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ORIGINAL ARTICLE

Preoperative sleep disruption and postoperative functional disability in lung surgery patients: a prospective observational study

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Abstract

Purpose Our aims were to evaluate the prevalence of preoperative acute sleep disruption in the hospital and to assess perioperative sleep quality and the effects of acute sleep disruption on postoperative functional recovery in a surgical setting.

Methods This prospective observational study included 24 patients aged ≥ 20 years who underwent video-assisted thoracoscopic surgical lobectomy for lung cancer under general anesthesia at a tertiary hospital in Japan between October 2016 and May 2017. Actigraphy was performed for 7 days in the hospital, including the night before surgery. We defined acute sleep disturbance as less than 85% preoperative sleep efficiency and analyzed its effect on postoperative functional disability using the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) and Mann–Whitney *U* testing. The perioperative change in sleep efficiency was compared using a Dunn analysis. A high score on the WHODAS 2.0 is indicative of impaired function.

Results Nineteen (79.1%) patients had low sleep efficiency in the hospital prior to surgery. Three months after surgery, the 12-item WHODAS 2.0 score was higher in patients with acute sleep disturbance than in those without it (38.8 versus 33.3, $p = 0.02$, effect size 0.5). Sleep efficiency decreased significantly on the 5th postoperative day in patients with acute sleep disturbance.

Conclusions Our results showed a high prevalence of acute sleep disturbance. Patients with acute sleep disruption had low postoperative sleep efficiency and impaired functional ability three months after surgery.

Keywords 12-item World Health Organization Disability Assessment Schedule 2.0 · Sleep disruption · Lung surgery · Observational study

Introduction

Despite improvements in surgical and anesthetic techniques, sleep disruption remains a challenging problem in surgical settings. Sleep disruption, including sleep fragmentation and poor sleep quality are prevalent after surgery, and can result in hyperalgesia and a delay in postoperative recovery [1–3].

In addition to postoperative sleep, preoperative sleep quality also affects postoperative patient outcomes, as patients with poor sleep quality before surgery tend to experience postoperative delirium [4].

Although previous studies have focused mainly on early postoperative outcomes such as the incidence of postoperative complications or length of hospital stay, patient-oriented outcomes such as functional recovery after discharge have recently started to attract attention [5–7]. However, few studies have investigated the effects of preoperative sleep disruption on postoperative patient-oriented outcomes. The World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) was developed by the World Health Organization as a standardized evaluation tool to measure health and disability [8]. The WHODAS 2.0 score is a valid and reliable assessment tool for surgical patients, and is used to measure the difference in health and disability before and

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after a specific intervention, such as a surgical procedure [8, 9].

We conducted a prospective observational study to examine the prevalence of sleep disruption at home and during hospitalization, the change in perioperative sleep quality, and the relationship between preoperative sleep quality and postoperative functional disability. We hypothesized that patients with low preoperative sleep quality in the hospital would have high functional disability following surgery.

Methods

Ethical standards

This prospective observational study was approved by the Institutional Review Board of Nara Medical University (Kashihara, Nara, Japan; Chairperson Prof. M. Yoshizumi, Approval no. 1378, August 25, 2016).

Trial registration

This study was registered in the following clinical trial registry: The relationship between video-assisted thoracic surgery and postoperative quality of life, https://upload.umin.ac.jp/cgibin/ctr/ctr_view_reg.cgi?recptno=R000027373, UMIN000024660.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained preoperatively from each study patient.

Patient selection

The study was conducted at Nara Medical University between October 2016 and May 2017. The study had the following inclusion criteria: (1) Japanese-speaking patients aged ≥ 20 years who were undergoing video-assisted thoracoscopic surgical lobectomy for lung cancer under general anesthesia; (2) anticipated hospital stay ≥ 7 days, including 1 day of hospitalization prior to surgery. Patients were excluded if they: (1) refused to participate in the study; (2) had taken sleep medication prior to arriving at the hospital; (3) had cognitive dysfunction, psychiatric disease, or motor dysfunction; or (4) were not able to complete the questionnaires on their own.

Sleep measures

Sleep was examined in three settings: at home, in the hospital the day before surgery, and in the hospital postoperatively.

Preoperative sleep disruption was evaluated at home using the Pittsburgh Sleep Quality Index (PSQI), which subjectively evaluates sleep quality over the previous 30 days [10]. The empirically determined cut-off value of the PSQI to distinguish those with chronic sleep disruption is ≥ 6 [10].

In the hospital, the gold standard for measuring sleep stage is polysomnography; however, it is difficult to conduct polysomnography for several days before and after surgery. Therefore, a wristwatch-like actigraphy device, which is composed of a 3-axis accelerometer and is easy to wear, was used. We used a wrist actigraph to continuously obtain a sleeping index. Actigraphy has a high correlation with polysomnography for total sleep time, wake time, and sleep efficiency [11]. Patients wore the WGT3X-BT monitor (ActiGraph, Pensacola, FL, USA) on their wrist from 1 day before surgery to 6 days after surgery, except during the operation period. Patients also kept sleep diaries and recorded their total sleep time and time in bed, which were needed to calculate sleep efficiency (total sleep time/time in bed) from the actigraph data (Fig. 1). Patients did not record the time spent on the bed, but the time they tried to go to sleep in their sleep diaries. Preoperative sleep efficiency < 85% was defined as acute sleep disruption [12].

Outcome measures

The primary outcome measure was the score of the 12-item WHODAS 2.0, which is the short version of the WHODAS 2.0, on 3 months after surgery. The 12-item WHODAS 2.0 is an assessment tool used to evaluate disability and health conditions over a 30-day period. It consists of six domains including cognition, mobility, self-care, getting along, life activities, and participation with 12 items. For each item, the patient can select one of the five choices. Depending on the choice selected, the score ranges from 0 (none) to 4 (extreme) [13]. The total score, calculated using the item-response theory, ranges from 0 to 100 (0 = no disability, 100 = full disability) [13]. The secondary outcome measure was the prevalence of preoperative sleep disruption and the change in sleep efficiency over the first 6 postoperative days.

Perioperative management

General anesthesia was induced using fentanyl or remifentanil with propofol and maintained using sevoflurane (end-tidal concentration: 1.5–1.8 vol%) or propofol with fentanyl,

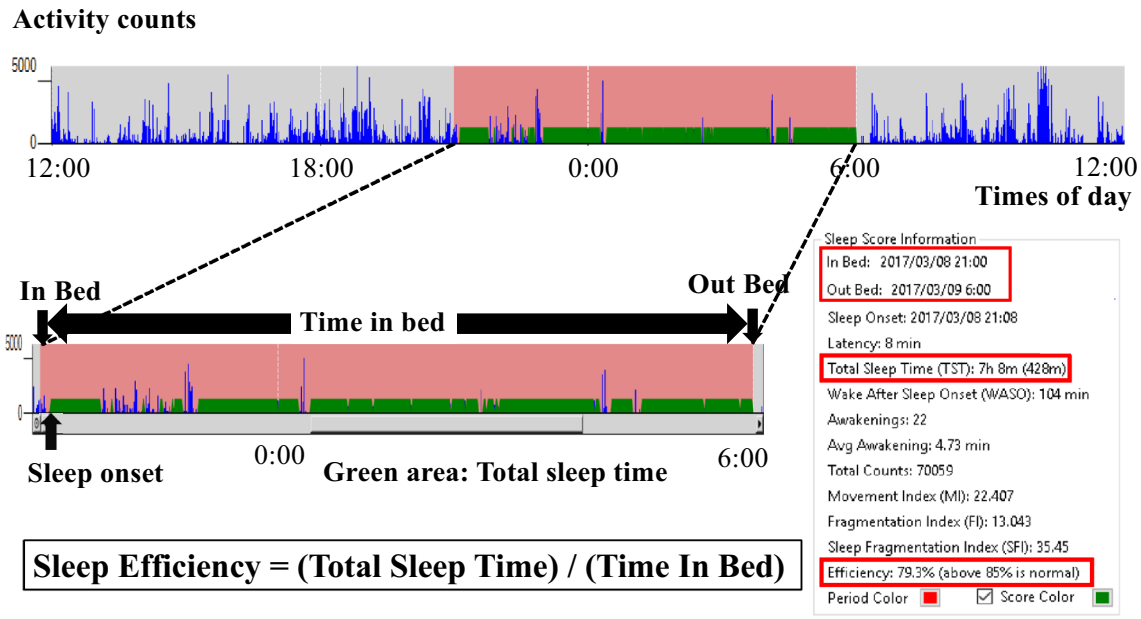

Fig. 1 The output from actigraph (reprehensive case). The *x*-axis and *y*-axis show the times of day and activity counts. The orange box shows the time spend on the bed recorded in patient's sleep diary, the green box shows the sleeping time which is automatically determined by the actigraph. The vertically extending blue jaggedness of each time zone indicates activity

remifentanil, and rocuronium. Propofol, when used to maintain general anesthesia, was titrated to achieve a target bispectral-index range of 40–60. The type of sedative and narcotic was dependent on the anesthesiologist. All patients received either intravenous patient-controlled analgesia or patient-controlled epidural analgesia postoperatively.

Demographic information, evaluation items, and follow-up

Prior to surgery, patient age, sex, height, weight, blood pressure (and presence of hypertension), respiratory function (including percent vital capacity and forced expiratory volume 1.0 s %, history of smoking, presence of diabetes mellitus, serum albumin level, total lymphocyte count, serum creatinine level, STOP-BANG ("Snoring, Tiredness during daytime, Observed apnea, high blood Pressure, Body mass index, Age, Neck circumference, Gender") sleep questionnaire score, anxiety and depression levels, catastrophic thoughts about pain, and the 12-item WHODAS 2.0 score were assessed. Anxiety and depression and catastrophic thoughts about pain were evaluated using the Hospital Anxiety and Depression Scale (HADS) [14] and the Pain Catastrophizing Scale [15], respectively. HADS is a self-assessment tool used to evaluate anxiety and depression that consists of 14 items. Patients with a HADS score greater than or equal to 11 are considered to have anxiety and depression. The Pain Catastrophizing Scale consists of 13 items, each of which is rated on a scale from 0 to 4. Points are allocated according to the answer to each item; if the total score is greater than or equal to 30, the level of catastrophic thinking is considered high. Additionally, a prognostic nutritional index was calculated as $10 \times$ serum albumin (g/dL) $+ 0.005 \times$ total lymphocyte count (per mm^3) [16]. Intraoperative data were recorded by the anesthesiologist and included the type of sedatives, type and amount of narcotics required to maintain anesthesia, duration of surgery, duration of anesthesia, water and blood balance, and postoperative pain management. On the second postoperative day, pain at rest and with coughing was evaluated using a numerical rating scale. The length of hospital stay was recorded upon discharge. Three months after surgery, patients were sent several self-assessment questionnaires by mail, including the 12-item WHODAS 2.0 and the persistent post-thoracotomy pain questionnaire, a screening questionnaire that identifies neuropathic components of pain [17]. Patients were provided with a stamped envelope for return postage. Our sample size was a viable sample, as the expected biologic effect previously had not been known, and thus could not have been used in a formal power analysis.

Statistical analyses

Data are presented as the median and interquartile range or number and percent. We classified patients into two groups according to their preoperative sleep efficiency and each evaluation item was analyzed with a univariate analysis that used a two-sided Fisher's exact test or a Mann–Whitney *U*

test. The change in sleep efficiency was analyzed by Dunn analysis. The null hypothesis was rejected if $p < 0.05$. We calculated not only the p value but also the Cohen's effect size for each score of the 12-item WHODAS 2.0 [18]. All data were analyzed using SPSS version 22.0 (IBM Inc., Armonk, NY, USA), except for the a priori comparisons and Dunn analysis, which were performed using Statflex version 6.0 (Arctech Inc., Tokyo, Japan).

Results

Twenty-four participants were enrolled in this study. There were no patients who received sleep medication after enrolled in our study. Seven patients had incomplete postoperative sleep data; 6 patients were discharged from the hospital within 4 days of surgery, and one patient had no sleep data for the third postoperative day. Therefore, the primary outcome was analyzed using the data from 24 patients, but the change in sleep efficiency was analyzed using data from 17 patient.

The patients' preoperative data are shown in Table 1. The median preoperative sleep efficiency [interquartile range] was 77.1 [9.0] and we saw 19 (79%) patients who had low sleep efficiency before surgery. Five patients (21%) had a score ≥ 6 on the PSQI, which was indicative of subjective sleep disruption. Of the 5 patients with chronic sleep disruption, 4 experienced acute sleep disruption, though one patient had normal sleep efficiency in the hospital. As shown in Table 1, we saw no statistically significant difference in the prevalence of acute sleep disruption between the patients with and without chronic sleep disruption ($p = 1$).

Intraoperative and postoperative data are shown in Tables 2 and 3. As shown in Table 4, the 12-item WHODAS 2.0 score before and after surgery was not significantly different in patients without acute sleep disruption. However, the patients with acute sleep disruption had a significantly higher 12-item WHODAS 2.0 scores postoperatively ($p = 0.02$; effect size: 0.5) than patients without acute sleep disruption. The analysis of each domain of the 12-item WHODAS 2.0 showed no statistical significant between two groups. However, we found that postoperative mobility, although not statistically significant ($p = 0.059$), had the medium effect size of 0.39.

The demographics and perioperative data for 17 patients with complete data on sleep efficiency are shown in Supplementary Tables 1–3, and there was no statistically significant difference. Figure 2 shows the perioperative change in sleep efficiency. Data from the day of surgery and the 1st postoperative day were excluded, since some patients were not able to complete their sleep diaries on those days. The sleep efficiency decreased significantly on the 5th postoperative day in patients with preoperative sleep disruption.

Table 1 Preoperative patients' demographics

	Total ($n = 24$)	Acute sleep disruption (+) ($n = 19$)	Acute sleep disruption (−) ($n = 5$)	p value
Preoperative data				
Age (years)	69 [4.3]	69 [3.9]	66 [6.8]	0.61
Male	17 (70.8)	14 (73.7)	3 (60)	0.6
BMI (kg/m^2)	22.6 [1.6]	22.6 [1.7]	22.5 [0.5]	0.97
Hypertension	12 (50)	10 (52.6)	2 (40)	1
%VC	104 [11]	108 [10]	98 [7.6]	0.28
FEV%	75 [5.0]	75 [5.1]	77 [4.0]	0.47
History of smoking	16 (66.6)	14 (73.7)	2 (40)	0.28
Diabetes mellitus	3 (12.5)	3 (15.7)	0 (0)	0.57
Serum albumin (g/dL)	4.3 [0.1]	4.2 [0.1]	4.5 [0.2]	0.21
Serum creatinine (mg/dL)	0.83 [0.1]	0.83 [0.1]	0.84 [0.2]	0.91
PNI	50.5 [3]	50.5 [2.8]	50.5 [3.8]	0.94
STOP-BANG				0.32
0–2 (Low risk)	9 (37.5)	6 (31.6)	3 (60)	
3–4 (Intermediate risk)	15 (62.5)	13 (68.4)	2 (40)	
Anxiety and depression	2 (8.3)	1 (5.2)	1 (20)	0.38
PCS 30 ≤	3 (12.5)	1 (5.2)	2 (40)	0.09
PSQI 6 ≤	5 (20.8)	4 (21)	1 (20)	1

All results are presented as median [interquartile range] or number (percent)

BMI body mass index, *VC* vital capacity, *FEV* forced expiratory volume, *PNI* prognostic nutritional index, *PCS* Pain Catastrophizing Scale, *PSQI* Pittsburgh Sleep Quality Index, *NRS* numerical rating scale

Table 2 Intraoperative patient's data

	Total ($n=24$)	Acute sleep disruption (+) ($n=19$)	Acute sleep disruption (−) ($n=5$)	p value
Types of sedatives				0.56
Sevoflurane or desflurane	18 (75)	15 (79)	3 (60)	
Propofol	6 (25)	4 (21)	2 (40)	
Dose of fentanyl (mcg/kg)	1.96 [1.4]	1.72 [1.7]	3.08 [1.4]	0.61
Dose of remifentanil (mcg/kg)	13.8 [4.8]	14.9 [4.0]	8.9 [6.6]	0.27
Duration of surgery (min)	138 [21]	136 [28.6]	140 [18.5]	0.91
Duration of anesthesia (min)	185 [23]	183 [21]	188 [24]	0.8
Water balance (mL/kg)	15.7 [4.8]	17.7 [4.4]	11.0 [3.7]	0.09
Postoperative pain management				1
Epidural anesthesia	21 (87.5)	17 (89.4)	4 (80)	
Intravenous fentanyl	3 (12.5)	2 (10.5)	1 (20)	

All results are presented as median [interquartile range] or number (percent)

Table 3 Postoperative patient's data

	Total ($n=24$)	Acute sleep disruption (+) ($n=19$)	Acute sleep disruption (−) ($n=5$)	p value
NRS of pain at rest on 2POD	3.0 [1]	3.0 [1.5]	2.0 [1.6]	0.38
NRS of pain with coughing on 2POD	6.0 [1]	5.5 [1.5]	6 [0.9]	0.87
Length of hospital stay (days)	8 [2]	8 [2]	8 [1]	0.88
Data at 3 months after surgery				
NRS of pain at rest	0.0 [0]	0.0 [0.4]	0.0 [0]	0.2
NRS of pain with coughing	0.0 [0.5]	0.0 [1.3]	0.0 [0]	0.12
Possible neuropathic pain				0.73
≦ 5 (No possible neuropathic pain)	0 (0)	0 (0)	0 (0)	
6–8 (Possible neuropathic pain components)	20 (83.3)	15 (78.9)	5 (100)	
9–11 (Probable neuropathic pain)	3 (12.5)	3 (15.7)	0 (0)	

All results are presented as median [interquartile range] or number (percent)

NRS numerical rating scale, *POD* postoperative days

Discussion

The findings of the current study suggest that in patients who underwent video-assisted thoracoscopic surgical lobectomy under general anesthesia, sleep was disrupted to a greater extent in the hospital than at home, and sleep efficiency was significantly lower on the 5th postoperative day than it was before surgery. Further, acute sleep disruption was associated with functional disability 3 months after surgery.

A previous observational study that included arthroplasty patients with a mean age of 76 years showed that 57% had chronic sleep disruption [19]. The high incidence rate found in that study can be attributed to the fact that the study group did not exclude patients who regularly took sleep medication. In our cohort, even though the prevalence of chronic sleep disruption was lower (20.8%), acute sleep disruption occurred in 19 patients (79.1%). Another study explored the relationship between psychological factors and sleep efficiency using actigraphy-based monitoring the night before surgery, and found that intrusive thoughts, anxiety, and emotional well-being were related to sleep duration the night before surgery [2]. We saw only two patients with anxiety and depression in our cohort. Additionally, in the hospital, environmental factors and health care practices, including noise, continuous ambient light, and frequent vital sign measurements and tests contribute to sleep disruption in older patients, who are vulnerable to change [20].

It is conceivable that surgical procedures or perioperative opioid administration affect postoperative sleep disruption. Previous studies showed that it took 4 days and 2 months for sleep to recover to preoperative levels after arthroplasty and cardiac surgery, respectively [21, 22]. However, the continuous change in objective sleep quality during the

Table 4 The pre- and postoperative data of 12-item WHODAS 2.0

	Total ($n=24$)	Acute sleep disruption (+) ($n=19$)	Acute sleep disruption (−) ($n=5$)	p value	Effect size
Preoperative 12-item WHODAS 2.0					
Total score	33.3 [4.1]	36.1 [4.1]	33.3 [1.0]	0.24	0.24
Each domain					
Cognition	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	0.27	0.22
Mobility	2.0 [1.0]	2.0 [1.0]	2.0 [0.3]	0.33	0.2
Self-care	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	0.61	0.11
Getting along	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	1	0
Life activities	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	0.35	0.19
Participation	2.0 [0.0]	2.0 [0.0]	2.0 [0.1]	0.92	0.02
Postoperative 12-item WHODAS 2.0					
Total score	37.5 [4.8]	38.8 [5.2]	33.3 [1.0]	0.02	0.5
Each domain					
Cognition	2.0 [0.3]	2.0 [0.5]	2.0 [0.0]	0.16	0.29
Mobility	3.0 [1.0]	4.0 [0.9]	2.0 [0.3]	0.059	0.39
Self-care	2.0 [0.8]	2.0 [0.8]	2.0 [0.3]	0.098	0
Getting along	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	0.35	0.19
Life activities	2.0 [0.0]	2.0 [0.0]	2.0 [0.0]	0.27	0.22
Participation	2.0 [0.5]	2.0 [0.9]	2.0 [0.1]	0.21	0.25

All results are presented as median [interquartile range]

12-item WHODAS 2.0 12-item World Health Organization Disability Assessment Schedule 2.0

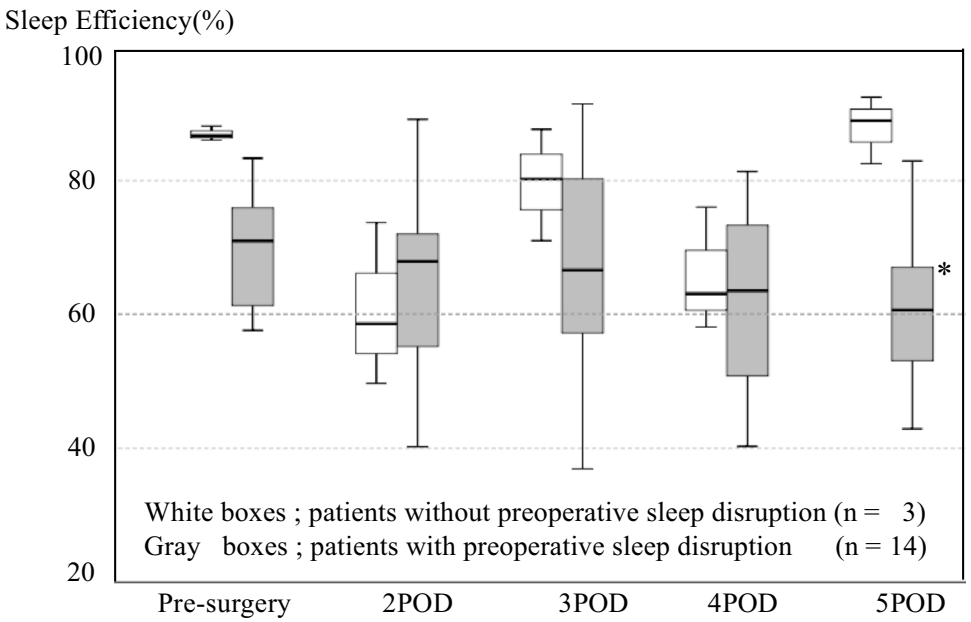

Fig. 2 Sleep efficiency results. The median sleep efficiency recorded by actigraphy is shown here for patients with preoperative sleep disruption (gray boxes) ($n=14$) versus those without preoperative sleep disruption (white boxes) ($n=3$) for the 5 monitoring periods. In the patients with preoperative sleep disruption, sleep efficiency decreases significantly on fifth postoperative day. In contrast, no POD dependence of perioperative sleep efficiency is seen in the patients without preoperative sleep disruption. The boxes show median and interquartile range; the whiskers show maximum or minimum value; *significant at $p<0.05$ by Dunn analysis compared with presurgical day; *POD* postoperative days

perioperative period has been poorly documented. Our preliminary study in women undergoing gynecological open abdominal surgery showed that sleep efficiency decreased significantly on the 3rd postoperative day and recovered to the preoperative level thereafter [23]. The exact reason why sleep efficiency decreased significantly 5 days after surgery in our cohort is unknown, but surgical stress and patient age may be related to the process of recovery of sleep efficiency.

Previous large-scale studies showed that fragmented sleep and longer wake time during the night was associated with slower walking speed and poorer daytime function [24, 25]. In addition to physical function, people with low sleep efficiency had a higher risk of cognitive impairment due to inflammatory dysregulation resulting from an immune defense response [26–29]. The relationship among sleep disruption, functional disability, and cognitive dysfunction may be explained by daytime sleepiness and fatigue [27, 30]. In our study, the sleep efficiency of patients with sleep disruption before surgery decreased significantly on the 5th postoperative day. Subsequent sleep efficiency data were not measured, but persistent sleep disruption associated with hospitalization and surgical procedures, which can affect physical and cognitive function, may have persisted since video-assisted thoracoscopic surgical lobectomy is a relatively invasive procedure. From our data, two domains of cognitive and mobility having approximately moderate effect size might contribute to postoperative functional disability, although understanding the etiology of the functional disability three months after surgery was beyond the scope of this study; thus, further studies should be conducted to elucidate its exact mechanisms.

The strengths of our study included that actigraph was used to measure patients sleep efficiency and 12-item WHODAS 2.0 was used to evaluate patient's health condition. It is recommended that the 12-item WHODAS 2.0 is superior to SF-12 to measure postoperative patients' status [31]. On the other hand, our study had some potential limitations. First, there was a difference between the measures of sleep that were used in the home and hospital. Both wrist actigraphy and the PSQI are validated tools by which sleep disruption is measured, although the PSQI is subjective. Accordingly, the PSQI is prone to self-interpretation bias; therefore, an objective evaluation of sleep disruption at home may have been beneficial. Second, actigraphy-based preoperative sleep efficiency was measured only once. It is thought that sudden changes in the environment affect sleep efficiency; therefore, it may have been preferable to take measurements over several days. However, in clinical practice, hospital stays are becoming shorter, and it is often difficult to hospitalize patients for examination. Third, this was a small study, which did not allow for the consideration of all potential covariates of postoperative functional disability. However, we tried to examine the various factors that might affect sleep and physical and mental function, such as nutritional status, anxiety and depression, and thoughts about pain. Finally, our sample size was also too small to show the exact transition of sleep efficiency. In the future, large-scale observational studies involving enough patients are needed.

In conclusion, this study found that the prevalence of acute sleep disruption after hospitalization was high even if patients did not experience sleep disruption at home. Further, we showed that acute sleep disruption was associated with functional disability three months after surgery. We see a need for further studies aimed at identifying the patients likely to experience sleep disruption during hospitalization, in addition to a need for improvements in the hospital sleep environment. Such studies would aid in reducing sleep disruption and improving postoperative physical and mental function.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this manuscript.

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