Original Article

The Prevalence and Related Risk Factors of Obstructive Sleep Apnea in Heart Failure Patients at the Indonesian Referral Hospital for Respiratory Diseases

Agus Dwi Susanto[1], Regina Annisa Harahap[1], Budhi Antariksa[1], Muhammad Abbas Basalamah[2], Fariz Nurwidya[1,3]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan Hospital, [2]Department of Cardiology, Persahabatan Hospital, [3]Department of Nutrition, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Abstract

Background: Obstructive sleep apnea (OSA) is closely associated with metabolic diseases such as hypertension and dyslipidemia. OSA is also frequently found in patients with heart failure. This study aims to determine the prevalence and factors which affect the incidence of OSA in patients with heart failure. **Methods:** This cross-sectional study was conducted on 70 samples of patients with heart failure in the cardiac outpatient clinic and inpatient ward of the Persahabatan Hospital, Jakarta, Indonesia. **Results:** Using the Berlin Questionnaire, 42 patients (60%) were found to be at high risk of OSA. Using the Chi-square test, it was found that age (P = 0.988), gender (P = 0.678), body mass index (P = 0.170), neck circumference (P = 0.605), abdominal circumference (P = 0.189), blood pressure (P = 0.922), and smoking (P = 0.678) factors did not have a significant correlation with OSA risk in patients with heart failure. While the tonsil size was found to have a significant correlation (P = 0.005). **Conclusions:** Patients with heart failure were at risk of having OSA, and tonsil size was significantly correlated with OSA incidence in patients with heart failure.

Keywords: Berlin Questionnaire, heart failure, obstructive sleep apnea, polysomnography, tonsils

Introduction

Obstructive sleep apnea (OSA) is closely linked to stroke, chronic renal failure, and heart diseases such as heart failure.[1,2] It has been reported that 36% of 700 patients with a functional class (FC) I-II heart failure suffer from OSA in Europe.[3,4]

OSA is characterized by recurrent incidences of decreased or cessation of airflow although breathing efforts are seen to be caused by partial or complete obstruction of the upper airway.[5] Apnea is defined as a reduction in peak sensitivity of the amplitude to heat ±90% of baseline for ±10 s. The severity of OSA can be determined polysomnography (PSG) examination and Berlin criteria questionnaire. Apnea–Hypopnea Index (AHI) is the number of apnea and hypopnea per hour of sleep, a standard used for the quantitative assessment of OSA severity. In OSA, the AHI score is ≥5–10 events/h. The diagnosis of OSAS was made through an AHI score >5–10 events/h of OSA, and the patient has excessive symptoms of drowsy at daytime, unrefreshing sleep, or chronic fatigue.[4,5] This study aims to determine the prevalence of OSA risk in patients with congestive heart failure (CHF) based on the Berlin Questionnaire and to find the risk factors for OSA.

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Methods

This cross-sectional study was conducted in the cardiac outpatient and inpatient ward of the National Referral Hospital for Respiratory Diseases, Persahabatan Hospital, Jakarta, Indonesia, from July to October 2015, and patients were recruited by consecutive sampling until the sample size was reached. The inclusion criteria were patients of stage I–II CHF, both men and women aged 40–70 years who

Address for correspondence: Dr. Agus Dwi Susanto, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Indonesia, Persahabatan Hospital, Jalan Persahabatan Raya No. 1, Rawamangun, Jakarta 13230, Indonesia.
E-mail: agus_ds2000@yahoo.com

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came to the cardiac outpatient clinic with FC I-II CHF. The patients underwent history taking, physical examination, and echocardiography. Patients with ejection fraction (EF) <50% underwent PSG examination in the inpatient ward. OSA patients were treated by continuous positive airway pressure. Exclusion criteria were OSA patients with a history of stroke and chronic obstructive pulmonary disease, patients without FC I-II CHF. Patients who were willing to participate in the study were required to complete and sign the informed consent.

The data collection in this study was conducted by interview using questionnaires based on Berlin criteria [Table 1],[1] and other questions regarding the history of FC I-II CHF through anamnesis, physical examination, and laboratory examination including blood glucose examination, HbA1C, and C-reactive protein. The patient then underwent an echocardiography examination continued with PSG examination in the inpatient ward.[6-8] The Berlin Questionnaire consists of ten questions about sleep disturbances, which can be used for screening patients who are at risk for the occurrence of sleep disorders. Patients are considered high-risk OSA if two or more categories are positive and low-risk OSA if only one or no positive category.[1] The PSG used in this study is the portable-type Alice PDX (Philips Co, Andover, USA).[9] This study has been approved by the Institutional Review Board of the Faculty of Medicine, Universitas Indonesia.

Bivariate analysis was performed using the Chi-square test. Multivariate analysis was performed on independent variables to determine the OSA risk factors in heart failure patients. Statistical analysis was performed in the obtained data using the Statistical Package for the Social Sciences (SPSS) software program version 20 (IBM Corp, Armonk, NY, USA). $P < 0.05$ was considered to be statistically significant.

Results

This study was conducted from August to October 2015 at the Persahabatan Hospital in patients with FC I-II CHF with EF <50%. The total sample in this study was 70 patients. Each patient was given the Berlin Questionnaire. From the questionnaire, the study found 42 patients (60%) had a risk for OSA, which have a score of 2 or more. Further, examination with PSG was performed for patients with the risk of OSA.

Most of the patients were aged 50–59 years, male, hypertensive heart disease as the etiology of CHF, normal weight, had neck circumference above the cut off value, hypertension, smokers, and high-risk OSA as seen in Table 2.

Of the 42 patients with high-risk OSA, 26 patients were randomly selected to undergo PSG examination. From the 26 patients examined with PSG, patients with mild OSA (AHI 5–15) were seven patients (26.7%), moderate OSA (AHI 15–30) were nine patients (34.5%), and severe OSA (AHI >30) were ten patients (38.8%). Symptoms of OSA in patients with heart failure include snoring, choking, and breathing efforts which cause the patient to wake up and feel fatigued when awake from the sleep [Table 3].

Table 1: Berlin Questionnaire

Height: M; Weight: Kg; Age: Male/female

Please choose the correct response to each question

Category 1

1. Do you snore?
   a. Yes
   b. No
   c. Do not know

If you snore

2. Your snoring is
   a. Slightly louder than breathing
   b. As loud as talking
   c. Louder than talking
   d. Very loud - can be heard in adjacent rooms
3. How often do you snore?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never
4. Has your snoring ever bothered other people?
   a. Yes
   b. No
   c. Do not know
5. Has anyone noticed that you quit breathing during your sleep?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

Category 2

6. How often do you feel tired or fatigued after your sleep?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month

e. Never or nearly never

7. During your waking time, do you feel tired, fatigued, or not up to par?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never
8. Have you ever nodded off or fallen asleep while driving a vehicle?
   a. Yes
   b. No

If yes

9. How often does this occur?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

Category 3

10. Do you have high blood pressure?
    a. Yes
    b. No
    c. Do not know

Category 1: Items 1, 2, 3, 4, and 5
- Item 1: If yes is the response, assign 1 point
- Item 2: If c or d is the response, assign 1 point
- Item 3: If a or b is the response, assign 1 point
- Item 4: If b is the response, assign 1 point
- Item 5: If a or b is the response, assign 2 points
- Category 1 is positive if the total score is 2 or more points

Category 2: Items 6, 7, and 8 (item 9 should be noted separately)
- Item 6: If a or b is the response, assign 1 point
- Item 7: If a or b is the response, assign 1 point
- Item 8: If a is the response, assign 1 point
- Category 2 is positive if the total score is 2 or more points

Category 3
- Category 3 is positive if the answer to item 10 is yes or if the BMI of the patient is greater than 30 kg/m2

High risk of OSA: Two or more categories scored as positive, Low risk of OSA: Only one or no category scored as positive, OSA: Obstructive sleep apnea, BMI: Body mass index

Table 2: Characteristics of study patients

Variable	Frequency, *n* (%)
Age (years)	
<40	3 (4.29)
40–49	6 (8.57)
50–59	31 (44.28)
60–69	21 (30)
≥70	9 (12.86)
Gender	
Male	47 (67.14)
Female	23 (32.86)
Diagnosis	
CHF caused by HHD	47 (67.14)
CHF caused by CAD	20 (28.57)
CHF caused by MR	3 (4.29)
Comorbid	
Hypertension with DM	23 (32.86)
Hypertension with DM and CKD	3 (4.29)
DM with obesity	16 (22.86)
Hypertension	10 (14.28)
DM	10 (14.28)
Obesity	6 (8.57)
MR	2 (2.86)
BMI	
Normal	38 (54.29)
Obesity	32 (45.71)
Neck circumference	
Normal	58 (82.86)
Above the cut off value	12 (17.14)
Abdominal circumference	
Normal	26 (37.14)
Above the cut off value	44 (62.86)
Tonsil size	
No tonsil (underwent tonsillectomy)	1 (1)
Tonsil not enlarged	58 (82)
Enlarged tonsil	12 (17)
Blood pressure	
Normal	33 (47.14)
Hypertension	37 (52.86)
Smoking	
Yes	47 (67.14)
No	23 (32.86)
Berlin questionnaire	
Low-risk OSA	28 (40)
High-risk OSA	42 (60)

BMI: Body mass index, CHF: Congestive heart failure, HHD: Hypertensive heart disease, CAD: Coronary artery disease, MR: Mitral regurgitation, DM: Diabetes mellitus, CKD: Chronic kidney disease, OSA: Obstructive sleep apnea

We then analyze the association between various factors with OSA in heart failure patients. Age was not significantly associated with OSA severity level (P = 0.988). The association between gender factor with OSA severity was also not statistically significant (P = 0.678). Although severe OSA was more prevalent in patients with obesity, which was found in 22 from 32 obese patients; however, body mass index (BMI) was not significantly associated with the severity of OSA (P = 0.170). The association of the neck circumference with OSA was not statistically significant (P = 0.605). There was a significant association (P = 0.005) between tonsil size and the severity of OSA in patients with heart failure.

In this study, severe OSA was more common in patients with high blood pressure (hypertension) as many as 22 from 37 patients with hypertension; however, the correlation between blood pressure factors and OSA severity was not statistically significant (P = 0.922). The association between a smoking factor and OSA severity was not statistically significant (P = 0.678). In this study, severe OSA was more common in patients with an EF of <40%, which was found in 29 from 43 patients; however, the association between EF and OSA severity was not statistically significant (P = 0.109).

Finally, we performed multivariate analysis using logistic regression test for variables with $P < 0.25$, which are BMI (0.170), abdominal circumference (P = 0.189), tonsil size (P = 0.007), and EF (P = 0.109). Based on logistic regression test results, there were no variables associated with OSA in patients with CHF, as described in Table 4.

Discussion

OSA is frequently found in CHF patients. In this study, we determined the prevalence and factors which affect the incidence of OSA in patients with CHF. This study found that patients with high-risk of OSA (score >2) based on the Berlin Questionnaire were 42 patients (60%). The previous report by Javaheri *et al*. found that 11% of 81 heart failure patients had OSA on PSG screening.[10] According to the literature, patients suffering from OSA usually have narrowed airway in the pharynx or tonsil hypertrophy. OSA can also be caused by cardiac vascular diseases such as heart failure. In patients with heart failure, fluid accumulation of the lower limbs remain in the lower limb during the day due to posture effect, but this fluid will shift toward the neck when sleeping, especially during the night. This fluid shifting will cause neck and vein congestion and edematous of the pharynx connective tissue, resulting in increased pressure on the pharynx and airway obstruction.[11]

This study found symptoms experienced in heart failure patients with OSA such as snoring, fatigue after waking, and sleep deprivation. A study by Nieto *et al*. involved 6132 patients and they found that the prevalence of snoring symptoms was present in 33.9% of the patients.[12] Snoring in OSA caused by pharyngeal collapse with the tongue, uvula, and soft palate toward the posterior covering the airway at the larynx area. It can also be caused by the upper airway collapse leading to decreased air volume capacity in the lungs, thus affecting ventilation control systems which cause the airway to collapse partly or completely.[11]

Patients with OSA were more prevalent at the age of 50–59 years, and this is consistent with cross-sectional studies

Table 3: Symptoms of obstructive sleep apnea in heart failure patients

OSA symptoms	Frequency, *n* (%)
Snoring, fatigue, and choking	39 (55.71)
Snoring and tired	3 (4.29)
Snoring and choking	1 (1.43)
Tired and choked	1 (1.43)
Snoring	22 (31.43)
Tired	3 (4.29)
Choking	1 (1.43)

OSA: Obstructive sleep apnea

Table 4: Multivariate analysis of obstructive sleep apnea risk factors in heart failure patients

Variables	*P*	OR	95% CI
BMI	0.067	0.370	0.128–1.073
Tonsil size	0.999	0.000	0.000
Abdominal circumference	0.854	0.877	0.217–3.546
Ejection fraction	0.214	2.000	0.670–5.969

OR: Odds ratio, CI: Confidence interval, BMI: Body mass index

conducted by Pahlesia *et al*.[13] and with a prospective study conducted by Mannarino *et al*.[14] This finding is different from a quasi-experimental study by Susanto *et al*. who found that the patients mostly aged 31–40 years,[15] and with a study by Knecht *et al*. involving elderly heart failure patients with age range 68–70 years.[16] Sin *et al*. study found that age was significantly associated with OSA incidence in female patients with heart failure, and Odds ratio for age >60 years was 6.04 (95% confidence interval: 1.75–20.0).[17] Left ventricular hypertrophy in patients with CHF is closely related to changes in blood pressure during sleep compared to waking, and increased blood pressure may also be aggravated by the OSA.[18]

This study found that the BMI factor has no significant correlation with the incidence of OSA. Meanwhile, a study conducted by Wiadnyana *et al*. found that OSA was more common in patients with a BMI >25.[19] Furthermore, Punjabi *et al*. found that 58% of cases of adult patients with OSA are closely related to BMI ≥25 kg/m^2.[20] Obesity can cause changes in the airways causing the size of the pharynx to shrink. Fat deposition in the neck can cause the pads on the pharynx-surrounding tissue and lateral pharynx muscle thickened, thus causing the airways to narrow and cause apnea in OSA patients with heart failure who have risk factors for obesity. Obesity is also an early cause of hypertension and insulin-resistant diabetes mellitus, which can cause endothelial vascular disorders. These events are the initial occurrence of heart failure in patients with OSA.[18]

There was no significant correlation between neck circumference and OSA incidence. Evidence suggests that the neck circumference does not affect OSA in heart failure because OSA that occurs in patients with heart failure is due to fluid shifts to the neck area at the time of lying down or sleeping position, especially at night when the fluid accumulation is supposed to be in the lower limb.[11]

In this study, OSA patients with a Berlin Questionnaire score of >2 were significantly associated with enlarged tonsils. This result is also in accordance with a study by Cahali *et al*.,[21] which found that the size of the tonsils did have a significant correlation with AHI ($P = 0.04$). The tonsil grade is closely related to the volume of true connective tissue with varying sizes according to the age and BMI.[21]

This study found that blood pressure and OSA occurrence did not have a significant correlation. In contrast, Mannarino *et al*. found that 64 patients with moderate-to-severe OSH have persistent hypertension.[14] Furthermore, Young *et al*. found that blood pressure will increase linearly along with the increase of AHI with $P = 0.003$ for systolic blood pressure and $P = 0.01$ for diastolic blood pressure.[22]

In this study, patients at high risk of OSA from the Berlin Questionnaire were more common in severe CHF patients with low EF (<40%) although it was not statistically significant. The direct mechanism of OSA can occur because of increased blood pressure may reduce the left ventricular EF.[23]

Conclusions

This study found heart failure patients with high-risk OSA based on Berlin Questionnaires is 60%. Twenty-six patients at high risk of OSA underwent PSG examination with the result of patients with mild OSA (AHI score 5–15) – seven patients (26.7%), moderate OSA (AHI score 15–30) –nine patients (34.5%), and severe OSA (AHI >30) –ten patients (38.8%). Tonsil size was found to have a significant correlation with the incidence of OSA in patients with heart failure.

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Conflicts of interest

There are no conflicts of interest.

References

1. Randerath WJ, Sanner BM, Somers VK, editor. Sleep Apnea: Current Diagnosis and Treatment: Physiology of Sleep and Dreaming. Switzerland: Karger; 2006.
2. Sagaspe P, Leger D, Taillard J, Bayon V, Chaumet G, Philip P. Might the berlin sleep questionnaire applied to bed partners be used to screen sleep apneic patients? Sleep Med 2010;11:479-83.
3. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, *et al*. Sleep apnea and cardiovascular disease: An American Heart Association/American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council On Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health). Circulation 2008;118:1080-111.
4. Shiomi T, Sasanabe R. Advances in diagnosis and treatment of sleep apnea syndrome in Japan. Japan Med Assoc J 2009;52:224-30.
5. Astuti P, Yunus F, Antariksa B, Ratnawati. The prevalence of clinical

symptoms of obstructive sleep apnea (OSA) in patients with asthma. J Indones Med Assoc 2014;61:273-9.
6. Sin DD, Logan AG, Fitzgerald FS, Liu PP, Bradley TD. Effects of continuous positive airway pressure on cardiovascular outcomes in heart failure patients with and without Cheyne-Stokes respiration. Circulation 2000;102:61-6.
7. Tkacova R, Niroumand M, Lorenzi-Filho G, Bradley TD. Overnight shift from obstructive to central apneas in patients with heart failure: Role of PCO2 and circulatory delay. Circulation 2001;103:238-43.
8. Wexler L, Javaheri S. Sleep apnea is linked to heart failure, but does treatment improve outcome? Cleve Clin J Med 2005;72:929-36.
9. United Health Care. Polysomnography and Portable Monitoring for Sleep Related Breathing Disorders: Medical Policy. Available from: http://sleepinformatics.com/uploads/UHC_Polysomnography_and_Portable_Monitoring040114.pdf. [Last assessed 28 September 2019].
10. Javaheri S, Parker TJ, Liming JD, Corbett WS, Nishiyama H, Wexler L, *et al*. Sleep apnea in 81 ambulatory male patients with stable heart failure. Types and their prevalences, consequences, and presentations. Circulation 1998;97:2154-9.
11. Kasai T, Bradley TD. Obstructive sleep apnea and heart failure: Pathophysiologic and therapeutic implications. J Am Coll Cardiol 2011;57:119-27.
12. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, *et al*. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283:1829-36.
13. Pahlesia R, Yunus F, Antariksa B, Ratnawati, Widodo D [Thesis]. Prevalence of Obstructive Sleep Apnea in Patients with Mild to Severe Chronic Obstructive Pulmonary Disease Based on Berlin Questionnaire and Continuing with Polysomnography in Persahabatan Hospital; 2010.
14. Mannarino MR, Di Filippo F, Pirro M. Obstructive sleep apnea syndrome. Eur J Intern Med 2012;23:586-93.
15. Susanto A. Sleep-related Breathing Disorder in Indonesia. The 19th Congress of Asia Pacific Society of Respirology: Bali. Indonesia; 2014.
16. Knecht KM, Alosco ML, Spitznagel MB, Cohen R, Raz N, Sweet L, *et al*. Sleep apnea and cognitive function in heart failure. Cardiovasc Psychiatry Neurol 2012;2012:402079.
17. Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med 1999;160:1101-6.
18. Floras J, Andreas S. Sleep apnoea and malignant ventricular arrhythmias in heart failure. Eur Heart J 2011;32:10-2.
19. Wiadnyana IP, Susanto AD, Amri Z, Antariksa B. The prevalence of obstructive sleep apnea and related factors among taxi drivers X in Jakarta. J Respir Indones 2010;30:32-8.
20. Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5:136-43.
21. Cahali MB, Soares CF, Dantas DA, Formigoni GG. Tonsil volume, tonsil grade and obstructive sleep apnea: Is there any meaningful correlation? Clinics (Sao Paulo) 2011;66:1347-52.
22. Young T, Peppard P, Palta M, Hla KM, Finn L, Morgan B, *et al*. Population-based study of sleep-disordered breathing as a risk factor for hypertension. Arch Intern Med 1997;157:1746-52.
23. Mirzaaghazadeh M, Bahtouee M, Mehdiniya F, Maleki N, Tavosi Z. The relationship between nocturnal hypoxemia and left ventricular ejection fraction in congestive heart failure patients. Sleep Disord 2014;2014:978358.