Risk factors of sleep disturbances in elderly patients after thoracic surgery: a preliminary clinical trial

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Abstract

Background

To identify the risk factors of sleep disturbances in elderly patients after thoracic surgery.

Methods

We enrolled 200 patients, all aged > 65, who underwent elective thoracic surgery and had American Society of Anesthesiology physical status II–III. We recorded general information, surgical diagnosis, type of operation, surgical duration, bleeding, nerve block, and dexmedetomidine dose given by controlled intravenous analgesia (PCIA). We used the Pittsburgh Sleep Quality Index (PSQI) at the end of PCIA to evaluate subjective sleep quality; we also recorded postoperative pain, nausea, and vomiting. We divided patients into a non-sleep disturbances group and a sleep disturbances group with PSQI $\geq$ 5 as the cutoff.

Results

A total of 76 (45%) of the patients had sleep disturbances after thoracic surgery. There were significant differences between groups in terms of chronic insomnia, hypertension, diabetes, BMI, age, surgical diagnosis, type of operation, surgical duration, bleeding, nerve block, and dexmedetomidine dose in PCIA. Logistic regression analysis revealed that chronic insomnia, BMI, diabetes, surgical diagnosis, type of operation, surgical duration, bleeding, and postoperative pain were independent risk factors of postoperative sleep disturbances. This analysis also showed that nerve block and dexmedetomidine dose in PCIA were significant protective factors of postoperative sleep disturbances.

Conclusion

Chronic insomnia, BMI, diabetes, surgical diagnosis, type of operation, surgical duration, bleeding, and postoperative pain are independent risk factors of postoperative sleep disturbances in elderly patients. Nerve block and the dose of dexmedetomidine in PCIA are protective.

Trial registration

ChiCTR2000035169; retrospectively registered on 01.08.2020.

Background

Insomnia is a subjective experience in which sleep time and sleep quality are not satisfied even though there are appropriate sleep opportunities and sleep environment, affecting social function during the day. Studies showed that, in the previous month, 5.4% of Chinese people experienced varying degrees of sleep disturbances, 25% met diagnostic criteria for insomnia, and 50% over the age of 65 suffered from insomnia [1, 2]. Insomnia affects daytime mental state, including fatigue, depression, or irritability, and

reduces life quality. It can also lead to cognitive impairment, reduce work efficiency, alertness, and judgment, especially for postoperative sleep disturbances. Postoperative sleep disturbances include insomnia, hypersomnia, narcolepsy, changed sleep structure and increased frequency waking [3, 4]. Postoperative sleep disturbances caused by general anesthesia might increase postoperative complications such as postoperative fatigue, severe anxiety and depression, delirium, and even severe stroke [5–7].

There are few studies of postoperative sleep disturbances in elderly patients. The aging of China's population and their particular medical environment will increase postoperative sleep disturbances in elderly patients. We aimed to identify the risk factors of sleep disturbance in elderly patients after thoracic surgery to provide reference for the development of effective preventive measures.

Methods

Study design and setting

This study enrolled 200 patients from August 2020 to November 2020. This prospective study was approved by the Ethics Committee of Henan Provincial People's Hospital [Ethics Committee: (2020) Lun Shen No. (100)], and written informed consent was obtained from the patients. The study was registered at www.chictr.org.cn (ChiCTR2000035169). The study protocol complied with the 1975 Declaration of Helsinki.

Characteristics of participants

We enrolled patients classified as American Society of Anesthesiologists status □ or □, were aged 65 years and older and were scheduled for elective thoracic surgery. We excluded patients with communication disturbances, inability to cooperate (e.g., language comprehension disturbances, mental illness), unstable angina pectoris or myocardial infarction within 3 months, New York Heart Association grade ≥3, severe cardiovascular and cerebrovascular diseases, those who underwent an unplanned second operation in the post-anesthesia care unit (PACU), those transferred to intensive care unit (ICU) after surgery, and those transferred from the ward to ICU after surgery.

We recruited patients in the PACU admission after August 2020. A nurse anesthetist and a PACU nurse scrutinized the medical records. During the reviewer training, the study protocol, definitions, and the case record form were explained. Initially, both reviewers practiced completing the case record forms for 20 cases together. Then, each reviewer independently examined half of the remaining 180 medical records to prepare a form for each case. Each reviewer subsequently checked every 20th form completed by the other reviewer, and a third reviewer (an anesthesiologist) randomly checked 60 of the total 200 case record forms. Finally, 200 forms were converted to electronic data for input to PASW SPSS Statistics for Windows ver. 26.0 (SPSS Inc., Chicago, IL, USA). We recorded the following: age; sex; smoking history; drinking history; chronic insomnia; hypertension; diabetes; American Society of Anesthesia classification; type of operation; surgical duration; bleeding; nerve block;

whether dexmedetomidine was included in PCIA; postoperative pain, nausea and vomiting; and the patient's subjective sleep quality evaluated by Pittsburgh Sleep Quality Index (PSQI) after 48 hours.

Preoperative preparations and anesthesia protocol

No patients received pretreatment before admission to the operating room. All patients were monitored using electrocardiography, pulse oximetry, invasive blood pressure recordings, and bispectral index. The anesthesiologist determined whether to perform PCIA with dexmedetomidine or thoracic paravertebral block after surgery, depending on the patient's condition. Subsequently, we administered a comprehensive evaluation of satisfaction with analgesia from patients and their family members at the end of PCIA (very satisfied; satisfied; general; dissatisfaction). We grouped very satisfied and satisfied as satisfaction. We considered this group as having no pain after surgery; If patients reported general or dissatisfaction, we classified them as dissatisfied, and defined this group as having postoperative pain. We used the Pittsburgh Sleep Quality Index (PSQI) questionnaire to evaluate their subjective sleep quality, including sleep quality, sleep time, sleep time, sleep efficiency, daytime dysfunction, sleep disturbances, and hypnotic drug use. The scale consists of nine questions, with 18 items, and each index is scored 0–3. The total score of each index is 21 points [8]. When the PSQI score is greater than or equal to 5, the patient is defined as having sleep disturbances. We divided patients into a non-sleep disturbances group and a sleep disturbances group.

Sample size calculation

The sample size was calculated with “Power and Sample Size.com,” an online power and sample size calculator. The primary objective of this study identified the risk factors of sleep disturbances in elderly patients after thoracic surgery. The calculation of the sample size was based on the pilot study finding that the incidence of sleep disturbances in elderly patients after thoracic surgery was approximately 45%. It was thus assumed that the incidence of sleep disturbances in elderly patients after thoracic surgery was 60%. To detect a clinically significant difference with a power of 80%, an alpha error of 0.05 (twosided), a total of 87 patients were required. To compensate for data that may be found to be missing during the retrospective review, the sample size was adjusted upward to 200 cases.

Statistical analysis

The data analysis was performed using the independent sample Student t-test, the Pearson’s chi-square test, and the Mann–Whitney U-test, and it employed the program PASW SPSS Statistics for Windows ver. 26.0 (SPSS Inc.). All descriptive data were presented as case (%), mean ± standard deviation, and median (interquartile range). Univariate analyses of each factor were performed to calculate the p-value, OR, and 95% confidence interval (CI). Multiple logistic regression analysis was performed by choosing the factors with a p-value of <0.10; p<0.05 was considered to be significant.

Results

In total, 200 patients met the inclusion criteria, and 16 patients declined to participate. We enrolled a total of 174 patients, five of whom developed delirium. The final analyses included 169 patients (Fig. 1).

The incidence of sleep disturbances in elderly patients after thoracic surgery was 45%. We performed univariable and multivariable analyses by selecting factors whose p-values were < 0.10: age, chronic insomnia, hypertension, diabetes, BMI, surgical diagnosis, type of operation, surgical duration, bleeding, nerve block, whether dexmedetomidine was included in PCIA, and postoperative pain (Table 1). We performed multiple logistic regression analysis by selecting factors whose p-values were < 0.10: chronic insomnia, diabetes, BMI, surgical diagnosis, type of operation, surgical duration, bleeding, nerve block, dose of dexmedetomidine in PCIA, and postoperative pain. Only nerve block ($p < 0.001$; OR, 0.085; 95% CI, 0.046–0.155) and dexmedetomidine ($p = 0.003$; OR, 0.772; 95% CI, 0.609–0.979) were marginally significant preventive factors for sleep disturbances in elderly patients after thoracic surgery. Chronic insomnia, BMI, diabetes, surgical diagnosis, type of operation, surgical duration, bleeding, and postoperative pain were independent risk factors of postoperative sleep disturbances in elderly patients (Table 2).

Table 1
Analysis of suspicious factors of postoperative sleep disturbances in two groups

Variable	Sleep disturbances group(n = 76)	non-sleep disturbances group(n = 93)	*p*-value
Smoking history	35.6	32.5	0.055
Drinking history	31.1	34.3	0.078
Chronic insomnia	47.7	36.0	0.014*
Hypertension	29.3	25.5	0.035*
Diabetes	27.9	22.5	0.027*
Body mass index(kg/m^2)	23.9 ± 4.3	19.4 ± 3.7	0.083
Age(yr)	78.3 ± 5.5	71.2 ± 4.7	0.077
Sex(female)	34/42	46/47	0.223
American Society of Anesthesia status			0.562
□	87.8	88.5	
□	12.2	11.5	
Type of operation			0.018*
Thoracoscopy	29.1	10.4	
Video assisted thoracoscopy	70.9	89.6	
Surgical diagnosis			0.031*
Benign tumor of lung	27.4	38.5	
Lung cancer	37.2	33.7	
Esophageal cancer	35.4	27.8	
Surgical duration	233.8 ± 108.3	185.06 ± 76.6	0.029*
Nerve block			0.011*
None	46.9	33.1	
TPVB	53.1	66.9	
Postoperative pain	48.8	22.7	0.005*

Note: Values are presented as number (%), mean ± standard deviation, or median (interquartile range).
s group, *$p < 0.05$ indicates statistical significance.

Variable	Sleep disturbances group(n = 76)	non-sleep disturbances group(n = 93)	*p*-value
Dose of dexmedetomidine in PCIA	38.9	55.6	0.011*
Bleeding	164.3 ± 33.2	101.1 ± 25.8	0.041*
Nausea	4.9	4.8	0.068
Vomiting	2.2	2.1	0.117

Note: Values are presented as number (%), mean ± standard deviation, or median (interquartile range). Combined with the non-sleep disturbances group, *$p < 0.05$ indicates statistical significance.

Table 2
Risk factors of postoperative sleep disorders in elderly patients undergoing thoracic surgery

Factors	B	S.E.	Wals	*p*-value	OR	95% CI
Chronic insomnia	0.421	0.098	18.475	0.000	1.523	1.257–1.845
Body mass index	0.919	0.454	4.107	0.043	2.508	1.031–6.102
Diabetes	0.364	0.154	5.569	0.018	1.439	1.064–1.948
Type of operation	0.535	0.184	8.418	0.004	1.707	1.190–2.450
Surgical diagnosis			11.453	0.003		
Lung cancer vs Benign tumor of lung	0.274	0.102	7.255	0.007	1.315	1.078–1.606
Esophageal cancer Vs Benign tumor of lung	0.720	0.292	6.076	0.014	2.055	1.159–3.645
Surgical duration	0.352	0.112	9.821	0.002	1.421	1.141–1.771
Nerve block	-2.466	0.308	64.283	0.000	0.085	0.046–0.155
Dose of dexmedetomidine in PCIA	-0.259	0.121	4.556	0.033	0.772	0.609–0.979
Postoperative pain	0.454	0.123	13.694	0.000	1.575	1.238–2.004
Bleeding	0.479	0.243	3.887	0.049	1.615	1.003–2.601

Note: Lung cancer vs Benign tumor of lung: Combined with the Benign tumor of lung, lung cancer is a independent risk factor of postoperative sleep disturbances in elderly patients. Esophageal cancer Vs Benign tumor of lung: Combined with the Benign tumor of lung, esophageal cancer is a independent risk factor of postoperative sleep disturbances in elderly patients.

Discussion

Postoperative sleep disturbances are manifestations of postoperative brain dysfunction, especially for elderly patients, and they are among the important risk factors for delirium, which had gradually attracted attention. Studies confirmed that extensive surgical trauma often leads to postoperative sleep disturbances, increasing the possibility of postoperative cognitive impairment [9]. The expansion of surgical incisions and the complexity of surgical types, the amount of bleeding increased, and the operation time prolonged all increase the degree of severity of surgical trauma of elderly patients; these

factors significantly increase the incidence of sleep disturbances in elderly patients. The operation time was associated with the duration of postoperative sleep disturbances, and this may have been due to the extensive surgical trauma and the severity of the patient's condition [10].

In the present study, we found the perioperative application of thoracic paravertebral block, dexmedetomidine, and reducing postoperative pain reduced the incidence of postoperative sleep disturbances in elderly patients; postoperative pain is the most harmful factor associated with postoperative sleep disturbances [11]; pain can prolong sleep latency and reduce total sleep time, while sleep disturbances increase pain sensitivity and reduce pain threshold, including pain experienced the following day. The degree of pain is also predicted by postoperative sleep quality [12]. General anesthesia disrupts sleep/wake-up cycles and other circadian rhythms [13], leading to postoperative fatigue, severe anxiety and depression, delirium, and even severe stroke [5, 7]. Volatile general anesthetics, including sevoflurane, isoflurane, and halothane, may cause short-term sleep disturbances and fragmentation [14]. Dexmedetomidine can induce bionic sleep [15], that is, natural sleep, and it does not produce dependence, tolerance, or addiction [16]. For elderly patients with minimal trauma, the application of total intravenous anesthesia combined with dexmedetomidine may reduce the incidence of postoperative sleep disturbances.

Sleep disturbances are associated with increased age [17]. In the present study, we showed that people with preoperative insomnia were more likely to have postoperative sleep disturbances. The reason may be that melatonin levels in the elderly are significantly lower than those of young people [18]. The physiological reserve of elderly patients decreases, and the prevalence of infirmity and comorbidities increases, all of which may affect the brain and central nervous system, leading to postoperative sleep disturbances [19]. Diabetes mellitus is a risk factor for long-term use of opioids and persistent pain after surgery; patients with diabetes are in chronic systemic proinflammatory states, characterized by high concentration of the inflammatory cytokine IL-6; persistent immune responses related to host defense prolong peripheral sensitization leading to pain hypersensitivity [20], and this further aggravates postoperative sleep disturbances.

We found that many factors influenced postoperative sleep disturbances, including surgical anesthetic- and patient-related factors. Other studies showed that postoperative sleep disturbances might be affected by psychological and postoperative environmental factors such as ward lighting and sound; elderly patients are a special population. We should comprehensively consider the factors associated with their postoperative sleep disturbances.

Some limitations of this study should be noted. First, postoperative sleep disorders are affected by many factors, including surgery, anesthesia and patient factors, as well as environmental factors which was not noticed by this study. Second, our study did not continue to track the recovery of patients with postoperative sleep disorders, which is the main direction of our future research.

Conclusions

Chronic insomnia, BMI, diabetes, surgical diagnosis, type of operation, surgical duration, bleeding, and postoperative pain are independent risk factors of postoperative sleep disturbances in elderly patients. Nerve block and the dose of dexmedetomidine in PCIA are protective.

Declarations

Consent for publication

All copyright owners agree to submit the paper to BMC Anesthesiology for publication. The author agrees that the copyright and related property rights of the paper shall be transferred to BMC Anesthesiology from the date of official publication of the paper.

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Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

BL: manuscript and data analysis. YL: sample detection and measurements.: human samples and data acquisition. JJ and FDT: sample detection and measurements. WZ and JQZ: design and clinical studies. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

This prospective study was approved by the Ethics Committee of Henan Provincial People's Hospital, and written informed consent was obtained from all patients.

Competing interests

The authors declare that they have no competing interests.

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References

1. Soldatos CR, Allaert FA, Ohta T, Dikeos DG: **How do individuals sleep around the world? Results from a single-day survey in ten countries**. *Sleep Med* 2005, **6**(1):5-13.
2. Crowley K: **Sleep and sleep disorders in older adults**. *Neuropsychol Rev* 2011, **21**(1):41-53.
3. Knill RL, Moote CA, Skinner MI, Rose EA: **Anesthesia with abdominal surgery leads to intense REM sleep during the first postoperative week**. *Anesthesiology* 1990, **73**(1):52-61.
4. Cavalcante AN, Hofer RE, Tippmann-Peikert M, Sprung J, Weingarten TN: **Perioperative risks of narcolepsy in patients undergoing general anesthesia: A case-control study**. *J Clin Anesth* 2017, **41**:120-125.
5. Haack M, Simpson N, Sethna N, Kaur S, Mullington J: **Sleep deficiency and chronic pain: potential underlying mechanisms and clinical implications**. *Neuropsychopharmacology* 2020, **45**(1):205-216.
6. Mashour GA, Lipinski WJ, Matlen LB, Walker AJ, Turner AM, Schoen W, Lee U, Poe GR: **Isoflurane anesthesia does not satisfy the homeostatic need for rapid eye movement sleep**. *Anesth Analg* 2010, **110**(5):1283-1289.
7. Gogenur I, Wildschiotz G, Rosenberg J: **Circadian distribution of sleep phases after major abdominal surgery**. *Br J Anaesth* 2008, **100**(1):45-49.
8. Veqar Z, Hussain ME: **Validity and reliability of insomnia severity index and its correlation with pittsburgh sleep quality index in poor sleepers among Indian university students**. *Int J Adolesc Med Health* 2017, **32**(1).
9. Ramos AR, Gardener H, Rundek T, Elkind MS, Boden-Albala B, Dong C, Cheung YK, Stern Y, Sacco RL, Wright CB: **Sleep disturbances and cognitive decline in the Northern Manhattan Study**. *Neurology* 2016, **87**(14):1511-1516.
10. Yilmaz H, Iskesen I: **Follow-up with objective and subjective tests of the sleep characteristics of patients after cardiac surgery**. *Circ J* 2007, **71**(10):1506-1510.
11. Dolan R, Huh J, Tiwari N, Sproat T, Camilleri-Brennan J: **A prospective analysis of sleep deprivation and disturbance in surgical patients**. *Ann Med Surg (Lond)* 2016, **6**:1-5.

12. Lautenbacher S, Huber C, Kunz M, Parthum A, Weber PG, Griessinger N, Sittl R: **Hypervigilance as predictor of postoperative acute pain: its predictive potency compared with experimental pain sensitivity, cortisol reactivity, and affective state**. *Clin J Pain* 2009, **25**(2):92-100.
13. Dispersyn G, Touitou Y, Coste O, Jouffroy L, Lleu JC, Challet E, Pain L: **Desynchronization of daily rest-activity rhythm in the days following light propofol anesthesia for colonoscopy**. *Clin Pharmacol Ther* 2009, **85**(1):51-55.
14. Luo M, Song B, Zhu J: **Sleep Disturbances After General Anesthesia: Current Perspectives**. *Front Neurol* 2020, **11**:629.
15. Akeju O, Hobbs LE, Gao L, Burns SM, Pavone KJ, Plummer GS, Walsh EC, Houle TT, Kim SE, Bianchi MT *et al*: **Dexmedetomidine promotes biomimetic non-rapid eye movement stage 3 sleep in humans: A pilot study**. *Clin Neurophysiol* 2018, **129**(1):69-78.
16. Keating GM: **Dexmedetomidine: A Review of Its Use for Sedation in the Intensive Care Setting**. *Drugs* 2015, **75**(10):1119-1130.
17. Paulose JK, Wang C, O'Hara BF, Cassone VM: **The effects of aging on sleep parameters in a healthy, melatonin-competent mouse model**. *Nat Sci Sleep* 2019, **11**:113-121.
18. Luboshitzky R, Shen-Orr Z, Tzischichinsky O, Maldonado M, Herer P, Lavie P: **Actigraphic sleep-wake patterns and urinary 6-sulfatoxymelatonin excretion in patients with Alzheimer's disease**. *Chronobiol Int* 2001, **18**(3):513-524.
19. Sterniczuk R, Rusak B, Rockwood K: **Sleep disturbance in older ICU patients**. *Clin Interv Aging* 2014, **9**:969-977.
20. Saito T, Hasegawa-Moriyama M, Kurimoto T, Yamada T, Inada E, Kanmura Y: **Resolution of Inflammation by Resolvin D1 Is Essential for Peroxisome Proliferator-activated Receptor-gamma-mediated Analgesia during Postincisional Pain Development in Type 2 Diabetes**. *Anesthesiology* 2015, **123**(6):1420-1434.

Figures

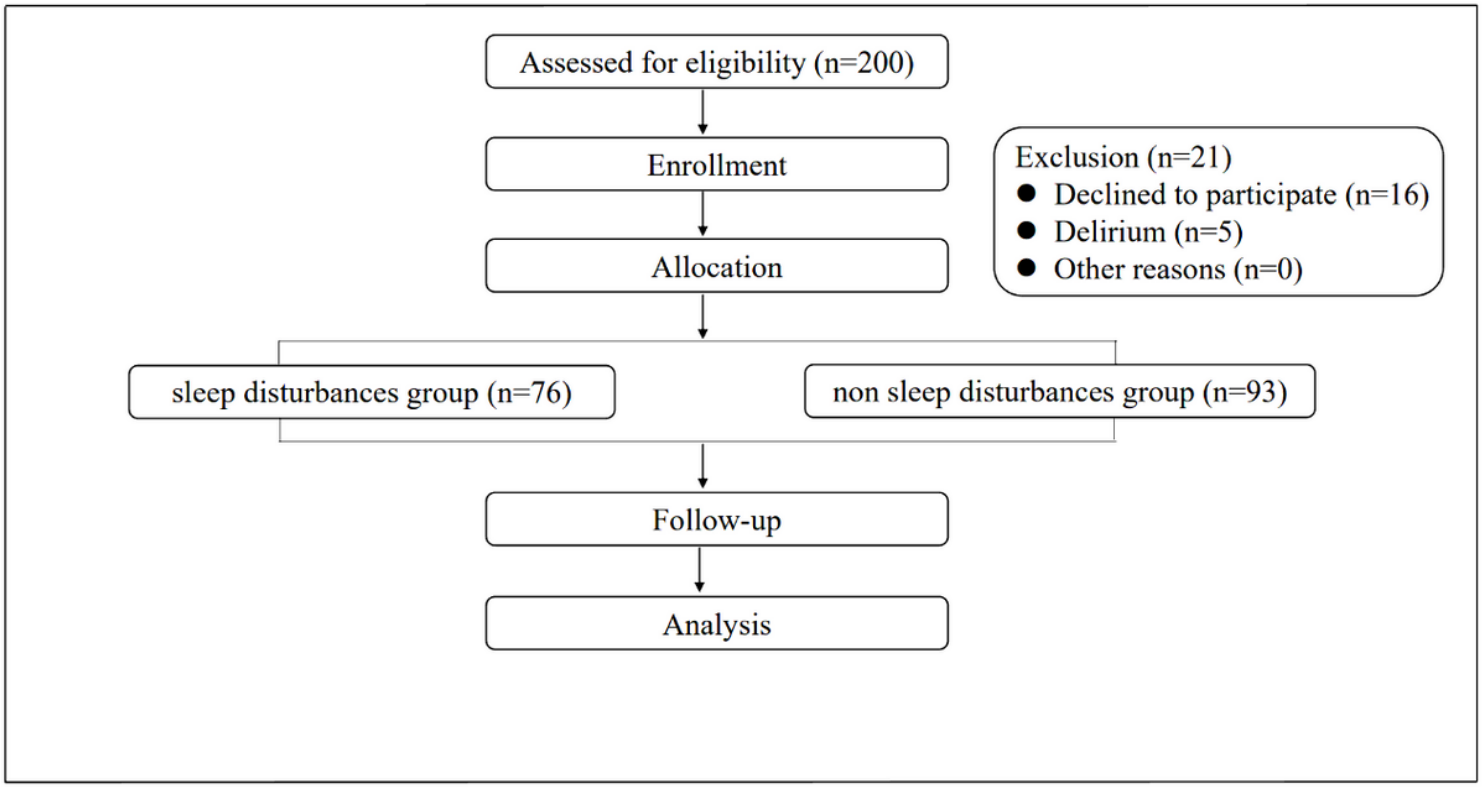

Figure 1

Study flow diagram