Effects of Continuous Positive Airway Pressure on Obstructive Sleep Apnea and Left Ventricular Afterload in Patients With Heart Failure

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Background—The objectives of this study were to determine the effects of continuous positive airway pressure (CPAP) on blood pressure (BP) and systolic left ventricular transmural pressure (LVP tm) during sleep in congestive heart failure (CHF) patients with obstructive sleep apnea (OSA). In CHF patients with OSA, chronic nightly CPAP treatment abolishes OSA and improves left ventricular (LV) ejection fraction. We hypothesized that one mechanism whereby CPAP improves cardiac function in CHF patients with OSA is by lowering LV afterload during sleep.

Methods and Results—Eight pharmacologically treated CHF patients with OSA were studied during overnight polysomnography. BP and esophageal pressure (P es) (ie, intrathoracic pressure) were recorded before the onset of sleep and during stage 2 non–rapid eye movement sleep before, during, and after CPAP application. OSA was associated with an increase in systolic BP (from 120.4±7.8 to 131.8±10.6 mm Hg, P<0.05) and systolic LVP tm (from 124.4±7.7 to 137.2±10.8 mm Hg, P<0.05) from wakefulness to stage 2 sleep. CPAP alleviated OSA, improved oxyhemoglobin saturation, and reduced systolic BP in stage 2 sleep to 115.4±8.5 mm Hg (P<0.01), systolic LVP tm to 117.4±8.5 mm Hg (P<0.01), heart rate, P es amplitude, and respiratory rate.

Conclusions—In CHF patients with OSA, LV afterload increases from wakefulness to stage 2 sleep. By alleviating OSA, CPAP reduces LV afterload and heart rate, unloads inspiratory muscles, and improves arterial oxygenation during stage 2 sleep. CPAP is a nonpharmacological means of further reducing afterload and heart rate during sleep in pharmacologically treated CHF patients with OSA. (Circulation. 1998;98:2269-2275.)

Key Words: blood pressure ■ lung ■ heart-assist device ■ respiration ■ physiology

The introduction of ACE inhibitors, whose beneficial effects are related to reductions in afterload, preload, and heart rate, represents the most important recent advance in the treatment of congestive heart failure (CHF), yet morbidity and mortality remain unacceptably high.1,2 Novel approaches to the investigation and treatment of CHF are required if further advances are to occur. One such approach may be the diagnosis and specific treatment of coexisting obstructive sleep apnea (OSA). We showed, in a group of patients with CHF, that abolition of coexisting OSA by nightly application of continuous positive airway pressure (CPAP) caused highly significant improvements in left ventricular (LV) function.3 These findings strongly suggested that pathological effects of OSA were contributing to the development of LV dysfunction in these patients and that CPAP was responsible for the improvement in LV function.3 At the transition from wakefulness to non–rapid eye movement sleep, sympathetic nervous system activity, blood pressure (BP), and afterload decrease in healthy individuals4 but increase in patients with OSA.5 Because the failing heart is particularly sensitive to the detrimental effects of increases in LV afterload,6,7 such OSA-related elevations in afterload during sleep could potentially play a role in the progression of cardiac failure. These observations led us to hypothesize7 that CPAP could improve LV function over time in CHF patients with OSA beyond that due to pharmacological therapy by 2 potential mechanisms: eliminating apnea-related surges in BP6 and raising intrathoracic pressure,7 both of which would reduce LV afterload during sleep. CPAP may also lower heart rate.8 Together, these effects will reduce the metabolic demands on the heart.9 We therefore tested the acute effects of CPAP on BP, intrathoracic pressure, LV transmural pressure (LVP tm), and heart rate during sleep in medically treated CHF patients with OSA.

Methods

Subjects
Inclusion criteria for patients were (1) chronic CHF secondary to ischemic or idiopathic dilated cardiomyopathy; (2) chronic exer-
tional dyspnea (NYHA class II or III); (3) appropriate pharmacological therapy for CHF, including afterload-reducing agents; (4) stable clinical status and an absence of medication changes for ≥1 month before entry; (5) a resting LV ejection fraction ≤45% measured by 99mTc equilibrium radionuclide angiography; and (6) OSA, defined as ≥15 obstructive apneas and hypopneas per hour of sleep on a previous sleep study, accompanied by at least 2 of the following: habitual snoring, restless sleep, nocturnal choking or dyspnea, morning headaches, or excessive daytime sleepiness. Exclusion criteria included a history of myocardial infarction or unstable angina within 3 months of entry into the study. The protocol was approved by the ethics committee of the University of Toronto, and all patients gave written informed consent.

Sleep Studies
Polysomnography and sleep staging were performed as previously described.3,10,11 Heart rate was determined from a precordial ECG. Thoracoabdominal movements were measured by a calibrated respiratory inductance plethysmograph (Respitrace; Ambulatory Monitoring, Inc).3,10 Oxymoglobin saturation (SaO$_2$) was measured with an ear oximeter (Oxyshuttle; Sensormedics Corp). The mean sleep SaO$_2$ mean low sleep SaO$_2$, and the mean nadir in SaO$_2$ for each apnea and hypopnea were also determined as previously described.3,10,11 Esophageal pressure (P$_{es}$), measured with a balloon catheter–pressure transducer system,3,10,11 was used as a measure of intrathoracic pressure. Obstructive apneas were defined as an absence of tidal volume for at least 10 seconds, during which inspiratory P$_{es}$ swings persisted. Hypopneas were defined as a ≥50% reduction in tidal volume from the baseline level for at least 10 seconds3,10,11 with paradoxical thoracoabdominal movements and P$_{es}$ swings with increased airways resistance compared with ventilatory periods. The apnea-hypopnea index was defined as the number of apneas and hypopneas per hour of sleep. Finger BP was measured by digital photoplethysmography (Finapres BP Monitor, Ohmeda 2300) with the patient supine and the hand secured on a horizontal splint. BP readings obtained with Finapres correlate well with intra-arterial measurements from the radial artery at rest and during vigorous respiratory maneuvers.12,13

Protocol
Patients with CHF and OSA were studied during 2 consecutive nights in the sleep laboratory. Medication remained unchanged during this time, and none were using sedatives. None had any previous exposure to CPAP. During the first night, CPAP (BiPAP STD, Respironics Inc) was titrated to the optimal pressure at which apneas and hypopneas were abolished or to the highest pressure tolerated by the patient during that night. On the second night, P$_{es}$ and BP were recorded in addition to routine polysomnographic variables. Baseline measurements were recorded during quiet breathing before sleep onset. Once the patients fell asleep, they were studied while off CPAP during the first part of the night (pre-CPAP), while on CPAP during the second part, and after CPAP withdrawal during the last part of the night (post-CPAP). After patients had at least 1 hour of stable non–rapid eye movement sleep, CPAP was applied for 2 to 3 hours at the optimal pressure determined during the first night. Thereafter, CPAP was withdrawn. Analyses during sleep were confined to stage 2 non–rapid eye movement sleep, because this represented the predominant sleep stage during which most obstructive events occurred and because it was the only sleep stage in which data from all 3 study conditions were acquired.

Data Analysis
End-expiratory P$_{es}$ during wakefulness before the onset of sleep was the reference value for all P$_{es}$ measurements. Respiratory rate was determined from the P$_{es}$ tracing as the frequency of inspiratory efforts during obstructive events and ventilatory periods. P$_{es}$ amplitude was measured. P$_{es}$ during systole was measured synchronously with systolic BP (when averaged over time, it is equivalent to mean P$_{es}$). Systolic LV P$_{es}$ was calculated as the difference between BP and P$_{es}$ measured synchronously during systole.

To determine the effect of OSA during stage 2 sleep on these cardiovascular and respiratory variables, mean values were derived from a 2-minute period of wakefulness before the onset of sleep and over 5 randomly chosen obstructive apneas and ventilatory periods between apneas during stage 2 sleep (Figure 1). For this purpose, a technician not involved in performing the study identified the beginning of the first episode of stage 2 sleep closest to the baseline period of wakefulness. The first apnea-ventilatory cycle during this period was marked as the first cycle to be analyzed. Subsequently, 4 apnea-ventilatory cycles were identified at randomly alternating intervals of every third and sixth cycle, for a total of 5 cycles. Mean±SEM apnea duration was 19.9±1.9 seconds and mean ventilatory duration was 28.6±2.5 seconds, so that the mean cycle length was 48.3±4.3 seconds. Mean stage 2 sleep values were compared with those during wakefulness by paired $t$ tests. Each apnea-ventilatory cycle was then subdivided into apneic and ventilatory components to determine the impact of each on these variables. A 1-way ANOVA for repeated measures with Dunnnett’s test was used to compare values obtained during these apneic and ventilatory periods with corresponding values during wakefulness.

To determine the effect of CPAP and its withdrawal on these variables during stage 2 sleep, the equivalent time period for the 5 pre-CPAP apnea-ventilatory cycles was analyzed beginning at the
onset of stage 2 sleep during CPAP application and for 5 apnea-ventilatory cycles (selected in the same manner as the 5 pre-CPAP cycles) after CPAP withdrawal during stage 2 sleep. One-way ANOVA for repeated measures with Dunnett’s test was used to compare mean stage 2 sleep values obtained before, during, and after CPAP application. All data are expressed as mean±SEM.

Results

Characteristics of the Patients

During the course of the study, 36 CHF patients were referred to the sleep laboratory because sleep apnea was suspected. Ten (28%) had no sleep apnea, 18 (50%) had predominantly central or mixed sleep apnea, and 8 (22%) had predominantly obstructive OSA. These latter 8 patients were recruited into the study. Ten (28%) had no sleep apnea, 18 (50%) had predominantly central or mixed sleep apnea, and 8 (22%) had predominantly obstructive OSA.4 They were generally middle-aged (49.8±6.6 years old) and obese (body mass index, 35.8±6.2 kg/m²). The average daytime clinic BP measured by cuff was 122.1±8.4 mm Hg systolic and 81.3±6.8 mm Hg diastolic. The cause of CHF was idiopathic dilated cardiomyopathy in 6 and coronary artery disease in 2. Severe LV functional impairment was evidenced by a mean LV ejection fraction of 25.5±4.2%. Four patients were in NYHA class II and 4 in class III. They were on optimal medical therapy for CHF, consisting of digoxin in 7, diuretics in 8, ACE inhibitors in 7, and β-blockers in 1. The patients had moderately severe OSA, as indicated by the high frequencies of apneas, hypopneas, and movement arousals and had moderate O₂ desaturation during obstructive events (Table 1).

Comparison of Wakefulness and Stage 2 Sleep

Figure 1 illustrates changes in BP and Pso2 amplitude from wakefulness to stage 2 sleep in a representative patient. Table 2 presents pooled data for all 8 patients. During stage 2 sleep, mean overall systolic BP increased significantly, by 11 mm Hg (P<0.05), compared with wakefulness, whereas diastolic BP did not. Mean BP also increased (from 87.4±6.2 to 96.9±7.5 mm Hg, P<0.05). Systolic LVPtm increased by 13 mm Hg from wakefulness to mean stage 2 sleep (P<0.05). However, neither Pso2 during systole, Pso2 amplitude, heart rate, nor respiratory rate changed significantly from wakefulness to stage 2 sleep.

During the ventilatory period of stage 2 sleep, there was a significant increase in systolic BP, by 14 mm Hg (P<0.05), and a significant decrease in Pso2 during systole by 2 mm Hg (P<0.05), resulting in a significant increase in systolic LVPtm of 16 mm Hg (P<0.01) compared with wakefulness. There was also a significant increase in Pso2 amplitude of 6 mm Hg (P<0.05). However, there were no significant changes in diastolic BP, heart rate, or respiratory rate compared with wakefulness. In contrast to the ventilatory period, there were minimal changes in these variables during the apnea, with only heart rate, which decreased by 3 bpm (P<0.05), differing significantly from the awake state. Consequently, during stage 2 sleep, variables oscillated between obstructive apneas and ventilatory periods such that diastolic BP, systolic BP, systolic LVPtm, heart rate, and Pso2 amplitude were all significantly greater and systolic Pso2 was significantly lower during the ventilatory period than during apnea (Table 2).

Effects of CPAP

A representative example of the effects of CPAP and CPAP withdrawal on obstructive hypopneas, Pso2, BP, and SaO2 in 1 patient appears in Figure 2. Grouped data for all 8 patients are shown in Figures 3 through 6. The mean CPAP applied on the

TABLE 1. Baseline Sleep Study Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Awake</th>
<th>Stage 2 Sleep</th>
<th>Apnea</th>
<th>Ventilatory Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time asleep, h</td>
<td>5.30±0.40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep stage, h</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stage 1</td>
<td>0.33±0.06</td>
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<tr>
<td>Stage 2</td>
<td>3.57±0.30</td>
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<tr>
<td>Slow wave</td>
<td>0.41±0.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REM</td>
<td>0.97±0.18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstructive AHI, No./h sleep</td>
<td>43.4±6.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Movement arousal, No./h</td>
<td>38.8±5.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean sleep SaO2, %</td>
<td>93.4±0.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean low sleep SaO2, %</td>
<td>91.3±0.9</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Mean nadir SaO2 during apneas</td>
<td>82.5±2.5</td>
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<td></td>
</tr>
</tbody>
</table>

Abbreviations: REM, rapid eye movement; AHI, apnea-hypopnea index; SaO2, oxyhemoglobin saturation.

TABLE 2. Effects of OSA on Cardiovascular and Respiratory Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Awake</th>
<th>Mean Stage 2 Sleep</th>
<th>Apnea</th>
<th>Ventilatory Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPso2, mm Hg</td>
<td>74.7±4.1</td>
<td>79.3±6.1</td>
<td>77.1±5.6</td>
<td>80.6±6.5‡</td>
</tr>
<tr>
<td>BPsys, mm Hg</td>
<td>120.4±7.8</td>
<td>131.8±10.6*</td>
<td>129.4±10.6</td>
<td>133.9±10.9*‡</td>
</tr>
<tr>
<td>Pesamp, mm Hg</td>
<td>−4.2±0.6</td>
<td>−5.4±1.0</td>
<td>−4.6±1.2</td>
<td>−6.1±1.0*‡</td>
</tr>
<tr>
<td>LVPtmso2, mm Hg</td>
<td>124.4±7.7</td>
<td>137.2±10.8*</td>
<td>133.9±10.0</td>
<td>140.2±10.6§</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>83.3±5.8</td>
<td>82.1±5.8</td>
<td>80.1±5.9*</td>
<td>83.9±5.6§</td>
</tr>
<tr>
<td>Pesys, mm Hg</td>
<td>9.3±1.4</td>
<td>12.2±1.4</td>
<td>9.1±1.3</td>
<td>15.2±2.0*‡</td>
</tr>
<tr>
<td>RR, breaths/min</td>
<td>19.9±2.6</td>
<td>20.5±1.7</td>
<td>19.1±1.7</td>
<td>20.8±1.8</td>
</tr>
</tbody>
</table>

BPso2 indicates diastolic blood pressure; BPsys, systolic blood pressure; Pesamp, systolic esophageal pressure; LVPtmso2, systolic LV transmural pressure; HR, heart rate; Pesys, amplitude of esophageal pressure swings; and RR, respiratory rate.

*P<0.05, †P<0.01 vs wakefulness.
‡P<0.05, §P<0.01 vs apnea.
experimental night was 9.3±0.6 cm H2O (range, 7 to 12 cm H2O). CPAP caused significant reductions in the apnea-hypopnea index (P<0.001) and the frequency of movement arousals (P<0.05), as well as increases in mean low SaO2 (P<0.01) (Figure 3). After withdrawal of CPAP, the apnea-hypopnea index increased significantly compared with CPAP (P<0.01) but remained significantly lower than pre-CPAP levels (P<0.05). Withdrawal of CPAP led to a decrease in mean low SaO2 (P<0.02) to values comparable to those pre-CPAP. The increase in the frequency of movement arousals from CPAP to CPAP withdrawal was not significant. As illustrated in Figure 4, diastolic BP did not change during CPAP, whereas systolic BP decreased by 16 mm Hg (P<0.01), systolic Pes increased by 4 mm Hg (P<0.01), and systolic LVPtm decreased by 20 mm Hg (P<0.01) compared with pre-CPAP. During the post-CPAP withdrawal period, diastolic BP remained unchanged. However, systolic BP increased (P<0.05), systolic Pes decreased (P<0.02), and systolic LVPtm increased (P<0.05) compared with CPAP but did not differ from pre-CPAP values. Mean BP was reduced by CPAP (from 96.9±7.5 to 86.8±5.8 mm Hg, P<0.05), and it increased to the pre-CPAP values (96.1±6.2 mm Hg) during the post-CPAP withdrawal period. As shown in Figure 5, CPAP caused a significant decrease in heart rate (P<0.01) and a very pronounced reduction (by 20%) in systolic LVPtm×heart rate product (P<0.001). During the post-CPAP period, heart rate remained unchanged and the systolic LVPtm×heart rate product increased (P<0.05) compared with CPAP. However, heart rate as well as the systolic LVPtm×heart rate product remained lower than pre-CPAP (P<0.05).

Figure 6 illustrates a substantial decrease of Pes amplitude (P<0.001), a decrease in respiratory rate (P<0.05), and a very pronounced reduction (by 58%) in Pes amplitude×respiratory rate product (P<0.001) on CPAP compared with pre-CPAP. Post-CPAP, Pes amplitude increased (P<0.01), respiratory rate remained unchanged, and Pes amplitude×respiratory rate product increased (P<0.05) compared with CPAP. Compared with pre-CPAP, Pes amplitude (P<0.01), respiratory rate (P<0.05), and Pes amplitude×respiratory rate product (P<0.001) were reduced.

Discussion
The first important observation from our study was that despite their adherence to optimum pharmacological therapy (which included either ACE inhibitors or the combination of hydralazine and nitrates) and the presence of normal daytime BP, these CHF patients with OSA experienced recurrent increases in LV afterload in association with OSA during stage 2 sleep that rose above levels during wakefulness (Figure 1 and Table 2). This was equally true of patients on β-blockers. These increases in LV afterload occurred mainly during ventilatory periods after apneas. They resulted primarily from surges in systolic BP, with reductions in intrathoracic pressure (ie, Pes) playing a minor role. Heart rate also increased during the ventilatory period. In contrast, during apneas, LV afterload did not increase and heart rate actually decreased compared with wakefulness. Therefore, these patients suffered from elevations in BP and LV afterload during

![Figure 2. Recording during stage 2 sleep before, during, and after CPAP application. Ventilatory period in this patient has a waxing and waning pattern of tidal volume (Vt) typical of Cheyne-Stokes ventilation, but hypopneas have an obstructive component, as indicated by recurrent generation of negative Pes during which airway resistance increased markedly compared with hyperpnea. Abolition of obstructive hypopneas and improvement in SaO2 by CPAP are accompanied by decreases in BP, these CHF patients with OSA experienced recurrent increases in LV afterload in association with OSA during stage 2 sleep.](image1)

![Figure 3. CPAP administration resulted in a significant reduction in apnea-hypopnea index (AHI) (from 55.3±9.9 to 15.0±5.3 per hour of stage 2 sleep), an increase in mean low stage 2 sleep SaO2 (from 89.6±1.1% to 93.4±0.9%), and a decrease in number of movement arousals (from 45.1±10.7 to 20.0±3.9 per hour of stage 2 sleep). Post-CPAP, there was an increase in AHI to 36.1±9.5 per hour of stage 2 sleep, a decrease in mean low stage 2 sleep SaO2 to 90.0±1.0%, and an increase in number of movement arousals to 34.6±9.2 per hour of stage 2 sleep. However, post-CPAP, AHI remained below pre-CPAP level. •P<0.05, **P<0.01 vs PRE-CPAP, †P<0.05 vs CPAP.](image2)
sleep that were not completely suppressed by pharmacological therapy.

In most respects, our patients resembled OSA patients without CHF: they had symptoms of OSA, were middle-aged men, and were obese. As shown in Figure 1, some had a pattern of OSA similar to that of patients without CHF, whereas others had a waxing and waning pattern of tidal volume suggestive of a Cheyne-Stokes ventilatory pattern alternating with obstructive apneas, as shown in Figure 2. In all cases, the obstructive nature of apneas and hypopneas was proved by continued Pn swings generated against the occluded upper airway or by a marked increase in airway resistance compared with the hyperpneic phase (see Figure 2). Nevertheless, among those patients with a Cheyne-Stokes breathing pattern, it is possible that centrally mediated periodic breathing could have entrained upper airway obstruction during the waning phase and surges in BP during the waxing phase.14,15

The demonstration of LV hypertrophy and dilated cardiomyopathy of unknown cause in patients with OSA who are normotensive while awake1,16 suggests that over time, nocturnal increases in LV afterload related to obstructive apneas will have detrimental effects on myocardial performance. Apnea-induced hypoxia at these times may further aggravate any underlying predisposition to cardiac ischemia and systolic and diastolic dysfunction.3,6–18 It is also noteworthy that 6 of the 8 patients studied had idiopathic dilated cardiomyopathy. This raises the question as to whether OSA might have played a role in the pathogenesis of their cardiac dysfunction.3 Because elevations in BP and LV afterload are related to OSA, one can anticipate that its elimination would result in reduced afterload during sleep beyond that achieved by pharmacological therapy.

The second important finding of our study was that CPAP abolished OSA and caused a 20 mm Hg reduction in systolic LVPm during stage 2 sleep. The reduction in systolic LVPm was due to the combined effects of a 4 mm Hg increase in systolic Pn (LVPm <sub>syst</sub>) fell significantly. Post-CPAP, BP <sub>syst</sub> remained unchanged, BP <sub>pul</sub> increased, Pes <sub>syst</sub> decreased, and LVPm <sub>syst</sub> increased. **P < 0.01 vs pre-CPAP; †P < 0.05 vs CPAP.**

**Figure 4.** Although CPAP application did not change diastolic BP (BP <sub>dias</sub>), it decreased systolic BP (BP <sub>syst</sub>) and increased systolic esophageal pressure (Pes <sub>syst</sub>) significantly, so that systolic LVPm (LVPm <sub>syst</sub>) fell significantly. Post-CPAP, BP <sub>syst</sub> remained unchanged, BP <sub>pul</sub> increased, Pes <sub>syst</sub> decreased, and LVPm <sub>syst</sub> increased. **P < 0.01 vs pre-CPAP; †P < 0.05 vs CPAP.**

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CPAP reduces afterload in HF patients with apnea

Figure 6. Application of CPAP resulted in marked decreases in esophageal pressure amplitude (Pes$_{amp}$), respiratory rate (RR), and Pes$_{amp}$×RR product. Post-CPAP, Pes$_{amp}$ increased, RR remained unchanged, and Pes$_{amp}$×RR product increased. However, post-CPAP, Pes$_{amp}$, RR, and Pes$_{amp}$×RR product did not rise back to pre-CPAP levels. *P<0.05, **P<0.01 vs pre-CPAP, †P<0.05, ‡P<0.01 vs CPAP.

than that observed in the awake CHF patients in our previous study.8

Patients with CHF are particularly susceptible to the adverse effects of increased LV afterload on heart function.7 Therefore, the above observations strongly suggest that one of the mechanisms responsible for the improvements in daytime LV ejection fraction (from 37% to 49%, P<0.001) observed in our previous series of CHF patients with OSA treated with long-term nocturnal CPAP3 was a sustained reduction in nocturnal LV afterload. It is worth noting that diastolic BP was not reduced by CPAP. Thus, coronary artery perfusion should not be adversely affected by its application. Because central apneas also cause surges in BP,15 it is possible that alleviation of the central components of apneas and hypopneas could have lowered BP in those patients with a Cheyne-Stokes respiratory pattern. If so, this would also help to explain chronic improvements in LV function in CHF patients with predominantly central sleep apnea.16

CPAP also lowered heart rate by 5 bpm. This reduction was similar to that observed during CPAP application to awake CHF patients in our previous study.3 CPAP could have lowered heart rate by 2 mechanisms: increasing vagal tone and decreasing sympathetic nerve firing rate. In patients with OSA but without CHF, Somers et al17 documented decreases in sympathetic nerve discharge to muscle when CPAP was applied during sleep. Indirect evidence suggests that CPAP can augment parasympathetic activity,18 probably by increasing lung volume and thereby stimulating pulmonary stretch receptors that augment vagal tone reflexively. The main clinical benefit of this reduced heart rate is a more advantageous myocardial O2 delivery/consumption ratio during the application of CPAP. Maintenance of diastolic BP at these lower heart rates will allow for augmented coronary blood flow and improved LV filling, while the lower systolic LVP$_{tm}$×heart rate product indicates a decrease in myocardial O2 consumption.9 In this context, afterload-reducing agents that also reduce heart rate have greater survival benefit than those that do not.2

The marked reduction in P$_{oa}$ amplitude indicates that CPAP unloaded the inspiratory muscles as well as the left ventricle. P$_{oa}$ amplitude×respiratory rate product, an index of inspiratory force generation over time,19,20 also fell significantly, by 58%, during application of CPAP. The most likely mechanisms by which this occurred were through relief of upper airway obstruction and by positive intrathoracic pressure–induced extrathoracic redistribution of lung water.21,22 Resulting in increased lung compliance.23 Because CPAP alleviated OSA-related hypoxia, this inspiratory muscle unloading occurred in the presence of improved oxygenation. This improvement in respiratory efficiency would also reduce the need to divert much of the already low cardiac output of these patients to these muscles.23

Another novel finding was that several of the beneficial effects of CPAP persisted into the post-CPAP period. These included reductions in apnea-hypopnea index, heart rate, systolic LVP$_{tm}$×heart rate product, P$_{oa}$ amplitude, respiratory rate, and P$_{oa}$ amplitude×respiratory rate product below pre-CPAP values. The mechanisms for these post-CPAP effects remain uncertain. One possibility is that exposure of the upper airway and lungs to positive pressure caused a shift in interstitial fluid into the vascular compartment and from the intrathoracic to the extrathoracic space,24 resulting in a sustained reduction in upper airway and pulmonary edema. Any resultant increase in upper airway luminal area and lung compliance might account for a reduced apnea-hypopnea index and lower inspiratory P$_{oa}$ amplitude. Similarly, an increase in lung compliance could lead to increased lung volume, with consequent stimulation of pulmonary stretch receptors provoking vagally mediated slowing of heart rate.8 A sustained reduction in interstitial pulmonary edema would also reduce stimulation of pulmonary irritant receptors and could lead to a sustained slowing of respiratory rate.25 Regardless of the mechanisms involved, these observations have important clinical implications, because they suggest that CPAP can have beneficial carryover effects. This might explain, for example, sustained reductions in dyspnea lasting into the daytime in CHF patients with OSA, even though CPAP was used only at night.7 Other investigators have also described carryover effects of CPAP. Genoves et al26 observed sustained increases in cardiac output during CPAP application and after its withdrawal in pigs with experimental CHF. Further research will be necessary to elucidate the mechanisms underlying these beneficial carryover effects.

Pharmacological therapy that reduces afterload in concert with either a reduction in heart rate or preload has become the...
cornerstone of contemporary therapy for CHF. Such pharmacological therapy has beneficial effects on hospitalization, morbidity, and mortality in the CHF population as a whole. However, our data suggest that these benefits may be attenuated in patients who also suffer from sleep-related breathing disorders. Although the prevalence of OSA in CHF patients is not certain, we found it in 22% of CHF patients referred to our laboratory, which suggests that it is common. Our data are therefore liable to be relevant to a significant proportion of the CHF population. The present findings combined with those of our previous study lead us to 2 conclusions. First, OSA adversely affects LV afterload in patients with CHF. Second, because CPAP eliminates OSA; improves oxygenation; reduces nocturnal BP, LV afterload, and heart rate; and may also reduce preload, it can be viewed as a potentially important nonpharmacological adjunct to the management of such patients, in whom its effects are above and beyond those of conventional drug therapy.

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References


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