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Risk of pneumonia in patients with insomnia: A nationwide population-based retrospective cohort study

Chia-Ling Lin[a], Ta-Chun Liu[b,*], Chi-Hsiang Chung[c], Wu-Chien Chien[d,e,1]

[a] Department of Nursing, Chang Gung University of Science and Technology, Taoyuan, Taiwan
[b] Department of Stem Cell Biology and Regenerative Medicine, Keck School of Medicine, University of Southern California, Los Angeles, USA
[c] Taiwanese Injury Prevention and Safety Promotion Association, Taipei, Taiwan
[d] Department of Medical Research, Tri-Service General Hospital and National Defense Medical Center, Taipei, Taiwan
[e] School of Public Health, National Defense Medical Center, Taipei, Taiwan

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ABSTRACT

Evidence is lacking regarding whether insomnia increases the risk of infectious disease. Accordingly, the present study examined the risk of pneumonia in patients with insomnia.

This study was a population-based retrospective cohort study on a cohort of 8061 patients with insomnia and a control cohort of 16,112 patients (matched by age, sex, and year of diagnosis) from the Taiwan National Health Insurance Research Database for the 2000–2010 period.

Overall incidence of pneumonia was 50.6 per 1000 person-years in the insomnia cohort, which was significantly higher than that in the control cohort (30.9 per 1000 person-years). Overall, the insomnia cohort exhibited a higher risk of pneumonia (HR = 2.43; CI, 2.24–2.62). By age group, the risk of pneumonia was significantly higher in the insomnia cohort for those aged ≤40 years (HR = 3.23, CI: 1.38–7.57), 41–65 years (HR = 2.62, CI: 2.07–3.32), and >65 years (CI: 2.21–2.61).

Compared with the controls, the insomnia cohort exhibited a higher risk of pneumonia, particularly in young adults.

Introduction

Insomnia is a common sleep disorder. In Taiwan, more than 25% of adults have experienced insomnia symptoms [9]. The association between insomnia and chronic disease, such as type 2 diabetes [25], hypertension (HT) [24], and acute myocardial infarction [14], has been extensively investigated. Despite the support for this association, the association between insomnia and infectious diseases has been relatively less studied.

Sleep plays major role in the regulation of the immune system function in humans. Previous studies have demonstrated that acute sleep deprivation is associated with the decrease in killer cell, monocyte and neutrophil, and phagocytic cell counts [8,22]. One study identified nuclear factor-kappa B activation as a molecular pathway by which sleep disturbance may influence immune system expression and the risk of inflammation-related disease [8].

Insomnia has affects both sleep quality and duration. Previous studies have mostly focused on the association between short sleep durations and respiratory infection. For example, Prather et al. demonstrated that a shorter sleep duration (measured behaviorally using an actigraphy) was associated with a greater risk of cold following experimental exposure to rhinovirus [19]. An observational study revealed that sleep duration exhibited a U-shaped association with pneumonia development risk in the female population [17]. A recent study demonstrated that short sleep duration, sleep disorder, and sleep disturbances were associated with a higher probability of developing a cold or respiratory infection [20].

However, few studies have explored the long-term effects of sleep disorders such as insomnia on pneumonia. Therefore, the present study investigated this risk in a cohort of patients with insomnia and compared it with that in a cohort of without insomnia by using the Taiwan National Health Insurance Database (NHIRD).

* Corresponding author.
E-mail addresses: d99426005@ntu.edu.tw (C.-L. Lin), tachunli@usc.edu (T.-C. Liu), g694810042@gmail.com (C.-H. Chung), chienwu@ndmctsgh.edu.tw (W.-C. Chien).
[1] Address: No. 161, Sec. 6, Ming-Chuang E. Rd., Neihu Dist., Taipei City 114, Taiwan. Fax: +886 2 87923147.

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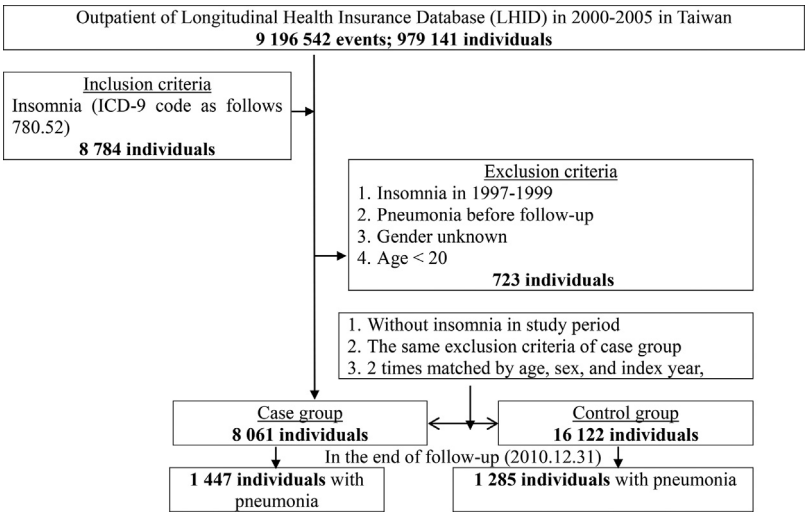

Fig. 1. The flowchart of study sample selection from National Health Insurance Research Database in Taiwan.

Materials and methods

Participants

Taiwan's National Health Insurance (NHI) program was launched as a single-payer system on March 1, 1995. As of 2014, the NHI program provides insurance for 99.9% of Taiwan's population. In the present study, data were collected from the Longitudinal Health Insurance Database 2005 (LHID2005), a subset of the NHIRD. The LHID2005 comprises 1 million people randomly selected from the NHIRD. To protect patient privacy, the National Health Research Institutes encrypted all personal identification numbers before releasing the LHID2005. In the LHID2005 dossier, the disease diagnosis codes are based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). This study was approved by the Ethics Review Board of National Taiwan University (IRB No. 201412130W).

The present study applied a retrospective cohort study design. The study cohort comprised patients aged ≥20 years who had received a diagnosis of insomnia between 2000 and 2005. They were identified according to the corresponding ICD-9 code (780.52; insomnia, unspecified). For the control cohort, we randomly selected patients without a history of insomnia. The insomnia and control cohorts were frequency-matched by age (5-year spans), sex, and year of diagnosis (Fig. 1).

Outcome measures

All study individuals were followed up from the index date until the onset of pneumonia (ICD-9-CM 480–486) in the subset file from the LHID2005, withdrawal from the NHI program, or the end of 2010, whichever occurred first.

Variable definitions

The individuals were grouped by sex, urbanization level (low, medium, and high; according to their registered address with the NHI) [15], and season of diagnosis outcome (spring, March–May; summer, June–August; autumn, September–November; and winter, December–February). The comorbidities considered in this study were asthma (ICD-9-CM code 493), chronic kidney disease (CKD; ICD-9-CM codes 585.3, 585.4, 585.5, and 585.9), chronic obstructive pulmonary disease (COPD; ICD-9-CM codes 490–496), cardiovascular disease (CVD; ICD-9-CM codes 410–414), depression (ICD-9-CM codes 296.2, 296.3, 300.4, and 311), HT (ICD-9-CM codes 401–405), and stroke (ICD-9-CM codes 430–438). Individuals with any of the aforementioned comorbidities were classified as having a comorbidity.

Statistical analysis

Descriptive statistics were used for basic information, including the percentage, mean, and standard deviation. Chi-squared and *t* tests were used to evaluate the distributions of categorical and continuous variables between the insomnia and control cohorts. The incidence densities of pneumonia were calculated according to age, sex, urbanization level, season of diagnosis outcome, and comorbidity. Cox proportional hazards regression models were used to determine the risk of pneumonia, and the results are presented as hazard ratios (HRs) with a 95% confidence interval (CI). The same variables were used in a multivariable analysis. All analyses were performed using SPSS version 21 (SPSS, Inc., Chicago, IL, USA).

Results

Demographic data

Demographic data of the study participants are presented in Table 1. The insomnia and control cohorts comprised 8061 and 16,112 patients, respectively. Most patients were older than 65 years (46.8% and 48.5% in the insomnia and control cohorts, respectively) and male. The main comorbidity in the insomnia cohort was COPD (23.2%) and that in the control cohort was HT (17.5%). In both cohorts, most patients were classified as living in a medium urbanization level (41.5% vs. 44.5%). The average follow-up duration was 3.5 (SD 2.9) years for the insomnia cohort and 3.7 (SD 3.6) years for the control cohort.

Incidence rates and adjusted HR of pneumonia by age, sex, urbanization level, and comorbidities

The incidence rates and adjusted HRs of pneumonia by age, sex, urbanization level, and comorbidities are presented in Table 2. During the follow-up period, the pneumonia incidence rate in the insomnia cohort was significantly higher than that in the control cohort (50.6 vs. 30.9 per 1000 person-years), and the risk of pneumonia was 2.43 times higher in the insomnia cohort than in the control cohort (adjusted HR, 2.43 [95% CI, 2.24–2.62]).

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