Prevalence, Risk Factors, Outcomes, and Treatment of Obstructive Sleep Apnea in Patients with Cerebrovascular Disease: A Systematic Review

Ruifang Dong, MD, Zhiling Dong, MD, Hongmei Liu, MD, Fangkun Shi, MD, and Junfeng Du, MD

Background: Obstructive sleep apnea (OSA) is known to increase the risk of cerebrovascular disease (CVD), and patients with CVD have high incidence of OSA. The study aimed to systematically evaluate the prevalence of OSA in patients with CVD. *Materials and Methods:* Medline, Embase, Science Citation Index, Wanfang, CNKI, and Wiley Online Library were thoroughly searched to identify relevant studies. Random-effects models were used to calculate the pooled rate estimates. Meta-regression and subgroup analysis were performed to explore potential sources of heterogeneity. *Results:* Thirty-seven studies with 3242 patients were analyzed. The prevalence of OSA (apnea hypopnea index [AHI] >10) ranged from 34.5% to 92.3%, the random-effects pooled prevalence was 61.9%. Furthermore, the prevalence of sleep disordered breathing (SDB) with AHI greater than 5 was 70.4%, with AHI greater than 20 was 39.5%, and with AHI greater than 30 was 30.1%. Only 8.3% of the SDB was primarily central apnea. Seventeen studies reported risk factors for OSA, 6 of which used multivariate analyses to extract risk factors. In univariate meta-regression analysis, male had higher prevalence than female ($P = .041$). OSA was associated with increased length of hospitalization in 2 studies, and 1 long-term study reported severe sleep apnea was associated with poor functional outcome. Among the 5 studies on treatment, 3 indicated that early treatment with CPAP was effective; the remaining studies did not find benefit from CPAP treatment and reported the CPAP acceptance was poor. *Conclusions:* There is high prevalence of OSA in patients with CVD (61.9%). Therefore, accurate diagnosis and treatment to OSA is very important so as to prevent CVD. **Key Words:** Obstructive sleep apnea/OSA—all cerebrovascular disease/stroke—prevalence—risk factors—outcome—treatment.

Introduction

Cerebrovascular disease (CVD) is the leading cause of adult death and disability worldwide, with cognitive impairment inflicting catastrophic consequences on patients and their families as well as placing a significant burden on the healthcare system and socioeconomic economy.[1,2] Sleep-disordered breathing (SDB) is a worldwide sleep-related respiratory abnormality including both central and obstructive forms.[3,4] Previous studies accumulating clinical and epidemiologic evidence suggested a strong causal relationship between SDB and CVD.[5-7] Obstructive sleep apnea (OSA) is the most common form

of SDB. It was proved to be the independent risk factor for CVD.[8,9] As a biological imperative for all humans, sleep can confer protection against acute cerebrovascular events after a period of rest.[10] Early large-scale risk ratio study showed a strong relationship between snoring and cerebral infarction, with a risk ratio of 10.3.[11] And the more frequencies of the snoring, the greater risk of stroke will be.

It is reported that the prevalence of OSA ranges from 3% to 7% among the general population[12] in contrary to a prevalence of 30%-70% in people who have a stroke.[13] Many studies have reported that OSA is frequent in patients with acute stroke and has been associated with poor outcomes.[14-16] Patients diagnosed with SDB (apnea hypopnea index [AHI] > 5) have a 1.58 relative odds of prevalent CVD, with a hazard ratio of 2.89.[17] After stratifying for severity, mild OSA (5 ≤ AHI <15) has a 2.44 times increased risk of cerebrovascular events, and moderate (15 ≤ AHI <30) or severe OSA (AHI ≥ 30) a 3.56-fold increased risk.[18] However, there are no guidelines about whether the presence of OSA should be routinely evaluated in CVD patients or how they should be evaluated. We aimed to gain better understanding of the prevalence, risk factors, outcomes, and treatment of OSA in patients with CVD.

Materials and Methods

Search Strategy

Medline, Embase, Science Citation Index, Wanfang, CNKI, and Wiley Online Library were thoroughly searched using keywords of "cerebrovascular disease/stroke", "cerebral infarction", "transient ischemic attack (TIA)", and "sleep apnea" (date until May 2017). Moreover, we get more relevant articles by snow-balling references. Only published full text articles were included, and unpublished studies were not considered.

Selections of Studies and Data Extraction

Studies were considered eligible for analysis if they met all of the criteria for inclusion: (1) the exposed population was patients with CVD; (2) the patients under study were adults (>18 years old); and (3) estimates of prevalence or frequency of OSA or data to calculate them were provided. We excluded studies if oximetry alone or snoring history was used to define OSA instead of sleep studies. For overlapping studies, only the most recent or complete studies were included.

Two reviewers independently extracted information about number of case, definition of OSA, mean age, diagnostic method, diagnostic criteria (AHI), time from CVD onset to testing, type of CVD, mean body mass index (BMI). If 2 reviewers had different opinions, third investigator would be asked to reach consensus.

Definition of Outcomes

The percentage of patients with SDB determined by AHI criteria of greater than 5, greater than 10, greater than 15, greater than 20, greater than 30, and greater than 40, as well as the percentage of patients with primarily central apnea was determined. The studies were analyzed for sleep study type including complete polysomnography (PSG) with electroencephalography (EEG), limited-channel without EEG or automatic continuous positive airway pressure (CPAP) in diagnostic mode. Sleep apnea severity was evaluated by AHI, which was calculated as the total number of apneas and hypopneas per hour of sleep. An apnea was defined as complete cessation of breathing for 10 seconds or longer. A hypopnea was defined as a 30% or greater reduction of nasal pressure or thermocouple monitored airflow, for at least 10 seconds, when followed by an oxygen desaturation of 4% or higher, arousal, or awakening.[19] For this study, OSA was defined as AHI greater than 10. Moreover, predominantly central sleep apnea was diagnosed when more than 50% of respiratory events were of the central type.

Statistical Analysis

We calculated pooled prevalence estimates and the 95% confidence intervals (CI), stratified by several criteria. The criteria included event type, first or recurrent event, sex, study design, time interval, testing method, AHI cut-off points. Q-text (reported as X^2 and P values) and the I^2 statistic were used to estimate heterogeneity between studies. In the presence of significant heterogeneity of variance among studies, random effects model was used.[20] Potential publication bias was assessed by Begg's funnel plot[21] and Egger's test[22]; if P is less than .05, then it is considered as statistically significant. Composite estimates of percentage of patients with AHI greater than 10 and heterogeneity statistics were derived for each subgroup. Meta-regression was used to estimate whether age or BMI correlated with the proportion of patients with AHI greater than 10. We used Stata 11.0 with the commands metan and metareg.

Results

One hundred and twenty-one records were selected by search strategy (Fig 1), 51 records were excluded after initial screening. Three studies were meta-analyses or systematic reviews, 3 studies were review, 2 studies were letter, 4 studies defining OSA by snoring, 5 studies testing with oximetry, 8 studies which did not report AHI cutoffs, 5 studies were duplicate to previous study. At last, 37 studies consisted of 3242 patients in this meta-analysis.[14,15,17,23-56]

The studies characteristics were summarized in Table 1. One study evaluated cerebral infarction, 7 studies evaluated stroke and transient ischemic attack, and the remaining