Sleep-Related Breathing Disorders Are Associated With Ventricular Arrhythmias in Patients With an Implantable Cardioverter-Defibrillator*

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**Study objectives:** The aim of this study was to examine the influence of sleep-related breathing disorders (SBDs) on the occurrence of ventricular arrhythmias in patients with reduced left ventricular ejection fraction (LVEF), and life-threatening ventricular tachyarrhythmias treated with an implantable cardioverter-defibrillator.

**Patients:** Thirty-eight patients with LVEF of $36 \pm 13\%$ (mean $\pm$ SD) underwent a sleep study. When an apnea-hypopnea index (AHI) $> 10$/h occurred, SBD was diagnosed.

**Measurements and results:** In patients with SBDs, ventricular arrhythmias (couples, triplets, short runs) were recorded simultaneously by Holter ECG and differentiated in episodes with and without disordered breathing. An apnea-associated arrhythmia index (AI) was defined as the number of ventricular arrhythmias occurring simultaneous to disordered breathing. Accordingly, a nonapnea-associated arrhythmia index (NAI) was calculated as the number of ventricular arrhythmias during normal breathing. SBDs were diagnosed in 14 patients: Cheyne-Stokes respiration (CSR) [$n = 8; \text{AHI, } 32.1 \pm 25.0$/h], and obstructive sleep apnea (OSA) [$n = 6; \text{AHI, } 34.1 \pm 14.6$/h]. Four patients in the OSA group and four patients in the CSR group had ventricular arrhythmias during sleep, revealed by Holter ECG. In these eight patients, the AI was significantly higher than the NAI ($20.9 \pm 18.8$/h vs $4.9 \pm 3.3$/h, respectively).

**Conclusions:** These data show that ventricular arrhythmias occurred significantly more often in association with disordered breathing in patients at high risk for arrhythmias and reduced LVEF. (CHEST 2002; 122:558–561)

**Key words:** implantable cardioverter defibrillator; left ventricular dysfunction; sleep-related breathing disorders; ventricular arrhythmias

**Abbreviations:** AHI = apnea-hypopnea index; AI = apnea-associated arrhythmia index; CSR = Cheyne-Stokes respiration; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; NAI = nonapnea-associated arrhythmia index; OSA = obstructive sleep apnea; PVC = premature ventricular contraction; REM = rapid eye movement; SBD = sleep-related breathing disorder

Sleep-related breathing disorders (SBDs) are associated with cardiac arrhythmias, conduction abnormalities, frequent arousals, and potentially life-threatening arrhythmias. It has been shown that patients with cardiac dysfunction frequently have SBDs. Only few data are available about ventricular arrhythmias and sleep apnea in patients with underlying severe cardiac diseases. Some authors have reported a nocturnal increase in frequency of ventricular arrhythmias in patients with heart disease. Other studies did not show a relationship or only showed a weak relationship between ventricular arrhythmias and SBDs. However, in the majority of these studies, patients without significant cardiac or respiratory comorbidities were examined.

We investigated patients with impaired left ventricular function and a history of malignant, drug-resistant ventricular tachyarrhythmia who received

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an implantable cardioverter-defibrillator (ICD). The goal was to assess the influence of SBDs on ventricular arrhythmias in these patients.

**Materials and Methods**

**Patients**

Of 43 consecutive ICD recipients, 38 patients gave informed consent to participate in a sleep study in our sleep laboratory. In these 38 patients, the indication for implantation of an ICD was documented spontaneous, life-threatening ventricular tachyarrhythmias. An invasive angiographic study was performed to assess left ventricular function before the sleep study. Underlying cardiac diseases included coronary heart disease (74%), dilatative cardiomyopathy (21%), and idiopathic ventricular tachyarrhythmia (5%). All patients except one were receiving individual therapy with angiotensin-converting enzyme inhibitors and class III antiarrhythmics.

**Measurements**

Polysomnography consisted of continuous polygraphic recording from surface leads for EEG, electro-oculography, and electromyography (CNS 1000 P; Viyas; Wuerzburg, Germany). Thoracoabdominal excursions were measured qualitatively by pneumatic respiration transducers placed over the rib cage and abdomen. Airflow was quantified by an oronasal thermocouple. Arterial blood saturation was recorded by oximetry. A microphone was placed at the fossa jugularis for detection of tracheal sounds. Body position and leg movements were recorded by electromyography. For ECG recording, a simultaneous Holter ECG was used to detect ventricular arrhythmias (couplets, triplets, short runs) during sleep.

Before each of the measurements, the clocks of the sleep laboratory and the Holter ECG were synchronized exactly and times were checked for accordance after the measurement. Polysomnography was terminated after final waking. All patients were adapted to the sleep laboratory at the time of the initial evaluation.

**Data Collection and Analysis**

Polysomnograms were scored by visual evaluation according to standard criteria. Polysomnography records were scored for sleep, breathing, oxygenation, and movement in 30-s periods. Sleep data were staged (stages 1, 2, 3, and 4 and rapid eye movement [REM] sleep) according to the system of Rechtschaffen and Kales.1 An abnormal breathing event during sleep was defined as having Cheyne-Stokes respiration (CSR) if they had absence of thoracoabdominal movement for at least 10 s and a crescendo-decrescendo pattern of the movements during hyperpnea, regularly alternating with central apneas and hypopneas at a rate of >10/h.

The average number of episodes of apnea and hypopnea per hour of sleep (the apnea-hypopnea score) was calculated as the summary measurement of SBD. SBD was diagnosed when an apnea-hypopnea index (AHI) >10/h was documented. When apnea and hypopnea were scored, the scorer was blinded to the results of the ECG.

In a second step, ventricular arrhythmias (including couplets, triplets, and ventricular short runs) were compared with associated episodes of disordered breathing in the two-channel ECG of the polysomnogram. The occurrence of ventricular arrhythmias within the time of the beginning and the end of an apnea or hypopnea was taken as apnea/hypopnea-associated events.

The total time of normal and disordered breathing episodes was measured by evaluation of the polysomnogram. An apnea-associated arrhythmia index (AI) was defined as the number of ventricular arrhythmias occurring simultaneous with disordered breathing episodes divided by the disordered breathing time period (in hours). Accordingly, a nonapnea-associated arrhythmia index (NAI) was calculated as the number of ventricular arrhythmias during normal breathing divided by the nondisordered breathing time period.

**Statistical Analysis**

All data were expressed as mean values ± SD. Comparisons of the sleep laboratory data were made with a Wilcoxon signed-rank test. A two-tailed, paired t test was used to compare the AI and the NAI.

**Results**

The sleep study was accomplished after a mean time period of 35.8 ± 18.1 months after ICD implantation. The polysomnography of 38 patients with an ICD yielded the diagnosis of SBD in 16 patients (42%): CSR respiration in 8 patients and obstructive sleep apnea (OSA) in 8 patients. Two patients with SBD (one patient with CSR and one patient with OSA) could not be evaluated because of insufficient technical quality of the Holter ECG recording. Of these 14 patients, 8 patients had ventricular arrhythmias during sleep. In these eight patients, 3,309 apneas and hypopneas, 185 apnea-associated ventricular short runs, and 162 nonapnea-associated short runs were found and evaluated for interference. The evaluation of Holter ECG for ventricular arrhythmias in coincidence with apneas/hypopneas during sleep showed a significant higher levels of AI vs NAI (21.8 ± 18.2 vs 4.9 ± 3.3; Fig 1). The comparison of

![Figure 1. Comparison of the number of ventricular arrhythmias occurring simultaneous to disordered breathing (AI) and ventricular arrhythmias occurring during the time of normal breathing (NAI) in all patients with SBDs and ventricular tachyarrhythmias during sleep. *Indicates patients with CSR.](http://journal.publications.chestnet.org/)
patients with an ICD with and without ventricular arrhythmias showed no significant difference in age, left ventricular ejection fraction (LVEF), underlying cardiac diseases, and polysomnographic-based data (Table 1). The sleep data of the 14 patients are shown in Table 2. No significant differences were detected in the amount of total sleep time, stages 1 and 2 sleep, stages 3 and 4 sleep, and REM sleep.

**Discussion**

Only few data are available regarding the relationship between SBD and ventricular arrhythmias in patients with underlying cardiac disease and impaired left ventricular function. In this study, the coincidence of disordered breathing and ventricular arrhythmias in patients with ICDs was investigated. Although it was not primarily expected when analyzing the data of the literature, we found a surprisingly high prevalence of SBD (41%) in the 38 patients with ICDs. In a subgroup of the patients with SBDs, premature ventricular contractions (PVCs) occurred significantly more often during disordered breathing.

This high prevalence of SBD in patients with ICDs is comparable with other studies in patients with impaired cardiac function. CSR was the most common SBD in our study group. It has been shown that CSR is associated with a higher mortality in patients with congestive heart failure. As a consequence, CSR probably has a relevant impact on the survival of these patients by increasing sympathetic neuronal activity, which is evoked by concomitant apneas or hypopneas leading to hypoxemia, hypercapnia, and arousals during sleep.

Several contributing factors of SBDs might have played a role in inducing PVCs: (1) activation of the sympathetic nervous system induced by linkage to episodes of hypoxemia, and (2) hypercapnia, arousals, and temporary hemodynamic alterations related to increased intrathoracic pressure changes during OSA. Hypoxemia has been estimated to provoke PVC, as described by Shephard et al; however, in their study, PVC occurred only in one patient with oxygen desaturations <60%, and only patients without cardiac or pulmonary comorbidity were examined. In other studies, a significantly higher level of PVCs was not found in patients with SBD.

Guilleminault and coworkers presented a large study of 400 patients with sleep apnea syndrome who were examined for the presence of various types of arrhythmias. In 4% of the patients, ventricular arrhythmias (defined as three or more beat runs) were found, and all had happened during an apneic event. In a study of ventricular arrhythmias, Flick and Block demonstrated in patients with COPD that oxygen desaturations can cause PVCs and that oxygen therapy could dramatically reduce the frequency of PVCs in a subgroup of patients. In this study, SBD was not taken into account because SBD was not regularly diagnosed at the time this study was conducted.

Our data show that PVCs occur significantly more often during disordered respiration than during normal breathing in patients with SBDs and ICDs. As underlying factors, we could not detect any significant difference in LVEF and AHI between the two groups with and without PVCs during sleep. The number of patients treated with class III antiarrhythmics, with a history of cardiac resuscitation, or patients with symptoms of SBD did not significantly differ in both groups. In another study, we could show that even ICD-treated ventricular tachyarrhythmias over 2 years were not significantly different in patients with and without SBDs.

Apneic-specific microchanges during SBD are a possible mechanism of inducing PVCs: systemic and pulmonary artery pressure alterations caused by elevated negative intrathoracic pressure during apneas might be a contributing factor.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SBD With</th>
<th>SBD Without</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>68.5 ± 7.2</td>
<td>62.0 ± 6.8</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>32.5 ± 5.3</td>
<td>35.0 ± 11.8</td>
<td>NS</td>
</tr>
<tr>
<td>CSR</td>
<td>3</td>
<td>4</td>
<td>NS</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme</td>
<td>6</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class III antiarrhythmics</td>
<td>6</td>
<td>7</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>4</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>AHI, per h</td>
<td>43.3 ± 22.1</td>
<td>31.2 ± 16.7</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2—Sleep Characteristics of Patients With Diagnosed SBD With or Without Ventricular Arrhythmias During Sleep

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>SBD With Arrhythmias</th>
<th>SBD Without Arrhythmias</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST, min</td>
<td>347 ± 49</td>
<td>300 ± 58</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 1 and 2, min</td>
<td>280 ± 74</td>
<td>260 ± 47</td>
<td>NS</td>
</tr>
<tr>
<td>Stage 3 and 4, min</td>
<td>42 ± 16</td>
<td>18 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>REM sleep, min</td>
<td>22 ± 20</td>
<td>26 ± 20</td>
<td>NS</td>
</tr>
<tr>
<td>REM/TST, %</td>
<td>8 ± 7</td>
<td>7 ± 7</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD. TST = total sleep time; see Table 1 for expansion of abbreviation.
possible explanation could be that ventricular dysrhythmias could be more common with arousals, which are known to be associated with surges in BP and presumably in sudden increase in catecholamine secretion. However, arousals provoked by intrinsic respiratory stimuli during CSR have relatively little effect on BP and heart rate.\textsuperscript{24}

The present article provides more specific information regarding what circumstances cause sleep apnea and arrhythmias to occur. The data show that in the group of patients at risk for severe ventricular tachyarrhythmias, an association and a simultaneous occurrence of apneas and disordered breathing were found. These data suggest that SBDs have the potential of inducing ventricular arrhythmias in patients with reduced left ventricular function. If we consider PVC as a precursor of ventricular tachyarrhythmias,\textsuperscript{23} it seems to be possible that SBDs could provoke malignant ventricular tachyarrhythmias in these patients.

In summary, we found a high prevalence of SBDs in patients with ICDs. Ventricular arrhythmias were significantly more often associated with apneas/hypopneas than with normal breathing in these patients. The data provide more specific information regarding what circumstances sleep apnea and arrhythmias occur. We could specifically show a coincidence between events of disordered breathing and arrhythmias that could be shown for obstructive events as well as for CSR events. Therefore, we conclude that SBD could be regarded as a risk factor for ventricular arrhythmias in these patients. These findings can be applied to a broader population of patients with ventricular arrhythmias, because no sustained tachyarrhythmic events that were treated by ICDs occurred in patients in these investigations. Patients with indication for ICD should therefore be considered for a sleep study if implantation of this device has been indicated. Furthermore, it has to be evaluated whether continuous positive airway pressure therapy, nocturnal oxygen therapy, or other effective therapies of SBD are able to improve the outcome of these patients.

ACKNOWLEDGMENT: The authors thank J. Juhász for his helpful comments and suggestions.

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