



# **Assessment of Biventricular Function in Patients with Obstructive Sleep Apnea and Atrial Fibrillation: A Cross-sectional Study Using Two-dimensional Speckle Tracking Imaging**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MZF designed the study, wrote the protocol and performed the echocardiographic study. Author BS performed the statistical analysis. Authors SK, BHM and RB enrolled patients and collected data from their medical records. Authors AJ and SK managed the literature searches and wrote the first draft of the manuscript. Author BAJ performed the polysomnographic study. Authors OS, FA and LN checked the accuracy of data and statistical results. Author MMS performed the final verification and validated the manuscript. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Background:** Obstructive sleep apnea syndrome (OSA) is a common but often under diagnosed condition. According to literature, OSA prevalence in atrial fibrillation (AF) patients varies from 21 to 85%. OSA is increasingly recognized as a risk factor for biventricular dysfunction. The present study aimed to compare left and right ventricular functions, assessed by conventional

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echocardiographic parameters and speckle tracking imaging, in non-valvular atrial fibrillation (NVAf) patients with and without severe OSA.

**Methods:** A cross-sectional analytic study was conducted. Forty successive patients with NVAf were included. All of them had a clinical screening for symptoms suggestive of OSA and underwent polysomnographic study. Patients were divided into two groups (group 1: without severe OSA with an apnea-hypopnea index (AHI) < 30 events per hour (e/h), and group 2: having severe OSA with an AHI ≥ 30 e/h). Echocardiography was performed in all patients. Left and right ventricular function parameters were measured including global longitudinal strain (GLS) and myocardial performance index (MPI).

**Results:** OSA was diagnosed in 90% of NVAf patients. The average AHI was 22.1 ± 13 e/h. Eleven patients (27.5%) had mild OSA, 9 patients (22.5%) had moderate OSA, and 16 patients (40%) had severe OSA. General clinical characteristics were comparable between groups. A statistically significant association was demonstrated between severe OSA and impairment of left ventricular GLS (-17.3 ± 4.5 vs. -14.9 ± 3%, in group 1 and 2 respectively, p = 0.02) and left ventricular MPI (0.37 ± 0.09 vs. 0.49 ± 0.13, in group 1 and 2 respectively, p = 0.01). Right ventricular lateral wall strain was non significantly lower in group 1 compared to group 2 (-22.5 ± 8.4 vs. -18.4 ± 5.8%, in group 1 and 2 respectively, p = 0.15). On multivariate logistic regression analysis, left ventricular GLS impairment (> -18%) and MPI > 0.37 were independent predictors of severe OSA.

**Conclusion:** Severe OSA was diagnosed in 40% of NVAf patients. Impairment of left ventricular GLS and left MPI were statistically associated with severe OSA.

*Keywords: Obstructive sleep apnea; atrial fibrillation; left ventricle; right ventricle; echocardiography.*

## ABBREVIATIONS

AF : Atrial fibrillation  
 AHI : Apnea-hypopnea index  
 e/h : event(s)/hour  
 GLS : Global longitudinal strain  
 LV : Left ventricle  
 MPI : Myocardial performance index  
 NVAf : Non-valvular atrial fibrillation  
 OSA : Obstructive sleep apnea  
 ROC : Receiver operating characteristics  
 RV : Right ventricle  
 TAPSE : Tricuspid annular plane systolic excursion

## 1. INTRODUCTION

Obstructive sleep apnea syndrome (OSA) is a common condition affecting about 4-5% of the adult population [1]. Because of its implication in several cardiovascular diseases, particularly heart failure, OSA which is often under diagnosed, represents a major public health concern [2]. Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. Its prevalence increases with age, from 0.1% among those under 55 years of age to 9% among people aged over 80 [3]. AF is associated with an increase in morbidity and mortality and may lead to heart failure and thromboembolic events. The prevalence of OSA in patients with AF varies from 21 to 85% according to recent

studies [4]. The aim of the present study was to compare in non-valvular atrial fibrillation (NVAf) patients, left and right ventricular functions by using conventional echocardiographic parameters and speckle tracking imaging depending on the presence or not of severe OSA.

## 2. MATERIALS AND METHODS

### 2.1 Study Design

This study was a cross-sectional analytic one (Department of cardiological investigations and resuscitation - La Rabta University Hospital – Tunis) and was conducted between July and October 2017.

### 2.2 Study Population

The enrolment involved randomly selected NVAf patients, aged over eighteen years and followed up in the outpatient consultation. Only patients, in whom the diagnosis of AF was documented, were included [5,6].

Non-inclusion criteria were

- A significant valvular heart disease [7].
- A history of coronary artery disease (coronary revascularization, history of typical anginal pain, electrocardiographic

abnormalities suggestive of coronary artery disease).

- Primary cardiomyopathies (hypertrophic, restrictive, dilated, arrhythmogenic right ventricular dysplasia and left ventricular noncompaction).
- A history of intracardiac device implantation.
- Obstructive or restrictive pulmonary disease (patients having a suggestive functional respiratory testing and/or receiving dedicated therapy).
- Pulmonary hypertension due to identifiable diseases other than OSA.

**Exclusion criterion was poor echogenicity:**

Prior to enrolment in the present study, none of the patients had received a previous diagnosis of OSA. All enrolled patients underwent overnight polysomnography and were stratified according to the severity of OSA, when present. The interpretation of polysomnography was performed by a pneumologist. Two study groups were established: group 1 for patients without severe OSA (apnea hypopnea index (AHI) < 30 events/hour (e/h)) and group 2 for patients with severe OSA (AHI ≥ 30 e/h).

## 2.3 Data Collection

### 2.3.1 Clinical screening of OSA

The Berlin questionnaire [8,9] was used to assess the clinical probability of OSA. The Berlin score was then compared to the polysomnographic data. The Berlin questionnaire included 10 questions divided in three categories: category 1 including five questions about snoring and apnea, category 2 including four questions about daytime sleepiness and category 3 with two questions about hypertension and obesity. A Berlin score ≥ 2 indicated a high probability of OSA and thus was considered as positive.

### 2.3.2 Atrial fibrillation

Atrial fibrillation was documented in all patients by a resting electrocardiogram or by an electrocardiographic holter showing the arrhythmia lasting longer than thirty seconds. AF was classified as paroxysmal, persistent, or permanent according to the European guidelines [10]. Symptoms related to AF and AF effect on quality of life was assessed by the EHRA classification [10].

### 2.3.3 Echocardiographic study

All patients underwent echocardiographic evaluation according to The American Society of Echocardiography guidelines [11] as well as an assessment of two-dimensional myocardial deformation with speckle tracking imaging. All echocardiographic studies were performed by the same experimented operator who was blinded to patient's data and groups. A Vivid E9 echocardiograph (GE Healthcare, General Electric), equipped with a 2D phased array M5S transducer (1.5–4.6 MHz) operating in second harmonic and a matrix 4D volume phased array transducer (1.5–4.0 MHz), was used. The electrocardiogram was systematically coupled with the ultrasound imaging. The standard echocardiography included the measurement of the end-diastolic and end-systolic diameters of the left ventricle (LV) in the longitudinal parasternal axis. The apical 4 and 2-chambers views were used for the measurement of LV and left atrial volumes by the Simpson biplane method. The trans-mitral pulsed wave Doppler velocities were recorded from the apical 4-chambers view with a 2 mm Doppler sample placed between the tips of the mitral leaflets. The evaluation of diastolic function was made with reference to the guidelines of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [12]. Continuous wave Doppler of tricuspid regurgitation was utilized to estimate the pressure gradient between the right ventricle (RV) and the right atrium according to the Bernoulli equation. The systolic velocity of the S<sub>m</sub>' and diastolic E' waves were collected by tissue Doppler and averaged from the lateral and the septal part of the mitral annulus. In 5-chambers apical view, the peak aortic velocity as well as the aortic mean gradient was measured with continuous Doppler. The LV myocardial performance index (MPI) was measured using tissue Doppler according to the description of Tei et al. [13]. MPI is defined as the ratio of the sum of the iso-volumetric contraction time and iso-volumetric relaxation time by the ejection time. This index is considered pathological if it is greater than 0.47. The RV systolic function was assessed using tricuspid annular plane systolic excursion (TAPSE) as well as the systolic wave S<sub>i</sub>' velocity of the lateral tricuspid ring and the RV lateral wall strain [14].

Gray scale loops obtained in second harmonic imaging and centered on the LV were recorded. Five to ten loops of single cardiac cycles were

performed in apical 4, 3 and 2-chambers views with a frame rate between 55 and 80 frames per second using the 4D volume. The data were recorded and stored in digital format for off-line analysis (EchoPac, ultrasound General Electric Vingmed Ultrasound AS). Measurement of the two-dimensional speckle tracking was performed when feasible from simultaneous three apical views using 4D matrix probe (Xplane mode); and if not from three single and nearly equal in duration cardiac cycles using the 2D M5S probe. The measurement was made in 18 segments LV model and the global longitudinal strain (GLS) was then automatically calculated. For the RV lateral wall strain, recording 2D images required a high frame rate of greater than 60 frames per second, using the best scan and depth to get the RV image as large as possible [15,16]. The RV lateral wall strain was calculated by averaging the 3 regions of interest (basal, medial and apical segments). Strain thresholds of LV and RV were respectively -18% and -20%.

### 2.3.4 Sleep study

All patients underwent overnight polysomnography using a standard technique with assessment of airflow through nasal cannula, respiratory effort by thoracoabdominal bands, oxygen saturation and heart rate with pulse oximetry. Apnea was defined as complete cessation of airflow for at least 10s. Hypopnea was defined as a reduction of at least 50% in airflow lasting at least 10s associated with a 4% decrease in nocturnal oxygen saturation. AHI was defined as the number of apneas and/or hypopneas per hour. An obstructive apnea was defined as the absence of airflow despite respiratory movement or exertion. According to international guidelines, diagnosis of OSA is made when AHI is greater than 5 e/h [17]. The latter index was also used to stratify the disease severity: mild with AHI ranging between 5 and 14 e/h, moderate with AHI between 15 and 29 e/h and severe with AHI  $\geq 30$  e/h [17].

## 2.4 Statistical Analysis

Statistical analysis was performed using SPSS software (version 23.0). Percentages were calculated to assess qualitative variables. Mean values and standard deviations were determined for the quantitative variables. Comparison of two independent averages was assessed by the nonparametric Mann and Whitney test. Categorical variables were compared using Fischer's exact test or chi square test as deemed

appropriate. To determine quantitative variables' threshold values with a certain sensitivity and specificity to predict an event, receiver operating characteristics (ROC) curves were used while making sure that the area under the curve was significantly greater than 0.5. In order to identify risk factors independently related to the event, a stepwise multivariate logistic regression analysis was conducted.

## 3. RESULTS

### 3.1 General Clinical Characteristics and Polysomnographic Data

Forty patients were included in the present study. General clinical characteristics are summarized in Table 1.

Atrial fibrillation was permanent in 23 patients (57.5%), persistent in 5 patients (12.5%) and paroxysmal in 12 patients (30%). AF age ranged from 6 months to 27 years, with an average of  $4.6 \pm 4.2$  years. The effects of AF on quality of life, assessed by the EHRA classification, are reported in Table 1.

Ninety percent of patients were found to have OSA. The average AHI was  $22.1 \pm 13$  e/h with extremes ranging from 1.1 to 52 e/h. Eleven patients had mild OSA (27.5%), 9 patients (22.5%) had moderate OSA and 16 patients (40%) had severe OSA. Data relating to the polysomnographic investigation and symptoms due to OSA are described in Table 2.

### 3.2 Echocardiographic Findings

Details of conventional and tissue Doppler echocardiographic parameters for both groups are reported in Table 3.

#### 3.2.1 Left ventricular systolic function

Averages of LV systolic parameters as well as percentages of impaired LV systolic parameters are listed in Table 3.

The mean value of LV ejection fraction according to the Simpson method was  $56 \pm 10.7\%$ . The LV ejection fraction was impaired in 17.5% of patients. The mean value of the GLS was  $-16.4 \pm 4.1\%$  with limits ranging from -4 to -25%. LV GLS was impaired in 65% of cases. The average value of left MPI was  $0.42 \pm 0.12$ . According to the latter index, 30% of patients had systolic ventricular dysfunction.

**Table 1. General characteristics of the study population**

Baseline characteristics	Study population (n=40)	Group 1 AHI < 30 e/h (n=24)	Group 2 AHI ≥ 30 e/h (n=16)	P
Sex (M/F)	14/26	9/15	5/11	0.68
Age* (years)	63.8 ± 10.7	61.8 ± 11.7	66.7 ± 8.7	0.16
Hypertension	27 (67.5%)	15 (62.5%)	12 (75%)	0.50
Diabetes mellitus	12 (30%)	6 (25%)	6 (37.5%)	0.49
Dyslipidaemia	21 (52.5%)	12 (50%)	9 (56%)	0.75
Smoking	8 (20%)	4 (17%)	4 (25%)	0.69
Prior ischemic stroke	5 (12.5%)	4 (17%)	1 (6%)	0.63
Body mass index* (Kg/m <sup>2</sup> )	28.6 ± 4.3	28.4 ± 4.3	29 ± 4.5	0.68
Neck circumference* (cm)	38.4 ± 4.6	38.4 ± 4.5	38.5 ± 5	0.90
Waist circumference* (cm)	111.6 ± 11.7	109.5 ± 12.5	114.8 ± 12.7	0.20
<b>Clinical form of AF</b>				
• Permanent AF	23 (57.5%)	11 (46%)	12 (75%)	
• Persistent AF	5 (12.5%)	4 (17%)	1 (6%)	0.18
• Paroxysmal AF	12 (30%)	9 (37.5%)	3 (19%)	
<b>Effect of AF on quality of life</b>				
• EHRA I	7 (17.5%)	4 (17%)	3 (19%)	
• EHRA II	19 (47.5%)	13 (54%)	6 (37.5%)	
• EHRA III	13 (32.5%)	6 (25%)	7 (44%)	0.51
• EHRA IV	1 (2.5%)	1 (4%)	0	

*Values are expressed in number (percentage) or in \* means (standard deviation). AF: Atrial fibrillation; AHI: Apnea hypopnea index; e/h: event(s)/hour*

**Table 2. Polysomnographic data and obstructive sleep apnea's symptoms**

<b>Variables</b>	<b>Study population (n=40)</b>	<b>Group1 AHI &lt; 30 e/h (n=24)</b>	<b>Group2 AHI ≥ 30 e/h (n=16)</b>	<b>P</b>
<b>Obstructive sleep apnea symptoms</b>				
<b>Snoring</b>	36 (90%)	20 (83%)	16 (100%)	0.13
<b>Daytime sleepiness</b>	34 (85%)	19 (79%)	15 (94%)	0.37
<b>Morning asthenia</b>	31 (77.5%)	18 (75%)	13 (81%)	0.71
<b>Sleep disorder</b>	20 (50%)	12 (50%)	8 (50%)	1
<b>Memory disorder</b>	31 (77.5%)	20 (83%)	11 (69%)	0.44
<b>Nocturia</b>	23 (57.5%)	9 (37.5%)	14 (87.5%)	<b>0.003</b>
<b>Cognitive impairment</b>	16 (40%)	9 (37.5%)	7 (44%)	0.75
<b>Polysomnographic data</b>				
<b>Apnea hypopnea index (e/h)</b>	22.1 ± 13	13 ± 7.6	35.6 ± 4.8	<b>&lt; 0.0001</b>
<b>Desaturation index</b>	19.3 ± 12.7	11 ± 6.1	31.7 ± 9.4	<b>&lt; 0.0001</b>
<b>Mean saturation (%)</b>	93.4 ± 2.5	94.2 ± 1.5	92.2 ± 3.2	<b>0.03</b>
<b>Mean heart rate (c/mn)</b>	64.9 ± 8.7	62.8 ± 7	68 ± 9	0.09

*Values are expressed in means (standard deviation). AHI: Apnea hypopnea index; e/h: event(s)/hour*

Table 3. Conventional echocardiographic parameters and two-dimensional speckle tracking

Variables	Study population (n=40)	Group1 AHI < 30 e/h (n=24)	Group2 AHI ≥ 30 e/h (n=16)	P
<b>Left heart chambers dimensions</b>				
Indexed left atrial volume* (ml/m <sup>2</sup> )	43.7 ± 20.2	42.2 ± 24.8	45.5 ± 12.8	0.16
End-distolic diameter* (mm)	49.4 ± 5.7	50.4 ± 5.4	48 ± 6.1	0.10
End-systolic diameter* (mm)	32.7 ± 7	33.3 ± 7	31.8 ± 7.3	0.48
End-diastolic volume* (ml)	74.4 ± 32.5	79 ± 24.8	69.2 ± 39.9	0.11
End-systolic volume* (ml)	33.8 ± 19.5	36.3 ± 19	31 ± 20.3	0.17
Inter ventricular septum* (mm)	11.9 ± 1.8	11.8 ± 1.8	12.1 ± 1.8	0.48
Indexed LV mass* (g/m <sup>2</sup> )	119 ± 35	123 ± 45	116 ± 28	0.57
<b>Left ventricular systolic function</b>				
LV EF* (Simpson) (%)	56 ± 10.7	55.5 ± 11.9	56.7 ± 9.2	1
Impaired LV EF (Simpson)	7 (17.5%)	5 (20.8%)	2 (12.5%)	0.6
LV GLS* (%)	-16.4 ± 4.1	-17.3 ± 4.5	-14.9 ± 3	<b>0.02</b>
Impaired LV GLS	26 (65%)	11 (45.8%)	15 (93.7%)	<b>0.004</b>
Left MPI *	0.42 ± 0.12	0.37 ± 0.09	0.49 ± 0.13	<b>0.01</b>
Impaired left MPI	12 (30%)	4 (16.6%)	8 (50%)	<b>0.016</b>
<b>Right ventricular systolic function</b>				
TAPSE* (mm)	18.7 ± 4.9	20.3 ± 5.3	17 ± 3.7	0.06
Impaired TAPSE	15 (37.5%)	7 (29.1%)	8 (50%)	0.28
S <sub>1</sub> ' wave velocity* (cm/s)	10.9 ± 3.5	10.9 ± 4.1	10.8 ± 2.5	0.63
Impaired S <sub>1</sub> ' wave velocity	12 (30%)	8 (33.3%)	4 (25%)	0.53
Right Ventricular lateral wall strain* (%)	-20.8 ± 7.6	-22.5 ± 8.4	-18.4 ± 5.8	0.15
Impaired Ventricular lateral wall strain	20 (50%)	9 (37.5%)	11 (68.7%)	0.15

Values are expressed in number (percentages) or in \* means (standard deviation). AHI: Apnea hypopnea index; e/h: event(s)/hour; LV: Left ventricle; LV EF: Left ventricle ejection fraction; GLS: Global longitudinal strain; MPI: Myocardial performance index; TAPSE: tricuspid annular plane systolic excursion

**Table 4. Univariate and multivariate analysis**

Variables	Odds ratio	CI (95%)	P
<b>Univariate analysis</b>			
LV GLS < -18%	16.8	[1.9 – 150.9]	<b>0.004</b>
Left MPI > 0.37	7.2	[1.6 – 32.4]	<b>0.01</b>
RV lateral wall strain < -20%	3.4	[0.7 – 15.6]	0.15
TAPSE < 17 mm	2.7	[0.6 – 11.7]	0.28
Permanent AF	3.5	[0.8 – 14.2]	0.10
Nocturia	11.6	[2.1 – 63.6]	<b>0.003</b>
<b>Multivariate analysis</b>			
LV GLS < -18%	16.6	[1.2 – 222.3]	<b>0.03</b>
Left MPI > 0.37	17.2	[1.2 – 248.2]	<b>0.03</b>
RV lateral wall strain < -20%	1.3	[0.03 – 48.4]	0.90
TAPSE < 17 mm	0.57	[0.01 – 20.1]	0.75
Permanent AF	2.5	[0.1 – 45.8]	0.51
Nocturia	1.8	[0.6 – 57.6]	0.72

CI: Confidence interval; LV: Left ventricle; GLS: Global longitudinal strain; MPI: Myocardial performance index; RV: Right ventricle; TAPSE: tricuspid annular plane systolic excursion; AF: Atrial fibrillation

The impairment of the Simpson biplane LV ejection fraction was observed in 5 patients (20.8%) vs. 2 patients (12.5%), in group 1 and 2, respectively (p = 0.6).

Fifty percent of patients in group 2 had a left MPI greater than 0.47 consistent with LV systolic dysfunction, whereas only 4 patients (16.6%) in group 1 had an abnormal left MPI (p = 0.016).

Referring to the ROC curve, a left MPI cut-off value of 0.37 differentiated between the presence or not of severe OSA, with a sensitivity of 81% and a specificity of 62%.

LV GLS was impaired in 11 patients (45.8%) vs. 15 patients (93.7%), in group 1 and 2, respectively (p = 0.004).

A statistically significant association was demonstrated between severe OSA and impairment of left ventricular GLS ( $-17.3 \pm 4.5$  vs.  $-14.9 \pm 3\%$ , in group 1 and 2 respectively, p = 0.02) and left ventricular MPI ( $0.37 \pm 0.09$  vs.  $0.49 \pm 0.13$ , in group 1 and 2 respectively, p = 0.01).

### 3.2.2 Left ventricular diastolic function

The study of LV diastolic function revealed that in the study population, 12 patients (30%) had diastolic dysfunction, 19 patients (47.5%) had normal diastolic function and 9 patients (22.5%) had indeterminate diastolic function.

In group 1, eight patients (33.3%) had diastolic dysfunction, 5 patients (20.8%) had

indeterminate diastolic function and 11 patients (45.8%) had normal diastolic function. In group 2, five patients (31.2%) had diastolic dysfunction, 3 patients (18.8%) had indeterminate diastolic function and the remaining patients had normal diastolic function. There was no significant difference between the two groups (p = 0.94).

### 3.2.3 Right ventricular systolic function

Averages of RV systolic parameters as well as percentages of impaired RV systolic parameters are reported in Table 3.

In the study population, TAPSE had an average value of  $18.7 \pm 4.9$  mm with extremes ranging from 11.9 to 31 mm. TAPSE was impaired in 37.5% of patients. TAPSE was impaired (<17mm) in 7 patients (29.1%) vs. 8 patients (50%), in group 1 and 2, respectively (p=0.28).

The S<sub>t</sub> wave at the lateral tricuspid ring had a mean value of  $10.9 \pm 3.5$  cm/s for all patients. S<sub>t</sub> was below 9.5 cm/s in 30% of cases. Regarding this parameter, 8 patients (33.3%) in group 1 had right ventricular dysfunction, while 4 patients (25%) in group 2 had an impaired S<sub>t</sub> (p = 0.53).

In the study population, the mean value of the RV lateral wall strain was  $-20.8 \pm 7.6\%$  with limits ranging from -8.5 to -37%. Right ventricular strain was impaired in 50% of patients. Impairment of the RV lateral wall strain was noted in 9 patients (37.5%) in group 1 vs. 11 patients (68.7%) in group 2, with no statistically significant difference (p = 0.15).



### 3.3 Multivariate Analysis

Multivariate logistic regression analysis revealed that LV GLS impairment ( $< -18\%$ ) and a left MPI  $> 0.37$  were independent predictors of severe OSA (Table 4).

### 3.4 Berlin Score

Twenty-five patients (62.5%) from the study population had a Berlin score  $\geq 2$ , indicating a high probability of OSA. The Berlin score was suggestive of OSA in 8 patients (50%) vs. 13 patients (81.3%), in group 1 and 2 respectively ( $p=0.05$ ).

### 3.5 New Combined Screening Test of OSA

In the present study, a new combined clinical and echocardiographic screening test of OSA was proposed. This test was considered positive if Berlin score was suggestive ( $\geq 2$ ), LV GLS was impaired ( $> -18\%$ ) and a left MPI  $> 0.37$ .

The comparison of this test results with the polysomnographic data, demonstrated that this new combined screening test had a sensitivity of 86.7% and a specificity of 75%, for predicting severe OSA in NVAf patients.

## 4. DISCUSSION

In the present study, OSA was diagnosed in 90% in NVAf patients. Severe OSA was found in 40% of patients. The echocardiographic study revealed that left MPI was impaired ( $> 0.47$ ) in 16.6% vs. 50% of patients, in group 1 and 2, respectively ( $p=0.016$ ). A left MPI threshold of 0.37 differentiated between the presence or not of severe OSA, with a sensitivity of 81% and a specificity of 62%. LV GLS was impaired in 45.8% vs. 93.7% of patients, in group 1 and 2, respectively ( $p=0.004$ ). TAPSE and RV later wall longitudinal strain were more impaired in patients with severe OSA without reaching the threshold of statistical significance.

In this study, the high prevalence of OSA among NVAf patients could be explained by a significant percentage of obese and hypertensive patients among the study population. Several observational studies have shown frequent coexistence of AF and OSA [4,18-21]. Abumuamar et al. [4] reported a prevalence of OSA of 85% in AF patients, with a prevalence of severe OSA of 28%.

Regarding echocardiographic findings, many studies have found similar results. Indeed, Varghese et al. [22] investigated the LV function using several parameters then compared them between patients with very severe OSA ( $AHI \geq 40$ ) and patients without OSA (control group). They found that there was no significant difference between the two groups regarding the conventional parameters of LV systolic function, including Simpson biplane LV ejection fraction and MPI. The diastolic function as well as the LV GLS were significantly more impaired in the group with severe OSA compared to the control group. According to the study conducted by Altekin et al. [23] including 58 patients with different degrees of OSA severity and a control group of 21 patients, the LV GLS were more impaired in case of OSA (Healthy patients:  $-25.58 \pm 2.16\%$ , Mild OSA:  $-23.93 \pm 3.96\%$ , Moderate OSA:  $-21.27 \pm 2.60\%$ , Severe OSA:  $-16.94 \pm 2.66\%$ ). Regarding LV GLS, the difference was significant in severe OSA patients compared to all other subgroups ( $p=0.03$ ). Conventional parameters, however, such as Simpson biplane LV ejection fraction and  $S'_m$  wave were comparable between the subgroups. Akyol et al. [24] studied MPI in 116 patients with different degrees of OSA severity and compared findings according to OSA severity. The left MPI was significantly higher in the group with severe OSA ( $MPI = 0.5 \pm 0.12$ ) than in the groups with moderate OSA ( $MPI = 0.48 \pm 0.09$ ) and mild OSA ( $MPI = 0.45 \pm 0.08$ ) ( $p=0.018$ ). Similarly, Romero et al. [25] found that right and left MPI correlated positively and significantly with the  $AHI$  ( $p = 0.40$ ,  $p = 0.002$ ; and  $p = 0.27$ ,  $p = 0.02$ , respectively).

Regarding the RV function, the association between RV dysfunction and OSA has been reported in several studies using several echocardiographic parameters [26-29]. Tavit et al. [26] demonstrated that RV systolic function, assessed by different echocardiographic parameters (TAPSE,  $S'_t$  wave velocity and right MPI), was significantly more impaired in the group with OSA compared to the control group. Zakhama et al. [27] showed that the  $S'_t$  wave velocity and the right MPI, were significantly worse in patients with OSA compared to the control group ( $p < 0.001$  and  $p = 0.024$ , respectively). More recently, Vitarelli et al. [28] investigated the impact of OSA on the RV function using longitudinal strain and three-dimensional ejection fraction. They demonstrated that both parameters were significantly more altered in patients with

OSA compared to the control group. Buonauro et al. [29] also demonstrated that OSA was significantly associated with an impairment of the RV GLS and the lateral wall longitudinal strain ( $p=0.05$  and  $p=0.04$ , respectively).

## 5. STUDY LIMITATIONS

The present study is a small scale one mainly because of limited accessibility to polysomnographic investigation. Moreover, echocardiographic monitoring of left and right functions after the implementation of OSA therapies (lifestyle changes, positive airway pressure or surgery) was not performed.

## 6. CONCLUSION

The present study demonstrated that OSA was very common among NVAf patients. OSA may be a contributing or causal factor of an apparently isolated AF and its screening, by a suitable tool such as echocardiography, is advisable. In case of severe OSA, myocardial dysfunction involved not only RV as commonly known but also LV. From this perspective, it is advisable to search for myocardial dysfunction by the appropriate parameters such as the longitudinal strain and MPI.

OSA treatment could be considered as an etiopathogenic treatment of cardiovascular disorders including AF and myocardial dysfunction. Recent studies support the reversibility of echocardiographic abnormalities by OSA treatment but the clinical interest and the prognosis improvement after treatment remains to demonstrate.

## CONSENT

All patients included in this study were informed orally about the objectives and the course of the study. All of them provided informed consent to the study.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Garvey JF, Pengo MF, Drakatos P, Kent BD. Epidemiological aspects of obstructive sleep apnea. *J Thorac Dis.* 2015;7(5): 920-9.
2. Sia C-H, Hong Y, Tan LWL, van Dam RM, Lee C-H, Tan A. Awareness and knowledge of obstructive sleep apnea among the general population. *Sleep Med.* 2017;36:10-7.
3. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: The Atrial Fibrillation and Risk Factors in Atrial Fibrillation (ATRIA) study. *JAMA.* 2001;285(18):2370-5.
4. Abumumar AM, Dorian P, Newman D, Shapiro CM. The prevalence of obstructive sleep apnea in patients with atrial fibrillation. *Clin Cardiol.* 2018;41(5):601-7.
5. European Heart Rhythm Association, European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GYH, Schotten U, et al. Guidelines for the management of atrial fibrillation: The task force for the management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Heart J.* 2010;31(19):2369-429.
6. Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. Focused update of the ESC Guidelines for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of Atrial Fibrillation. Developed with the special contribution of the European Heart Rhythm Association. *Eur Heart J.* 2012;33(21):2719-47.
7. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38(36): 2739-91.
8. Massierer D, Martinez D, Fuchs SC, Pellin PP, Garcia MS, Zacharias AL, et al. Obstructive sleep apnea, detected by the Berlin Questionnaire: An associated risk factor for coronary artery disease. *Cad Saude Publica.* 2012;28(8):1530-8.
9. Faria AC, da Costa CH, Rufino R. Sleep apnea clinical score, Berlin Questionnaire, or Epworth sleepiness scale: Which is the best obstructive sleep apnea predictor in

- patients with COPD? *Int J Gen Med.* 2015;8:275-81.
10. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J.* 2016;37(38): 2893-962.
  11. Schiller NB. Two-dimensional echocardiographic determination of left ventricular volume, systolic function, and mass. Summary and Discussion of the 1989 Recommendations of the American Society of Echocardiography. *Circulation.* 1991;84(3 Suppl):I280-287.
  12. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2016;29(4):277-314.
  13. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JK, Rodeheffer RJ, et al. New index of combined systolic and diastolic myocardial performance: A simple and reproducible measure of cardiac function- A study in normals and dilated cardiomyopathy. *J Cardiol.* 1995;26(6):357-66.
  14. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr.* 2010;23(7):685-713.
  15. Kalogeropoulos AP, Georgiopoulou VV, Howell S, Pernetz M-A, Fisher MR, Lerakis S, et al. Evaluation of right intraventricular dyssynchrony by two-dimensional strain echocardiography in patients with pulmonary arterial hypertension. *J Am Soc Echocardiogr.* 2008;21(9):1028-34.
  16. Ishizu T, Seo Y, Atsumi A, Tanaka YO, Yamamoto M, Machino-Ohtsuka T, et al. Global and regional right ventricular function assessed by novel three-dimensional speckle-tracking echocardiography. *J Am Soc Echocardiogr.* 2017;30(12):1203-13.
  17. Lemarié É, Valeyre D, Housset B, Godard P. Syndrome d'apnées hypopnées obstructives du sommeil de l'adulte: Des recommandations pour la pratique clinique. *Rev Mal Respir.* 2010;27:804-5.
  18. Gami AS, Pressman G, Caples SM, Kanagala R, Gard JJ, Davison DE, et al. Association of atrial fibrillation and obstructive sleep apnea. *Circulation.* 2004;110(4):364-7.
  19. Braga B, Poyares D, Cintra F, Guilleminault C, Cirenza C, Horbach S, et al. Sleep-disordered breathing and chronic atrial fibrillation. *Sleep Med.* 2009;10(2): 212-6.
  20. Stevenson IH, Teichtahl H, Cunningham D, Ciavarella S, Gordon I, Kalman JM. Prevalence of sleep disordered breathing in paroxysmal and persistent Atrial fibrillation patients with normal left ventricular function. *Eur Heart J.* 2008;29(13):1662-9.
  21. Szymański FM, Płatek AE, Karpiński G, Koźluk E, Puchalski B, Filipiak KJ. Obstructive sleep apnoea in patients with atrial fibrillation: Prevalence, determinants and clinical characteristics of patients in Polish population. *Kardiol Pol.* 2014;72(8): 716-24.
  22. Varghese MJ, Sharma G, Shukla G, Seth S, Mishra S, Gupta A, et al. Longitudinal ventricular systolic dysfunction in patients with very severe obstructive sleep apnea: A case control study using speckle tracking imaging. *Indian Heart J.* 2017;69(3):305-10.
  23. Altekin RE, Yanıkoğlu A, Karakaş MS, Ozel D, Yıldırım AB, Kabukçu M. Evaluation of subclinical left ventricular systolic dysfunction in patients with obstructive sleep apnea by automated function imaging method; an observational study. *Anadolu Kardiyol Derg AKD Anatol J Cardiol.* 2012;12(4):320-30.
  24. Akyol S, Cortuk M, Baykan AO, Kiraz K, Borekci A, Seker T, et al. Biventricular myocardial performance is impaired in proportion to severity of obstructive sleep Apnea. *Tex Heart Inst J.* 2016;43(2): 119-25.
  25. Romero-Corral A, Somers VK, Pellikka PA, Olson EJ, Bailey KR, Korinek J, et al. Decreased right and left ventricular

- myocardial performance in obstructive sleep apnea. *Chest*. 2007;132(6):1863-70.
26. Tavi Y, Kanbay A, Sen N, Ciftçi TU, Abaci A, Yalçın MR, et al. Comparison of right ventricular functions by tissue Doppler imaging in patients with obstructive sleep apnea syndrome with or without hypertension. *Int J Cardiovasc Imaging*. 2007;23(4):469-77.
27. Zakhama L, Herbegue B, Abouda M, Antit S, Slama I, Boussabah E, et al. Impact of obstructive sleep apnea on the right ventricle. *Tunis Med*. 2016;94(8-9):612-5.
28. Vitarelli A, Terzano C, Saponara M, Gaudio C, Mangieri E, Capotosto L, et al. Assessment of right ventricular function in obstructive sleep apnea syndrome and effects of continuous positive Airway Pressure Therapy: A pilot study. *Can J Cardiol*. 2015;31(7):823-31.
29. Buonauro A, Galderisi M, Santoro C, Canora A, Bocchino ML, Lo Iudice F, et al. Obstructive sleep apnoea and right ventricular function: A combined assessment by speckle tracking and three-dimensional echocardiography. *Int J Cardiol*. 2017;243:544-9.

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