OBSTRUCTIVE SLEEP APNEA IN HEART FAILURE PATIENTS:
EVIDENCE FOR PERSISTENT CONDUCTION DISTURBANCES
OR SINUS NODE DYSFUNCTION

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Bradycardia is a common finding in patients with obstructive sleep apnea and might be pronounced in heart failure patients. The aim of the present study was to determine the relationship between nocturnal hypoxemia, apnea-hypopnea index, and electrophysiological parameters of sinus node and atrioventricular conduction properties. Electrophysiological studies were performed in 12 patients with heart failure. Polygraphic studies were done in all of the patients. Patients with an AHI $>10$/h were classified as sleep apnea patients. Mild sleep apnea was diagnosed in 50% of the patients ($AHI 17.8 \pm 4.4$ vs. $5.1 \pm 3.6$/h). There were no differences with respect to the resting heart rate, PQ interval, or QRS duration between the two groups. Sinus node recovery time was normal in all of the patients ($993 \pm 291$ vs. $1099 \pm 62$ ms, $P=0.45$). There was no abnormal atrioventricular conduction. Nevertheless, sleep apnea patients showed decreased atrioventricular conduction time ($AH$ intervals ($134 \pm 42$ vs. $102 \pm 25$ ms, $P=0.1$) and infranodal conduction time ($HV$) intervals ($59 \pm 9$ vs. $43 \pm 7$ ms, $P=0.01$). We conclude that mild sleep apnea was not associated with abnormal findings in sinus node function or $AV$ conduction properties in patients with heart failure. Decreased $AH/HV$ intervals might be a consequence of apnea associated sympathetic activation.

Key words: electrophysiology, sleep apnea

INTRODUCTION

Obstructive sleep apnea (OSA) is a well-established risk factor for arterial hypertension and might contribute to heart failure (1), coronary artery disease (2, 3), and cardiac death (4). Moreover, it has been recognized for many years that
OSA is associated with cardiac arrhythmias, in the majority of cases sinus-arrhythmia, atrial fibrillation (5), and bradycardia (6). Bradycardia, which is reported in 18-50% (7, 8) in severe sleep apneics, might be a consequence of sinus node dysfunction or atrio-ventricular block.

Sleep apnea is a common finding in heart failure patients with an incidence of nearly 50% (9). There are several pathophysiological links between OSA and heart failure: Negative intrathoracic pressure is known to decrease left ventricular filling and emptying (10), with a consecutive fall of cardiac output and stroke volume (11). As a result of upper airway obstruction large negative intrathoracic pressure swings have been demonstrated in OSA, comparable with those occurring during repeated Müller maneuvers. In this regard, hemodynamic effects on cardiac function of apnea or Müller maneuvers are more pronounced in patients with congestive heart failure (12). Furthermore, there are structural adaptations (hypertrophy) of the left ventricle to obstructive sleep apnea in patients with dilated cardiomyopathy (13). This might be, at least in part, a consequence of apnea-associated rise in left ventricular afterload, which is determined by left ventricular transmural pressure (11).

Therefore, sleep apnea-associated bradycardia, or anatomic alterations of the sinus node, or the atrioventricular conduction system might be strengthened in patients with heart failure. The aim of the present study was to determine the relationship between sleep apnea and electrophysiological studies of the sinus node and AV-conduction properties in heart failure patients.

PATIENTS AND METHODS

The study was approved by a local Ethics Committee and was performed in accordance with the guidelines of the Declaration from Helsinki for Human Research.

The study included patients with symptomatic heart failure (NYHA class II-III) referred to the clinic because of syncope or ventricular tachycardia. They were receiving stable doses of their medicaments without exacerbations of symptoms during the last 4 weeks. A further inclusion criterion was suspected sleep apnea (history of snoring, obesity, etc). Exclusion criteria were: CPAP therapy, atrial fibrillation, antiarrhythmic therapy with class I or III antiarrhythmic agents, or NYHA class IV.

Electrophysiological studies

Electrophysiological studies were done in the afternoon in a non-sedated state. After local anesthesia (2% lidocaine) two 6 Fr quadripolar catheters and one 5 Fr bipolar catheter were inserted through the femoral veins. Catheters were advanced in the right atrium, across the tricuspid valve and in the apex of the right ventricle. Surface ECG form leads I to III and intracardiac recordings were displayed simultaneously on a computer screen. Measurements of time intervals were performed manually. Electrophysiological evaluation of sinus node function and AV-conduction were carried out in a standardized manner that has been described in detail elsewhere (14). Atrial pacing started just below sinus cycle lengths, with decremented steps of 60 ms until an atrial cycle length of 330 ms was reached. The assessment of AV conduction included the measurements of
atrioventricular conduction time (AH) and infranodal conduction time (HV) intervals, and the determination of the atrioventricular Wenckebach point.

**Polygraphy**

Polygraphy (Schwarzer, Germany) was performed between 10.00 p.m. and 6.00 a.m. Oro-nasal airflow was recorded by a thermistor, abdominal and thoracic respiration efforts were measured using impedance plethysmography, SaO\textsubscript{2} by finger pulse-oxymetry, and the electrocardiogram from a precordial lead. An apnea was defined as cessation of airflow, a reduction of <50% was defined as hypopnea. Apnea and hypopnea with duration of >10 s and a decrease in oxygen saturation >4% were considered to be pathological. The apnea-hypopnea-index (AHI) was calculated as the number of respiratory events per hour of sleep. An AHI >10 episodes per hour was considered diagnostic of the sleep apnea syndrome. Minimum nocturnal oxygen saturation was defined as the lowest saturation reached during sleep after manual exclusion of clear artefacts. Exclusion criteria were the existing CPAP therapy, atrial fibrillation, therapy with class I or III antiarrhythmic agents, or NYHA-class IV.

**Statistical evaluation**

Data were analyzed with the Statistical Package for Social Sciences (SPSS 11.0 for Windows, Munich, Germany). For comparison of the groups, the Mann-Whitney U Test was used. Correlation coefficients were generated with the Spearman test. Significant difference between groups was assumed at the level of error <5%.

**RESULTS**

Twelve patients (age 66.6 ±5.6 yr, body mass index 28.3 ± 3.7 kg/m\textsuperscript{2}) were included in the study (9 male, 3 female). Mild sleep apnea was diagnosed in 6 (50%) of the patients (AHI 17.8 ± 4.4/h vs. 5.1 ± 3.6/h). There was no difference with respect to resting heart rate, PQ-interval, or QRS duration between the two groups. The patients with OSA had longer QT intervals (346 ±312 vs. 396 ±35 ms, P=0.03). Sinus node recovery time was normal in all of the patients (993 ± 291 vs. 1099 ± 62 ms, P=0.45) (Table 1). Three patients without sleep apnea showed a slightly elongated AH interval. There was no abnormal atrioventricular conduction in sleep apnea patients.

Nevertheless, sleep apnea patients showed decreased AH intervals (134 ± 42 vs. 102 ± 25 ms, P=0.1, *Fig. 1*) and HV intervals (59 ± 9 vs. 43 ± 7 ms, P=0.01).

<table>
<thead>
<tr>
<th></th>
<th>Control n=6</th>
<th>OSA n=6</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR [RR-Interval] (ms)</td>
<td>773 ±184</td>
<td>857 ±87</td>
<td>0.33</td>
</tr>
<tr>
<td>PQ Interval (ms)</td>
<td>190 ±46</td>
<td>158 ±23</td>
<td>0.16</td>
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<tr>
<td>QRS Duration (ms)</td>
<td>99 ±13</td>
<td>144 ±43</td>
<td>0.32</td>
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<tr>
<td>Wenckebach (ms)</td>
<td>388 ±105</td>
<td>351 ±20</td>
<td>0.4</td>
</tr>
<tr>
<td>QT Interval (ms)</td>
<td>346 ±31</td>
<td>396 ±35</td>
<td>0.03</td>
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*Table 1.* Electrophysiological parameters in OSA patients and in the control group.
There was a significant correlation between the AHI and AH-intervals ($r=-0.70$, $P=0.01$) and the AHI and HV intervals ($r=-0.62$, $P=0.03$). Sinus node recovery time was not different between the patients with OSA and the control group ($P=0.4$). Furthermore, there was no correlation between SNRT and AHI ($r=0.129$, $P=0.25$, Fig. 2).

Nocturnal oxygen desaturation was decreased only in patients with sleep apnea (87.2 ± 4.3 vs. 86.8 ± 4.9%). There was no association between minimum oxygen saturation and AH intervals ($r=0.168$, $P=0.62$), HV intervals ($r=0.15$, $P=0.65$), or SNRT ($r=0.36$, $P=0.25$).
DISCUSSION

The present study revealed normal electrophysiological findings of sinus node function and AV conduction in heart failure patients. Interestingly, AH and HV intervals were shorter in OSA patients. Since AV conduction is mainly influenced by the vegetative nerve system, this might be explained by an increased sympathetic activation in OSA patients (15).

There are only few studies assessing electrophysiological parameters in sleep apnea syndrome. Grimm et al (17) examined 15 patients with ventricular asystole ≥5 s. They found only mild abnormalities of sinus node function or AV conduction in these patients. Anyhow, in that study most of the patients (54%) were without an underlying heart disease. Tilkian et al (8) found no abnormalities of electrophysiological parameters in a small group of 5 sleep apnea patients.

Nocturnal bradycardia might occur even in patients without anatomic abnormalities of the sinus node or AV conduction. Koehler et al (16) found an association between nocturnal bradyarrhythmias and sleep stage (predominance during REM sleep) in patients with sleep apnea. Since nocturnal bradycardia was eliminated by intravenous injection of atropine, an increased vagal tone, possibly associated with apnea-related hypoxia (17) has been postulated as the cause of nocturnal bradycardia.

There is growing evidence that effective CPAP–treatment prevents nocturnal bradycardia (6). Therefore, such bradycardia constitutes only a relative indication to implant a pacemaker in OSA patients. Garrique et al (18) found an excessively high prevalence of undiagnosed sleep apnea syndrome (59%) in patients with long term pacing. This implies that some of the pacemaker implantations would have been dispensable, if sleep apnea had been diagnosed and treated.

In summary, our study supports the concept that OSA is not associated with anatomic abnormalities of the sinus node or atrio-ventricular conduction, even in patients with heart failure. Decreased AH/HV-intervals might be a consequence of apnea associated sympathetic activation.

Conflicts of interest: The authors had no conflicts of interest to declare in relation to this article.

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