

Obstructive sleep apnea, diagnosed by the Berlin questionnaire and association with coronary artery disease severity

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Original Article

Abstract

BACKGROUND: Obstructive sleep apnea syndrome (OSAS) is a highly prevalent sleep-related disorder that is associated with increased risk of hypertension (HTN) and coronary heart disease. This study aimed to evaluate the correlation between the OSAS and coronary artery disease (CAD) severity.

METHODS: The cross-sectional study was conducted from September 2012 to December 2013. We enrolled 127 patients with chronic stable angina who were referred for coronary angiographic studies in Shahid Chamran and Nour Hospitals in Isfahan, Iran. The Berlin questionnaire (BQ) was used for estimate the probability of OSAS in patients as a low or high probability. Demographic characteristics and metabolic risk factors including diabetes mellitus, HTN, obesity, and smoking also were recorded. The severity of CAD was assessed and compared based on the Gensini score with Mann–Whitney U statistical test. Independent t-test for continuous variables and chi-square test for categorical variables were used.

RESULTS: Totally, 65.4% of subjects were considered as high and 34.6% as low probability for OSAS, which 81.1% of them had CAD. There was a significant difference between body mass index, systolic blood pressure, diastolic blood pressure, and ischemic heart disease drug consumption with OSAS probability ($P < 0.0500$). CAD was accompanied by OSAS significantly ($P = 0.0260$). The Gensini score was significantly higher in patients with high OSAS probability (100.4 ± 69.1 vs. 65.3 ± 68.9 ; $P = 0.0030$). OSAS also increase odds of CAD based on regression analysis (odds ratio, 95% confidence interval = 2.7).

CONCLUSION: This study indicates that more severe CAD is associated with high OSAS probability identified by BQ.

Keywords: Coronary Artery Disease, Obstructive Sleep Apnea Syndrome, Berlin Questionnaire

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Introduction

Cardiovascular diseases (CVD) are of the most important causes of morbidity and mortality in both developed and developing countries with a rising pattern of occurrence all over the world.¹ Over 17 million people die annually from CVD related disorders of which most of them occurs in countries with low to intermediate income, thus there is the world-wide concern to find suitable ways of controlling and management of CVD disorders.^{2,3} Obstructive sleep apnea syndrome (OSAS) is a highly prevalent sleep-related disorder characterized by

repeated partial or complete closure of the pharynx, gasping episodes, sleep fragmentation, and daytime sleepiness that affect 5% of the adult population.^{4,6}

This syndrome is associated with increased risk of hypertension (HTN), coronary heart disease, atrial and ventricular arrhythmias, and ultimately increases the mortality rates due to cardiovascular disorders.⁷⁻⁹ The effects of OSAS on cardiovascular system have been established as a multi factorial phenomenon by the American College of Cardiology and American Heart Association.¹⁰⁻¹²

OSAS is under-diagnosed most of the times,

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especially by primary care physicians who regularly visit the patients; and only about 75% of even severe OSAS patients are diagnosed.^{13,14} Polysomnography is the golden standard method for sleep apnea diagnosis.¹⁵ The use of validated questionnaires like Berlin questionnaire (BQ) can be simpler and inexpensive alternative methods;^{16,17} which it has acceptable sensitivity and specificity among the instruments for OSAS diagnosis.¹⁸ The BQ indicates the presence of sleep apnea by addressing the presence and frequency of snoring behavior, wake time sleepiness or fatigue, and history of obesity or HTN.¹⁶ The evaluation of specificity and sensitivity of the BQ in Iran is currently underway in Isfahan, Iran, by Amra et al.¹⁹

The aim of the present study was to explore the correlation between the OSAS (diagnose by BQ) and coronary artery disease (CAD) severity with the application of coronary artery angiography, Gensini scoring evaluation system.

Materials and Methods

The present analytical cross sectional study was conducted from September 2012 to December 2013. We enrolled 127 patients with chronic stable angina who were referred for coronary catheterization studies to our university hospitals including Nour and Shahid Chamran hospitals, Isfahan, Iran. Chronic stable angina is defined as a chest pain or discomfort that most often occurs with activity or stress. Angina is due to poor blood flow through the blood vessels in the heart.²⁰ Inclusion criteria were all male and female presented with chronic stable angina and candidate for coronary catheterization. People who do not consent to participate in the study and catheterization, patients with heart failure, cardiomyopathy, severe valvular heart diseases, congenital heart disease, chronic obstructive pulmonary disease, history of ischemic heart disease (IHD), or acute coronary syndrome during the last month, patients with recent cerebral hypoxia and recently had oxygen therapy and patients with body mass index (BMI) more than 40 kg/m² were defined as exclusion criteria. The design of the study was approved by research and ethical committees of Isfahan University of Medical Sciences, Isfahan, Iran. Informed consents also were taken from the patients for their approval of involvement in the study. Cases were selected using a simple non-random sampling model.

After taking medical history and physical examination, the patients evaluated for OSAS. BQ

filled out for each patient to estimate the probability of OSAS. According to the questionnaire, patients were divided into two groups; high and low probability.¹⁶ The BQ consists 10 questions in three categories that having two positive categories define as high probability situation. The first category consists of five questions on snoring. Being symptomatic for more than 3-4 times a week in 2 questions or more, renders this category positive. The second category consists of three item on daytime somnolence that are considered positive if in 2 or more questions the patient is symptomatic for 3-4 times a week. The third category has two questions on the history of HTN and/or BMI > 30 kg/m² and will be considered positive with each of these questions being positive. Illiterate and low-educated patients filled out the questionnaire with the assistance of an investigator.

Coronary angiography usually was performed using the left and right Judkins catheters through common femoral artery. Coronary catheterization and the severity of coronary disorder were recorded by the same cardiologist based on the Gensini score.²¹ Calculation of Gensini score was carried as previously reported.¹⁸ Severity score depending on the degree of stenosis [25% (1 score), 50% (2 score), 75% (4 score), 90% (8 score), 99% (16 score), and 100% (32 score) stenosis] and its location score (proximal, middle, or distal tract) along the target vessel and the type of coronary vessel involved (left anterior descending, left circumflex artery, or right coronary artery) (Figure 1). The mean of Gensini score for each participant was recorded.

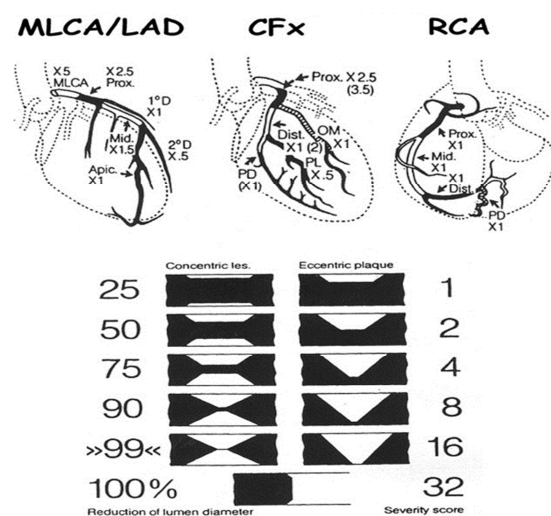


Figure 1. Gensini score calculation
 RCA: Right coronary artery; CFx: Circumflex; LAD: Left anterior descending artery; MLCA: Main left coronary artery

Demographic characteristics and metabolic risk factors including diabetes mellitus, HTN, obesity, smoking, and IHD drugs consumption including antiplatelet, beta adrenergic receptor blocker, statins and angiotensin converting enzyme inhibitors or angiotensin receptor blocker also were recorded.

Continuous variables were expressed as mean \pm standard deviation and were compared by independent sample t-test for normal variables and Mann–Whitney test for non-normal variables. Categorical variables were compared using a chi-square test and presented as frequencies with percentages. Simple and multiple logistic regression analysis were used to assess the crud and adjust effect of OSAS on CAD. The effect was hierarchically first adjusted by age and sex (Model 1), and then adjusted by BMI, HTN, diabetes mellitus, smoking, and drug consumption (Model 2). For all analyses, statistical package SPSS (version 15.0, SPSS Inc., Chicago, IL, USA) was used. All P values were 2-tailed with significance defined as $P < 0.0500$.

Results

The participant's mean of age was 59.00 ± 9.01 years. The youngest and the oldest participants had 32 and 82 years old, respectively. Of the participants, 74 (58.3%) were male. The mean BMI of participants was 26.67 ± 4.59 . Totally, 65.4% of

subjects were considered as high and 34.6% as low probability for OSAS, which 81.10% of them had CAD. There was significant difference between BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), HTN and IHD drug consumption with OSAS probability ($P < 0.0500$) (Table 1). 72 (86.7%) cases of high probable OSAS subjects had CAD; while it was 31 (70.5%) cases in low probable OSAS subjects ($P = 0.0260$). The Gensini score was also significantly higher in patients with high probability of OSAS comparing subjects with low probability (100.4 ± 69.1 vs. 65.3 ± 68.9 ; $P = 0.0030$) (Table 1).

Simple and multiple logistic regression analysis were used to assess the crud and adjust effect of OSAS on CAD. The effect was adjusted with age and sex in model 1 and with age, sex and other metabolic risk factors (is described) in model 2. As it shown for all models, OSAS had significant effect on CAD incidence by increases odds of CAD based on regression analysis (Table 2).

Discussion

Our finding demonstrated that OSAS identified by the BQ was associated with a significant risk of incidence and severity of CAD. The association between OSAS and CAD has been reported in previous studies.²²⁻²⁶

Table 1. Sleep apnea obstructive syndrome probability and demographic and risk factor characteristics, Gensini score and coronary artery disease (CAD) cases [mean \pm standard deviation or frequency (%)]

Variables	Sleep apnea obstructive syndrome		P
	High (n = 83)	Low (n = 44)	
Demographic characteristics			
Age	59.30 ± 9.20	57.54 ± 8.70	0.2980
BMI	27.32 ± 4.90	25.44 ± 3.70	0.0160
SBP	142.60 ± 17.20	126.23 ± 19.30	0.0040
DBP	93.80 ± 14.50	79.70 ± 13.10	0.0020
Sex (male) (%)	46 (55.4)	28 (63.6)	0.3720
Risk factors (%)			
HTN	60 (72.3)	14 (31.8)	< 0.0001
Diabetic	24 (28.9)	10 (22.7)	0.4540
Obesity	38 (45.8)	14 (31.8)	0.1280
Smoker	28 (33.7)	12 (27.3)	0.4560
IHD drug consumption (%)			
Use	66 (86.8)	24 (57.1)	< 0.0001
Gensini score	100.4 ± 69.1	65.3 ± 68.9	0.0030*
CAD (%)			
Positive	72 (86.7)	31 (70.5)	0.0260
Negative	11 (13.3)	13 (29.5)	

Use independent t-test for continuous variables and chi-square test for categorical variables; * Use Mann–Whitney U-test; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HTN: Hypertension; IHD: Ischemic heart disease; CAD: Coronary artery disease

Table 2. Odds ratio (OR) confidence interval (95% CI) of obstructive sleep apnea syndrome (OSAS) effect on coronary artery disease (CAD) with and without controlling other variables using logistic regression

CAD existence	Model	OR (95% CI)	P
CAD	Crud	2.75 (1.11, 6.79)	0.0290
	Model 1	2.80 (1.08, 7.27)	0.0340
	Model 2	4.74 (1.29, 17.29)	0.0180

Model 1: Adjust age, sex; Model 2: Adjust age, sex, BMI, HTN, diabetes mellitus, smoking and IHD drug consumption; OR: Odds ratio; CI: Confidence interval; CAD: Coronary artery disease; BMI: Body mass index; HTN: Hypertension; IHD: Ischemic heart disease

Martinez et al.²⁷ and Massierer et al.²⁸ reported that OSAS diagnosis based on BQ greatly increases the risks of CAD in patients having significant coronary artery lesions according to coronary angiography particularly in younger women. Although, at older ages, other risk factors especially metabolic risk factors play a more important role in CAD and IHD incidence. Lu et al.²⁹ indicated that higher Gensini score was in moderate to severe OSAS patients significantly. This results also reported by Hayashi et al.,³⁰ about revealed a positive correlation between Gensini score and the severity of sleep apnea. Our results was similar to research by Massierer et al.²⁸ which revealed there was an association between BMI, SBP, DBP and risk factors such as HTN and OSAS. BMI values were observed to increase significantly incidence of OSAS in our study which is in agreement with previous studies.³¹ Furthermore, Gus et al.¹⁷ demonstrated high risk for OSAS assessed by the BQ was highly prevalent and associated with resistant HTN and using antihypertensive drugs. This event can be justified by theory that breathing disorders during sleep can result in high SPB.³² Our findings also showed OSAS increases odds ratio (OR) for the presence of CAD [OR, 95% confidence interval (CI) = 4.7] like Martinez et al.²⁷ study that presented OR (95% CI) 4.5 for CAD with same risk factor adjustments.

Our study had some limitations. This study was simple non-random sampling model because we enrolled just patients with chronic stable angina and did not enrolled patient with other type of angina like acute coronary syndrome or Prinzmetal angina. In addition, the study method was analytical cross-sectional study. Evaluation of acute coronary events and OSAS is recommended for future studies.

Conclusion

This study indicates that more severe CAD is associated with high OSAS probability identified by

BQ. Moreover, this study confirmed the association between OSAS and CAD again.

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Conflict of Interests

Authors have no conflict of interests.

References

1. Talaei M, Sarrafzadegan N, Sadeghi M, Oveisgharan S, Marshall T, Thomas GN, et al. Incidence of cardiovascular diseases in an Iranian population: the Isfahan Cohort Study. *Arch Iran Med.* 2013; 16(3): 138-44.
2. Sadeghi M, Talaei M, Oveisgharan S, Rabiei K, Dianatkah M, Bahonar A, et al. The cumulative incidence of conventional risk factors of cardiovascular disease and their population attributable risk in an Iranian population: The Isfahan Cohort Study. *Adv Biomed Res.* 2014; 3: 242.
3. Sadeghi M, Talaei M, Zand I, Oveisgharan S, Iranipour R, Esteki Ghashghaei F, et al. Heart rate and cardiovascular events: a nested case-control in Isfahan Cohort Study. *Arch Iran Med.* 2014; 17(9): 633-7.
4. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep* 1999; 22(5): 667-89.
5. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993; 328(17): 1230-5.
6. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. *Am J Respir Crit Care Med* 2002; 165(9): 1217-39.
7. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 2005; 365(9464): 1046-53.
8. Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawabit R, Kirchner HL, et al. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *Am J Respir Crit Care Med* 2006; 173(8): 910-6.

9. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005; 353(19): 2034-41.
10. 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. *J Am Coll Cardiol* 2008; 52(8): 686-717.
11. Bradley TD, Floras JS. Obstructive sleep apnoea and its cardiovascular consequences. *Lancet* 2009; 373(9657): 82-93.
12. Kasai T, Bradley TD. Obstructive sleep apnea and heart failure: pathophysiologic and therapeutic implications. *J Am Coll Cardiol* 2011; 57(2): 119-27.
13. Mold JW, Quattlebaum C, Schinnerer E, Boeckman L, Orr W, Hollabaugh K. Identification by primary care clinicians of patients with obstructive sleep apnea: a practice-based research network (PBRN) study. *J Am Board Fam Med* 2011; 24(2): 138-45.
14. Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep* 2008; 31(8): 1071-8.
15. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep* 2005; 28(4): 499-521.
16. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999; 131(7): 485-91.
17. Gus M, Goncalves SC, Martinez D, de Abreu Silva EO, Moreira LB, Fuchs SC, et al. Risk for Obstructive Sleep Apnea by Berlin Questionnaire, but not daytime sleepiness, is associated with resistant hypertension: a case-control study. *Am J Hypertens* 2008; 21(7): 832-5.
18. Abrishami A, Khajehdehi A, Chung F. A systematic review of screening questionnaires for obstructive sleep apnea. *Can J Anaesth* 2010; 57(5): 423-38.
19. Amra B, Nouranian E, Golshan M, Fietze I, Penzel T. Validation of the persian version of berlin sleep questionnaire for diagnosing obstructive sleep apnea. *Int J Prev Med* 2013; 4(3): 334-9.
20. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012; 60(24): e44-e164.
21. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. *Am J Cardiol* 1983; 51(3): 606.
22. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000; 342(19): 1378-84.
23. Schafer H, Koehler U, Ewig S, Hasper E, Tasci S, Luderitz B. Obstructive sleep apnea as a risk marker in coronary artery disease. *Cardiology* 1999; 92(2): 79-84.
24. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population-based study. *Am J Respir Crit Care Med* 2005; 172(12): 1590-5.
25. Borgel J, Sanner BM, Bittlinsky A, Keskin F, Bartels NK, Buechner N, et al. Obstructive sleep apnoea and its therapy influence high-density lipoprotein cholesterol serum levels. *Eur Respir J* 2006; 27(1): 121-7.
26. Parish JM, Somers VK. Obstructive sleep apnea and cardiovascular disease. *Mayo Clin Proc* 2004; 79(8): 1036-46.
27. Martinez D, da Silva RP, Klein C, Fiori CZ, Massierer D, Cassol CM, et al. High risk for sleep apnea in the Berlin questionnaire and coronary artery disease. *Sleep Breath* 2012; 16(1): 89-94.
28. Massierer D, Martinez D, Fuchs SC, Pellin PP, Garcia MS, Zacharias AL, et al. Obstructive sleep apnea, detected by the Berlin Questionnaire: an associated risk factor for coronary artery disease. *Cad Saude Publica* 2012; 28(8): 1530-8.
29. Lu G, Xu ZW, Zhang YL, Yang ZJ, Zhang XL, Yin KS. Correlation among obstructive sleep apnea syndrome, coronary atherosclerosis and coronary heart disease. *Chin Med J (Engl)* 2007; 120(18): 1632-4.
30. Hayashi M, Fujimoto K, Urushibata K, Uchikawa S, Imamura H, Kubo K. Nocturnal oxygen desaturation correlates with the severity of coronary atherosclerosis in coronary artery disease. *Chest* 2003; 124(3): 936-41.
31. Kepez A, Niksarlioglu EY, Hazirolan T, Hayran M, Kocabas U, Demir AU, et al. Evaluation of association between obstructive sleep apnea and coronary risk scores predicted by tomographic

coronary calcium scoring in asymptomatic patients. *Anadolu Kardiyol Derg* 2011; 11(5): 428-35.

32. Javadi HR, Jalilolghadr S, Yazdi Z, Rezaie MZ. Correlation between Obstructive Sleep Apnea Syndrome and Cardiac Disease Severity. *Cardiovasc Psychiatry Neurol* 2014; 2014: 631380.

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