Original Article

Impact of Obstructive Sleep Apnea and Snoring on Left Ventricular Mass and Diastolic Function in Hypertensive Nigerians

Akintunde AA[1,2], Kareem L[1], Bakare A[1], Audu M[1]

[1]Department of Medicine, Division of Cardiology, Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, Nigeria, [2]Goshen Heart Clinic, Osogbo, Nigeria

Address for correspondence:
Dr. AA Akintunde,
P.O. Box 3238, Osogbo, Nigeria.
E-mail: iakintunde2@yahoo.com

Abstract

Background: Systemic hypertension (HTN) and obstructive sleep apnea (OSA) are individually associated with left ventricular structural and functional adaptations. However, little is known about the impact of OSA on the left ventricle in Africans with HTN. **Aim:** The aim of this study is to determine the association between OSA and left ventricular mass (LVM) and diastolic dysfunction in Nigerian hypertensive subjects. **Subjects and Methods:** A total of 104 hypertensive subjects were enrolled for this study. Risk for OSA was assessed with the Berlin score. Clinical history and examination were performed. Echocardiography was performed and diastolic dysfunction was diagnosed using the pulse wave Doppler. Statistical analysis was performed using the statistical package for social sciences 17.0. (Chicago Ill, USA). Comparism between groups was done using *t*-test and Chi-square and $P < 0.050$ was taken as statistically significant. **Results:** LVM, posterior wall and interventricular septum were significantly higher among hypertensive patients with high risk for OSA than those with low risk (263.610 g [11.202] g vs. 208.714 g [47.060] g; 12.100 mm [2.712] mm vs. 10.711 mm [2.101] mm; 13.210 [3.114] mm vs. 11.700 mm [2.402] mm respectively). A similar finding was reported between hypertensive snorers and hypertensive non-snorers. Fasting blood glucose was also significantly higher among hypertensive snorers than non-snorers. However, mean transmitral early (E) to late (A) flow E/A ratio was lower among hypertensive with low risk of OSA and snorers than those with a high risk and non-snorers respectively. Left Ventricular hypertrophy was also more common among hypertensive with high risk of OSA than non-snorers and low risk of OSA (39/55, 70.9% vs. 28/49, 57.1% respectively, $P < 0.05$). **Conclusion:** OSA is associated with significant additional left ventricular changes in hypertensive subjects. Therefore, aggressive effort at managing OSA and snoring among hypertensive subjects may further reduce their cardiovascular risk.

Keywords: Africa, Hypertension, Sleep apnea, Snoring

Introduction

Obstructive sleep apnea (OSA) and snoring are common, but underdiagnosed conditions that carry increased cardiovascular (CV) risk leading to increased CV morbidity and mortality.[1] Hypertension (HTN) is a clinical condition with multiple etiologies and complications.[2] It is the most common CV risk factors in Nigeria.[2,3] The CV risk of HTN is a function of the level of blood pressure (BP), the presence of target organ damage, associated clinical conditions and presence of other CV risk factors.[4] OSA is a CV risk factor.[5,6] OSA is characterized by recurrent upper airway obstruction leading to hypopnea and apnea, hypoxia, reduced intra-thoracic pressure during breathing effort and frequent awakenings with subsequent sleep fragmentation.[1,5] The seventh report of the Joint National Council (VII) on Prevention, Detection, Evaluation and Treatment of High BP included OSA as a new cause of secondary HTN and also a CV risk factor.[7] The prevalence of HTN continue to increase world-wide including Nigeria.[1-3] HTN is associated with increased risk for left

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ventricular hypertrophy (LVH).[8,9] LVH is an important determinant of CV morbidity and mortality from various studies.[7] In a report from Nigeria, up to one-fifth of a population cohort were discovered to have a high risk for OSA using the Berlin score as compared with about one-fourth of Americans in another report.[10,11] The association between OSA and HTN has been well-described.[7,12] Neurohormonal abnormalities such as increased activation of adrenergic and renin angiotensin aldosterone systems are similarly found in OSA and systemic HTN.[13] LVH and diastolic dysfunction are associated with HTN and OSA.[14]

Since OSA is often associated with systemic HTN, it will be essential to identify the impact of coexistence of OSA and HTN on left ventricular mass (LVM) and diastolic function in Nigerians. The aim of this study was to describe the impact of sleep apnea on LVM and left ventricular diastolic function (LVDF) in treated Nigerian hypertensive subjects.

Subjects and Methods

A total of 104 subjects were consecutively recruited for this study. They included hypertensive subjects receiving their treatment at the Cardiology Clinic of Ladoke Akintola University of Technology, Ogbomoso. The study was carried out between January and December 2012.

The study location was the Cardiology clinic of Ladoke Akintola University of Technology Teaching Hospital, Ogbomoso, Nigeria. It was a cross-sectional study. HTN was diagnosed according to international clinical criteria.[7,15] Clinical and demographic parameters including age, gender, body weight (in kg), height (in m), waist circumference (WC) and hip circumference of all participants were taken. Blood sample was taken after at least 8 h of overnight fasting and used to determine the fasting blood sugar (FBS) using the glucose oxidase method. Informed consent was taken from each participant. Ethical approval was obtained from the institutional ethical review board.

The epworth sleepiness scale (ESS) was used to determine excessive daytime sleepiness (EDS). It is an eight item self administered questionnaire. Possible score ranges were from 0 to 24. For this study, an ESS score of more than 11 was taken to mean EDS. The Berlin questionnaire was used to identify the risk of having clinical OSA. The questionnaire consists of three categories related to the risk of having sleep apnea. Patients can be classified into high risk or low risk based on their responses to the individual items and their overall scores in the symptom categories. Subjects were categorized as high risk for having OSA if there were two or more categories where the score were positive and low risk if there was only one or no categories where the score was positive.[15] The Berlin questionnaire has been documented to be clinically sensitive and correlates significantly with the presence of OSA among various population.[16] Clinically suspected obstructive sleep apneas was defined in accordance with the 2001 international classification of sleep disorders.[15]

Echocardiography was performed according to the American Society of Echocardiography guideline with the patient in the left lateral decubitus position. The left ventricular posterior wall and interventricular wall dimensions were taken. Transmitral E and wave velocities were also determined. LVM and relative wall thickness (RWT) were determined. Systolic function was assessed by the left ventricular ejection fraction (EF) according to the Teicholz formula. LVM was measured according to the Penn convention using the Devereux formula.[17] LVH was considered present if the LVM index is ≥ 134 g/m^2 and 110 g/m^2 for males and females respectively. RWT was derived by 2 × posterior wall thickness (PWT)/left ventricular internal diastolic dimension.[17,18]

Statistical analysis was performed using the statistical package for social sciences version 17.0 (Chicago Ill, USA) Numerical data were summarized using means and standard deviation while categorical data were summarized using frequencies and percentages. Comparism between groups was done using *t*-test and Chi-square. $P < 0.05$ was taken as statistically significant.

Results

More than half of our hypertensive patients (55/104, 52.9%) were found to be at high risk for OSA while snoring was present in 50.0% of the study population. Hypertensive subjects with low risk for OSA were similar in age and gender distribution with hypertensive subjects with high risk for OSA. Mean WC, body mass index (BMI) and waist hip ratio were significantly higher among hypertensive subjects with high risk for OSA than those with low risk as shown in Table 1. Mean systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse rate were similar between the hypertensive subjects with high and low risk for OSA as shown in Table 1, although they were higher among the hypertensive subjects with high risk of OSA.

Hypertensive subjects with high risk for OSA were noted to have a significantly higher PWT in diastole, interventricular septal thickness in diastole (IVSd), mitral E/A ratio, LVM, RWT, LVM index and the proportion of participants with LVH than those with low risk of OSA as shown in Table 2. Left ventricular internal dimension in diastole (LVIDd) and systole, EF and fractional shortening were similar between hypertensive subjects with high risk of OSA and those hypertensive with low risk for OSA.

The mean ages were similar between hypertensive snorers and hypertensive non-snorers in this study. Mean SBP, DBP, LVIDd and mitral E/A ratio were higher among hypertensive snorers although they did not reach statistical significance. However, mean FBS, PWT in diastole, IVSd, LVM and BMI were significantly higher among hypertensive snorers than hypertensive non-snorers as shown in Table 3.

Discussion

This study revealed that OSA is associated with additional impact in the left ventricular dimension and LVM among Nigerian hypertensive subjects and that they may have additional increased CV risk. This is related to the associated increased frequency of LVH, a higher chamber wall dimension including PWT, interventricular septal thickness and even increased mean FBS. It is also related to significantly higher LVM among hypertensive subjects with increased risk of OSA than those with low risk for OSA. A similar finding was demonstrated in this study between hypertensive snorers and non-snorers.

This is in agreement with other similar studies that have demonstrated that OSA is associated with increased LVM and left ventricular chamber dimensions.[19-21] However, other studies have demonstrated that this change is particularly related to the pattern and contribution of obesity among these hypertensive subjects[22] while others have demonstrated no significant additional impact of OSA on the left ventricular structure and function among hypertensive and diabetic subjects.[23]

OSA is closely associated with many CV risk factors such as HTN, atherosclerosis, obesity, diabetes and dyslipidemia.[7,12,24,25] Repeated episodes of hypoxia, hypercapnia, microarousals and changes in intrathoracic pressure in OSA trigger pathophysiological mechanisms such as hyperactivity, oxidative stress, systemic inflammation, hypercoagulability and even endothelial dysfunction.[26-28] All these changes results in additional impact on the left ventricular remodeling pattern and may consequently produce increased LVM and chamber dimension. The apnea and hypopnea episode in OSA is also associated with increased inflammation, endothelial dysfunction and coagulation abnormalities.[20,24] This may be responsible for a higher BP profile among hypertensive subjects with high risk for OSA in this study and also among hypertensive snorers. The increased CV risk profile of hypertensive subjects with high risk for OSA and snoring may also be responsible for the elevated FBS compared with those with low risk of OSA. Increased FBS is associated with insulin resistance and endothelial dysfunction and can ultimately lead to frank diabetes.[7,12,15,27]

This study therefore revealed that OSA and/or snoring are associated with the double burden on the myocardium of hypertensive subjects with these conditions. It is however, possible that this burden may be alleviated by the use of antihypertensive therapy. This may be what is responsible for the finding in this study with respect to diastolic function. LVH is associated with increased prevalence of diastolic dysfunction.[29,30] However, we found out that the mean transmitral E/A velocity was lower among subjects with high risk for OSA and hypertensive snorers than those with low risk and hypertensive non-snorers respectively. This may be due to the fact that the study participants were already on treatment majority of who are on Angiotensin converting

Table 1: Demographic and clinical parameters between hypertensive with low and high risk of OSA

Variable	Low risk (49)	High risk (55)	*P*
Age (years)	58.8 (12.6)	58.6 (11.2)	0.82
Gender (females) (%)	29 (59.2)	34 (61.8)	0.73
WC (cm)	88.2 (11.4)	96.6 (11.9)	<0.001*
SBP (mmHg)	133.7 (15.2)	137.3 (21.1)	0.36
DBP (mmHg)	81.5 (11.8)	82.1 (14.0)	0.84
BMI (kg/m^2)	24.6 (5.4)	27.8 (5.1)	<0.01*
WHR	0.90 (0.006)	0.94 (0.007)	0.01*
PR (min^{-1})	80.5 (13.3)	84.7 (15.0)	0.21

*Statistically significant. WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WHR: Waist hip ratio, PR: Pulse rate, OSA: Obstructive sleep apnea

Table 2: Echocardiographic parameters of hypertensive subjects with low and high risk of OSA

Variable	Low risk (49)	High risk (55)	*P*
LVIDd (mm)	49.1 (4.1)	50.9 (12.1)	0.71
LVIDs (mm)	32.6 (5.1)	37.3 (14.8)	0.42
PWTd (mm)	10.7 (2.1)	12.1 (2.7)	0.02*
IVSd (mm)	11.7 (2.4)	13.2 (3.1)	0.02*
EF (%)	65.2 (8.9)	60.6 (20.0)	0.60
FS (%)	34.0 (5.4)	30.0 (11.1)	0.37
E/A ratio	0.81 (0.21)	1.2 (0.44)	0.04*
LVM (g)	208.7 (47.0)	263.6 (112.8)	0.02*
RWT	0.44±0.07	0.50 (0.16)	0.03*
LVMI (g/m$^{2.7}$)	53.3 (11.3)	73.2 (30.9)	0.01*
LVH (n) (%)	28 (57.1)	39 (70.9)	<0.01*

*Statistical significant. LVIDd: Left ventricular internal dimension in diastole, LVIDs: Left ventricular internal dimension in systole, PWTd: Posterior wall thickness in diastole, IVSd: Interventricular septal thickness in diastole, EF: Ejection fraction, FS: Fractional shortening, LVM: Left ventricular mass, RWT: Relative wall thickness, LVMI: Left ventricular mass index, LVH: Left ventricular hypertrophy, OSA: Obstructive sleep apnea, E/A: transmitral early (E) to late atrial (A) flow velocity

Table 3: The clinical and echocardiographic parameters between hypertensive snorers and non-snorers

Variable	Hypertensive non-snorers (52)	Hypertensive snorers (52)	*P*
Age (years)	58.6 (12.02)	58.1 (11.7)	0.81
Waist circumference (cm)	88.1 (10.7)	97.2 (12.2)	<0.001*
SBP (mmHg)	132.5 (13.8)	138.6 (22.12)	0.12
DBP (mmHg)	81.0 (12.4)	82.7 (13.6)	0.54
FBS (mmol/l)	5.1 (1.7)	5.7 (0.82)	0.04*
LVIDd (mm)	49.3 (3.6)	51.0 (12.7)	0.70
PWTd (mm)	10.6 (1.8)	12.0 (2.7)	0.01*
IVSd (mm)	11.8 (2.0)	13.4 (3.2)	0.02*
E/A ratio	0.98 (0.37)	1.2 (0.46)	0.32
LVM (g)	208.3 (40.7)	268.8 (11.7)	0.01*
BMI (kg/m^2)	24.4 (4.73)	28.3 (5.5)	<0.001*

*Statistically significant. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FBS: Fasting blood glucose, LVIDd: Left ventricular internal dimension in diastole, PWTd: Posterior wall thickness in diastole, IVSd: Interventricular septal thickness in diastole, LVM: Left ventricular mass, BMI: Body mass index, E/A: Transmitral early (E) to late atrial (A) flow velocity

enzyme inhibitors, Angiotensin receptor blockers, which have been reported to improve diastolic function and reverse CV remodeling.[7,9,14]

An important association of high risk for OSA and snoring in this study was obesity. Hypertensive snorers and those with high risk for OSA had a significantly higher mean WC and BMI than those with low risk for OSA and hypertensive non-snorers. While obesity may be associated with increased LVM, Sukhija *et al*.[19] showed that OSA was an independent predictor of LVH after controlling for other factors including BMI and WC.

Some other relationships between OSA and HTN have been reported by other authors from other part of the world. Myslinski *et al*. reported that left ventricular end diastolic dimension was increased in hypertensive subjects with ineffectively treated HTN and also was positively correlated with apnea and hypopnea index.[31]

This study revealed no significant association between left ventricular dimension and OSA. This may be because the mean WC and BMI in were significantly higher in that study by Myslinski *et al*. than this present study. Another possible reason may be because our patients are treated hypertensives and the use of antihypertensives might have altered the remodeling pattern. However, Wachter *et al*. showed that OSA is not associated with increased LVM and/or impaired LVDF independently of obesity, HTN or advancing age.[32]

The clinical significance of this study is that Nigeria hypertensive subjects with snoring or increased risk for OSA may have a higher CV risk due to the increased LVM, chamber wall dimension and a higher chance of LVH and may therefore require further attention in order to reduce the CV risk. Continuous positive airway pressure has been shown to ameliorate the increased CV burden in these subjects including lifestyle modification aimed at reducing weight among obese subjects.[13,21,31] One limitation of this study is that it is a cross-sectional study and do not have the power to determine the causality of statistically related variables. Further research is therefore necessary including prospective study designs as well as randomized trials in order to determine the relationship of LVM and OSA among hypertensive subjects.

In conclusion, this study revealed that OSA and snoring are possibly associated with increased CV risk due to the significant increased LVM, chamber wall dimension, FBS, obesity and frequency of LVH in Nigerian hypertensive subjects. Further attention may therefore be needed among them to further reduce their CV risk.

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