

# Using Speckle-Tracking Echocardiography to Evaluate Subclinical Left Ventricular Dysfunction in Patients with Obstructive Sleep Apnea Syndrome

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## Abstract

**Purpose:** This study aims to evaluate left ventricular (LV) functions using speckle-tracking echocardiography (STE)-based analyses in the early stages of obstructive sleep apnea (OSA). **Methods:** Twenty-one healthy individuals and 79 OSA patients enrolled in the study. The OSA group was classified according to Apnea-Hypopnea Index (AHI) as mild, moderate, and severe. Two-dimensional tissue Doppler imaging and STE was performed. **Results:** The control and OSA groups were comparable for sex ( $P = 0.450$ ) and age ( $P = 0.560$ ), while diabetes ( $P < 0.001$ ) and hypertension ( $P < 0.001$ ) diagnoses and body mass index ( $P < 0.001$ ) were higher in the OSA patients. In OSA group, global longitudinal strain (GLS) ( $-13.32 \pm 3.19\%$ ,  $P < 0.001$ ), global circumferential strain (GCS) ( $-18.33 \pm 3.40\%$ ,  $P < 0.001$ ) and global radial strain (GRS) ( $37.91 \pm 8.11\%$ ,  $P = 0.005$ ) were reduced. GLS and GCS have a decreasing trend toward severe OSA, while GRS increased in mild and moderate OSA. According to linear regression analysis, GRS ( $\beta: -1.47$ ,  $P = 0.001$ ), GCS ( $\beta: -1.34$ ,  $P = 0.001$ ), GLS ( $\beta: -1.54$ ,  $P < 0.001$ ), systolic pulmonary artery pressure ( $\beta: 0.99$ ,  $P = 0.001$ ), and deceleration time ( $\beta: 0.13$ ,  $P = 0.03$ ) have an independent relationship with AHI. **Conclusions:** In our study, STE technique can be a practical method for manifesting LV functional impairment at the early stages of OSA.

**Keywords:** Global strain parameters, left ventricular dysfunction, obstructive sleep apnea, speckle-tracking echocardiography

## INTRODUCTION

Obstructive sleep apnea (OSA) is a syndrome characterized by recurrent apnea and hypopnea episodes during sleep, primarily affecting the middle-aged population.<sup>[1]</sup> Global estimates suggest that 936 million people worldwide have mild-to-moderate OSA, and 425 million have moderate-to-severe OSA.<sup>[2]</sup> In some observational studies, the prevalence of OSA may be as high as 50% among patients with heart failure. OSA can play a crucial role in heart failure by causing repetitive hypoxia and apnea episodes, hormonal and metabolic impairment, systemic inflammation, and mechanical hemodynamic disturbances.

Extensive research has shown the link between OSA and cardiac remodeling causing heart failure. For example,

Borrelli *et al.* found a 62% prevalence of OSA in heart failure.<sup>[3]</sup> Though, these results were based on basic echocardiographic parameters. Most of the studies have focused on left ventricular (LV) hypertrophy, decreased LV ejection fraction (EF), and LV diastolic dysfunction in the presence of OSA and heart failure.<sup>[3-5]</sup>

The strain is a measure of myocardial deformation. Furthermore, strain analysis is defined as a current LV function index method in recent echocardiography guidelines.<sup>[6,7]</sup> There

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are three different types of strain reflecting cardiac axes: global longitudinal strain (GLS), circumferential, longitudinal strain (global circumferential strain [GCS]), and global radial strain (GRS).<sup>[8]</sup> LV GLS has been introduced as a relevant clinical marker of LV function.<sup>[9]</sup> To date, some studies have investigated the LV mechanics in patients with OSA using speckle-tracking echocardiography (STE).<sup>[10]</sup>

This paper's central hypothesis is that OSA with normal LV EF would have impairment in myocardial deformation. This situation could result in diastolic dysfunction in the early stages of the disease. Based on this hypothesis, our study has three main objectives: (1) to evaluate subclinical LV dysfunction with STE; (2) to investigate LV diastolic parameters and hypertrophic changes in OSA patients compared to a healthy control group; and (3) to ascertain determinant factors for Apnea-Hypopnea Index (AHI).

## METHODS

### Patients

For this study, 88 consecutive newly diagnosed OSA patients aged between 18 and 100 in the Respiratory Medicine Division of Suleyman Demirel University Hospital were evaluated between January 2013 and January 2014. Patients with any of the following conditions were excluded: concomitant lung disease (including chronic obstructive pulmonary disease, bronchial asthma, or intestinal lung disease); heart failure (typical symptoms and signs, depressed LV EF, and elevated natriuretic peptides); valvular heart disease (hemodynamically significant regurgitation/stenosis); coronary heart disease (history of percutaneous intervention or coronary artery bypass graft surgery); atrial fibrillation or any arrhythmia; chronic renal and hepatic disease; a history of malignancy; or a suboptimal echo window. Nine individuals were excluded from the study based on concomitant lung disease ( $n = 5$ ), a poor echocardiographic image ( $n = 3$ ), and atrial fibrillation ( $n = 1$ ), leaving 79 OSA patients (48 males and 31 females).

The control group was composed of 21 volunteers who were first admitted to the respiratory sleep clinic with an AHI of less than five and found normal cardiovascular examination by an experienced cardiologist between December 2014 and January 2014. Moreover, they did not meet the exclusion criteria.

The study was conducted under the Declaration of Helsinki. The Ethical Committee approved the study for Clinical Studies of Suleyman Demirel University (Registration Number: 181). All participants gave written informed consent.

### Polysomnography

Polysomnography (PSG) was performed in a quiet, partially soundproof room with stable humidity and temperature. Data were examined with a Compumedics (44-channel E-series, Australia) PSG device. Electroencephalography, two-channel electrooculography, electromyography, oronasal airflow, thoracic and abdominal movements, body position, and pulse oximetry (oxygen saturation measured from the fingertip) were

monitored during the procedure. According to the American Sleep Disorders Association criteria, an experienced chest disease specialist scored the PSG results.<sup>[11]</sup>

Apnea is defined as a cessation of the airflow signal for 10 s per hour. Hypopnea is identified as a  $\geq 30\%$  decrease in the airflow signal, associated with cortical arousal or oxygen desaturation of  $\geq 3\%$ . The number of apnea plus hypopnea incidents per hour of sleep is calculated as the AHI. Patients with an AHI of less than five were considered OSA negative. This index was used to stratify OSA severity, as mentioned above.

### Standard echocardiographic measurements

In the standard echocardiographic examination, patients were placed in the left lateral decubitus position using a Phillips iE33 Echocardiography machine with a 2.5 MHz transducer. Images were acquired from apical four-chamber, two-chamber, and three-chamber views using two-dimensional (2D), M-mode, color Doppler, continuous-wave Doppler, and pulse-wave Doppler according to recommendations in the American Society of Echocardiography (ASE) guidelines.<sup>[7,12]</sup> The left ventricle (LV) and left atrium (LA) dimensions were evaluated in M-mode during LV diastole from 2D parasternal images. LA size and volume were also evaluated from apical four-chamber and two-chamber views at ventricular end-systole (modified Simpson's method). LA volume indices (LAVIs) were calculated by dividing the LA volumes by the body surface area.<sup>[7]</sup> The sample volume of pulsed-wave Doppler was taken at the mitral leaflets' tip level from the apical four-chamber view for mitral inflow velocity assessment. The peak mitral inflow in early diastole (E wave), the late diastolic atrial filling velocity (A wave), their ratio (E/A ratio), mitral deceleration time (DecT), and aortic ejection time (ET) parameters were measured. The sample volume with measurements of myocardial systolic (S'), early (E'), and late (A') diastolic velocities were applied at the septal and lateral sides of the mitral annulus using pulsed-wave tissue Doppler imaging (TDI) to assess myocardial velocities. All the TDI measures were obtained by averaging values at the septal and lateral mitral annulus. LV isovolumic contraction time (IVCT) and isovolumic relaxation time (IVRT) were acquired from the pulse wave Doppler traces. The Myocardial Performance Index (MPI) was calculated from the formula  $(IVCT \times IVRT)/ET$ .

### Speckle-tracking echocardiography

A specific software package, QLAB V6.0 (Advanced Quantification Software version 6; Phillips), was used to perform the STE analysis from the apical and parasternal short-axis offline images at a frame rate of 70–90 frames/s. Three consecutive cardiac cycles were apical four-chamber, two-chamber, three-chamber views, and parasternal short-axis basal, mid, and apical views were recorded. They averaged<sup>[13]</sup> in Digital Imaging and Communications in Medicine format for offline STE analysis by an experienced cardiologist. Images were acquired at end-expiration during breath hold.

Records were examined in the region of interest (ROI) tab; then, the views were drawn to include the entire myocardium. The

ROI thickness was the same in all the patients independently from LV hypertrophy.

The first step in this process was to mark the mitral annulus endocardial borders and apex on the apical two-, three-, and four-chamber images. Second, automatic tracing was performed [Figure 1]. Endocardial borders were reviewed during end-systolic frames, and images were settled in motion for tracking confirmation. Areas that cannot be tracked were excluded. Third, peak systolic strain was measured and averaged for determining GLS. Before conducting radial strain analysis, the anatomical structures were marked manually as anterior, inferior, and interventricular parts on the short-axis basal, mid, and apical images and endocardial borders were determined by software. Then, borders were again reviewed during end-systolic frames, and images were settled in motion for tracking confirmation. Peak systolic GCS and GRS values were calculated by averaging from analyzed ventricular segments. The software could track 95% of segments longitudinal for GLS and 93% for GRS and GCS, respectively.

Finally, a bullseye image showing left ventricle whole-strain parameters was obtained [Figure 2a and b].

**Statistical analysis**

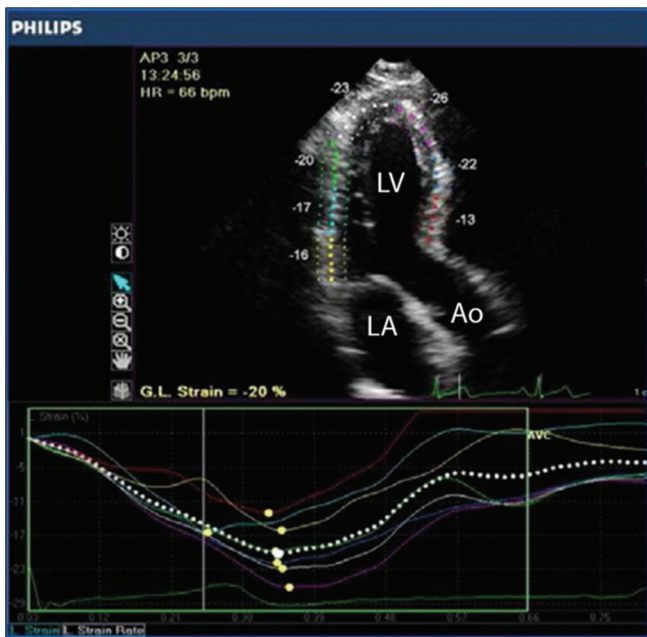
Data management and analysis were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). The fitting of variables to normal distribution was carried out with analytical methods (Kolmogorov–Smirnov tests). The Student’s *t*-test was used to compare parametric variables, and the Chi-square test was used to compare nonparametric variables. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Since 2D echocardiographic data, diastolic parameters, and LV strain values were all determined to show normal distribution, these parameters were compared using a one-way ANOVA test between the OSA groups. The homogeneity of the variances was calculated using the Levene test.

Descriptive analyses were performed using the median and interquartile range for nonnormally distributed variables. Systolic blood pressure, posterior wall (PW) thickness, mitral inflow E/A ratio, and tissue Doppler mitral lateral annulus IVRT were determined to have normal distribution between these parameters in the OSA groups. The analysis was performed using the Kruskal–Wallis test and evaluated using the Bonferroni correction. *P* < 0.05 was considered to show statistically significant results.

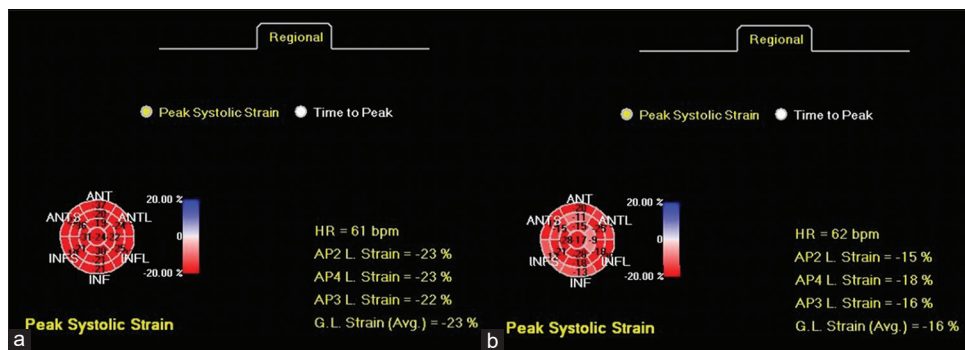
Correlation with the AHI was examined using the Pearson test. Those results with significant correlations were taken into the first univariable linear regression analysis (unadjusted), and variables found *P* < 0.05 were considered in an ordered multivariate logistic regression model (adjusted).

**RESULTS**

Table 1 summarizes the demographic and clinical characteristics of the control and OSA groups. The two groups were comparable for sex (*P* = 0.450), age (*P* = 0.560), smoking (*P* = 0.970), and heart rate (*P* = 0.057). However, diabetes (*P* < 0.001) and hypertension (*P* < 0.001) diagnoses, body mass index (*P* < 0.001), and systolic (*P* < 0.001) and diastolic (*P* = 0.002) blood pressure were higher in the OSA patients than in the healthy controls.



**Figure 1:** Determination of endocardial borders in speckle-tracking evaluation in a mild obstructive sleep apnea patient



**Figure 2:** (a) Global longitudinal strain and bullseye image of a participant in control group. (b) Global longitudinal strain and bullseye image of severe obstructive sleep apnea patient

Table 2 shows the standard echocardiographic characteristics of the subgroups. LV EF with Simpson’s method was 63.12% ± 2.78% in the control group and 61.81% ± 3.45% in the OSA group ( $P < 0.001$ ). LV septal wall thickness ( $P = 0.007$ ), LV

internal dimensions ( $P = 0.023$ ), and LV mass index ( $P < 0.001$ ) were higher in the OSA subgroups. DecT ( $P < 80.001$ ) and IVRT ( $P < 0.001$ ) were also longer in OSA. While E/A ( $P < 0.001$ ) and E/E’ ratios ( $P < 0.001$ ), which are parameters of diastolic function, were impaired in the OSA group. The MPI increased with OSA ( $P < 0.001$ ). If we look at the estimated systolic pulmonary artery pressure (sPAP) of the two groups, it was measured as 23.09 ± 3.80 mmHg in the control group and 32.89 ± 6.46 mmHg in the OSA group ( $P < 0.001$ ).

The next section of the study showed LV GLS (-%13.32 ± 3.19 vs. -%18.60 ± 4.60,  $P < 0.001$ ), GCS (-%18.3 ± 3.4 vs. -%22.27 ± 2.40,  $P < 0.001$ ), and GRS (37.9% ± 8.1% vs. 42.47% ± 5.00%,  $P = 0.005$ ) variables were decreased in OSA patients compared to the control group, as presented in Table 3. Figure 3 shows a clear trend of decreasing GLS and GCS as we moved from the control to the severe OSA patients, while GRS increased in mild and moderate OSA patients compared to the healthy group. Interestingly, GRS decreased in the severe OSA subgroup.

There was a significant positive correlation between AHI and GCS ( $r = -0.53$ ,  $P < 0.001$ ), GRS ( $r = -0.68$ ,  $P < 0.001$ ),

**Table 1: Demographic, clinical variables of the all groups**

	Control (n=21), n (%)	OSA (n=79), n (%)	P
Age (years)	49.2±8.6	50.5±9.1	0.560
Sex (male/female)	15/6	48/31	0.450
Smoking	7 (33)	23 (29)	0.970
DM	0	13 (16)	<0.001
HT	0	31 (39)	<0.001
Hypothyroidism	0	3 (3.7)	0.360
BMI (kg/m <sup>2</sup> )	25.5±3.4	29.9±4.6	<0.001
HR (beat/min)	76.6±9.5	81.9±11.9	0.057
SBP (mmHg)	111.8±8.9	124.5±11.5	<0.001
DBP (mmHg)	69.4±7.0	75.9±8.9	0.002
AHI (IQR)	0 (0-3)	35.6 (8-22)	<0.001

Data are expressed as, n (%) or mean±SD. OSA: Obstructive sleep apnea, DM: Diabetes mellitus, HT: Hypertension, BMI: Body mass index, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, AHI: Apnea-Hypopnea Index, IQR: Interquartile range, SD: Standard deviation

**Table 2: Two-dimensional, M-mode. and Doppler echocardiographic measurements of the study population**

	Control (n=21)	Mild OSA (n=20)	Moderate OSA (n=21)	Severe OSA (n=38)	P*
LA Vol (mL)	35.72±3.16	37.4±4.52	37.91±3.15	42.67±3.64	<0.001
LAVI (mL/m <sup>2</sup> )	19.63±4.61	21.15±5.35	25.54±6.52	31.51±6.11	<0.001
LV EF (%)	63.12±2.78	62.60±3.60	61.88±3.20	60.95±3.55	0.008
LV EDV (mL)	88.37±5.24	88.95±3.31	89.12±3.59	90.22±4.32	0.101
LV ESV (mL)	32.18±2.15	32.83±3.24	32.76±3.21	33.92±3.51	0.023
IVS (mm)	10.32±1.14	10.29±1.43	11.44±1.31	11.91±1.59	<0.001
PW (mm)	9.56±1.34	9.58±0.98	10.08±1.25	10.75±1.45	0.001
LVDD (mm)	48.32±4.43	48.85±5.12	49.48±4.85	49.85±3.81	0.527
LVsD (mm)	30.61±1.39	31.39±2.81	32.18±2.82	32.67±2.69	0.023
LVMI	88.51±14.42	91.48±24.30	105.51±26.92	110.10±25.12	0.002
E (cm/sn)	7.62±1.3	7.48±1.09	7.39±1.53	6.99±1.33	0.304
A (cm/sn)	6.46±1.89	7.52±1.21	8.14±1.31	8.78±1.56	<0.001
DecT (s)	169.23±13.20	177.45±31.53	189.45±33.12	219.61±25.31	<0.001
ET (s)	281.71±21.34	271.65±35.87	261.85±44.85	249.68±23.42†	0.002
E/A ratio	1.33±0.70	1.02±0.22†	0.92±0.21†	0.82±0.26†	<0.001
E/E’ ratio	6.53±1.63	6.88±1.98	7.92±2.43	10.58±2.10†‡***	<0.001
IVRT (s)	86.42±14.81	110.05±22.62	114.80±21.06†	119.18±20.47†	<0.001
S’ wave (cm/sn)	11.17±1.87	10.02±2.21	10.02±2.00	9.30±1.90†	0.010
E’ wave (cm/sn)	12.11±2.57	11.72±3.56	10.06±3.15	9.41±2.35†‡	0.001
A’ wave (cm/sn)	11.41±2.38	12.19±1.90	12.84±2.63	13.04±2.04	0.010
TDI IVCT	48.00±7.25	46.91±9.64	52.15±12.05	57.68±9.34	<0.001
TDI IVRT	90.33±9.89	98.00±18.55	109.55±19.65	112.28±19.37	<0.001
TDI ET	281.52±13.95	284.65±27.53	270.95±23.10	269.31±27.69	0.093
LV MPI	0.46±0.11	0.60±0.15	0.66±0.14	0.71±0.11	<0.001
sPAP (mmHg)	23.09±3.80	30.80±7.2	32.20±4.34	34.36±6.76	<0.001

†Compared with control group,  $P < 0.05$ , ‡Compared with mild OSA group,  $P < 0.05$ , \*\*\*Compared with moderate OSA group,  $P < 0.05$ , \*Tested with one-way ANOVA and Kruskal-Wallis, *post hoc* comparisons made with Tukey’s and Mann-Whitney U-test and evaluated with Bonferroni correction, †Compared to the control group  $P < 0.05$ . Data are expressed as, n (%) or mean±SD. OSA: Obstructive sleep apnea, LAVI: Left atrial volume index, IVS: Interventricular septum, PW: Posterior wall, LV: Left ventricular, LVDD: LV diastolic dimension, LVsD: LV systolic dimension, LV EF: LV ejection fraction, with Simpson’s method, LVMI: LV mass index, LV ESV: LV end-systolic volume, LV EDV: LV end-diastolic volume, DecT: Deceleration time, TDI: Tissue Doppler imaging, ET: Ejection time, IVRT: Isovolumic relaxation time, IVCT: Isovolumic contraction time, LV MPI: LV myocardial performance index, sPAP: Systolic pulmonary pressure, SD: Standard deviation

GLS ( $r = -0.62, P < 0.001$ ), interventricular septum thickness (IVS) ( $r = 0.40, P < 0.001$ ), PW ( $r = 0.35, P < 0.001$ ), sPAP ( $r = 0.46, P < 0.001$ ), LAVI ( $r = 0.28, P = 0.013$ ), E/E' ( $r = 0.51, P < 0.001$ ), LV MPI ( $r = 0.23, P = 0.041$ ), and DecT ( $r = 0.48, P < 0.001$ ) variables [Table 4].

Linear regression analysis was performed to determine the parameters that correlate independently with the AHI. GRS ( $\beta: -1.47; 95\%$  confidence interval [CI]:  $-1.97-0.98, P = 0.001$ ), GCS ( $\beta: -1.34; 95\%$  CI:  $-2.04-1.10, P = 0.001$ ), GLS ( $\beta: -1.54; 95\%$  CI:  $-1.93-1.04, P < 0.001$ ), sPAP ( $\beta: 0.99, 95\%$  CI:  $0.49-1.53, P = 0.001$ ), and DecT ( $\beta: 0.13; 95\%$  CI:  $0.20-0.24, P = 0.03$ ) were found to be independently associated with AHI [Table 4].

### DISCUSSION

OSA is frequently associated with many cardiovascular diseases and severe clinical outcomes, including heart failure. The current study's main goal was to evaluate LV functions using STE-based analyses in OSA patients before developing the overt clinical disease. We found that GLS, GCS, and GRS values decreased in OSA patients compared to a healthy control group, while LV functions were still intact in 2D echocardiographic imaging. One interesting finding was that GRS increased in mild and moderate OSA patients while it decreased significantly in the severe OSA group. However, GLS and GCS were decreasing from the control to severe OSA groups. The second goal of this research was to look for LV diastolic parameters and LV hypertrophic changes in OSA patients compared to the control group. Diastolic functions were found impaired with the OSA progression; in addition, the LV was more hypertrophic in OSA patients. Another objective of the study was to determine independent factors for AHI. We found that GLS, GCS, GRS, sPAP, and DecT have an independent relationship with AHI.

Prior studies have noted the significance of heart failure development in OSA patients compared with the general population.<sup>[14-16]</sup> However, the traditional systolic function parameter LV EF was normal in most OSA patients despite heart failure signs.<sup>[17,18]</sup> In addition, it is difficult to detect cardiac changes with conventional 2D echocardiography. GLS is a recent marker for subclinical LV pump dysfunction, and we found that GLS was decreasing from the healthy control group toward severe OSA patients. This result seems to be consistent with other researches.<sup>[18-20]</sup> A possible explanation for the decrease in LV longitudinal strain may be the susceptibility of subendocardial fibers to hypoxia in OSA patients.

Furthermore, a higher prevalence of diabetes and hypertension in the OSA groups could affect LV longitudinal function GLS even with preserved diastolic function. Myocardial longitudinal shortening and myocyte apoptosis cause a decrease in longitudinal and circumferential strain values. While GLS and GCS decrease in the mild OSA group, GRS increases. The reason for this finding is not apparent, but it may be associated with adaptive mechanisms such as

**Table 3: The left ventricular global strain values of the obstructive sleep apnea subgroups and the control group**

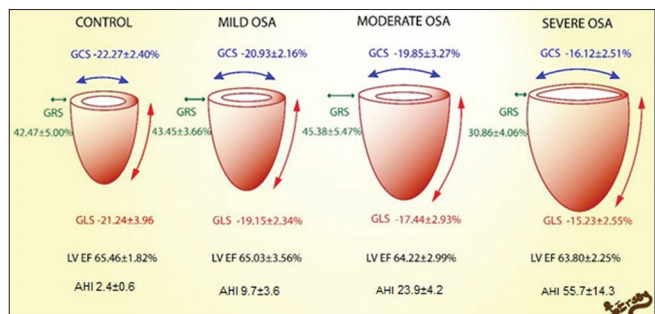
	Control (n=21)	OSA (n=79)	P
GLS (%)	-18.60±4.60	13.32±3.19	<0.001
GCS (%)	-22.27±2.40	18.33±3.40	<0.001
GRS (%)	42.47±5.00	37.91±8.11	0.005

Data are expressed as, n (%) or mean±SD. OSA: Obstructive sleep apnea, GLS: Global longitudinal strain, GCS: Global circumferential strain, GRS: Global radial strain, SD: Standard deviation

**Table 4: Linear regression analysis of Apnea-Hypopnea Index with clinical and echocardiographic measurements**

	r	P	β	CI		P
				Lower bound	Upper bound	
Age	0.7	0.015	-	-	-	-
SBP	0.32	0.004	-	-	-	-
DBP	0.22	0.043	-	-	-	-
GCS	-0.53	<0.001	-1.34	-2.04	-1.10	0.001
GRS	-0.68	<0.001	-1.47	-1.97	-0.98	0.001
GLS	-0.62	<0.001	-1.54	-1.93	-1.04	0.001
IVS	0.40	<0.001	-	-	-	-
PW	0.35	<0.001	-	-	-	-
sPAP	0.46	<0.001	0.99	0.49	1.53	0.001
DecT	0.48	<0.001	0.13	0.20	0.24	0.031
IVCT	0.23	0.035	-	-	-	-
LV MPI	0.23	0.041	-	-	-	-
LAVI	0.28	0.013	-	-	-	-
E/E'	0.51	<0.001	-	-	-	-

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, GLS: Global longitudinal strain, GCS: Global circumferential strain, GRS: Global radial strain, IVS: Interventricular septum, PW: Posterior wall, sPAP: Systolic pulmonary artery pressure, DecT: Deceleration time, IVCT: Isovolumic contraction time, LV: Left ventricular, LV MPI: LV myocardial performance index, LAVI: Left atrial volume index, CI: Confidence interval



**Figure 3:** An illustration showing global strain (GLS, GRS, and GCS) patterns changing normal to severe OSA. Data are expressed as number (%) or mean ± SD. Abbreviations: OSA: Obstructive sleep apnea, GLS: Global longitudinal strain, GCS: Global circumferential strain, GRS: Global radial strain, AHI: Apnea-Hypopnea Index, SD: Standard deviation

radial thickening to preserve LV EF. In the later stages of OSA, all strain parameters decreased significantly compared to the control group. This situation's main reason may be increased cardiac afterload, and LV adaptive mechanisms are not responding to this condition and causing LV subclinical

dysfunction. There are investigations in which TDI has been used to represent an early stage of myocardial abnormality despite preserved global LV function.<sup>[17,21,22]</sup> The TDI is an angle-dependent technique, and it has significant test variabilities, causing important limitations. STE does not need angle interrogation.<sup>[23]</sup> All global strain value reduction broadly supports the results of other studies in this area linking OSA with subclinical dysfunction.<sup>[10,18,19]</sup>

When we look at the second aim of this study, our results showed relevant connections between OSA and LV hypertrophy, LV mass index diastolic dysfunctions, and enlargement of the left ventricle and atrium, consistent with other researches.<sup>[24-26]</sup> In our results, as the OSA severity increased from the healthy control group, LV hypertrophy, LA diameter, LV diameter, LV mass index, and LV MPI also increased. We found that as for diastolic parameters, like E, E/A ratio decreased, A, E/E' ratio and IVRT, DecT, and ET elevated in OSA progression. These findings can be explained with some hypotheses: compensatory changes occur against an increase in LV afterload; nocturnal hypoxia and sympathetic hyperactivity can increase blood pressure; and respiratory effort during apnea can cause severe negative intrathoracic pressure, resulting in raised transmural pressure. These data must be interpreted with caution because our study participants tended to be obese, hypertensive, and diabetic. These factors are well-known causes of LV hypertrophy and diastolic dysfunction.

Another significant aspect of our study underlines that the AHI, which reflects OSA severity, correlates with GRS, GCS, E/E' ratio, DecT, IVS, PW, and sPAP. Patients with a higher AHI had more impaired horizontal strain patterns and diastolic reserve. These relationships may partly be explained by nocturnal apnea and hypoxia episodes increasing LV afterload during sleep. This mechanism could be the first step of cardiac remodeling and result in impaired global strain patterns in OSA patients.

Our study excluded situations that could increase pulmonary pressure, such as chronic pulmonary disease and asthma. In our finding, sPAP was higher in OSA patients than healthy controls, in agreement with previous studies.<sup>[27,28]</sup> In a physio-pathogenetic view, repetitive hypoxia can cause pulmonary vasoconstriction, while endothelial remodeling increases endothelin-1 release, NO release decreases, and OSA-related pulmonary pressure increases.<sup>[29]</sup>

Our study has some limitations. The main drawback was a single-center experience, and one cardiologist performed the echocardiography. This situation cannot exclude selection or procedure bias. Our control group had no hypertension or diabetes, and the OSA patients were overweight individuals. Hypertension, diabetes, and obesity could affect diastolic and LV dimension results. Furthermore, this work is also limited by not considering medications like renin-angiotensin antagonists that could affect early remodeling. In addition, the severe OSA group included the highest number of patients. Our study lacks hemodynamic data. An assessment by right heart catheterization might have provided more accurate

information about sPAP. This study's final limitation relates to not considering markers such as B-type natriuretic peptide and N-terminal pro-brain natriuretic peptide diagnosing heart failure.

Strain parameters are a proven method that has entered guidelines and consensus documents, as in the ASE and the European Association of Cardiovascular Imaging.<sup>[30]</sup> Merely one of its main limitations, which is the time-consuming offline analysis, might make it difficult to apply STE to every clinical setting, particularly to the outpatient clinic. Furthermore, there is no agreement on STE strain parameters for OSA presence and severity. Future follow-up studies seeking to use STE should attempt to determine predictive LV strain value on OSA patients' outcomes.

## CONCLUSIONS

Cardiac mechanic evaluation with STE will be a regular part of the echocardiographic imaging. Furthermore, impaired cardiac mechanics project the first step in the complex cascade of cardiac remodeling in OSA patients. Our study results indicate that LV strains and diastolic functions were impaired in OSA patients while LV EF was in the normal range. STE technique can be a practical method for manifesting LV functional impairment at the newly diagnosed stages of OSA.

## Ethical statement

The study was conducted under the Declaration of Helsinki. The Ethical Committee approved the study for Clinical Studies of Suleyman Demirel University (Registration Number: 181). All participants gave written informed consent.

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## Conflicts of interest

There are no conflicts of interest.

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