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Influence of sleep apnea syndrome on cardiovascular function

（睡眠時無呼吸症候群の心血管機能への影響）

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ABSTRACT

Background: Sleep-disordered breathing is common in individuals with left ventricular (LV) dysfunction and has been treated with nocturnal positive airway pressure. We investigated whether treatment of central sleep apnea-hypopnea with bilevel positive airway pressure (BPAP) in ambulatory patients with idiopathic dilated cardiomyopathy (IDCM) might improve LV function.

Methods: Fifty-two consecutive patients with IDCM who underwent both cardiac catheterization and standard polysomnography were enrolled in the study; individuals with obstructive sleep apnea syndrome were excluded. Subjects with an apnea-hypopnea index (AHI) of ≥20 episodes per hour were randomized to receive medical therapy either alone (n = 11) or together with BPAP (n = 10).

Results: The LV end-diastolic pressure, pulmonary capillary wedge pressure, and plasma concentration of brain natriuretic peptide were significantly greater, and the LV ejection fraction (LVEF) was significantly lower, in patients with an AHI of ≥20/h (n = 21, 40.4%) than in those with an AHI of <20/h (n = 31, 59.6%). The LVEF (30.5 ± 1.6 vs. 50.8 ± 3.5%, $P < 0.001$) and plasma concentration of brain natriuretic peptide (162.8 ± 44.5 vs. 32.7 ± 17.6 pg/mL, $P = 0.02$) were significantly increased and decreased, respectively, after treatment with BPAP (daily use, 4.8 ± 0.3 h) for 3 months, whereas these parameters remained unchanged in the controls.

Conclusions: Our findings suggest that treatment of coexisting central sleep apnea-hypopnea with BPAP improves LV function in ambulatory patients with IDCM.

BPAP should thus be considered as a nonpharmacological adjunct to conventional drug therapy in such patients.

Key words: cardiomyopathy, left ventricular function, central sleep apnea, bilevel positive airway pressure

Abbreviations

AHI, apnea-hypopnea index

BPAP, bilevel positive airway pressure

BNP, brain natriuretic peptide

CPAP, continuous positive airway pressure

IDCM, idiopathic dilated cardiomyopathy

LV, left ventricular

LVEF, LV ejection fraction

NYHA, New York Heart Association

INTRODUCTION

Idiopathic dilated cardiomyopathy (IDCM), which is characterized by cardiac enlargement and impaired systolic function of one or both ventricles, has an age-adjusted prevalence of 36 cases per 100,000 population and accounts for 10,000 deaths annually in the United States.[1] This condition is an important cause of congestive heart failure, which remains a major and growing public health problem despite recent advances in therapy.[1] Improvement in the prognosis of individuals with left ventricular (LV) dysfunction associated with overt congestive heart failure will thus require the development of additional and novel therapeutic approaches. One such potential approach is the early diagnosis and specific treatment of coexisting sleep-disordered breathing in patients with LV dysfunction.[2-6]

Nocturnal treatment of sleep apnea by continuous positive airway pressure (CPAP) in individuals with congestive heart failure not only alleviates sleep-disordered breathing but also improves LV function, ameliorates the symptoms of heart failure, and reduces sympathetic activation by decreasing the secretion of norepinephrine.[7–11] However, the increased effort required to complete expiration against the applied pressure often results in a sensation of dyspnea in individuals treated with CPAP.[12–14] The Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure (CANPAP) trial showed that CPAP attenuates central sleep apnea and improves cardiovascular function in patients with heart failure, but it did not demonstrate any beneficial effect of CPAP on survival.[15] Ventilation by bilevel positive airway pressure (BPAP) almost completely abolished Cheyne-Stokes respiration in patients with

congestive heart failure,[16] suggesting that this approach is a noninvasive option for treatment of such patients. BPAP with room air for 1 h was also found to reduce systemic vascular resistance, reflecting cardiac afterload, as well as systolic blood pressure and heart rate in patients with congestive heart failure,[17] indicating that the reduction in LV transmural pressure during inspiration and expiration induced by this approach might alleviate congestive heart failure. BPAP was thus proposed to have excellent potential for improving LV performance.[17] The long-term effects of treatment with BPAP on cardiac function and its mechanisms of action have not been systematically evaluated, however, in patients with IDCM.

We have now performed a randomized prospective controlled trial to determine whether BPAP might improve LV function during daytime wakefulness and survival in ambulatory patients with IDCM and central sleep apnea-hypopnea.

METHODS

Study Subjects

Fifty-two consecutive ambulatory patients (aged 21 to 67 years) with IDCM (New York Heart Association [NYHA] functional class I, II, or III) who underwent both cardiac catheterization and standard polysomnography were enrolled in the study (Fig. 1). The diagnosis of IDCM was based on both clinical and histopathologic findings after echocardiography [LV ejection fraction (LVEF) of <45%], coronary angiography, and LV endomyocardial biopsy. Ischemic and primary valvular heart disease were excluded by angiography and echocardiography. Exclusion criteria included a history of alcohol abuse;[18] diabetes mellitus and hypertension based on the criteria of the World Health Organization; endocrine disorders;[19] obstructive sleep apnea syndrome; and chronic obstructive pulmonary disease (FEV_1/FVC ratio<70%). The study protocol was approved by the appropriate institutional review committee, and subjects provided written consent to participation after being informed in detail of the purpose and methods of the study.

Polysomnography

Overnight polysomnography was performed according to standard techniques.[20] Breathing variables monitored included chest and abdominal movement, surface intercostal electromyogram, oronasal airflow with thermistor and airflow using nasal pressure. Apnea, hypopnea, sleep stages, and electroencephalographic arousal were scored according to established criteria.[20–22] Central sleep apnea was defined as the absence of airflow for ≥10 s without thoracoabdominal motion and changes in surface

intercostal electromyogram, and central hypopnea as a reduction of ≥50% in airflow and thoracoabdominal motion from baseline, also for ≥10 s without airflow limitation.[15] Central sleep apnea syndrome was defined as the occurrence of ≥15 episodes of apnea or hypopnea per hour of sleep (apnea-hypopnea index, AHI), more than 50% of which were determined to be central rather than obstructive.[15]

Echocardiography

Standard echocardiography, including measurement of transmitral flow velocity indices, was performed. LVEF was calculated according to a modification of Simpson's method.[23] Mitral regurgitation was graded by color flow Doppler imaging.[24]

Cardiac Catheterization

LV pressure, pulmonary capillary wedge pressure, and cardiac output were measured. We calculated the peak positive first derivative of LV pressure with respect to time (*dP/dt*) and the pressure half-time.[25]

Treatment with BPAP

The health insurance system in Japan covers the cost of CPAP or BPAP treatment only for individuals with an AHI of ≥20/h. Study subjects were thus stratified according to the AHI, and those with an index of ≥20/h were randomly assigned to receive standard medical therapy either alone (11 patients, non-BPAP group) or together with nasal BPAP (10 patients, BPAP group) until the end of the study (Fig. 1). BPAP was administered with a BPAP S instrument (Respironics). On the night after the baseline sleep analysis, those patients assigned to receive BPAP underwent overnight titration of the pressure in order to adjust it to abolish apnea, hypopnea, and oxygen desaturation or to determine the highest level tolerated. Both inspiratory and expiratory pressures were initially set at

4 cm H_2O and were increased by 1 cm H_2O in a stepwise manner until apnea was eliminated. The expiratory pressure was adjusted to abolish obstructive events. The inspiratory pressure alone was then increased to eliminate hypopnea, oxygen desaturation, snoring, and arousal from sleep.[16] Urine samples were obtained on the two consecutive days involving overnight sleep analysis both before and during treatment with BPAP. Patients in the BPAP group were sent home with a pressure device and instructed to use it for at least 4 h per night on at least 70% of nights. These patients visited their hospitals once a month, and compliance with the pressure treatment protocol was assessed each month during the study from each individual's recorded usage of the device. The time and cause of death and BPAP use were ascertained from medical records. Quality of life was assessed with the Specific Activity Scale[26] both before and after 3 months of treatment with or without BPAP. Physicians who interpreted the polysomnography, cardiac catheterization, and echocardiography data obtained before or after 3 months of treatment with or without BPAP were blinded to treatment assignment.

Statistical Analysis

Data are presented as means ± SE. Clinical characteristics were compared between patients with an AHI of <20/h and those with an index of ≥20/h with Fisher's exact test, the Mann-Whitney *U* test, or Student's unpaired two-tailed *t* test. Baseline characteristics were compared between the BPAP and non-BPAP groups with Fisher's exact test, the Mann-Whitney *U* test, or Student's unpaired two-tailed *t* test. Parameters at baseline and after treatment with BPAP were compared with Student's paired *t* test. Parameters at baseline were compared between the survivors and nonsurvivors of the non-BPAP group

with Student's unpaired two-tailed *t* test. All analyses were performed with the SPSS 12.0 software package (SPSS, Chicago, IL). A *P* value of <0.05 was considered statistically significant.

RESULTS

Characteristics of the Study Subjects

The prevalence of individuals with an AHI of ≥20/h among the patients with IDCM enrolled in the study was 40.4% (21/52). The LV end-diastolic pressure, pulmonary capillary wedge pressure, LV end-diastolic and end-systolic internal dimensions, and plasma concentration of brain natriuretic peptide (BNP) were significantly greater, and the LVEF was significantly lower, in the patients with an AHI of ≥20 /h than in those with an index of <20/h (Table 1).

Effects of BPAP on Polysomnographic and Hemodynamic Variables

Among the subjects with an AHI of ≥20/h, all of whom satisfied the definition for central sleep apnea syndrome, there were no significant differences in baseline polysomnographic and hemodynamic parameters, history of ventricular tachycardia, prevalence of atrial fibrillation, or standard medical therapy between those assigned to the BPAP group and those assigned to the non-BPAP group (Table 2). In the treatment group, BPAP was administered at mean inspiratory and expiratory levels of 10.9 ± 0.9 and 7.9 ± 0.9 cm H_2O, respectively, for at least 4 h per night (daily use, 4.8 ± 0.3 h) during the study. All patients assigned to receive BPAP treatment were able to tolerate it for 3 months. In the BPAP group, the AHI, frequency of arousals, and amount of norepinephrine in 24-h urine specimens were significantly decreased for the first night the patients received pressure treatment compared with the values for the previous night of natural sleep (Table 3). The LVEF, deceleration time of the peak early velocity of LV inflow, and Specific Activity Scale were significantly increased, and the LV end-systolic

internal dimension, heart rate, systolic and diastolic blood pressures, and plasma level of BNP were all significantly decreased, in these 10 patients after 3 months of treatment with BPAP (Table 4).

There were no significant changes in any of the measured parameters in the non-BPAP group during this 3-month period. Moreover, four patients in the non-BPAP group, but none of those in the pressure treatment group, died from worsening heart failure during a mean follow-up time of 31.0 ± 2.3 months. Patients in the BPAP group continued use of the pressure device during the follow-up period. Comparison of baseline data revealed that the LVEF and lowest oxygen saturation during sleep were significantly lower, whereas the plasma BNP concentration was significantly greater, in the nonsurvivors than in the survivors of the non-BPAP group.

DISCUSSION

We have shown that treatment for 3 months with BPAP resulted in a significant increase in LVEF and significant decreases in heart rate, systolic and diastolic blood pressures, and the plasma concentration of BNP in patients with IDCM and an AHI of ≥20/h. These various parameters did not change during the same 3-month period in similar patients not treated with BPAP. Moreover, four of the 11 patients in the non-BPAP group died during follow-up compared with none of the 10 patients in the treatment group. Our results suggest that sleep-disordered breathing has detrimental effects on LV function in individuals with IDCM, and that these effects can be ameliorated by treatment with BPAP.

A BPAP device allows independent adjustment of inspiratory and expiratory airway pressures and can eliminate sleep-disordered breathing at lower levels of expiratory airway pressure than those required with CPAP.[27] Moreover, application of BPAP may help to increase and stabilize functional residual capacity, improve pulmonary compliance (thereby decreasing the effort of breathing), and improve the ventilation-perfusion relation in the presence of an elevated pulmonary capillary wedge pressure.[28] An increased pulmonary capillary wedge pressure confers an increased risk for Cheyne-Stokes respiration, central sleep apnea, and death.[29] In patients with IDCM and central apnea or hypopnea, the expiratory positive airway pressure does not need to be as high as the inspiratory positive airway pressure because persistent hypopnea or oxygen desaturation is eliminated by increasing the inspiratory positive airway pressure alone.

A recent large randomized trial showed that CPAP improved cardiac function in heart failure patients but had no effect on the occurrence of death or need for transplantation after 2 years.[15] The subjects of the CPAP group in this previous CANPAP trial were 63.2 ± 9.1 years old, had an AHI of 40 ± 15/h and LVEF of 24.8 ± 7.9%, and included individuals with a NYHA functional class of II, III, or IV whose cardiomyopathy was ischemic (65%), idiopathic dilated (33%), or hypertensive (2%). The differences in outcome between the CANPAP study and our study may thus be attributable to differences in the age of the patients, in baseline LVEF, in baseline severity of sleep apnea syndrome or NYHA functional class, or in the cause of LV dysfunction. Philippe et al. showed that both adaptive servo-pressure support and CPAP alleviated central sleep apnea in 25 heart failure patients, but only adaptive servo-pressure support completely corrected central sleep apnea and Cheyne-Stokes respiration at 6 months, reducing the AHI to <10/h.[30] The LVEF increased significantly in the adaptive servo-pressure support group but not in the CPAP group. BPAP should thus be considered as a supplemental nonpharmacological treatment in IDCM patients with moderate to severe sleep-disordered breathing. Further large-scale studies focusing on the long-term use of BPAP as well as its effects on LV function and mortality are required to confirm the efficacy of this treatment approach.

In the 10 patients with an AHI of ≥20/h in the BPAP group, such treatment reduced both the frequency of nocturnal arousals and 24-h urinary norepinephrine excretion as well as increased the lowest oxygen saturation. Reduced sympathetic activity, improved myocardial oxygen delivery, and the change in intrathoracic pressure likely contributed to the increase in LV function in this group of patients.[2,3,7,9,31] The

sustained increase in LVEF and reductions in heart rate, systolic blood pressure, and diastolic blood pressure induced by BPAP were thus probably achieved as a result both of elimination of cyclical surges in LV wall tension during sleep and of chronic downward resetting of sympathetic outflow.[32–34] The effects of nocturnal treatment with BPAP thus appear to persist during daytime wakefulness. Furthermore, recognition by general practitioners of the pathogenic role of sleep-disordered breathing in the development of LV dysfunction would likely result in an improvement in patient care.

The cardiac index did not differ significantly between patients with an AHI of ≥20 or <20/h, indicating that prolonged circulation time during daytime wakefulness alone did not play a key role in initiating sleep-disordered breathing.[2] In contrast, the plasma level of BNP was significantly increased in patients with an AHI of ≥20/h and was decreased in these individuals after 3 months of regular treatment with BPAP. The plasma concentration of BNP, which is secreted predominantly from the left ventricle in response to changes in LV wall stretching, is related to LV filling pressures and wall stress.[35] It is a sensitive indicator of the progression of LV dysfunction and its prognostic impact has been established by several studies.[36–38] Sleep-disordered breathing thus plays an important role in the pathophysiology of LV dysfunction, and the impact of this role can be ameliorated by targeted therapy.

Study Limitations

We did not perform polysomnography after treatment of patients with BPAP for 3 months. Whether or not there was a persistent improvement in central apnea with or without BPAP treatment is thus not known. In addition, the BPAP device used in our study did not include memory, hence, the compliance was assessed from self-reported

use of positive pressure therapy, which might provide some insufficient information. We also did not measure esophageal pressure with continuous overnight monitoring as an index of respiratory effort, given that such measurements can disturb sleep, especially in individuals with central sleep apnea syndrome without daytime sleepiness.[2,20] Instead, we recorded the intercostal electromyogram. Intercostal muscles play an important role in lung ventilation. Activity of the parasternal portion of the internal intercostal muscles is associated with inspiratory airflow,[39] with the normal expansion of the rib cage during inspiration being primarily mediated by the intercostal muscles.[40]

Clinical Implications

In this randomized prospective control trial, we have demonstrated long-term beneficial effects of BPAP on hemodynamics, without apparent adverse effects, in ambulatory patients with IDCM and moderate to severe sleep-disordered breathing. The assessment of sleep-disordered breathing as a potential contributing factor to the progression of LV dysfunction thus appears to be clinically important for the initial evaluation and long-term follow-up of patients with IDCM.

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FIGURE LEGENDS

Fig. 1. Study protocol and subject survival. The mean follow-up time was 31.0 ± 2.3 months.

Table 1. Comparison of baseline characteristics between patients with an apnea-hypopnea index (AHI) of <20 or ≥20 /h.

Characteristic	AHI < 20/h (*n* = 31)	AHI ≥ 20/h (*n* = 21)	*P*
Clinical characteristics			
NYHA functional class I/II/III	18/11/2	3/12/6	<0.001
NYHA functional class score	1.5 ± 0.1	2.1 ± 0.1	<0.001
Age (years)	50.4 ± 2.2	51.6 ± 2.0	0.70
Body mass index (kg/m^2)	24.4 ± 0.6	24.0 ± 1.1	0.72
Polysomnographic measurements			
AHI (/h)	7.5 ± 1.1	27.3 ± 2.1	<0.001
Lowest SpO_2 (%)	86.1 ± 1.3	82.0 ± 2.3	0.11
Sleep stage (%)			
Stage 1	22.2 ± 4.5	41.9 ± 5.6	0.02
Stage 2	59.3 ± 4.2	44.9 ± 6.5	0.09
Stages 3 + 4	1.7 ± 0.9	0.15 ± 0.1	0.08
Rapid eye movement	15.0 ± 2.3	13.0 ± 2.3	0.54
No. of arousals/h	28.5 ± 5.8	41.2 ± 4.2	0.05
Hemodynamic variables			
LV end-diastolic internal dimension (mm)	60.5 ± 0.8	64.3 ± 1.7	0.03

LV end-systolic internal dimension (mm)	48.7 ± 1.0	54.5 ± 1.6	0.002
LVEF (%)	38.9 ± 1.2	33.0 ± 1.5	0.004
Deceleration time of peak early velocity (ms)	189.1 ± 9.0	167.6 ± 8.8	0.11
Left atrial dimension (mm)	36.6 ± 0.9	40.6 ± 1.4	0.02
Peak +*dP/dt* (mmHg/s)	1182.5 ± 53.6	1197.1 ± 67.8	0.86
Peak –*dP/dt* (mmHg/s)	1498.8 ± 67.7	1459.1 ± 116.9	0.75
Pressure half-time (ms)	41.0 ± 1.9	43.7 ± 2.7	0.40
LV end-diastolic pressure (mmHg)	13.7 ± 1.0	23.1 ± 1.4	<0.001
Pulmonary capillary wedge pressure (mmHg)	10.9 ± 0.8	15.4 ± 1.4	0.004
Cardiac index (L min^{-1} m^{-2})	3.2 ± 0.2	2.9 ± 0.2	0.17
Heart rate (beats/min)	73.1 ± 3.2	79.4 ± 3.8	0.20
Systolic blood pressure (mmHg)	121.6 ± 2.4	127.5 ± 3.8	0.19
Diastolic blood pressure (mmHg)	76.5 ± 2.5	78.8 ± 2.8	0.55
Plasma BNP (pg/mL)	46.5 ± 8.0	170.7 ± 33.9	<0.001

Data are means ± SE. NYHA, New York Heart Association; AHI, apnea-hypopnea index; SpO_2, oxygen saturation; LV, left ventricular; LVEF, LV ejection fraction; *dP/dt* , first derivative of left ventricular pressure with respect to time; BNP, brain natriuretic peptide.

Table 2. Baseline characteristics of patients with an apnea-hypopnea index of ≥20/h according to treatment group.

Characteristic	Non-BPAP group (n = 11)	BPAP group (n = 10)	P
Age (years)	50.8 ± 2.4	50.0 ± 3.4	0.47
Body mass index (kg/m^2)	23.6 ± 1.1	24.4 ± 2.2	0.70
NYHA functional class I/II/III	2/5/4	1/6/3	1.00
NYHA functional class score	2.2 ± 0.2	2.2± 0.2	0.95
Sinus rhythm/atrial fibrillation	9/2	9/1	0.53
No. with ventricular tachycardia	4	2	0.41
Mitral regurgitation (mild/moderate/severe)	3/1/2	2/0/2	0.91
Medications (%)			
Angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers	81.9	80.0	0.92
Digoxin	18.2	20.0	0.92
Diuretics	72.7	80.0	0.70
Nitrates	9.1	10.0	0.94
Beta-blockers	63.6	70.0	0.76

Quantitative data are means ± SE. BPAP, bilevel positive airway pressure.

Table 3. Acute effects of treatment with bilevel positive airway pressure on polysomnographic parameters.

Parameter	Before	After	*P*
AHI (/h)	28.3 ± 3.9	5.2 ± 1.2	<0.001
Central apnea	11.2 ± 0.2	0.60 ± 0.2	<0.001
Obstructive apnea	1.7 ± 0.6	1.5 ± 0.6	0.82
Mixed apnea	2.1 ± 1.6	0.5 ± 0.2	0.28
Hypopnea	13.2 ± 2.5	2.7 ± 0.7	0.001
Lowest SpO_2 (%)	75.1 ± 4.7	89.2 ± 1.8	0.02
Sleep stage (%)			
Stage 1	42.9 ± 4.7	33.2 ± 6.0	0.22
Stage 2	41.5 ± 6.0	48.5 ± 7.2	0.47
Stages 3 + 4	0.01 ± 0.01	0.6 ± 0.4	0.13
Rapid eye movement	15.1 ± 2.4	17.0 ± 1.3	0.51
No. of arousals/h	40.2 ± 4.6	11.9 ± 1.3	<0.001
24-h urinary norepinephrine (nmol/mmol creatinine)	49.9 ± 6.7	29.6 ± 3.7	0.03

Data are means ± SE and are for the night before and the first night of treatment with bilevel positive airway pressure (n = 10).

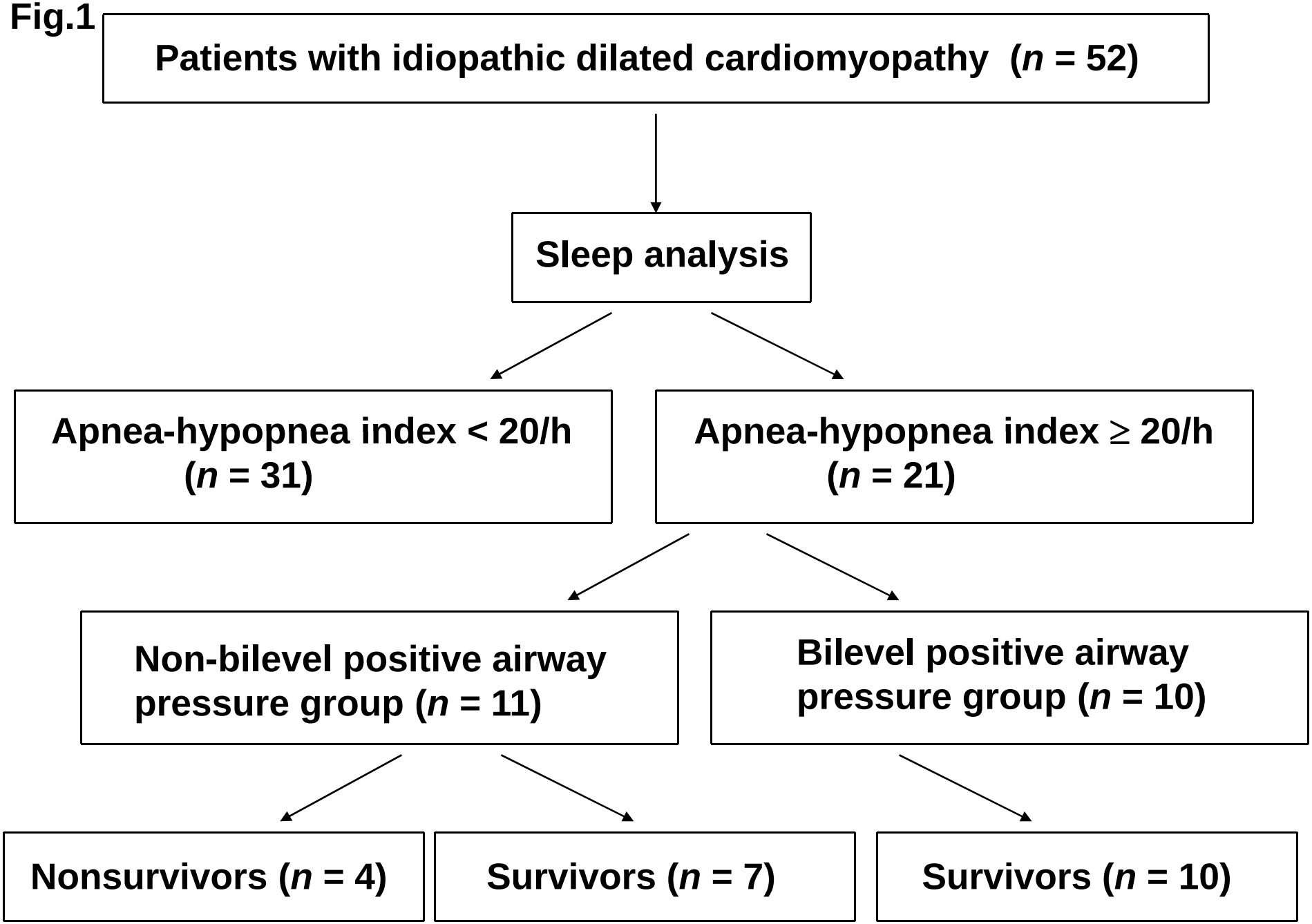
Table 4. Effects of treatment for 3 months with bilevel positive airway pressure on hemodynamic variables.

Parameter	Baseline	After 3 months	*P*
*Non-BPAP group (*n = *11)*			
NYHA functional class score	2.2 ± 0.2	2.0 ± 0.2	0.61
LV end-diastolic internal dimension (mm)	64.1 ± 2.2	63.5 ± 2.2	0.82
LV end-systolic internal dimension (mm)	53.5 ± 2.4	51.7 ± 2.8	0.63
LVEF (%)	34.6 ± 2.6	37.8 ± 3.7	0.49
Left atrial dimension (mm)	39.7 ± 2.3	40.9 ± 1.5	0.68
Deceleration time of peak early velocity (ms)	173.3 ± 12.8	161.5 ± 9.4	0.48
Heart rate (beats/min)	78.5 ± 6.1	74.5 ± 6.9	0.66
Systolic blood pressure (mmHg)	123.6 ± 4.6	121.0 ± 7.5	0.76
Diastolic blood pressure (mmHg)	76.8 ± 3.4	73.0 ± 4.0	0.48
Plasma BNP (pg/mL)	177.7 ± 52.6	139.0 ± 55.7	0.62
Specific Activity Scale (METs)	3.7 ± 0.5	4.0 ± 0.4	0.69
*BPAP group (*n = *10)*			
NYHA functional class score	2.2 ± 0.2	1.3 ± 0.2	0.002
LV end-diastolic internal dimension (mm)	65.4 ± 9.3	59.0 ± 9.4	0.14
LV end-systolic internal dimension (mm)	55.4 ± 2.1	43.5 ± 2.6	0.002
LVEF (%)	30.5 ± 1.6	50.8 ± 3.5	<0.001
Left atrial dimension (mm)	41.5 ± 2.0	37.4 ± 2.3	0.19

Deceleration time of peak early velocity (ms)	151.7 ± 9.2	207.2 ± 15.7	0.01
Heart rate (beats/min)	82.3 ± 3.9	70.0 ± 2.6	0.01
Systolic blood pressure (mmHg)	126.9 ± 4.5	109.6 ± 3.1	0.006
Diastolic blood pressure (mmHg)	77.3 ± 3.7	65.8 ± 3.5	0.04
Plasma BNP (pg/mL)	162.8 ± 44.5	32.7 ± 17.6	0.02
Specific Activity Scale (METs)	3.5 ± 0.4	5.4 ± 0.3	<0.001

Data are means ± SE.

Fig.1


Patients with idiopathic dilated cardiomyopathy (*n* = 52)
Sleep analysis
Apnea-hypopnea index < 20/h (*n* = 31)
Apnea-hypopnea index ≥ 20/h (*n* = 21)
Non-bilevel positive airway pressure group (*n* = 11)
Bilevel positive airway pressure group (*n* = 10)
Nonsurvivors (*n* = 4)
Survivors (*n* = 7)
Survivors (*n* = 10)