Original Article

Obstructive sleep apnea characteristic in systolic heart failure patients

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Abstract. The aim of the current study was to outline the demographic, clinical and polysomnographic characteristics of sleep apnea in patients with heart failure.

A retrospective, clinical study was conducted on 29 heart failure patients in our tertiary care center. Patients who reported snoring, witnessed apnea episodes and excessive daytime sleepiness underwent full-night polysomnography. Baseline features, types and frequencies of sleep disorders were noted. In addition, we have compared mild-moderate Obstructive sleep apnea (OSA) patients to severe OSA cases in terms of demographic, clinical and polysomnographic variables.

Of these 29 cases, three patients (10.3%) had mild OSA, while 6 patients (20.7%) were diagnosed with moderate OSA and severe OSA was determined in 15 (51.7%) patients. Four patients (13.8%) were diagnosed with central sleep apnea (CSA) and one patient (3.5%) had normal polysomnographic result. The mean age of the total group consisting of 11 females (37.9%) and 18 males (62.1%) with a mean age of 57.8±10.9 (range: 29.0-74.0) years. Severe OSA patients were older ($p=0.02$), had a lower ejection fraction ($p=0.02$), higher arterial oxygen desaturation index ($p<0.001$), prolonged mean apnea duration ($p=0.02$), and lower minimum arterial oxygen concentration ($p=0.02$).

Our results indicate that OSA may occur in the vast majority of heart failure patients that suffer from sleep disorders. Close collaboration between disciplines is crucial for effective management of these cases.

Key words: Obstructive sleep apnea; central sleep apnea; heart failure; apnea hypopnea index; polysomnography

1. Introduction

Obstructive sleep apnea (OSA) is a sleep-related breathing disorder characterized by repeated episodes of upper airway occlusion during sleep. In the United States, OSA affects approximately 3%–9% of women and 10%–17% of men (1). The risk of cardiovascular (CV) diseases can be increased via intermittent hypoxia, sleep fragmentation, chronic sympathetic activation, and systemic inflammation in sleep apnea (2-4). The association of OSA and various CV events as well as long term outcomes have not been fully elucidated yet (4-7).

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Received: 06.10.2015
Accepted: 13.10.2015

In heart failure (HF) patients, both OSA and central sleep apnea (CSA) can be observed. Distinguishing between OSA and CSA in HF patients is critical since their pathophysiologies and treatments are distinct. However, it should be kept in mind that overlapping of these two entities can be possible.

Obstructive sleep apnea ensources from upper airway collapse, while CSA is related with reductions in central respiratory drive (5,6). During OSA, the respiratory effort spent against the narrowed upper airway causes the rib cage and abdomen to distort and move out of phase. In contrast, respiratory movements are either absent or attenuated in CSA (4,6,8).

The apnea-hypopnea index (AHI) thresholds are used for diagnosis and categorization of the severity of OSA. Severity of OSA is classified by the American Academy of Sleep Medicine with respect to AHI (mild defined as an AHI of 5-15, moderate as 15-30, and severe as >30) and degree of daytime sleepiness (1,2). Focusing almost exclusively on AHI may lead clinicians and researchers miss the opportunities for better risk-

stratification of cases via other OSA-related variables (5,7,9). A number of less-studied and less popular variables may be pathophysiologically more relevant and offer a better predictive ability than AHI. Some of these variables are as follows: intermittent hypoxemia (level of arterial oxygen saturation), sleep fragmentation or sleep deprivation (e.g. number of awakenings, symptoms (daytime sleepiness, snoring), family history of snoring etc. It must be remembered that AHI, that is currently used to express the severity of OSA, may not be always sufficient for predicting the CV outcomes (4,5,7,8). Instead, an expanded set of personal and polysomnographic factors of the patient may provide greater accuracy and may possess an improved predictive value rather than AHI alone.

From this point of view, we evaluated polysomnographic parameters other than AHI such as arterial oxygen desaturation index, mean apnea duration, numbers of REM, arousal index, minimum arterial oxygen concentration, and mean arterial oxygen saturation. In this study, we aimed to outline the characteristics as well as clinical and polysomnographic features of sleep apnea in patients with HF. Thus, we hope that data obtained from our series may contribute to a better understanding of these adjunctive conditions and develop strategies for early recognition and more effective management.

2. Materials and methods

2.1. Study design

This retrospective clinical study was performed between September 2013 and January 2014 after the approval of the local Institutional Review Board (2013/3-08.09.2013). Information from the sleep laboratory and computer archives were obtained from patient files. Heart failure patients that suffer from at least two of the three complaints (snoring, excessive daytime sleepiness and witnessed apnea episodes) underwent full-night polysomnography.

Prior to sleep study, a complete otolaryngological examination was carried out to rule out any obstructive pathology in the upper airway. None of the patients reported use of alcohol or sleeping pills.

Obstructive sleep apnea was defined as having an apnea–hypopnea index (AHI) ≥5, of which ≥50% were obstructive in nature. Cases with 5≤AHI<15 were termed as mild OSA, while those with 15≤AHI<30 were assigned as moderate OSA. Patients with AHI≥30 constituted the severe OSA subgroup.

Stable systolic HF was due to ischemic or non-ischemic dilated cardiomyopathy with a left ventricular ejection fraction of <35% on an echocardiogram, current treatment with optimal medical therapy, and no hospital admission within 1 month before the sleep study.

The exclusion criteria consisted of: [1] treatment for sleep-disordered breathing, e.g use of oral appliances, arterial oxygen inhalation, and positive airway pressure (PAP) therapy before the sleep study; [2] a history of pharyngeal or orthognathic surgery; [3] a history of stroke with neurologic deficit or other neuromuscular disease; [4] diagnosis of another sleep disorder; [5] having more than 50% central events; [6] obese patients.

2.2. Sleep study

Sleep apnea was diagnosed in all patients based on the results of full-night polysomnography (Embla 4500, RemLogic, Embla Systems LLC, USA) at our sleep laboratory. The following physiologic variables were monitored simultaneously and continuously: four channels for the electroencephalogram; two channels for the electro-oculogram; two channels for the surface electromyogram (submentonian region and anterior tibialis muscle); one channel for an electrocardiogram; airflow detection via two channels through a thermocouple (one channel) and nasal pressure (one channel); respiratory effort of the thorax (one channel) and of the abdomen (one channel) using plethysmography; snoring (one channel) and body position (one channel); oxyhemoglobin saturation; and pulse rate. Two specialists visually scored all recordings according to standardized criteria for investigating sleep.

Generally accepted definitions and scoring methods were used (1,10). Apnea was defined as cessation of inspiratory airflow for ≥10 seconds. Obstructive apnea was defined as the absence of airflow in the presence of rib cage and abdominal excursions. Central apnea was defined as the absence of rib cage and abdominal excursions with an absence of airflow (1,10).

2.3. Outcome parameters

In our series, age, gender, body-mass index, smoking habit, hypertension, diabetes mellitus, ejection fraction, snoring, witnessed apnea episodes, excessive daytime somnolence, AHI, arterial oxygen desaturation index, mean apnea duration, no. of REMs, arousal index, minimum arterial oxygen concentration, mean saturation, treatment modality applied were noted and documented in our series of 29 HF patients.

2.4. Statistical Analyses

Data were analysed using the Statistical Package for Social Sciences (SPSS) software

(version 10.0 for Windows). Continuous variables with normal distribution were expressed as mean±standard deviation, while those without normal distribution are displayed as median±interquartile range. Parametric methods were used in the analysis of the variations that have normal distribution, and nonparametric methods were used in the analysis of the variations that do not have normal distribution. In the comparison of two independent groups, Independent-Samples T test and Mann-Whitney U tests were used. In the comparison of categorical data, Pearson Chi-Square and Fisher Exact tests were used. All differences associated with a p value less than 0.05 were considered statistically significant.

3. Results

The sleep study revealed that 15 cases had severe OSA, 6 patients had moderate OSA and 3 patients had mild OSA. Four patients (13.8%) were diagnosed with central sleep apnea (CSA) and one patient (3.5%) had normal sleep study results. The mean age of the total group consisting of 11 females (37.9%) and 18 males (62.1%) with a mean age of 57.8±10.9 (range: 29.0-74.0) years. The mean body-mass index was 25.8±4.9 (range, 17.6 to 35.4) kg/m^2.

Demographic and clinical characteristics in addition to polysomnographic variables in our series are demonstrated on Tables 1 and 2. Comparative presentations of variables under investigation are shown on Table 3.

Table 1. Demographical and clinical features of our study group.

	Average value (min-max)
Age (years)*	57.8±10.9 (29.0-74.0)
Body mass index _(kg/m^2)*	25.8±4.9 (17.6-35.4)
Ejection fraction**	23.9±7.0 (15.0-35.0)
Apnea hypopnea index**	37.5±19.5 (6.0-78.2)
Epworth Sleepiness Scale	9.20±3.54 (2.0-22.0)
Arterial oxygen desaturation index*	18.7±12.6 (0-43.7)
Mean apnea duration**	20.5±4.6 (12.0-31.8)
No. of REM (/hour)*	3.8±1.7 (1.0-7.0)
REM sleep (%)	10.73±7.5 (2.9-29.4)
Minimum O_2 concentration**	78.6±9.2 (50.0-90.0)
Mean saturation**	89.7±4.8 (76.0-95.0)
Smoking habit (packs year)**	32.2±14.8 (20.0-60.0)

(REM= Rapid Eye Movements; min= minimum; max= maximum; *= Expressed as mean±standard deviation; **= median±interquartile range)

Table 2. Frequency of demographical and clinical variables in OSA patients of our series

		n (%)
Diagnosis	Mild-moderate OSA (5≤AHI<30)	9 (37.5%)
	Severe OSA (AHI≥30)	15 (62.5%)
Gender	Female	7 (29.2%)
	Male	17 (70.8%)
Snoring	No	9 (37.5%)
	Yes	15 (62.5%)
Witnessed apnea episodes	No	1 (4.2%)
	Yes	23 (95.8%)
Excessive daytime somnolence	No	12 (50%)
	Yes	12 (50%)
Hypertension	No	16 (66.7%)
	Yes	8 (33.3%)
Diabetes mellitus	No	17 (70.8%)
	Yes	7 (29.2%)
Smoking habit	No	15 (62.5%)
	Yes	9 (37.5%)
Treatment modality	Positive airway pressure (BiPAP-CPAP)	21 (66.7%)
	None	3 (12.5%)

(OSA= Obstructive sleep apnea; CPAP= Continuous positive airway pressure; BiPAP= Bilevel positive airway pressure)

Table 3. Comparison of mild to moderate and severe OSA patients in our series with respect to demographical and clinical variables.

		Mild-moderate OSA (n, %)	Severe OSA (n, %)	p Value
Age (years)*		50.0±12.1	61.1±8.9	0.02†
Gender	Female	2 (28.6%)	5 (29.4%)	1
	Male	5 (71.4%)	12 (70.6%)	
Body mass index*		25.9±4.4	25.7±5.3	0.91
Snoring	No	4 (57.1%)	5 (29.4%)	0.36
	Yes	3 (42.9%)	12 (70.6%)	
Witnessed apnea episodes	No	0	1 (5.9%)	‡
	Yes	7 (100%)	16 (94.1%)	
Excessive daytime somnolence	No	3 (42.9%)	9 (52.9%)	1
	Yes	4 (57.1%)	8 (47.1%)	
Hypertension	No	4 (57.1%)	12 (70.6%)	0.65
	Yes	3 (42.9%)	5 (29.4%)	
Diabetes mellitus	No	3 (42.9%)	14 (82.4%)	0.13
	Yes	4 (57.1%)	3 (17.6%)	
Smoking habit	No	4 (57.1%)	11 (64.7%)	1
	Yes	3 (42.9%)	6 (35.2%)	
Ejection fraction**		20.0±5.0	26.2±5.9	0.02†
Apnea hypopnea index**		20.7±8.8	36.0±20.0	<0.001†
Arterial oxygen desaturation index*		6.0±3.4	23.9±11.2	<0.001†
Epworth Sleepiness Scale		7.90±3.29	11.52±6.61	0.04†
Mean apnea duration**		18.0±1.7	21.0±4.0	0.02†
No. of REM (/hour)*		4.6±1.5	3.4±1.7	0.13
REM sleep (%)		10.8±3.3	12.6±8.7	0.37
Arousal Index**		5.0±10.0	5.0±18.2	0.41
Minimum O2 concentration**		84.0±2.0	80.0±4.0	0.02†
Mean saturation**		91.0±3.0	90.0±2.0	0.60
Treatment modality	Positive airway pressure (APAP-BiPAP-CPAP)	4 (57.1%)	12 (70.6%)	‡
	ASV	0	5 (29.4%)	
	None	3 (42.9%)	0	
Smoking habit (packs year)**		20.0±0	35.0±20.0	0.08

(REM= Resting Eye Movements; ASV= Adaptive Servo Ventilation; *= Expressed as mean±standard deviation; **= median±interquartile range; †= statistically significant; ‡= Data is inappropriate for statistical analysis)

4. Discussion

In this study, we attempted to outline the demographic and clinical profiles of sleep apnea in patients with HF. In addition, we compared the mild-moderate OSA group to severe OSA cases with respect to demographic, clinical and polysomnographic variables.

Obstructive sleep apnea is recognized as an established cardiac risk factor and is associated with some cardiovascular disorders. Prevalence of OSA in patients with HF was reported to vary between 12% and 53%, which is greater than that in the general population (7-10%). However, the cause of this circumstance is obscure. Interestingly, in comparison to the general population, HF patients have a lower body mass index (BMI) for any given severity of OSA (11,12). This suggests that factors other than weight may play a greater role in the pathogenesis of OSA in patients with HF than in the general population. OSA may be linked with both systolic and diastolic impairment of the left ventricle. The cause of high prevalence of OSA in HF patients are vague, but oedema of neck soft tissues may facilitate the collapse of pharyngeal tissue and lead to the further tightening of airways. Involvement of OSA in the development of HF suggests that treatment of OSA can be useful for amelioration of these secondary

conditions (3-6). The current consensus for treatment of OSA is usage of CPAP for ventilatory support as a tool for the secondary prevention of cardiac problems (7,12-14). In our series, we noted that CPAP was by far the most preferred method.

The hazardous effect of OSA on left ventricle function may be due to the increased negative intrathoracic pressure, asphyxia during apnea periods, arousals at the end of apnea, and injury at the level of vascular wall. Furthermore, OSA may be linked with hypertension and exaggerated adrenergic responses which may subsequently predispose to hypertensive heart failure. Mechanisms leading to diastolic dysfunction in OSA include myocardial hypertrophy and high blood pressure due to intermittent hypoxia. Reduced right ventricular contractility, impaired ejection fraction (EF) and hypertrophy have all been reported in OSA patients (3-6). These findings may be either attributed to OSA related disturbed haemodynamics or may be secondary to pulmonary hypertension.

Successful treatment of OSA is supposed to improve right ventricular function and improvement in LV dimensions and contractility have been observed after CPAP. Most of the current evidence supports the use of continuous positive airway pressure (CPAP) in reduction of blood pressure with concomitant improvement in patients' cognition and daytime sleepiness (6,7,9). In our series, CPAP and Bilevel positive airway pressure (BPAP) were the most commonly used modalities of treatment. Due to possible cardiovascular risks and doubtful efficacy of a surgical intervention in this subgroup of patients, we suggest that CPAP and biPAP are the main therapeutic options.

The finding that HF patients have a lower body-mass index for a given AHI than the general population suggests that factors unrelated to obesity might contribute more to the pathogenesis of OSA in patients with heart failure. One such factor might be fluid redistribution from oedematous legs to peripharyngeal tissues when the patient takes recumbent position for sleep. This circumstance leads to impinging on the pharyngeal lumen and may subsequently result in collapse during sleep.

Since most of the demographic and clinical variables are similar in mild to moderate and severe OSA groups; we think that onset of the disease is the critical period rather than the advancement of the severity of OSA. “The more severe OSA, the worse EF becomes” reminds that there may be a vicious circle between OSA and HF. Which pathology triggers the other yields an issue similar to the well-known “chicken or the egg” causality dilemma.

Some limitations of our study must be noted. First, the retrospective design and relatively small size of our series interferes with extrapolation of our results to larger population. Moreover, some details of history and other factors (e.g. ethnicity) prone to affect the outcome that may not be completely documented. In addition, HF patients were at various levels for severity and variation of HF status may result in the degree of soft tissue edema. Lastly, polygraphic studies employed rather than full polysomnography might not be the preferred method for congestive HF patients sleep status assessments. Due to these restrictions, associations should be interpreted with caution.

In conclusion, the present study found that OSA might occur frequently in patients with HF. Even though overlapping of these two entities is possible, early recognition and appropriate treatment is crucial for avoidance of complications, reduction of morbidity and mortality as well as improvement of long-term outcomes. More effective management of sleep disorders can be feasible owing to the close collaboration between experts in sleep apnea and cardiologists.

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