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Subclinical Right Ventricular Dysfunction and Left Atrial Remodeling Across Obstructive Sleep Apnea Severities: A Cross-Sectional Speckle-Tracking Echocardiographic Study

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Abstract

Background and Objectives:
Obstructive sleep apnea (OSA) is strongly linked to cardiovascular morbidity, yet the extent of subclinical right heart remodeling and left atrial enlargement across disease severities remains inadequately characterized. This study aimed to evaluate cardiometabolic characteristics, conventional echocardiographic parameters, and right ventricular (RV) myocardial mechanics using two-dimensional speckle-tracking echocardiography (2D-STE) in patients with severe versus mild-to-moderate OSA.

Methods:
This single-center, cross-sectional observational study enrolled 173 consecutive adult patients (aged ≥18 years) evaluated at a tertiary cardiovascular referral center between January 2023 and January 2025. All participants underwent overnight in-laboratory polysomnography (PSG) and comprehensive transthoracic echocardiography within a 4-week interval. Patients were stratified into mild-to-moderate OSA ($5.0 \leq AHI < 30.0$ events/h; n=87) and severe OSA (AHI ≥ 30.0 events/h; n=86) groups. Multivariable binary logistic and linear regression analyses were performed to identify independent determinants of severe disease and myocardial impairment. Receiver operating characteristic (ROC) curve analysis evaluated the diagnostic discriminative value of echocardiographic parameters.

Results:
Patients with severe OSA were significantly older (53.4 ± 11.2 vs. 47.1 ± 12.8 years, P = 0.001), had a higher body mass index (34.8 ± 4.2 vs. 30.9 ± 3.9 kg/m², P < 0.001), and exhibited a higher male predominance (72.1% vs. 49.4%, P = 0.002) compared to those with mild-to-moderate OSA. Severe OSA was associated with a significantly elevated comorbidity burden, including a higher prevalence of prior cerebrovascular accidents (24.4% vs. 9.2%, P = 0.007). Echocardiographically, patients in the severe group demonstrated marked subclinical myocardial impairment, characterized by significantly reduced RV free-wall longitudinal strain (RV-FWLS: 19 ± 7% vs. 25 ± 4%, P < 0.001) and impaired conventional systolic parameters. Multivariable linear regression identified continuous apnea-hypopnea index (AHI) as an independent predictor of impaired RV-FWLS (B = -0.067, P < 0.001) and elevated pulmonary artery systolic pressure (B = +0.077, P = 0.007). Furthermore, ROC analysis revealed that left atrial volume index (LAVI) possessed superior diagnostic accuracy for identifying severe OSA (AUC = 0.931, P < 0.0001) compared to RV-FWLS and conventional hemodynamics.

Conclusion:
Severe OSA is independently associated with pronounced subclinical right ventricular longitudinal strain impairment and left atrial remodeling. Two-dimensional speckle-tracking echocardiography and LAVI provide robust diagnostic utility for identifying high-risk patients, emphasizing the critical need for early cardiovascular screening and aggressive management in severe sleep apnea populations.

Keywords: Sleep Apnea, Obstructive; Right Ventricular Function; Speckle-Tracking Echocardiography; Left Atrial Remodeling; Cardiovascular Diseases.

Introduction:

Obstructive sleep apnea (OSA) is a common sleep-related breathing disorder characterized by recurrent upper-airway obstruction during sleep, intermittent hypoxemia, sleep fragmentation, autonomic activation, and fluctuations in intrathoracic pressure(1, 2).An estimated 936 million adults aged 30 to 69 years worldwide may have mild-to-severe OSA, including approximately 425 million with moderate-to-severe disease(2). Despite its high prevalence, OSA remains underdiagnosed in clinical practice.

OSA frequently coexists with cardiovascular and metabolic disorders, including hypertension, type 2 diabetes, coronary artery disease, atrial fibrillation, heart failure, pulmonary hypertension, and cerebrovascular disease(1, 3). These associations may reflect the effects of intermittent hypoxemia, sympathetic overactivity, oxidative stress, endothelial dysfunction, inflammation, and abnormal intrathoracic pressure. However, obesity, age, and preexisting cardiovascular disease are important shared risk factors; therefore, associations identified in observational studies should not be interpreted as evidence of causality(1, 3).

The apnea-hypopnea index (AHI) remains the principal measure used to classify OSA severity, with severe OSA generally defined as an AHI of at least 30 events per hour. However, AHI quantifies respiratory-event frequency and may not fully capture the physiological burden of OSA. The duration and depth of oxygen desaturation may differ substantially among individuals with similar AHI values. In cohort studies, hypoxic burden was more strongly associated with cardiovascular mortality than AHI, suggesting that measures of nocturnal hypoxemia may provide complementary clinical information(4).

Cardiac remodeling and right-ventricular dysfunction may represent important cardiovascular manifestations of OSA. A systematic review and meta-analysis found that OSA was associated with right-ventricular dilatation, increased right-ventricular wall thickness, and impaired right-ventricular systolic indices, including tricuspid annular plane systolic excursion, right-ventricular S′ velocity, and right-ventricular fractional area change(5). OSA has also been linked to abnormal glucose metabolism and insulin resistance, although these relationships may be partly influenced by obesity and other comorbidities(6).

While left ventricular dysfunction in OSA has been extensively investigated, the assessment of right ventricular (RV) mechanics and left atrial (LA) remodeling across disease severities has received comparatively less attention, despite the profound impact of intermittent hypoxia, negative intrathoracic pressure swings, and recurrent nocturnal pulmonary vasoconstriction on the thin-walled right heart and cardiac chambers. Conventional echocardiographic parameters (such as TAPSE or tissue Doppler S′) often fail to detect early, subclinical right ventricular impairment due to the complex geometry of the RV. Consequently, two-dimensional speckle-tracking echocardiography (2D-STE) has emerged as a sensitive, angle-independent modality capable of unmasking subclinical myocardial dysfunction.

Accordingly, this single-center cross-sectional study was conducted to evaluate and compare cardiometabolic characteristics, conventional echocardiographic indices, left atrial enlargement, and RV myocardial mechanics (using 2D-STE) between adults with polysomnography-confirmed severe OSA and those with mild-to-moderate OSA. The study was designed to characterize associations across OSA severity groups and to generate hypotheses for future longitudinal research; it was not intended to establish causality.

Methods

Study Design and Setting

This single-center, cross-sectional observational study was conducted at Rajaie Cardiovascular Medical and Research Center (Tehran, Iran), a tertiary cardiovascular referral center, between January 2023 and January 2025. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was formally approved by the Institutional Ethics Committee of Rajaie Cardiovascular Medical and Research Center (Approval Code: IRB140312). Written informed consent was obtained from all participants prior to enrollment.

Study Population and Eligibility Criteria

Adult patients (aged ≥18 years) consecutively referred to the center's sleep disorders laboratory for clinically suspected sleep-disordered breathing were prospectively screened. Patients were eligible for inclusion if they underwent both diagnostic overnight polysomnography (PSG) and comprehensive transthoracic echocardiography (TTE) within a maximum interval of 4 weeks.

Inclusion required a confirmed diagnosis of obstructive sleep apnea (OSA), defined as an apnea–hypopnea index (AHI) ≥5.0 events/hour according to the American Academy of Sleep Medicine (AASM) criteria. For patients with mild OSA (AHI 5.0–14.9 events/h), documented clinical symptoms (e.g., excessive daytime sleepiness, witnessed apneas, choking/gasping) or

established cardiometabolic comorbidities were required. Participants were stratified into two clinical severity groups:
1) Mild-to-moderate OSA ($5.0 \leq AHI < 30.0$ events/h)
2) Severe OSA ($AHI \geq 30.0$ events/h).

Exclusion criteria were:
1) Predominant central sleep apnea (>50% central apneas/hypopneas of total respiratory events);
2) Severe parenchymal lung disease or severe chronic obstructive pulmonary disease (GOLD Stage III–IV);
3) Significant primary left-sided valvular heart disease (greater than moderate stenosis or regurgitation);
4) Known congenital heart disease or prior cardiac surgery involving pericardiotomy;
5) Inadequate acoustic windows or uninterpretable PSG recordings;
6) Prior treatment for OSA (including positive airway pressure therapy or oral appliances).

Clinical and Comorbidity Ascertainment
Baseline demographics, anthropometric measurements, and lifestyle habits (including cigarette smoking) were documented. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Cardiometabolic comorbidities were defined based on standardized criteria:
- Hypertension:Systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or active antihypertensive medication use.
- Diabetes Mellitus: Fasting plasma glucose ≥126 mg/dL, HbA1c ≥6.5%, or current use of hypoglycemic agents.
- Dyslipidemia: Documented history of hyperlipidemia or current lipid-lowering therapy.
- Coronary Artery Disease (CAD):Documented history of myocardial infarction, coronary revascularization, or angiographically proven stenosis ≥50%.
- Cerebrovascular Accident (CVA):Neurologically confirmed ischemic/hemorrhagic stroke or transient ischemic attack.
- Depression: Documented clinical diagnosis by a specialist or ongoing antidepressant therapy.
- Polycythemia: Hemoglobin >16.5 g/dL in women or >18.5 g/dL in men, or hematocrit >48% in women or >52% in men.

Polysomnographic Evaluation
Overnight full in-laboratory polysomnography was performed using standard diagnostic sleep systems (SOMNOscreen plus, SOMNOmedics GmbH, Randersacker, Germany). Continuous physiological monitoring included electroencephalography (EEG), electrooculography (EOG), submental and bilateral anterior tibialis electromyography (EMG), modified Lead II electrocardiography (ECG), nasal pressure cannula, thoracoabdominal respiratory inductance plethysmography, and continuous finger pulse oximetry.

PSG recordings were manually scored by experienced certified sleep technologists blinded to clinical and echocardiographic data, according to the AASM Manual for the Scoring of Sleep and Associated Events (Version 2.6). Apnea was defined as a drop in peak signal excursion by ≥90% from pre-event baseline lasting ≥10 seconds. Hypopnea was defined as a ≥30% reduction in nasal airflow for ≥10 seconds accompanied by an oxygen desaturation of ≥3% or an EEG arousal. The apnea–hypopnea index (AHI) was calculated as the total number of apneas and hypopneas per hour of total sleep time (TST).

Echocardiographic Assessment

Comprehensive transthoracic echocardiography was performed using high-end ultrasound systems (Vivid E95, GE Healthcare, Horten, Norway) equipped with an M5S active matrix phased-array transducer (1.5–4.6 MHz). All examinations were conducted within 4 weeks of PSG by an experienced cardiologist/echocardiographer who was blinded to the patients' PSG severity classifications, adhering strictly to current American Society of Echocardiography (ASE) and European Association of Cardiovascular Imaging (EACVI) guidelines.

- **Left Heart Indices:** Left ventricular ejection fraction (LVEF) was measured using the biplane Simpson's method of disks. Left atrial volume was obtained at end-systole from apical 4- and 2-chamber views and indexed to body surface area (LAVI, mL/m²). Interventricular septal thickness (IVSd) and posterior wall thickness (PWd) were measured at end-diastole.

- **Right Heart Structure and Hemodynamics:** Right atrial volume was determined at end-systole and indexed to BSA (RAVI, mL/m²). Right ventricular end-diastolic and end-systolic volume indices (RVEDVI, RVESVI) were acquired from RV-focused apical 4-chamber views. **sPAP** (Systolic pulmonary artery pressure) was calculated using the modified Bernoulli formula (4 × tricuspid regurgitation peak velocity² + right atrial pressure). Right atrial pressure (RAP) was estimated based on the inferior vena cava (IVC) diameter and its inspiratory collapsibility.

- **Right Ventricular Systolic Function:** Conventional RV systolic function was quantified using tricuspid annular plane systolic excursion (TAPSE) via M-mode, pulsed-wave tissue Doppler imaging systolic velocity of the lateral tricuspid annulus (RV S'), and RV fractional area change [FAC (%) = ((end-diastolic area – end-systolic area) / end-diastolic area) × 100].

- **Two-Dimensional Speckle-Tracking Echocardiography:** Offline speckle-tracking analysis was performed on RV-focused apical 4-chamber views at a frame rate of 60–80 frames/second using dedicated workstation software (EchoPAC v204, GE Healthcare). The RV endocardial border was manually traced at end-diastole. Peak systolic RV free-wall longitudinal strain (RV-FWLS) and RV septal longitudinal strain were computed. In accordance with current conventions, absolute values (|%|) are presented, where lower numerical values reflect worse myocardial contractility and functional impairment.

Statistical Analysis

Analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software (Ostend, Belgium). Distribution normality was assessed using the Shapiro–Wilk test. Continuous variables are expressed as mean ± standard deviation (SD) for normally distributed data or median (interquartile range [IQR]) for skewed distributions, and compared between groups using the independent-samples t-test or Mann–Whitney U test, as appropriate. Categorical variables are reported as frequencies and percentages (n, %) and compared using Pearson's χ^2 or Fisher's exact test.

To identify clinical and demographic factors independently associated with severe OSA (defined as AHI ≥\ge≥ 30 events/h), multivariable binary logistic regression analysis was conducted. To avoid residual confounding, the full multivariable model was simultaneously adjusted for established cardiovascular and metabolic risk factors, comprising age, sex, BMI,

smoking status, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, chronic heart failure, history of cerebrovascular accident, dyslipidemia, and polycythemia. Adjusted odds ratios (aORs) with their corresponding 95% confidence intervals (CIs) were estimated. Multicollinearity among covariates was evaluated using variance inflation factors (VIF < 2.5 considered acceptable). Overall goodness-of-fit was assessed via the likelihood ratio test and McFadden's pseudo-R2R^2R2.

To determine independent determinants of continuous myocardial and hemodynamic alterations (specifically RV-FWLS and PASP), multivariable linear regression models were constructed with continuous AHI, age, sex, BMI, hypertension, diabetes mellitus, and coronary artery disease as covariates. Model assumptions, including absence of multicollinearity (variance inflation factor <2.5) and residual normality, were verified.

Receiver operating characteristic (ROC) curve analyses were performed to determine the discriminative ability of echocardiographic indices for identifying severe OSA. Optimal cut-off points were identified using the maximum Youden index (J). Comparison of areas under the ROC curves (AUC) was conducted using the DeLong test. A two-sided p-value <0.05 was considered statistically significant for all analyses.

Results

1. Study Population and Baseline Characteristics

A total of 173 consecutive adult patients fulfilling the study inclusion criteria who underwent comprehensive diagnostic in-laboratory polysomnography (PSG) and transthoracic echocardiography were analyzed. Based on the Apnea–Hypopnea Index (AHI), patients were stratified into two groups: mild-to-moderate OSA (5.0≤AHI<30.0 events/h , n=87) and severe OSA (AHI≥30.0 events/h ,n=86).

Baseline demographic, anthropometric, and clinical characteristics stratified by OSA severity are detailed in **Table 1**. The distributional normality of continuous variables was confirmed via the Shapiro–Wilk test. Patients in the severe OSA cohort were significantly older (53.4±11.2 vs. 47.1±12.8 years , Student's t= −3.45 , P=0.001) and exhibited significantly higher body mass index (34.8±4.2 vs. 30.9±3.9 kg/m^2 , t=−6.29 ,P<0.001) compared with those in the mild-to-moderate cohort. Categorical comparisons using Pearson's chi-square and Fisher's exact tests demonstrated a notable male preponderance in severe OSA (72.1% vs. 49.4%, $\chi 2$=9.38 , P=0.002). Among baseline cardiovascular comorbidities, a history of cerebrovascular accident (CVA) was significantly more prevalent in the severe OSA group (24.4% vs. 9.2%, $\chi 2$=7.42 , P=0.007). Trends toward higher prevalence in the severe group were noted for hypertension (19.8% vs. 10.3, P=0.077), diabetes mellitus (20.9 vs. 11.5%, P=0.091), and polycythemia (16.3% vs. 8.0%, P=0.089), although these did not reach statistical significance at the alpha level of 0.05.

Regarding polysomnographic parameters, non-parametric analysis (Mann–Whitney U test) confirmed that patients with severe OSA had markedly higher median AHI [61.0 (43.0–82.0) vs. 17.0 (13.0–22.0) events/h, U=0.0, P<0.001] and higher total nocturnal respiratory events [297.23±215.76 vs. 156.83±148.81, U=2239.0 , P<0.001].

2. Conventional and Speckle-Tracking Echocardiographic Findings

Comparative analysis of cardiac structural, hemodynamic, and functional parameters is presented in **Table 2**.

Left Heart Remodeling: Resting left ventricular ejection fraction (LVEF) was preserved across the study population, with no statistically significant difference between severe and mild-to-moderate groups (52.4±5.1% vs. 53.1±4.8%, t=0.94, P=0.350 . Conversely, left atrial volume index (LAVI) was markedly enlarged in the severe OSA group (32.53±3.52 vs. 25.57±2.79 mL/m^2 , U=513.5, P<0.001). Mild but statistically significant increases in left ventricular end-diastolic dimension (LVEDD: 48.7±5.5 vs. 46.9±4.8 mm , t= −2.29, P=0.023) and interventricular septal thickness (IVSD: 10.9±1.5 vs. 10.3±1.2 mm , t=−2.90 P=0.004) were also observed in severe OSA.

Right Heart Remodeling and Hemodynamics: Systolic pulmonary artery pressure (sPAP) was substantially higher in severe OSA (36.81±8.24 vs. 28.45±6.12 mmHg ,U=1968.5, P<0.001). Right heart chambers demonstrated significant anatomical enlargement: right atrial volume index (RAVI: 29.14±4.11 vs. 24.23±3.65 mL/m^2 , U=1625.0 , P<0.001), right ventricular end-diastolic volume index (RVEDVI: 48.21±5.34 vs. 42.15±4.87 mL/m^2 ,U=1782.0, P<0.001), and right ventricular end-systolic volume index (RVESVI: 27.25±3.61 vs. 23.41±3.12 mL/m^2 ,U=1891.0 , P<0.001) were all significantly increased in severe OSA patients.

Right Ventricular Functional and Deformation Mechanics: Conventional indices of RV systolic function showed significant reduction in severe OSA, including tricuspid annular plane systolic excursion (TAPSE: 18.72±4.29 vs. 23.52±3.25 mm , U=5981.0, P<0.001) and RV fractional area change (RVFAC: 38.4±6.1% vs. 43.2±5.4% , U=5214.0 , P<0.001). In two-dimensional speckle-tracking echocardiography, subclinical myocardial deformation was markedly impaired in severe OSA: RV free-wall longitudinal strain was significantly lower (18.93±6.55% vs. 24.99±4.31% , U=5643.5 , P<0.001), as were RV septal strain (15.20±4.02% vs. 18.42±3.68% , U=5410.0 , P<0.001) and average RV strain (17.84±5.42% vs. 22.65±3.91% , U=5520.5 , P<0.001 P).

3. Independent Predictors of Severe OSA

To determine independent clinical factors associated with severe OSA classification, a multivariable binary logistic regression model was constructed (**Table 3**). Covariates entered into the model included age, sex, BMI, smoking status, hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, heart failure, CVA, hyperlipidemia, and polycythemia. The overall regression model demonstrated robust goodness-of-fit (Omnibus test of model coefficients: Likelihood Ratio $\chi 2$=74.88 , degrees of freedom =12, P=2.25×10^{-7} ; McFadden's pseudo-R^2 =0.227).

Following full multivariable adjustment, three variables remained independently associated with increased odds of severe OSA:

1. **Male sex:** adjusted Odds Ratio (aOR) =3.53 (95% CI:1.62–7.72, CI:1.62–7.72, P=0.0015).
2. **Body mass index:** aOR=1.21 per 1 kg/m^2 increment (95% CI:1.09–1.34 , P=0.0002).
3. **History of CVA:** aOR=4.51 (95% CI:1.45–14.04, P=0.0092).

Age and traditional cardiometabolic comorbidities were not independently predictive of severe OSA classification after adjusting for sex and BMI.

4. Continuous Association Between AHI, RV Mechanics, and Pulmonary Pressures

To evaluate whether nocturnal apnea severity exerts a direct, independent effect on right ventricular deformation mechanics and pulmonary hemodynamics, two multivariable linear regression models were constructed (**Table 4**), adjusting for potential confounders including age, sex, BMI, hypertension, diabetes mellitus, and coronary artery disease.

Determinants of RV Free-Wall Strain: The overall regression model was statistically significant (F(7,165)=7.91, P<0.001P , multiple R^2 =0.251, adjusted R^2 =0.219). Continuous AHI was an independent negative predictor of RV free-wall strain (B= −0.067 , SE=0.014 , standardized β=−0.334, t=−4.70, P<0.001, 95% CI:−0.094 to −0.039). This indicates that for each 10-event/h elevation in AHI, RV free-wall strain declined by an average of 0.67% in absolute deformation magnitude, independent of age, obesity, or underlying cardiovascular disease. In addition, male sex (B=−2.381, t=−2.60, P=0.010) and diabetes mellitus (B=−3.004, t=−2.45, P=0.015) were independently associated with impaired RV free-wall strain.

Determinants of sPAP: The multivariable linear regression model for sPAP was likewise significant (F(7,165)=2.24 , P=0.033, multiple R^2 =0.087, adjusted R^2 =0.048R). AHI emerged as the sole independent predictor of elevated sPAP (B=+0.077, SE=0.029, standardized β=+0.207, t=2.72, P=0.007, 95% CI:0.021–0.134), reflecting an estimated increase of 0.77 mmHg in sPAP for every 10-unit increase in AHI.

5. Diagnostic Performance and ROC Curve Analysis

The discriminatory capacity of echocardiographic and anthropometric indices for identifying patients with severe OSA (AHI≥30 events/h) was evaluated using receiver operating characteristic (ROC) curves (**Table 5**). Cut-off thresholds were determined using Youden's J statistic.

Left Atrial Volume Index (LAVI): LAVI demonstrated exceptional diagnostic accuracy, yielding an area under the curve (AUC) of **0.931** (95% CI:0.898–0.965, P<0.001). An optimal cut-off value of **≥29.0 mL/m^2** provided a sensitivity of **83.7%** and a specificity of **83.9** (Youden's index J=0.676).

RV Free-Wall Strain: Strain imaging demonstrated strong discriminatory performance, with an AUC of **0.754** (95% CI:0.682–0.827, P<0.001). A threshold of **≤16.0%** yielded high specificity (**96.6**) for detecting severe OSA (sensitivity 51.2%, Youden's index J=0.478J).

Other Indices: Modest discriminatory capabilities were noted for sPAP (AUC=0.656, 95% CI:0.573–0.738; optimal cut-off ≥31.0 mmHg , sensitivity 37.2%, specificity 93.1%), BMI (AUC=0.653 , 95% CI:0.571–0.734; optimal cut-off ≥34.0 kg/m^2 , sensitivity 55.8%, specificity 73.6%), and average RV strain (AUC=0.593, 95% CI:0.508–0.678).

Pairwise AUC Comparisons (DeLong's Test): Pairwise testing revealed that the diagnostic performance of LAVI was statistically superior to all other investigated parameters (P<0.0001 for all comparisons). Furthermore, RV free-wall strain showed significantly superior discriminatory performance compared with average RV strain (ΔAUC=0.161, Z=3.65, P<0.001) and sPAP (ΔAUC=0.099, Z=2.39, P=0.017).

Table 1. Baseline Demographic, Clinical, and Polysomnographic Characteristics of the Study Population (N=173)

Characteristic	Overall (N=173)	Mild-to-Moderate OSA (n=87)	Severe OSA (n=86)	Test Statistic (t / χ 2 / U)	P -value
Age (years), mean ± ± SD	50.2±12.4	47.1±12.8	53.4±11.2	t=−3.45	0.001
Male sex, n (%)	105 (60.7%)	43 (49.4%)	62 (72.1%)	χ2=9.38	0.002
BMI (kg/m2), mean ± ± SD	32.8±4.5	30.9±3.9	34.8±4.2	t=−6.29	< 0.001
Smoking history, n (%)	56 (32.4%)	25 (28.7%)	31 (36.0%)	χ2=1.05	0.305
Hypertension, n (%)	26 (15.0%)	9 (10.3%)	17 (19.8%)	χ2=3.12	0.077
Diabetes Mellitus, n (%)	28 (16.2%)	10 (11.5%)	18 (20.9%)	χ2=2.85	0.091
Coronary Artery Disease, n (%)	31 (17.9%)	12 (13.8%)	19 (22.1%)	χ2=2.07	0.150
Atrial Fibrillation, n (%)	45 (26.0%)	20 (23.0%)	25 (29.1%)	χ2=0.84	0.358
Heart Failure (CHF), n (%)	37 (21.4%)	15 (17.2%)	22 (25.6%)	χ2=1.83	0.176
History of CVA, n (%)	29 (16.8%)	8 (9.2%)	21 (24.4%)	χ2=7.42	0.007
Hyperlipidemia, n (%)	46 (26.6%)	19 (21.8%)	27 (31.4%)	χ2=2.00	0.157
Polycythemia, n (%)	21 (12.1%)	7 (8.0%)	14 (16.3%)	χ2=2.89	0.089

Polysomnography Indices					
- AHI (events/h), mean ± SD	41.60±31.91	17.62±6.33	65.92±28.97	U=0.0	< 0.001
- Median (IQR)	30.0 (16.0–62.0)	17.0 (13.0–22.0)	61.0 (43.0–82.0)	—	—
- Total Episodes, mean ± ± SD	226.60±197.66	156.83±148.81	297.23±215.76	U=2239.0	< 0.001

Continuous data are presented as mean ±\pm± SD or median (interquartile range); categorical data are presented as frequencies and percentages. AHI: Apnea-Hypopnea Index; BMI: Body Mass Index; CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; CVA: Cerebrovascular Accident.

Table 2. Conventional and Speckle-Tracking Echocardiographic Parameters Stratified by OSA Severity

Echocardiographic Parameter	Overall (N=173)	Mild-to-Moderate OSA (n=87)	Severe OSA (n=86)	Test Statistic (U / t)	P -value
Left Heart Indices					
- LVEF (%)	52.7±4.9	53.1±4.8	52.4±5.1	t=0.94	0.350
LAVI (mL/m2 mL)	29.03±4.75	25.57±2.79	32.53±3.52	U=513.5	< 0.001
LVEDD (mm)	47.8±5.2	46.9±4.8	48.7±5.5	t=−2.29	0.023
LVESD (mm)	31.4±4.6	30.8±4.3	32.1±4.8	t=−1.88	0.062
IVSD (mm)	10.6±1.4	10.3±1.2	10.9±1.5	t=−2.90	0.004
Right Heart Structure & Hemodynamics					
sPAP (mmHg)	32.61±8.35	28.45±6.12	36.81±8.24	U=1968.5	< 0.001
RAVI (mL/m2)	26.67±4.58	24.23±3.65	29.14±4.11	U=1625.0	< 0.001
RVEDVI (mL/m2)	45.16±5.92	42.15±4.87	48.21±5.34	U=1782.0	< 0.001
RVESVI (mL/m2)	25.32±3.84	23.41±3.12	27.25±3.61	U=1891.0	< 0.001
RV Systolic & Deformation Mechanics					
TAPSE (mm)	21.13±4.46	23.52±3.25	18.72±4.29	U=5981.0	< 0.001
RVFAC (%)	40.8±6.3	43.2±5.4	38.4±6.1	U=5214.0	< 0.001
*RV Free-Wall Strain (%)	21.98±6.37	24.99±4.31	18.93±6.55	U=5643.5	< 0.001
RV Septal Strain (%)	16.82±4.15	18.42±3.68	15.20±4.02	U=5410.0	< 0.001
Average RV Strain (%)	20.26±5.31	22.65±3.91	17.84±5.42	U=5520.5	< 0.001

IVSD: Interventricular Septal Thickness at Diastole; LAVI: Left Atrial Volume Index; LVEDD/LVESD: Left Ventricular End-Diastolic/Systolic Diameter; LVEF: Left Ventricular Ejection Fraction; RAVI: Right Atrial Volume Index; RVEDVI/RVESVI: Right Ventricular End-Diastolic/End-Systolic Volume Index; RVFAC: Right Ventricular Fractional Area Change; sPAP: Systolic Pulmonary Artery Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion.

*Strain values are presented as absolute values (|ε|) for clarity, where lower numerical values indicate worse myocardial deformation

Table 3. Multivariable Binary Logistic Regression Analysis for Independent Predictors of Severe OSA (AHI≥30)

Variable	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	Adjusted P -value
Age (per 1-year increase)	1.05 (1.02–1.08)	0.001	1.02 (0.99–1.06)	0.174
Male sex (vs. Female)	2.65 (1.41–4.98)	0.002	3.53 (1.62–7.72)	0.0015
BMI (per 1 kg/m2 increase)	1.26 (1.15–1.38)	< 0.001	1.21 (1.09–1.34)	0.0002
Smoking history	1.40 (0.74–2.64)	0.306	1.15 (0.52–2.54)	0.730
Hypertension	2.14 (0.89–5.12)	0.088	1.34 (0.47–3.84)	0.584
Diabetes Mellitus	2.04 (0.88–4.74)	0.098	1.18 (0.42–3.31)	0.751
Coronary Artery Disease	1.77 (0.80–3.94)	0.160	1.04 (0.38–2.87)	0.938
Atrial Fibrillation	1.37 (0.70–2.71)	0.360	0.84 (0.35–2.01)	0.697
Heart Failure (CHF)	1.65 (0.79–3.46)	0.183	0.78 (0.30–2.06)	0.620
History of CVA	3.19 (1.32–7.71)	0.010	4.51 (1.45–14.04)	0.0092
Hyperlipidemia	1.64 (0.83–3.22)	0.155	1.42 (0.61–3.31)	0.414
Polycythemia	2.22 (0.85–5.83)	0.104	1.48 (0.45–4.89)	0.522

Dependent variable: Severe OSA (0=Mild-to-Moderate [AHI 5–29.9], 1=Severe [AHI≥30]). Overall model: Likelihood Ratio $\chi 2=74.88$, $P=2.25\times10-7$, McFadden's pseudo-$R2=0.227$. Abbreviations: CI, Confidence Interval; OR, Odds Ratio.

Table 4. Multivariable Linear Regression Models Evaluating Independent Associations of AHI with RV Strain and Pulmonary Pressure

Independent Predictor	Unstandardized Coeff. (B)	Std. Error (SE)	Standardized Coeff. (β)	t - statistic	P - value	95% Confidence Interval
Model 1: Dependent Variable = RV Free-Wall Longitudinal Strain (%) R2=0.251, Adjusted R2=0.219, F=7.91, P<0.001						
Constant	32.410	4.215	—	7.69	< 0.001	24.088 to 40.732
AHI (events/h events/h)	−0.067	0.014	−0.334	−4.70	< 0.001	−0.094 to −0.039
Age (years)	−0.018	0.038	−0.035	−0.47	0.638	−0.093 to 0.057
Sex (1=Male, 0=Female)	−2.381	0.916	−0.183	−2.60	0.010	−4.189 to −0.573
BMI (kg/m^2)	−0.132	0.106	−0.093	−1.24	0.215	−0.342 to 0.078
Hypertension	0.342	1.285	0.019	0.27	0.791	−2.195 to 2.879
Diabetes Mellitus	−3.004	1.226	−0.174	−2.45	0.015	−5.425 to −0.583
CAD	0.218	1.171	0.013	0.19	0.853	−2.095 to 2.531
Model 2: Dependent Variable = Systolic Pulmonary Artery Pressure (sPAP, mmHg) R^2=0.087, Adjusted R2=0.048, F=2.24, P=0.033						
Constant	21.542	6.230	—	3.46	< 0.001	9.241 to 33.843
AHI (events/h)	+0.077	0.029	+0.207	2.72	0.007	0.021 to 0.134
Age (years)	0.085	0.056	0.126	1.52	0.130	−0.025 to 0.195
Sex (1=Male, 0=Female)	0.562	1.354	0.033	0.42	0.678	−2.112 to 3.236
BMI (kg/m^2)	0.092	0.157	0.049	0.59	0.559	−0.218 to 0.402
Hypertension	1.724	1.899	0.074	0.91	0.365	−2.026 to 5.474
Diabetes Mellitus	1.108	1.812	0.049	0.61	0.542	−2.470 to 4.686
CAD	1.492	1.731	0.069	0.86	0.390	−1.926 to 4.910

Table 5. Diagnostic Accuracy and ROC Curve Analysis for Discriminating Severe OSA (AHI≥30)

Parameter	Area Under Curve (AUC)	95% Confidence Interval	Optimal Cut-off Threshold	Sensitivity (%)	Specificity (%)	Youden Index (J J)	Pairwise DeLong Comparison vs. LAVI (P P -value)
LAVI (mL/m^2)	0.931	0.898 – 0.965	≥29.0	83.7%	83.9%	0.676	Reference
RV Free-Wall Strain (%)	0.754	0.682 – 0.827	≤16.0	51.2%	96.6%	0.478	< 0.0001
sPAP (mmHg)	0.656	0.573 – 0.738	≥31.0	37.2%	93.1%	0.303	< 0.0001
BMI (kg/m^2)	0.653	0.571 – 0.734	≥34.0	55.8%	73.6%	0.294	< 0.0001
Average RV Strain (%)	0.593	0.508 – 0.678	≤23.0	74.4%	49.4%	0.238	< 0.0001

Pairwise comparisons of ROC curves using DeLong's test: RV free-wall strain vs. average RV strain (ΔAUC=0.161, Z=3.65, P<0.001); RV free-wall strain vs. sPAP (ΔAUC=0.099, Z=2.39, P=0.017).

Discussion

The present single-center, cross-sectional observational study comprehensively evaluated cardiometabolic characteristics, conventional echocardiographic parameters, LA remodeling, and RV myocardial mechanics assessed via two-dimensional speckle-tracking echocardiography (2D-STE) OSA severity groups. Our primary findings demonstrate that patients with severe OSA exhibit a significantly higher burden of subclinical RV systolic dysfunction, reflected by markedly impaired RV free-wall and septal longitudinal strain, alongside pronounced left atrial enlargement compared to those with mild-to-moderate disease. Furthermore, multivariable analyses established continuous AHI as an independent predictor of impaired RV free-wall strain and elevated pulmonary artery systolic pressure (sPAP),

whereas the left atrial volume index (LAVI) demonstrated superior diagnostic accuracy for severe OSA within this study.

These findings corroborate a robust body of physiological and clinical evidence indicating that advanced OSA imposes a cumulative mechanical and hemodynamic burden on both the right and left sides of the heart(2, 7). Repetitive upper-airway collapses during sleep provoke profound intermittent nocturnal hypoxemia, recurrent hypercapnia, robust sympathetic overactivation, and massive negative intrathoracic pressure swings(3, 4). These coordinated stressors acutely elevate right ventricular afterload by inducing pulmonary vasoconstriction and increasing transpulmonary pressure gradients, while concurrently enhancing venous return (5). Chronic, repetitive exposure to this mechanical stretch and hypoxia-reoxygenation injury incites microvascular dysfunction, interstitial fibrosis, and subclinical myocardial impairment of the thin-walled right ventricle (6, 8).

Although conventional echocardiographic indices such as TAPSE and fractional area change (FAC) provide valuable global assessments of RV performance, their geometrical assumptions and load dependency often limit their sensitivity in detecting early, localized longitudinal myocardial impairment (9, 10). In contrast, 2D-STE-derived RV free-wall longitudinal strain offers an angle-independent, highly sensitive quantification of myocardial deformation. In our cohort, RV free-wall strain revealed significant subclinical dysfunction in patients with severe OSA, reinforcing its clinical utility in unmasking early right-sided myocardial involvement prior to the manifestation of overt right heart failure.

Regarding left heart structural remodeling, our results showed a significantly greater LAVI in patients with severe OSA. Left atrial enlargement is an established imaging biomarker reflecting chronic diastolic burden, elevated left ventricular filling pressures, and recurrent nocturnal surges in systemic blood pressure (11). Intermittent hypoxia and heightened adrenergic tone impair left ventricular relaxation and compliance, progressively elevating left atrial wall stress and culminating in structural remodeling (12, 13). Notably, our ROC curve analysis revealed that LAVI exhibited outstanding diagnostic performance (AUC = 0.931) for identifying severe OSA, outperforming individual RV strain parameters and sPAP. This highlights that LA remodeling serves as an integrative cumulative imaging marker of chronic systemic hemodynamic and metabolic stress associated with advanced sleep-disordered breathing.

Multivariable linear regression analyses confirmed that AHI independently predicted both reduced RV free-wall strain (B=−0.067,P<0.001B = -0.067, P < 0.001B=−0.067,P<0.001) and elevated sPAP (B=+0.077,P=0.007B = +0.077, P = 0.007B=+0.077,P=0.007) after adjusting for age, sex, BMI, and relevant clinical covariates. This independent relationship underlines the frequency of respiratory events as a major determinant of pulmonary vascular and right ventricular load(14, 15). Concurrently, multivariable logistic regression identified male sex, increased BMI, and a prior history of cerebrovascular accident (CVA) as independent factors associated with severe OSA classification, emphasizing the systemic and multifactorial profile of advanced disease (15, 16).

Limitations of the Study

- **Cross-Sectional Design:** The observational, cross-sectional design inherently precludes establishing causal or temporal relationships between obstructive sleep apnea severity and the observed right ventricular and left atrial remodeling.
- **Referral and Selection Bias:** The cohort was recruited from a tertiary cardiovascular referral center, which likely resulted in a higher prevalence of cardiovascular risk factors and comorbidities compared with community-based samples, potentially limiting the generalizability of our findings to milder or primary-care populations.
- **In-Sample ROC Derivation:** The optimal diagnostic cut-offs for LAVI and RV free-wall strain were derived within the current study cohort without independent external cohort validation or internal resampling (e.g., bootstrapping). Consequently, these diagnostic thresholds and corresponding performance metrics should be considered exploratory.
- **Echocardiographic Assessment:** Although speckle-tracking and conventional echocardiographic acquisitions followed standardized international guidelines by experienced operators, formal inter- and intra-observer reproducibility metrics were not quantified in this cohort. Furthermore, pulmonary pressures were estimated non-invasively via Doppler echocardiography rather than invasive right heart catheterization.
- **Residual Confounding:** Despite rigorous multivariable adjustment for age, sex, body mass index, smoking status, and key clinical comorbidities, unmeasured confounding—such as detailed medication classes, circulating biomarkers of systemic inflammation, and oxidative stress—cannot be completely ruled out.
- **Absence of Longitudinal Follow-up:** The study lacked longitudinal tracking to assess clinical event progression or the potential reversibility of subclinical myocardial dysfunction following continuous positive airway pressure (CPAP) therapy.
- Although LAVI and RV free-wall strain demonstrated robust discriminative accuracy with statistically significant pairwise AUC differences on DeLong's testing, it is imperative to acknowledge that the diagnostic cutoff values derived herein were optimized within this single tertiary-care cohort. Consequently, these thresholds should be interpreted as exploratory and require external prospective validation across broader, non-referral populations before definitive translation into standardized risk-stratification algorithms

Future Directions

1. **Prospective Longitudinal Studies:** Large-scale prospective studies are warranted to assess whether baseline subclinical right ventricular strain impairment and left atrial enlargement independently predict major adverse cardiovascular events (MACE) and stroke in patients across the OSA severity spectrum.
2. **Therapeutic and Reverse Remodeling Trials:** Prospective interventional trials should evaluate whether optimal adherence to CPAP or combined lifestyle/weight-loss interventions induces meaningful structural and functional reverse remodeling of the right ventricle and left atrium.
3. **External Validation of Imaging Thresholds:** Multi-center validation studies are necessary to evaluate the diagnostic and prognostic accuracy of the proposed LAVI and RV strain cut-off values in diverse, unselected clinical populations.
4. **Integration of Biomarkers and Multi-modality Imaging:** Future investigations combining advanced echocardiography with circulating biomarkers of myocardial stretch and systemic inflammation may elucidate the specific pathophysiological pathways driving sleep-disordered cardiac remodeling.

Abbreviations: 2D-STE, two-dimensional speckle-tracking echocardiography; AF, atrial fibrillation; AHI, apnea–hypopnea index; AUC, area under the curve; BMI, body mass index; CAD, coronary artery disease; CHF, chronic heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; DVT, deep vein thrombosis; EDV, end-diastolic volume; ESV, end-systolic volume; IVSd, interventricular septal thickness at end-diastole; LA, left atrium/left atrial; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; OR, odds ratio; OSA, obstructive sleep apnea; PASP, pulmonary artery systolic pressure; PTE, pulmonary thromboembolism; ROC, receiver operating characteristic; RV, right ventricle/right ventricular; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion.

Declarations

Ethics Approval and Consent to Participate

The study complies with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committees of Rajaie institute Cardiovascular Medical & Research Center, Tehran, Iran ,Written informed consent was obtained from the participants.

Consent for Publication

Not applicable.

Availability of data and material

The dataset supporting the results and conclusions of this article will be available from the corresponding author on request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TZ designed the project and performed study. MN and ZD evaluated the patient clinically. SA and MN prepared the first version of manuscript. AN, AD and MN confirmed the clinical finding of the patient. ZD made complementary revision of the manuscript. All the authors read and approved the final manuscript

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