Relationship Between Severity of Obstructive Sleep Apnea and PR Interval

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ABSTRACT

Introduction: Relationship between obstructive sleep apnea (OSA) and electrocardiogram and OSA severity index relationship that may affect the PR interval were studied.

Patients and Methods: This study included 85 people who had OSA diagnosed at our clinic between January 2013 and August 2013. Their polysomnography (PSG) reports were evaluated by physicians who are expert in their fields. Individuals with severe OSA diseases were categorized as group 1, and individuals with mild to moderate OSA were categorized as group 2.

Results: Age distribution of individuals who participated to the study ranged from 20 years to 85 years (mean ± standard deviation, 45.5 ± 13.2 years). Fifty-one (60%) of those individuals were men, and 34 (40%) of them were women. The PR interval for the group who had severe OSA on PSG (group 1) was 163.1 ± 35.2 ms, and it was 147.8 ± 29.3 in group 2.

Conclusion: It was observed that individuals having severe OSA had higher PR intervals than individuals who had mild to moderate OSA. It was determined that results were statistically significant ($p< 0.05$, $p= 0.032$). We believe that apnea-hypopnea index, oxygen desaturation index, and arousal values, which are indications of OSA severity and parameters of hypoxia-reoxygenation, contribute to PR prolongation.

Key Words: PR interval time; sleep apnea, obstructive

Obstrüktif Uyku Apnesi Şiddeti ve PR Süresi Arasındaki İlişki

ÖZET

Giriş: Obstriktif uyku apnesi (OSA) şiddeti ile elektrokardiyogramdaki PR süresinin genişlemesi arasındaki ilişki ve PR süresini etkileyebilecek OSA şiddet indeksleri ile ilişkisi araştırılmıştır.

Hastalar ve Yöntem: Bu çalışma; kliniğimizde Ocak 2013 ve Ağustos 2014 tarihleri arasında, OSA tanısı almış 85 kişiyi içermektedir. Polisomnografi (PSG) raporları alanında uzman hekim tarafından değerlendirildi. Şiddetli uyku apne hastalığı olan bireyler grup 1 olarak adlandırılırken, orta, hafif uyku apne hastalığı olan bireyler grup 2 olarak belirlendi.

Bulgular: Çalışmaya katılan tüm bireylerin yaş dağılımı; minimum 20 yıl, maksimum 85 yıldır (ortalama ± standart sapma 45.5 ± 13.2 y). Bu kişilerin 51'i (%60) erkek, 34'ü (%40) kadındır. Polisomnografi şiddetli OSA tanısı alan bireyleri içeren grup 1'de PR süresi 163.1 ± 35.2 milisaniye (ms) iken grup 2'de 147.8 ± 29.3 milisaniye olduğu görüldü.

Sonuç: Şiddetli OSA tanısı alan bireylerin, hafif ve orta şiddette OSA tanısı alan bireylere göre PR sürelerinin yüksek olduğu görüldü. Sonucun istatiksel olarak anlamlı olduğu tespit edildi ($p< 0.05$, $p= 0$). OSA şiddeti göstergesi ve hipoksi-reoksijenizasyon parametreleri olan AHI (apne-hipopne indeksi), ODI (oksijen desaturasyon indeksi); arousal değerleri PR uzamasında katkı sağladığına inanmaktayız.

Anahtar Kelimeler: PR aralığı süresi; obstrüktif uyku apnesi

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INTRODUCTION

Obstructive sleep apnea (OSA) syndrome (OSAS) is a health problem observed in 2-4% of the population and has significant cardiovascular effects[1-3]. One-third of OSAS mortalities and morbidities are associated with coronary syndrome, coronary heart disease, heart failure, and cerebrovascular ischemia[3]. One-third of patients with hypertension also have OSAS[3]. However, the relationship between OSA and these diseases and the etiopathogenic mechanisms have not been explained clearly.

Frequent apnea occurring in patients with OSA increases negative intrathoracic pressure and cardiac preload and afterload. The disruptions in cardiac electrical activity that occur thereafter have a cardiovascular mechanical stress effect and can cause sudden cardiac death[4].

Sudden cardiac death in patients with OSA usually occurs during sleep from midnight to early hours of the morning (03:00-06:00), whereas sudden cardiac death in normal cardiac patients occurs later (06:00-12:00)[4]. These sudden deaths were thought to occur due to cardiac arrhythmia, and several studies have been conducted on that topic. However, the reasons have not been clarified, and many factors contribute to night-time arrhythmia, stroke, and myocardial infarction in patients with OSA. Night-time arousal plays a particular role in patients with OSA by initiating sudden cardiac side effects and activating particular aspects of the cardiovascular system[5].

Cardiac arrhythmias occur as a result of decreased oxygen delivery to the myocardium during apnea-hypopnea events, which causes large differences in intrathoracic pressure, hypoxia, and hypercapnia in patients with OSA[6]. Changes in heart rate, hemodynamics, and the endothelium occur as a result of changes that occur during intermittent hypoxia and sympathetic activities[5,6].

In this study, we examined changes in the PR interval during respiratory events in patients with mild to moderate and severe OSA. PR prolongation (> 200 ms), defined as a first-degree block at the atrioventricular (AV) node level with respect to the apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and arousal index (AI) in patients with OSA, was assessed.

PATIENTS and METHODS

Clinical Characteristics of the Patients

The sleep laboratory data were generated by subjects who presented to our clinic between January 2013 or August 2014 with snoring, complaints of witnessed apnea, or were suspected of having sleep apnea. The study included 85 patients. None of the patients had been referred previously to a sleep laboratory.

The patients were questioned about snoring, witnessed apnea, and daytime sleepiness status as acceptance criteria before the polysomnography (PSG) investigation. Data on age, sex, smoking, hypertension, diabetes mellitus, hyperlipidemia, family coronary artery disease, congestive heart disease, and atrial fibrillation were gathered from all participants. Patients using medications that affected the autonomic nervous system or thyroid and those who were taking medications for chronic liver failure or liver disease were excluded from the study.

Respiratory function tests, chest X-ray, electrocardiogram (ECG), and physical examinations were performed on all patients. Hemogram, liver function tests, urea, creatinine and fasting glucose levels, lipid profile, and thyroid function tests were also evaluated. Patients were excluded if they were diagnosed with acute myocardial infarction; had a pacemaker, implantable defibrillator, heart disease, valvular heart disease, or severe chronic pulmonary disease; or were undergoing dialysis.

Patients were also evaluated according to medication use history, such as digoxin, diltiazem, verapamil, and amiodarone, which can prolong the PR interval. Written informed consent was obtained from each volunteer, and the risks and nature of the study were explained.

Electrocardiographic Evaluation

Sleeping ECG was obtained from electronic records. Heart rate and PR interval were obtained by computed ECG (ALICE 6 LDe model, 31 canal PSG system; Phillips Healthcare, Andover, MA, USA). The PR interval was measured during sleep from the earliest detection of atrial depolarization in any lead to the earliest detection of ventricular depolarization in any lead.

Overnight Polysomnography Evaluation

Overnight polysomnography was recorded with Alice® 6 Polysomnography System (ALICE 6 LDe model, 31 canal PSG system), which recorded the following parameters: ECG; central, temporal, and occipital electroencephalogram; bilateral electrooculogram; submental and anterior tibias electromyogram; nasal airflow using a nasal cannula and pressure transducer; nasal-oral airflow using thermistor; and respiratory effort using chest and abdominal piezo electric belts. The electromyogram, electrooculogram, and electroencephalogram leads were applied according to the international 10/20 electrode placement system. Oxyhemoglobin saturation was monitored using a pulse oximeter. Sleep stages were scored according to the criteria of American Academy of Sleep Medicine. Apnea was defined as decrements in airflow ≥ 90% from baseline for ≥ 10 hypopneas were defined as a 30% or greater decrease in flow lasting at least 10 s and associated with a 4% or greater oxyhemoglobin desaturation. The number of apneas and hypopneas per hour of sleep was calculated to obtain the apnea-hypopnea index (AHI). Cortical arousals were identified according to American Sleep Disorders Association criteria (1992) as abrupt shifts in

EEG frequency lasting 3-15 s. Arousals were subsequently classified as spontaneous or respiratory-related according to the absence or presence of an immediately preceding respiratory event. Respiratory events were derived primarily from nasals cannula pressure transducer. The oxygen desaturation index was defined as the total number of episodes of oxyhemoglobin desaturation ≥ 4% from immediate baseline- ≥ 10 s but < 3 min- divided by the total sleep time (hours). The mean and minimal arterial oxyhemoglobin saturations and cumulative time spent with an arterial oxyhemoglobin saturation < 90% were also calculated. OSAS severity was assessed as mild, moderate and severe according to the AHI values of 5-14, 15-29, and > 30, respectively.

The local ethics committee approved the study and patients who agreed to participate in the study gave informed consent.

Statistical Analysis

Data were analyzed using SPSS (v 15.0; IBM Corp, Armonk, NY, USA). Means with standard deviations or percentages were used to describe the sample. Independent t test were used for difference between groups with respect to basic characteristic and associated diseases of OSA patients. Comparison for categorical variables was done using the chi-square test. Spearman correlation test was used for relationship between PR and AHI, AI, ODI, cumulative time spent with arterial oxyhemoglobin saturation < 90%, and mean oxygen concentration.

RESULTS

Subject Characteristics

Eighty-five patients were included in the study (34 women and 51 men; mean age, 45.5 ± 13.2 years), and all patients had a diagnosis of OSA. The mean body mass index (BMI) was 29.6 ± 4.8 kg/m^2. Patients were divided into severe OSA and mild to moderate OSA groups. No differences in characteristics (BMI, sex, age, and coronary artery disease, heart failure, hyperlipidemia, hypertension, or diabetes) were observed between groups. About 8% of patients had diabetes mellitus, 31% had hypertension, and 17.2% had hyperlipidemia. Twenty four (28%) patients were obese (BMI > 30 kg/m^2), and 10 (11%) were morbidly obese (BMI > 35 kg/m^2) (Table 1).

No relationships were found between the PR interval and patient age (r= 0.12), sex (r= 0.078), BMI (r= 0.13), or the presence or absence of other diseases (r< 0.05) (Table 2). The PR interval was increasingly prolonged as OSA severity increased (Table 3, Figure 1).

Moderate correlations were detected between the PR interval and AHI (r= 0.49), ODI (r= 0.47), and final AI (r= 0.41) (Figure 2A,B,C).

No association was found between cumulative time spent with arterial oxyhemoglobin saturation < 90% (time with < 90% SaO_2) and the PR interval or between mean oxygen saturation and the PR interval.

Table 1. Demographic parameters and baseline characteristics

	OSA (mild to moderate)	OSA (severe)	p value
Age (yrs.)	47.2 ± 13.2	50.3 ± 13.4	NS
Sex (female/male)	24/25	10/26	NS
BMI (kg/m^2)	29.2 ± 5.5	30.3 ± 3.7	NS
DM	3 (6%)	4 (11%)	NS
CAD	6 (12%)	5 (12.5%)	NS
Hyperlipidemia	8 (16%)	7 (19%)	NS
CHF	0	0	NS

BMI: Body mass index; OSA: Obstructive sleep apnea; DM: Diabetes mellitus; CAD: Coronary artery disease; CHF: Congestive heart failure.

Table 2. BMI and PR interval difference in men and women study groups

	Men	Women	p value
BMI (kg/m^2)	29.00 ± 3.81	30.74 ± 5.92	NS
PR interval (ms)	156.4 ± 34.64	151.1 ± 29.5	NS

*** No significant difference was determined with respect to the PR interval and BMI when patients were separated according to men and women groups.

Table 3. PR interval of OSA groups

	OSA (mild to moderate)	OSA (severe)	p value
PR interval	147.8 ± 29.3	163.1 ± 35.2	0.032

*** Significant difference was determined with respect to the PR interval when patients were separated according OSA severity groups.

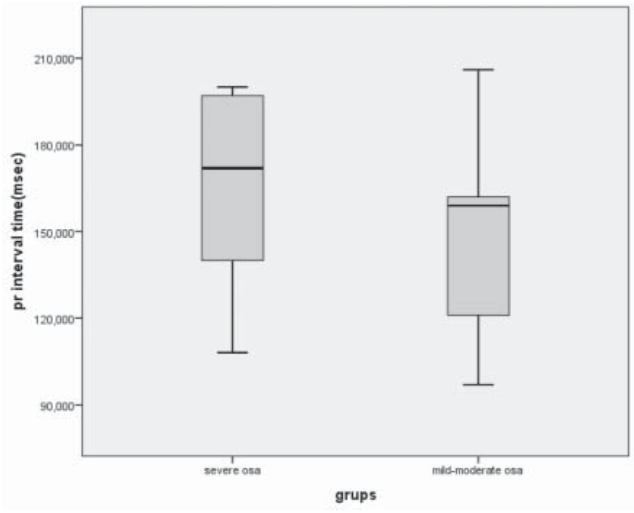

Figure 1. Relationship between PR interval and OSA severity groups.

* There are significant differences between PR interval between severe and mild to moderate OSA group (p= 0.032).

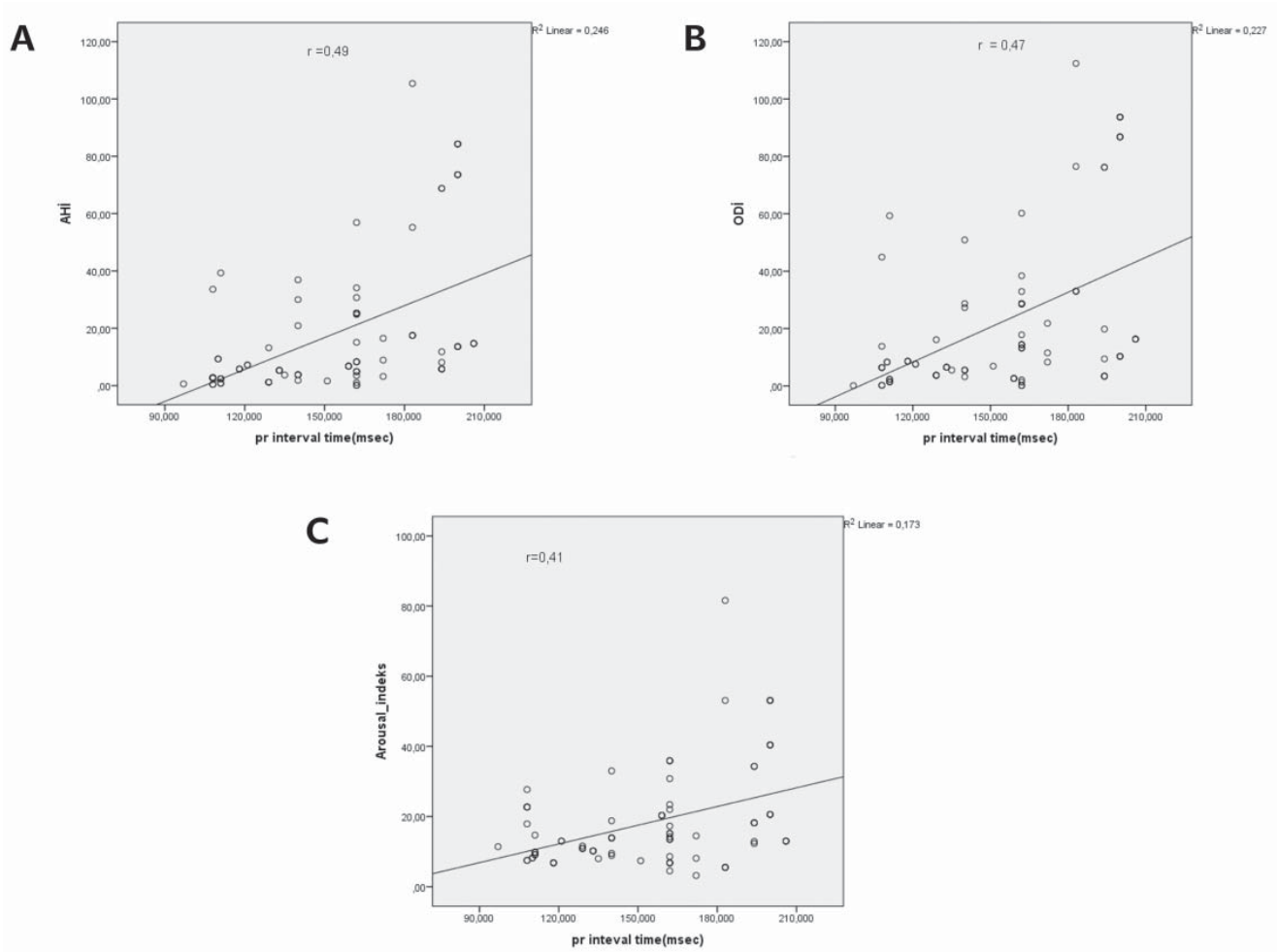

Figure 2. A,B,C. Correlation of PR interval with OSA severity parameters.

* Relationship of AHI with PR interval (r= 0.49); of ODI with PR interval (r= 0.47); and of arousal index with PR interval (r= 0.41).

DISCUSSION

The relationships between OSA and various cardiovascular diseases, such as hypertension, ischemic heart disease, and congestive heart failure, have been demonstrated. Thus, OSA is likely to occur in patients with cardiovascular disease. On the other hand, respiratory diseases related to sleep cause an arrhythmogenic effect in the relationship between respiratory and cardiovascular diseases.

A prolonged PR interval an arrhythmia observed in 1-2% of the healthy population generally has a good prognosis. However, if the PR interval is > 300 ms, intervention with a pacemaker may be required. The PR interval in patients in our study did not exceed 300 ms; therefore, no intervention was needed.

In our study, the PR interval was evaluated by ECG taken over a long period during a PSG investigation and was used to diagnose diseases associated with sleep. We separated our patients into two OSA severity groups and compared the PR interval between the groups. A significant increase in the PR interval was identified in patients with severe OSA compared to those with mild to moderate OSA. We found direct relationships between AHI, ODI and AI, which pathologically affect prolongation of the PR interval.

Many pathophysiological conditions can predispose patients with OSA to develop a prolonged PR interval, either directly or indirectly. Left ventricular diastolic dysfunction may develop in patients with OSA if these factors become severe, which can increase left atrial pressure indirectly, increase atrial size, and prolong the P wave[7].

Parasympathetic activity is dominant over heart rate during sleep in healthy subjects, whereas sympathetic and parasympathetic activities may dominate over heart rate in patients with OSA[8]. Respiratory events, such as apnea, hypopnea, and arousal, that occur during sleep in patients with OSA create arrhythmogenic effects, causing structural changes in the myocardium and other cardiac structures[9]. Adrenergic discharges occur as result of activation of the sympathetic system when a patient with OSA is exposed to intermittent

hypoxia[3]. The basis for the change in transmission of AV conduction is due to a dominant effect of arousal over autonomic neural conduction in the AV node. Arousal increases vagal tone in the transmission structures of the heart, which increases the PR interval. Maeno et al. demonstrated that apnea/hypopnea prolongs the P wave independently[10]. Somer et al. showed that baroreflex distortion and the increase of chemo-reflex response are due to sympathetic and parasympathetic changes in patients[11]. In addition, temporary increases in autonomic neural conduction in the atrium change pacemaker activity. As a result, distance increases between new evolved areas from the AV node[12]. These pacemaker shifts cause temporary changes in P waves on ECG.

Intrathoracic pressure fluctuations occur as a result of hyperventilation reoxygenation cycles and arousal that occur after hypoxia during sleep. These intrathoracic pressure fluctuations increase left atrial pressure[13]. The increased negative intrathoracic pressure increases venous return, leading to right atrial stress. Increased atrial stress causes atrial fibrosis, which disrupts atrial transmission[14].

In our study, we found correlations between prolongation of the PR interval and AHI, ODI, and AI, which are indications of hypoxia-reoxygenation severity. These results support the pathophysiological mechanisms discussed above.

We examined a heterogeneous sample group and conducted a PSG examination, which are gold standards for evaluating OSA. However, several limitations of our study should be mentioned. The ECG records were taken only at night; therefore, the PR interval could not be compared between day and night. We plan to evaluate 24-h ECG and PSG results in a future study for more comprehensive results.

OSA and other respiratory diseases associated with sleep represent a diversity of diseases that particularly affect the cardiovascular system.

CONFLICT of INTEREST

The authors declared no conflict of interest regarding the publication of this paper.

AUTHORSHIP CONTRIBUTIONS

Concept/Desing: HK
Analysis/Interpretation: HK
Data acquisition: HK
Writing: HK
Critical Revision: FA, RA
Final Approval: All of authors

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