# Left ventricular function assessed with two-dimensional speckle tracking and three-dimensional echocardiography in patients with obstructive sleep apnea

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**Summary**

*Objective:* To investigate left ventricular function by two-dimensional (2D) speckle tracking and three-dimensional (3D) echocardiography in obstructive sleep apnea (OSA) patients. *Subject and method:* Patients who were diagnosed with OSA based on the results of full polysomnography and had apnea-hypopnea index values > 5 events/hour of sleep were included in the study. All patient underwent polysomnography recording. Comprehensive 2-dimensional echocardiography were performed to all subjects according to American Society of Echocardiography guidelines [5], followed by real-time 3D echocardiography. *Result:* From June 2021 to June 2022, there were 46 OSA patients were included in the study. Mean age of OSA patients 51.3 ± 11.7 years. Men 63% (29/46), women 37% (15/46). The apnea-hypopnea index, percentage of total sleep time with an oxygen saturation level < 90%, arousal index increased in OSA patients. E/E' increased (12.6 ± 4.3), GLS mildly reduced (-16.5 ± 3.8%) while other echocardiographic parameters were in normal range. Results of ANOVA showed an increase in the following LA parameters on 3D echocardiography according to the levels of OSA severity: LV mass index, 3D maximum LA volume, 3D maximum LA volume index, E/E' were significantly higher in the severe OSA group compared with the moderate OSA and the mild OSA (p<0.05 for all). There was a decrease in the E' velocity and global longitudinal strain (GLS) (p<0.05 for all). *Conclusion:* In patients with obstructive sleep apnea, the severity of OSA was associated with lower E' velocity, greater E/E' ratio, larger 3D LV volume, greater LV mass index, and poorer left ventricular global longitudinal strain.

*Keywords:* Obstructive sleep apnea, left ventricular diastolic function, 3D echocardiography, speckle-tracking echocardiography.

## 1. Background

Obstructive sleep apnea (OSA) is a disorder characterized by recurrent upper airway collapse during sleep causing intermitted hypoxia and sleep fragmentation. Studies showed that severe OSA is an independent risk factor for fatal cardiovascular events and development of heart failure. OSA is associated with hypoxemia leading to relative cardiac ischemia, catecholaminergic toxicity, and periodic elevations in negative intra-thoracic pressure, which alter ventricular and atrial volumes and function [1], [2]. The severity of OSA was associated with impaired left ventricular (LV) diastolic function independently of obesity. The impairment of LV diastolic function is a major cause of heart failure with preserved ejection fraction [3]. Few studies have evaluated the association of OSA with abnormalities in cardiac structure and function. Our aim is to investigate the relation between OSA and left ventricular function assessed by two-dimensional (2D) and three-dimensional (3D) echocardiography.

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## 2. Subject and method

Patients with obstructive sleep apnea were recruited to the study in Bach Mai Hospital.

*Inclusion criteria for OSA patients:* Patients who were diagnosed with OSA based on the results of full polysomnography and had apnea-hypopnea index values > 5 events/hour of sleep [4].

*Exclusion criteria:* Body mass index (BMI) > 35kg/m$^2$, history of coronary artery disease and atrial fibrillation, cardiomyopathy, severe arrhythmias and pulmonary and valvular heart disease, and poor-quality imaging on 2DE and/or 3D echocardiography.

*Ethical issue:* The study was approved by the ethics committee of Bach Mai Hospital, informed consent was obtained from each patient.

*Polysomnography:* Each patient underwent polysomnography recording. Levels of OSA severity were defined according to apnea-hypopnea index as follows: mild (5-15 events/hour of sleep), moderate (15.1-30 events/ hour of sleep) and severe (>30.1 events/hour of sleep) [4].

*Echocardiography*: Comprehensive 2-dimensional echocardiography were performed to all subjects according to American Society of Echocardiography guidelines (2015) [5], followed by real-time 3D echocardiography using the CVx Philips Medical ultrasound system (USA 2019), performed by an experienced cardiologist who were blinded to the polysomnographic. Global longitudinal strain was measured on 2D speckle-tracking echocardiography. 3D echocardiography was performed with a matrix-array transducer (3MHz) for acquisition of “full-volume” real-time pyramidal volumetric data sets along 5 consecutive cardiac cycles. Apical 2-chamber and 4-chamber views were extracted from the pyramidal data set during expiration. The 3D echocardiography data sets were digitally stored and analyzed. The left ventricular ejection fraction (LVEF) was evaluated using the pyramidal 3D echocardiography data set of apical 4-chamber and 2-chamber views (Figure 2). Maximum LA volume, maximum LA volume indexed for body surface area (BSA) were measured and calculated: The LA internal endocardial border of each frame was defined by automated processing and manually adjusted. From these data, a 3D model of LA volume was generated (Figure 3).

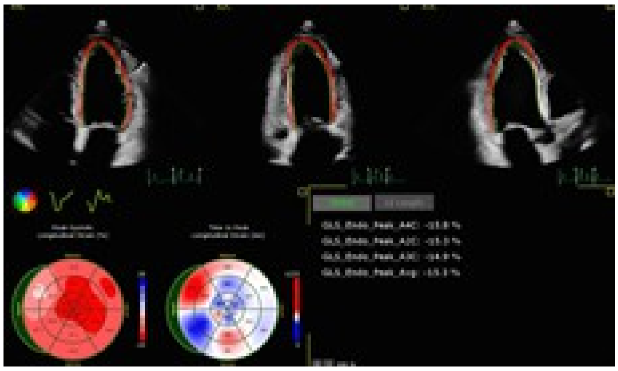

**Figure 1.** Measurement of left ventricular global longitudinal strain (GLS) using 2D speckle-tracking echocardiography

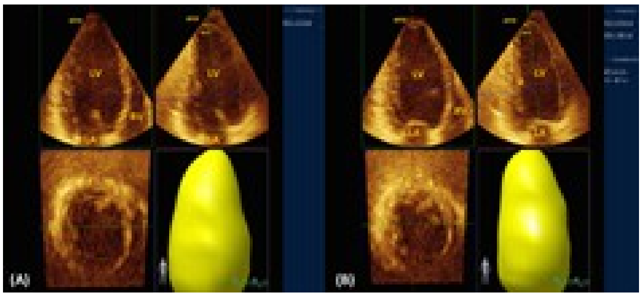

**Figure 2.** Measurement of left ventricular ejection fraction (EF) using three-dimensional echocardiography. Fig.2A: End-diastolic tracing. Fig.2B: End-systolic tracing.

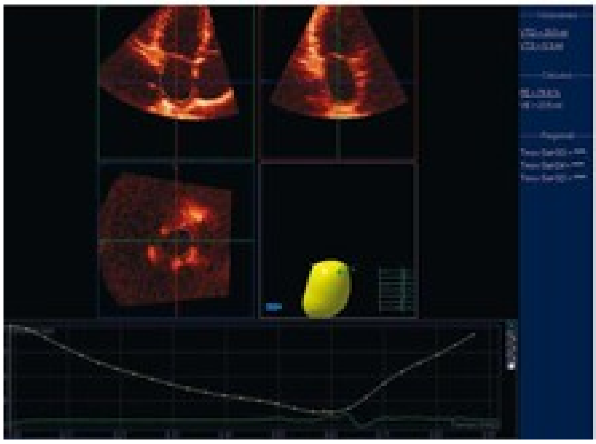

**Figure 3.** Measurement of left atrial volume using real-time three-dimensional echocardiography

*Statistical analysis*

Data were summarized as mean ± standard deviation for continuous variables with normal distribution; median [95% confidence interval] for other continuous variables and number of subjects (%) for categorical variables. ANOVA test was used to compare the group factors. Categorical variables were compared using Fisher's exact test. The level of significance was set at $p<0.05$.

## 3. Result

### *3.1. Patient's characteristics*

From June 2021 to June 2022, there were 46 OSA patients were included in the study. Mean age of OSA patients 51.3 ± 11.7 years. Men 63% (29/46), women 37% (15/46).

**Table 1. Patients' characteristics and polysomnographic results**

| Parameters | Patients with OSA (n = 46) $\overline{X}$ ± SD or n (%) |
|---|---|
| Age (year) | 51.3 ± 11.7 |
| Men | 29 (63%) |
| Hypertension | 19 (41.3%) |
| Systolic blood pressure (mmHg) | 139.8 ± 18.2 |
| Diastolic blood pressure (mmHg) | 86.6 ± 15.9 |
| Heart rate (bpm) | 77.9 ± 13.3 |
| Diabetes mellitus | 4 (8.7%) |
| Apnea-hypopnea index (events/hour) | 29.5 ± 19.7 |
| Arousal index per hour | 19.8 ± 11.2 |
| Oxygen sarturation < 90% (percentage of total sleep time) (%) | 15.7 ± 13.4 |

Regarding the polysomnographic findings, the apnea-hypopnea index, percentage of total sleep time with an oxygen saturation level < 90%, arousal index increased in OSA patients [4] (Table 1).

### *3.2. Echocardiographic findings*

Table 2 showed that E/E' increased (12.6 ± 4.3), GLS mildly reduced (-16.5 ± 3.8%) while other echocardiographic parameters were in normal range [5].

**Table 2. Two-dimensional and Doppler echocardiography results**

| Parameters | Patients with OSA (n = 46) $\overline{X}$ ± SD or n (%) |
|---|---|
| LAd (mm) | 34.3 ± 11.5 |
| 2D LA volume index (ml/m$^2$) | 26.7 ± 11.8 |
| LVEDd (mm) | 44.3 ± 5.6 |
| 2D LVEF (%) | 66.5 ± 9.6 |
| LV mass index (g/m$^2$) | 85.3 ± 17.4 |
| E velocity (cm/s) | 70.1 ± 18.5 |
| A velocity (cm/s) | 69.3 ± 20.9 |
| E' velocity (cm/s) | 7.1 ± 4.2 |
| E/E' | 12.6 ± 4.3 |
| GLS (%) | -16.5% ± 3.8 |
| 3D LA maximum volume (ml) | 45.3 ± 11.7 |
| 3D LA maximum volume index (ml/m$^2$) | 29.7 ± 9.5 |
| 3D LVEF (%) | 65.7 ± 6.3 |

**Table 3. Left atrial parameters on 2DE and RT3DE according to the levels of OSA severity**

| Parameters | Severe OSA (n = 11) $\bar{X} \pm SD$ | Moderate OSA (n = 23) $\bar{X} \pm SD$ | Mild OSA (n = 12) $\bar{X} \pm SD$ | p |
|---|---|---|---|---|
| LV mass index (g/m$^2$) | 96.7 ± 7.5 | 87.8 ± 10.7 | 82.5 ± 6.5 | <0.05 |
| 2D maximum LA volume (mm) | 46.4 ± 11.5 | 45.2 ± 10.7 | 43.7 ± 9.6 | >0.05 |
| 2D maximum LA volume index (ml/m$^2$) | 30.9 ± 9.1 | 29.6 ± 11.5 | 28.4 ± 10.5 | >0.05 |
| E' velocity | 4.2 ± 1.1 | 8.5 ± 3.7 | 11.3 ± 1.7 | <0.05 |
| E/E' | 15.3 ± 1.2 | 12.3 ± 2.5 | 9.7 ± 1.6 | <0.05 |
| 3D maximum LA volume (ml) | 59.6 ± 33.0 | 41.7 ± 9.9 | 34.1 ± 13.5 | <0.05 |
| 3D maximum LA volume index (ml/m$^2$) | 31.4 ± 11.3 | 24.9 ± 10.5 | 20.3 ± 6.3 | <0.05 |
| 2D LVEF (%) | 65 ± 10.6 | 65 ± 8.9 | 66 ± 9.7 | >0.05 |
| 3D LVEF (%) | 64 ± 9.3 | 65 ± 7.6 | 65 ± 11.6 | >0.05 |
| GLS (%) | -14.6 ± 1.8 | -17.3 ± 2.5 | -19.5 ± 1.7 | <0.05 |

Results of analysis of variance showed an increase in the following LA parameters on 3D echocardiography according to the levels of OSA severity: LV mass index, 3D maximum LA volume, 3D maximum LA volume index, E/E' were significantly higher in the severe OSA group compared with the moderate OSA and the mild OSA (p<0.05 for all). There was a decrease in the E' velocity and global longitudinal strain (GLS) (p<0.05 for all). There was not any significant difference between 3 groups regarding the 2D maximum LA volume and 2D maximum LA volume index, 2D LVEF, 3D LVEF (p>0.05 for all) (Table 3).

## 4. Discussion

Previous studies have shown that severe OSA is an independent risk factor for fatal cardiovascular events and progression of heart failure [1]. The severity of OSA was associated with impaired LV diastolic function independently of obesity [2], [3]. In our study, the severity of OSA was associated with higher LVMI but not with reduced EF assessed by either 2D or 3D echocardiography. Our results were similar to the Multi-Ethnic Study of Atherosclerosis, which included 318 participants, higher apnea-hypopnea index was associated with higher LV mass index but not with reduced EF assessed by cardiac MRI [6]. The severity of OSA was directly linked with the enlargement of 3D LA volume while this was not seen with 2D LA volume. OSA impairs LA wall compliance and passive contraction independently of obesity and gradually changes the LA morphology which can be better assessed by 3D echocardiography [7]. 2D LV volume assessment takes geometric assumption and may be limited in patients who have severe anatomic alterations in the left atrium [8], [9]. LA volume analysis using 3D echocardiography has shown to be a prognostic marker of major cardiovascular events and is promising regarding accuracy, feasibility, and reproducibility [10].

The association between OSA and LV diastolic function has been examined before. OSA and LV diastolic dysfunction frequently co-occur, as 23% to 37% of patients with clinically diagnosed sleep disordered breathing have LV diastolic dysfunction on imaging [6]. The intermittent bouts of hypoxia may cause direct myocardial injury as well as predispose to inflammation and oxidative stress. Emerging data suggest OSA may be a risk factor for cardiac fibrosis, as evidenced by elevated circulating levels of galectin-3 [6]. In our study, the severity of OSA tended to be associated with lower E', higher E/E', and poorer GLS. The subtle changes in LA volumes and function could be related to diastolic impairment. Early LA emptying results in a smaller motion of the mitral valve annulus, which can be evidenced by low annular early diastolic velocity (E′). This impaired emptying contributes to a larger residual volume before LA contraction. According to the Frank-Starling mechanism, the presence of such volumetric changes affects atrial contraction, which becomes of critical importance during left ventricular filling. This atrial overload may lead to the increase of maximum LA volume and the decrease of diastolic function. In the ECHO-SOL Ancillary Study, increase in apnea-hypopnea index was associated with lower E′, greater E/E′ ratio, and higher prevalence of diastolic dysfunction, greater LV mass index, as well as lower GLS. These associations persisted after adjustment for hypertension and diabetes mellitus [11].

## 5. Conclusion

In patients with obstructive sleep apnea, the severity of obstructive sleep apnea was associated with lower E′ velocity, greater E/E′ ratio, larger 3D LV volume, greater LV mass index, and poorer left ventricular global longitudinal strain.

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