Reprinted From

The NEW ENGLAND JOURNAL of MEDICINE

VOL. 348 NO. 13

ESTABLISHED IN 1812 MARCH 27, 2003 WWW.NEJM.ORG

ORIGINAL ARTICLE

Cardiovascular Effects of Continuous Positive Airway Pressure in Patients with Heart Failure and Obstructive Sleep Apnea

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ABSTRACT

BACKGROUND

Obstructive sleep apnea subjects the failing heart to adverse hemodynamic and adrenergic loads and may thereby contribute to the progression of heart failure. We hypothesized that treatment of obstructive sleep apnea by continuous positive airway pressure in patients with heart failure would improve left ventricular systolic function.

METHODS

Twenty-four patients with a depressed left ventricular ejection fraction (45 percent or less) and obstructive sleep apnea who were receiving optimal medical treatment for heart failure underwent polysomnography. On the following morning, their blood pressure and heart rate were measured by digital photoplethysmography, and left ventricular dimensions and left ventricular ejection fraction were assessed by echocardiography. The subjects were then randomly assigned to receive medical therapy either alone (12 patients) or with the addition of continuous positive airway pressure (12 patients) for one month. The assessment protocol was then repeated.

RESULTS

In the control group of patients who received only medical therapy, there were no significant changes in the severity of obstructive sleep apnea, daytime blood pressure, heart rate, left ventricular end-systolic dimension, or left ventricular ejection fraction during the study. In contrast, continuous positive airway pressure markedly reduced obstructive sleep apnea, reduced the daytime systolic blood pressure from a mean (±SE) of 126±6 mm Hg to 116±5 mm Hg ($P=0.02$), reduced the heart rate from 68±3 to 64±3 beats per minute ($P=0.007$), reduced the left ventricular end-systolic dimension from 54.5±1.8 to 51.7±1.2 mm ($P=0.009$), and improved the left ventricular ejection fraction from 25.0±2.8 to 33.8±2.4 percent ($P<0.001$).

CONCLUSIONS

In medically treated patients with heart failure, treatment of coexisting obstructive sleep apnea by continuous positive airway pressure reduces systolic blood pressure and improves left ventricular systolic function. Obstructive sleep apnea may thus have an adverse effect in heart failure that can be addressed by targeted therapy.

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N Engl J Med 2003;348:1233-41.

Reprinted from THE NEW ENGLAND JOURNAL OF MEDICINE
(ISSN 0028–4793) Vol. 348:1233-1241 (March 27, 2003).

HEART FAILURE AFFECTS APPROXIMATELY 4,700,000 people in the United States, with annual costs of approximately $20 billion.[1] Despite advances in pharmacologic therapy, morbidity, mortality, and rates of hospitalization for heart failure remain high.[2-4] These data emphasize the importance of identifying all treatable conditions that could aggravate heart failure. One such condition may be obstructive sleep apnea.

Sleep-related breathing disorders, including obstructive and central sleep apnea, often coexist with heart failure. The largest epidemiologic studies, which involved 450 and 81 patients with chronic heart failure, found rates of prevalence of obstructive sleep apnea of 37 percent and 11 percent, respectively.[5,6] In addition, obstructive sleep apnea is associated with significantly increased odds of having heart failure.[7]

Normally, sleep is accompanied by reductions in central sympathetic outflow, heart rate, blood pressure, and cardiac output.[8] However, recurrent obstructive apnea disrupts sleep and subjects the heart to bouts of hypoxia, exaggerated negative intrathoracic pressure, and bursts of sympathetic activity provoking surges in blood pressure and heart rate.[8-10] Such nocturnal stress can be relieved by therapy with continuous positive airway pressure.[10] Randomized trials involving patients without heart failure also suggest that treating obstructive sleep apnea with continuous positive airway pressure can lower daytime blood pressure,[11,12] but the results of randomized trials of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea have yet to be published.

We previously reported a significant improvement in the left ventricular ejection fraction in eight patients with heart failure and obstructive sleep apnea who were treated with continuous positive airway pressure for one month.[13] However, that study was not randomized, lacked a control group, included only patients with nonischemic dilated cardiomyopathy, and did not assess other cardiovascular variables. We therefore undertook a randomized, controlled trial involving patients with heart failure to test the primary hypothesis that treatment of obstructive sleep apnea with continuous positive airway pressure would improve the left ventricular ejection fraction when patients were awake and the secondary hypothesis that continuous positive airway pressure would lower daytime blood pressure.

METHODS

STUDY SUBJECTS

The study subjects were recruited from the heart failure clinics of Mount Sinai Hospital and Toronto General Hospital in Toronto. Patients referred to these clinics routinely undergo overnight polysomnography. The entry criteria were a history of heart failure due to ischemic or nonischemic dilated cardiomyopathy (defined as a left ventricular end-diastolic dimension above 27 mm per square meter of body-surface area[14]) for at least six months; a left ventricular ejection fraction of 45 percent or less at rest, as quantified by gated radionuclide angiography; assignment to New York Heart Association functional class II, III, or IV; the absence, within the previous three months, of exacerbations of heart failure while the patient was receiving stable, optimal pharmacologic therapy at the highest tolerated doses[15]; and evidence, during a clinical sleep study, of obstructive sleep apnea, defined as at least 20 episodes of apnea and hypopnea per hour of sleep, of which more than 50 percent were obstructive.

The exclusion criteria were primary valvular heart disease; the presence of an implanted cardiac pacemaker; and unstable angina, myocardial infarction, or cardiac surgery within the previous three months. The protocol was approved by the research ethics board of the University of Toronto. Written informed consent was obtained from all patients at enrollment.

SLEEP STUDIES

The patients were evaluated with the use of the Epworth Sleepiness Scale[16] and then underwent baseline overnight sleep studies in a hospital sleep laboratory. Sleep stages and arousals were scored according to standard criteria.[17,18] Thoracoabdominal movements were monitored by respiratory inductance plethysmography,[17] and oxyhemoglobin saturation was monitored by oximetry. Signals were recorded on a polysomnographic system. The desaturation index was the number of times per hour of sleep that the oxyhemoglobin saturation fell below 90 percent. The lowest saturation value was also recorded. Obstructive and central apneas and hypopneas were scored as previously described.[5,10] The number of apneas and hypopneas per hour of sleep was calculated.

CARDIOVASCULAR ASSESSMENTS

Two hours after the patient awakened, blood pressure and heart rate were measured continuously by digital photoplethysmography, with the patient supine, and averaged over a period of 15 minutes. Next, two-dimensional echocardiographic images were acquired from the parasternal long and short axes, apical long axis, apical four-chamber, and subcostal views by an echocardiographer who was unaware of the patient's treatment assignment. The left ventricular end-diastolic and end-systolic dimensions were determined, and the left ventricular ejection fraction was calculated according to a modification of Simpson's method.[19]

INTERVENTION

The patients were then randomly assigned to either a control group that continued to receive optimal drug therapy or a treatment group that received continuous positive airway pressure in addition to optimal drug therapy. The night after the base-line sleep study, those assigned to continuous positive airway pressure underwent overnight titration of continuous positive airway pressure, during which the pressure was adjusted to abolish apnea and hypopnea, or to the highest level tolerated. Patients in the treatment group were sent home with a continuous-positive-airway-pressure device and were instructed to use it every night for at least six hours. The number of hours during which the device was switched on was documented by a built-in meter. All procedures were repeated one month after the base-line study.

STATISTICAL ANALYSIS

The data are given as means ±SE. The base-line characteristics of the control group and the group that received continuous positive airway pressure were compared by two-tailed unpaired t-tests for continuous variables and Fisher's exact test for nominal variables. Two-way repeated-measures analysis of variance and Tukey's test were used to compare differences within and between groups in variables measured at base line and one month later. P values of less than 0.05 were considered to indicate a statistically significant difference.

RESULTS

CHARACTERISTICS OF THE PATIENTS

Twenty-four patients participated, 12 with ischemic and 12 with nonischemic dilated cardiomyopathy. All had a history of habitual snoring. Twelve patients were randomly assigned to the control group, and 12 to the group given continuous positive airway pressure; all 24 completed the study. Most of the patients were middle-aged, overweight men with mild-to-moderate symptoms of heart failure and a markedly depressed left ventricular ejection fraction. At base line there were no significant differences between the two groups in age, sex distribution, body-mass index, cardiac diagnosis, New York Heart Association class, left ventricular ejection fraction, or medications (Table 1). Twenty-two patients had normal sinus rhythm, and two in the control group had atrial fibrillation. The scores on the Epworth Sleepiness Scale were similar in the two groups. There were no significant differences between the two groups in the base-line frequency

Table 1. Base-Line Characteristics of the Control Group and the Group Given Continuous Positive Airway Pressure.*

Characteristic	Control Group (N=12)	Group Receiving Continuous Positive Airway Pressure (N=12)
Age — yr	55.2±3.6	55.9±2.5
Sex — M/F	10/2	11/1
Body-mass index†	32.3±2.5	30.4±1.8
Score on Epworth Sleepiness Scale‡	5.7±0.9	6.8±0.7
Cause of heart failure — no. of patients		
Ischemic dilated cardiomyopathy	6	6
Nonischemic dilated cardiomyopathy	6	6
NYHA class — no. of patients		
II	8	9
III	4	2
IV	0	1
Left ventricular ejection fraction — %	28.5±1.8	25.0±2.8
Hypertension — no. of patients (%)	5 (42)	7 (58)
Medications — no. of patients (%)		
Digoxin	8 (67)	8 (67)
Diuretics	11 (92)	9 (75)
Angiotensin-converting–enzyme inhibitors	12 (100)	10 (83)
Hydralazine	0 (0)	2 (17)
Nitrates	3 (25)	1 (8)
Beta-blockers	5 (42)	7 (58)

* NYHA denotes New York Heart Association. Plus–minus values are means ±SE. There were no significant differences between the two groups in any of the variables.

† The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ The Epworth Sleepiness Scale ranges from 0 to 24, with scores of 10 or higher indicating excessive daytime sleepiness.

of apneas and hypopneas, desaturation index, lowest oxyhemoglobin saturation value, frequency of arousals from sleep, or distribution of sleep stages (Table 2).

EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE

There were no significant changes in body-mass index from base line to one month in either group (Table 2). In the control group, there were no significant changes in the frequency of apneas and hypopneas or any of the other polysomnographic variables during the study. In the treatment group, continuous positive airway pressure was administered at a mean of 8.9±0.7 cm of water (range, 6 to 14) for 6.2±0.5 hours per night during the study. As compared with base line, the treatment group had significant reductions in the frequency of obstructive apneas and hypopneas and arousals from sleep and significant improvements in the desaturation index and the lowest oxyhemoglobin saturation value ($P<0.01$ for all differences), which were more pronounced than in the control group.

There were no changes in medications during the study in either group. Control patients had no significant changes in blood pressure or heart rate (Table 3), but the group treated with continuous positive airway pressure had a reduction in daytime systolic blood pressure of 10±4 mm Hg ($P=0.02$ for the comparison with base line) and a reduction in heart rate of 4±2 beats per minute ($P=0.007$). The fall in systolic blood pressure was proportional to the base-line value ($r=0.596$, $P=0.04$). The changes in systolic blood pressure were significantly greater in the patients treated with continuous positive airway pressure than in the control group ($P=0.008$). The changes in heart rate also tended to be more pronounced in the patients treated with continuous

Table 2. Anthropomorphic and Polysomnographic Data.*

Variable	Control Group			Group Receiving Continuous Positive Airway Pressure		
	Base Line	1 Mo	P Value†	Base Line	1 Mo	P Value†
Body-mass index‡	32.3±2.5	32.3±2.3	NS	30.4±1.8	31.0±1.8	NS
Episodes of apnea and hypopnea (no./hr of sleep)						
Total	45.2±5.3	44.7±6.8	NS	37.1±6.4	8.3±2.8	<0.001§
Obstructive	34.8±5.3	36.1±5.6	NS	30.3±4.7	3.6±0.7	<0.001¶
Central	7.0±2.6	7.2±3.0	NS	5.9±3.6	4.7±2.9	NS
Desaturation index (no./hr of sleep)‖	17.7±5.3	16.4±4.8	NS	12.7±3.2	0.8±0.5	<0.001**
Lowest oxyhemoglobin saturation (%)	78.4±2.2	76.9±3.6	NS	82.3±1.2	89.6±1.1	0.004††
Total sleep time (min)	286.2±11.7	303.7±16.2	NS	296.7±17.8	306.8±21.2	NS
Stage I and II sleep (% of total sleep time)	78.4±2.8	80.1±4.9	NS	82.3±3.7	75.1±4.2	NS
Stage III and IV sleep (% of total sleep time)	8.5±3.0	8.0±3.5	NS	10.0±2.6	12.7±3.3	NS
REM sleep (% of total sleep time)	13.2±1.8	11.8±2.7	NS	7.7±1.6	12.2±2.1	NS
Arousals (no./hr of sleep)	42.9±5.5	42.3±6.2	NS	31.4±6.1	12.8±1.7	0.003‡‡

* NS denotes not significant, and REM rapid eye movement. Values are means ±SE. There were no significant differences in base-line values between the control group and the group given continuous positive airway pressure.
† P values are for comparisons between base-line values and one-month values within the group.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ $P=0.002$ for the comparison between the groups.
¶ $P<0.001$ for the comparison between the groups.
‖ The desaturation index is the number of times per hours of sleep that the oxyhemoglobin saturation falls below 90 percent.
** $P=0.008$ for the comparison between the groups.
†† $P=0.01$ for the comparison between the groups.
‡‡ $P=0.03$ for the comparison between the groups.

positive airway pressure than in the controls, but the difference was not significant (P=0.09).

After one month, there was no significant change in left ventricular ejection fraction in the control group (an increase of 1.5±2.3 percent, based on left ventricular end-diastolic and end-systolic volumes of 221±14 and 160±13 ml, respectively, at base line and 215±14 and 149±9 ml, respectively, at one month). In contrast, the group treated with continuous positive airway pressure had a significant absolute increase of 8.8±1.6 percent in the left ventricular ejection fraction (P<0.001) and a relative increase of 35 percent (Fig. 1), based on left ventricular end-diastolic and end-systolic volumes of 184±14 and 140±13 ml, respectively, at base line and 192±14 and 129±12 ml, respectively, at one month. The improvement was significantly greater than that in the control group (P=0.009).

This effect of continuous positive airway pressure on the left ventricular ejection fraction was similar in patients receiving beta-blockers and those not receiving beta-blockers (increases of 9.1±2.4 percent [P=0.008] and 8.5±2.1 percent [P=0.02], respectively). In addition, subjects with ischemic dilated cardiomyopathy and those with nonischemic dilated cardiomyopathy had similar improvements in the left ventricular ejection fraction during treatment with continuous positive airway pressure (increases of 8.1±1.3 percent [P=0.02] and 9.7±3.0 percent [P=0.02], respectively). There were no significant changes in left ventricular end-diastolic or end-systolic dimensions in the control group, but there was a significant reduction in end-systolic dimension in the group treated with continuous positive airway pressure (P=0.009). This reduction was significantly greater than that in the control group (P=0.02) (Fig. 2).

DISCUSSION

Our results demonstrate that nocturnal continuous positive airway pressure significantly improves the daytime left ventricular systolic function of patients with heart failure and coexisting obstructive sleep apnea whose condition is stable. One month of therapy with continuous positive airway pressure resulted in a 9 percent absolute increase and a 35 percent relative increase in left ventricular ejection fraction, in conjunction with significant reductions in left ventricular end-systolic dimension, daytime systolic blood pressure, and heart rate. Because continuous positive airway pressure reduced the frequency of obstructive events and arousals and improved arterial oxygenation during sleep, we attribute these cardiovascular effects primarily to the alleviation of obstructive sleep apnea.

In our previous uncontrolled study, involving eight patients with nonischemic dilated cardiomyopathy and obstructive sleep apnea, therapy with continuous positive airway pressure also resulted in a significant augmentation of the left ventricular ejection fraction.[13] The present study confirms, in the more rigorous setting of a randomized trial, that one month of nocturnal continuous positive airway pressure causes substantial improvement in the daytime left ventricular ejection fraction. Our study also broadens the application of these findings to both ischemic and nonischemic causes of heart failure. By demonstrating that continuous positive airway pressure also lowers daytime systolic blood pressure

Table 3. Heart Rate and Blood Pressure.*

Variable	Control Group			Group Receiving Continuous Positive Airway Pressure		
	Base Line	1 Mo	P Value	Base Line	1 Mo	P Value
Heart rate (beats/min)	67±4	67±4	NS	68±3	64±3	0.007†
Systolic blood pressure (mm Hg)	128±7	134±8	NS	126±6	116±5	0.02‡
Diastolic blood pressure (mm Hg)	60±4	58±3	NS	62±4	59±2	NS

* NS denotes not significant. Plus–minus values are means ±SE. There were no significant differences in base-line values between the control group and the group given continuous positive airway pressure. Unless otherwise specified, P values are for the comparisons between base-line values and one-month values within the group.
† P=0.09 for the comparison between the groups.
‡ P=0.008 for the comparison between the groups.

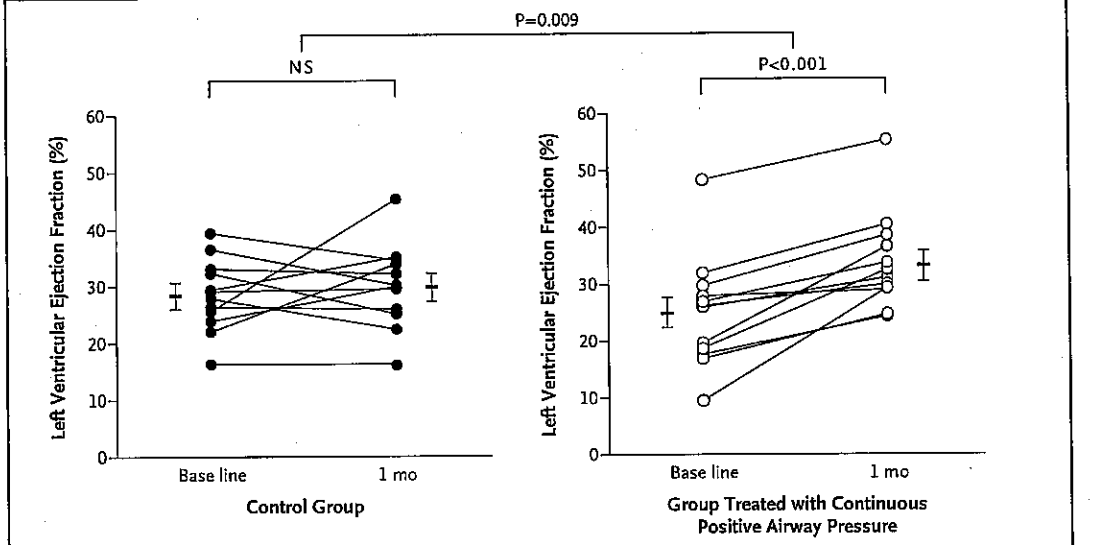

Figure 1. Individual Values for the Left Ventricular Ejection Fraction in All Patients.

In the control group, there was no significant change in the left ventricular ejection fraction from base line to one month (from a mean [±SE] of 28.5±1.8 to 30.0±2.1 percent). In contrast, the left ventricular ejection fraction increased in all 12 subjects treated with continuous positive airway pressure, and the mean increase was significant (from 25.0±2.8 to 33.8±2.4 percent, P<0.001). The change in the left ventricular ejection fraction from base line to one month was significantly greater in the group treated with continuous positive airway pressure than in the control group (8.8±1.6 percent vs. 1.5±2.3 percent, P=0.009). The one patient in the group that received continuous positive airway pressure who had a base-line left ventricular ejection fraction of 48 percent met the pretrial screening eligibility criterion (the left ventricular ejection fraction was 39 percent). NS denotes not significant. Short horizontal lines and I bars are means ±SE.

and heart rate, our study provides evidence that this improvement in the left ventricular ejection fraction is achieved at a lower myocardial workload and points to sustained reduction in afterload as one likely mechanism for this improvement.

In dogs, experimentally induced obstructive sleep apnea leads to nocturnal and daytime systemic hypertension and impairment of left ventricular systolic function.[9,20] These observations are supported by epidemiologic studies indicating that obstructive sleep apnea increases the likelihood that hypertension will develop[21] and is associated with increased odds of heart failure, independently of other known risk factors.[7]

Obstructive sleep apnea has several adverse effects with the potential both to impair ventricular systolic function and to raise systemic vascular resistance. Acutely, inspiratory efforts during obstructive apnea generate exaggerated negative intrathoracic pressure, which leads to both an increase in left ventricular afterload and a decrease in left ventricular preload, which in turn cause a reduction in stroke volume.[8,9,22-24] Intermittent hypoxia during obstructive apnea may impair cardiac contractility directly or reduce cardiac output indirectly by increasing pulmonary-artery pressure.[25,26] It may also induce a mismatch between the supply of oxygen and the demand, provoking myocardial ischemia in those with coronary disease.[27] Apnea-induced hypoxia, hypercapnia, and arousal from sleep trigger sympathetic vasoconstrictor outflow that raises systemic blood pressure and further increases afterload.[28-30] These adverse hemodynamic and sympathetic effects are more pronounced in subjects with heart failure.[31,32] Long-term exposure to elevated sympathetic neural activity can induce hypertrophy and apoptosis of myocytes and predispose patients to cardiac arrhythmias.[33,34] None of these adverse nocturnal effects of obstructive apnea are remedied by pharmacologic therapy.[35]

In contrast, continuous positive airway pressure reverses many of these pathophysiological effects during sleep. In patients with obstructive sleep apnea but without heart failure, continuous positive airway pressure attenuates apnea-related surges in sympathetic vasoconstrictor tone.[29] In patients with

heart failure, short-term abolition of obstructive apnea by continuous positive airway pressure dampens negative intrathoracic-pressure swings and lowers systemic blood pressure, causing a reduction in left ventricular afterload.[10] By abolishing hypoxic dips, continuous positive airway pressure also augments the myocardial oxygen supply while reducing oxygen demand.

In the present study, we found that the effects of nocturnal continuous positive airway pressure carry over into wakefulness. After one month, subjects treated with continuous positive airway pressure had a 9 percent absolute and a 35 percent relative rise in left ventricular ejection fraction and a 3-mm decrease in left ventricular end-systolic dimension during wakefulness. These improvements in systolic function were accompanied by a decrease in systolic blood pressure of 10 mm Hg and a decrease in heart rate of 4 beats per minute, suggesting a concomitant lowering of myocardial oxygen requirements.

The mechanisms contributing to this sustained increase in left ventricular ejection fraction were probably abolition of cyclical surges in left ventricular wall tension during sleep and chronic downward resetting of sympathetic outflow and peripheral resistance secondary to the abolition of obstructive apnea.[29,36] Similar improvements in the left ventricular ejection fraction that were associated with reductions in the plasma norepinephrine concentration have been described in patients with heart failure and Cheyne–Stokes respiration who were treated with continuous positive airway pressure.[17,37] Our observation, that continuous positive airway pressure used only at night leads to improvement in the left ventricular ejection fraction that persists into the daytime, is similar to the sustained improvement in left ventricular systolic function that occurs after removal of a left ventricular assist device. With both mechanical interventions, myocardial workload is reduced and heart failure is alleviated. Over time, this change may lead to sustained aftereffects, including reduction in sympathetic outflow, up-regulation of myocardial β-adrenergic–receptor responsiveness,[37,38] restoration of the expression of cardiac metabolic genes, and improvement in contractility.[39]

Improvements in cardiovascular function in response to continuous positive airway pressure occurred relatively rapidly in our study in patients in stable condition who were receiving optimal medical therapy, including combinations of drugs that reduce vascular resistance (Table 1). Furthermore, the magnitude of change in the left ventricular ejection fraction did not differ between the majority of patients treated with continuous positive airway pressure who were receiving beta-blockers and the minority who were not. Those with ischemic and those with nonischemic dilated cardiomyopathy had similar improvements in left ventricular ejection fraction, a result indicating that continuous positive airway pressure has beneficial effects beyond those of contemporary pharmacologic therapy that are independent of the cause of heart failure. Although it is possible that the response to continuous positive airway pressure might differ between patients with ischemic cardiomyopathy and those with nonischemic cardiomyopathy, a larger study would be required to detect this difference.

Among patients with heart failure, the daytime systolic blood pressure is higher in those with obstructive sleep apnea.[40] In patients with normal

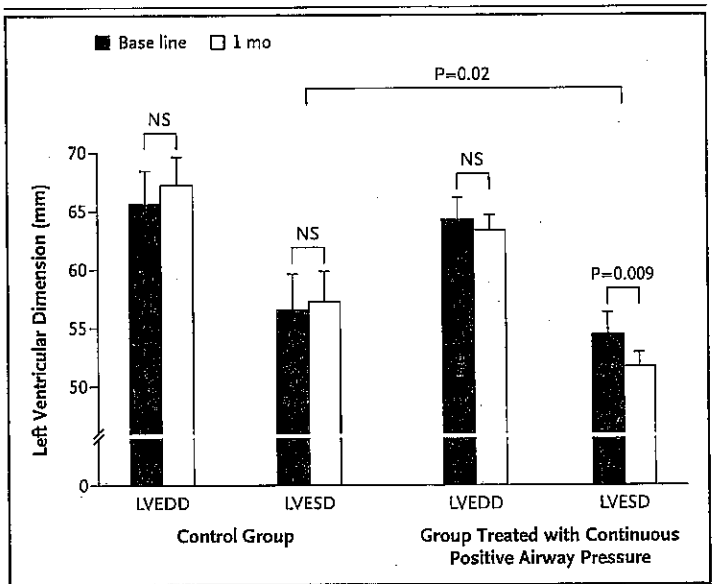

Figure 2. Mean (±SE) Changes in Left Ventricular Dimensions.

There were no significant changes in left ventricular end-diastolic dimension (LVEDD) or left ventricular end-systolic dimension (LVESD) during the study period in the control group (LVEDD changed from 65.6±2.8 to 67.2±2.4 mm, and LVESD from 56.6±3.0 to 57.3±2.5 mm). In the group treated with continuous positive airway pressure, there was no significant change in LVEDD during the study period (LVEDD changed from 64.3±1.8 to 63.4±1.8 mm). However, there was a significant reduction in LVESD (from 54.5±1.8 to 51.7±1.2 mm, P=0.009). The change in LVESD from base line to one month was significantly greater in the group that received continuous positive airway pressure than in the control group (−2.8±1.1 vs. 0.7±0.8 mm, P=0.02). NS denotes not significant.

blood pressure who have obstructive sleep apnea without heart failure, continuous positive airway pressure has been reported to lower the daytime systolic blood pressure.[11,12] In the present study, the blood-pressure–lowering effect of continuous positive airway pressure was most pronounced in those with the highest initial systolic pressures. The reductions in blood pressure induced by continuous positive airway pressure, coupled with improvements in the left ventricular ejection fraction, provide further evidence that obstructive apnea exerts pressor effects during wakefulness that can contribute to left ventricular dysfunction.[9,20]

The presence of obstructive sleep apnea was not associated with reports of daytime sleepiness, as indicated by normal scores on the Epworth Sleepiness Scale (under 10).[16] Nevertheless, compliance was excellent among those randomly assigned to continuous positive airway pressure, indicating that patients with heart failure and obstructive apnea need not have daytime sleepiness to derive cardiovascular benefits from continuous positive airway pressure. Our data also suggest that continuous positive airway pressure can be readily tolerated across a wide spectrum of age and severity of heart failure, since our patients ranged in age from 28 to 72 years and had class II, III, or IV symptoms of heart failure.

Although the patients were aware of their treatment assignments, the key measurements of cardiovascular outcome were obtained by persons blinded to treatment assignment. The control group had no significant changes in sleep or cardiovascular outcomes, a result confirming the stability of their condition during the study. Therefore, the changes detected in the treatment group can be attributed specifically to continuous positive airway pressure, even in the absence of a placebo intervention.

In general, therapies that lower blood pressure (i.e., afterload) and heart rate and improve the left ventricular ejection fraction reduce cardiovascular morbidity and mortality among patients with heart failure.[2,3] Ideally, therefore, larger randomized trials should be undertaken to determine whether the beneficial effects of continuous positive airway pressure on cardiovascular function translate into similar long-term outcomes. However, such studies may be difficult if not impossible to conduct because of the ethical concerns that would arise if continuous positive airway pressure, which is now standard therapy for obstructive apnea in patients without heart failure, were withheld from a control group over prolonged periods.

In conclusion, treatment of obstructive sleep apnea by nocturnal continuous positive airway pressure in medically treated patients with heart failure improves daytime left ventricular systolic function while lowering systolic blood pressure. Since nocturnal continuous positive airway pressure does not induce such responses in patients with heart failure but without sleep apnea,[41] our findings imply that obstructive apnea has specific detrimental effects on ventricular function and blood pressure that are at least partially reversible.[8-10,20]

Because obstructive sleep apnea has been reported to occur in up to one third of patients with stable heart failure,[5] continuous positive airway pressure could become an important nonpharmacologic adjunct to conventional drug therapy in this population. Our results therefore raise the question of whether routine screening for sleep apnea should be performed in patients with heart failure. Currently, the standard method for the diagnosis of sleep apnea is polysomnography conducted in a sleep laboratory, an expensive and not universally available procedure. However, the development and validation of less expensive and more readily available techniques, such as ambulatory monitoring, may make widespread screening for sleep apnea feasible in patients with heart failure. Nevertheless, there needs to be greater awareness among physicians that obstructive sleep apnea may have an adverse pathophysiological role in heart failure that can be addressed by targeted therapy.

Supported by a grant (MOP-11607) from the Canadian Institutes of Health Research, a research fellowship from the Japan Information Center for Respiratory Failure Patients (to Dr. Kaneko), a Career Scientist Award from the Heart and Stroke Foundation of Ontario (to Dr. Floras), a Senior Scientist Award from the Canadian Institutes of Health Research (to Dr. Bradley), unrestricted Research Fellowships from Respironics (to Drs. Usui, Plante, and Tkacova), unrestricted postdoctoral support from Merck Frosst, SmithKlineBeecham, and Roche Pharmaceuticals (to Dr. Kubo), and a Canadian Hypertension Society–Merck Frosst Canada Research Fellowship and a grant from the Gardiner Foundation of Toronto (to Dr. Ando).

Drs. Floras and Bradley report having received research funding unrelated to the current study from Respironics, ResMed, and Tyco. Dr. Usui reports having received grant support from Respironics.

We are indebted to Fiona Rankin, B.Sc., and Candice Silversides, M.D., for their technical assistance.

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