European Review for Medical and Pharmacological Sciences 2018; 22: 1415-1420

Correlation between coronary artery lesion quantitative score and OSAHS and relative risk factors

T. ZHANG[1], C. ZHANG[2], R.-X. CHEN[1], B. SHAO[1], G.-A. LIU[1]

[1]Cardiology Center, Suzhou Kowloon Hospital, Shanghai Jiaotong University, Suzhou, China
[2]Department of Respiration and Critical Care Unit, Peking University First Hospital, Beijing, China

Abstract. – OBJECTIVE: The purpose of this study was to investigate the relationship of obstructive sleep apnea hypopnea syndrome (OSAHS) with coronary artery lesion quantitative score Syntax Score (SX score) and risk factors for coronary heart disease (CHD).

PATIENTS AND METHODS: A total of 115 patients with OSAHS admitted to the Department of Cardiology in our hospital from January 2011 to June 2015 were selected. Philips Respironics Alice 5 Polysomnography was used for sleep monitoring. The patients were divided into mild group (n=32), moderate group (n=36) and severe group (n=47) according to apnea hypopnea index (AHI). Coronary angiography was performed for the patients, and SX score was calculated. Fasting venous blood was extracted from all patients with OSAHS and sent for detection of blood routine, coagulation, liver and kidney function, blood lipid and other indexes, and all patients received color Doppler echocardiography.

RESULTS: The body weight and body mass index (BMI) of patients with OSAHS in severe group were higher than those in the mild group and moderate group ($p<0.05$). The content of fibrinogen (FIB) of patients in severe group was higher than that in mild group ($p<0.01$). The levels of total cholesterol (TC) ($p<0.05$), blood uric acid ($p<0.05$), and serum creatinine ($p<0.01$) of patients in the severe group were significantly higher than those in mild group and moderate group, but there were no differences between mild group and moderate group ($p>0.05$). Echocardiography suggested that the left atrium diameter 1 (LAD) and pulmonary artery pressure (PAP) of patients in severe group were larger than those in the mild group and moderate group ($p<0.01$), and the right ventricle anteroposterior diameter (RVD) in the mild group was smaller than those in the moderate group ($p<0.05$) and severe group ($p<0.01$). The score of patients with OSAHS in the severe group was higher than those in the mild group and moderate group ($p<0.01$), and SX score was increased with AHI (r=0.416, $p<0.01$). Logistic regression analysis showed that AHI and SX score could not be used as indicators to judge the prognosis of patients.

CONCLUSIONS: There is a positive correlation between AHI and SX score in patients with OSAHS, indicating that with the aggravation of respiratory sleep disorder, SX score is increased significantly and the severity of coronary artery lesion is increased accordingly.

Key Words:
OSAHS, Sleep monitoring, Coronary angiography, SX score.

Introduction

Obstructive sleep apnea hypopnea syndrome (OSAHS) is a common and frequently-occurring disease, clinically manifested as irregular snoring, and sleep rhythm disorders, and often accompanied by hypertension, chronic pulmonary heart disease, type 2 diabetes, stroke, coronary heart disease (CHD) and so on[1-5]. The effects of OSAHS on the cardiovascular system are similar to the traditional risk factors of CHD known to us (diabetes mellitus, hypertension, obesity, etc.). Epidemiological data suggest that cardiovascular disease and related mortality have a causal link with OSAHS[2-4]. The coronary artery calcification score was detected with Computerized Tomography (CT). The results suggested that the risk of CHD in the patients with OSAHS is increased and the degree of coronary artery lesion is higher. Sharma found that the stenosis degree of coronary artery lesion is more serious in patients with OSAHS than that in patients without OSAHS, and OSAHS patients are more prone to multiple vessel lesions.

The Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX research) has introduced

Corresponding Author: Tao Zhang, MD; e-mail: ximenxiaobaozi@sina.com

the concept of SYNTAX score (SX score) based on American Heart Association (AHA), American College of Cardiology (ACC)/AHA, Leaman and other score systems, as well as expert opinions[6]. SX score is a new score system for risk stratification based on the anatomical characteristics of coronary artery lesion[7-10]. It evaluates the complexity of coronary artery lesion quantitatively according to the lesion location, severity, bifurcation, calcification, and other anatomical characteristics. In this study, through comparisons of blood routine, coagulation, biochemical indexes, echocardiography and coronary artery SX score among patients with mild, moderate and severe OSAHS, the correlation between OSAHS and clinical indicators was analyzed, and the effects of OSAHS on the severity of coronary artery lesions were discussed.

Patients and Methods

Patients

A total of 115 patients hospitalized in Department of Cardiology in our hospital from January 2011 to June 2015 and diagnosed with OSAHS by Polysomnogram (PSG) were included in this investigation. There were 86 males and 29 females, aged 36-78 years old, with an average age of (56.38±8.74) years old. The patients received coronary angiography in the same period of hospitalization. Exclusion criteria: a. Patients with serious liver and kidney dysfunction. b. Patients undergoing continuous positive airway pressure (CPAP). c. Patients using respiratory depressant (such as diazepam). This study was approved by the Ethics Committee of Suzhou Kowloon Hospital, Shanghai Jiaotong University. Signed written informed consents were obtained from all participants.

Methods

Clinical data: age, sex, smoking history, history of hypertension, history of diabetes mellitus, weight, height and other general conditions of the patients were collected and recorded. Fasting venous blood was collected and sent for determination of blood routine, coagulation, biochemical and other indexes, and the patients received echocardiography.

Sleep apnea monitoring: all patients underwent PSG with Philips Respironics Alice 5 Polysomnography (PSG) in the sleep treatment room after hospitalization. Patients with OSAHS were grouped according to the apnea hypopnea index (AHI): mild group (5 times/h<AHI<15 times/h), moderate group (15 times/h<AHI<30 times/h) and severe group (AHI>30 times/h).

SX score calculation: Coronary angiography was performed on all selected patients. According to the SX score scoring method, all vessels with a diameters ≥ 1.5 mm and all vessels with diameter stenosis of intraluminal lesion ≥ 50% should be scored. The left and right dominant types of the coronary artery, the weight of the vessels in the lesion site, and the severity of the lesions in patients were recorded, including coarctation of diameter of coronary artery, total occlusion, trifurcation lesions, double bifurcation lesions, lesions of aortic orifice, severe vascular tortuosity, lesion length >20 mm, thrombus, and diffuse lesions infiltrating into small vessels. SYNTAX Score Calculator was used to calculate SX score.

Follow-up: all patients were regularly followed up by phone or outpatient visit every 3 months after discharge from the hospital. The occurrence of major adverse cardiovascular and cerebrovascular events (MACCE) in patients was recorded. Primary endpoint: all-cause mortality. Secondary endpoints: stroke (cerebral infarction, cerebral hemorrhage), myocardial infarction and revascularization again.

Statistical Analysis

All statistics were performed using Statistical Product and Service Solutions (SPSS) 20.0 software (IBM Corp., Armonk, NY, USA). Normal-distributed quantitative data were expressed as ($\bar{x} \pm s$). One-way analysis of variance (ANOVA) was used in comparisons among multiple groups, and least significant digit (LSD) method was used for comparisons between two groups. Enumeration data were compared by x^2-test. Spearman correlation test was used for the correlation analysis. Logistic regression analysis was used to evaluate relevant risk factors. $p<0.05$ suggested statistical significance.

Results

Comparisons of General Conditions

There were no statistically significant differences in the age, sex, height, hypertension, diabetes mellitus and the proportion of smokers among three groups of patients with OSAHS ($p>0.05$). The body weight and BMI level of patients with OSAHS in the severe group were higher than

Table I. Comparisons of general conditions among different OSAHS level groups.

	Mild group (n=32)	Moderate group (n=36)	Severe group (n=47)	F/χ^2
Age (y)	57.34±7.96	56.89±8.32	57.47±9.22	0.328
Male/Female	21/11	29/7	39/8	2.346
Hypertension n (%)	21 (65.63)	25 (69.44)	38 (80.85)	3.245
Diabetes n (%)	6 (18.75)	5 (13.89)	9 (19.15)	0.719
History of smoking n (%)	18 (56.25)	26 (72.22)	30 (63.83)	2.447
Height (cm)	170.12±8.48	169.27±7.53	171.08±7.64	1.623
Weight (kg)	75.95±11.83	76.14±13.91	85.27±12.78*	8.128
BMI (kg/m^2)	25.89±2.99	26.45±4.34	28.36±3.92*	6.349

Note: *p<0.05 in comparison with mild and moderate OSAHS group.

those in the mild group and moderate group (p<0.05) (Table I).

Comparisons of Laboratory Indexes

There were no significant differences in the contents of red blood cell (RBC), platelet (Plt), hemoglobin (Hb) and dimer among three groups (p>0.05). The content of fibrinogen (FIB) in the severe group was higher than that in the mild group (p<0.01). There were no statistically significant differences in low-density lipoprotein-cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), thyroglobulin (TG), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) among three groups of patients with OSAHS (p>0.05). The levels of total cholesterol (TC) (p<0.05), uric acid (p<0.05) and serum creatinine (p<0.01) in the severe group were higher than those in the mild group and moderate group, but there were no differences between the mild group and the moderate group (p>0.05) (Table II).

Comparisons of Echocardiographic Indexes

Echocardiography showed that there were no statistically significant differences in left ventricular end-diastolic diameter (LVD) and left ventricular ejection fraction (LVEF) among three groups (p>0.05). The left atrium diameter 1 (LAD) and pulmonary artery pressure (PAP) in the severe group were larger than those in the mild group and moderate group (p<0.01). The right ventricle anteroposterior diameter (RVD) in the mild group was smaller than those in the moderate group (p<0.05) and severe group (p<0.01) (Table III).

Comparisons of Coronary Artery SX Score in Patients with OSAHS Among Mild Group, Moderate group and Severe Group

SX score of patients with OSAHS in the severe group was higher than those in the mild group and

Table II. Comparisons of laboratory indexes among different OSAHS level groups.

	Mild group (n=32)	Medium group (n=36)	Severe group (n=47)	F/χ^2
RBC (1012/L)	4.52 ± 0.47	4.56 ± 0.33	4.49 ± 0.51	2.125
Hb (g/L)	133.17 ± 14.72	138.46 ± 12.64	140.54 ± 13.83	1.639
Plt (109/L)	196.09 ± 57.19	223.25 ± 65.57	220.34 ±53.48	1.107
D-D (ug/mL)	0.26 ± 0.20	0.27 ± 0.22	0.28 ± 0.21	0.074
FIB (g/L)	2.93 ± 0.69	3.18 ± 1.05	3.46 ± 0.87**	3.673
TC (mmol/L)	4.71 ± 0.86	4.82 ± 0.73	5.14 ± 0.69*	5.215
LDL-c (mmol/L)	2.85 ± 0.82	2.74 ± 0.76	3.05 ± 0.74	2.338
HDL-c (mmol/L)	1.24 ± 0.43	1.32 ± 0.39	1.15 ± 0.45	4.248
TG (mmol/L)	2.13 ± 1.15	2.15 ± 1.08	2.20 ± 0.96	0.416
AST (U/L)	24.32 ± 14.47	26.35 ± 12.92	27.78 ± 11.28	1.291
ALT (U/L)	23.28 ± 8.16	24.74 ± 9.73	26.32 ± 10.24	2.354
UA (umol/L)	323.16 ± 72.51	335.27 ± 87.15	372.83 ± 88.49*	5.162
Cr (umol/L)	68.34 ± 15.28	69.59 ± 14.83	82.67 ± 17.52**	8.936

Note: *p<0.05; **p<0.01 in comparison with mild and moderate OSAHS group.

Table III. Comparisons of echocardiographic indexes among different OSAHS level groups.

	Mild group (n=32)	Moderate group (n=36)	Severe group (n=47)	F/χ^2
LVD (mm)	50.83±3.94	51.41±3.95	52.46±3.89	2.173
LVEF (%)	60.44±5.42	59.56±5.37	59.47±6.36	0.935
LAD (mm)	34.28±3.97	35.71±4.48	37.71±3.65**	3.452
PAP (mmHg)	30.82±2.53	30.23±1.94	32.31±2.87**	6.274
RVD (mm)	14.32±2.36	15.58±1.83#	16.25±3.14##	4.198

Note: #p<0.05; ##p<0.01 in comparison with mild OSAHS group. **p<0.01 in comparison with mild and moderate OSAHS group.

moderate group (p<0.01), and SX score was increased with AHI (r=0.416, p<0.01).

Analysis of risk Factors Related to MACCE in Patients with OSAHS

The occurrence of MACCE was used as the dependent variable, where no MACCE was defined as "0", and the occurrence of MACCE was defined as "1". The body weight, BMI, FIB, TC, blood uric acid, creatinine, LAD, RVD, PAP, and coronary artery SX score were used as independent variables for Logistic regression analysis. The results showed that the above indexes failed to serve as independent risk factors for the occurrence of MACCE in OSAHS patients (p>0.05) (Table IV).

Discussion

OSAHS can cause multiple-system and multiple-organ damage in the whole body[1]. Obesity, sex, age, smoking are all-important factors affecting the prevalence of OSAHS and the severity of the disease[2-4]. The results of this investigation showed that as the body weight and BMI were increased, the severity of OSAHS was increased. This conclusion is consistent with previous findings. Possible mechanisms include: 1) Obesity causes excessive accumulation of adipose tissue in the pharyngeal airways and compression of neck fat. 2) The enlargement of the soft palate, the lateral wall of the pharynx, the tongue, or the parapharyngeal fat pad results in abnormal upper airway structure. 3) The diaphragm moves up and the airway is more prone to collapse and occlusion. 4) Obesity can cause endocrine abnormalities, and decreased leptin may result in respiratory depression. There was no difference in sex of patients with OSAHS in each group[2,11-13]. However, studies have shown that the prevalence of OSAHS in men is 1.5-3 times that in women, and the sex difference can be reduced after female menopause[12]. Some scholars believed that female menopause is an important risk factor for the increased incidence of OSAHS. It is considered that it is related to changes in hormone levels, subsequent weight gain and abnormal distribution of body fat in postmenopausal women. We found that there were no significant differences in smoking, age, and other risk factors among patients with mild, moderate, and severe OSAHS.

Table IV. Logistic regression analysis of risk factors related to MACCE in patients with OSAHS.

	B	SE	Wald	95%CI	p
Weight	-0.041	0.052	0.716	0.789-1.025	0.399
BMI	0.217	0.318	2.245	0.924-1.413	0.201
UA	0.006	0.024	0.839	0.936-1.027	0.354
Cr	-0.007	0.032	0.224	0.943-1.039	0.657
SX score	0.058	0.025	2.376	0.978-1.286	0.052
AHI	-0.008	0.132	0.073	0.915-1.048	0.936
CHO	-0.625	0.731	3.051	0.427-1.247	0.343
PAP	0.032	0.329	0.047	0.825-1.234	0.746
LA	0.021	0.216	0.005	0.712-1.105	0.831
RV	-0.189	0.127	1.486	0.635-1.072	0.228
FIB	0.343	0.379	1.834	0.849-1.348	0.325

Note: p<0.05 suggested statistical significance.

This result may be related to some limitations of the selected patients.

The data of this study showed that the FIB level in the patients with severe OSAHS was higher than those in the mild group and moderate group. It suggested that patients with severe OSAHS had hypercoagulable state, compared with those in the other two groups. Previous researches have shown that the level of plasma FIB in patients with severe OSAHS is increased and has a positive correlation with AHI level[14]. The increased plasma FIB level in patients with OSAHS may be associated with intermittent hypoxia.

The results of our work also suggested that patients with severe OSAHS had more severe renal dysfunction than those in the other two groups. Analysis of possible causes: firstly, secondary hypertension often exists in patients with OSAHS, and long-term elevated blood pressure is the direct cause of kidney damage. Secondly, OSAHS can promote systemic oxidative stress, inflammation and endothelial dysfunction, causing renal ischemia and hypoxia. Finally, chronic intermittent hypoxia in patients with OSAHS can cause renal tubular cell apoptosis or transformation of epithelial cells and mesenchymal cells, resulting in renal fibrosis under the synergistic effects of various factors[1,3,14,15]. We found that blood uric acid level of patients with OSAHS in the severe group was significantly increased, compared with those in the mild group and moderate group, which is consistent with previous findings. The renal function of patients with severe OSAHS was significantly impaired, and uric acid excretion disorder could be found, making blood uric acid level increased. At the same time, hyperuricemia is an important part of the metabolic syndrome, and the severity of OSAHS is closely related to the metabolic syndrome. In this investigation, there were no significant correlations of ALT and AST with AHI level in patients with OSAHS. Previous studies[11,15] have proposed that the severity of OSAHS is positively correlated with levels of ALT, AST, etc. However, the number of related literature is relatively small, and most of them included a small sample of patients. Therefore, the relationship between OSAHS and aminotransferase levels remains to be further explored. In this report, blood TC level in the patients with severe OSAHS was higher than that in the mild group, but there was no significant difference between mild group and severe group. The mechanism of dyslipidemia induced by OSAHS is not clear. It may be related to the enhanced oxidative stress and sympathetic activity that lead to a potential dyslipidemia pathway disorder.

Our findings showed that severe OSAHS can lead to the expansion of LAD and RVD, and the increase of PAP in patients, but has nothing to do with LVEF and LVD. Repeated nocturnal hypoxia, hypercapnia, changes in the negative pressure in pleural cavity, rapid rise in pulmonary artery pressure and other factors may be important causes of changes in cardiac function and structure. The increased pulmonary artery pressure caused by OSAHS is the result of a combination of multiple factors: a. Apnea can cause reduction of alveolar ventilation and unbalanced ratio of ventilation/blood flow, leading to hypoxemia reflex and pulmonary vasoconstriction. b. Hypercapnia can enhance the contraction of pulmonary artery blood vessels during hypoxia. c. Others, such as intrathoracic pressure changes and the effects of sleep phase[1,4,12].

SX score is an angiographic grading method used to assess the complexity of coronary artery lesion. This study suggested that as the severity of OSAHS was increased, the severity and complexity of coronary artery lesion were also increased. Especially in patients with severe OSAHS, SX score level was significantly higher than those in the other two groups, so they were more prone to severe coronary artery lesion. The patients were followed-up, and by logistic regression analysis, it was found that there are no associations of OSAHS condition and SX score with MACCE of patients at present. It may be because the number of subjects was relatively small and the follow-up time was relatively short, and it remains to be further studied in the future.

Conclusions

We showed that in patients with OSAHS, with the aggravation of respiratory sleep disorder, SX score was increased significantly and the severity of coronary artery lesion increased accordingly. Early intervention should be taken in patients with cardiovascular disease complicated with OSAHS to reduce the risk of acute cardiovascular events and improve prognosis.

Conflict of Interest

The Authors declare that they have no conflict of interest.

References

1) Luo H, Scholp A, Jiang JJ. The finite element simulation of the upper airway of patients with moderate and severe obstructive sleep apnea hypopnea syndrome. Biomed Res Int 2017; 2017: 7058519.
2) Jiang YQ, Xue JS, Xu J, Zhou ZX, Ji YL. Efficacy of continuous positive airway pressure treatment in treating obstructive sleep apnea hypopnea syndrome associated with carotid arteriosclerosis. Exp Ther Med 2017; 14: 6176-6182.
3) Arous F, Boivin JM, Chaouat A, Rumeau C, Jankowski R, Nguyen DT. Awareness of obstructive sleep apnea-hypopnea syndrome among the general population of the Lorraine region of France. Eur Ann Otorhinolaryngol Head Neck Dis 2017; 134: 303-308.
4) Mutlu LC, Tulubas F, Alp R, Kaplan G, Yildiz ZD, Gurel A. Serum YKL-40 level is correlated with apnea hypopnea index in patients with obstructive sleep apnea sindrome. Eur Rev Med Pharmacol Sci 2017; 21: 4161-4166.
5) Agha B, Johal A. Facial phenotype in obstructive sleep apnea-hypopnea syndrome: a systematic review and meta-analysis. J Sleep Res 2017; 26: 122-131.
6) Farooq V, Head SJ, Kappetein AP, Serruys PW. Widening clinical applications of the SYNTAX Score. Heart 2014; 100: 276-287.
7) Ružičić D, Dobrić M, Vuković M, Hrnčić D, Đorđević S, Ružičić M, Aleksandrić S, Đorđević-Dikić A, Beleslin B. The correlation of SYNTAX score by coronary angiography with breast arterial calcification by digital mammography. Clin Radiol 2017 Dec 29. pii: S0009-9260(17)30566-4. doi: 10.1016/j.crad.2017.12.002. [Epub ahead of print]
8) Aksu U, Gulcu O, Bilgi Z, Topcu S, Sevimli S, Bayram E, Tanboga IH. The association of the Syntax score II with carotid intima media thickness and epicardial fat tissue. Indian Heart J 2017; 69: 752-756.
9) Nishigawa K, Fukui T, Takanashi S. Preoperative SYNTAX score to assess the late outcomes after coronary endarterectomy for the diffusely diseased left anterior descending artery. Interact Cardiovasc Thorac Surg 2017; 25: 780-784.
10) Dinckal MH, Ozkaynak B, Mert B, Sahin I, Sigirci S, Gulsen K, Ayca B, Okuyan E. The relationship between antibeta 2 glycoprotein antibodies and SYNTAX score in patients undergoing coronary artery by-pass graft surgery. Eur Rev Med Pharmacol Sci 2014; 18: 2556-2561.
11) Jokubauskas L, Baltrusaityte A. Relationship between obstructive sleep apnoea syndrome and sleep bruxism: a systematic review. J Oral Rehabil 2017; 44: 144-153.
12) Zhang W, Si LY. Obstructive sleep apnea syndrome (OSAS) and hypertension: pathogenic mechanisms and possible therapeutic approaches. Ups J Med Sci 2012; 117: 370-382.
13) Buccheri A, Chine F, Fratto G, Manzon L. Rapid maxillary expansion in obstructive sleep apnea in young patients: cardio-respiratory monitoring. J Clin Pediatr Dent 2017; 41: 312-316.
14) Zhang X, Yin K, Wang H, Su M, Yang Y. Effect of continuous positive airway pressure treatment on elderly Chinese patients with obstructive sleep apnea in the prethrombotic state. Chin Med J (Engl) 2003; 116: 1426-1428.
15) Li F, Huang H, Song L, Hao H, Ying M. Effects of obstructive sleep apnea hypopnea syndrome on blood pressure and C-Reactive protein in male hypertension patients. J Clin Med Res 2016; 8: 220-224.