Temporal Worsening of Sleep-Disordered Breathing in the Acute Phase of Myocardial Infarction

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Background  Sleep apnea is an important risk factor for cardiovascular diseases, but whether the severity of sleep-disordered breathing (SDB) changes in the acute phase of myocardial infarction (MI) has not been well determined, nor has it been determined what type of SDB, central or obstructive, (CSA or OSA) is exacerbated.

Methods and Results  Polysomnography was performed in patients with acute phase of MI during the acute (days 3–5) and chronic (day 14) phases. On the same day, the ventilatory equivalent (VE)/carbon dioxide production (VCO₂) slope, urinary catecholamines secretion and arterial carbon dioxide tension were assessed before sleep. The apnea/hypopnea index was significantly decreased in the chronic phase (13.26±11.30 vs 6.97±5.67, p<0.05). The distribution of the types of SDB was unchanged, indicating both CSA and OSA can be exacerbated in the acute phase of MI. The VE/VCO₂ slope and arterial carbon dioxide tension before sleep were also unchanged. Urinary norepinephrine secretion was slightly decreased, although the difference was not significant.

Conclusions  SDB is temporarily worsened in the acute phase of AMI and both CSA and OSA are worsened in AMI. (Circ J 2006; 70: 1553 – 1556)

Key Words: Ischemic heart disease; Myocardial infarction; Sleep apnea; Sleep-disordered breathing

Sleep apnea is a recognized risk factor for various cardiovascular diseases,1-2 including hypertension,3,4 stroke,5 congestive heart failure, and ischemic heart disease (IHD).6 Sleep apnea can also influence hemodynamics; for example, elevating the pulmonary capillary wedge pressure in patients with congestive heart failure. Hypertension, which has close relationship with sleep apnea, increases afterload of left ventricle and can also induce cardiac rupture. Moreover, sleep apnea is closely related to arrhythmia, which is one of the major causes of death in the acute phase of myocardial infarction (MI). However, there are only a few reports of worsening of sleep disordered breathing (SDB) in the acute phase of IHD.6-11 There are no reports documenting change in the severity of SDB during the acute phase of MI, as analyzed by polysomnography (PSG), so we used this technique in the present study. We also analyzed the factors that are supposed to be related to the severity of SDB.

Methods

Patients  To assess the effect of MI on sleep apnea and to exclude the effect of heart failure, we selected only patients in Killip class 1 and because we performed cardiopulmonary exercise testing, we selected only those patients who had been successfully revascularized with percutaneous coronary intervention soon after admission. Acute MI (AMI) was defined as peak creatinine kinase 3-fold greater than normal. The entry criteria were AMI, single-vessel disease and successful revascularization soon after admission. We excluded patients with residual ischemia, abnormal spirometric tests, total sleep time less than 180 min in any of the sleep studies, heart failure or inability to perform exercise testing. From November 2004 to October 2005, 12 patients meeting the entry criteria were enrolled after giving informed consent.

PSG  Our preliminary study using a simple diagnostic device (Morpheus, Compumedics, Abbotsford, Vic., Australia) revealed that the apnea/hypopnea index (AHI) dramatically decreased within 5 days after the onset of AMI. It was also revealed that in the acute phase of MI, sleep is disturbed in most patients and it is quite difficult to determine the AHI without analyzing the electroencephalogram (EEG). Therefore, we decided to perform PSG to determine how the AHI changes during the acute phase of MI. This preliminary study also suggested that the AHI decreases, particularly within 2 days after the onset of AMI. However, because we had to attach several sensors (including EEG) to perform PSG and had to perform cardiopulmonary exercise testing to assess the ventilatory equivalent (VE)/carbon dioxide production (VCO₂) slope, we recorded the first PSG on days 3–5 after MI (acute phase) and a second PSG on day 14 (chronic phase). The third PSG was performed 6 months later only in patients with an AHI >10.0 on the second PSG. PSG was performed using standard techniques and a digital polygraph (Alice 4, Respironics, Murraysville, PA, USA) equipped with EEGs, electro-oculograms, submental electromyogram, tibialis electromyograms, electrocardiograms, chest and abdominal movement recording using respiratory effort bands, body position monitoring, oronasal airflow monitoring using a flow-sensor, and arterial oxygen hemoglobin saturation monitoring using a pulse-oximeter. An episode of apnea was defined as the cessation of inspiratory airflow lasting for at least 10 s. An episode of central apnea (CSA) was defined as the absence of chest and abdominal movement and the absence of airflow. An episode of obstructive sleep apnea (OSA) was defined as the absence of
airflow in the presence of chest and abdominal movement. Hypopnea was defined as a reduction in airflow lasting at least 10 s and associated with at least a 3% decrease in atrial oxyhemoglobin saturation (SpO₂), an electroencephalographic arousal, or both. The AHI was calculated by dividing the number of the episodes of apnea and hypopnea by total sleep time. PSG was analyzed through non-computer analysis by 2 well-trained observers who were unaware of the clinical background of the patients and the AHI was calculated as the mean value of the 2 observations.

Exercise Testing and VE/V̇CO₂ Slope Calculation
Symptom-limited cardiopulmonary exercise testing was performed using a treadmill. After a 3-min rest period, exercise began with a 3-min warm up and intensity was increased incrementally using the Ramp method. The first cardiopulmonary exercise test was performed on day 4 after MI, and the second one on day 14. In the first exercise test, considering the risk of cardiac rupture, we limited the exercise intensity within 3 Mets, and stopped exercise before the systolic blood pressure increased over 150 mmHg. In the second exercise test, we encouraged patients to exercise to exhaustion. None of them experienced angina pectoris, ischemic ST changes, or severe arrhythmias during the exercise test. Oxygen consumption, V̇CO₂, and VE were measured continuously using a breath-by-breath analyzer (RM-300i, Minato Ikagaku, Osaka, Japan). The VE/V̇CO₂ slope was calculated by linear regression analysis.

Statistical Analysis
All descriptive data are expressed as the mean±SD. Student’s t-test was used to assess the difference in the data obtained from the tests performed twice for each patient. A p-value <0.05 was considered to indicate statistical significance. All calculations were performed with Stat View software (SAS Institute Inc, Cary, NC, USA).

Results
The clinical characteristics of the patients are summarized in Table 1. All patients were being administered β-blockers and all patients underwent PSG twice. Several other examinations were also performed twice for each patient. The AHI was significantly lower in the second PSG, indicating that sleep apnea worsened in the acute phase of MI but recovered in the chronic phase (13.26±11.30 vs 6.97±5.67, p<0.05; Fig 1A). The minimum SpO₂
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was not different between the acute and chronic studies (89.75±2.34 vs 91.25±3.86, p=NS; Fig 1B). The distribution of the types of sleep apnea was similar in the acute and chronic phases, indicating that all types of sleep apnea are worsened in the acute phase of MI (Fig 1C). There was not a significant difference in total sleep time between the acute and chronic studies (365.7±95.9 vs 392.0±63.2, p=NS; Fig 2A). As for sleep stages, although the percentage of stage 1 and REM sleep were slightly different, the distribution of sleep stages was similar in both studies (Fig 2B). The VE/VCO₂ slope, which has a close relationship with the severity of CSA in patients with congestive heart failure (CHF), did not change significantly between the acute and chronic phases (32.93±5.39 vs 33.40±4.15, p=NS; Fig 3A). Arterial carbon dioxide tension before sleep also did not differ between the acute and chronic phases (39.67±3.36 vs 39.23±3.76, p=NS; Fig 3B). Urinary norepinephrine secretion was slightly decreased in the chronic phase; however, the difference was not significant (141.69±45.80 vs 107.83±37.52, p=NS; Fig 3C).

Among the 12 patients, had a more than 5-unit decrease in AHI between the 2 studies; however, even in these 6 patients, the distribution of the types of sleep apnea was similar in the acute and chronic phases, and the VE/VCO₂ slope did not change (40.43±3.06 vs 41.35±3.08, p=NS). Urinary norepinephrine secretion did not change significantly (137.62±57.99 vs 102.15±77.93, p=NS). The wash-out rate and heart (H)/mediastium (M) ratio calculated from iodine-123 (¹²³I) metaiodobenzylguanidine scintigraphy showed no significant difference between those with a more than 5-unit decrease in AHI (Decrease group) and those with a less than 5-unit decrease in AHI (No change group) (Decrease group: H/M ratio 1.88±0.18, No change group: H/M ratio 1.88±0.18, p=NS).
wash-out rate 46.57±7.03% vs No change group: H/M ratio 1.78±0.36, wash-out rate 32.22±17.86%). Of the 12 patients, 3 had an AHI >10.0 on the second PSG, and a third PSG (6 months after the onset) was performed in which the AHI was unchanged (data not shown).

Discussion

Sleep apnea syndrome has a detrimental effect on hemodynamics\(^3\),\(^4\),\(^7\) and provokes arrhythmias\(^1\) and both the hemodynamic instability and the arrhythmia are recognized as important factors that worsen the prognosis of the patients with AMI. However, to date, SDB in the acute phase of MI has not been well analyzed and in the present study, we found that the AHI obtained with PSG temporarily worsened in this phase. Because sleep is disturbed in the acute phase of MI, total sleep time is difficult to determine without EEG recordings. There have been several reports of the severity of SDB in the acute phase of MI, but those researchers calculated the AHI with a relatively incorrect monitoring system without an EEG\(^8\),\(^9\),\(^11\). In the present study, we have shown that AHI determined with PSG significantly improves in the chronic phase and our study indicates that both CSA and OSA are worsened in the acute phase of MI. Our study also revealed no change in the AHI between the second (day 14) and third PSG (6 months later), which indicates that temporal worsening of SDB in the setting of AMI occurs within 2 weeks after the onset and that PSG performed on day 14 has good diagnostic value for determining the severity of SDB.

It has been reported that the VE/VCO\(_2\) slope correlates with the severity of CSA in patients with CHF\(^12\)–\(^14\) and we have also observed this correlation between the VE/VCO\(_2\) slope and the severity of CSA in the settings of CHF. Therefore, we speculated that this correlation would be observed in patients with AMI, and that temporal worsening of the AHI might correlate with the VE/VCO\(_2\) slope. However, after the acute and chronic phases. Our PSG data indicated that all types of SDB could be worsened in the acute phase of MI. The relationship between the VE/VCO\(_2\) slope and the severity of SDB in patients with CHF was observed only in patients with CSA. The present results suggest that the mechanisms are different between SDB in AMI and CSA in CHF. In our study, the only difference between the acute and chronic studies was the urinary norepinephrine secretion, but that difference was not significant. Therefore, sympathetic nerve activation associated with AMI might play a role in the temporal worsening of SDB. Further studies should be performed to determine the mechanism of temporal worsening of SDB in AMI.

In the present study, we found that both CSA and OSA are worsened in AMI. Oxygen administration is usually performed in the acute phase of MI. Although there is a report of the favorable effect of oxygen administration for OSA\(^15\) oxygen administration for this indication has not been well established. However, it is impractical to use continuous positive airway pressure or other ventilators\(^16\) in the acute phase of MI and suitable treatment for SDB in the setting of AMI needs further evaluation.

Study Limitations

For ethical reasons, neither PSG nor exercise testing could be performed immediately after the onset of AMI and the delay in performing the acute studies could possibly affect the results of the present study.

References