Original article

Relationship between sleep-disordered breathing and renal dysfunction in acute coronary syndrome

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ABSTRACT

Background: Sleep-disordered breathing (SDB) is associated with cardiovascular complications. However, the effect of SDB on renal function in patients with acute coronary syndrome (ACS) treated by percutaneous coronary intervention (PCI) remains unclear.
Methods: We enrolled 154 consecutive ACS patients without heart failure. A sleep study was performed immediately after PCI.
Results: The mean apnea-hypopnea index (AHI) was 16.4 ± 13.1, and 33 patients (21%) had severe SDB, defined as AHI ≥ 25. Estimated glomerular filtration rate (eGFR) values on admission (60 ± 12 mL/min/1.73 m^2 vs. 67 ± 17 mL/min/1.73 m^2, $p = 0.046$) and at discharge (54 ± 15 mL/min/1.73 m^2 vs. 63 ± 15 mL/min/1.73 m^2, $p = 0.002$) were lower in patients with severe SDB than in those patients without severe SDB. Multiple linear regression analysis showed that AHIs were significantly correlated with absolute changes in eGFR values from admission to discharge ($\beta = 0.201$, $p = 0.004$). Median 24-h urinary noradrenaline excretion measured on the same day of the sleep study was higher [297 (interquartile range {IQR}: 232–472) vs. 174 (IQR: 107–318) μg/day, $p = 0.021$] in patients with severe SDB. On multivariate logistic regression analysis, the presence of severe SDB was a significant predictor (adjusted odds ratio 3.76, 95% confidence interval 1.06–13.9, $p = 0.047$) for eGFR of less than 45 mL/min/1.73 m^2 at discharge. This association was independent of age, eGFR on admission, and a presentation of ST-segment elevation myocardial infarction.
Conclusion: In patients with ACS who undergo PCI, severe SDB is associated with impaired renal function on admission and its deterioration during hospitalization. Further studies will be needed to conclude that SDB would be a therapeutic target in ACS.

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Introduction

Transient and persistent worsening renal function during hospitalization is associated with all-cause mortality in patients with heart disease [1,2]. Furthermore, in patients with acute coronary syndromes (ACS), deteriorating renal function is related to high mortality rates during the early and late post-ACS period [3,4]. Therefore, potential risk factors or mechanisms for kidney injury after exposure to contrast medium during invasive strategies such as percutaneous coronary intervention (PCI) have been investigated [5,6]. Animal studies have shown that new attractive targets such as sympathetic hyperactivity may play an important role in forecasting kidney injury during the acute phase of a critical situation [7,8].

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Sleep-disordered breathing (SDB) is known to induce sympathetic hyperactivity [9], promote cardiovascular complications, and lead to poor outcomes in patients with coronary artery disease [10,11]. Interestingly, several researchers have reported high prevalence of SDB among chronic kidney disease and hypothesized that SDB might contribute to loss of kidney function [12,13]. However, to the best of our knowledge, studies examining the influence of SDB on renal function in patients with ACS who undergo PCI have not yet been reported. The present study investigated the hypothesis that SDB is related to renal dysfunction in patients with ACS who undergo PCI.

Methods

Patients

Between May 2011 and March 2014, we recruited 252 consecutive patients with ACS who were admitted to our institute and underwent coronary angiography within 24 h after admission. We excluded 5 patients who died within 7 days of admission, 7 patients with chronic kidney disease requiring chronic peritoneal dialysis or hemodialysis, 41 patients who had congestive heart failure with a New York Heart Association functional class of 2 or above and/or history of pulmonary edema, 10 patients who did not meet the coronary anatomical criteria required for PCI, 13 patients who required emergency bypass grafting, and 22 patients with spastic angina. We studied the remaining 154 patients with ACS who underwent PCI immediately after coronary angiography (mean age 66 ± 12 years; 79% men). ACS was classified into two types: (1) ST-segment elevation acute myocardial infarction (STEMI), in which the patient had been admitted within 24 h after the onset of chest pain that had lasted for 30 min with ST-segment elevation of 0.2 mV or higher in at least two contiguous leads and elevation of the creatinine kinase or its MB isozyme level to at least twice the upper limit of normal or (2) non-ST-segment elevation ACS, in which the patient had experienced an episode of ischemic chest pain lasting at least 10 min with transient or persistent ST-segment depression (≥ 0.5 mm), T-wave inversion (≥ 1 mm), and/or elevation of the troponin T level beyond the upper limit of normal [6]. The Ethics Committee of our institution approved the present study, and all patients provided written informed consent. This study was registered with the UMIN protocol registration system with the identification number UMIN000022423.

Laboratory and clinical assessments

Serum creatinine (sCr) levels were measured in all patients on admission and within 2 days before discharge. The estimated glomerular filtration rate (eGFR) was calculated according to the Japanese equation from sCr developed by Matsuo et al. [14]. To assess the risk of renal deterioration, the Mehran score was calculated as described previously [5]. Anemia was defined according to the World Health Organization criteria (hemoglobin level ≤ 13 g/dL for men and ≤ 12 g/dL for women) [15]. Renal dysfunction at discharge was defined as an eGFR of less than 45 mL/min/1.73 m^2 [16–18]. Contrast-induced nephropathy was defined as a greater than 25% increase in the sCr level or a greater than 0.5 mg/dL sCr level within 3 days after the intravascular administration of contrast medium [19]. Left ventricular ejection fraction was measured on admission by echocardiography.

To evaluate sympathetic nervous system activity, 24-h urinary noradrenaline excretion was measured on the day of the sleep study for a subset of 63 consecutive patients among the total of 154. The samples were collected in acidified containers containing 20 mL of 6 mol/L hydrochloric acid and stored at 4 °C before analysis.

PCI procedure and assessment

All patients received 200 mg aspirin, a 300-mg loading dose of clopidogrel, and 70–100 U/kg intravenous standard heparin before PCI. Glycoprotein IIb/IIIa inhibitors were not available in Japan at the time of the study. In patients with STEMI, an intravenous infusion of 0.9% sodium chloride was immediately started on admission at a continuous rate of 2 mL/kg/h, which was continued before and during primary PCI. The infusion rate was reduced to 1 mL/kg/h at the end of the procedure and was stopped the next morning. In patients with non-ST-segment elevation ACS, an intravenous infusion of 0.9% sodium chloride was started on admission at a continuous rate of 1 mL/kg/h; the infusion was continued through PCI and stopped the next morning. Sodium bicarbonate and N-acetylcysteine were not used in this study. All patients underwent PCI according to standard clinical practice. The SYNTAX (SYNergy between PCI with TAXUS™ and Cardiac Surgery) score was calculated as described previously [20].

Sleep study

The sleep study was conducted using an apnomonitor Type 4 (SAS-2100, NIHON KOHDEN, Tokyo, Japan) [21–23] within 7 days after admission. The variables measured included nasal airflow and
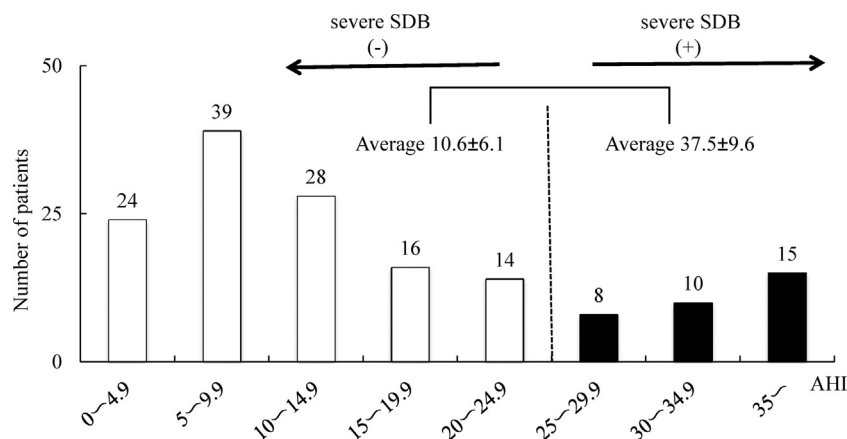

Fig. 1. Distribution of the AHI in patients with acute coronary syndrome. Black bars indicate patients with an AHI of ≥ 25 ($n = 33$), and white bars indicate patients with an AHI of <25 ($n = 121$). AHI, apnea hypopnea index; SDB, sleep-disordered breathing.