Determination of right ventricular dysfunction using the speckle tracking echocardiography method in patients with obstructive sleep apnea

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Abstract

Background: *The speckle tracking echocardiography (STE) method shows the presence of right ventricular (RV) dysfunction before the advent of RV failure and pulmonary hypertension in patients with cardiopulmonary disease. We aimed to assess subclinical RV dysfunction in obstructive sleep apnea (OSA) using the STE method.*

Method: *Twenty-one healthy individuals and 58 OSA patients were included. According to severity as determined by the apnea–hypopnea index (AHI), OSA patients were examined in three groups: mild, moderate and severe. RV free wall was used in STE examination.*

Results: *Right ventricle strain (ST %) and systolic strain rate (STR-S 1/s) were decreasing along with the disease severity (ST — healthy: –34.05 ± –4.29; mild: –31.4 ± –5.37; moderate: –22.75 ± –4.89; severe: –20.89 ± –5.59; p < 0.003; STR-S — healthy: –2.93 ± –0.64; mild: –2.85 ± –0.73; moderate: –2.06 ± –0.43; severe: –1.43 ± –0.33; p < 0.03). Correlated with the disease severity, the RV early diastolic strain rate (STR-E) was decreasing and the late diastolic strain rate was increasing (STR-E — healthy: 2.38 ± 0.63; mild: 2.32 ± 0.84; moderate: 1.66 ± 0.55; severe: 1 ± 0.54; p < 0.003; STR-A — healthy: 2.25 ± 0.33; mild: 2.32 ± 0.54; moderate: 2.79 ± 0.66; severe: 3.29 ± 0.54; p < 0.03). The STR-E/A ratio was found to be in a decreasing trend along with the disease severity (healthy: 1.08 ± 0.34; mild: 1.06 ± 0.46; moderate: 0.62 ± 0.22; severe: 0.34 ± 0.23; p < 0.03).*

Conclusions: *Subclinical RV dysfunction can be established in OSA patients even in the absence of pulmonary hypertension and pathologies which could have adverse effects on RV functions. In addition to the methods of conventional, Doppler and tissue Doppler echocardiography, using the STE method can determine RV dysfunction in the subclinical phase.* (Cardiol J 2012; 19, 2: 130–139)

Key words: speckle tracking echocardiography, right ventricle, obstructive sleep apnea

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Introduction

Previous studies have shown the adverse effects of obstructive sleep apnea (OSA) on myocardial functions [1]. Right ventricle (RV) function plays a crucial role in the morbidity and mortality of patients with cardiopulmonary disease. Early determination of RV dysfunction before pulmonary arterial hypertension (PAH) development is important in preventing progression to heart failure and even death [2].

Global RV functions are usually assessed by means of RV fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE); however, both techniques have intrinsic limitations [3]. A conventional two-dimensional (2D) echocardiography does not allow a comprehensive evaluation, because the RV has a complex crescent shape and is wrapped around the left ventricle (LV). The tissue Doppler echocardiography method is more sensitive than the 2D echocardiography method for determining subclinical cardiac dysfunction, but it is influenced by the cardiac translational motion and tethering of adjacent myocardial tissue and it has high inter-observational variability [4, 5].

The 2D speckle tracking echocardiography (2D-STE) method assesses myocardial deformation and the myocardial deformation rate by tracking speckles in the myocardium on grayscale (B-mode) images. It can be used to evaluate both global and regional myocardial strain (ST %) and the strain rate (STR 1/s) without the limitation of a Doppler beam angle. In previous studies using the 2D-STE method, the coexistent RV dysfunction has been determined in patients with congenital heart diseases, systemic sclerosis, pulmonary hypertension, systemic hypertension, diabetes mellitus and pulmonary thromboembolism. Besides these, results of these studies were found to be correlated well with the TAPSE, FAC, myocardial performance index (MPI), and isovolumic acceleration (IVA) parameters [6].

The assessment of radial functions in the parasternal view is difficult because of the anterior location of the RV leading to significant artifacts. The circumferential functions of the RV are not usually assessed. For these reasons, in the evaluation of RV functions, only the longitudinal ST and STR parameters are used. It is debatable whether the interventricular septum should be included as a part of the assessment of global RV function with the 2D-STE method. The interventricular septum is influenced more by the LV than the RV, with the exception of the advanced RV dysfunction. Therefore, the RV free wall in the apical four-chamber view is used for ST and STR assessment [5, 7].

In our study, we aimed to investigate the relationship between the subclinical RV dysfunction and disease severity in OSA patients without pulmonary hypertension and LV dysfunction with standard and tissue Doppler echocardiography and 2D-STE methods.

Methods

Determination of patient and control groups

Patients between the ages of 30 and 60 with an OSA diagnosis who were examined at the Akdeniz University, Faculty of Medicine, Chest Diseases Polyclinic between March 2009 and October 2010 were included in this study after conducting polysomnographies at the sleep laboratory. To create a control group, we chose healthy individuals between the ages of 30 and 60 with no cardiovascular diseases who came to the Akdeniz University, Faculty of Medicine, Cardiology outpatient clinic for various reasons. The healthy group used in the study included patients suitable for the study from the perspective of cardiac structure and functions, those with no night snoring or day-time sleepiness, who scored less than 10 on the Epworth Sleepiness Scale, and had low risk of OSA in the Berlin survey form evaluation [8, 9].

Exclusion criteria were as follows: angina and angina equivalent symptoms, abnormal electrocardiography, abnormal cardiovascular stress test and abnormal myocardial scintigraphy, an LV ejection fraction (LVEF) lower than 50%, mean pulmonary artery pressure (MPAP) > 25 mm Hg, a moderate or severe degree of valvular stenosis or insufficiency, a documented history of coronary and peripheral vascular diseases, diabetes mellitus, hypothyroidism and hyperthyroidism, renal failure, hepatic failure, restrictive and obstructive pulmonary disease, connective tissue disorders, atrial fibrillation, pacemaker, congenital cardiac disease, pericardial disease, and smoking. In the physical examination, patients with a systolic blood pressure value of > 140 mm Hg and diastolic blood pressure value of > 90 mm Hg after averaging three separate blood pressure measurements taken at ten minute intervals, as well as patients receiving antihypertensive treatment, were accepted as hypertensive. Also, patients who were receiving OSA treatment were excluded. Informed consent was given by everyone included in the study, which was approved by the local ethical committee of Akdeniz University Medical School.

All individuals' blood pressures, pulse rates and anthropometric measures were recorded before echocardiographic examination. Body mass index (BMI) and body surface areas (BSA) were derived from the anthropometric measures.

Polysomnography

Polysomnography was performed with 16 channels Embla (Medcare Inc, Iceland) with continuous monitoring from a sleep technician. The system consists of four channels of electroencephalography, two channels of electrooculography, submental electromyography, oronasal air flow, thoracic and abdominal movements, pulse oximeter oxygen saturation, tibial electromyography, body position detector, electrocardiogram, and tracheal sound.

Apnea was defined as complete stopping of airflow lasting more than 10 s. Hypopnea was defined as 30% or more reduction in respiratory airflow lasting more than 10 s and accompanied by a decrease of more than 4% in oxygen saturation. The average number of episodes of apnea and hypopnea per hour of sleep was defined as the apnea–hypopnea index (AHI). According to the severity, included patients were classified as having mild OSA (AHI 5––15), moderate OSA (AHI 16–30); or severe OSA (AHI > 30). Sleep stages were scored following the standard criteria with 30-s epochs and were reviewed and verified by a certified sleep physician [10].

Echocardiography

Echocardiography was performed in the left lateral decubitus position with an ultrasound machine GE-Vingmed Vivid 7 system (GE-Vingmed Ultrasound AS, Horten, Norway) and 3S-RS (3.5 MHz) probe. Averages of three consecutive cycles were measured for all echocardiographic data. Images were obtained from parasternal and apical positions using 2D, M-mode and Doppler echocardiographic techniques. Examinations were performed by two experienced cardiologists who were unaware of the disease presence and severity of the individuals. The LV end-diastolic and end-systolic dimensions, interventricular septum and posterior wall thickness were measured with M-mode echocardiography. LV mass was determined by the Devereux formula, and the LV mass index (LVMI) was derived by dividing the LV mass by the BSA [11]. LVEF was measured using the biplane Simpson's method. LV inflow velocity was recorded from the pulse wave Doppler sample volume placed proximal to mitral leaflet tips in the apical four-chamber view. Early diastolic peak flow velocity (E), and late diastolic peak flow velocity (A) were recorded, and the E/A ratio and the deceleration time (DecT) of E wave were calculated [3].

RV global systolic function was assessed as the TAPSE by the 2D difference of the end-diastolic and end-systolic lines traced between the center of the ultrasound fan origin and the junction of the RV lateral tricuspid annulus in the apical four-chamber view. Right atrium volume (RAV) was calculated by the area-length method in apical four-chamber view and the right atrial volume indices (RAVI) were derived by dividing the RAV by the BSA. Tricuspid inflow velocities were obtained with pulsed wave Doppler recording in the apical four-chamber view, by placing the sample volume at the tips of the tricuspid valve leaflets. The peak early diastolic (E) and late diastolic (A) tricuspid inflow velocities and the DecT were measured. Right ventricular outflow tract acceleration time (RVAT) was calculated as the time interval between the onset of systolic velocity and peak systolic velocity. The mean pulmonary artery (PA) pressure (MPAP) was calculated with the Mahan formula $[90 - (0.62 \times RVAT)]$. The systolic PA pressure (SPAP) was estimated from the sum of the estimated right atrial (RA) pressure and the pressure gradient between RA and RV, which is calculated using the tricuspid regurgitant peak velocity [12].

Tissue Doppler imaging (TDI) was recorded from the apical four-chamber view with the pulse-wave Doppler sample volume placed on the septal mitral annulus and the tricuspid lateral annulus. Peak systolic (S) velocity, peak early (E') and peak late (A') diastolic myocardial annular velocity, isovolumic relaxation time (IVRT), and isovolumic contraction time (IVCT) were measured. The ratio between the early diastolic mitral flow (E) and early diastolic myocardial velocity (E') was calculated (E/E'). Myocardial performance index (MPI) was calculated with the Tei index formula for both ventricles. Isovolumic acceleration (IVA) for the RV was calculated by dividing the isovolumic contraction peak velocity by the time interval between the onset of this wave and its peak velocity [3, 12].

2D-STE analysis was performed with a software package (Echopac PC, version 8.0, GE Healthcare) from the apical view. Standard grayscale 2D images were obtained at a frame rate of 70–90 frame/s. The RV free wall endocardial border was traced manually from an end-systolic frame. Then, the epicardial border was automatically detected by the software and the region of interest (ROI) was manually adjusted to include the entire myocardial wall. The quality tracking was verified and the ROI was modified, and corrected by the observer if nec-
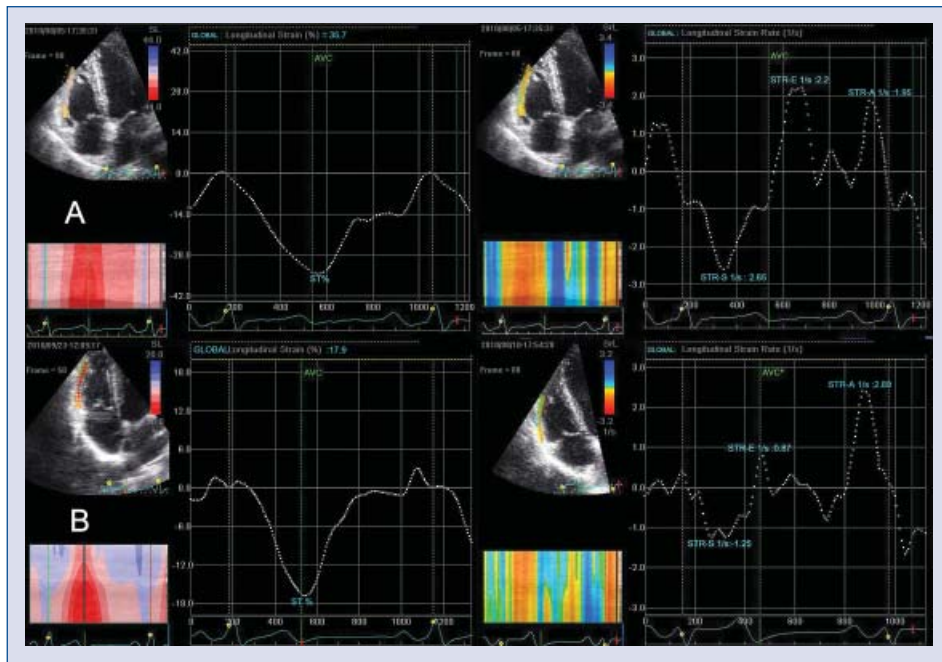
Figure 1. ST-STR graphic result of 2D-STE analysis of RV free wall, and ST, STR-S, STR-E and STR-A values. Comparative display of RV-ST, RV-STR-S, RV-STR-E, and RV-STR-A parameters in a healthy individual (**A**) and in an obstructive sleep apnea patient. **Left panel.** Global RV-ST curves; **Right panel.** Global RV-STR curves. Obstructive sleep apnea patient (**B**) has lower RV-ST, RV-STR-S and RV-STR-E and higher RV-STR-A compared to healthy individual (**A**).

essary to obtain optimal tracking. The apical four--chamber images of the RV free wall were processed by the software. Strain (RV-ST), systolic strain rate S (RV-STR-S), early diastolic strain rate (RV-STR-E), and late diastolic strain rate (RV-STR-A) curves were obtained. The early and late diastolic strain rate ratio (RV-STR-E/RV-STR-A) was calculated. The ST-STR graphic result of 2D-STE analysis of RV free wall, and the ST, STR-S, STR-E and STR-A values on this graphic are presented in Figure 1.

Statistical analysis

The study data was analyzed with SPSS v. 18.0 for Windows. Numeric variables were presented as mean ± standard derivation or median (minimum––maximum), and categorical variables as rates. Three or more group comparisons were performed by one--way ANOVA for normally distributed variables and by the Kruskal-Wallis test for ordinal variables or continuous variables not distributing normally. The Tukey test was used for *post-hoc* analysis after performing ANOVA. The Mann-Whitney U test with Bonferroni correction was used for *post-hoc* analysis after performing the Kruskal-Wallis test. The alpha critical value for the Mann-Whitney U test in Bonferroni correction was accepted as 0.03 because the Mann-Whitney U test loses its value below 0.03.

The normality analysis was performed by the Kolmogorov-Smirnov test. The Pearson correlation test was used in order to assess the relation between the severity and presence of OSA with all of the echocardiographic (standard tissue Doppler and speckle tracking imaging) variables. All the hypotheses were constructed as two-tailed, and an alpha critical value of 0.05 was accepted as significant.

Inter- and intra-observer variability

Intra-observer variability was determined by the observer repeating the measurement of the global longitudinal ST and STR in 20 random OSA patients or control subjects two weeks after the first measurement. Inter-observer variability was determined by another observer measuring these variables in the same database. The Blant-Alman analysis method was used to determine inter- and intraobserver variability.

Results

In our study, 79 individuals, consisting of 21 healthy individuals, 20 mild OSA patients, 19 moderate OSA patients, and 19 severe OSA patients, were included. The BMI values of OSA groups were found to be higher than the healthy group; howev-

Table 1. Clinical, demographic characteristics and AHI levels of the patients.

	Healthy (n = 21)	Mild OSA (n = 20)	Moderate OSA (n = 19)	Severe OSA (n = 19)
Age [years]	45.38 ± 4.5	46.95 ± 6.4	46.79 ± 5	46.68 ± 7.6
Female	11 (52.4%)	5 (25%)	5 (26.3%)	3 (15.8%)
Male	10 (47.6%)	15 (75%)	14 (73.7%)	16 (84.2%)
BMI [kg/m^2]	26.35 ± 4.14	28.68 ± 3.44	29.05 ± 2.26	29.80 ± 2.38†
BSA [m^2]	1.84 ± 0.16	1.97 ± 0.17	2 ± 0.18	2.01 ± 0.14
SBP [mm Hg]	120.95 ± 10.56	118.75 ± 6.04	120.26 ± 6.76	121.05 ± 8.09
DBP [mm Hg]	75.48 ± 6.69	76 ± 6.19	73.68 ± 5.97	75.79 ± 5.07
Pulse [bpm]	74.33 ± 10.89	76 ± 7.15	77.21 ± 5.52	78.21 ± 6.24
AHI [per hour]	N/A	10.73 ± 2.57	20.52 ± 2.60‡	58.1 ± 16.27‡,*

†p < 0.03 compared to healthy individuals; ‡p < 0.03 compared to mild OSA patients; *p < 0.03 compared to moderate OSA patients; AHI — apnea––hypopnea index; BMI — body mass index; BSA — body surface area; OSA — obstructive sleep apnea; SBP — systolic blood pressure; DBP — diastolic blood pressure

Table 2. Standard two-dimensional, Doppler and tissue Doppler left ventricular echocardiographic parameters of the patients and the control group.

	Healthy	Mild OSA	Moderate OSA	Severe OSA
EF [%]	64.24 ± 3.75	64.25 ± 3.76	63.68 ± 5.37	63.21 ± 3.17
DVI [mL/m^2]	37.38 ± 9.22	37.34 ± 10.34	36.78 ± 7.76	33.9 ± 9.64
SVI [mL/m^2]	13.44 ± 3.38	13.22 ± 3.67	13.42 ± 3.45	13.32 ± 4.77
IVSD [cm]	0.89 ± 0.9	1.03 ± 0.1†	1.03 ± 0.13†	1.13 ± 0.13†
PWD [cm]	0.88 ± 0.07	1.03 ± 0.09†	1.04 ± 0.12†	1.11 ± 0.13†
LVMI [g/m^2]	86.46 ± 18.74	93.25 ± 16.63	94.50 ± 22.87	103.51 ± 22.89
LAVI [mL/m^2]	21.63 ± 4.65	22.15 ± 4.75	27.44 ± 6.99†	32.31 ± 5.11†,‡
E/A	1.19 ± 0.24	0.96 ± 0.16†	1.01 ± 0.3	1.11 ± 0.28
DecT [ms]	163 ± 26.2	227.35 ± 31.1†	216.35 ± 60.41†	199.36 ± 39.5†
IVRT [ms]	88.29 ± 12.49	106.3 ± 12.83†	108.84 ± 12.91†	113.26 ± 10.42†
MPI	0.46 ± 0.08	0.48 ± 0.08	0.55 ± 0.06†	0.6 ± 0.13†,‡
E/E′	8.13 ± 2.22	8.62 ± 2.68	11.31 ± 2.87†,‡	13.89 ± 2.32†,‡,*

†p < 0.03 compared to healthy individuals; ‡p < 0.03 compared to mild OSA patients; *p < 0.03 compared to moderate OSA patients; DecT — deceleration time; DVI — diastolic volume index; E/A — ratio between diastolic early (E) and late diastolic mitral inflow (A) velocities; E/E′ — ratio between early diastolic mitral inflow velocity and early diastolic annular velocity; EF — ejection fraction; IVRT — isovolumic relaxation time; IVSD — interventricular septum diastolic thickness diameter; LAVI — left atrial volume index; LVMI — left ventricular mass index; MPI — myocardial performance index; OSA — obstructive sleep apnea; SVI — systolic volume index; PWD — posterior wall diastolic thickness diameter

er, no differences were observed between OSA groups. Detailed demographic, clinical variables and AHI levels of the groups are presented in Table 1.

Echocardiographic data belonging to LV and results of comparisons made between data of groups are presented in Table 2. While the LV wall thickness of individuals with OSA was observed to be higher than those in the healthy group, there were no LVMI differences between groups. The left atrial volume index, DecT, and IVRT values of the OSA group were found to be higher than the healthy group. The E/A value was found to be lower in the mild OSA group than the healthy group; however, no differences between other groups were ob-

served. While the MPI and E/E' values were correlated with the disease severity, differences in values were observed among groups especially from the moderate OSA group onward.

The echocardiographic data belonging to RV and RA and the results of comparison made between data of groups are presented in Table 3. No differences were observed between groups in terms of A, S velocities and PAP. It was observed that RAVI, DecT, A' velocity, E/ E' ratio and MPI values proportionally increased along with the disease severity. Furthermore, the difference was more noticeable in moderate and severe OSA groups. TAPSE, E velocity, E/A ratio, E' velocity and IVA values of

Table 3. Standard two-dimensional, Doppler and tissue Doppler right ventricular echocardiographic parameters of the patients and the control group.

	Healthy	Mild OSA	Moderate OSA	Severe OSA
RAVI [mL/m²]	15.56 ± 4.94	17.31 ± 6.24	21.89 ± 7.91	28.85 ± 7.97[†,‡]
TAPSE [mm]	24.76 ± 1.55	22.30 ± 2.39	21.11 ± 1.56[†]	19.42 ± 1.64[†,‡,*]
E [m/s]	0.75 ± 0.11	0.73 ± 0.01	0.64 ± 0.13[†]	0.57 ± 0.09[†,‡]
A [m/s]	0.48 ± 0.09	0.46 ± 0.09	0.46 ± 0.07	0.49 ± 0.09
E/A ratio	1.62 ± 0.23	1.44 ± 0.24	1.42 ± 0.22	1.37 ± 0.19[†]
DecT [ms]	162.33 ± 43.89	194.25 ± 44.95	206.37 ± 46.32	242.26 ± 54.63[†]
S [m/s]	0.17 ± 0.03	0.16 ± 0.03	0.15 ± 0.02	0.14 ± 0.02
E' [m/s]	0.16 ± 0.03	0.14 ± 0.03	0.13 ± 0.03[†]	0.11 ± 0.03[†]
A' [m/s]	0.15 ± 0.02	0.16 ± 0.01	0.18 ± 0.05	0.19 ± 0.03[†,‡]
E/E' ratio	4.19 ± 1.22	4.37 ± 1.22	5.77 ± 1.27[†,‡]	7.12 ± 2.29[†,‡]
MPI	0.43 ± 0.09	0.46 ± 0.09	0.53 ± 0.08[†]	0.56 ± 0.11[†,‡]
IVA [m/s²]	4.51 ± 0.65	4.38 ± 1.51	3.5 ± 0.98[†]	2.52 ± 1.1[†,‡]
SPAP [mm Hg]	25.61 ± 5.43	27.62 ± 4.32	29.78 ± 4.24	32.06 ± 3.71
MPAP [mm Hg]	19.91 ± 2.78	18.12 ± 5.39	17.73 ± 4.7	18.74 ± 4.36

[†]$p < 0.03$ compared to healthy individuals; [‡]$p < 0.03$ compared to mild OSA patients; [*]$p < 0.03$ compared to moderate OSA patients; A — tricuspid valve late diastolic velocity; A' — tricuspid anulus late diastolic myocardial velocity; DecT — deceleration time; E — tricuspid valve early diastolic velocity; E' — tricuspid annulus early diastolic myocardial velocity; IVA — myocardial acceleration during isovolumic contraction; MPAP — mean pulmonary artery pressure; MPI — myocardial performance index; OSA — obstructive sleep apnea; RAVI — right atrium volume index; SPAP — systolic pulmonary artery pressure; S' — tricuspid annulus systolic myocardial velocity; TAPSE — tricuspid annular plane systolic excursion

Table 4. Right ventricle ST and STR parameters of the patients and the control group.

	Healthy	Mild OSA	Moderate OSA	Severe OSA
RV-ST [%]	−34.05 ± −4.29	−31.4 ± −5.37	−22.75 ± −4.89[†,‡]	−20.89 ± −5.59[†,‡]
RV-STR-S [1/s]	−2.93 ± −0.64	−2.85 ± −0.73	−2.06 ± −0.43[†,‡]	−1.43 ± −0.33[†,‡,*]
RV-STR-E [1/s]	2.38 ± 0.63	2.32 ± 0.84	1.66 ± 0.55[†]	1 ± 0.54[†,‡]
RV-STR-A [1/s]	2.25 ± 0.33	2.32 ± 0.54	2.79 ± 0.66[†]	3.29 ± 0.54[†,‡]
RV-STR-E/A ratio	1.08 ± 0.34	1.06 ± 0.46	0.62 ± 0.22[†,‡]	0.34 ± 0.23[†,‡,*]

[†]$p < 0.03$ compared to healthy individuals; [‡]$p < 0.03$ compared to mild OSA patients; [*]$p < 0.03$ compared to moderate OSA patients; OSA — obstructive sleep apnea; RV — right ventricle; ST — strain; STR-S — systolic strain rate; STR-E — early diastolic strain rate; STR-A — late diastolic strain rate

moderate and severe OSA groups were noted to be lower than healthy and mild OSA groups.

The ST and STR parameters of the RV free wall are summarized in Table 4. RV-ST and RV-STR-S values were observed to be lower in the moderate and severe OSA groups than in the healthy and mild OSA groups. While no differences were observed between moderate and severe OSA groups in terms of RV-ST values, the RV-STR-S value of the severe OSA group was lower than the moderate OSA group. While the RV-STR-E value began to decrease starting from the moderate OSA group along with the disease severity, the RV-STR-A value was observed to be increasing. The RV-STR-E/A value began to decrease along with the disease severity, starting from the moderate OSA group, with statistical significance.

The relationship between AHI and LV MPI with RV functions was evaluated in a correlation analysis. There was nocorrelation found between the AHI and E/A value and S velocity value. A relationship between LV-MPI with RAVI and E/A values was not found. The 2D-STE parameters correlated better with AHI than the other echocardiographic parameters. A lower degree of correlation was observed between LV-MPI values and RV functions. The correlation analysis was repeated after performing BMI adjustment and it was observed that the relationship between AHI and LV-MPI with RV functions still remained. The results of the correlation analysis are given in Table 5. The relationship between AHI and RV-ST, and RV-STR-E/A are summarized in Figure 2.

Intra- and inter-observer variables

Twenty patients were randomly selected for the assessment of intra- and interobserver variables in measurements of RV-ST, RV-STR-S, RV-STR-E,

Table 5. Correlation of the AHI and the left ventricular MPI ratio with the echocardiographic right ventricular parameters.

	AHI		LV-MPI	
	r	p	r	p
TAPSE	–0.520	< 0.001	–0.488	< 0.001
TR-S′	–0.326	0.013	–0.265	0.018
MPI	0.342	0.009	0.340	0.002
IVA	–0.415	0.001	–0.410	< 0.001
RAVI	0.467	< 0.001	0.198	0.08
E/A	0.480	0.095	0.339	0.11
E/E′	0.573	< 0.001	0.273	0.015
RV-ST [%]	–0.694	< 0.001	0.379	0.001
RV-STR-S [1/s]	–0.710	< 0.001	–0.356	< 0.001
RV-STR-E/A	–0.704	< 0.001	–0.329	0.003

AHI — apnea-hypopnea index; E/A — ratio of tricuspid valve early and late diastolic myocardial velocity; E/E′ — ratio of tricuspid valve early diastolic velocity and tricuspid annulus early myocardial velocity; IVA — myocardial acceleration during isovolumic contraction; LV — left ventricle; MPI — myocardial performance index; RAVI — right atrium volume index; RV — right ventricle; RV-ST — right ventricle strain; RV-STR- E/A — ratio of right ventricle early diastolic and late diastolic strain rate; RV-STR-S — right ventricle systolic strain rate; S′ — tricuspid annulus systolic myocardial velocity; TAPSE — tricuspid annular plane systolic excursion

and RV-STR-A. The mean difference for interobserver agreement for RV-ST was 0.32 (95% confidence interval [CI] and –0.8 to 0.85). The mean difference for intraobserver agreement for RV-ST was 0.56 (95% CI –0.44 to 1.04). The mean differences for interobserver agreement for RV-STR were 0.78 (95% CI 0.52 to 0.85), –0.69 (95% CI –0.88 to –0.52), –0.7 (95% CI –0.86 to –0.53) for RV-STR-S, RV-STR-E, and RV-STR-A, respectively. The mean differen-

ces for intraobserver agreement for RV-STR were 0.81 (95% CI 0.51 to 0.84), –0.69 (95% CI –0.86 to –0.52), –0.46 (95% CI –0.68 to –0.24) for RV-STR-S, RV-STR-E, and RV-STR-A, respectively.

Discussion

OSA is characterized by repeated episodes of upper respiratory tract obstruction during sleep and arterial oxygen desaturation. OSA is often associated with certain cardiovascular risk factors such as hypertension, diabetes, and obesity. Repeated episodes of hypoxia, hypercapnia and changes in intrathoracic pressure may trigger pathophysiological mechanisms such as sympathetic hyperactivity, oxidative stress, systemic inflammation, hypercoagulability and endothelial dysfunction. Those pathophysiologic changes may have a direct or an indirect negative effect on myocardial structure and functions [13].

In our study, we observed that ST and STR-S values that display the systolic functions of the RV decrease correlated with disease severity. We observed that the RV systolic dysfunction was starting from the moderate OSA group onward. In terms of diastolic function parameters, we observed that the STR-E and STR-E/A values were decreased along with disease severity. But the STR-A value was found to be increased along with disease severity. The AHI correlated with RV functions better than the LV-MPI. There was a stronger relationship between AHI and 2D-STE parameters compared to other echocardiographic parameters. The relationship between the degree of RV dysfunction and OSA was found to be independent of BMI.
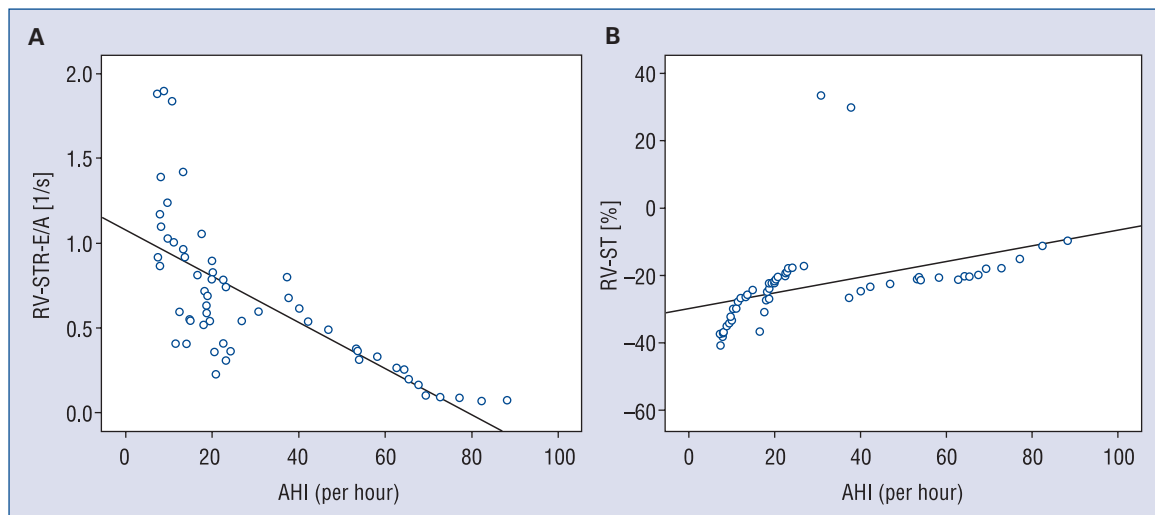

Figure 2. Relationship between AHI and RV-STR-E/A ratio (**A**), RV-ST (**B**); AHI — apnea-hypopnea index; RV-ST — right ventricular strain; RV-STR-E/A — ratio of right ventricular early and late diastolic strain rates.

While the cause of RV dysfunction in OSA was not certain, repetitive nocturnal arterial oxygen desaturation and hypercapnia, large intrathoracic negative pressure swings and acute increases in PAP may be the responsible mechanisms [14]. Experimental intermittent hypoxia administered for part of the day for just a few weeks results in pulmonary artery remodeling and RV hypertrophy in rodents [15]. Pulmonary vasoconstriction that arises in the hypoxic and hypercapnic stages, as well as endothelium dysfunction in the pulmonary vascular bed caused by oxidative stress triggered by OSA, are responsible for the development of pulmonary remodeling in OSA patients. Endothelial nitric oxide synthesis in the pulmonary bed is adversely affected by endothelium dysfunction in OSA [16]. The generation of negative intrathoracic pressure against an occluded airway is the unique feature of OSA which causes increased venous return, volume overload and distension of the RV during apnea periods. In OSA, the LV dysfunction may lead to RV dysfunction. RV functions are often influenced in LV pathologies as a result of direct injury extension, afterload, changes, or ventricular interdependence, which is mainly due to the close anatomical association between the two ventricles [17, 18]. Myocardial oxygen demands may be increased because of structural changes in RV. Insufficient supply of this increased demand may cause RV ischemia and dysfunction [13].

Chronic obstructive pulmonary disease, morbid obesity and LV failure may accompany OSA disease. Pulmonary hypertension and RV failure are commonly seen in these cases. However, in studies that have examined OSA patients without additional diseases which could have adverse effects on RV functions, a moderate degree of pulmonary hypertension (MPAP: 20–30 mm Hg) has been observed in 20–40% of cases, and a correlation between PAP levels and RV functions was noted. Also, in asymptomatic OSA patients, increases in PAP with exercise and decreases in their functional capacity were observed [14]. Therefore, the evaluation of RV functions in OSA patients is necessary for prognosis of the disease.

In our study, RV functions were first evaluated with 2D and Doppler echocardiography. While the TAPSE value decreased with the severity of the disease, and was found to be especially low in the severe OSA group compared to other groups, a moderate correlation was observed between the TAPSE value and AHI. In our study, the tricuspid E velocities decreased from the moderate OSA group and the tricuspid E/A ratios decreased from the severe OSA group onward, but no differences were observed between the tricuspid A velocities of groups. Also, no correlation was found between the AHI and Tri E/A ratios. The RV 2D echocardiographic and Doppler echocardiographic parameters displayed the shortcomings of these methods in the determination of early stage RV dysfunction.

Because of the shortcomings of the conventional echocardiography and pulse Doppler examinations, the relationship between OSA and RV functions have been examined using the tissue Doppler method in recent years. Besides the systolic and diastolic parameters determined by the tissue Doppler method, in various studies the RV MPI and IVA parameters were used to evaluate global RV functions in OSA patients [4, 19, 20]. While no differences were observed between groups in S wave velocity from tissue Doppler parameters, the IVA value decreased from the moderate OSA group onward, related to the severity of the disease. The related result proved that the IVA value non-related to volume load was more sensitive than S waves in determining subclinical cardiac damage [21, 22]. Tricuspid E/E' values were found to be increased along with the severity of OSA. In a previous study, observation of the correlation between the E/E' value and the invasively measured RA pressure showed that there is a correlation between the increasing RV filling pressure and the related parameter [23]. In OSA patients, the increased E/E' value indicates the presence of increased RV filling pressure and subclinical myocardial dysfunction.

The new echocardiographic method of speckle tracking assesses myocardial strain and strain rate by tracking speckles in the myocardium on gray-scale (B-mode images) and can be used to evaluate both global and regional myocardial strain without being limited by Doppler beam angle, tethering effect and load dependency [24]. In a study which compared the healthy individuals and patients with RV dysfunction, the ST and STR values were found to be decreased proportionally to the RV dysfunction severity, and these values were found to be related to systolic function parameters such as TAPSE and RV FAC. While there are differences between groups in the RV global ST and STR values, there was no difference among groups in terms of RV segments. A high degree of inter- and intra--observer compatibility in the study indicates the reliability of the 2D-STE values used in the evaluation of RV functions [25].

In our study, ST and STR-S values related to RV systolic functions were found to be decreased along with the severity of the disease. While the

ST values were not different among severe and moderate OSA patients, the STR-S value of severe OSA patients were found to be lower than that of the moderate OSA patients. This could be the result of a previously affected STR-S parameter in RV systolic dysfunction caused by OSA. Similar findings were observed in the study conducted by Tugcu et al. [26]. The RV free wall basal and mid segment systolic ST and STR values were calculated with the 2D-ST method and the results were compared between healthy individuals and OSA patients without pulmonary hypertension. The ST and STR-S values of both segments were found to be lower in OSA patients compared to the control group.

In our study, besides the systolic functions of RV, we also assessed the diastolic RV functions with the 2D-STE method. While the STR-E and STR-E/STR-A values were found to be decreased along with the disease severity, the STR-A values were found to be increased. These results indicated that RV systolic and diastolic longitudinal functions in OSA were corrupted from the moderate OSA group onwards.

The stronger correlation of RV strain and strain rate parameters with the AHI suggests to us that the RV dysfunction can be determined using the 2D--STE method in the subclinical phase. In our study, the presence of a weaker correlation between LV--MPI and RV functions supports the hypothesis that the direct effect of OSA has a potent impact on RV functions.

Limitations of the study

The first limitation of our study is the use of the Epworth and Berlin scales rather than the AHI in the selection of control individuals. However, in daily clinical practice, we use those methods for the selection of appropriate patients for the polysomnography test. In addition, previous reports have demonstrated the correlation of the Epworth Sleepiness Scale with the AHI [27].

Secondly, our study population was relatively small, and finally, the RV dimensions and wall thickness were not measured because conventional echocardiography calculations of these variables are difficult due to the atypical and abnormal shape of the RV. The RV functions were corroborated by an independent method, such as magnetic resonance imaging or radionuclide ventriculography, which may limit the ability to detect and quantify significant associations between OSA severity and the degree of RV dysfunction. Despite the subjects excluded with diseases which have adverse effects on myocardial function, such as diabetes, coronary artery disease and hypertension, the BMI of OSA patients was found to be higher than that of normal healthy individuals. This difference may have an effect on the results of our study; however, even after adjustment of the BMI, the RV mechanical parameters were still correlated with the OSA presence and severity. This showed us that our study findings were not affected by the BMI.

Conclusions

In OSA patients, before the development of RV failure and pulmonary hypertension, it is important to detect subtle RV dysfunction for the prevention of cardiac complications. Even in the absence of pathologies which could have adverse effects on RV functions, OSA itself may lead to RV dysfunction. Besides the direct effect of OSA on RV myocardial functions, the accompanying LV dysfunction may have additional effects on RV dysfunction via interventricular interactions. In addition to conventional and Doppler echocardiographic methods, with the 2D-STE method, the RV functions can be assessed in detail and subtle RV dysfunction can be detected. Additional studies using the 2D-STE method are necessary to determine the ST and STR values for the diagnosis of RV dysfunction. In addition, prospective studies using the 2D-STE method are needed to demonstrate the impact of RV functions on the prognosis of OSA.

Conflict of interest: non declared

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