SCIENTIFIC RESEARCH

ASSESSMENT OF LEFT ATRIAL VOLUME AND FUNCTION IN REAL-TIME THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN OBSTRUCTIVE SLEEP APNEA

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SUMMARY

Aims: To evaluate the volumetric and functional abnormalities of the left atrium (LA) using real-time three-dimensional echocardiography (RT3DE) in patients with obstructive sleep apnea (OSA) compared with a control group.

Methods: Patients with OSA and age-and sex-matched control subjects were recruited to the study in Bach Mai hospital. All patients underwent polysomnography recording. Comprehensive 2-dimensional echocardiographic (2DE) was performed on all subjects according to American Society of Echocardiography guidelines, followed by RT3DE. Maximum LA volume, maximum LA volume indexed for body surface area (BSA), minimum LA volume, and LA volume before contraction were obtained.

Results: From June 2021 to June 2022, there were 46 OSA patients and 30 controls were included in the study. The mean age of OSA patients was 51.3 ± 11.7. Men accounted for 63% (29/46). The apnea-hypopnea index, percentage of total sleep time with an oxygen saturation level < 90%, arousal index were higher in OSA patients compared with controls. There was a significantly higher 2D LA volume index and E/E' ratio in the OSA patients compared with the controls (p<0.05). RT3D echocardiography results showed a larger maximum LA volume indexed for BSA, LA volume before atrial contraction, total LA systolic volume, and active LA systolic volume and a higher active LA ejection fraction in the OSA patients compared with controls (p<0.05 for all). There was an increase in the following LA parameters on RT3DE according to the levels of OSA severity: 3D maximum LA volume, 3D maximum LA volume index, 3D LA volume before LA contraction; 3D LA total systolic volume, 3D LA active systolic volume, 3D LA active systolic ejection fraction (p<0.05). On the other hand, 2D maximum LA volume and 2D maximum LA volume index did not differ according to the severity of OSA (p>0.05)

Conclusion: There was a significant increase in LA volume and augmentation of LA active systolic function in patients with OSA. The severity of OSA was directly linked with the enlargement of 3D LA volume while this was not seen with 2D LA volume.

Keywords: *Left atrial volume, obstructive sleep apnea, echocardiography, three-dimensional echocardiography, left atrial enlargement.*

I. INTRODUCTION

Obstructive sleep apnea (OSA) is a highly prevalent disorder characterized by recurrent upper airway collapse during sleep causing intermitted hypoxia and sleep fragmentation. OSA has been demonstrated to be associated with cardiovascular conditions such as hypertension, heart failure, ischemic heart disease, and cerebrovascular accident [1], [2]. There are suggested mechanisms associated with hypoxemia leading to relative cardiac ischemia, catecholaminergic toxicity, and periodic elevations in negative intra-thoracic pressure, which alter ventricular and atrial volumes. OSA contributes to the development of left ventricular (LV) diastolic dysfunction, which is associated with heart failure and increased mortality. Left ventricular diastolic dysfunction progressively impairs the emptying of the left atrium, as a result, the intra-atrial pressure gradually increases to maintain proper ventricular filling, which leads to atrial myocardial overstretching and dilation. These atrial volumetric and functional changes are associated with cardiovascular events such as atrial fibrillation, stroke, and death[3], [4]. Left atrial (LA) volume can be evaluated using two-dimensional echocardiography (2DE). 2DE assessment of LA volume considers geometric assumption and may have limitations in patients with severe anatomic alterations in the left atrium [5]. LA volume assessment using real-time three-dimensional echocardiography (RT3DE) has been proven as a prognostic marker of major cardiac events and is promising in terms of accuracy, feasibility, and reproducibility [6]. We aim to evaluate the volumetric and functional abnormalities of the left atrium using RT3DE in patients with OSA compared with a control group.

II. METHODS

Patients and materials:

Patients with OSA and control subjects were recruited for 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.

Inclusion criteria for the controls: Volunteers from the outpatient clinic who were matched for age and sex to the patients' group and had normal polysomnography, had the same cardiovascular risk factors as the OSA patients.

Exclusion criteria: Body mass index (BMI) > 35 kg/m^2, history of coronary artery disease and atrial fibrillation, cardiomyopathy, severe arrhythmias, pulmonary and valvular heart disease, and poor-quality imaging on 2DE and/or RT3DE.

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

Polysomnography

Each patient underwent polysomnography recording. The recordings were visually scored using the American Academy of Sleep Medicine criteria. The variables analyzed were total sleep time, sleep efficiency (sleep time/recording time x 100), apnea-hypopnea index (apnea and hypopnea events per hour of sleep), arousals per hour, and oxygen saturation. Levels of OSA severity were defined according to the 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) [7].

Echocardiography

Comprehensive 2-dimensional echocardiographic were performed on all subjects according to American Society of Echocardiography guidelines [5], followed by real-time 3D echocardiography using the CVx Philips Medical ultrasound system (USA 2019), performed by an experienced cardiologist who was blinded to the polysomnographic.

RT3DE was performed with a matrix-array transducer (3 MHz) for the 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 RT3DE data sets were digitally stored and analyzed. Maximum LA volume, maximum LA volume indexed for body surface area (BSA), minimum LA volume, and LA volume before contraction asobtained. 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 1). The left ventricular ejection fraction (LVEF) was also evaluated using the pyramidal RT3DE data set of apical 4-chamber and 2-chamber views

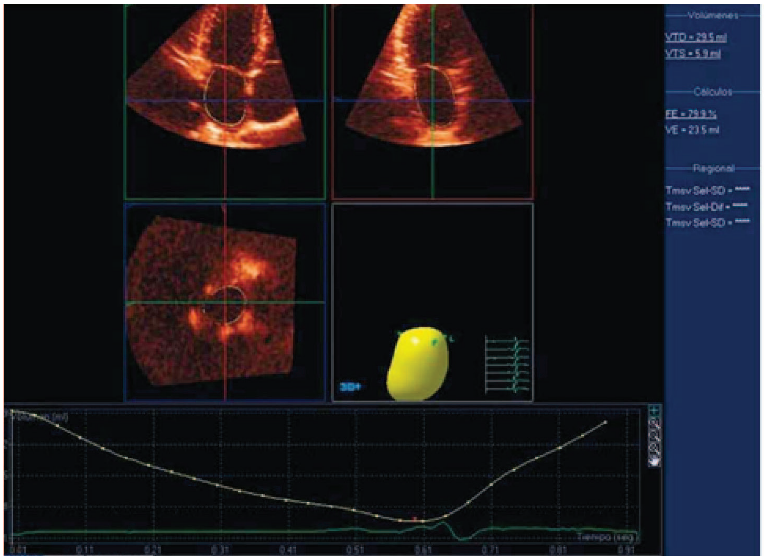

Figure 1. *Measurement of left atrial volume using RT3D echocardiography*

Statistical Analysis

Data are presented as mean ± SD or as frequencies. ANOVA test was used to compare the group factor (OSA vs controls) with the following factors: RT3DE, polysomnographic, and demographic variables. The level of significance was set at $p<0.05$.

III. RESULTS

Patient's characteristics:

From June 2021 to June 2022, there were 46 OSA patients and 30 controls were included in the study. The mean age of OSA patients 51.3 ± 11.7. Men 63% (29/46), women 37% (15/46). Table 1 showed that the mean age did not significantly differ between groups. The frequencies of male gender, hypertension, and diabetes were similar in both groups. Additionally, BMI, heart rate, and systolic and diastolic blood pressure values were not significantly different in both groups.

Table 1. *Patients' characteristics and polysomnographic results*

Parameters	Patients with OSA (n = 46) X ± SD or n (%)	Controls (n = 30) X ± SD or n (%)	p
Age (year)	51.3 ± 11.7	51.3 ± 12.9	>0.05
Men	29 (63%)	18 (60%)	>0.05
Hypertension	19 (41.3%)	12 (40.0%)	>0.05
Systolic blood pressure (mmHg)	139.8 ± 18.2	136.1 ± 19.5	>0.05
Diastolic blood pressure (mmHg)	86.6 ± 15.9	85.7 ± 14.5	>0.05
Heart rate (bpm)	77.9 ± 13.3	75.9 ± 14.6	>0/05
Diabetes mellitus	4 (8.7%)	3 (10.0%)	>0.05
Sleep efficiency (%)	82.4 ± 11.3	81.2 ± 14.6	>0.05
Total sleep time (min)	362.7 ± 89.3	355.8 ± 84.7	>0.05
Apnea-hypopnea index (events/hour)	29.5 ± 19.7	2.5 ± 1.3	<0.01
Arousal index per hour	19.8 ± 11.2	9.7 ±4.3	<0.01
Oxygen saturation <90% (percentage of total sleep time) (%)	15.7 ± 13.4	0.5 ± 0.3	<0.01

Regarding the polysomnographic findings, the apnea-hypopnea index, percentage of total sleep time with an oxygen saturation level < 90%, and arousal index were higher in patients compared with controls (table 1).

Two-Dimensional Echocardiographic and Doppler Findings

Table 2 showed that the 2D LA diameter, left ventricular 2D echocardiographic measurements of ejection fraction, mitral pulsed Doppler diastolic flow velocities, LV mass index between the 2 groups were similar. There was a significantly higher 2D LA volume index and E/E' ratio in the OSA patients compared with the controls (p<0.05).

T**able 2.** *Two-dimensional and Doppler echocardiography results*

Parameters	Patients with OSA (n = 46) X ± SD or n (%)	Controls (n = 30) X±SD or n (%)	p
LAd (mm)	34.3 ± 11.5	33.3 ± 4.9	> 0.05
2D LA volume index (ml/m^2)	26.7 ± 11.8	21.5 ± 7.4	**< 0.05**
LVEDd (mm)	44.3 ± 5.6	42.3 ± 6.8	> 0.05
LVEF (%)	66.5 ± 13.7	66.5 ± 13.7	> 0.05
LV mass index (g/m^2)	85.3 ± 17.4	81.2 ± 16.9	> 0.05
E velocity (cm/s)	70.1 ± 18.5	68.6 ± 17.7	> 0.05
A velocity (cm/s)	69.3 ± 20.9	67.9 ± 19.5	> 0.05
E/E'	12.6 ± 4.2	7.4 ± 2.7	**< 0.05**

Real-Time 3-Dimensional Echocardiographic Findings

Table 3 described the RT3D echocardiography results showing a larger maximum LA volume indexed for BSA, LA volume before atrial contraction, total LA systolic volume, and active LA systolic volume and a higher active LA ejection fraction in the OSA patients compared to controls (p<0.05 for all). However, the minimum LA volume, total LA ejection fraction, and passive LA ejection fraction were similar among the different groups (p>0.05 for all).

Table 3. *Three-dimensional echocardiographic results*

Parameters	Patients with OSA (n = 46) X ± SD or n (%)	Controls (n = 30) X ± SD or n (%)	p
3D LA maximum volume (ml)	45.3 ± 11.7	26.3 ± 5.9	<0.05
3D LA maximum volume index (ml/m^2)	29.7 ± 9.5	19.5 ± 7.4	<0.05
3D LA minimum volume (ml)	17.7 ± 3.6	16.3 ± 4.8	>0.05
3D LA volume before atrial contraction (ml)	30.5 ± 10.6	21.5 ± 6.3	<0.05
3D LA total systolic ejection fraction (%)	58.9 ± 9.5	56.7 ± 7.9	>0.05
3D LA active systolic volume (ml)	13.7 ± 3.5	7.6 ± 4.7	<0.05
3D LA active systolic ejection fraction (%)	38.3 ± 9.5	31.7 ± 7.3	<0.05
3D LA passive ejection fraction (%)	33.6 ± 7.2	35.5 ± 51	>0.05
3D LV ejection fraction (%)	65.7 ± 6.3	66.9 ± 7.8	>0.05

Results of the analysis of variance showed an increase in the following LA parameters on RT3DE according to the levels of OSA severity: 3D maximum LA volume, 3D maximum LA volume index, 3D LA volume before

LA contraction; 3D LA total systolic volume, 3D LA active systolic volume, 3D LA active systolic ejection fraction were significantly higher in the severe OSA group compared with the moderate OSA and the mild OSA ($p<0.05$ for all). There was no significant difference between 3 groups regarding the 2D maximum LA volume and 2D maximum LA volume index (table 4)

Table 4. *Left atrial parameters on 2DE and RT3DE according to the levels of OSA severity*

Parameters	Severe OSA (n = 11)	Moderate OSA (n= 23)	Mild OSA (n =12)	p
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
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
3D LA volume before atrial contraction (ml)	43.7 ± 25.6	25.9 ± 5.9	21.3 ± 12.7	<0.05
3D LA total systolic volume (ml)	33.4 ± 14.5	27.3 ± 6.2	23.2 ± 10.5	<0.05
3D LA active systolic volume (ml)	20.1 ± 11.5	13.4 ± 7.0	7.7 ± 4.9	<0.05
3D LA active systolic ejection fraction (%)	42.7 ± 12.6	34.5 ± 13.9	29.9 ± 11.5	<0.05

IV. DISCUSSION

Longitudinal studies have proved that severe OSA is an independent risk factor for fatal cardiovascular events and the progression of heart failure [1]. The severity of OSA was associated with impaired LV diastolic function independently of obesity [4], [7]. Left atrial volume index is an important measure for the assessment of LV diastolic function and reflects chronic LA overload without being affected by hemodynamic state compared with measures derived by Doppler and tissue Doppler velocity [8], [9]. It seems to be important to evaluate LAVI in patients with OSA. It is previously reported that an increase in 2D LAVI is related to the degree of LV diastolic dysfunction, age, sex, blood pressure, and the degree of obesity [8], [9]. However, the relationship between 3D LAVI and OSA has not yet been fully studied.

The main findings of the current study were a significant increase in LA volume and augmentation of LA active systolic function. The severity of OSA was directly linked with the enlargement of 3D LA volume while this was not seen with 2D LA volume. Other studies showed that OSA impaired LA wall compliance and passive contraction independently of obesity. The results of the present study directly evaluate the impact of OSA on LA enlargement assessed by RT3DE. Oxidative stress activation due to intermittent hypoxia during sleep may contribute to a weakening of the atrial wall and result in atrial overstretching and dilatation. Another mechanism may be the rise of transmural pressure, which is caused by increased negative intrathoracic pressure during apneic episodes, it might stretch the atrium outward [7], [10], [11].

2D LV volume assessment considers geometric inferences and has limitations in cases in which there are severe anatomic alterations in the left atrium. LA volume analysis using RT3DE has shown to be a prognostic marker of major cardiovascular events and is promising regarding accuracy, feasibility, and reproducibility. Accuracy in determining LA size is important for clinical evaluation because of the association of major adverse cardiovascular outcomes with an enlarged left atrium [12].

The effect of OSA treatment on 3D LA volume and function, as well as its potential impact on the development of atrial arrhythmias, deserves future investigation.

V. CONCLUSION

There was a significant increase in LA volume and augmentation of LA active systolic function in patients with OSA. The severity of OSA was directly linked with the enlargement of 3D LA volume while this was not seen with 2D LA volume.

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