use	13.72	5.67	2.47 to 24.96	0.02	9.96	3.79	2.44 to 17.48	0.01
Anticonvulsant drug use	3.27	3.38	-3.43 to 9.97	0.34				
Sedative-hypnotic use	5.63	3.24	-0.80 to 12.05	0.09				
Malignant brain tumor	8.03	2.24	3.59 to 12.48	0.001	4.26	1.59	1.09 to 7.43	0.01
Age	0.01	0.10	-0.18 to 0.21	0.92				
BMI	-0.18	0.27	-0.72 to 0.37	0.52				
CCI	0.31	0.97	-1.61 to 2.24	0.75				
KPS	-0.80	0.22	-1.24 to -0.36	0.001	-0.32	0.16	-0.65 to -0.04	0.047
CAIS	1.42	0.19	1.03 to 1.80	0.001	0.55	0.24	0.08 to 1.02	0.02

The final multivariable linear regression model yielded adjusted $R^2 = 0.6$, $p = 0.001$

BMI Body Mass Index, CCI Charlson Comorbidity Index, KPS Karnofsky performance scale, *B* B coefficient (slope) of linear regression model, CI confidence interval. CAIS, Chinese version of the Athens Insomnia Scale; CESS, Chinese version of the Epworth Sleepiness Scale; CPSQI, Chinese version of the Pittsburgh Sleep Quality Index; TBFI, Taiwanese version of Brief Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale.

Variables	Univariate				Multivariate			
CESS	1.17	0.30	-9.56 to 6.25	0.001	0.28	0.24	-0.20 to 0.75	0.25
CPSQI	0.82	0.19	0.45 to 1.19	0.001	0.13	0.18	-0.23 to 0.50	0.46
BFI	2.68	0.48	1.73 to 3.63	0.001	0.55	0.44	-0.33 to 1.43	0.22
HADS-Anxiety	1.62	0.28	1.07 to 2.18	0.001	0.47	0.27	-0.07 to 1.01	0.09
HADS-Depression	1.92	0.24	1.44 to 2.40	0.001	0.87	0.27	0.33 to 1.41	0.002
The final multivariable linear regression model yielded adjusted $R^2 = 0.6$, $p = 0.001$								
BMI Body Mass Index, CCI Charlson Comorbidity Index, KPS Karnofsky performance scale, B coefficient (slope) of linear regression model, CI confidence interval. CAIS, Chinese version of the Athens Insomnia Scale; CESS, Chinese version of the Epworth Sleepiness Scale; CPSQI, Chinese version of the Pittsburgh Sleep Quality Index; TBFI, Taiwanese version of Brief Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale.								

After considering an effect size of 0.3, derived from the variance explained by predictors (0.6), a two-tailed α of 0.05, and numbers of predictors ($k = 9$), a post hoc power of 0.98 was suggested.

Discussion

Similar to the finding of a population-based study [38], we found that patients with untreated benign and malignant brain tumors exhibited similar sleep complaints at the untreated stage; specifically, the patients had a high prevalence of self-reported insomnia and poor sleep quality. Patients with brain tumors experience a disruption of sleep–wake patterns that is associated with major dysfunction in the hypothalamic–pituitary axis that affects both Process S (homeostasis) and Process C (circadian) in the Two-Process Model of Sleep Regulation [39]. Furthermore, patients may experience sleep disturbance due to injury to the suprachiasmatic nucleus, which leads to disruption in the circadian rhythm [39]. In addition, depression and anxiety, psychologically predisposing factors, may contribute to sleep disturbances [40]. Notably, the findings of our study regarding the psychological relationship between mood and sleep disturbances among patients with untreated malignant and benign tumors were contradictory, with results for patients with untreated malignant brain tumors supporting a positive association and those in patients with untreated benign brain tumors disproving the association. Because the exact underlying mechanism could not be ascertained by the current study, future studies investigating the matter are warranted.

The $I < 0$ value has become the most clinically relevant circadian marker [41]. Our findings revealed that 70% and 57.7% of the patients with malignant and benign tumors, respectively, experienced circadian

rhythm disruption before cancer-related treatments, which are much higher rates than those reported for other advanced cancers (ranging from 31.3–54.9%) [42]. A recent scoping review further suggested that circadian disruption is linked to not only physical and psychological symptoms (e.g., fatigue, appetite loss, pain, and depression) but also to low quality of life and survival [42]. Thus, health-care providers should provide timely and effective interventions that target circadian rhythm disruption in patients with untreated brain cancer to optimize recovery in this population.

We determined that only 4.4% and 5.7% of the patients with malignant and benign brain tumors, respectively, experienced excessive daytime sleepiness before any treatment, which are much lower rates than those previously reported (25–70%) [12, 38]. One of the reasons for the discrepancy between our findings and prior reports is the type of cancer-related treatment the patients underwent; a previous study reported that > 90% of the patients with primary brain tumors who underwent cranial radiation therapy experienced excessive daytime sleepiness [5]. Cranial radiation therapy may affect melatonin and hypocretin (orexin) secretion, which contributes to excessive daytime sleepiness in patients with brain tumors [39]. This is the first investigation to report a low frequency of excessive daytime sleepiness in patients with untreated malignant and benign brain tumors, and further investigation is required to verify our findings.

Although previous investigations [43, 44] have suggested that insomnia is associated with poor quality of life in cancer survivors, knowledge regarding the matter in patients with brain tumors is still limited. Our study revealed that self-reported insomnia is the only sleep parameter associated with quality of life among patients with untreated primary brain tumors. Patients with brain cancer who have insomnia may experience impaired neuropsychological functioning, which may subsequently impact work productivity as well as the return-to-work process, leading to deficits in quality of life [45]. Programs aimed at improving sleep quality and quantity should be implemented to help patients with primary brain tumors to improve or maintain their quality of life as much as possible.

Limitations

Although we adopted standardized, multifaceted sleep assessments to evaluate sleep disturbance in patients with untreated malignant and benign brain tumors, our study still has several limitations. First, we enrolled patients from only three medical centers in northern Taiwan, limiting the external generalizability of our findings. Second, only approximately one-third of the participants completed the actigraphy assessment, which may compromise the internal validity of the objective sleep data.

Conclusion

The current study determined that the prevalence of insomnia, poor sleep quality, and excessive daytime sleepiness was 59.2%, 77.7%, and 4.9%, respectively, in patients with primary brain tumors. Approximately 60% of the patients with primary brain tumors experienced circadian rhythm disruption. Insomnia was the only sleep parameter that independently correlated with quality of life. Moreover, patients with untreated

malignant brain tumors with depressive symptoms tend to have a worse quality of life. Further research on adults with untreated benign or malignant tumors is required to determine the association between sleep disturbances and tumor histology. Future studies that explore sleep trajectory before and after treatment in patients with benign or malignant tumors are warranted.

Declarations

Author contributions

PCL, PYC, KCW, JHL, and HYC conceptualized and designed the study, assisted in data collection, analyzed the data, and drafted the initial manuscript; PCL, PYC, and HYC critically analyzed the data and reviewed the manuscript. PCL, PYC, KCW, JHL, MRL, MCW, and HYC helped in data collection and critically reviewed the manuscript. All authors have approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability

Data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest: The authors declare no potential conflicts of interest regarding the authorship and publication of this article.

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