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Echocardiographic evaluation may provide more accurate patient selection for polysomnography in patients with obstructive sleep apnea: Predicting the severity of disease by echocardiography

Tıkayıcı uyku apnesi olan hastalarda ekokardiyografik değerlendirme polisomnografi için daha doğru hasta seçimi sağlayabilir: Ekokardiyografi ile hastalığın şiddetini tahmin etme

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ABSTRACT

Aim: Obstructive sleep apnea (OSA) may influence the cardiac function by several mechanisms. The aim of the present study was to evaluate the impact of OSA on left and right cardiac function and determine the echocardiographic parameters which can help to predict the severity of OSA.

Methods: In this cross-sectional analysis, 60 patients with suspected OSA were evaluated with transthoracic echocardiography before polysomnography between January and June 2017. On the basis of apnea-hypopnea index (AHI), the patients were classified into non-severe (AHI<30) (n = 30) and severe (AHI≥30) OSA (n = 30). The correlation between echocardiographic parameters and the apnea-hypopnea index (AHI) / Epworth Sleepiness Scale (ESS) was assessed.

Results: Regarding left ventricular (LV) echocardiographic parameters: left ventricular outflow (LVOT) proximal diameter, left ventricular mass index, posterior wall enddiastolic diameter (PWEDD) and interventricular septum enddiastolic diameter (IVSEDD) were significantly higher in severe OSA patients. With respect to right ventricular (RV) functional parameters: RV fractional area change (RVFAC) and myocardial performance index (MPI) values were significantly higher in severe OSA patients. We found significant positive correlations between AHI and LVOT proximal diameter, IVSEDD, RVMPI, RV E and A velocities, body mass index, neck circumference and ESS. By using the model created with 'PWEDD, LVOT diameter and RV A velocity' we were able to predict most of the patients' group correctly before polysomnography.

Conclusion: We conclude that we can predict the severity of the disease in patients with suspected OSA by using echocardiography.

ÖZ

Amaç: Tıkayıcı uyku apnesi (TUA) çeşitli mekanizmalarla kalp fonksiyonunu etkileyebilir. Bu çalışmanın amacı, TUA'nın sol ve sağ kalp fonksiyonu üzerindeki etkisini değerlendirmek ve TUA'nın ciddiyetini öngörmede yardımcı olabilecek ekokardiyografik parametreleri belirlemektir.

Yöntemler: Bu kesitsel analizde Ocak ve Haziran 2017 ayları arasında TUA şüphesi olan 60 hasta polisomnografi öncesi transtorasik ekokardiyografi ile değerlendirildi. Apne-hipopne indeksine (AHİ) dayanarak, hastalar ağır olmayan (AHI <30) (n=30) ve ağır (AHI≥30) TUA (n=30) olarak sınıflandırıldı. Ekokardiyografik parametreler ile apne-hipopne indeksi (AHİ) / Epworth Uykululuk Skalası (ESS) arasındaki korelasyon değerlendirildi. Regresyon analizi ile TUA ciddiyetini ön gördürebilecek model araştırıldı.

Bulgular: Sol ventrikül (LV) ekokardiyografik parametreler ile ilgili olarak; sol ventrikül çıkış akımı (LVOT) proksimal çapı, sol ventrikül kitle indeksi, arka duvar diyastol sonu çapı (ADDSÇ) ve interventriküler septum diastol sonu çapı (IVSDSÇ) ağır OSA hastalarında anlamlı olarak yüksek bulundu. Sağ ventrikül (RV) fonksiyonel parametrelerine göre; Sağ ventrikül fraksiyonel alan değişimi (SağVFAC) ve miyokardiyal performans indeksi (MPI) değerleri ağır OSA hastalarında anlamlı olarak yüksek bulundu. AHI ve LVOT proksimal çapı, IVSDSÇ, SağVMPI, SağV E ve A hızları, vücut kitle indeksi, boyun çevresi ve ESS arasında anlamlı pozitif korelasyon bulundu. "ADDSÇ, LVOT çapı ve SağV A hızı" ile oluşturulan modeli kullanarak, hastaların çoğunu polisomnografi öncesi doğru şekilde tahmin etmeyi başardık.

Sonuç: TUA şüphesi olan hastalarda ekokardiyografi kullanarak hastalığın ciddiyetini tahmin etmek mümkün olabilir.

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INTRODUCTION

Obstructive sleep apnea (OSA) is the most common form of sleep-related breathing disorders. It is characterized by repeated partial or complete closure of the pharynx, gasping episodes, unrefreshing sleep and excessive daytime sleepiness. It is defined by as the occurrence of more than five apneas / hypopneas per hour in polysomnography [1]. OSA is highly prevalent in the general population, affecting at least 9-15% of middle aged adults [2]. Definitions of OSA are based on respiratory and neurophysiological indices but recent data show that cardiovascular consequences may be more serious. It is associated with an increase in cardiovascular morbidity and mortality due to complications such as systemic and pulmonary hypertension, coronary artery disease, heart failure and arrhythmias [3]. The risk of cardiovascular complications appears to be mediated by the complex interaction between the mechanical and chemical effects (hypoxia, hypercapnia) or repetitive upper airway closure and its effect on the autonomic nervous system [4]. Studies have assessed the effects of OSA on the left ventricle (LV) [3]. Early determination of right ventricular (RV) dysfunction and pulmonary hypertension in patients with OSA is also important, although data on RV dysfunction and structural changes in this group of patients are limited. Recently, several echocardiographic studies have reported alterations in the structure and function of RV in patients with OSA, but the outcomes from these studies have been inconsistent [4]. Most of the studies were small and assessed few echocardiographic parameters, whereas large, randomized, controlled trials evaluating the impact of OSA on the alterations of the RV are lacking.

Accurate evaluation of RV morphology and function remains challenging in clinical practice due to its complex geometric shape. Although cardiac magnetic resonance imaging is considered as the gold standard for morphological and functional assessment of the right ventricle, conventional echocardiography remains the first-resort imaging modality in routine clinical practice due to its low-cost, safety, noninvasive nature and simplicity [5-6]. Novel techniques, including 2D and 3D speckle-tracking echocardiography, are very sensitive and can reveal alterations in RV structure and function in early disease stages. However, these techniques require expertise and have not been extensively validated for the assessment of RV function.

There is no 'gold standard' for the diagnosis of OSA, which makes it difficult to calibrate any test for diagnosis. Traditionally, polysomnography (PSG) in an attended setting (sleep laboratory) has been used as a reference standard for the diagnosis of OSA. Polysomnography measures several sleep variables, one of which is the apnea-hypopnea index (AHI), which is defined as the apneas and hypopneas per hour of sleep. The AHI has been widely used to diagnose OSA. The Epworth sleepiness scale (ESS), is a simple, self-administrated questionnaire which is shown to provide a measurement of the subject's general level of daytime sleepiness [7]. Polysomnography laboratories are very busy all over the world and patients have to wait for a long time to have the test. Therefore, a method that would facilitate proper patient selection for polysomnography would be very useful.

In this study, we aimed to investigate the impact of untreated OSA on left and right ventricular function as measured with echocardiography, the correlation between echocardiographic parameters and AHI/ESS and determine the echocardiographic parameters which can predict severe OSA. To the best of our knowledge, this is the first study that investigates the predictor echocardiographic parameters for severe OSA.

MATERIALS AND METHODS

Study population

Between January and June 2017, 60 patients with suspected OSA undergoing polysomnography were included in the study. They had symptoms including snoring, witnessed apnea and daytime sleepiness. All patients had to provide written, informed consent prior to inclusion in the study, which was approved by the local ethics committee.

Pulmonary function tests of all participants were evaluated. Individuals who had a sleep-related respiratory disease other than OSA, diagnosed pulmonary disease, left ventricular dysfunction (EF<50%), ischemic or valvular heart disease,

atrial fibrillation, or renal insufficiency (serum creatinine >2 mg/dl), were excluded.

All patients were subjected to a thorough clinical and laboratory evaluation. Echocardiographic examinations for the detection of LV/RV function were performed before the polysomnography and ESS evaluations. Echocardiographic examinations were performed exclusively for this study by two experienced physicians, with the exception of routine practice in patients scheduled for polysomnography. All patients underwent overnight polysomnography using a standard technique and the average AHI was calculated [8]. On the basis of AHI, patients were classified into non-severe (AHI < 30) and severe (AHI ≥ 30) OSA groups [9]. The ESS score was calculated for each patient using the Turkish version of the validated ESS questionnaire [10]. Body mass indices (BMI) of the patients were calculated as weight (kg) divided by the height-squared (m^2). Neck circumferences were also measured.

Echocardiography

Echocardiographic examinations were performed with a 2-4 MHz transducer attached to a Vivid S5 echocardiography machine (GE, Norway). Single lead electrocardiography was recorded continuously during the examination in the left lateral decubitus position. All measurements were taken at 3 consecutive cycles and the averages were recorded. Analysis was performed according to the recommendations found in the guidelines of the American Society of Echocardiography.

Left ventricular end-diastolic and end-systolic diameters (LVEDD, LVESD), interventricular septum and posterior wall end-diastolic diameters (IVSEDD, PWEDD) and left ventricular outflow tract (LVOT) proximal diameters were measured in the parasternal long axis view [11]. EF was calculated according to the Simpson formula. The left atrium (LA) diameters were calculated in the parasternal long axis and apical 4-chamber views. IVSEDD, PWEDD and internal diameters were used to calculate LV mass (LVM) using the following equation:

LVM = 1.04 x 0.8 [(LV Wall thickness + internal dimension) - (internal dimension)] + 10.6 [12].

BSA was calculated using the Sclich formula, which varies according to gender [13]. To evaluate the diastolic functions of the LV, the mitral inflow velocities were evaluated from the apical 4-chamber view. The early diastolic velocity of the lateral mitral annulus (Em) was recorded with tissue Doppler imaging (TDI).

Right ventricular diameters were measured in the parasternal long axis and apical 4-chamber views. Systolic pulmonary arterial pressure (sPAP), fractional area change (FAC), Sm velocity, tricuspid annular plane systolic excursion (TAPSE), TDI-derived myocardial performance index (MPI), tricuspid E wave velocity, A wave velocity, deceleration time (DT), E/A ratio, Ea velocity and Ea/Aa ratio were measured.

The maximal tricuspid regurgitation velocity was measured by continuous-wave Doppler echocardiography from the apical 4-chamber view. Systolic pulmonary pressure was calculated as follows:

4X (tricuspid systolic jet)^2 + right atrial pressure.

Early (E) and late (A) right ventricular inflow velocities were measured with pulsed wave Doppler by placing the sample volume in between the tips of the tricuspid valve in the apical 4-chamber view.

Pulsed wave TDI was obtained in the apical 4-chamber view by placing a 5-10 mm sample volume at the lateral side of the tricuspid annulus. Measurements were recorded during end-expiratory apnea [14]. On the TDI images annular peak systolic velocity (S'), early (Ea) and late (Aa) (peak annular diastolic velocities) and systolic velocity duration were measured as ejection time (ET), isovolumetric relaxation time (IVRT, time between the end of ET and the beginning of E') and isovolumetric contraction time (IVCT, time between the end of Aa and the beginning of ET) were measured. Tricuspid valve closure and opening time (TCO), which was measured from the cessation of the Aa wave to the beginning of the Ea wave, encompassed IVCT, ET and IVRT. The TDI-derived MPI, as a global estimate of both systolic and diastolic functions of the RV, was calculated with the following formula :

TDI-MPI = (TCO-ET)/ET [15].

TAPSE was calculated by placing an M-mode cursor through the tricuspid annulus and measuring the amount of longitudinal motion of the annulus at peak systole in the apical 4-chamber view.

RV FAC was obtained by tracing the RV endocardium both in end-systole and end-diastole from the annulus, along with the free wall to the apex, and then back to the annulus along with the interventricular septum in the apical 4-chamber view. RV FAC was calculated using the following formula:

FAC = (end-diastolic area - end-systolic area) / end-diastolic area x 100 [16].

Polysomnography Analysis

Full-night polysomnographic recording was applied with a Grass-telefactor - PMA AS40 in the sleep laboratory. Polysomnographies were scored manually by the same examiner. Measured parameters included electroencephalography (C4/A1, O2/ A1, F4/A1, F3/A2), electro-oculography, electrocardiogram, oronasal airflow - either by nasal cannula or thermal sensors - pulse oximetry, thoracoabdominal movements, submental and pretibial electromyography and snoring noises. Staging was performed according to the guidelines of the American Sleep Academy Association 2012 criteria [17].

Statistical Analysis: Data are presented as mean ± standard deviation for normally distributed continuous variables, median (minimum-maximum) for non-normally distributed continuous variables and count, percentages for categorical variables. The differences in categorical variables between groups were compared using the Chi-Square test. Normally distributed continuous variables were evaluated by the Student's t test. The degree of association between continuous variables was calculated by the Pearson's correlation coefficient. A multiple logistic regression was performed to identify the independent risk factors of outcome variable. Receiver operating characteristic (ROC) curves were used to describe the performance of diagnostics value of continuous variables. P-value <0.05 was considered statistically significant.

RESULTS

Clinical characteristics: A total of 60 patients were enrolled in the study. Among the 60 patients included, the median age was 50.9 ± 13.7 years and 34 patients (56.6%) were male. The mean AHI value was 34.06 ± 25.3. The patients were classified as severe OSA (AHI≥30) (n= 30) and non-severe OSA (AHI<30) (n=30). Both study groups were similar with regard to age, gender, the prevalence of hypertension and diabetes, smoking year, blood pressure, body mass index (BMI) and heart rate values (p > 0.05). Neck circumference values were higher in the severe OSA group (40.2 ± 3.8 vs. 37.7 ± 4.4, p=0.021, respectively). The baseline demographic and clinical data are presented in Table 1.

Table 1. General characteristics of the patients

	AHI ≥30 n:30	AHI <30 n:30	P
Male gender (n, %)	20 (66.7)	14 (46.7)	0.118
DM (n, %)	9 (30.0)	8 (26.7)	0.774
HT (n, %)	13 (43.3)	7 (23.3)	0.100
Smoke (n, %)	16 (53.3)	15 (50.0)	0.796
FH (n, %)	6 (20.0)	11 (36.7)	0.152
Age (years)	53.6 ±14.0	48.2±13.0	0.130
Sys BP (mmHg)	143.3 ±22.6	136.0 ±25.2	0.241
Dia BP (mmHg)	90.0+14.6	84.3+12.3	0.110
BMI (kg/m2)	31.8 ± 6.9	28.9 ±5.4	0.064
Neck Circumference (cm)	40.2 ± 3.8	37.7 ± 4.4	0.021*
Heart Rate	81.2 ±10.3	75.9 ±11.4	0.063
ESS	6.63 ± 5.65	5.26 ± 4.68	0.313

BMI: Body Mass Index, DM: Diabetes Mellitus, Dia: Diastolic, ESS: Epworth Sleepiness Scale, FH: Family history, HT: Hypertension, Sys: Systolic

Conventional LV echocardiographic parameters: Regarding LV echocardiographic parameters, LVOT diameter, IVSEDD and PWEDD were significantly higher in severe OSA patients (22.25 ± 2.09 mm vs. 20.43 ± 4.23 mm, p=0.039; 11.13 ± 1.61 mm vs. 10.16 ± 1.46 mm, p=0.018; 11.10 ± 1.60 mm vs. 10.10 ± 1.42 mm, p=0.013 respectively). LVMI was also higher in this group (99.39 ± 25.51 gr/m² vs 87.71 ± 18.84 gr/m², p=0.048, respectively). There was a statistical trend for significance for left ventricular A velocity (p = 0.056) to be higher in the severe OSA group

(Table 2).

Conventional echocardiographic RV functional parameters: With respect to RV functional parameters, RVFAC and MPI values were significantly higher in severe OSA patients (47.94 ± 7.36% vs. 41.23 ± 12.18%, p=0.012; 0.43 ± 0.31 vs. 0.29 ± 0.16, p=0.034, respectively) whereas TAPSE and PVR values were similar in both groups. Right ventricular A velocity was also higher in the severe OSA group (0.58 ± 0.14 m/sn vs. 0.48 ± 0.13, p=0.008, respectively). No significant difference was determined between the two groups in terms of right atrial and right ventricular dimensions, right atrial area, and systolic pulmonary pressure (Table 3).

Table 2. Left ventricular echocardiographic parameters

	AHI ≥ 30 (n:30)	AHI < 30 (n:30)	p
PWEDD(mm)	11.10 ±1.60	10.10 ± 1.42	0.013*
IVSEDD(mm)	11.13 ±1.61	10.16 ± 1.46	0.018*
LVOT Diameter(mm)	22.25 ± 2.09	20.43 ± 4.23	0.039*
LVMI (gr/m^2)	99.39 ± 25.51	87.71 ± 18.84	0.048*
E (m/s)	0.61 ± 0.14	0.63 ± 0.18	0.726
A (m/s)	0.79 ± 0.15	0.70 ± 0.18	0.056
Em (cm/s)	9.81 ± 4.23	10.60 ± 4.90	0.505
Am (cm/s)	12.95 ± 5.19	11.67 ± 3.48	0.266
LAVI (mm/m^2)	21.1 ± 5.3	19.9 ± 4.4	0.336
LA D1(mm)	35.93 ± 4.46	34.50 ± 3.55	0.174
LVSD(mm)	26.5 ± 3.62	26.63 ± 4.05	0.894
LVDD(mm)	45.46 ± 3.56	44.73 ± 3.86	0.448
LVOT VTI	19.67 ± 5.09	20.91 ± 7.16	0.443
DT (ms)	232.16 ± 78.87	230.3 ± 90.31	0.932

A: Peak late diastolic mitral inflow velocity, Am: Late diastolic myocardial velocity, DT: Deceleration time, E: Peak early diastolic mitral inflow velocity, Em: Early diastolic myocardial velocity, IVSEDD: Interventricular septum end-diastolic diameter, , LVMI: Left ventricular mass index, LVDD: Left ventricular diastolic diameter, LVSD: Left ventricular systolic diameter, LVOT: Left ventricular outflow tract, LA D1:Left atrium anteroposterior diameter, PWEDD: Posterior wall end-diastolic diameter , Sys: Systolic, * p value < 0,05

Correlation analysis: We found significant positive but weak correlations between AHI and LVOT proximal diameter, IVSEDD, RVMPI, right ventricular E and A velocities, BMI, neck circumference and ESS. Within echocardiographic parameters, the absolute value of the correlations with RV A velocity, PWEDD, IVSEDD, LVOT diameter and RVMPI were higher than the one with ESS (Table 4).

Logistic regression analysis end regression model: The log regression model created with PWEDD, LVOT diameter and RV A velocity identified 73% of the patients' group correctly. 70% of the patients with severe OSA (AHI ≥ 30) were determined correctly and 76% of the other group of patients (AHI < 30) were predicted correctly by using this model (Table 5).

Table 3. Right Ventricular Echocardiographic Parameters

	AHI ≥ 30 (n:30)	AHI < 30 (n:30)	p
A (m/s)	0.58 ± 0.14	0.48 ± 0.13	0.008**
RVFAC (%)	47.94 ± 7.36	41.23 ± 12.18	0.012*
MPI	0.43 ± 0.31	0.29 ± 0.16	0.034*
DT (ms)	253.62 ± 89.44	246.81 ± 89.33	0.773
TR vel (cm/s)	1.88 ± 0.48	1.92 ± 0.61	0.823
PAP (mmHg)	15.49 ± 7.68	17.59 ± 9.31	0.382
TCO(s)	388.33 ± 60.42	385.6 ± 43.42	0.841
TAPSE(mm)	19.59 ± 10.22	20.00 ± 8.82	0.871
RA long axis (mm)	46.23 ± 5.09	46.06 ± 5.68	0.905
RA minor axis (mm)	37.26 ± 6.48	37.36 ± 6.05	0.951
RA area (cm^2)	14.17 ± 2.79	13.53 ± 3.70	0.451
RV diameter	27.03 ± 3.41	26.93 ± 3.36	0.909
RVOT (mm)	23.61 ± 2.88	23.0 ± 4.13	0.505
RVOT VTI	16.99 ± 5.27	17.0 ± 4.58	0.998
E (m/s)	0.518 ± 0.17	0.46 ± 0.13	0.177
Ea (cm/s)	10.83 ± 3.27	11.71 ± 3.67	0.333
Aa (cm/s)	16.6 ± 5.77	15.32 ± 3.92	0.321
Sa (cm/s)	14.47 ± 4.42	13.52 ± 3.61	0.365
PVR (dyn*s/cm5)	1.39 ± 0.84	1.32 ± 0.52	0.708

A: Peak late diastolic tricuspid inflow velocity, Aa: Late diastolic velocity of tricuspid lateral annulus, DT: Deceleration time E: Peak early diastolic tricuspid inflow velocity, Ea: Early diastolic velocity of tricuspid lateral annulus, MPI: Myocardial performance index , PAP: Pulmonary arterial pressure , PD: Peritoneal dialysis, PVR: Pulmonary vascular resistance, TR vel: Tricuspid regurgitation flow velocity, RA: Right atrium, RV: Right ventricle, RVOT: Right ventricle outflow tract, RVFAC: Right ventricular fractional area change, Sa: Systolic myocardial velocity of tricuspid annulus, TAPSE: Tricuspid plane systolic excursion, TCO: Tricuspid closure opening time. * p value < 0,05, **p value <0,01

DISCUSSION

To our knowledge, this is the first study to predict patients with severe OSA using conventional echocardiography and TDI. Various echocardiographic evaluations were found to be related to severity of many clinical conditions in previous studies [18]. We evaluated the patients with suspected OSA who were scheduled to undergo polysomnography. Echocardiographic examinations were performed

Table 4. Correlations between Echocardiographic/Clinical findings and AHI

RV Echocardiographic findings			LV Echocardiographic findings			General Clinical Findings		
	r	p		r	p		r	p
	r	p		r	p		r	p
MPI	0.33	0.010*	IVS	0.31	0.015*	ESS	0.29	0.027*
FAC	0.21	0.107	PW	0.32	0.012*	Neck Circumference	0.39	0.002
PVR	0.00	0.987	LVEDD	0.13	0.330	BMI	0.42	0.001**
TCO	0.07	0.595	LVEDD	0.03	0.826	Weight	0.40	0.002**
RV	0.17	0.191	LA D1	0.14	0.289	Boy	0.06	0.652
RVOT	0.19	0.142	LA D2	0.10	0.430	Age	0.22	0.089
RVOTVTI	-0.05	0.707	LA D3	0.12	0.375	Sys BP	0.16	0.223
Dia. Area	0.07	0.604	LAVI	0.23	0.859	Dia BP	0.23	0.079
Sys Area	-0.05	0.683	LVOT	0.34	0.008**	Heart rate	0.14	0.271
TAPSE	-0.02	0.852	LVOT VTI	0.00	0.983			
TR vel.	-0.14	0.294	LV E vel	-0.06	0.649			
PAP	-0.22	0.125	LV A vel	0.19	0.151			
RV E vel.	0.26	0.044*	Em	-0.16	0.217			
RV A vel.	0.35	0.006**	Am	0.09	0.475			
RV DT	0.09	0.510	LV DT	0.11	0.399			
Ea	0.21	0.101						
Aa	0.07	0.602						
Sa	0.04	0.738						
RA long axis	0.05	0.680						
RA minor axis	0.06	0.660						
RA area	0.02	0.909						

BMI: Body Mass Index, DM: Diabetes Mellitus, Dia: Diastolic, ESS: Epworth Sleepiness Scale, FH: Family history, HT: Hypertension, Sys: Systolic, Aa: Late diastolic velocity of tricuspid lateral annulus, Am: Late diastolic velocity of mitral lateral annulus , DT: Deceleration time , Ea: Early diastolic velocity of tricuspid lateral annulus , Em: Early diastolic velocity of mitral lateral annulus, IVSEDD: Interventricular septum end-diastolic diameter , LA D1:Left atrium anteroposterior diameter, LA D2:Left atrium long axis diameter, LV A vel: Peak late diastolic mitral inflow velocity, LV E vel: Peak early diastolic mitral inflow velocity, LVDD: Left ventricular diastolic diameter , LVMI: Left ventricular mass index , LVOT: Left ventricular outflow tract, LVSD: Left ventricular systolic diameter , MPI: Myocardial performance index , PAP: Pulmonary arterial pressure, PVR: Pulmonary vascular resistance , PWEDD: Posterior wall end-diastolic diameter, RV A vel: Peak late diastolic tricuspid inflow velocity, RV E: Peak early diastolic tricuspid inflow velocity, RA: Right atrium, RV: Right ventricle, RVOT: Right ventricle outflow tract, RVFAC: Right ventricular fractional area change, Sa: Systolic myocardial velocity of tricuspid annulus, Sys: Systolic , TAPSE: Tricuspid plane systolic excursion, TCO: Tricuspid closure opening time , TR vel: Tricuspid regurgitation flow velocity, * p value < 0,05 , **p value <0,01

Table 5. Log regression model

	OR	95,0% C.I.	P
PWEDD > 11 mm	5.05	1.28 - 19.94	0.021
LVOT D >21.5 mm	8.12	2.09-31.59	0.003
RV A vel. > 0.475 cm/s	5.18	1.28-20.96	0.021

LVOT: Left ventricular outflow tract, PWEDD: Posterior wall end-diastolic diameter, RV A vel: Peak late diastolic tricuspid inflow velocity

before polysomnographies. According to the results of our study, we found some structural and functional alterations in the left and right ventricles. The major new finding of our study is that we have shown the possibility of predicting the patients with severe OSA by the use of certain echocardiographic parameters. This could help in the selection of patients to undergo polysomnography primarily and determining the appropriate treatment.

We tried to create a regression model predicting severe OSA using the parameters associated with the severity of OSA in the t test and correlation analysis. In many model experiments, the most significant model was the one including 'PWEDD, LVOT proximal diameter and RV A velocity'.

The current gold standard for diagnosis and management of OSA is in-laboratory (in-lab) polysomnography, however the limited availability of testing options for patients has led to long wait times and increased disease burden within the population.

Tests that predict severe OSA may provide a priority ranking in sleep tests. Our predictive values are not an alternative to polysomnography, but can be helpful to identify patients who will be given priority in polysomnography [19].

In our study, it was found that the patients with severe OSA (AHI ≥ 30) showed a statistically significant increase in both IVSEDD and PWEDD compared to the patients with AHI <30. Additionally, severe OSA patients showed a significant increase in LVMI. This is in line with previous studies on this topic [20]. It is known that intermittent hypoxia causes left ventricular hypertrophy and also plays an important role in the cardiovascular complications of OSA [21]. Although the negative effect of intermittent hypoxia on the cardiovascular system has not been completely clarified, multiple mechanisms, including sympathetic overactivation, oxidative stress, inflammation, metabolic deregulation, and endothelial dysfunction have been suggested to be involved. Hypoxemia, hypercapnia and acidosis induced by chronic intermittent hypoxia in OSA patients, could activate the sympathetic nervous system. This results in increased LV afterload and heart rate, which promote myocardial oxygen demand and chronically contribute to LV hypertrophy and failure. In addition, systemic inflammation and free radical generation triggered by OSA, play important role in intermittent hypoxia-induced remodeling of LV [22]. In our study, we showed that severe OSA is associated with left ventricular hypertrophy. Hypertension prevalence and blood pressure values were similar in both groups in the study. Our findings showed the association between left ventricular hypertrophy and severe OSA, independent of hypertension. Hedner, J. et al. reported this association similarly [23] and the meta-analysis which evaluated the LV structure in OSA patients, also reported that OSA induces the cardiac abnormality independent of hypertension. In the analysis, they eliminated the effect of systemic hypertension by excluding the studies which hypertensive patients enrolled. We found that PWEDD ≥ 12 mm increases the likelihood of severe OSA fivefold, in a patient examined for the suspicion of OSA.

Unlike previous studies, we investigated the LVOT diameter and found it to be significantly higher in patients with severe OSA. To our knowledge, this is the first study which highlights the association between LVOT diameter and severe OSA. Although there is no data on the association between the increase in LVOT diameter and the severity of OSA, it could also be the result of LV remodeling and hypertrophy due to intermittent hypoxia. The normal value for the LVOT proximal diameter is 20.3 ± 2.3 mm [24]. Using ROC analysis, we determined 21.5 mm to be the maximum LVOT diameter. We found that a LVOT diameter > 21.5 mm increases eightfold the likelihood of severe OSA in a patient with suspected OSA.

The conclusions about the correlation between the severity of OSA and RV remodeling and function from various studies have differed. Several studies reported that OSA patients presented with right cardiac dysfunction but some others did not reveal any changes in RV morphology and function in OSA patients. Several mechanisms were considered to explain the association between RV dysfunction and OSA. Permanent pulmonary hypertension was thought to be an important factor, leading to RV overload and inducing the release of inflammatory factors and resulting with RV dysfunction [25]. Some other studies reported the increased venous return and overload due to the intrathoracic negative pressure against an occluded airway, resulted in remodeling of RV. In addition, stimulation of central and peripheral chemoreceptors and increase in sympathetic nerve activity by intermittent hypoxia and CO2 retention might be another mechanism of RV dysfunction.

In our study, there were no differences between the two groups in terms of right ventricular dimensions, right atrial area, PVR and systolic pulmonary pressure. With respect to right ventricular functional parameters, RVMPI and RVFAC values were significantly higher in the severe OSA group; whereas TAPSE and lateral TDI Sm values were similar in both groups. Maripov et al. demonstrated that RVMPI was significantly high in patients with OSA compared to the controls, in their meta-analysis including twenty-five studies [2]. They reported that patients with OSA had decreased TAPSE, RV Sm and RV FAC. The findings of the present study showed a similar increase in RV MPI but there were no differences in the TAPSE and RV Sm values of the two groups. Interestingly, there was an increase in RVFAC value in the severe OSA group in our study, which might be due to differences in study design. Most previous studies compared patients with OSA and healthy control groups, but we compared severe with non-severe OSA patients, so the mean AHI value of our control group was higher than those of previous studies. In addition, there are conflicting results about RVFAC and RV Sm values [2,26]. Dobrowolski et al. and Shivalkar et al. reported an increase in RV Sm; Kasikcioglu et al and Vitarelli et al. indicated that RV Sm was lower in patients with OSA [4,26-29]. The difficulty of accurate evaluation of RV morphology and function in clinical practice due to its complex geometric shape might be another reason for the discrepancy between the studies. When we examined the correlations between AHI and echocardiographic parameters, we found significant correlations between AHI and IVSEDD, PWEDD, LVOT diameter, RVMPI, right ventricular E and A velocities. None of the correlations were strong, although all but right ventricular E velocity were stronger than the correlation between AHI and ESS.

There is little data on the association between RV A velocity and the severity of OSA in previous studies. Kasikcioglu et al. reported an increase in RV A velocity in patients with severe OSA, but it was not statistically significant [4]. We found that RV A velocity was higher in the severe OSA group. The increase in RV A velocity was considered as a sign of RV diastolic dysfunction. The mean value of RV A velocity is 0,40 m/s and the upper reference value is 0,58 (0,55-0,60) m/s [15]. We accepted 0.475 m/s as the upper limit of RV A velocity that we determined using ROC analysis. We found RV A velocity > 0.475 m/s to increase the likelihood of severe OSA fivefold in a patient with suspected OSA.

Limitations: This was a cross sectional study including a relatively small number of patients with OSA. The small number of patients is an important limitation especially for predictive analysis. For more reliable results of the predicted values, the results should be examined in large-scale studies. We believe that this study should be a guide for larger studies to be carried out in the future.

Most of the patients with OSA have high BMI, which makes echocardiographic examination difficult. We tried to overcome this difficulty as the examinations were performed by experienced physicians.

Conclusion: To our knowledge, this is the first study that investigates the predictor echocardiographic parameters for severe OSA. Our findings indicate that we can predict 73% of patients with suspected OSA, whether they have severe OSA or not, before polysomnography. At this point, using echocardiography, it may be possible to select patients for polysomnography more accurately.

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REFERENCES

1. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep. 1999;22:667-89. PMID: 10450601.
2. Maripov A, Mamazhakypov A, Sartmyrzaeva M, Akunov A, Muratali Uulu K, Duishobaev M, et al. Right Ventricular Remodeling and Dysfunction in Obstructive Sleep Apnea: A Systematic Review of the Literature and Meta-Analysis. Can Respir J. 2017;2017:1587865. PMID: 28814913. PMCID: 5549475.
3. Kendzerska T, Gershon AS, Hawker G, Leung RS, Tomlinson G. Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. PLoS Med. 2014;11:e1001599. PMID: 24503600. PMCID: 3913558.
4. Kasikcioglu HA, Karasulu L, Tartan Z, Kasikcioglu E, Cuhadaroglu C, Cam N. Occult cardiac dysfunction in patients with obstructive sleep apnea syndrome revealed by tissue Doppler imaging. Int J Cardiol. 2007;118:203-5. PMID: 16997399.
5. Grunig E, Peacock AJ. Imaging the heart in pulmonary hypertension: an update. Eur Respir Rev. 2015;24:653-64. PMID: 26621979.
6. Vonk Noordegraaf A, Haddad F, Bogaard HJ, Hassoun PM. Noninvasive imaging in the assessment of the cardiopulmonary vascular unit. Circulation. 2015;131:899-913. PMID: 25753343.
7. Lattimore JD, Celermajer DS, Wilcox I. Obstructive sleep apnea and cardiovascular disease. J Am Coll Cardiol. 2003;41:1429-37. PMID: 12742277.
8. Practice parameters for the indications for polysomnography and related procedures. Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. Sleep. 1997;20:406-22. PMID: 9302725.
9. Fleetham J, Ayas N, Bradley D, Ferguson K, Fitzpatrick M, George C, et al. Canadian Thoracic Society guidelines: diagnosis and treatment of sleep disordered breathing in adults. Can Respir J. 2006;13:387-92. PMID: 17036094.
10. Izci B, Ardic S, Firat H, Sahin A, Altinors M, Karacan I. Reliability and validity studies of the Turkish version of the Epworth Sleepiness Scale. Sleep Breath. 2008;12:161-8. PMID: 17922157.
11. de Simone G, Devereux RB, Ganau A, Hahn RT, Saba PS, Mureddu GF, et al. Estimation of left ventricular chamber and stroke volume by limited M-mode echocardiography and validation by two-dimensional and Doppler echocardiography. Am J Cardiol. 1996;78:801-7. PMID: 8857486.
12. Devereux RB, Lutas EM, Casale PN, Kligfield P, Eisenberg RR, Hammond IW, et al. Standardization of M-mode echocardiographic left ventricular anatomic measurements. J Am Coll Cardiol. 1984;4:1222-30. PMID: 6238987.
13. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. Nutrition. 1989;5:303-11; discussion 12-3. PMID: 2520314.
14. Wang AY, Wang M, Lam CW, Chan IH, Zhang Y, Sanderson JE. Left ventricular filling pressure by Doppler echocardiography in patients with end-stage renal disease. Hypertension. 2008;52:107-14. PMID: 18474835.
15. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23:685-713; quiz 86-8. PMID: 20620859.
16. Anavekar NS, Skali H, Bourgoun M, Ghali JK, Kober L, Maggioni AP, et al. Usefulness of right ventricular fractional area change to predict death, heart failure, and stroke following myocardial infarction (from the VALIANT ECHO Study). Am J Cardiol. 2008;101:607-12. PMID: 18308007.
17. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8:597-619. PMID: 23066376.
18. Altay H, Altın C, Coner A, Muderrisoglu H, Giray S. Parathyroid hormone and ischemic cerebrovascular event. Endoc Metab Immune Drug Targets. 2019; 19: 1134-1140. PMID: 30806331
19. Stewart, S. A., Skomro, R., Reid, J., Penz, E., Fenton, M., Gjevre, J., & Cotton, D. (2015). Improvement in obstructive sleep apnea diagnosis and management wait times: A retrospective analysis of a home management pathway for obstructive sleep apnea. Canadian respiratory journal, 22(3), 167-170. DOI: 10.1155/2015/516580
20. 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;32:384-90. PMID: 22705609.
21. Xie S, Deng Y, Pan YY, Ren J, Jin M, Wang Y, et al. Chronic intermittent hypoxia induces cardiac hypertrophy by impairing autophagy through the adenosine 5'-monophosphate-activated protein kinase pathway. Arch Biochem Biophys. 2016;606:41-52. PMID: 27412517.
22. Yu L, Li H, Liu X, Fan J, Zhu Q, Li J, et al. Left ventricular remodeling and dysfunction in obstructive sleep apnea : Systematic review and meta-analysis. Herz. 2019. DOI: 10.1007/s00059-019-04850-w
23. Hedner J, Ejnell H, Caidahl K. Left ventricular hypertrophy independent of hypertension in patients with obstructive sleep apnoea. J Hypertens. 1990;8:941-6. PMID: 2174947.
24. Kou S, Caballero L, Dulgheru R, Voilliot D, De Sousa C, Kacharava G, et al. Echocardiographic reference ranges for normal cardiac chamber size: results from the NORRE study. Eur Heart J Cardiovasc Imaging. 2014;15:680-90. PMCID: 4402333.
25. Sajkov D, McEvoy RD. Obstructive sleep apnea and pulmonary hypertension. Prog Cardiovasc Dis. 2009;51:363-70. DOI: 10.1016/j.pcad.2008.06.001
26. Dobrowolski P, Florczak E, Klisiewicz A, Prejbisz A, Rybicka J, Sliwinski P, et al. Pulmonary artery dilation indicates severe obstructive sleep apnea in patients with resistant hypertension: the Resist-POL Study. Pol Arch Med Wewn. 2016;126:222-9. PMID: 27129085.
27. Dobrowolski P, Klisiewicz A, Florczak E, Prejbisz A, Bielen P, Sliwinski P, et al. Independent association of obstructive sleep apnea with left ventricular geometry and systolic function in resistant hypertension: the RESIST-POL study. Sleep Med. 2014;15:1302-8. PMID: 25260432.
28. Vitarelli A, Terzano C, Saponara M, Gaudio C, Mangieri E, Capotosto L, et al. Assessment of Right Ventricular Function in Obstructive Sleep Apnea Syndrome and Effects of Continuous Positive Airway Pressure Therapy: A Pilot Study. Can J Cardiol. 2015;31:823-31. PMID: 25980631.
29. Shivalkar B, Van de Heyning C, Kerremans M, Rinkevich D, Verbraecken J, De Backer W, et al. 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. PMID: 16580533.