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Research Article

Obstructive Sleep Apnea Syndrome in Acute Coronary Syndrome Patients

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ABSTRACT

Objective: There is increasing evidence linking obstructive sleep apnea syndrome (OSAS) with cardiovascular pathogenesis. OSAS diagnostic methodologies have recently come to standards, and there is not enough in-depth research in the field of sleep medicine and cardiology. In this study, we aimed to evaluate the presence of OSAS and its relationship with severity of coronary artery disease in patients with acute coronary syndrome (ACS).

Materials and Methods: 192 patients who applied with acute coronary syndrome and who underwent coronary angiography were included in the study. 96 patients were ST segment elevation myocardial infarction (STEMI) and 96 patients were non-ST segment elevation myocardial infarction (NSTEMI). SYNTAX scores of the patients were calculated. Patients were administered Berlin questionnaire and Epworth sleepiness score (ESS) before discharge. The scales were compared between the two groups and the patients' SYNTAX score.

Results: The rate of high risk patients according to Berlin questionnaire and ESS was found statistically significant in NSTEMI patients compared to the STEMI group ($p < 0.001$, $p = 0.023$). The total amount of points determined in Berlin questionnaire and ESS was statistically significant in NSTEMI patients compared to the STEMI group ($p < 0.001$). In Pearson correlation analysis, a significant positive correlation was found between the SYNTAX score and the total score determined in the Berlin questionnaire, and between the SYNTAX score and ESS ($r = 0.865$, $p < 0.001$ and $r = 0.761$, $p < 0.001$).

Conclusion: In this study, the relationship between OSAS and ACS was evaluated. Berlin questionnaire and ESS results were higher than the literature, and a positive correlation was found between the SYNTAX score and OSAS risk.

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Introduction

Obstructive sleep apnea syndrome (OSAS) has a close relationship with cardiovascular diseases [1]. Sleep Apnea; It has been found to be associated with increased risks of hypertension, heart failure, stroke / stroke and atrial fibrillation [1, 2]. Polysomnography is the gold standard for the diagnosis of sleep apnea [3]. Portable home monitoring with Type III portable polysomnography monitors is an alternative to make OSAS diagnosis more easily in different clinical situations [4]. In addition, a simpler alternative to the diagnosis of OSAS is to use validated and

validated questionnaires [5, 6]. The Berlin questionnaire and Epworth Sleepiness Scale (ESS) are the two most widely used of these surveys [5, 6]. The questions in these questionnaires were selected from risk factors or behaviours that consistently predict the presence of sleep apnea [5]. In studies conducted in various populations, OSAS has been found to be closely related to acute coronary syndrome (ACS) [7, 8]. The evaluation of OSAS diagnostic methodologies is still new and has not been thoroughly investigated in the field of cardiology [5, 6]. In this study, we aimed to evaluate the relationship between OSAS and

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coronary artery disease severity in ACS patients in our country, using the SYNTAX score and these two questionnaires.

Materials and Methods

A total of 192 patients, including 96 non-ST segment elevation myocardial infarction (NSTEMI) and 96 ST segment elevation myocardial infarction (STEMI), who applied with ACS at two different centers between March 2018 and July 2019, were included in the study. The most frequently used Berlin questionnaire and ESS were used in the literature on the day when patients were discharged after their treatment was completed [5, 6]. ESS is a test used to demonstrate daytime sleepiness. It consists of eight questions. Each question is filled by the patient by giving 0-3 points. If there is no possibility of falling asleep in all questions, it gets 0 if it is low, 2 if it is medium and 3 if it is high. If the total score is 10 or more, it indicates the presence of excessive daytime sleepiness. The Berlin questionnaire is a survey organized for OSAS community surveys. There are 10 questions in 3 categories in total. 2 points in categories 1 and 2 and ≥ 1 score in category 3 are considered significant. If each category is evaluated by itself and 2 or more categories are positive, OSAS risk is considered high. Age, weight, height, neck circumference, waist circumference of the patients were learned by using patient records and the hospital's automation system. Hypertension was defined as the detection of systolic blood pressure ≥ 140 mmHg and / or diastolic blood pressure ≥ 90 mmHg with at least two measurements or active use of antihypertensive drugs.

Diabetes mellitus defined fasting plasma glucose levels above 6.9 mmol / l or 11.1 mmol / l above any measurement or antidiabetic drug use. Hyperlipidemia was defined as 11.1 mmol / l or higher total cholesterol levels or a history of statin use. Patients who smoked before going to hospital were considered smokers. Patients with severe heart valve disease, acute rheumatic fever history, prosthetic valve, decompensated heart failure, malignancy, kidney or liver dysfunction, acute or chronic inflammatory disease, hematological disease and chronic obstructive pulmonary disease were excluded from the study. The study complies with the principles set out in the Helsinki Declaration and was approved by the local corporate ethics committee. The coronary angiography of the patients was performed using the Judkins technique (Siemens Axiom Artis Zee 2011; Siemens Healthcare, Erlangen, Germany) using the femoral or radial artery. Each coronary artery was evaluated in at least 2 positions. Based on this coronary angiography result, the SYNTAX score was calculated for all patients by an experienced interventional cardiologist unaware of the clinical or laboratory results of the patients. The SYNTAX score was determined for all coronary lesions with $> 50\%$ diameter stenosis in ≥ 1.5 mm vein, according to SYNTAX score calculator 2.1 (Link).

ESS is a test used to show daytime sleepiness. It consists of 8 questions in total. Each question is filled by the patient himself to give 0-3 points.

In this survey, the possibility of falling asleep in certain situations is questioned on an ordinary day when the patient is not overly tired. The scoring method is the same in all questions, it gets 0 if there is no possibility of falling asleep, 1 if it is low probability to fall asleep, 2 if it is medium probability and 3 if it is high probability. If the total score is 10 or more, it indicates the presence of excessive daytime sleepiness. Berlin questionnaire, on the other hand, is a questionnaire for OSAS societies. There are 10 questions in 3 categories in total. 2 points in categories 1 and 2 and ≥ 1 score in category 3 are considered significant. If each category is evaluated by itself and 2 or more categories are positive, OSAS risk is considered high.

Statistical Analysis

Statistical analyzes were performed with SPSS 20.0 (Statistical Package for Windows, Chicago, Illinois, USA) program. Kolmogorov-Smirnov test was used to examine the normal distribution of data. The numerical variables (normal-median) with normal distribution (non-parametric) median) and normal (non-parametric) median) values were expressed as percentages. Student-t test or Mann-Whitney U-test was used for numerical variables and chi-square test was used for analysis of categorical variables. It was considered significant for variables with $p < 0.05$.

Results

Basal features and laboratory parameters of the study groups are shown in (Table 1). In the ST segment elevation myocardial infarction (NSTEMI) group, the rates of diabetes mellitus, hypertension and family history of heart disease were higher than the ST segment elevation myocardial infarction (STEMI) group, but were not statistically significant. In the NSTEMI group, body mass index, neck and waist circumference levels were found higher than the STEMI group, but were not statistically significant ($p > 0.05$). In the NSTEMI group, the average SYNTAX score and ejection fraction rates were higher than the STEMI group ($p < 0.001$).

The rate of high-risk patients in NSTEMI patients compared to ESS was statistically significant compared to the STEMI group ($p = 0.024$). The total amount of points determined in ESS was statistically significant in NSTEMI patients compared to the STEMI group ($p < 0.001$). The rate of high-risk patients in NSTEMI patients compared to the Berlin questionnaire was statistically significant compared to the STEMI group ($p < 0.001$). The total amount of points detected in the Berlin questionnaire was statistically significant in NSTEMI patients compared to the STEMI group ($p < 0.001$). In the Pearson correlation analysis, a significant positive correlation was found between the SYNTAX score and the total score determined in the Berlin questionnaire, and between the SYNTAX score and ESS ($r = 0.644$, $p < 0.001$).

Table 1: Basal features and laboratory parameters of the study groups.

Variables	NSTEMI (n=96)	STEMI (n=96)	p value
Age (year)	60.2 \pm 4.6	59.6 \pm 4.5	0.723
BMI*, kg/m ²	29.3 \pm 12.1	28.6 \pm 12.1	0.345
Waist circumference, cm	90.41 \pm 8.53	87.23 \pm 5.14	0.412
Neck circumference, cm	37.46 \pm 3.11	35.89 \pm 3.19	0.648
Male gender, n (%)	60 (62.5)	65 (67.7)	0.506

Diabetes mellitus, n (%)	37 (39.1)	26 (27.1)	0.131
Hypertension, n (%)	37 (46.3)	27 (33.8)	0.107
Hyperlipidemia, n (%)	30 (37.5)	25 (31.3)	0.405
Cigarette, n (%)	44 (45.8)	45 (46.8)	0.525
Family history of heart disease	34 (42.5)	24 (30.0)	0.100
ESS total score	10.8 ± 5.2	6.1 ± 4.5	<0.001
ESS high-risk patient rate	46 (47.9)	32 (33.3)	0.024
Berlin questionnaire total score	3.2 ± 1.7	1.8 ± 1.4	<0.001
Berlin questionnaire high-risk patient rate	44 (45.8)	26 (27.1)	<0.001
SYNTAX score	14.6 ± 7.9	7.8 ± 4.3	<0.001
Ejection Fraction	53 ± 6.7	42 ± 10.6	<0.001

*BMI: Body mass index.

Discussion

In our study, it was found that the susceptibility to OSAS was high in the NSTEMI group. Thus, a positive correlation was found between SYNTAX score and OSAS risk in our study. One of the most important risk factors in cardiovascular diseases is increased sympathetic activity [9]. Findings from animal models and human studies have many evidence that OSAS is associated with increased sympathetic activation. In an experiment in rats, subjects' exposure to intermittent hypoxia for 14-30 days was associated with increased production of catecholamines and a significant increase in blood pressure [10]. In addition, in rats, chronic intermittent hypoxia has been observed to increase chemoreflex-induced sympathetic outflow through the renin-angiotensin system [11]. An experimental randomized controlled study provided data on the effects of intermittent hypoxia on the vascular system. In this study, 10 healthy men were exposed to intermittent hypoxia or a fake procedure for 6 hours a day; Average blood pressure increased by 4 mmHg after 4 days of hypoxia and nitric oxide derivatives decreased by 55%, which was associated with increased pressure and cerebral vascular resistance response to hypoxia [12]. Consistent with increased sympathetic activity, a study in OSAS patients observed high levels of peripheral nerve activity, plasma norepinephrine, and urinary catecholamines in patients [13].

Endothelial dysfunction is one of the key points in ACS pathophysiology [14]. There are studies showing that OSAS is associated with endothelial dysfunction and causes decreased endothelial repair capacity. In a study, endothelium-dependent vasodilation, measured by the blood flow of the forearm after intraarterial infusion of acetylcholine in patients with OSAS, was impaired compared to the normal control group [15]. In addition, the levels of circulating nitric oxide and endothelial progenitor cells required to maintain endothelial repair capacity decreased in patients with OSAS [16]. There is also a close relationship between the severity of coronary artery disease and inflammation [17]. In in vitro studies, in cell culture models of intermittent hypoxia, unlike continuous hypoxia, nuclear factor-mediated inflammatory pathways of kappa-B (nF-κB) are preferably activated on hypoxia-inducible factor (HiF) -1-dependent pathways [18]. In addition, the findings of numerous cross-sectional, case-control and non-randomized interventional studies have revealed that the levels of proinflammatory cytokine IL-6 and C-reactive protein increase in patients with OSAS and decrease with OSAS therapy [19, 20].

Therefore, OSAS has the potential to play a role in inflammatory pathophysiology by co-inflammatory disease. The results of the Berlin

questionnaire and ESS scale found at the end of our study were higher than the studies conducted in Poland and China [7, 8]. Comparing these populations with our study group, comorbidities such as mean BMI and accompanying diabetes mellitus were found to be higher in our study group, so higher results of Berlin questionnaire and ESS could be explained in our study group. In our study, the results of BUA and ESS scale were found higher in NSTEMI patients than in STEMI patients. In NSTEMI patients, comorbidities such as diabetes mellitus, hypertension, and obesity are more common than STEMI patients, and these comorbidities are in close relationship with OSAS [21].

Another important finding in our study was that the total number of answers given to the Berlin questionnaire and ESS questions in favor of OSAS showed a positive correlation with the SYNTAX score. SYNTAX score is the gold standard in determining the severity of coronary artery disease [22]. It was observed that total mortality and morbidity increased as the SYNTAX score increased in coronary artery patients. The findings of our study should be interpreted with some limitations. The sample size is relatively limited and OSAS pre-diagnosis was evaluated without using the gold standard sleep tests. In addition, patients were not followed up for a long time and cardiovascular endpoints were not determined. In this study, the relationship between OSAS and ACS was evaluated. Berlin questionnaire and ESS scale results were higher than general population and a positive correlation was found between SYNTAX score and OSAS risk. The results of the study show that OSAS risk should be taken into consideration in patients treated with ACS or followed up with coronary artery disease. However, in order to clarify this hypothesis, multicenter, large-scale, randomized and prospective studies are required.

Conflicts of Interest

None.

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