

# Predictor factors of sleep-disordered breathing in heart failure

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**Background** Heart failure (HF) is characterized by its high mortality, frequent hospitalizations, and reduced quality of life. Sleep-disordered breathing (SDB), one of the common comorbidities, accelerates the progression of HF.

**Objectives** The objectives of the study were (a) to investigate the prevalence and type of SDB in HF patients and (b) to determine the predictors of SDB.

**Materials and methods** In a cross-sectional analytic study, all eligible patients of Assiut Chest and Cardiology Department admitted (100 patients) during the period from August 2015 to March 2016 were included in this study. Clinical assessment, full-night attended polysomnography, and echocardiography were recorded and compared between patients with (SDB) (85 patients) and those without SDB (15 patients).

**Results** SDB was found in 85% of patients [53% had obstructive sleep apnea (OSA) and 32% had central sleep apnea (CSA)]. OSA patients are characterized by higher BMI and neck and waist circumference. There was a higher prevalence of hypertension, as well as mean blood pressure, systolic blood pressure, diastolic blood pressure, in OSA patients. Loud snoring was the only clinical symptom associated with OSA as compared with CSA. CSA patients

had a significant reduction in PaCO<sub>2</sub>. OSA patients showed a significant increase in desaturation index and time spent with oxygen saturation less than 90%. Maximum heart rate and brady/tachy index were significantly increased in OSA. Cycle length was significantly increased in CSA.

**Conclusion** The prevalence of sleep apnea was high in patients with stable HF (85%). OSA was the predominant type (53%). The predictors of SDB were BMI ( $\geq 30$ ), systemic hypertension, neck circumference more than 40 cm, waist circumference more than 110 cm, and ejection fraction (left ventricular ejection fraction) ( $\leq 45\%$ ).

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## Introduction

Heart failure (HF) is a highly prevalent syndrome with an estimated annual incidence of half a million. Despite therapeutic advances in pharmacology, HF remains a leading cause of morbidity, as well as frequent hospitalizations and a reduced quality of life [1]. Sleep-disordered breathing (SDB), one of the most common comorbidities in HF, occurs in 50–80% of patients, and is known to accelerate the progression of the condition, thus increasing morbidity and mortality [2,3].

The present study aimed (a) to investigate the prevalence and type of SDB in HF patients and (b) to determine the predictors of SDB in HF patients.

## Materials and methods

This cross-sectional analytic study was carried out in the Chest and Cardiology Department, Faculty of Medicine, Assiut University Hospital, during the period from August 2015 to March 2016.

The study design was approved by the Scientific Ethics Committee of Faculty of Medicine of Assiut University.

Informed consent was obtained from the patients.

Among 100 patients who were admitted during this period and fulfilled the inclusion criteria, only 85 patients had SDB. Patients were classified into two groups: group 1, the SDB group (85 patients), and group 2, the without SDB (no SDB) group (15 patients). Group 1 patients were further subclassified into those with central sleep apnea (CSA) and those with obstructive sleep apnea (OSA) based on the predominant ( $>50\%$ ) type of sleep apnea.

## Exclusion criteria

Patients with recent unstable angina or myocardial infarction within 3 months of the study, those with a history of chronic lung disease (i.e. obstructive pulmonary disease), pregnant woman, those with a history of stroke or clinical signs of peripheral or central nervous system disorders were excluded from the study.

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All patients were subjected to a comprehensive clinical assessment, an overnight-attended polysomnography, and echocardiography.

#### *Clinical assessment and sleep history*

Clinical data of patients were recorded, including age, sex, anthropometric measures (height, weight, BMI, and neck and waist circumference), history of diabetes mellitus, and history of hypertension. New York Heart Association classification (NYHA) functional classification of HF was determined. The standard HF therapy was noted for each patient (angiotensin-converting enzyme inhibitors,  $\beta$ -blockers, diuretics, and amiodarone). Sleep history was as follows: daytime symptoms included morning headache and excessive daytime sleepiness and nighttime symptoms included loud snoring, disturbed sleep rhythm, witnessed apnea, bad dreams, and frequent nocturia). Epworth Sleepiness Score was used in our study. Results of at least 10 are considered to represent significant excessive daytime sleepiness [4].

#### *Echocardiography*

All participants underwent transthoracic echocardiography (Vivid S5; GE Healthcare, United States), which was performed in the left lateral decubitus position. Images were obtained in different views (parasternal long-axis as well as apical four chambers, two chambers, and three chambers) according to current standards, by personnel blinded to the results of polysomnography [5].

Left atrial diameter, left ventricular (LV) end-diastolic internal dimension, LV end-systolic internal dimension, interventricular septal thickness, and LV posterior wall thickness were determined from M-mode measurements. In addition, left ventricular ejection fraction (LVEF) was measured according to the modified Simpson's method using apical four and two chamber views. Right ventricle diameter and pulmonary artery systolic pressure (PASP) were also measured. PASP can be determined using the modified Bernoulli equation:  $(PASP) = 4 \times (\text{peak TR velocity})^2 + \text{RAP}$ .

The maximum velocity of the tricuspid valve regurgitant jet ( $v$ ) is measured using continuous wave Doppler and added to the estimated right atrial pressure (RAP) [6].

#### *Polysomnography*

All patients underwent full-night attended polysomnography (Somnstar 4100; Sensor-Medics Co., Yorba Linda, California, USA) in the sleep laboratory

of the Assiut university hospital. The polysomnogram systematically monitors the electroencephalogram (C3–A2, C4–A1), electro-oculogram, electromyogram of the chin, electrocardiogram, body positions, nasal and oral airflow, thoracic and abdominal effort, limb movements, pulse oximetry, and snoring sound level. The polysomnograms were all scored manually according to the American academy of sleep medicine [7].

#### **Cheyne–Stokes respiration**

Cheyne–Stokes respiration is defined as three consecutive central apneas and/or central hypopneas separated by a crescendo and decrescendo change in breathing amplitude with a cycle length of at least 40 s and the central apnea index of at least 5 per hour [7]. Cycle length is the duration of the central apnea plus the duration of a respiratory phase. If central hypopneas occur, the cycle length is defined as the time from the zenith in the respiratory phase preceding the central hypopnea to the zenith of the next respiratory phase [7]. Minimum and maximum heart rate was recorded. Brady/tachy index, which is the average number of bradycardia and tachycardia events per hour, was also recorded.

#### **Statistical analysis**

Data were analyzed using SPSS (Statistical Package for Social Science), version 16 (IBM Inc., Armonk, New York, USA) software was used for analysis of results. The results in this study were expressed as mean  $\pm$  SD or number and percentage. Comparison between two groups was made using the  $t$ -test and the one-way analysis of variance test for comparison between more than two groups. The difference was considered significant when  $P$  value of less than 0.05. Logistic regression analysis was performed to detect predictors of SDB in HF.

#### **Results**

Table 1 shows demographic data and clinical examination in HF patients with SDB and those no SDB. Group 1 patients with SDB had significantly higher age group, BMI, neck and waist circumference, and serum cholesterol level. Moreover, the prevalence of hypertension, as well as mean blood pressure (MBP), systolic blood pressure (SBP), and diastolic blood pressure (DBP), was significantly increased in patients with SDB.

As shown in Table 2, patients with OSA had a significant increase in BMI and the prevalence of hypertension (MBP, SBP and DBP) as compared with the CSA and the no SDB group. However, cases with CSA

**Table 1 Demographic data and clinical examination findings in heart failure patients with sleep-disordered breathing and those without sleep-disordered breathing**

	Group 1 (SDB) (n=85)	Group 2 (no SDB) (n=15)	P-value
Age (years)	56.35±7.23	51.13±4.32	0.014*
Sex			
Male	54 (63.5)	10 (66.7)	0.815
Female	31 (36.5)	5 (33.3)	
BMI			
Overweight: (>25 kg/m <sup>2</sup> )	14 (16.5)	6 (40.0)	0.080
Obese (>30 kg/m <sup>2</sup> )	71 (83.5)	9 (60.0)	
Neck circumference (cm)	42.07±2.50	39.87±1.51	0.001*
Waist circumference (cm)	117.13±15.43	104.67±4.42	0.005*
Hypertension	41 (48.2)	3 (20.0)	0.042*
Mean BP (70–105) (mmHg)	96.50±13.82	88.44±12.34	0.001*
SBP (90–140) (mmHg)	126.47±27.03	117.33±17.15	0.010*
DBP (60–90) (mmHg)	81.52±14.35	74.00±7.36	0.004*
Diabetes	32 (37.6)	2 (13.3)	0.067
Smoking	45 (52.9)	6 (40.0)	0.355
Cholesterol level (0–200) (mg/dl)	196.28±48.47	128.57±36.24	0.000*

Values expressed as mean±SD or *n* (%). DBP, diastolic blood pressure; SBP, systolic blood pressure. *P*-value is determined between the two (SDB vs. no SDB) groups. \*Significant difference.

**Table 2 Anthropometric measures, demographic data, and comorbidities among obstructive sleep apnea, central sleep apnea and no sleep-disordered breathing in heart failure patients**

	OSA (n=53)	CSA (n=32)	No SDB (n=15)	<i>P</i> <sub>1</sub>	<i>P</i> <sub>2</sub>	<i>P</i> <sub>3</sub>
Age (years)	53.13±5.27	61.69±6.93	51.13±4.32	0.001*	0.178	0.001*
Sex						
Male	36 (67.9)	18 (56.2)	10 (66.7)	0.279	0.927	0.498
Female	17 (32.1)	14 (43.8)	5 (33.3)			
BMI (kg/m <sup>2</sup> )	35.50±3.73	30.97±2.06	30.65±2.41	0.001*	0.001*	0.945
Neck circumference (cm)	42.09±2.51	42.03±2.51	39.87±1.51	0.963	0.002*	0.000*
Waist circumference (cm)	119.57±16.56	113.09±12.59	104.67±4.42	0.089	0.004*	0.026*
Hypertension	33 (62.3)	8 (25.0)	3 (20.0)	0.001*	0.004*	0.994
Mean BP (70–105) (mmHg)	106.01±13.42	85.73±12.43	88.44±13.71	0.001*	0.002*	0.452
SBP (90–140) (mmHg)	135.85±26.49	110.94±20.06	117.33±17.15	0.001*	0.018*	0.142
DBP (60–90) (mmHg)	86.60±13.29	73.13±12.03	74.00±7.36	0.001*	0.001*	0.498
Diabetes mellitus	20 (37.7)	12 (37.5)	2 (13.3)	0.983	0.001*	0.178
Cholesterol level (0–200) (mg/dl)	200.58±48.70	189.15±47.99	128.57±36.24	0.260	0.000*	0.001*

Values expressed as mean±SD or *n* (%). CSA, central sleep apnea; DBP, diastolic blood pressure; No SDB, no sleep-disordered breathing; OSA, obstructive sleep apnea; SBP, systolic blood pressure. *P*<sub>1</sub> between OSA versus CSA. *P*<sub>2</sub> OSA versus no SDB. *P*<sub>3</sub> CSA versus no SDB. \*Significant difference.

recorded a statistically significant difference in age, neck and waist circumference, and serum cholesterol level as compared with the no SDB group.

As shown in Table 3, CSA was significantly higher in NYHA functional class (III and IV) as compared with the OSA and the no SDB group. It was observed that the Epworth Sleepiness Scale was significantly higher in OSA patients. OSA patients showed a significant increase in daytime and night-time symptoms of sleep apnea compared with no SDB patients. The prevalence of loud snoring was significantly increased in patients with OSA as compared with CSA patients.

Table 4 shows that CSA patients had a significant respiratory alkalosis and a decrease in the mean value of PaCO<sub>2</sub> associated with marked atrial fibrillation (AF) as compared with OSA and no SDB.

As regards polysomnographic parameters (Table 5), the respiratory disturbance index (RDI) was significantly increased in OSA patients. Patients with CSA had a significant increase in the Cheyne–Stokes respiration index as well as cycle length when compared with the OSA and the no SDB group.

As regards respiratory oxygenation during sleep, patients with OSA had a significantly more severe arterial

**Table 3 Clinical scores for heart failure and sleep disorders between obstructive sleep apnea, central sleep apnea, and no sleep-disordered breathing in heart failure patients**

	OSA (n=53)	CSA (n=32)	No SDB (n=15)	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
NYHA class						
Class I and II	10 (18.9)	1 (3.1)	15 (100.0)	0.078	0.001*	0.001*
Class III and IV	43 (81.1)	31 (96.9)	0 (0.0)			
ESS scale	11.08±1.93	10.63±1.34	7.80±1.74	0.367	0.002*	0.002*
Daytime symptoms						
Morning headache	34 (64.2)	17 (53.1)	6 (40.0)	0.315	0.003*	0.401
Excessive daytime sleepiness	28 (52.8)	15 (46.9)	2 (13.3)	0.595	0.007*	0.026*
Night-time symptoms						
Loud snoring	30 (56.6)	12 (37.5)	5 (33.3)	0.002*	0.011*	0.782
Disturbed sleep rhythm	22 (41.5)	19 (59.4)	2 (13.3)	0.110	0.044*	0.003*
Witnessed sleep apnea	18 (34.0)	12 (37.5)	0 (0.0)	0.741	0.021*	0.017*
Bad dreams	35 (66.0)	19 (59.4)	5 (33.3)	0.536	0.023*	0.096
Frequent nocturia	34 (64.2)	17 (53.1)	7 (46.7)	0.315	0.022*	0.680

Values expressed as mean±SD or n (%). CSA, central sleep apnea; ESS, Epworth Sleepiness Scale; NYHA class, New York Heart Association classification; OSA, obstructive sleep apnea; SDB, sleep-disordered breathing. P<sub>1</sub> between OSA versus CSA. P<sub>2</sub> OSA versus no SDB. P<sub>3</sub> CSA versus no SDB. \*Significant difference.

**Table 4 Comparison in arterial blood gases and electrocardiography changes between each of obstructive sleep apnea, central sleep apnea, and no sleep-disordered breathing groups with heart failure**

	OSA (n=53)	CSA (n=32)	No SDB (n=15)	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
Arterial blood gases						
pH (7.35–7.45)	7.42±0.02	7.46±0.03	7.43±0.02	0.001*	0.145	0.003*
PaCO <sub>2</sub> (35–45) (mmHg)	39.89±3.67	34.72±2.41	38.73±3.08	0.001*	0.220	0.000*
PaO <sub>2</sub> (95–98) (mmHg)	79.00±5.14	79.47±4.81	81.80±3.10	0.774	0.069	0.122
HCO <sub>3</sub> <sup>-</sup> (18–22) (mmol/l)	19.53±2.41	21.34±1.47	19.13±1.60	0.000*	0.674	0.000*
SaO <sub>2</sub> (97–98)	95.94±0.86	96.09±1.00	96.47±0.83	0.542	0.235	0.176
ECG changes						
Arrhythmia: AF	9 (17.0)	22 (68.8)	5 (33.3)	0.001*	0.307	0.022*
Ventricle arrhythmia	15 (28.3)	3 (9.4)	0 (0.0)	0.039*	0.048*	0.558

Values expressed as mean±SD or n (%). AF, atrial fibrillation; CSA, central sleep apnea; OSA, obstructive sleep apnea; PaCO<sub>2</sub>, arterial carbon dioxide tension; PaO<sub>2</sub>, arterial oxygen tension; SDB, sleep-disordered breathing. P<sub>1</sub> between OSA versus CSA. P<sub>2</sub> OSA versus no SDB. P<sub>3</sub> CSA versus no SDB. \*Significant difference.

oxyhemoglobin desaturation and time spent with oxygen saturation below 90%. Moreover, a significant reduction in minimum and average oxygen saturation was observed in OSA patients when compared with CSA and no SDB patients. As regards heart rate recording during sleep, OSA patients showed a significant reduction in minimum heart rate and a significant increase in maximum heart rate and brady/tachy index.

As shown in Table 6, LVEF was significantly reduced in patients with CSA as compared with OSA and no SDB patients. Patients with HF reduced ejection fraction (≤45%) had a significantly higher prevalence of CSA, whereas HF patients with preserved ejection fraction (>45%) had a significantly higher prevalence of OSA.

As regards LV dimensions, CSA patients had a significant increase in LV end diastolic and LV end systolic diameter, whereas in patients with OSA, both posterior wall diameter and interventricular septal

diameter were significantly increased. There was no significant difference in PASP between both OSA and CSA. OSA was significantly higher in patients with hypertensive heart disease, whereas CSA had a significantly higher prevalence in ischemic heart disease and dilated cardiomyopathy.

Table 7 shows that the possible predictive factors of SDB in HF were BMI of at least 30, systemic hypertension, neck circumference more than 40 cm, waist circumference more than 110 cm, LVEF (≤45%), NYHA functional class III and IV, AF, male sex, and age more than 50 years.

## Discussion

In the current study, we have studied the prevalence of SDB in HF, and found that 85% of patients with HF had SDB; OSA accounted for 53%, whereas CSA sleep apnea accounted for (32%). Our results are consistent

**Table 5 Baseline polysomnographic parameters between obstructive sleep apnea, central sleep apnea, and no sleep-disordered breathing in heart failure patients**

	OSA (n=53)	CSA (n=32)	No SDB (n=15)	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
Respiratory events						
Obstructive apnea index (n/h)	15.50±11.32	4.17±2.90	2.08±0.78	0.001*	0.001*	0.022*
Mixed apnea index (n/h)	1.13±1.34	0.85±1.10	0.11±0.25	0.593	0.004*	0.001*
Central apnea index (n/h)	2.66±2.98	19.29±6.26	0.43±0.72	0.000*	0.001*	0.003*
Hypopnea index (n/h)	16.51±11.99	10.33±5.93	1.39±0.50	0.004*	0.001*	0.004*
RDI (n/h)	36.03±18.76	34.76±9.15	3.99±0.71	0.549	0.000*	0.000*
CSR (index/h)	4.74±2.39	43.85±8.96	3.17±0.16	0.001*	0.342	0.001*
Cycle length (at least 40 s)	51.60±10.12	64.13±12.99	41.55±11.23	0.002*	0.321	0.002*
Oxygenation						
Desaturation index (n/h)	73.13±19.28	50.02±19.23	35.80±7.05	0.001*	0.006*	0.000*
Basal SaO <sub>2</sub> asleep	95.47±2.87	96.63±1.07	97.20±0.86	0.010	0.421	0.078
Minimum SaO <sub>2</sub> asleep	54.50±8.00	65.21±17.18	88.00±3.76	0.007*	0.003*	0.001*
Average SaO <sub>2</sub>	74.44±6.31	82.45±8.67	90.33±3.92	0.000*	0.001*	0.001*
SaO <sub>2</sub> <90% (min)	76.69±30.41	62.94±44.29	2.13±2.97	0.000*	0.000*	0.001*
Heart rate						
Basal HR (60–90) (beats/min)	70.87±5.12	66.56±2.61	70.40±4.00	0.001*	0.667	0.001*
Min. HR (beats/min)	42.08±6.65	46.78±6.34	60.07±1.71	0.010*	0.002*	0.003*
Max. HR (beats/min)	133.92±11.66	114.56±11.00	98.00±3.66	0.004*	0.003*	0.002*
Brady/tachy index	49.60±14.07	36.84±9.95	4.63±4.91	0.001*	0.001*	0.004*
Arousal index (n/h)	27.60±5.62	24.47±7.80	4.65±0.98	0.107	0.000*	0.000*

Average SaO<sub>2</sub>, average arterial oxygen saturation; Brady/tachy index, average number of bradycardia and tachycardia events per hour; CSA, central sleep apnea; CSR index, number of CSR events per total sleep time; CSR, Cheyne–Stokes respiration; Cycle length, the length of one CSR cycle spent in seconds; Max. HR, maximum heart rate; Min. HR, minimum heart rate; Min. SaO<sub>2</sub>%, minimum arterial oxygen saturation; OSA, obstructive sleep apnea; Oxygen desaturation index (events/h); RDI, respiratory disturbance index; SaO<sub>2</sub> less than 90% in minutes, time in bed with oxygen saturation less than 90% in minutes; SDB, sleep-disordered breathing. P<sub>1</sub> between OSA versus CSA. P<sub>2</sub> OSA versus no SDB. P<sub>3</sub> CSA versus no SDB.

**Table 6 Echocardiographic parameters between each of obstructive sleep apnea, central sleep apnea, and no sleep-disordered breathing**

	OSA (n=53)	CSA (n=32)	No SDB (n=15)	P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
LVEF (52–72)	50.45±12.54	32.72±8.08	47.73±10.23	0.001*	0.349	0.000*
LVEF						
Reduced (EF≤45)	26 (49.0)	30 (93.8)	10 (66.7)	0.001*	0.093	0.014*
Preserved (EF>45)	27 (51.0)	2 (6.2)	5 (33.3)			
LVEDD (4.2–5.8) (cm)	5.60±1.13	6.45±0.54	5.59±0.81	0.001*	0.912	0.002*
LVESD (2.5–3.9) (cm)	4.02±1.04	4.94±0.66	3.88±0.69	0.000*	0.619	0.000*
PWd (0.6–1.0) (cm)	1.10±0.31	0.91±0.10	1.02±0.19	0.017*	0.829	0.029*
IVSD (0.6–1.0) (cm)	1.18±0.13	1.12±0.08	1.09±0.11	0.021*	0.231	0.150
LV FS (35–45)	29.23±9.19	21.69±1.89	30.60±8.74	0.000*	0.313	0.000*
Left atrial diameter (3–4) (cm)	3.95±0.47	4.35±0.77	3.67±0.21	0.073	0.128	0.009*
Right ventricle diameter (2.0–2.8) (cm)	1.82±0.37	1.98±0.27	1.93±0.18	0.052	0.268	0.459
PASP (>35) (mmHg)	46.64±9.97	46.22±6.75	40.93±6.17	0.708	0.029*	0.013*
Cause of HF						
Ischemic heart disease	23 (43.4)	18 (56.2)	7 (46.7)	0.003*	0.822	0.001*
Dilated cardiomyopathy	11 (20.8)	14 (43.8)	3 (20.0)	0.024*	0.949	0.100*
Hypertensive heart disease	19 (35.8)	0 (0.0)	5 (33.3)	0.000*	0.857	0.003*

Values expressed as mean±SD or n (%). CSA, central sleep apnea; FS, fraction of shortening; HF, heart failure; IVSD, interventricular septal diameter; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; OSA, obstructive sleep apnea; PASP, pulmonary artery systolic pressure; PWd, posterior wall diameter; SDB, sleep-disordered breathing. P<sub>1</sub> between OSA versus CSA. P<sub>2</sub> OSA versus no SDB. P<sub>3</sub> CSA versus no SDB.

with previous studies. Paulino *et al.* [8] evaluated 316 French patients with stable HF and found that the prevalence of SDB was high (81%), (70% were classified as having OSA, whereas 30% were classified as having CSA). Moreover, Ferreira and colleagues [9] investigated 103 patients with HF on

optimal treatment. SDB was found in 72.8% of patients (60% had OSA and 9.3% had CSA). In another recent study by Damy and colleagues [10], who studied 384 patients with HF, SDB was discovered in 88% of patients (62% had OSA and 26% had CSA). In contrast, previous studies

**Table 7** Logistic regression analysis revealing the possible predictors for sleep-disordered breathing in patients with heart failure

	P-value	OR	95% CI	
			Lower	Upper
Age (>50 years)	0.001*	1.421	1.342	2.342
Sex (male)	0.013*	1.908	1.654	2.763
BMI $\geq$ 30 (kg/m <sup>2</sup> )	0.004*	3.622	1.40	6.360
Neck circumference (>40) (cm)	0.004*	3.423	1.671	4.559
Waist circumference (>110) (cm)	0.002*	3.470	2.883	6.018
Hypertension	0.004*	3.620	0.90	4.10
Atrial fibrillation	0.013*	1.195	1.061	1.346
ESS scale	0.121	1.251	0.890	2.871
NYHA class (III and IV)	0.002*	1.320	0.895	5.675
PaCO <sub>2</sub> ( $\leq$ 35) (mmHg)	0.423	1.345	0.987	3.871
LVEF ( $\leq$ 45)	0.003*	3.100	1.06	4.140

CI, confidence interval; ESS, Epworth Sleepiness Score; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OR, odds ratio. \*Significance.

reported a lower prevalence of SDB, with a clear predominance of CSA over OSA. Javaheri and colleagues [11] reported that the prevalence of SDB in 81 outpatients with stable HF was 51% (10% had OSA and 40% had CSA). Moreover, Vazir and colleagues [12] demonstrated that the prevalence of SDB was 53% (15% OSA and 38% CSA). This variability in the reported prevalence of SDB may be attributed to the small number of patients involved, or the use of different monitoring techniques to measure airflow. SDB in those studies was evaluated with cardiorespiratory polygraphy instead of standard polysomnography.

As regards patient characteristics of SDB in HF, we observed that patients with SDB were characterized by old age (56.35 $\pm$ 7.23 vs. 51.13 $\pm$ 4.32 years in no SDB) and male sex (63.5 vs. 36.5%). Similarly, Paulino and colleagues [8] demonstrated that HF patients with SDB had significantly older age group (mean age; 60 $\pm$ 13 vs. 55 $\pm$ 14 years in no SDB) and male sex (86 vs. 67%). Arzt and colleagues [13] also reported a higher prevalence of SDB in men than in women (49 vs. 36%) and also found that the rate of SDB increased as age increased (the prevalence in patients $\leq$ 50 years was 31%, whereas in those $>$ 80 years the prevalence was 59%). The sex-related differences may be attributed to differences in sleep characteristics between the two sexes; men have less stable sleep architecture compared with women, with a greater number of sleep-wake transitions and shorter slow wave sleep, which may predispose to respiratory control system instability and central apneas [14].

Our study revealed that patients with CSA were characterized by significantly old age (61.69 $\pm$ 6.93 vs. 53.13 $\pm$ 5.27 years in OSA). In accordance with previous

studies, Sin and colleagues [15] evaluated the risk factors for CSA and OSA on 450 patients with HF; patients with CSA were older than those with OSA (64.8 $\pm$ 11.1 vs. 58.2 $\pm$ 12.6 years). Older patients with HF have less compliant left ventricles with higher filling pressures compared with younger ones. This possibly may place them at a higher risk for nocturnal hyperventilation and CSA.

In addition to age and sex, obesity was an important risk factor for the development of SDB in HF. Patients with OSA had a significant increase in the mean BMI (35.50 $\pm$ 3.73 vs. 30.97 $\pm$ 2.06 kg/m<sup>2</sup> in CSA). Paulino and colleagues [8] reported a significant increase in BMI in OSA patients (28.3 $\pm$ 5.4 vs. 27.9 $\pm$ 5.1 kg/m<sup>2</sup> in CSA). Sin and colleagues [15] also demonstrated higher BMI in patients with OSA (32.3 $\pm$ 7.0 vs. 26.3 $\pm$ 4.5 kg/m<sup>2</sup>) than in those with CSA. A possible explanation is that obese individuals frequently have short, thick necks and peripharyngeal fatty deposits that may contribute to pharyngeal obstruction [15]. Herrscher *et al.* [16] demonstrated that BMI of at least 30 kg/m<sup>2</sup> was the only independent predictor of moderate-to-severe SDB in HF patients [odds ratio (OR)=3.62, 95% confidence interval (CI) 1.40–9.36,  $P=0.008$ ]. Thus, BMI may be used as one of the selection criteria for referral of HF patients to a sleep specialist [16]. In contrast, Friedman *et al.* [17] reported that OSA was highly prevalent in nonobese patients with HF (mean BMI 30.2 $\pm$ 1.3 vs. 33.8 $\pm$ 1.3 kg/m<sup>2</sup> in HF patients without OSA). This can be attributed to the fact that HF patients often experience varying degrees of chronic fluid overload resulting in redistribution of excess fluid from the legs to the chest and neck when supine during sleep and may predispose to OSA resulting in increased peripharyngeal edema and cervical congestion that compresses the upper airway and obstructs airflow [17].

Our results revealed that neck circumference, which is an indirect measure of fat deposition around the neck has been shown to be an important and independent predictor of SDB among HF patients ( $42.07 \pm 2.50$  vs.  $39.87 \pm 1.51$  cm in no SDB). Similarly, Ferreira and colleagues [9], who studied 103 patients with HF to identify the possible risk factors for sleep apnea in HF patients reported that an increased neck circumference has been associated with an increased risk for SDB in HF ( $41.0$  vs.  $38.0$  cm in no sleep apnea,  $P=0.003$ ). Moreover, Loo and colleagues [18], who studied 332 HF patients (mean age:  $62 \pm 10$  years) to determine a possible predictor of SDB, demonstrated that neck circumference is one of the predictors of SDB among HF patients (OR=1.06; 95% CI 1.02–1.10;  $P=0.001$ ). This can be attributed to the fact that increased fat around the neck, related to an android pattern of adiposity, may contribute to pharyngeal narrowing and collapsibility. Another additional mechanism, the redistribution of excess fluid from the legs to the neck during sleep, resulting in increased peripharyngeal edema and cervical congestion, compresses the upper airway and obstructs airflow [19].

Waist circumference is another predictor, which has been found as a risk factor for SDB among HF patients. Our findings are similar to those of Loo and colleagues [18], who found that waist circumference (OR=1.06; 95% CI 1.01–1.13,  $P=0.001$ ) is one of the independent predictors of SDB among HF patients.

In our study, we observed that the prevalence of systemic hypertension was significantly higher in patients with OSA (62.3 vs. 20.0% in no SDB), with a significant increase in the mean value of SBP, DBP, and MBP. This is in accordance with the findings of Logan and colleagues [20], who demonstrated that, in medically treated patients with HF, the prevalence of systolic hypertension was significantly increased in patients with OSA (83%), with a significant increase in daytime SBP ( $190.43 \pm 43.12$  vs.  $140.54 \pm 23.11$  mmHg in no SDB). OSA plays a linking role between hypertension and HF. Intermittent apnea-related hypoxia, as well as the intrathoracic pressure swings and arousals associated with respiratory events, augment sympathetic nervous system activity, which may contribute to elevated blood pressure [21].

On comparing clinical symptoms suggestive of sleep apnea between CSA and OSA, our study revealed that

loud snoring was the prevalent night-time symptom in patients with OSA (56 vs. 33.3% as compared with CSA). Similarly, Javaheri and colleagues [21] found that 78% of patients with OSA had nocturnal snoring, and only 28% of patients with CSA had nocturnal snoring. Moreover, Bitter and colleagues [22] investigated more than 1500 HF (LVEF  $\leq 45\%$ , NYHA  $\geq$ II) patients for possible symptoms of sleep apnea and found that snoring was the only symptom independently associated with OSA (66 vs. 25%).

In this study, we demonstrated that most predictors of SDB among HF patients were BMI of at least 30, systemic hypertension, neck circumference more than 40 cm, waist circumference ( $>110$  cm), and LVEF ( $\leq 45\%$ ). Similarly, Loo and colleagues [18] studied 332 HF patients (mean age:  $62 \pm 10$  years) to determine possible predictors of SDB and demonstrated that neck circumference (OR=1.09; 95% CI 1.01–1.12,  $P=0.002$ ), waist circumference (OR=1.06; 95% CI 1.01–1.13,  $P=0.001$ ), BMI (OR=1.19; 95% CI 1.10–1.30,  $P=0.001$ ), and age (OR=1.06; 95% CI 1.02–1.10,  $P=0.001$ ) were independent predictors of SDB. Moreover, in a large prospective study by Woehrle and colleagues [23], who investigated the prevalence of SDB and its predictors in patients with stable chronic HF, the authors found that HF patients with SDB often do not show characteristic symptoms, suggesting that the presence of one or more predictors of SDB [e.g. male sex (OR=1.90, 95% CI 1.67–2.17)], age more than 60 years (OR=1.41, 95% CI 1.34–1.49), obesity (OR=1.29, 95% CI 1.22–1.36), LVEF less than 25% (OR=1.10, 95% CI 1.06–1.39), and AF (OR=1.19, 95% CI 1.06–1.34) should prompt clinicians to perform device-based screening for SDB.

## Conclusion

The prevalence of sleep apnea was high in patients with stable HF despite optimized therapy (85%). OSA was the predominant type (53%). The possible predictive factors of SDB in HF were BMI of at least 30, systemic hypertension, neck circumference more than 40 cm, waist circumference ( $>110$  cm), and LVEF ( $\leq 45\%$ ).

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**Conflicts of interest**

There are no conflicts of interest.

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