Original Article

Effect of obstructive sleep apnea syndrome on serum C-reactive protein level, left atrial size and premature atrial contraction

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Abstract: Objective To assess the changes of serum C–reactive protein (CRP) level, left atrial size and atrial premature contraction (PAC) in patients with obstructive sleep apnea syndrome (OSAS). Methods This study involved 277 patients with OSAS diagnosed after an overnight polysomnography, who underwent a 24-h Holter electrocardiography and ambulatory blood pressure monitoring for detection of PAC. According to the apnea–hypopnea index (AHI), 137 patients with PAC identified from these patients were classified into 3 groups, namely the mild (5≥AHI<15), moderate (15≥AHI<30) and severe (AHI≥30) groups. Serum CRP level was assessed by a high-sensitivity radio-immunomassay. The left atrial diameter and echocardiographic parameters were recorded by transthoracic Doppler echocardiography (TTE). Results We found a high prevalence of PAC in those OSAS patients (137/277, 49.4%). Serum CRP was significantly higher in severe OSAS group (5.01±4.68 mg/L) than in the moderate (3.03±1.94 mg/L) and mild OSAS (2.98±1.82 mg/L) groups (P=0.040 and 0.033, respectively). The left atrial diameter was significantly increased in severe OSAS group (40.1±7.9 mm) as compared to that in moderate (37.9±5.5 mm) and mild (33.7±3.8 mm) groups (P=0.025 and 0.002, respectively). The severity of OSAS was positively correlated to both CRP (r=0.304, P=0.034) and left atrial diameter (r=0.411, P=0.003). After adjusting for gender, age and body mass index (BMI), a strong correlation was found between the left atrial diameter and CRP (r=0.594, P=0.0005). Conclusion There is a high prevalence of PAC in OSAS patients. The progression of OSAS is associated with increased serum CRP level and left atrial size in patients with premature atrial complexes. Our study suggests that inflammation associated with OSAS might contribute to atrial structural and electrical remodeling in OSAS patients with PAC.

Key words: obstructive sleep apnea syndrome; premature atrial contraction; C–reactive protein; left atrial remodeling

Introduction

Obstructive sleep apnea syndrome (OSAS) is a condition of disordered breathing in which the upper airway closes repeatedly during sleep. These repetitive partial or complete cessations of airflow during sleep result in oxygen desaturation, arousals from sleep and generation of exaggerated negative intrathoracic pressure that directly or indirectly affects the cardiovascular system by several pathways, such as sympathetic activation, inflammation, oxidative stress, and endothelial dysfunction.

The relationships between OSAS and cardiac arrhythmias have been explored over the past 3 decades. Atrial arrhythmia is the most frequently encountered arrhythmia in OSAS patients with a high prevalence ranging from 32% to 49%[13]. Recent epidemiological[14–18], animal[19–21] and clinical[22–25] studies have shown that the occurrence and post-cardioversion recurrence of atrial arrhythmias including atrial fibrillation (AF) are associated with inflammatory processes. An enlarged left atrium is an independent risk factor for atrial arrhythmias[26]. Some researches have suggested that ongoing inflammation leads to fibrosis and structural remodeling of the atrium, thus promoting arrhythmias[27–29]. Inflammation is a hallmark of the pathophysiology of OSAS and represents a pathway linking OSAS to increased cardiovascular morbidity[30–34]. C-reactive protein (CRP) is a sensitive marker of inflammation, and several studies have demonstrated an independent relationship between OSAS and elevated CRP levels[35–39].

In clinical practice, premature atrial contraction (PAC) is a commonly seen arrhythmia in OSAS patients undergoing 24-h Holter electrocardiography. We hypothesize that PAC might be the precursor of other complex cardiac arrhythmias[39–40]. In this study, we investigated the effect of OSAS on serum CRP level and left atrial size in patients with PAC, and explored the association between inflammation (as shown by CRP levels) and the left atrial size in these patients.

Methods

Patients

We conducted a retrospective study of 277 patients with the diagnosis of OSAS after an overnight polysomnography (PSG) at the Sleep Medicine Center of Nanfang Hospital between December 2004 and May 2010. An apnea–hypopnea index (AHI) of no less than 5/ hour was considered diagnostic of OSAS. All the 277 patients underwent a 24-h Holter ECG and ambulatory blood pressure examination, and 137 (49.4%) patients who were found to have at least 1 episode of PAC were selected for further study. The patients with PAC,
including 81 (29.2%) with exclusive PAC and 56 (20.2%) with both PAC and PVC, were classified into 3 groups according to the severity of OSAS defined by the apnea-hypopnea index (AHI), namely the mild (5 ≤ AHI < 15), moderate (15 ≤ AHI < 30) and severe OSAS (AHI ≥ 30) groups.23 Serum levels of CRP were measured with a high-sensitivity radio-immunoassay. Transthoracic Doppler echocardiography was performed. The sonographer and the reporting cardiologist were blinded to the patients’ sleep study findings. Patients with congestive heart disease, valvular disease, rheumatic heart disease, chronic pulmonary disease, connective tissue diseases or chronic inflammatory diseases were excluded.

Sleep study

Overnight polysomnography (PSG) monitoring was performed with the Emblettta sleep system (Embla, USA) to obtain the data of the electroencephalogram, electrooculogram, electromyogram, ECG, airflow, chest and abdominal efforts and arterial oxyhaemoglobin saturation (SPO2). Apnea was defined as continuous cessation of airflow at the nose and mouth lasting over 10 s, and hypopnea as a reduction of thoracoabdominal motion by ≥50% associated with a fall in the baseline oxygen saturation by ≥4%. The AHI was calculated as the total number of episodes of apnea and hypopnea per hour of sleep.

Twenty-four-hour Holter recordings were taken using a standard 3-channel flash card recorder (RZ153; GE Electronics, Germany). The ECG signal was digitalized and stored using a commercially available computer-based system. All the recordings were visually scanned and analyzed using the RZ153 Holter Analysis System. Patients with at least 1 episode of PAC over 24 h were included in the study group.

Echocardiography

All the transthoracic echocardiography examinations were randomly performed by one of 3 experienced sonographers blinded to the results of PSG using an Acuson Sequoia 512 with a 2.5-MHz transducer. The echocardiographic images were obtained in the parasternal long-axis and short-axis, apical long-axis, and apical four-chamber view according to current standards. End-diastolic left atrial diameter (LA) and left ventricular (LV) internal diameter were determined from the apical four-chamber view 2-D measurement. Interventricular septal thickness (IVSD), and LV posterior wall thickness (LVPW) were determined from the M-mode measurements in the parasternal long-axis. The LV ejection fraction (LVEF) was also obtained. Transmural diastolic flow was obtained by pulse-wave Doppler from an apical four-chamber view. Color Doppler was used to visualize the transmural flow; the pulsed Doppler sample volume was placed at the level of mitral leaflet tips, with the ultrasonic beam perpendicular to the inflow jet. The peak velocities of the early (E-wave) and late (A-wave) phase of the mitral inflow pattern from Doppler recordings were measured and their ratio (E/A) was calculated.

Statistical analysis

All the values are expressed as Mean±SD. One-way ANOVA was used to test the differences between the 3 groups. Dunnett T3 method was used to compare the differences in CRP level and left atrial diameter between the groups. All statistical analyses were carried out using SPSS version 13.0 for Windows (SPSS Inc, Chicago, IL). The differences were considered statistically significant at the level of P<0.05.

RESULTS

Tab.1 shows that the 3 groups of patients with PAC were roughly matched for age and gender distribution. The patients with an increasing severity of OSAS tended to have a greater body mass index (BMI) and higher blood pressure. There were no significant differences between the 3 groups in LV internal diameter, IVSD, LVPW, LVEF, or diastolic function characterized by the E/A ratio. The serum CRP level and the left atrial diameter increased with the severity of OSAS, significantly higher in severe OSAS group (5.01±4.68 mg/L) than in the moderate (3.03±1.94 mg/L) and mild OSAS (2.98±1.82 mg/L) groups (P=0.040 and 0.035, respectively); the left atrial diameter increased even more obviously in severe OSAS group (40.1±7.9 mm) as compared to that in moderate (37.9±5.5 mm) and mild OSAS (33.7±3.8 mm) groups (P=0.025 and 0.002, respectively).

After adjusting for age, gender and BMI, the severity of OSAS was positively correlated to serum CRP level and left atrial diameter (r=0.304, P=0.034, and r=0.411, P=0.003, respectively). There was also a significant correlation between serum CRP level and left atrial diameter (r=0.383, P=0.004). The correlation was even more significant after adjusting for gender, age and BMI (r=0.594, P=0.0005).

DISCUSSION

There has been an increasing awareness of the relationship between cardiac arrhythmia and sleep apnea. Most of the previous studies addressed atrial fibrillation in OSAS patients for its association with high morbidity and mortality rates and economic burden. This study represents the first attempt to examine PAC as a condition of arrhythmia in OSAS patients by assessing sleep study findings. Patients with an increasing severity of OSAS tended to have a greater body mass index (BMI) and higher blood pressure. There were no significant differences between the 3 groups in LV internal diameter, IVSD, LVPW, LVEF, or diastolic function characterized by the E/A ratio. The serum CRP level and the left atrial diameter increased with the severity of OSAS, significantly higher in severe OSAS group (5.01±4.68 mg/L) than in the moderate (3.03±1.94 mg/L) and mild OSAS (2.98±1.82 mg/L) groups (P=0.040 and 0.035, respectively); the left atrial diameter increased even more obviously in severe OSAS group (40.1±7.9 mm) as compared to that in moderate (37.9±5.5 mm) and mild OSAS (33.7±3.8 mm) groups (P=0.025 and 0.002, respectively).

After adjusting for age, gender and BMI, the severity of OSAS was positively correlated to serum CRP level and left atrial diameter (r=0.304, P=0.034, and r=0.411, P=0.003, respectively). There was also a significant correlation between serum CRP level and left atrial diameter (r=0.383, P=0.004). The correlation was even more significant after adjusting for gender, age and BMI (r=0.594, P=0.0005).

DISCUSSION

There has been an increasing awareness of the relationship between cardiac arrhythmia and sleep apnea. Most of the previous studies addressed atrial fibrillation in OSAS patients for its association with high morbidity and mortality rates and economic burden. This study represents the first attempt to examine PAC as a condition of arrhythmia in OSAS patients by assessing the prevalence of PAC in OSAS patients in relation to serum CRP and the left atrial diameter.

Our results suggest a high prevalence of PAC (49.4%) in Chinese OSAS patients, which is consistent with the observation by Gami et al18 that there is a high prevalence of atrial fibrillation in OSAS patients. This seems to justify the hypothesis that PAC in association with OSAS may not be as benign as previously
The impact of medications e.g ACEI probably taken by the hypertensive patients could not be evaluated. Moreover, its retrospective design and the absence of follow-up data do not allow us to draw definite conclusions. To extend these preliminary results, it is necessary to undertake a case-controlled multi-center study and a longitudinal follow-up to evaluate the role of OSAS and CRP in left atrial remodeling and atrial arrhythmias.

References

摘要:目的 评估血清C-反应蛋白(CRP)的浓度,左房大小和房性早搏与睡眠呼吸暂停综合症(OSAS)的关系。方法 经多导睡眠呼吸监测诊断为OSAS的277名患者行24 h动态心电图和动态血压检查。将患有房性早搏的137名患者根据呼吸暂停低通气指数(AHI)分成3组,即轻度组(AHI≤15),中度组(15<AHI≤30)和重度组(AHI≥30)。比较3组患者的血清CRP浓度、左房直径,分析二者与OSAS严重程度之间的关系。结果 OSAS患者中,房性早搏的发生率较高,为49.4% (134/277)。轻、中、重度OSAS患者中的CRP值分别为(2.98±1.82) mg/L,(3.03±1.94) mg/L,(5.01±4.68) mg/L,左房直径分别为(33.7±3.8) mm,(37.9±5.5) mm,(40.1±7.9) mm。血清CRP水平和左房直径与OSAS的严重程度成正相关(r=0.304,P=0.034; r=0.411,P=0.0003)。在排除性别、年龄和体质量指数的影响下,CRP和左房直径也呈正相关(r=0.594, P=0.0005)。结论 OSAS患者房性早搏的发病率较高。在这些患有房性早搏的OSAS患者中,CRP水平和左房直径的大小与OSAS的严重程度成正相关的关系,提示炎症激活介导的左房重构和电重构可能在OSAS患者房性早搏的发生中起重要作用。

关键词:睡眠呼吸暂停综合症;房性早搏;C-反应蛋白;左房重构

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