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ORIGINAL ARTICLE

Continuous positive airway pressure treatment improves cardiovascular outcomes in elderly patients with cardiovascular disease and obstructive sleep apnea

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Abstract Obstructive sleep apnea (OSA) is associated with the progression of cardiovascular disease (CVD), particularly in the middle-aged population. However, the clinical importance of OSA as a risk for CVD in the elderly population remains controversial. Moreover, evidence for the effectiveness of continuous positive airway pressure (CPAP) treatment for the secondary prevention of CVD in elderly patients is lacking. We assessed whether CPAP treatment improves cardiovascular outcomes in elderly patients with OSA and CVD. In this retrospective cohort study, we enrolled 130 elderly patients aged 65–86 years with moderate to severe OSA (apnea–hypopnea index $\geq$15/h) and a history of hospitalization due to CVD, who underwent polysomnography between November 2004 and July 2011. Patients were divided into the CPAP group (n = 64) or untreated OSA group (n = 66). The main outcome measures were cardiovascular death and hospitalization due to CVD. During the mean follow-up period of 32.9 $\pm$ 23.8 (standard deviation) months, 28 (21.5 %) patients either died or were hospitalized. The Kaplan–Meier curves indicated that event-free survival was significantly lower in the untreated OSA group than in the CPAP group ($P < 0.005$). A multivariate analysis showed that the risk was significantly increased in the untreated OSA group (hazard ratio 5.13; 95 % confidence interval 1.01–42.0; $P < 0.05$). Moderate to severe OSA not treated with CPAP was an independent risk factor for relapse of a CVD event, and adequate CPAP treatment improved cardiovascular outcomes in elderly patients.

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Introduction

Obstructive sleep apnea (OSA) is a highly prevalent disorder in the general population, characterized by repetitive upper airway obstruction during sleep [1]. The Sleep Heart Health Study showed that the prevalence of moderate to severe sleep-disordered breathing (SDB) was estimated at 10 % in persons aged 40–49 years, and 20–21 % in persons aged $\geq$70 years [1]. A previous study has shown that the prevalence of sleep apnea tends to increase with age, although its severity decreases [2]. OSA has been widely recognized to promote the progression of cardiovascular disease (CVD), mostly among middle-aged populations [3–20]. On the other hand, some authors observed that SDB among elderly patients was not an independent risk factor for hypertension [21] or mortality [22–26] in aged cohorts, and that age [23, 26] and burden of illness [24, 26] were independent risk factors for mortality. Thus it is commonly known that the prevalence of SDB among elderly persons is also high, but OSA among them differs from that of the middle-aged in some ways [27].

Takama and Kurabayashi [28] reported that the presence of OSA was a strong predictor of fatal cardiovascular events in patients with CVD. The subjects studied in their report were markedly older than those of previously published reports, with a mean age of approximately 70 years. Among patients with CVD, OSA appears to promote poor cardiovascular outcomes in the elderly population. Recently, Martinez-Garcia et al. [29] reported that untreated, severe OSA in elderly patients was associated with an approximately twofold increase in cardiovascular mortality compared with elderly patients without OSA.

In recent years, aging of the population has become one of the most serious problems worldwide, and the secondary prevention of CVD in such a high-risk elderly population is an urgent subject. In middle-aged populations, continuous positive airway pressure (CPAP) treatment is reported to improve cardiovascular outcomes in patients with OSA and CVD [4–6, 16, 30–32]. However, whether CPAP treatment for elderly patients with CVD contributes to a decrease in new cardiovascular events remains unclear. Furthermore, a therapeutic strategy for OSA in this patient population has not yet been established. Therefore, we conducted this study to assess whether CPAP improves cardiovascular outcomes in elderly patients with OSA and CVD.

Patients and methods

Patients

A total of 1,693 patients underwent a fully attended polysomnography at Tokyo Medical University Hospital between November 2004 and July 2011. From this database, we retrospectively selected consecutive elderly patients aged ≥65 years with moderate to severe SDB who had a history of hospitalization due to CVD before polysomnography, and classified them into two groups: a CPAP group and an untreated OSA group. CVD included the following: heart failure; coronary artery disease, such as myocardial infarction and angina pectoris; atrial or ventricular tachyarrhythmia, such as atrial fibrillation/flutter and ventricular tachycardia/fibrillation; ischemic and hemorrhagic stroke; and aortic dissection. Exclusion criteria included patients with central sleep apnea (>50 % apneic events), cancer, chronic kidney disease on hemodialysis, and previous positive airway pressure (PAP) treatment.

Ethical considerations

The present study was conducted in accordance with the recommendations of the Declaration of Helsinki (1975), and the protocol was approved by the ethical review board of Tokyo Medical University. Written informed consent was obtained from all patients to make use of their medical records.

Sleep study and PAP treatment

SDB was diagnosed in all patients based on the results of overnight polysomnography using a digital polygraph (Alice 4 and 5; Philips Respironics, Murrysville, PA, USA) in our sleep laboratory. Sleep stages and arousals were scored according to standard criteria [33, 34]. Thoracoabdominal movements were monitored by respiratory inductance plethysmography, and oxyhemoglobin saturation was monitored by oximetry. Signals were recorded on a polysomnographic system. Obstructive and central apneas and hypopneas were scored as previously described [35]. The number of apneas and hypopneas per hour of sleep (apnea–hypopnea index (AHI)) was calculated. Moderate to severe SDB was defined as AHI ≥15/h. We defined patients with predominantly central sleep apnea as having an AHI of ≥15/h, of which >50 % were central events. These patients were excluded from further analysis.

Patients with moderate to severe OSA were recommended for CPAP treatment, regardless of their symptoms. All patients who were treated with CPAP had been titrated manually on the second night in the sleep laboratory with full polysomnography to determine the appropriate pressure level for each patient. Thereafter, CPAP treatment was performed at home. Patients who had refused CPAP treatment initially or discontinued it within the first month after initiation were enrolled in the untreated OSA group. Patients who had been treated with CPAP were entered into the CPAP group, but those who had discontinued CPAP treatment between the first month after initiation of CPAP treatment and the day of outcome measures were excluded from the data analyses, because the association between the effect of CPAP treatment and cardiovascular events was unclear. Adherence to CPAP was assessed by reading the time counter on the device.

Outcome measures

The major outcome measures of interest were cardiovascular death or rehospitalization due to heart failure, acute coronary syndrome, arrhythmias, stroke, and aortic dissection between the day of the baseline polysomnography and September 2011. The medical records were reviewed by two investigators. Each event was defined as follows: heart failure was defined as decompensated heart failure, based on the Framingham criteria accompanied by a worsening of clinical signs and symptoms of heart failure; acute coronary syndrome included acute myocardial infarction, regardless of ST-segment elevation, and unstable angina pectoris; arrhythmias included ventricular tachycardia, atrial flutter, and atrial fibrillation that required hospitalization because of a hemodynamic emergency; stroke was defined as ischemic or hemorrhagic stroke which required hospitalization; aortic dissection included acute dissection of the thoracic and/or abdominal aorta. We counted only one event per patient, and once the event occurred the patient's follow-up was concluded.

Statistical analysis

Continuous data are expressed as mean ± standard deviation (SD), and categorical variables are expressed as frequencies

of occurrence and percentages. The baseline characteristics were compared using Student's *t* test for continuous variables, and the Chi-square test for categorical variables. A two-sided *P* value of less than 0.05 was considered to indicate a statistically significant difference. Event-free survival between the groups was compared using the Kaplan–Meier estimates with the log-rank test. The hazard ratio (HR) was calculated using the Cox proportional hazards model. Univariate analysis was based on the proportional hazards model to determine the associations between CVD events and the following pretreatment variables: age; gender; body mass index; past history or presence of hypertension, dyslipidemia, or diabetes; presence of atrial fibrillation; systolic/diastolic blood pressure; heart rate; subjective sleepiness expressed according to the Epworth Sleepiness Scale; left ventricular ejection fraction on echocardiograms; plasma brain natriuretic peptide; plasma norepinephrine; estimated glomerular filtration rate; medications; AHI; and study groups. Variables that were regarded as significant were included in the multivariate analysis. All statistical analyses were performed using a statistical software package (JMP 7; SAS Institute, Cary, NC, USA).

Results

Initially, 146 elderly patients were enrolled in this study; of these, 80 were classified into the CPAP group and 66 into the untreated OSA group. In the CPAP group 16 patients discontinued CPAP treatment, leaving 64 patients for inclusion in the final analyses.

Patients' characteristics

The baseline characteristics of the patients were comparable between the groups (Table 1). The CPAP group included a significantly larger number of male patients than the untreated OSA group ($P = 0.0003$). The diastolic blood pressure in the CPAP group was higher than that in the untreated OSA group ($P < 0.05$). Other variables such as age, body mass index, history of hypertension, dyslipidemia, diabetes, atrial fibrillation, heart rate, systolic blood pressure, hemoglobin, estimated glomerular filtration rate, plasma brain natriuretic peptide, plasma norepinephrine, left ventricular ejection fraction, and use of angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers, β-blockers, mineralocorticoid receptor antagonists, and statins as medications were not significantly different between the groups. Regarding the previous history of CVD, there was no statistically significant difference between the groups (Table 2).

With respect to the sleep characteristics (Table 3), the CPAP group had a significantly higher AHI, obstructive apnea index, central apnea index, and arousal index ($P < 0.0001$, $P = 0.0002$, $P < 0.005$, and $P = 0.0008$, respectively). The median value of nightly CPAP usage in the

Table 1 Baseline characteristics of patients

	All patients (n = 130)	Untreated OSA group (n = 66)	CPAP group (n = 64)	P value
Age (years)	72.8 ± 5.0	73.1 ± 5.0	72.5 ± 5.1	0.46
Male gender	93 (71.5)	38 (57.6)	55 (85.9)	0.0003
Body mass index (kg/m^2)	25.8 ± 4.4	25.8 ± 3.7	25.8 ± 5.1	0.92
Heart rate (beats/min)	65.8 ± 14.9	67.6 ± 15.5	63.8 ± 14.1	0.18
Systolic BP (mmHg)	123.1 ± 19.3	121.7 ± 22.4	124.5 ± 15.6	0.41
Diastolic BP (mmHg)	70.4 ± 10.9	68.2 ± 11.9	72.5 ± 9.4	<0.05
Hypertension	101 (77.7)	51 (81.0)	50 (80.7)	0.97
Dyslipidemia	80 (61.5)	42 (65.6)	38 (62.3)	0.70
Diabetes	48 (36.9)	25 (39.7)	23 (37.1)	0.77
Atrial fibrillation	13 (10.0)	8 (17.4)	5 (10.4)	0.33
Hemoglobin (g/dl)	13.2 ± 1.7	12.9 ± 1.9	13.5 ± 1.6	0.05
eGFR (ml/min)	65.1 ± 36.8	62.9 ± 24.4	67.3 ± 24.2	0.30
BNP (pg/ml)	176.4 ± 237.9	206.2 ± 267.2	146.1 ± 201.6	0.15
PNE (pg/ml)	331.7 ± 202.8	342.0 ± 237.1	321.1 ± 162.0	0.58
LVEF (%)	56.6 ± 14.0	55.4 ± 14.8	57.7 ± 13.2	0.35
β-Blockers	56 (43.1)	30 (46.2)	26 (41.9)	0.63
ACE-inhibitors/ARBs	90 (69.2)	49 (75.4)	41 (66.1)	0.25
MRAs	29 (22.3)	14 (21.5)	15 (24.2)	0.72
Statins	61 (46.9)	34 (52.3)	27 (42.9)	0.64

Values are expressed as mean ± SD or number (%), unless otherwise indicated

ACE angiotensin-converting enzyme, *ARB* angiotensin-II receptor blocker, *BNP* brain natriuretic peptide, *BP* blood pressure, *eGFR* estimated glomerular filtration rate, *LVEF* left ventricular ejection fraction, *MRA* mineralocorticoid receptor antagonist, *PNE* plasma norepinephrine

CPAP group was 5.0 ± 1.7 h and the median value of AHI downloaded from CPAP devices was 4.3 ± 3.0/h.

Impact of CPAP treatment on event-free survival

During the mean follow-up period of 32.9 ± 23.8 months, 28 (21.5 %) patients either died or were rehospitalized because of CVD, the frequencies of CVD events being 7 (10.9 %) patients in the CPAP group and 21 (31.8 %) in the untreated OSA group ($P < 0.005$). The mortality rate was not significantly different between the groups. However, the total rate of rehospitalization due to CVD was significantly higher in the untreated OSA group ($P < 0.01$). Furthermore, the rate of rehospitalization due to heart failure was significantly higher in the untreated OSA group than in the CPAP group ($P < 0.05$, Table 4).

The causes of rehospitalization were not in the same category of CVD as that at baseline. Of 17 heart failure events, 15 patients had a previous history of heart failure; the other 2 patients had no history of heart failure although they had a history of coronary artery disease. Of four arrhythmic events, two patients had a previous history of arrhythmia and the other two had no history of arrhythmia, although one had a history of coronary artery disease and the other had an aortic dissection. There was no recurrence of aortic dissection. The first onsets of aortic dissection were seen in one patient with coronary artery disease and one with heart failure. All stroke events were the recurrences of previous strokes.

The Kaplan–Meier event-free survival curves indicated that event-free survival was significantly lower in the untreated OSA group than in the CPAP group ($P < 0.005$, log-rank test; Fig. 1). Univariate Cox regression analyses revealed that the following were each associated with CVD events: age; female gender; history of hypertension; use of β-blockers and angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers; low levels of estimated glomerular filtration rate, hemoglobin, and left ventricular ejection fraction; high levels of brain natriuretic peptide; and untreated OSA (Table 5). In the multivariate Cox regression analysis, female gender (HR 4.20; 95 % confidence interval (CI) 1.13–17.5; $P < 0.05$) and untreated OSA (HR 5.13; 95 % CI 1.01–42.0; $P < 0.05$) were independent predictors of CVD events.

Table 2 Previous history of CVD

	All patients (n = 130)	Untreated OSA group (n = 66)	CPAP group (n = 64)	P value
Coronary artery disease	59 (45.4)	29 (43.9)	30 (46.9)	0.74
Heart failure	54 (41.5)	31 (47.0)	23 (35.9)	0.20
Arrhythmias	34 (26.2)	20 (30.3)	14 (21.9)	0.27
Stroke	24 (18.5)	12 (18.2)	12 (18.8)	0.93
Aortic dissection	16 (12.3)	6 (9.1)	10 (15.6)	0.26

Values are given as the number (%)

CPAP continuous positive airway pressure, *CVD* cardiovascular disease, *OSA* obstructive sleep apnea

Discussion

The main finding of this study was that CPAP treatment significantly reduced CVD events, including rehospitalization due to heart failure, acute coronary syndrome, arrhythmia, stroke, and aortic dissection in elderly patients with moderate to severe OSA and CVD. Concurrently, untreated, moderate to severe OSA was independently associated with CVD events in this population sample. Therefore, adequate CPAP treatment could be an effective

Table 3 Baseline sleep study data of patients

	All patients (n = 130)	Untreated OSA group (n = 66)	CPAP group (n = 64)	P value
ESS score	6.5 ± 4.2	5.7 ± 4.2	7.2 ± 4.0	0.08
Total sleep time (min)	373.6 ± 75.0	376.5 ± 76.3	370.6 ± 74.0	0.66
Apnea–hypopnea index (/h)	42.9 ± 21.0	34.6 ± 18.0	51.5 ± 20.5	<0.0001
Obstructive apnea index (/h)	17.0 ± 17.5	11.5 ± 14.0	22.9 ± 19.0	0.0002
Central apnea index (/h)	1.1 ± 2.2	0.6 ± 1.2	1.7 ± 2.7	0.17
Lowest SpO_2 (%)	79.1 ± 8.8	80.1 ± 7.9	78.0 ± 9.5	0.06
CT90 (%)	7.7 ± 13.0	6.8 ± 13.1	8.6 ± 13.0	0.43
Arousal index (/h)	43.8 ± 18.1	38.7 ± 17.0	49.2 ± 17.6	0.0008
Periodic leg movements index (/h)	33.2 ± 33.5	37.3 ± 39.2	28.2 ± 24.6	0.26

Values are expressed as mean ± SD or number (%), unless otherwise indicated

CPAP continuous positive airway pressure, *CT90* total sleep time spent with $SpO_2 < 90$ %, *ESS* Epworth Sleepiness Scale, *OSA* obstructive sleep apnea, *SpO_2* oxyhemoglobin saturation

strategy for the secondary prevention of CVD in elderly patients with CVD and moderate to severe OSA.

According to previously published reports, the clinical significance of OSA in the elderly is inconclusive. In an observational study involving elderly patients, those with sleep apnea (defined as a respiratory disturbance index of 10 events per hour of sleep) had 2.7 times greater mortality than those without it, but this was not statistically significant (95 % CI 0.95–7.47) [23]. Another study showed that elderly individuals (mean age 72.5 years) with a respiratory disturbance index of ≥30 had significantly shorter survival, but the Cox proportional hazards analysis revealed that only age, CVD, and pulmonary disease, but not respiratory disturbance index, were the independent predictors of death [26]. However, some recent reports have shown that severe OSA was a high risk factor for cardiovascular mortality in elderly patients [28, 29]. Kobayashi et al. [27] proposed that there were some clinical differences between middle-aged-onset OSA and elderly-onset OSA among elderly patients with OSA. Compared with the middle-aged-onset group, the elderly-onset group had lower values of arousal index, maximal negative esophageal pressure, adequate nasal CPAP level, and fewer cardiovascular complications. These results indicate that cardiovascular risks are not uniformly associated with OSA in the elderly population. Unfortunately, we were unable to estimate the onset times of OSA, but we assume that large numbers of subjects in our study would have had a high risk for CVD events, because they had a history of hospitalization due to CVD.

Although the clinical significance of OSA was not assessed by comparing elderly patients with and without OSA in this study, we determined that untreated, moderate to severe OSA was significantly associated with reduced cardiovascular event-free survival rate in elderly patients with CVD and OSA not treated with CPAP compared with those treated with CPAP. CPAP treatment appears to inhibit the development of CVD. CPAP directly reduces the intrathoracic negative pressure and reduces venous return. Accordingly, it reduces the intramural pressure, causes lowering of the pulmonary capillary wedge pressure, and increases cardiac output in patients with heart failure [36–38]. Furthermore, CPAP indirectly reduces sympathetic nervous activity [39–42], oxidative stress [43–46], and inflammation [45, 47] by improving SDB. It is

Table 4 Details of CVD events

	All patients (n = 130)	Untreated OSA group (n = 66)	CPAP group (n = 64)	P value
Acute coronary syndrome	2 (1.5)	1 (1.5)	1 (1.6)	0.98
Heart failure	17 (13.1)	13 (19.7)	4 (6.3)	<0.05
Arrhythmias	4 (3.1)	3 (4.6)	1 (1.6)	0.31
Ventricular tachycardia	1 (0.8)	1 (1.5)	0 (0)	
Atrial fibrillation	2 (1.5)	2 (3.0)	0 (0)	
Atrial flutter	1 (0.8)	0 (0)	1 (1.6)	
Stroke	2 (1.5)	1 (1.5)	1 (1.6)	0.98
Aortic dissection	2 (1.5)	2 (3.0)	0 (0)	0.10
Cardiovascular death	1 (0.8)	1 (1.5)	0 (0)	0.24
Total CVD events	28 (21.5)	21 (31.8)	7 (10.9)	<0.005
Readmission due to CVD	27 (20.8)	20 (30.3)	7 (10.9)	<0.01

Values are expressed as mean ± SD or number (%)

CPAP continuous positive airway pressure, *CVD* cardiovascular disease, *OSA* obstructive sleep apnea

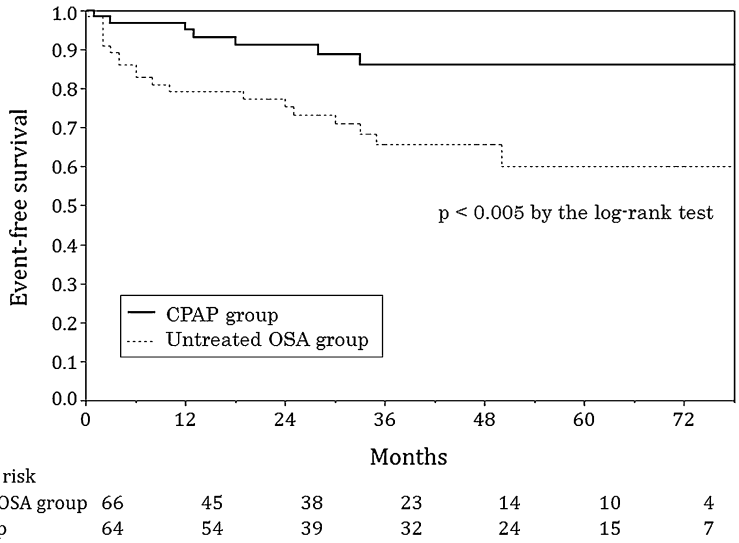

Fig. 1 Kaplan–Meier estimates of event-free survival for each group during follow-up. The cumulative event-free survival was significantly lower in the untreated obstructive sleep apnea (OSA) group than in the continuous positive airway pressure (CPAP) group (P < 0.005 by the log-rank test)

Table 5 Univariate and multivariate analysis of Cox proportional hazards model for determining CVD events

	Univariate analysis			Multivariate analysis		
	HR	95 % CI	*P* value	HR	95 % CI	*P* value
Age (per 1 year)	1.09	1.02–1.18	<0.05	1.07	0.94–1.23	0.29
Female gender	3.98	1.86–8.68	<0.0005	4.20	1.13–17.5	<0.05
Body mass index (kg/m^2)	0.95	0.89–1.03	0.22			
Heart rate (beats/min)	1.02	0.99–1.06	0.13			
Systolic BP (mmHg)	1.01	0.99–1.03	0.23			
Diastolic BP (mmHg)	1.00	0.96–1.04	0.95			
Hypertension	3.47	1.03–21.6	<0.05	4.90	0.83–94.9	0.08
Dyslipidemia	0.59	0.27–1.31	0.19			
Diabetes	0.96	0.41–2.13	0.92			
Atrial fibrillation	2.57	0.14–7.28	0.70			
Hemoglobin (per 1 g/dl)	0.59	0.47–0.75	<0.0001	0.76	0.53–1.06	0.11
eGFR (per 1 ml/min)	0.96	0.94–0.98	<0.0001	0.99	0.95–1.02	0.49
BNP ≥200 pg/ml	5.69	2.65–12.5	<0.0001	1.96	0.38–10.2	0.42
PNE ≥450 pg/ml	1.83	0.71–4.21	0.20			
LVEF (per 1 %)	0.96	0.94–0.98	<0.005	0.97	0.93–1.02	0.20
ESS score	0.91	0.78–1.04	0.17			
β-Blockers	2.75	1.25–6.46	<0.05	2.16	0.47–11.7	0.33
ACE-inhibitors/ARBs	3.26	1.13–13.7	<0.05	1.82	0.17–51.4	0.64
MRAs	1.02	0.37–2.40	0.96			
Statins	0.85	0.38–1.85	0.69			
Apnea–hypopnea index (/h)	0.99	0.97–1.01	0.19			
Untreated OSA	3.15	1.39–8.05	<0.01	5.13	1.01–42.1	<0.05

ACE angiotensin-converting enzyme, *ARB* angiotensin-II receptor blocker, *BNP* brain natriuretic peptide, *BP* blood pressure, *eGFR* estimated glomerular filtration rate, *ESS* Epworth Sleepiness Scale, *LVEF* left ventricular ejection fraction, *MRA* mineralocorticoid receptor antagonist, *OSA* obstructive sleep apnea, *PNE* plasma norepinephrine

thought that the direct and indirect effects of CPAP contribute to the prevention of coronary plaque rupture, thrombotic formation, arrhythmias, and cardiac dysfunction. A significant reduction of rehospitalization for heart failure in the CPAP group has been observed in this study, which may be explained by the fact that the impact of the direct physical effects of CPAP treatment is greater on patients with heart failure than on patients with other CVD. Because this was a retrospective, observational study, it is unlikely that an observer bias affected the event rate of rehospitalization.

Daida et al. [48] reported that the rate of cardiovascular death (fatal myocardial infarction, fatal stroke, and other cardiovascular death) was 2.7 % in 3597 Japanese ACS patients (mean age 67 years old) during a 2-year follow-up. In our study, mortality was extremely low. Lavie and Lavie [49] reported that elderly patients with moderate sleep apnea had lower mortality than the matched population cohorts, and severe sleep apnea had the same mortality as the matched population cohorts. In another report, Lavie et al. [25] stated that the mortality rates in male patients with sleep apnea decreased with age. They proposed that sleep apnea might activate adaptive pathways in the elderly. The mechanism of this protective effect is unclear, but this effect might have affected our mortality data. Further investigation of this topic is warranted.

Concerning heart failure events, more patients had a history of heart failure in the untreated OSA group, although this was not statistically significant. This might have been a source of bias for the high incidence of hospitalization due to heart failure observed in the untreated OSA group. However, in a subgroup analysis of 54 patients who had a history of heart failure, the recurrence rates of heart failure events were 35.5 % (11/31) in the untreated OSA group and 17.4 % (4/23) in the CPAP group. Another two heart failure events were de novo heart failure from coronary artery disease, both in the untreated OSA group. Therefore, taking the high incidence of heart failure in the untreated OSA group into consideration, CPAP treatment may reduce the rates of occurrence and recurrence of heart failure.

Kasai et al. [6] have reported that compliance to CPAP treatment was an important factor affecting prognosis in patients with heart failure and OSA, but there are only a few previous reports that provide clear data regarding CPAP adherence. In our study, adherence to CPAP treatment was considered to be comparatively strong, because the median value of nightly CPAP device usage was 5.0 h. We did not find any obvious effect of CPAP adherence on the event rates in this study.

One recent investigation has revealed that OSA is a risk factor for cardiovascular death not only in men but also in women, and that adequate CPAP treatment reduces mortality [7]. We enrolled 37 elderly women with moderate to severe OSA in our study. Women tended to not receive CPAP. Among the 37 women with moderate to severe OSA, only 9 (24.3 %) belonged to the CPAP group. On the other hand, 55 (59.1 %) of 93 men with moderate to severe OSA belonged to the CPAP group. To date, SDB has been virtually ignored as a cardiovascular risk in women. However, women had a 4.2-fold increase in CVD events compared with men by multivariate analysis. These facts suggest that CPAP treatment for OSA is very important in preventing CVD events in elderly women as well as in elderly men.

This real-world study indicates the importance for clinicians of recognizing and providing appropriate treatment for OSA, particularly in the elderly population. In our study, although CPAP treatment for OSA did not reveal a significant decrease in mortality, it prevented rehospitalization due to CVD events. We propose that CPAP treatment for elderly patients with OSA and CVD would lead to a better quality of life and would also be beneficial from an economic perspective.

The present study had several limitations. First, this was a small, retrospective cohort study. Intervention for OSA was not randomized. Prospective, randomized controlled trials would more strongly support the effectiveness of CPAP treatment for the secondary prevention of CVD in the elderly population. Second, many of the enrolled patients in this study had undergone polysomnography because of suspicion of SDB; therefore, we were unable to enroll a sufficient number of patients without SDB as our controls. Third, because of the small number of cardiovascular deaths, our results ultimately lacked the statistical evidence to more firmly implicate the effects of SDB on mortality in patients with CVD. Fourth, we could not follow the changes in body mass index, diet or exercise practice, and medical therapies during follow-up periods, including the patients' adherence to the medical therapies. These factors might have biased the final results.

Conclusions

To the best of our knowledge, we have provided the first report that CPAP treatment in elderly patients with OSA and CVD is associated with prevention of future cardiovascular events. We found that CPAP treatment significantly reduced rehospitalization due to CVD, but not cardiovascular death, in elderly patients with OSA and CVD. Although additional research is required, we believe that CPAP treatment promises to be an effective strategy for the secondary prevention of CVD in elderly patients with OSA and CVD.

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Conflict of interest The authors declare no potential conflicts of interest associated with this study.

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