Sleep-Disordered Breathing and Myocardial Ischemia in Patients With Coronary Artery Disease*

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Study objectives: To examine the occurrence of nocturnal myocardial ischemia and its relationship to sleep-disordered breathing (apneas and oxygen desaturations) in randomly selected men and women undergoing coronary angiography because of angina pectoris.

Design: An observational study using an overnight sleep study and Holter recording to examine disordered breathing (oxyhemoglobin desaturations ≥ 4% and apnea-hypopneas), heart rates, and ST-segment depressions (≥ 1 mm, ≥ 1 min).

Setting: University Hospital, Umeå, a teaching hospital in northern Sweden.

Patients: One hundred thirty-two men and 94 women referred for consideration of coronary intervention were randomly included, by lot.

Results: ST-segment depressions occurred in 59% (134 of 226) of the patients, and nocturnal ST-segment depressions occurred in 31% (69 of 226). A ST-segment depression occurred within 2 min after an apnea-hypopnea or desaturation in 12% (27 of 226) of patients. This temporal association was seen in 19% of nocturnal ST-segment depressions (71 of 366), more frequently in men (p < 0.01) and in more severely disordered breathing (p < 0.001). Most of these ST-segment depressions were preceded by a series of breathing events: three or more apnea-hypopneas or desaturations or both in 70% (50 of 71).

Conclusion: Episodes of nocturnal myocardial ischemia are common in patients with angina pectoris. However, a temporal relationship between sleep-disordered breathing and myocardial ischemia is present only in a minority of the patients, but occurs more frequently in men and in more severely disordered breathing.

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Key words: angina pectoris; anoxemia; coronary disease; myocardial ischemia; sleep apnea syndromes

Abbreviations: AHI = apnea-hypopnea index; ODI = oxygen desaturation index

Sleep-disordered breathing is characterized by frequent pauses in breathing during sleep, apneas, and hypopneas. Disordered breathing is a risk factor for myocardial infarction,1 and in a sleep clinic population, severely disordered breathing has been associated with increased mortality with a predominance of cardiovascular deaths.2

Disordered breathing results in oxyhemoglobin desaturation, sympathetic activation, and hemodynamic changes with an increase in preload and afterload.3,4 The hemodynamic stress induced by disordered breathing may be of particular importance in patients with coronary artery disease, in whom sleep-disordered breathing is common.5,6 In selected patients with coronary disease, sleep apnea is associated with myocardial ischemia and nocturnal angina.7 The aim of the present study was to examine the relationship between sleep-disordered breathing and myocardial ischemia in a large sample of randomly selected patients with angina pectoris and coronary artery disease verified by angiography.

Materials and Methods

Patients

Men and women ≥70 years old referred for coronary angiography because of disabling angina pectoris were included in the
study. Participants were randomly selected, by lot, from all eligible patients that day for an overnight sleep study. The presence of coronary disease was verified before inclusion.

The study was approved by the institutional ethics committee, and all subjects gave informed consent.

Sleep Studies

The following variables were recorded during 1 night of sleep in the hospital: oronasal airflow using a three-way thermistor (ZE-732A; Nihon Khoden; Tokyo, Japan), blood oxygen saturation and heart rate by pulse oximetry with a finger transducer (Biox 3700; Ohmeda; Louisville, CO), respiratory and body movements using a pressure-sensitive bed (polyvinylidenefluoride-foil; Apnomat; Duorek Ltd; Raisio, Finland), and sleep position with a body position indicator (Vitalog Monitoring; Redwood City, CA).

All signals were continuously sampled and stored in a Macintosh II computer (Apple Computer; Cupertino, CA) and displayed on-line. The duration of sleep was estimated from the pressure-sensitive bed recording.

Desaturations and apneas were manually scored without knowledge of the clinical characteristics. A desaturation was defined as a decrease in oxygen saturation of ≥ 4%. An apnea was defined as a cessation of airflow lasting at least 10 s, and hypopnea as a reduction in airflow lasting ≥10 s, with a nadir at least 50% below an estimated baseline amplitude within 2 min before or after the event, associated with an oxygen desaturation or a pulse alteration. Sleep-disordered breathing was measured as oxygen desaturation index (ODI) and apnea-hypopnea index (AHI), calculated as the average number of episodes of desaturation and apnea or hypopnea per hour of sleep, respectively. The computer used for the sleep study was time synchronized with the ECG tape recorder. A relationship between apnea/desaturation and ST-segment depression was considered to exist if the ST-segment depression occurred within 2 min after the breathing event.

All subjects completed a questionnaire concerning the occurrence of nocturnal chest pain.

Holter Monitoring

Monitoring was started between 3:00 PM and 6:00 PM, and continued until the patient woke up the following morning. A two-channel tape recorder (Tracker TR1; Reynolds Medical; Hertford, UK) was used, recording leads V2 and V5. The frequency response was 0.05 to 100 Hz (2 decibels). The recordings were analyzed with computerized equipment (Danica Biomedical AB; Borlänge, Sweden) with manual verification and printout. The ST-segment was measured 0.06 s after the J point, and depressions of at least 1 mm compared to baseline with a duration of at least 1 min were considered to indicate myocardial ischemia.

Statistical Analysis

Data were analyzed with the Statistica 4.0 software modules (StatSoft; Tulsa, OK). Group data were expressed as mean ± SD for continuous variables, and as rates for variables on a nominal scale. Differences between two means were assessed with t test for unpaired data, or the Mann Whitney U test when appropriate. Differences between proportions were analyzed with the χ2 test. In all statistical tests, the null hypothesis was rejected at the 5% level (p < 0.05).

Results

One hundred forty-four men and 106 women ≤ 70 years old were included. Sixteen patients (5 men, 11 women) refused to participate. After exclusions for technical failures, complete analysis of oxygen desaturation and Holter recording were obtained in 132 men and 94 women. Complete apnea analysis was obtained in 127 men and 92 women. All patients had stable angina pectoris in Canadian Cardiovascular Society class II (16%; n = 36) or III (84%; n = 190).

One-vessel disease was found in 19%, two-vessel disease in 27%, and three-vessel disease in 39%. Left main stem stenosis was found in 15%. No interaction was found between the severity of disordered breathing and the extent of coronary disease. Left ventricular function was visually assessed from the left ventriculography, and scored as good (74%), fair (21%), and poor (5%), corresponding to ejection fractions of approximately > 0.5, 0.35 to 0.5, and < 0.35, respectively.

Clinical characteristics and medical treatment of the patients are presented in Tables 1, 2. Mean values for ODI and AHI were 6.4 (range, 0 to 69) and 10.0 (range, 0 to 98), respectively.

Occurrence of ST-Segment Depressions

The duration of the recordings and the episodes of ST-segment depressions are shown in Table 3. An ST-segment depression was recorded in 134 of 226 patients (59%), and 69 patients (31%) had at least one ST-segment depression during sleep. Nocturnal ST-segment depressions were more common (39%...
vs 19%; \( p < 0.01 \)) and of longer duration (6.8 min/h vs 2.3 min/h; \( p < 0.05 \)) in men than in women, respectively. Patients with left main stem stenosis had a higher occurrence of nocturnal ST-segment depressions than those without (45% vs 28%; \( p = 0.05 \)).

**Relationship Between Disordered Breathing and ST-Segment Depressions**

More severely disordered breathing did not significantly increase the frequency or duration of ST-segment depressions during sleep (Table 4). ST-segment depressions occurred more frequently in men than in women, regardless of disordered breathing.

There was no difference in ODI or AHI in patients with and without nocturnal ST-segment depressions (ODI, 6.8 vs 6.3; AHI, 10.3 vs 9.8).

**Temporal Association Between Desaturations/Apneas and ST-Segment Depressions**

In 27 patients (12%; 22 men and 5 women; \( p < 0.01 \)), at least one ST-segment depression occurred within 2 min after an apnea or desaturation. The proportion of ST-segment depressions within 2 min after a breathing event was 19% (71 of 366 events). Patients with an ST-segment depression associated with a breathing event had more severely disordered breathing compared with those without: ODI, 13.9 vs 5.4 (\( p < 0.001 \)) and AHI, 18.2 vs 8.8 (\( p < 0.001 \)), respectively. Mean values of lowest oxygen saturation during sleep were 82.1 vs 87.1 (\( p < 0.001 \)). Seventy percent of patients (19 of 27) with ST-segment depressions associated with breathing events had ODI ≥ 5. Patients with left ventricular dysfunction were not significantly more likely to have ST-segment depressions related to disordered breathing events (11 of 59 vs 16 of 167; \( p = 0.07 \)). ST-segment depressions occurring within 2 min after a breathing event were often preceded by pronounced desaturations or evolved after repetitive apneas/desaturations (Fig 1, 2). Desaturations of > 6%, > 8%, and > 10% preceded 42% (30 of 71), 27% (19 of 71), and 13% (9 of 71) of these ST-segment depressions, respectively; repetitive apneas or desaturations or both (three or more events) preceded 70% (50 of 71). Fifteen patients had ≥ 50% of their ST-segment depressions within 2 min after an apnea or desaturation (42 of 56 events).

**Heart Rate Changes Preceding ST-Segment Depressions**

An increase in heart rate of > 10 beats/min within 2 min before the onset of ST-segment depressions was observed in 59% of ST-segment depressions (42 of 71) with, and in 48% of ST-segment depressions (141 of 295) without, a temporal relationship to breathing disturbances (\( p = 0.09 \)). The corresponding proportions of ST-segment depressions preceded by an increase in heart rate of > 20 beats/min were 21% (15 of 71) and 10% (30 of 295), respectively (\( p < 0.05 \)).

**Nocturnal Angina and Occurrence of Disordered Breathing**

Forty-three men (33%) and 41 women (44%) reported that they occasionally woke up because of...
chest pain. Disordered breathing (ODI > 5) was more common in patients with a history of nocturnal chest pain than in those without (38 of 84 vs 37 of 126; p < 0.05).

**DISCUSSION**

Although disordered breathing is common in patients with symptomatic coronary disease,\textsuperscript{5,6} published data about the relationship between nocturnal oxygen desaturations or apneas and myocardial ischemia are based on small and selected patient groups.\textsuperscript{7,11–13} In one study of 10 men with nocturnal angina and angiographically verified coronary disease, 5 had apneas or hypopneas within 90 s before ischemia was detected using computerized vectorcardiography.\textsuperscript{7} When Holter monitoring was performed in 19 patients (16 men, 3 women) on the second to sixth night after acute myocardial infarction, ST-segment depressions were detected within 2 min after oxygen desaturations in 9 patients.\textsuperscript{11} In another study, 30 men scheduled for coronary bypass surgery were examined by Holter monitoring and pulse oximetry.\textsuperscript{12} Ten patients had ischemic episodes; three were associated with respiratory events. When repeated sleep studies were performed in 21 patients, 144 episodes of myocardial ischemia were recorded in 6 patients (59 episodes in 1 patient), of which 123 episodes were concomitant with apneas and oxygen desaturations.\textsuperscript{13}

In our study, only 19% of nocturnal ST-segment depressions (71 of 366) appearing in 12% of the

<table>
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<th>Variables</th>
<th>Women</th>
<th>ST Dur</th>
<th>Men</th>
<th>ST Dur</th>
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<td>7.9</td>
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<td>2.7</td>
<td>33 (9/27)</td>
<td>8.0</td>
<td>33 (15/45)</td>
<td>5.9</td>
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<tr>
<td>ODI ≥ 15</td>
<td>36 (5/14)</td>
<td>2.3</td>
<td>42 (8/19)</td>
<td>8.1</td>
<td>39 (13/33)</td>
<td>5.9</td>
</tr>
</tbody>
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*Data are presented as % (no./total patients) unless otherwise indicated. ST Dur = mean duration of ST-segment depressions (in minutes) per hour calculated for patients showing ST-segment depressions.

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21948/) **Figure 1.** An example of sleep-disordered breathing (oxyhemoglobin desaturation and apnea) showing a temporal relationship with ST-segment depression. Sat = oxyhemoglobin saturation, %; HR = heart rate, beats per minute; Therm = thermistor tracing.
patients (27 of 226; 17% of men; 5% of women) had a temporal relationship to disordered breathing. A temporal relationship was more often found in patients with severely disordered breathing and pronounced desaturations (Fig 2). ST-segment depressions were often preceded by an increase in heart rate (59%; 42 of 71), or series (three or more) of breathing events (70%; 50 of 71), or pronounced desaturations (27%; 19 of 71), suggesting that disordered breathing with changes of heart rate was a common cause of ischemia. Since 59% of the ST-segment depressions (42 of 71) were preceded by an increase in heart rate (> 10 beats/min), both decreased oxygen supply (oxygen desaturation) and increased oxygen demand (increased heart rate) could have contributed to myocardial ischemia associated with breathing events.14,15

Holter monitoring has been extensively used to examine the occurrence of symptomatic as well as asymptomatic myocardial ischemia.16,17 The validity of the method in patients with coronary disease has been shown by comparison with radionuclide techniques,18 hemodynamic measurements,19 and positron tomography.20 Studies using Holter monitoring have discovered silent ischemia in 60 to 100% of patients with symptomatic myocardial ischemia.16,21,22 There is a circadian variation with a lower incidence of ischemia during the night.9,15,23 Our results (Table 3) correspond well with those of previous reports. Furthermore, we found a lower incidence (p < 0.01) and a shorter duration (p < 0.05) of nocturnal ischemia in women as compared with men, and only 5% (5 of 94) of the women had a temporal association between breathing events and ischemia (p < 0.01). Sex-related differences in vectorcardiographic changes during ischemia have previously been reported.24

We found that disordered breathing was more common in patients with a history of nocturnal angina. A sleep study may therefore be of value in patients with complaints of nocturnal chest pain. We did not find any significant relationship between the severity of disordered breathing and the severity of coronary disease, but the investigation was not designed to specifically explore this question.

All patients took their anti-anginal medication (Table 2) as usual. Probably, this reduced the number of nocturnal ST-segment depressions, but reflects a normal, everyday situation.

In most of the present patients with documented coronary disease, there was no relationship between nocturnal breathing disturbances and the occurrence of myocardial ischemia. Eighty-one percent of the nocturnal ST-segment depressions were not preceded by apneas or desaturations, and the occurrence of ST-segment depressions did not increase in patients with more severely disordered breathing (Table 4). Thus, mechanisms other than breathing disturbances explain the majority of nocturnal ST-segment depressions in patients with coronary disease, ie, heart rate changes and reduction in coronary flow.9,15

The prognostic consequences of disordered breathing in the present group of patients requires further study.

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REFERENCES