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Original Article

Prognostic implication of obstructive sleep apnea diagnosed by post-discharge sleep study in patients presenting with acute coronary syndrome

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ABSTRACT

Objective: We aimed to determine the prognostic implications of obstructive sleep apnea (OSA) diagnosed during the recovery phase of acute coronary syndrome (ACS).
Methods: Patients presenting with ACS and treated with percutaneous coronary intervention were recruited prospectively for a home-based sleep study within 30 days of hospital discharge. Major adverse cardiac and cerebrovascular events (MACCEs) assessed included cardiac death, myocardial infarction, stroke, unplanned revascularization, and hospitalization for heart failure.
Results: Of the 85 patients recruited, 68 successfully completed the study. The median time from percutaneous coronary intervention to sleep study was 14 days (interquartile range: 7.5–27 days). OSA was diagnosed in 24 patients (35.3%) (apnea–hypopnea index $\geqslant$15). A drug-eluting stent was implanted into the target lesion in 45 patients (66.2%). None of the study patients had received treatment for OSA. At 24-month follow-up, the MACCE incidence was 34.9% in the OSA group and 5.1% in the non-OSA group ($P = 0.008$, log-rank test). After adjusting for the possible confounding effect of age, gender, coronary intervention indications, hypertension, smoking, and body mass index, OSA remained an independent predictor of MACCEs (adjusted hazard ratio, 6.95; 95% confidence interval, 1.17–41.4; $P = 0.033$).
Conclusion: OSA diagnosed in patients treated with percutaneous coronary intervention for ACS by post-discharge sleep studies conducted 2 weeks after percutaneous coronary intervention was independently associated with MACCEs at 24-month follow-up.

1. Introduction

In the past two decades, much research on obstructive sleep apnea (OSA) has focused on its association with cardiovascular disease, revealing and recognizing the vasculopathic effects of OSA [1–3]. Intermittent hypoxemia, intrathoracic pressure changes and arousal-induced reflex sympathetic activation have been implicated as the underlying pathophysiological mechanisms [3]. The enormous significance of these findings has completely changed sleep medicine. Several population surveys have shown that OSA is independently associated with an increased long-term risk of fatal and non-fatal cardiovascular events [4–6]. However, in patients presenting with acute coronary syndrome (ACS), the relationships between OSA and cardiovascular outcomes remain unclear, and the current data are limited and conflicting [7–9].

The reliability of diagnostic sleep studies performed during the acute phase of ischemic insults has been a major source of controversy surrounding the prognostic implications of OSA in ACS patients. Some data have described how sleep studies conducted at different times appear to affect OSA prevalence [10–12]. In a study of 18 patients admitted to coronary care units for a variety of cardiac conditions, OSA prevalence decreased from 56% during the acute phase to 18% at the six-week follow-up [10]. In 28 patients presenting with ACS and diagnosed with OSA during hospitalization, repeat sleep studies conducted at the six-month follow-up showed OSA resolution in 79% of patients [11]. A recent report showed that sleep studies performed during the acute phase of myocardial infarction functioned as independent predictors of

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OSA [12]. These studies suggest that some of the OSA diagnosed during the acute phase of ACS may be transient, and that sleep studies should be performed during the recovery period to achieve better diagnostic accuracy.

Data on the relationships between OSA diagnosed during the ACS recovery period and subsequent cardiovascular outcomes have thus far been scarce. If a worse prognostic implication were demonstrated during recovery period diagnosis, it would further support the screening and treatment of OSA in patients presenting with ACS. Alternatively, OSA might merely be a marker of ACS. In this study, we sought to determine the prognostic implications of OSA diagnosed during the ACS recovery phase.

2. Methods

2.1. Study design and patient population

This was a single-center, prospective, observational study conducted at a tertiary institution in a multi-ethnic Asian country from February 2011 to December 2012. We recruited patients aged 21–80 years who were admitted to our institution for ACS and treated via percutaneous coronary intervention. We defined ACS as ST segment elevation myocardial infarction, non-ST segment elevation myocardial infarction or unstable angina according to the current standard clinical guidelines [13]. Patients with known OSA, who had received continuous positive airway pressure therapy or previous intervention treatment of the target vessel, who had experienced cardiogenic shock, chronic renal failure on dialysis or atrial fibrillation, or who were unable to provide informed consent were excluded. All of the recruited patients were scheduled to undergo a home-based overnight sleep study within 30 days of hospital discharge. The study was approved by the local institutional review board (National Healthcare Group Domain Specific Review Board; reference: C/2010/00341), and all of the subjects provided written informed consent.

2.2. Overnight sleep study

All of the sleep studies were performed using a portable level-3 diagnostic device (Embletta Gold, Natus Medical, Inc., Oakville, Ontario, Canada) that had been previously validated against full in-laboratory polysomnography [14]. The parameters measured included nasal airflow (nasal cannula), thoraco-abdominal movements (inductive respiratory bands), arterial oxygen saturation (pulse oximetry), snoring episodes derived from the integrated pressure transducer, limb movement, and body position (continuous actigraphy).

Outputs from the portable diagnostic device were analyzed by an investigator who was blinded to the patients' clinical characteristics. Apnea was defined as cessation of airflow for >10 s, and hypopnea was defined as 30–90% reduction in airflow from baseline lasting 10 s, in conjunction with desaturation of $\geqslant$4%. Apnea was classified as 'obstructive' if paradoxical thoraco-abdominal movement was detected, and 'central' if no thoraco-abdominal movement was present. Mean percutaneous blood oxygen saturation (SpO_2), lowest SpO_2 and total percentage of time $SpO_2 < 90\%$ were also recorded. As OSA was the sleep-disordered breathing of interest, patients with predominantly central sleep apnea were excluded from the analysis.

Each apnea–hypopnea index (AHI) was calculated as the total number of apneic and hypopneic episodes per hour of recording time in bed. The scoring was performed according to the American Academy of Sleep Medicine guidelines [15]. The recruited patients were classified into OSA (AHI $\geqslant$ 15) and non-OSA (AHI < 15) groups. OSA was defined as AHI $\geqslant$ 15 based on the latest clinical guidelines released by the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine [16].

2.3. Data collection and long-term follow-up

The following baseline demographic and clinical data were collected from the medical records of the recruited patients: gender, ethnicity, age, body mass index (BMI), cardiovascular risk factors (i.e. smoking, hypertension, hyperlipidemia, diabetes mellitus, family history of premature coronary artery disease), concomitant medical history (i.e. previous percutaneous coronary intervention, coronary artery bypass surgery, myocardial infarction, stroke, chronic renal failure), laboratory results, left ventricular ejection fraction, time from discharge to home sleep study, and discharge medications (i.e. aspirin, thienopyridine, beta blocker, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, lipid-lowering therapy).

The follow-up period began from the time of percutaneous coronary intervention during the index hospital admission. The clinical outcomes of the patient cohort were conducted via clinical chart reviews and telephone calls by an investigator who was blinded to the patients' sleep results. All of the information was recorded prospectively. The outcomes were collected after 24-month follow-up. The MACCEs (cardiac death, myocardial infarction, unplanned revascularization, stroke, and hospital admission for congestive heart failure) comprised the primary endpoint of the study. All of the morbidities recorded were defined according to current standard guidelines.

2.4. Statistical analysis

The categorical variables were presented as numbers and percentages, and continuous variables were described as means with standard deviations or medians with ranges/interquartile ranges. Differences in the characteristics between the OSA and non-OSA groups were analyzed using the independent sample *t*-test for continuous data, or χ^2/Fisher's exact test for categorical data.

The MACCE cumulative incidence curves were constructed using the Kaplan–Meier method and compared using the log-rank test. A Cox proportional hazards multivariate analysis was performed to adjust for possible confounders such as age, gender, different ACS presentations (i.e. ST segment elevation myocardial infarction versus non-ST segment elevation myocardial infarction and unstable angina; the latter two categories were grouped together due to small number of unstable angina patients ($n = 3$)), hypertension, smoking and BMI. All of the statistical analyses were carried out using STATA v. 13 (StataCorp LP; College Station, TX, USA), assuming a two-sided test with a 5% level of significance.

3. Results

3.1. Baseline demographic and clinical characteristics

Eighty-five patients presenting with ACS were successfully recruited during their hospitalization periods and scheduled to undergo a home-based portable sleep study. Out of these 85 patients, 15 subsequently withdrew and defaulted the study. Among the 70 patients who underwent the study, 68 completed it successfully. Most of the study patients (86.8%) were male, and the average age was 54.2 ± 8.8 years.

Based on AHI $\geqslant$ 15, OSA was present in 24 patients (35.3%), whereas 44 patients (64.7%) were classified as non-OSA. None of the patients in the OSA group accepted continuous positive airway pressure therapy or any other treatments for OSA during the follow-up period. The baseline demographic and clinical characteristics of the patients are shown in Table 1. Patients in