Sleep apnoea in ischaemic heart disease: differences between acute and chronic coronary syndromes

P Moruzzi, S Sarzi-Braga, M Rossi, M Contini

Abstract

Objective—To evaluate the incidence of sleep apnoea in acute and chronic coronary syndromes.

Design—Analysis of sleep and breathing characteristics in a polysomnographic study.

Setting—Cardiology department in tertiary referral centre.

Patients—23 patients were studied soon after acute myocardial infarction (group 1), 22 after clinical stabilisation of unstable angina (group 2), and 22 who had stable angina (group 3). Conditions liable to cause sleep apnoea, such as obesity, chronic obstructive pulmonary disease, neurological disorders, or the use of benzodiazepines, were exclusion criteria.

Main outcome measures—Sleep apnoea and hypopnoea, oxygen saturation, and sleep indices evaluated soon after clinical stabilisation in groups 1 and 2 and also in group 3.

Results—Sleep apnoea, mainly of the central type, was equally present in groups 1 and 2 (mean (SD) apnoea-hypopnoea index: 11.10 (19.42) and 14.79 (20.52), respectively) and more severe than in group 3 (2.82 (6.43), p < 0.01). Total time spent at SaO2 < 90%, although significantly greater in group 1 (5.15 (3.71)) and group 2 (5.31 (2.14)) than in group 3 (0.89 (2.4), p < 0.05) were detected in group 1 (5.15 (3.71)) and group 2 (5.31 (2.14)) than in group 3 (2.83 (1.51)).

Conclusions—Sleep apnoea, chiefly of the central type, not only characterises acute myocardial infarction, as found by others, but also unstable angina studied after recent stabilisation. Patient selection by exclusion of other causes of breathing disorders shows that coronary disease related apnoea is absent in the chronic coronary syndrome. In acute syndromes the lack of clinically significant apnoea related oxygen desaturation, together with the low associated incidence of major ischaemic and arrhythmic events, suggests that sleep apnoea is benign in these circumstances, despite a worsening of sleep quality.

Sleep apnoea may be present in several cardiovascular diseases, such as congestive heart failure, systemic arterial hypertension, and coronary artery disease.

According to some investigators, sympathetic activation can induce apnoea. If this were the case, increased adrenergic drive might help to explain the prevalence of sleep apnoea in such conditions as congestive heart failure and systemic arterial hypertension, but not in all varieties of coronary artery disease. Thus, while acute myocardial infarction and unstable angina are associated with sympathetic overactivity, chronic coronary artery disease without compromised left ventricular function is not. On the other hand, it is also possible that apnoea facilitates ischaemic attacks through hypoxia and the ensuing sympathetic activation.

In order to try to explain the association between coronary artery disease and sleep apnoea, patient selection must be strict enough to exclude the presence of non-cardiovascular causes of apnoea. Our aim in this study was to evaluate sleep and the breathing patterns during sleep in patients suffering from stable coronary artery disease, recent myocardial infarction, and unstable angina, to determine whether there is a difference between coronary stability and coronary instability in relation to the incidence of sleep apnoea. These conditions may differ not only because of different degrees of sympathetic activation, but also with regard to other characteristics such as left ventricular function and thrombogenesis, which might influence or be influenced by sleep apnoea. In stable coronary artery disease, for example, left ventricular function and thrombogenesis are often normal; in unstable angina, an increase in thrombogenesis contributes to clinical instability, while ventricular function may be normal, at least at baseline; and in myocardial infarction there is often an associated reduction in left ventricular function and enhanced thrombogenesis.

We thought that evaluating the prevalence of sleep apnoea and its relation to sleep stages under these different conditions might help in separating cause from effect with regard to breathing alterations in coronary artery disease. In particular, we wanted to see whether there is a link between coronary disorders associated with sympathetic activation and sleep apnoea.

Methods

We studied 67 patients (56 men and 11 women), ranging in age from 32 to 70 years, mean (SD)
Table 1  Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Group 1 (myocardial infarction)</th>
<th>Group 2 (unstable angina)</th>
<th>Group 3 (stable angina)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.00 (7.53)</td>
<td>54.45 (9.97)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>22/1</td>
<td>16/6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.76 (3.33)</td>
<td>24.56 (3.15)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>53.04 (11.17)†</td>
<td>62.19 (11.91)*</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>59.2 (6.64)</td>
<td>59.38 (8.23)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td>Smoker</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Total number in group</td>
<td>23</td>
<td>22</td>
</tr>
</tbody>
</table>

Values are numbers of patients or mean (SD). *p < 0.05 v group 3; †p < 0.01 v group 3.

The day before the study, an echocardiogram, to evaluate left ventricular ejection fraction, and a spirometric test, to exclude the presence of any restrictive or obstructive limitation of respiratory function, were performed in all cases. Patients with abnormal spirometric tests were not included in the study.

The indices used to assess sleep were total sleep time, sleep latency, sleep efficiency (total sleep time × 100/time in bed), number of arousals per hour of sleep, and evaluation of sleep stages as percentages of total sleep time. Sleep stages were identified blind by two observers through non-computer analysis, according to the guidelines established by the UCLA brain information service committee. To evaluate breathing disorders we included in the analysis the number of episodes of apnoea and hypopnoea per hour of sleep, total time spent in apnoea–hypopnoea, mean duration of apnoea–hypopnoea, longest apnoea duration, minimum arterial oxygen saturation (So2) and time spent at So2, less than 90%.

Apnoea episodes were considered to be interruptions in air flow lasting for more than 10 seconds; hypopnoea episodes were defined as periods in which there was at least a 50% reduction in respiratory flow for 10 seconds or more. Apnoea and hypopnoea episodes were classified as central if no chest or abdominal movement was observed, obstructive if chest and abdominal movements occurred during airflow reduction, and mixed when respiratory effort, initially absent, began just before the restoration of airflow.

RESULTS

As shown in table 1, the three groups were comparable for age, sex, and body mass index. Patients in groups 1 and 2 were more likely to have hypertension. Smoking and the use of β blockers were accurately accounted for (table 1) and considered in the analysis.

In group 1, extension of the necrosis was evaluated by the creatine kinase (CK) peak. Patients in group 2 were studied soon after clinical stabilisation. In group 3, the diagnosis of ischaemic heart disease was established by exercise stress testing. Coronary angiography was performed whenever necessary (62 patients). All patients gave informed consent for the study, and the research protocol was approved by the local ethics committee on human research.

A polysomnographic study (Somnostar 4100, SensorMedics bv, Bilthoven, Netherlands) was performed in all patients during their stay in hospital. Overnight recording included a four channel electroencephalogram (EEG) (C4A1, O2A1, C3A2, and O1A2), an electro-oculogram, a submental electromyogram, a three channel ECG, and evaluation of oro-nasal airflow by a thermistor, rib cage and abdominal movements by strain gauges, and oxygen saturation by digital oximetry (SensorMedics).

To evaluate breathing disorders we included in the analysis the number of episodes of apnoea and hypopnoea per hour of sleep, total time spent in apnoea–hypopnoea, mean duration of apnoea–hypopnoea, longest apnoea duration, minimum arterial oxygen saturation (So2) and time spent at So2, less than 90%.

Apnoea episodes were considered to be interruptions in air flow lasting for more than 10 seconds; hypopnoea episodes were defined as periods in which there was at least a 50% reduction in respiratory flow for 10 seconds or more. Apnoea and hypopnoea episodes were classified as central if no chest or abdominal movement was observed, obstructive if chest and abdominal movements occurred during airflow reduction, and mixed when respiratory effort, initially absent, began just before the restoration of airflow.

STATISTICS

Data are expressed as mean (SD). Statistical analysis was performed by χ² analysis and Kruskal and Wallis analysis of variance; in case of statistical significance, comparisons between two groups were performed using the Mann–Whitney U test. Statistical significance was assumed at p < 0.05.

RESULTS

As shown in table 1, the three groups were comparable for age, sex, and body mass index. Patients in groups 1 and 2 were more likely to have hypertension. Smoking and the use of β blockers were accurately accounted for (table 1) and considered in the analysis.

In group 1, extension of the necrosis was evaluated by the creatine kinase (CK) peak. Patients in group 2 were studied soon after clinical stabilisation. In group 3, the diagnosis of ischaemic heart disease was established by exercise stress testing. Coronary angiography was performed whenever necessary (62 patients). All patients gave informed consent for the study, and the research protocol was approved by the local ethics committee on human research.

A polysomnographic study (Somnostar 4100, SensorMedics bv, Bilthoven, Netherlands) was performed in all patients during their stay in hospital. Overnight recording included a four channel electroencephalogram (EEG) (C4A1, O2A1, C3A2, and O1A2), an electro-oculogram, a submental electromyogram, a three channel ECG, and evaluation of oro-nasal airflow by a thermistor, rib cage and abdominal movements by strain gauges, and oxygen saturation by digital oximetry (SensorMedics).

The day before the study, an echocardiogram, to evaluate left ventricular ejection fraction, and a spirometric test, to exclude the presence of any restrictive or obstructive limitation of respiratory function, were performed in all cases. Patients with abnormal spirometric tests were not included in the study.

The indices used to assess sleep were total sleep time, sleep latency, sleep efficiency (total sleep time × 100/time in bed), number of arousals per hour of sleep, and evaluation of sleep stages as percentages of total sleep time. Sleep stages were identified blind by two observers through non-computer analysis, according to the guidelines established by the UCLA brain information service committee. To evaluate breathing disorders we included in the analysis the number of episodes of apnoea and hypopnoea per hour of sleep, total time spent in apnoea–hypopnoea, mean duration of apnoea–hypopnoea, longest apnoea duration, minimum arterial oxygen saturation (So2) and time spent at So2, less than 90%.

Apnoea episodes were considered to be interruptions in air flow lasting for more than 10 seconds; hypopnoea episodes were defined as periods in which there was at least a 50% reduction in respiratory flow for 10 seconds or more. Apnoea and hypopnoea episodes were classified as central if no chest or abdominal movement was observed, obstructive if chest and abdominal movements occurred during airflow reduction, and mixed when respiratory effort, initially absent, began just before the restoration of airflow.

STATISTICS

Data are expressed as mean (SD). Statistical analysis was performed by χ² analysis and Kruskal and Wallis analysis of variance; in case of statistical significance, comparisons between two groups were performed using the Mann–Whitney U test. Statistical significance was assumed at p < 0.05.
Table 3  Respiratory variables in subgroups with apnoea-hypopnoea index (AHI) > 10

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time at SaO2 &lt; 90% (min)</td>
<td>0.89 (2.40)†</td>
<td>1.42 (3.23)‡</td>
<td>0.01 (0.05)</td>
</tr>
<tr>
<td>Mean SaO2 (%)</td>
<td>96.0 (0.82)</td>
<td>96.0 (1.07)</td>
<td>96.5 (0.71)</td>
</tr>
<tr>
<td>Minimum SaO2 (%)</td>
<td>86.75 (5.50)</td>
<td>85.13 (4.39)</td>
<td>90.0 (0.02)</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>75</td>
<td>80</td>
<td>95</td>
</tr>
</tbody>
</table>

Values are mean (SD).

*p < 0.05 v group 3; †p < 0.01 v group 3.

AHI, apnoea-hypopnoea index; REM, rapid eye movement; SaO2, arterial oxygen saturation.
index > 10). We also observed this nocturnal respiratory pattern for the first time in patients with a recent episode of unstable angina without previous myocardial necrosis. In these subjects the number of apnoea episodes per hour of sleep was even higher than after myocardial infarction, possibly because of the shorter time interval between the acute phase of the disease and the time of the study.

On the other hand, in patients with chronic coronary artery disease without previous episodes of coronary instability of any kind, the apnoea–hypopnoea index was not only less than in the other two study groups but also less than in the general population, probably because of patient selection. Thus sleep apnoea seems to be related in some way not only to myocardial infarction as such but also to the acute coronary syndrome as a whole.

Moreover, if we consider those few stable angina patients with significant sleep breathing disorders, the apnoea episodes were mostly of the obstructive type, as is usually observed in the general population. On the other hand, in groups 1 and 2, a clear prevalence of central sleep apnoea was observed. This could mean that patients with coronary instability not only show a higher incidence of sleep apnoea than patients with coronary artery disease or the general population, but also that such apnoea episodes probably have a different aetiology from episodes in subjects with a stable coronary circulation.

The results of our study do not allow us to draw definitive conclusions about the causes of disordered breathing during sleep in patients with coronary instability. As to a possible role of myocardial dysfunction, congestive heart failure is also characterised by apnoeic episodes, mostly of the central type, but they are associated with periodic breathing, which never occurred in our population. Furthermore, the absence of any correlation between the apnoea–hypopnoea index and the left ventricular ejection fraction, which was within normal limits in all three groups of patients, rules this out as a cause of the sleep apnoea syndrome. In addition, ischaemic or arrhythmic events during sleep that are apt to lead to left ventricular failure never occurred in our study.

Subgroup analysis also excludes an apnoeic effect of pharmacological treatment, especially of β blockade, in our population.

In our opinion, the prevalence of central apnoea episodes in groups 1 and 2 is more in favour of defective central ventilatory control. Chemoreceptor dysfunction does not seem to provide the best explanation, with normal cardiac performance and no episodes of Cheyne–Stokes respiration. As sympathetic hyperactivity is a feature common to both the postinfarction period and unstable angina, we hypothesise a possible inhibitory effect of sympathetic tone on respiratory drive in these patients. This effect has been demonstrated in animal studies by catecholamine infusion into the carotid artery and pacing of the vasomotor centres. The apparently protective effect of β blockers against apnoea observed in groups 1 and 2 is consistent with this hypothesis. Stress condition is another characteristic of coronary instability which might play a role in activating the adrenergic nervous system.

We cannot exclude the possibility that apnoea—as suggested by others—could facilitate coronary thrombosis and instability through hypoxia and platelet activation, both before and after an acute ischaemic event. In our opinion, however, this is more likely to be the case with obstructive than with central types of apnoea. In fact, obstructive sleep apnoea episodes, being more organic than functional in origin, are likely to be present before the occurrence of coronary syndromes, and above all are usually associated with a noticeably higher degree of oxygen desaturation than observed in our study population. The mild degree of oxygen desaturation found in our patients, together with the brief mean apnoea duration and normal cardiac function, could explain the lack of clinical complications, either ischaemic or arrhythmic, in patients with recent myocardial infarction and unstable angina. A study carried out in more compromised patients would be of interest in evaluating the clinical importance of sleep apnoea in coronary instability.

With regard to sleep architecture, the incidence of sleep apnoea episodes in groups 1 and 2 could explain the increased number of arousals, at least in those cases in which there was a clear temporal relation between respiratory and EEG events. However, there was no significant worsening in sleep quality, considered as percentage distribution of sleep stages and sleep efficiency.

**CONCLUSIONS**

In subjects without risk factors for obstructive respiratory disorders, acute coronary syndromes—unlike chronic coronary artery disease—are associated with the occurrence of sleep apnoea episodes, mostly of the central type, which is in some way related to the ischaemic event. Sympathetic hyperactivity, which is both associated with such conditions and a cause of apnoeic episodes in animal studies, might explain this finding. The lack of significant complications in apnoea patients suggests that sleep apnoea is benign in these circumstances, at least when other causes of apnoea are excluded.