KARDİYAK KO-MORBİDİTESİ OLMAYAN OBSTRÜKTİF UYKU APNE SENDROMLU HASTALARDA SOL VENTRİKÜL FONKSİYONLARININ DEĞERLENDİRİLMESİ

ASSESSMENT OF THE LEFT VENTRICULAR FUNCTIONS IN OSAS PATIENTS WITHOUT CARDIAC CO-MORBIDITY

Burcu Oktay ARSLAN[1] Hikmet FIRAT[2] Ramazan AKDEMİR[3] Sadık ARDIÇ[4]

[1]SBÜ. Dr. Suat Seren Göğüs Hastalıkları ve Göğüs Cerrahisi E.A.H, Göğüs Hastalıkları ve Uyku Bozuklukları Merkezi, İzmir, Türkiye
[2]SBÜ Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları ve Uyku Bozuklukları Merkezi, Ankara, Türkiye
[3]Sakarya Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Sakarya, Türkiye
[4]İzmir Özel Can Hastanesi, Göğüs Hastalıkları ve Uyku Bozuklukları Merkezi, İzmir, Türkiye

Anahtar sözcükler: OUAS, Diyastolik disfonksiyon, kardiak ko-morbidite

Keywords: OSAS, diastolic dysfunction, cardiac co-morbidity

Geliş tarihi: 21 / 06 / 2018 Kabul tarihi: 11 / 02 / 2019

ÖZ

Amaç: *Obstrüktif uyku apne sendromunun (OUAS) belirgin kardiyak hastalık ve hipertansiyon olmaksızın myokardiyal fonksiyonları etkileyebileceği öne sürülmektedir. Bu çalışmada hipertansiyon ve kardiyak ko-morbiditeleri dışlanan OSAS'lı hastalarda sol ventrikül fonksiyonlarının değerlendirilmesi amaçlanmıştır.*

Yöntem ve Gereç: *OUAS ön tanısı ile hastanemiz uyku laboratuarına başvuran, koroner arter hastalığı myokard perfüzyon sintigrafisi ile dışlanan ve polisomnografik (PSG) tetkik ile OUAS tanısı alan 40 hasta çalışmaya dahil edildi. Kardiyak hastalık öyküsü ve risk faktörü bulunmayan, OUAS tanısı PSG tetkiki ile dışlanan 16 olgu ise kontrol grubunu oluşturdu. Tüm hastalara 2 boyutlu transtorasik ekokardiyografik tetkik uygulandı. Hasta ve kontrol grubu arasında ekokardiyografik parametreler açısından farklılıklar ve ekokardiyografik bulguların PSG sonuçları ile olan ilişkisi değerlendirildi.*

Bulgular: *Çalışmaya 56 vaka (16 kadın, 40 erkek) dahil edildi. Hasta ve kontrol grubu arasında yaş, cinsiyet, sigara içimi, beden kitle indeksi yönünden anlamlı farklılık saptanmadı (p>0.05). Ekokardiyografik parametreler değerlendirildiğinde;*

ABSTRACT

Aim: *Obstructive sleep apnea syndrome (OSAS) could have an influence on myocardial functions even before the development of hypertension and the other cardiovascular diseases. The purpose of this study was to evaluate the left ventricular functions of the patients with OSAS excluded from the diagnosis of HT and other cardiovascular diseases.*

Material and Methods: *Forthy patients diagnosed as OSAS with polysomnographic (PSG) analysis and in whom coronary artery disease was ruled out with myocardium perfusion scintigraphy were included in the study. Control group consisted of 16 volunteers in whom OSAS was excluded with PSG analysis. All patients underwent two dimensional trans-thoracic echocardiographic examinations. Differences between patient and control group with regard to echocardiograhic parameters and relation with PSG finding and echocardiographic parameters were evaluated.*

Results: *A total of 56 participants enrolled the study. There were no significant differences between patient and control group with regard to age, sex, smoking habits and body mass index.*

diyastol sonu sol ventrikül çapı (LVIDD) (p=0.01), sol atrium çapı (LAD) (p=0.008), aort çapı (AD) (p=0.006), stroke volüm (SV) (p=0.03) OSAS'lu hasta grubunda kontrol grubuna göre istatistiksel olarak anlamlı yüksek tespit edildi. Yapılan korelasyon analizinde AHI ile LVIDD, LAD, SV ve AD arasında ilişki tespit edilmedi (p>0.05). Bununla birlikte uykuda %90'ın altında geçirilen desaturasyon süresi ile LVIDD (p:0.02, r.0.347) ve SV (p:0.01, r:0.376) arasında pozitif yönde anlamlı bir korelasyon tespit edildi.

***Sonuç:** OUAS'lu hastalarda sol ventrikül diyastolik fonksiyon bozukluğu, uykuda hipoksik geçirilen süre ile ilişkili görünmektedir. Ekokardiyografik tetkik ile diyastolik fonksiyon bozukluğu tespit edilen ancak kardiyak yönden ek sorunu bulunmayan olgular OUAS açısından değerlendirilmelidir.*

When the echocardiographic parameters were evaluated; left ventricular internal dimension at the end of diastole (LVIDD), left atrial diameter (LAD), aortic dimension (AD) and stroke volume (SV) were significantly higher in patient group compare to control group (p=0.01, p=0.008, p=0.006, p=0.03 respectively). Additionaly, there was a significant positive correlation between the desaturation period spent under 90% and LVIDD (p:0.02, r=0.347) and SV (p=0.01, r=0.376).

***Conclusion:** Left ventricular diastolic dysfunction seems to be associated with the desaturation time spent under %90 in patients with OSAS. Patients in whom diastolic dysfunction was detected by echocardiographic examination without any other cardiac disease should be evaluated for OSAS.*

s not useful to predict PE patients in this study

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by repeated partial or complete closure of the upper airway during sleep (1). Prevalence of OSA in the general adult population ranged from 9% to 38% (2). Cardiovascular disturbances are the most important complications of OSAS that are related to increased mortality and morbidity (3,4). These complications include systemic and pulmonary hypertension, arrhythmias, heart failure, stroke and coronary artery disease (5). Systemic hypertension (HT) is the most common cardiac co-morbidity in patients with OSAS, the prevalence of which reaches 50% in this population (6). Age, diabetes mellitus and obesity are considered as an independent but additive factor associated with both OSAS and HT (7,8). These factors are also contributors to left ventricular diastolic dysfunction which is an important cause of cardiovascular morbidity (9,10). Coronary artery disease (CAD) is another common co-morbidity in OSAS patients that affects left ventricular (LV) functions (11). Left ventricular diastolic dysfunctions have been shown to be associated with OSAS (12). However, whether LV dysfunction in OSAS is a reality beyond HT has been explored extensively and remains controversial (10). It has been suggested that left ventricular dysfunction could occur even before the development of hypertension and the other cardiovascular manifestations of OSAS (12). Proposed mechanisms that affect cardiac performance in patients with OSA include mechanical and several ischemic effects such as neurohumoral, inflammatory, endothelial and oxidative effects (13). Repetitive episodes of obstructive events result in hypoxia, hypercapnia, increased sympathetic activation and large intra-thoracic pressure swings (14). Previous studies have discussed that all these consequences of apneic events might contribute the developing of systolic and diastolic dysfunctions (15).

The purpose of this study was to evaluate the left ventricular functions of the patients with OSAS excluded from the diagnosis of HT and other cardiovascular diseases.

METHODS

Patients

Consecutive patients who had not been diagnosed as having OSAS in the past and who had been admitted to the sleep laboratory of our clinic with the presumptive diagnosis of OSAS were included in the study. All patients underwent a standard questionnaire and physical examination. Patients with the history of cardiac, renal, immunological or other

systemic diseases, or those who were on drugs due to disease, were excluded from the study. All patients with the presumptive diagnosis of OSAS and without a previous history of systemic disease underwent the standard 16-channel polysomnographic analysis. OSAS was diagnosed as apnea–hypopnea index (AHI) ≥5 with at least one of the following complaints: (1) excessive daytime sleepiness and (2) witnessed apnea reported by the bed partner or family members. Patients with AHI≥5 and diagnosed with OSAS underwent myocardium perfusion scintigraphy to rule out coronary artery disease. After these investigations, 40 patients in whom OSAS was diagnosed and coronary artery disease excluded were included in the study. Those who did not meet these criteria were excluded from the study. The control group was composed of volunteers who did not have a history of cardiological disease and risk factors. They also underwent polysomnographic analysis to rule out OSAS. Sixteen subjects, in whom OSAS and CAD were eliminated, were included as control group. Fifthy six subjects who were included in the study underwent echocardiographic study.

Polysomnography

Sixteen-channel [electroencephalography, electro-oculography, electromyography of the chin and the leg (anterior tibialis), electrocardiography, oxygen saturation (from fingertips), respiratory effort (thoracic, abdominal) and nasal air flow (nasal pressure transducer), body position and tracheal microphone] polysomnography recordings were obtained for 6–8 h with the Embla ®-flaga instrument. Polysomnography recordings were analyzed by a physician experienced in sleeping disorders using Somnologica 3.2 software. Patients with a minimal sleep efficacy of 60% were included. Apnea was defined as complete cessation of airflow for at least 10 s; hypopnea was defined as a 30% decrease in airflow accompanied by development of at least 4% drop in oxygen saturation, or 50% decrease in airflow accompanied by development of arousal or at least 3% drop in oxygen saturation (16). The diagnosis of obstructive sleep apnea syndrome was defined by AHI. All the apneas and hypopneas scored in the study were obstructive in type. Desaturation period spent under 90% during sleep and oxygen desaturation index was also recorded.

Echocardiography

All patients underwent a complete two-dimensional trans-thoracic echocardiographic evaluation from multiple windows. Echocardiographic evaluations were performed at day time in all patients. All studies were performed with Vivid-3 echocardiograph and a 2.5 MHz transducer. Echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography. Studies were recorded on compact disks for storage and review. Two-dimensional echocardiographic calculations were obtained by parasternal long axis, apical three and four chamber views. Left ventricular ejection fraction (LVEF) was calculated by Teicholz formula. Left ventricular internal dimension at the end of diastole (LVIDD), left atrial diameter (LAD), aortic dimension (AD) and stroke volume (SV) were calculated. Left atrial maximal and minimal volume calculated and left atrial ejection fraction were calculated as the ratio of end diastolic area to end-systolic area of the left atrium using apical three chamber views.

All the participants signed written informed consent to participate to the study. The study complied with the declaration of Helsinki and was approved by the local research ethics committee (Diskapi Yildirim Beyazit Training and Research Hospital-2009/2).

Statistical analyses

The analysis of the data was carried out using the SPSS 11.5 software. Continuous variables were shown as mean ± standard deviation or

median (min–max), while categorical variables were expressed with percentile band. The Shapiro–Wilks test was used to investigate whether or not continuous variables showed parametric distribution, and the Student's t test or the Mann–Whitney test were utilized to assess whether or not there was a significant difference between groups in terms of measured characteristics. The significance of the linear correlation between continuous variables was evaluated with the Spearman correlation test. The chi-square or Fisher's exact test was used for categorical comparisons. A p value of <0.05 was considered to be statistically significant.

RESULTS

A total of 56 participants enrolled in the study. Control group consisted of 16 subjects with AHI<5 events/hours. 40 patients with AHI≥5 events/hour were included in the study as the patient group. The mean age of the entire study population was 47.4 ± 8.0. There were no statistically significant differences between patient and control group with regard to age, sex, smoking habits and body mass index (BMI). None of the patients had a history of hypertension, coronary artery disease, congestive cardiac failure, chronic obstructive pulmonary disease, diabetes mellitus or any other systemic diseases. None of the patients was on medical treatment due to any reason. The demographic characteristics of the study population were demonstrated in Table 1.

All the echocardiographic parameters of the entire study population were found in normal range. However, a significant difference was found in left ventricular internal dimension at the end of diastole (LVIDD), left atrial diameter (LAD), aortic dimension(AD) and stroke volume(SV) between patient and control group (p=0.01, p=0.008, p=0.006, p=0.03 respectively). Echocardiographic parameters of the patient and the control group were illustrated in Table 2.

Table 1. Demographic characteristics of the study population.

	Control group (n=16)	Patient group (n=50)	P value
Age (year)	44.5±4.8	48.6±8.8	>0.05
Male gender, n (%)	14(73.6)	37(74)	>0.05
BMI* (kg/m2)	28.6±2.8	29.3±3.5	>0.05
Current smoker, n(%)	25% (n=4)	27.5% (n=11)	>0.05

*BMI: body mass index

Table 2. Echocardiographic parameters of the patient and control group

ECO paremeters	Control Group	Patient Group	P value
LVIDD,(mm)	4.55±0.29	4.79±0.31	0.001
LVIDS,mm	3.12±0.18	3.18±0.23	>0.05
LVSD,mm	1.05±0.05	1.07±0.06	>0.05
LVPWD,mm	1.06±0.05	1.07±0.06	>0.05
EF,%	60±2.8	62±4.8	>0.05
FS,%	32.2±2.01	32.3±5.7	>0.05
SV, ml	60.6±6.5	66.3±9.4	0.003
LAD,mm	2.95±0.15	3.07±0.14	0.008
AD,mm	2.9±0.17	3.11±1.8	0.006

LVIDD: left ventricular internal dimension at the end of diastole, LVIDS: left ventricular internal diameter in systole, LVSD: left ventricular systolic diameter, LVPWD: left ventricular posterior wall dimension, EF: left ventricular ejection fraction, FS: left ventricular fraction shorting, SV: stroke volume, LAD: left atrium dimension, AD: aortic dimension.

When the relation between echocardiographic parameters and PSG findings were evaluated, no significant correlation was found between LVIDD, LAD, AD, SV and sleep parameters including apnea hypopnea index, number of apnea and hypopnea ($p>0.05$). Similarly, no correlation was found between the desaturation period spent under 90%, LAD and AD in patients with OSAS. However, there was a weak but positive correlation between the desaturation period spent under 90% and LVIDD ($p=0.02$, $r=0.347$) and SV ($p=0.01$, $r=0.376$) (Figure 1).

DISCUSSION

The primary objective of the current study was to investigate the early echocardiographic alterations in patients with OSAS who had no other detected cardiovascular diseases. For this purpose, baseline echocardiographic examination was performed on participants. LVIDD, LAD, AD and SV were significantly higher in patient group compared to control group. Additionally, statistically significant correlation was found between the desaturation period spent under 90% and LVIDD and SV.

There are several studies evaluating the cardiac functions by echocardiography in subjects with obstructive sleep apnea syndrome. Enlarged left atrial size is one of the impaired diastolic function markers in patients with OSAS (17). In one study, it was shown that 64% of patients had left atrial enlargement with severe OSAS (18). In supporting these finding, LAD was found higher in patients with OSAS in the current study. Also LA enlargement is frequent in the normotensive, otherwise healthy obese and correlates well with LV mass (19). Increased left ventricular mass is associated with left ventricular diastolic dysfunction (15). Increase in LVIDD was reported in patients with cardiac heart failure (CHF) and OSAS was significantly greater than that in patients with isolated CHF (20). Another study found no relation between OSAS and LVIDD (21). Increase in LVIDD is also associated with left ventricular diastolic dysfunction. Stroke volume is the difference between the end diastolic volume and the end systolic volume. Increase in the end-diastolic

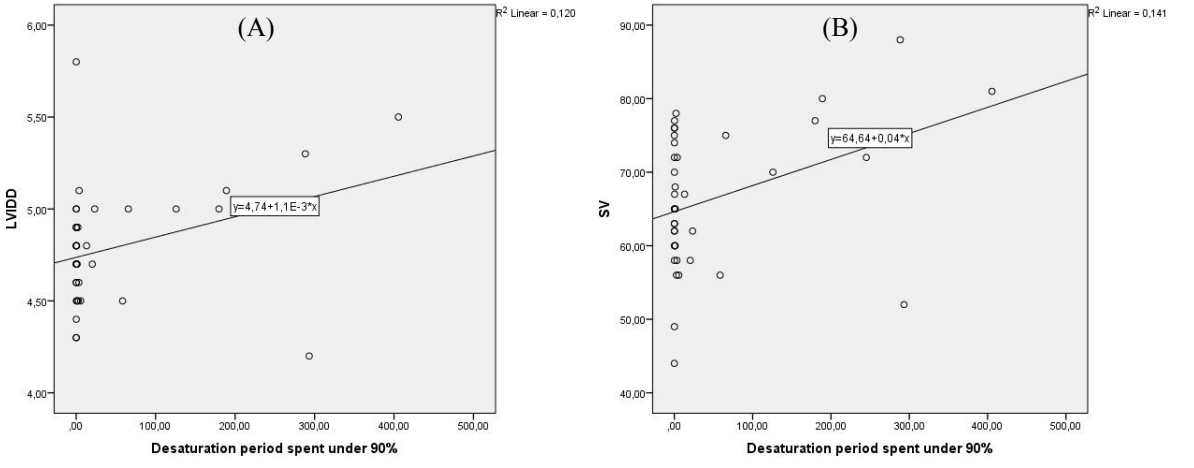

Figure I (A). Scatter plot graph of desaturation period spent under 90% and LVIDD. **(B).** Scatter plot graph of desaturation period spent under 90% and SV.

LVIDD: left ventricular internal dimension at the end of diastole
SV: stroke volume

volume, increased sympathetic stimulation could result in increased stroke volume (22). At the early stages of the diastolic dysfunction, stroke volume may be increased. Increase in aortic diameter could be due to increased stroke volume. Left ventricular diastolic dysfunction is common in hypertensive OSAS patients (12). In this study it was shown that even in the absence of hypertension and any other cardiovascular disease, left ventricular diastolic functions could be effaced in OSAS patients. Potential risk factors for left ventricular dysfunction include coronary artery disease, valvular heart disease, obesity, aging and diabetes mellitus. In the present study, the presence of CAD was ruled out by myocardium perfusion scintigraphy. None of the patient had hypertension and diabetes mellitus. There was no statistically significant difference regarding BMI and age between patient and control groups.

Studies have reported relationship between severity of OSAS and left ventricular diastolic dysfunction. Same of the studies have shown positive correlation between LVDD and AHI reflecting the severity of OSAS (23,24,12). Two studies have suggested that nadir arterial oxygen saturation but not AHI was associated with the LV diastolic function markers (25,26). In this study we have found a positive correlation between the desaturation period spent under 90% and LVIDD and SV. Although it is not clear the mechanism underlying diastolic dysfunction in OSA patients, hypoxemia seems to play an important role in this relation.

Ischemic effects of apneic events have been studied by several investigators. Hypoxemia due to obstructive events causes neurohumoral, inflammatory, endothelial and oxidative consequences. All these consequences may contribute to cardiovascular derangements (27). Apnea related to hypoxemia also increases sympathetic nervous system activity that results in systemic vasoconstriction and increased left ventricular (LV) after load (28) .Elevations in nocturnal blood pressure and sympathetic nervous system activity in OSAS subjects create ventricular pressure overload (29). Recurrent LV strain over several hours of apneic events may lead to chronic daytime LV dysfunction. Hypoxemia related to apnea can also impair LV myocardial contractility (30). However, not only ischemic effects but also mechanical effects of obstructive apnea have been mentioned in relation with echocardiographic alterations by previous studies. In patients with OSA during apneic event, large negative intra-thoracic pressures are generated during inspiratory efforts which increase transmural pressures across the myocardium, thus increasing after load (31). Another consequence of the increased negative intra-thoracic pressures is the leftward shift of the interventricular septum related to enhanced venous return and right ventricle dilatation. All of these effects of enhanced negative intra-thoracic pressure have been demonstrated to affect left ventricular functions(32). It is possible that if these effects are repeated over months or years (as occurs in OSA), then susceptible individuals might develop sustained left ventricular dysfunction (33).

The potential limitations of the current study must be addressed. Baseline echocardiographic examination was performed for this study. Because of this we were not able to evaluate the detailed echocardiographic parameters. Additionally, we also had relatively small sample size.

In conclusion; left ventricular diastolic functions could be effaced in patients with OSAS even in the absence of hypertension and any other cardiovascular disease. Left ventricular diastolic disfunction seems to be associated with the desaturation time spent under %90. Patients in which diastolic dysfunction was detected by echocardiographic examination without any other cardiac disease should be evaluated for OSAS.

KAYNAKLAR

1. Shahar E, Whitney C, Redline S, Lee E, Newman A, Javier Nieto F, O'Connor G, Boland L, Schwartz J, Samet J. Sleep-disordered breathing and cardiovascular disease: Cross-sectional results of the sleep heart health study. Am J Respir Crit Care Med 2001;163:19-25.
2. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage SC. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev 2017;34:70-81.
3. Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: A 7-year follow-up. Am J Respir Crit Care Med 2002;166:159-65.
4. Marin J, Carrizo S, Vicente E, Agusti A. 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;365:1046-53.
5. Vrints H, Shivalkar B, Hilde H, Vanderveken OM, Hamans E, Van de Heyning P, De Backer W, Verbraecken J. Cardiovascular mechanisms and consequences of obstructive sleep apnoea. Acta Clin Belg 2013;68(3):169-78.
6. Peppard PE, Young T, Palta M, Skatrud J. Prospective study ofthe association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378-84.
7. Duran J, Esnaola S, Rubio R, Iztueta A. Obstructive sleep apnea hypopnearelated clinical features in a population-basedsample of subjects aged 30 to 70 yr. Am J Respir Crit Care Med 2001;163:685—9
8. Pedrosa RP, Drager LF, Gonzaga CC, et al. Obstructive sleepapnea: the most common secondary cause of hypertension associated with resistant hypertension. Hypertension 2011;58:811-7.
9. Wachtell K, Palmieri V, Gerdts E, et al. Prognostic significance of left ventricular diastolic dysfunction in patients with left ventricular hypertrophy and systemic hypertension (the LIFE Study). Am J Cardiol 2010;106:999-1005.
10. Bodez D, Damy T, Soulat-Dufour L, Meuleman C, Cohen A. Consequences of obstructive sleep apnoea syndrome on left ventricular geometry and diastolic function. Arch Cardiovasc Dis 2016;109(8-9):494-503. doi: 10.1016/j.acvd. 2016.02.011.
11. Zhang J, Song Y, Ji Y, Song Y, Cai S, Yu Y, Liu S, Zhang W. Correlation between coronary artery disease and obstructive sleep apnea syndrome and analysis of risk factors. Exp Ther Med 2018;15(6):4771-6.
12. Aslan K, Deniz A, Cayli M, Bozdemir H, Sarica Y, Seydaoglu G. Early left ventricular functional alterations in patients with obstructive sleep apnea syndrome. Cardiol J 2013;20(5):519-25.
13. Arias M, García-Río F, Alonso-Fernández A, Mediano O, Martínez I, Villamor J. Obstructive sleep apnea syndrome affects left ventricular diastolic function: Effects of nasal continuous positive airway pressure in men. Circulation 2005;112:375-83.
14. Shivalkar B, Van de Heyning C, Kerremans M, Rinkevich D, Verbraecken J, De Backer W, Vrints C. Obstructive sleep apnea syndrome: More insights on structural and functional cardiac alterations, and the effects of treatment with continuous positive airway pressure. J Am Coll Cardiol 2006;47:1433-9.
15. Niroumand M, Kuperstein R, Sasson Z, Hanly P. Impact of obstructive sleep apnea on left ventricular mass and diastolic function. Am J Respir Crit Care Med 2001;163:1632-6.
16. American Academy of Sleep Medicine: International Classification of Sleep Disorders: Diagnostic and Coding Manual ne. Westchester, Ill, American Academy of Sleep Medicine, 2005.
17. Dursunoglu D, Dursunoglu N, Evrengül H, et al. Impact of obstructive sleep apneoa on left ventricular mass and global functions . Eur Respir J 2005;26:283-8.
18. Cloward T, Walker J, Farney R, Anderson J. Left ventricular hypertrophy is a common echocardiographic abnormality in severe obstructive sleep apnea and reverses with nasal continuous positive airway pressure. Chest 2003;124:594-601.
19. Sasson Z, Rasooly Y, Gupta R, Rasooly I. Left atrial enlargement in healthy obese: Prevalence and relation to left ventricular mass and diastolic function. Can J Cardiol 1996;12:257-63.

20. hen Q, Xu D, Lin S, Lai W. [sleep-disordered breathing and left ventricular remodeling in patients with chronic heart failure]. Nan Fang Yi Ke Da Xue Xue Bao 2006;26:486-9.

21. Varol E, Akcay S, Ozaydin M, Ozturk O, Cerci SS, Sahin U. Influence of obstructive sleep apnea on left ventricular mass and global function: sleep apnea and myocardial performance index. Heart Vessels 2010; 25(5): 400-4.

22. De Backer D. Stroke volume variations. Minerva Anestesiol. 2003;69(4):285-8.

23. Altintas N, Aslan E, Helvaci A, Malhotra A. Relationship between obstructive sleep apnea severity index and left ventricular function and volume. Ann Saudi Med 2012; 32(4): 384–90.

24. Akar Bayram N, Çiftçi B, Durmaz T, et al. Effects of continuous positive airway pressure on left ventricular function assessed by tissue Dopples imaging in patients with obstructive sleep apnoea syndrome. Eur J Echocardiogr 2009; 10(3):376-82.

25. Kraiczi H, Peker Y, Caidahl K, Samuelsson A, Hedner J. Blood pressure, cardiac structure and severity of obstructive sleep apnea in a sleep clinic population. J Hypertens. 2001 Nov;19(11):2071-8.

26. Chan J, Sanderson J, Chan W, et al. Prevalence of sleep-disordered breathing in diastolic heart failure. Chest 1997;111(6):1488-93.

27. McNicholas W, Bonsigore M, Bonsignore M. Sleep apnoea as an independent risk factor for cardiovascular disease: Current evidence, basic mechanisms and research priorities. Eur Respir J 2007;29:156-78.

28. Fletcher E. Invited review: Physiological consequences of intermittent hypoxia: Systemic blood pressure. J Appl Physiol 2001;90:1600-5.

29. Bradley T, Hall M, Ando S, Floras J. Hemodynamic effects of simulated obstructive apneas in humans with and without heart failure. Chest 2001;119:1827-35.

30. Laaban J, Pascal-Sebaoun S, Bloch E, Orvoën-Frija E, Oppert J, Huchon G. Left ventricular systolic dysfunction in patients with obstructive sleep apnea syndrome. Chest 2002;122:1133-8.

31. Dursunoglu N, Dursunoglu D, Ozkurt S, et al. Effects of cpap on left ventricular structure and myocardial performance index in male patients with obstructive sleep apnoea. Sleep Med 2007;8:51-9.

32. Virolainen J, Ventilä M, Turto H, Kupari M. Effect of negative intrathoracic pressure on left ventricular pressure dynamics and relaxation. J Appl Physiol 1995;79:455-60.

33. Dursunoğlu D, Dursunoğlu N. Cardiovascular diseases in obstructive sleep apnea. Tuberk Toraks 2006;54:382-96.

Yazışma Adresi:

Dr. Burcu Oktay Aslan
SBÜ. Dr. Suat Seren Göğüs Hastalıkları ve Göğüs Cerrahisi E.A.H, Göğüs Hastalıkları ve Uyku Bozuklukları Merkezi, İzmir, Türkiye
dr.arslanburcu@gmail.com