High Prevalence of Sleep Apnea Syndrome in Patients With Long-Term Pacing
The European Multicenter Polysomnographic Study

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Background—Cardiovascular diseases leading to pacemaker implantations are suspected of being associated with a high rate of undiagnosed sleep apnea syndrome (SAS). We sought to determine the prevalence and consequences of SAS in pacemaker patients according to pacing indications: heart failure, symptomatic diurnal bradycardia, and atrioventricular block.

Methods and Results—Ninety-eight consecutive patients (mean age, 64 ± 8 years) not known to have sleep apnea were included; 29 patients were paced for dilated cardiomyopathy (29%), 33 for high-degree atrioventricular block (34%), and 36 for sinus node disease (37%). All underwent Epworth Sleepiness Scale assessment and polysomnography with the pacemaker programmed to right ventricular DDI pacing mode (lower pacing rate, 50 pulses per minute). SAS was defined as an apnea-hypopnea index ≥ 10/h. Mean Epworth Sleepiness Scale was in the normal range (7 ± 4), although 13 patients (25%) had an abnormal score ≥ 11/h. Fifty-seven patients (59%) had SAS; of these, 21 (21.4%) had a severe SAS (apnea-hypopnea index ≥ 30/h). In patients with heart failure, 50% presented with SAS (mean apnea-hypopnea index, 11 ± 7) compared with 68% of patients with atrioventricular block (mean apnea-hypopnea index, 24 ± 29) and 58% with sinus node disease (mean apnea-hypopnea index, 19 ± 23).

Conclusions—In paced patients, there is an excessively high prevalence of undiagnosed SAS (59%). Whether treating SAS would have changed the need for pacing is unknown. Treatment effects should be further evaluated particularly because these patients are less symptomatic than typical SAS patients. In any case, SAS should be systematically searched for in paced patients owing to potential detrimental effects on their cardiovascular evolution. (Circulation. 2007;115:1703-1709.)

Key Words: bradycardia ■ heart failure ■ nervous system, autonomic ■ pacing ■ sleep apnea syndromes

Bradycardic rhythm disorders frequently are observed in patients with obstructive sleep apnea (OSA),1 particularly in those exhibiting severe nocturnal oxygen desaturations.2,3 Sinus bradycardia and sinoatrial and atrioventricular (AV) block commonly occur.1,3 This phenomenon has been attributed to the effect of sleep apnea–induced hypoxemia, resulting in increased vagal tone and thus cardiac rhythm disturbances.4–6 Compared with nonbradycardic patients, individuals with nighttime bradycardia exhibit a significant increase in nocturnal rhythm abnormalities associated with OSA.7,8 The diagnosis of sleep respiratory disturbances is therefore crucial because nasal continuous positive airway pressure reverses heart block in a significant percentage of patients with OSA.3,9,10 Therefore, pacemakers should be reserved for those with persistent heart block despite continuous positive airway pressure treatment or when compliance is poor.9

Clinical Perspective p 1709

On the other hand, both OSA and central sleep apnea (CSA) are highly prevalent in patients with left ventricular dysfunction,11 being observed in 40% to 50% of patients with compensated cardiac failure and ejection fraction < 40%.12–14 This prevalence can increase up to 80% when patients are evaluated soon after an acute episode of cardiac failure.15 CSA clearly is associated with an increased arrhythmic risk; sustained ventricular tachycardia in these patients is observed almost exclusively during severe CSA.13 As in OSA patients, arrhythmias can potentially be reduced by continuous positive airway pressure.16,17

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TABLE 1. Patients Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sinus Node Dysfunction (n=36; 37%)</th>
<th>AV Block (n=33; 44%)</th>
<th>Heart Failure (n=29; 29%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>66±6</td>
<td>63±9</td>
<td>62±9</td>
</tr>
<tr>
<td>Women, %</td>
<td>25</td>
<td>27</td>
<td>24</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27±4</td>
<td>26±4</td>
<td>26±6</td>
</tr>
<tr>
<td>Epworth Sleepiness Score</td>
<td>7±5</td>
<td>7±5</td>
<td>7±3</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>65±19</td>
<td>65±10</td>
<td>25±6†</td>
</tr>
<tr>
<td>Ischemic disease, %</td>
<td>19</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Treated hypertension, %</td>
<td>51</td>
<td>54</td>
<td>45†</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>8</td>
<td>9</td>
<td>14</td>
</tr>
</tbody>
</table>

LV indicates left ventricular. Values are mean±SD where appropriate. N=98.

*p<0.05; †p<0.01.

Because pacemaker implantations are performed predominantly in patients with daytime and nighttime symptomatic bradycardia, it seems reasonable to expect a higher incidence of OSA in patients with long-term pacing compared with the general population. In addition, with the increasing use of biventricular pacing to treat severe cardiac failure, a high prevalence of both CSA and OSA might be expected in this subgroup.

The current prospective clinical study, the European Multicenter Polysomnography Study, was designed to assess the prevalence of sleep respiratory disturbances in patients with long-term pacing. For this purpose, we performed full sleep studies in a population of pacemaker patients during spontaneous nocturnal atrial rhythm. The secondary goal of the study was to determine the nature, central or obstructive, and the severity of nocturnal respiratory events according to the type of rhythm abnormality (sinus dysfunction or AV block) and the severity of cardiac failure.

Methods

Study Population

A total of 98 consecutive patients from 11 cardiology centers in France, the United Kingdom, and Belgium were included in this study. Patients were selected on the basis of having a pacemaker implanted for at least 1 month for symptomatic sinus node dysfunction, permanent AV block, or severe heart failure with a QRS width >120 ms (biventricular pacing device); patient characteristics are given in Table 1. In addition, patients were required to have a mean spontaneous nocturnal atrial rate ≥50 bpm. Patients were excluded from participating in the study if they had any of the following: recent (<6 months) myocardial infarction, unstable angina, permanent atrially paced rhythm, or coronary revascularization by coronary artery bypass grafting or percutaneous intervention in the preceding 6 months.

All patients provided written informed consent to the study protocol, which was approved by the clinical research and ethics committee of each participating institution.

Study Protocol

Patient evaluation included historic data collection, assessment of the functional cardiac status (New York Heart Association classification), echocardiography, 24-hour Holter recording, and sleep study. Subjective sleepiness was assessed by the Epworth Sleepiness Scale, which is a validated 8-item self-completion questionnaire.18

Sleep Study

All polysomnographic recordings included at least the following parameters: inductance plethysmography for thoracic/abdominal movements; thermistor and/or nasal pressure for oronasal airflow; pulse oximetry for oxygen saturation; and electroencephalogram, electro-oculogram, and electromyogram for sleep recording.

Apneic events were classified as central, obstructive, or mixed, depending on the absence or presence of breathing efforts. Episodes of apnea were defined as complete cessation of airflow for ≥10 seconds. Hypopnea was defined as either a reduction in flow or amplitude of the thoracic and abdominal signals >50% lasting for at least 10 seconds or ≥30% and associated with an arousal and/or a desaturation of 3%.19 Cheyne-Stokes respiration was characterized by the presence of central apneas and/or hypopneas alternating with periods of crescendo-decrescendo tidal volume. During Cheyne-Stokes respiration periods, central apneas or hypopneas were scored and included in the apnea-hypopnea index (AHI). Hypopneas were classified as obstructive on the basis of a reduction in flow while the respiratory efforts either were increased or not reduced in proportion to the flow reduction. This was confirmed by the presence of inspiratory flow limitation on the nasal pressure signal.20 An AHI threshold ≥10/h was used for the diagnosis of sleep apnea syndrome (SAS).21 Sleep scoring was performed locally in each center. However, to ensure quality control and specifically to check the accuracy of the classification of hypopneas, a random analysis of the polysomnographic tracings was performed by one of the investigators (J.-L.P.) who was blinded to the initial results. Approximately 25% of the tracings were reviewed, and only minor corrections were made to the respiratory events scoring.

Pacing Protocol

The pacemaker setup was changed between 12 and 24 hours before the polysomnography so that eventual heart rhythm–induced sleep apnea changes were likely to occur. Pacemaker programming was optimized to promote spontaneous atrial and ventricular rhythm with respect to individual indications for pacing. Accordingly, before the polysomnography, the pacemaker was programmed as follows: DDD pacing at 50 bpm and a long AV delay (between 200 and 250 ms) to promote spontaneous ventricular activation in patients with sinus node dysfunction, DDD pacing at 50 bpm and an optimized AV delay in patients with complete AV block, and DDI pacing (with right ventricular pacing) at 50 bpm and a long AV delay (between 200 and 250 ms) to promote spontaneous ventricular activation in patients with heart failure.

After the polysomnography, the pacemaker was programmed in the original mode used before the study protocol.

Statistical Analysis

All descriptive data are presented as mean±SD. Differences between groups were compared by 1-way ANOVA or the Kruskal-Wallis test (for variables with a nonnormal distribution). Multiple comparisons were assumed with Bonferroni or Kruskal-Wallis tests, controlling for the comparison-wise error rate. Frequency of variables was assessed by Fisher exact test. Spearman’s rank test was used for correlations. Values of P<0.05 were considered significant.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patient Characteristics

Baseline characteristics of the patients are presented in Table 1. The mean age of this cohort was 63±8 years (77% of men); mean body mass index (BMI) was 26.8±5.2 kg/m²; and left ventricular ejection fraction was 60±19%. The following concomitant diseases were observed: coronary heart disease (22%), arterial hypertension (49%), and diabetes mellitus (10%).
Thirty-six patients (37%) were implanted with a dual-chamber pacemaker for sinus dysfunction; 33 patients (34%) received implants for high-degree AV block; and 29 patients (29%) underwent cardiac resynchronization therapy for severe heart failure. Heart failure patients had a significantly lower left ventricular ejection fraction (P<0.01) and presented with a lower prevalence of systemic hypertension (P<0.05) compared with patients undergoing pacing for sinus node dysfunction or AV block.

**Sleep Studies**
Details of the findings of the sleep studies are summarized in Table 2.

**Sleep Parameters and Pacing Characteristics**
The total sleep time was comparable in the 3 groups. During polysomnography, the percentage of ventricular pacing was 97% in sinus node dysfunction patients and 15% in AV block patients and 12% in patients with heart failure. Heart failure patients had a significantly lower percentage of spontaneous ventricular activation. In terms of percentage of atrial pacing, no significant difference existed between the 3 patient groups (Table 2).

**SAS Prevalence**
The overall prevalence of SAS was 59% (95% confidence interval, 49 to 69), which was significantly different from the values previously obtained in the general population22 (21%; 95% confidence interval, 19 to 22; P<0.001). The mean BMI values were not significantly different between the 2 populations. In patients with sinus node dysfunction, 58% were identified as having SAS that was clinically silent to the patients themselves and their physicians; 27% were severely affected (AHI >30/h). In patients with AV block, 68% were identified as having SAS, with 27% severely affected (AHI >30). In severe heart failure patients, 50% were identified as having SAS, but only 5% were severely affected. There was a trend for a difference in SAS prevalence between the 3 major centers (n=27, 26, and 16, representing 70% of the whole population participating in the study): 48%, 73% and 44%, respectively (P=0.09). This was explained at least in part by differences in terms of recruitment, the highest prevalence of SAS being found in the AV block and sinus node dysfunction groups.

The prevalence of SAS was determined in patients with treated hypertension and without hypertension: 56% versus 60% (P=NS) for patients with sinus node dysfunction, 65% versus 71% (P=NS) for patients with AV block, and 53% versus 48% (P=NS) for heart failure patients. Patients with and without diabetes or stable coronary heart disease were similarly affected: 60% versus 57% (P=NS) and 58% versus 61% (P=NS), respectively.

In the 3 groups, >70% of the sleep respiratory events were hypopneas (Table 2). Patients were identified as having mainly obstructive rather than central apnea (16±17% versus 8±6% of the total number of events; P=0.03). More than 75% of hypopneas were classified as obstructive. Even in the heart failure patients, obstructive events were observed more frequently than central events both for apneas (19±23% versus 8±12%; P=0.03) and hypopneas. Fewer than 5% of the patients had a predominant CSA syndrome in all 3 groups.

The Epworth score was low and comparable in the 3 patient groups (7±5 in sinus node dysfunction patients, 7±5 in AV block patients, and 7±3 in patients with heart failure;
No correlation existed between the symptoms related to sleep apnea (Epworth score) and disease severity (AHI value; $r=0.01$, $P=NS$; Figure 1). Interestingly, AHI also was not correlated with either age ($r=-0.04$, $P=NS$) or BMI ($r=0.14$, $P=NS$; Figure 2).

**Discussion**

The present study provides new information on the prevalence and characteristics of sleep-disordered breathing in patients who are paced long term.

First, ~60% of patients with long-term pacing for a spectrum of indications exhibited sleep-disordered breathing. Second, obstructive apneas and hypopneas represented the predominant abnormal respiratory events in paced patients. Third, in this population of patients, the presence of sleep apnea could not be predicted by symptoms or complaints traditionally reported by SAS patients. Finally, no correlation existed between age, BMI, and severity of SAS.

**Prevalence of SAS in the General Population**

Three large studies have established SAS prevalence in the community. These studies estimated the prevalence in men to be between 17% and 26% for an AHI $\geq 5$ and between 7% and 14% for an AHI $\geq 15$. In the elderly population (age, 70±7 years), overall, the prevalence of SAS increases steadily with age and ranges from 30% to 80% in the oldest compared with ~4% in middle-aged men and 2% in middle-aged women. In the present study, when age is taken into account and despite the use of more stringent criteria for the diagnosis of SAS, patients with long-term pacing were observed to have a much higher prevalence of SAS. This was shown nicely by a comparison of the means and confidence intervals between the present and previously published data (21% versus 59%; $P<0.01$).

**Prevalence of SAS in Pacemaker Patients**

Fietze et al published a study reporting the same prevalence of sleep-disordered breathing in patients with and without a pacemaker. They observed that in a population of patients who received a pacemaker for bradycardia, the prevalence of respiratory disturbance index $>10$/h was only 32%, which is markedly lower than that observed in the present study (65%). Several differences in study design may explain these conflicting results. In the former study, sleep apnea monitoring used the MESAM IV device (MAP, Munich, Germany) that is based only on heart rate, snoring, and oxygen saturation (pulse oximetry) and does not gather information on sleep or airflow. Hypopneas, which represent the most common respiratory events in moderate sleep apnea, generally are not associated with significant desaturations and are unlikely to have been identified with the MESAM. Moreover, because sleep duration was not assessed, the calculated respiratory disturbance index can only approximate the actual AHI. Possible differences exist between centers because a trend was observed in the present study that possibly is explained by differences in patient recruitment, the highest prevalence of sleep apnea being found in the AV block and sinus dysfunction groups.
Furthermore, in the present study, atrial pacing rate was programmed at 50 pulses per minute to promote spontaneous rhythm; Fietze et al. provided no details about the atrial pacing rate in their study. We have previously demonstrated that overdrive pacing can modify the severity of sleep apnea in some subgroups of apneic patients; thus, the degree of atrial pacing also may account in part for the prevalence discrepancies between the 2 studies. In our study, the treatment of heart rhythm abnormalities may have decreased the degree of SAS, at least relative to central events. However, this is not the case with obstructive events. After our initial report on the absence of an effect of atrial overdrive on obstructive events, this has been further confirmed by several reports. On the other hand, the prevalence of central events could have been higher before heart rhythm treatment, especially in case of associated heart failure. This could have further reduced the overall prevalence of SAS. To definitely address this question, further studies prospectively evaluating polysomnography before and after pacemaker implantation are needed.

**Impact of High SAS Prevalence on Pacemaker Patient Management**

Severe SAS (AHI ≥30) was found in 27% of patients paced for high-degree AV block and 27% of patients implanted for sinus node dysfunction, which appear to be very high compared with already published data for patients not equipped with a pacemaker. Surprisingly, AHI values did not correlate with age or BMI. In patients already implanted, new technologies can help to identify SAS and to evaluate treatment effects by using specific sensors located at the tip of the pacing leads. This, together with physician awareness of this important association, may lead to better patient management. Whether SAS should be treated in this subset of patients, however, remains to be studied. On the one hand, OSA represents a recognized cardiovascular risk factor, including for arrhythmias. On the other hand, however, treating OSA patients with no or few symptoms remains much discussed and sometimes difficult because the perceived clinical benefit may prove insufficient to justify continuous positive airway pressure.

**SAS Causing Heart Rhythm Disorders**

SAS is classically associated with prominent nocturnal bradyarrhythmias. The simplest hypothesis to explain the high prevalence of SAS in paced patients is to postulate that it is associated with potentially symptomatic bradycardia episodes, the latter possibly being the underlying manifestation that leads to pacemaker implantation while SAS is unknown. Grimm et al. reported a 40% pacemaker implantation in SAS patients with nocturnal arrhythmias. It is conceivable that in patients in whom SAS was not identified, the indications of pacemakers may have been more frequent.

Several arguments exist, however, against the hypothesis of underdiagnosed SAS and excessive pacemaker implantation. First, SAS patients demonstrating arrhythmias usually exhibit the most severe oxygen desaturation, whereas the majority of patients in the present study had only moderate nocturnal hypoxemia. Second, the occurrence of SAS in our study was not significantly associated with classic OSA risk factors such as age or BMI. This suggests that other contributing mechanisms may result in a specific process in patients requiring pacemaker implantation.

**Patients With Heart Failure**

Even if 50% of the heart failure population presented with sleep-disordered breathing, it was surprising to find only 5% of heart failure patients presenting with an AHI ≥30, whereas most of the clinical studies have reported a much higher percentage (around 40% to 50%), with patients demonstrating mainly central events. It is likely that our heart failure population was different from those previously described. It is well known that the prevalence of SAS in such patients is proportional to the severity and instability of heart failure. Actually, our patients received medical treatment optimization just before cardiac resynchronization, allowing a return to functional New York Heart Association class II or III. Moreover, it has been well established by a large multicenter study in Canada how much cardiac treatment optimization influences CSA and Cheyne-Stokes respiration prevalence.

**Study Limitations**

In this evaluation of the prevalence of SAS, we could have included a control group for direct comparison. However, we believe that the comparison with data from recent and large epidemiological studies is valid. Specifically, this comparison allows us to take into account various confounders that are difficult to match in a case-control design owing to the consecutive and multicenter nature of the present study. In this context, the absence of correlation between AHI and either age or BMI also is reassuring because it suggests that the 2 major confounding factors in studies of SAS prevalence were not involved.

Atrial pacing could not be suppressed completely in patients with symptomatic bradycardia for ethical reasons. Consequently, patients who received a pacemaker for sinus node dysfunction could not be studied with 100% spontaneous atrial activity (basic atrial pacing rate programmed to 50 pulses per minute). However, the percentage of atrial pacing was <20% in the 3 patient groups, which suggests that spontaneous atrial rate was rarely below 50 bpm. Moreover, although it could have promoted CSA by further altering cardiac output, it is unlikely to play a role in the occurrence of OSA. Conversely, it also is unlikely that atrial pacing, when present, resulted in altering SAS prevalence.

**Conclusions**

Patients with long-term pacing exhibit a high prevalence of SAS despite the indication for pacing. In this population, SAS is mainly obstructive and associated with few symptoms, although it is severe in many cases. Consequently, systematic screening of these patients should be performed owing to the potential cardiovascular consequences of SAS. Further studies are needed in this subgroup of patients to define the optimal treatment strategy.
In the present work, we have demonstrated, in a series of consecutive patients in whom pacemakers have been implanted long term, that sleep apnea prevalence was very high (ie, >50%). Differences existed according to the underlying disease requiring pacing, with a higher prevalence of sleep apnea in sinus node dysfunction and atrioventricular block compared with heart failure. A vast majority of abnormal respiratory events were obstructive in nature. No correlation existed between sleep apnea and age, body mass index, or symptoms. In clinical practice, the suggestion is to search for sleep apnea in patients requiring pacemaker implantation or currently treated by pacemakers. This is still recommended in patients with very few symptoms of sleep-disordered breathing (eg, the absence of excessive daytime sleepiness, as well as in young and lean subjects). Whether treating sleep apnea would have altered the pacing indication is unknown; however, a nasal continuous positive airway pressure trial, the first-line treatment of sleep apnea, could be evaluated on the basis of tolerance, treatment compliance, and treatment efficacy on cardiac rhythm.
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