Nocturnal Oxygen Desaturation in Coronary Artery Disease

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SUMMARY

Nocturnal oxygen desaturation and sleep apnea may provoke myocardial ischemia and arrhythmias in patients with coronary artery disease (CAD). Additionally, these factors may accelerate coronary atherosclerosis in the long term and they may play a role in the progression of the disease process. On the other hand, studies related to this subject are limited. This study was conducted to investigate the nocturnal oxygen desaturation and apneas during sleep in patients with CAD and to assess the possible association of these factors with CAD.

We studied 22 male patients with CAD confirmed by coronary angiography who did not have symptomatic pulmonary disease and fourteen male healthy controls without known heart disease. Patients were randomly selected from men undergoing coronary angiography. Controls were age and sex matched and selected from the population registry. The normal controls were of similar body mass index to the patients. None of them were obese. The patients and controls underwent standard polysomnography.

Men with CAD and controls had a similar apnea-hypopnea index (2.3 ± 3.8 vs. 1.2 ± 1.7). Mean oxygen desaturation index was higher among patients than controls (2.1 vs. 0.5 , $p < 0.05$). Patients with CAD spent 3.1% (9.7 ± 13.6) of total sleep time desaturated, while the same proportion in controls were 0.5% (1.9 ± 4.1) ($p < 0.05$). Although both groups of patients were of similar heart rates at initial, the development of bradycardia during sleep was significantly higher in patients compared with controls (43.3% vs. 25.3% , $p < 0.05$).

The results demonstrate that sleep disordered breathing, in particular nocturnal oxygen desaturation, occurs more common in patients with CAD compared to controls. Additionally, patients are at higher risk of developing bradycardia during sleep. This findings suggest that oxygen desaturation during sleep might contribute to the progression of CAD. (Jpn Heart J 1999; 40: 23–29)

Key words: Sleep apnea, Nocturnal oxygen desaturation, Coronary artery disease

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THE term of "sleep disordered breathing" consists of apnea, hypopnea and oxygen desaturation. The most important form of sleep disorder is obstructive sleep apnea syndrome (OSAS) because of its high prevalence and potential for the development of cardiovascular diseases. Sleep disordered breathing has been shown to be a significant risk factor in the development of ischemic heart disease.^{1,2)} The combined effects of systemic hypertension, hypoxemia and increased sympathetic activity during sleep are thought to promote the development of atherosclerosis.³⁾ On the other hand, patients with coronary artery disease (CAD) and obstructive sleep apnea (OSA) may have an increased cardiac risk due to apnea-associated oxygen desaturation.⁴⁾ Nocturnal oxygen desaturation could be detrimental to those patients with CAD in whom hypoxemia poses potential threats. The aim of this study was to determine the prevalence and characteristics of sleep disordered breathing in patients with coronary artery disease.

MATERIALS AND METHODS

Twenty two male patients with angiographically proved CAD and fourteen controls without known heart disease were studied between November 1996 and April 1997. Patients were recruited from the cardiology outpatient clinic in our hospital with symptoms of CAD. Patients were randomly selected from all eligible patients. All patients underwent coronary angiography and left ventriculography. Left ventricular function was scored as normal by echocardiography, corresponding to ejection fraction more than 0.5. Controls were age and sex matched and selected from the population registry.

Patients with intrinsic pulmonary diseases, unstable angina pectoris, unstable congestive heart failure, myocardial infarction ≤ 30 days before the study, acute pulmonary edema, congenital heart disease, primary valvular heart disease, intrinsic renal and liver disorders, use of benzodiazepines or theophylline, untreated hypothyroidism, or kyphoscoliosis were excluded from the study. Control subjects with history or signs and symptoms, or both, of cardiopulmonary disease were excluded. For uniformity, we studied only male patients.

The patients and controls underwent standard polysomnography. The overnight polysomnographic study was performed without nocturnal sedation. Overnight recordings of oronasal air-flow, abdominal and chest movements, oxygen saturation, body position, single-lead electrocardiogram, electro-oculograms, electroencephalograms and submental electromyogram were registered on a Sensormedics/Somnotrac 4250 recorder. Sleep staging⁵⁾ and apnea scoring were performed manually. An obstructive apnea was defined as cessation of airflow for > 10 s in the presence of thoracoabdominal movements. A central apnea was

defined as the absence of airflow for > 10s together with absence of thoracoabdominal movements. Hypopnea was defined as a reduction of airflow lasting > 10s associated with at least a 4% decrease in arterial oxygen saturation (SaO₂). Oxygen desaturation index (ODI) was calculated as the average number of episodes of desaturation, apnea index (AI) was calculated apnea per hour of sleep and apnea-hypopnea index (AHI) was calculated as apnea or hypopnea per hour of sleep.

All data are presented as mean ± SD. Mann Whitney U and Student-t tests were used to compare variables between the two groups of patients. A *p* value of < 0.05 was considered significant.

RESULTS

Clinical characteristics of the patients and controls are shown in Table I. The normal controls were of similar age and body mass index to the patients. None were obese. There was no symptomatic lung disease despite the history of heavy smoking in both groups. Patients more often had a history of hypertension (*p* < 0.05). None of the patients had nocturnal angina pectoris. One-vessel disease was found in 45%, two-vessel disease in 23% and three-vessel disease in

Table I. Clinical Characteristics of CAD Patients and Controls

Characteristics	Patients (<i>n</i> = 22)	Controls (<i>n</i> = 14)	<i>p</i> Value
Age, yr	53.6 ± 15.3	52.0 ± 16.0	NS
BMI, kg/m ²	25.3 ± 4.8	25.8 ± 7.1	NS
Smoking, %	72	67	NS
Diabetes mellitus, %	4	—	NS
Hypertension, %	45	—	< 0.05
Left ventricular function, %			
Normal	100		

Variables expressed as mean ± SD, *BMI = body mass index; **NS = Not significant.

Table II. Polysomnographic Characteristics of Patients and Controls

	Patients (<i>n</i> = 22)	Controls (<i>n</i> = 14)	<i>p</i> Value
AI	1.9 ± 0.7	1.1 ± 0.4	NS
AHI	2.3 ± 3.8	1.2 ± 1.7	NS
Duration of apnea			
Average (s)	12.6 ± 2.5	16.3 ± 4.1	NS
Longest (s)	20.6 ± 4.6	31.5 ± 11.5	NS
ODI	2.1 ± 3.1	0.5 ± 1.1	< 0.05
Duration of desaturation (min)	9.7 ± 13.6	1.9 ± 4.1	< 0.05
Duration of desaturation (%)	3.1	0.5	< 0.05

Variables expressed as mean ± SD, AI = apnea index; AHI = apnea-hypopnea index; ODI = oxygen desaturation index.

32%. Sixteen patients were taking calcium channel blockers, nine patients were taking angiotensin-converting enzyme inhibitors for control of angina pectoris and one was taking amiodarone as an antiarrhythmic agent. All patients had a normal left ventricular function. Five of 22 patients (23%) had a history of myocardial infarction.

Results of overnight polysomnography are shown in Table II. There were no differences between AI, AHI and apnea duration in both groups. The AI ranged from 0 to 11.7, mean 1.9 among the patients compared with 0 to 4.5, mean 1.1 among controls. The AI was greater than 5 in 18% and 10 in 9% of the patients. The CAD patients had longer episodes of apnea and had significantly greater ODI when compared with controls ($p < 0.05$). The patients also had longer duration of desaturation. The apneas were predominantly obstructive in both CAD and control groups (70% and 67% of all apneas, respectively).

The patients were of similar awake and sleep state oxygen saturation to the control subjects (Table III). The lowest SaO₂ was 87% in patients and 90% in controls ($p < 0.05$). Patients had a greater percentage of sleep time spent at an

Table III. The SaO₂* Values of Patients and Controls

	Patients (n = 22)	Controls (n = 14)	p Value
SaO ₂ awake	93.4 ± 2.8	94.2 ± 2.2	NS
SaO ₂ sleep	93.9 ± 1.7	94.5 ± 2.6	NS
SaO ₂ lowest	87.2 ± 9.5	90.5 ± 2.2	< 0.05
% time spent at SaO ₂ < %90	3.9 ± 1.6	0.3 ± 0.2	< 0.05

Variables expressed as mean ± SD, SaO₂ = arterial oxygen saturation.

Table IV. Sleep Structure of Patients and Controls

	Patients (n = 22)	Controls (n = 14)	p Value
Total sleep time (minute)	314.0 ± 87	366.0 ± 63	< 0.05
Awake, %	34.3 ± 11.3	24.9 ± 10.4	NS
NREM, %	59.5 ± 11.6	67.7 ± 13.6	NS
REM, %	5.9 ± 4.9	7.2 ± 7.7	NS
Sleep efficiency, %	65.0 ± 11.3	74.0 ± 10.8	< 0.05

Variables expressed as mean ± SD.

Table V. The Heart Rate Characteristics of Patients and Controls During Sleep and Awake

	Patients (n = 22)	Controls (n = 14)	p Value
Mean heart rate (awake)	63.9 ± 10.3	65.8 ± 6.0	NS
Mean heart rate (sleep)	61.8 ± 9.5	64.7 ± 3.8	< 0.05
Development of bradycardia (%)	43.3 ± 40.8	25.3 ± 23.5	< 0.05
Development of tachycardia (%)	0.48 ± 2.1	2.7 ± 5.0	< 0.05

Variables expressed as mean ± SD.

$\text{SaO}_2 < 90\%$ (equivalent to $\text{PO}_2 < 65 \text{ mmHg}$).

The sleep structures of the patients and controls are shown in Table 4. While the total sleep time was 314 minutes in patients, it was 366 minutes in controls ($p < 0.05$). There were no differences between awake, NREM and REM stages of sleep in both groups. The sleep efficiency was significantly higher in controls than in patients (74% and 65%, respectively). Of nocturnal desaturation episodes, 78% occurred during NREM sleep in patients and 67% in controls.

The heart rate profiles of both groups during awake and sleep are shown in Table V. The patients had similar initial heart rates to the controls. The mean heart rate and development of tachycardia during sleep in controls were significantly higher than patients ($p < 0.05$). The development of bradycardia during sleep was higher in patients compared with controls ($p < 0.05$).

DISCUSSION

We have shown that nocturnal oxygen desaturation and bradycardia during sleep occur more commonly in patients with coronary artery disease compared to controls. In our study, we were unable to show acute effects due to these abnormalities, but as pointed out by Block,⁶ sleep disordered breathing and nocturnal hypoxemia may contribute to the progression of coronary heart disease.

The clinical characteristics of the patients and controls were similar, except for hypertension. The patients more often had a history of hypertension which is a well known coronary risk factor. Obesity which is involved in the pathogenesis of OSA⁷ was not observed in either group.

The sleep apnea syndrome is present in 1–5% of the male adult population.⁸ The prevalence of this syndrome in normal communities increases with the level of obesity.⁸ The normal controls in our study did not have sleep apnea. This can be attributed to the small number ($n = 14$) and absence of obesity in controls.

Although the patients were more prone to development of sleep apnea compared to controls, there were no differences regarding mean AI and AHI between the groups. Using a diagnostic threshold value of $\text{AI} > 5$ and $\text{AI} > 10$, we found prevalence rates of 18% and 9% sleep apnea in our patients, respectively. This result shows that the prevalence of OSA in patients with CAD (18%) is higher than in the normal population (1–5%).

In two case control studies it has been shown that there is a relation between nocturnal angina pectoris and sleep apnea.^{9,10} Nocturnal angina disappeared after onset of home CPAP (continuous positive airway pressure).⁹ Since our patients did not have nocturnal angina pectoris we could not analyse this observation in our patients.

Jensen *et al.*¹¹ found that episodic and constant hypoxemia were common

during the first week after acute myocardial infarction. Two previous studies have shown a high incidence of sleep apnea in patients with myocardial infarction.^{1,12)} Reported mean values of lowest nocturnal oxygen saturation were similar to our findings.

Recently Moose *et al.*¹³⁾ and Andreas *et al.*¹⁴⁾ have shown a significant association between sleep disordered breathing and CAD. Moose *et al.*¹³⁾ reported that AHI was higher than 10 in 37% of the CAD patients and in 20% of the controls. In the Andreas *et al.* study,¹⁴⁾ the reported apnea index was > 10/h sleep in 25 of 50 (50%) patients. It is interesting that the prevalence of sleep apnea was so high even in those normal controls who had not any known heart disease in Moose's study. We think that the prevalence of sleep apnea in our patients and controls seems to be more realistic than those studies.

In OSAS, the heart rate slows in proportion to the duration of the apnea and the degree of oxyhemoglobin desaturation.¹⁴⁾ In our study, the development of bradycardia during sleep was higher in CAD patients compared with controls. This bradycardic response may be cardioprotective, limiting the myocardial oxygen content and oxygen delivery may be at a low point. Increased risk of sudden cardiac death in CAD patients may be explained by sleep disordered breathing associated with the development of bradycardia during sleep.

The mechanism of the relationship between hypoxemia and ischemic heart disease is unknown. On the other hand, there is strong experimental evidence linking hypoxia with atherosclerosis¹⁵⁾ and sleep disordered breathing may influence the progression of atherosclerosis. For that reason, early diagnosis and suitable therapy of CAD patients at high risk not only abolishes the sleep disordered breathing but also improves long-term outcome.

In conclusion, sleep disordered breathing, in particular nocturnal oxygen desaturation occurs more commonly in patients with CAD compared to controls. Additionally, patients are at higher risk of developing bradycardia during sleep. These findings suggest the need both for investigation of the underlying mechanism(s) and the prognosis in the long term.

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