Association of Left Atrial Enlargement with Increased Left Ventricular Mass in Adult Nigerians with Long Standing Hypertension

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ABSTRACT

Left atrial enlargement (LAE) is associated with increased risk of death and hospitalizations. We sought to determine the relationship between left atrial size and common demographic and echocardiographic parameters in adult Nigerians with long standing hypertension. A two dimensional echocardiography was performed on 81 patients with long standing hypertension and 80 normotensive controls after physical examination. The left ventricular mass (LVM) was calculated and indexed to body surface area to obtain the left ventricular mass index (LVMI). The hypertensive group was divided into those with left ventricular hypertrophy (LVH) and those without LVH based on their LVMI. Pearson’s Correlation Coefficient test was used to determine the relationship between LAE and demographic and echocardiographic parameters. The echocardiographic parameters were significantly higher in the hypertensive group than controls. Within hypertensives, they were significantly higher in those with LVH than those without LVH. The prevalence of LAE in the hypertensive population was 50.6%. It was more prevalent in those with LVH than those without LVH with rates of 80.5% versus 19.5% (χ2 = 9.586; p=0.002). The strongest correlate of LAE was LVM (r = 0.565; p<0.001) followed by LVH (r = 0.550; p<0.001). LAE is significantly associated with increased LVM and LVH in patients with long standing hypertension. This emphasizes the need for early institution and development of drugs that inhibit LVH in hypertensive patients.

Keywords: Left atrial enlargement, Left ventricular mass, Hypertension.

INTRODUCTION

Left atrial enlargement (LAE) is associated with increased risk of atrial fibrillation, stroke and death in both sexes.1,3 Studies have shown that the left atrial diameter has a graded independent association with all-cause mortality and death in men and women.4 It has been demonstrated that a left atrial dimension≥42mm is associated with increased risk of death and hospitalizations.5 The left atrium (LA) plays a major role in cardiac physiology by collecting blood during systole and modulating left ventricular filling during diastole.6 Left ventricular diastolic dysfunction or mitral valve disease may lead to increased left atrial pressure or volume overload which if chronically maintained, may result in left atrial remodelling and enlargement.7 Multiple studies have established till date that changes in left ventricular (LV) structure and function, evaluated by indicators such as left ventricular mass (LVM), left ventricular mass index (LVMI) and an impairment of diastolic and systolic function are a common implication of long standing hypertension.8,9 Another important indicator however is the left atrial size, an anatomic alteration of which has been associated...
independently with the occurrence of heart failure, hypertensive heart disease and other cardiovascular events. The enlargement of the left atrium in hypertensive patients is commonly seen in association with an overall increase in LVM and LVH. Similarly, LAE is a common echocardiographic finding in patients with different abnormal LV geometric patterns. Controversies however exist as to the individual geometric pattern associated with LAE. Aging is also said to be associated with left atrial dilatation. Left atrial conduit function deteriorates with age while reservoir and pump function are maintained. The independent association between LAE and LVH in patients with long standing hypertension has not yet been fully explored in Nigerian studies to determine whether similar findings occur in the Nigerian setting. The aim of our study is to determine the relationship between left atrial size and common demographic and echocardiographic parameters in adult Nigerians with long standing hypertension. The individual LV geometric pattern associated with these will also be determined. This will help to establish LAE as an independent cardiac event associated with LVH in hypertensive patients in Nigeria and the most likely left ventricular geometric pattern encountered when the two conditions coexist.

**MATERIALS AND METHODS**

**Patient Population**

A cross sectional survey of 81 hypertensive subjects and 80 age and sex matched controls with an age range of 24 to 70 years was carried out between May 2012 and April 2017 at Benue State University Teaching Hospital (BSUTH) Makurdi in Nigeria. Ethical approval was obtained from the Research Ethics Committee of the BSUTH before commencing the survey. Informed consent in written form was obtained from the subjects prior to commencing the study. Consecutive patients who had been diagnosed hypertensive for more than seven years, and referred for echocardiography from the medical out patients department (MOPD) of BSUTH were recruited for the study. The hypertensive patients were already on drug treatment for hypertension at the time of the study. The controls were normotensive subjects with normal body mass index (BMI) drawn from patient relations and staff of the hospital. Patients with history and examination findings suggestive of myocardial infarction, valvular heart disease or congestive heart failure were excluded from the study. Blood pressure was measured in all subjects by standard protocol. Hypertension was defined as a systolic blood pressure reading of ≥ 140mmHg or a diastolic blood pressure reading of ≥ 90mmHg or being on antihypertensive treatment. Weight was measured using a weighing scale while height was measured using a stadiometer and BMI was calculated. Subjects with BMI ≥ 30kg/m² were considered obese. Because the incidence of increased LA size could be related to LVM and age, the hypertensive population was divided into two sub-groups (with LVH and without LVH). The LVH group was further subdivided into two (age < 50 and age > 50 years).

**Echocardiography Examination**

Echocardiography was performed using Phillips HD11 XE and a 2.5 MHz transducer with subjects in the left lateral decubitus position and head of the bed maintained at 30°. Two dimensional targeted M-mode measurements were obtained in the parasternal long axis view. LA dimension (LAD) was measured according to the American Society of Echocardiography (ASE) from the leading edge of the posterior wall of the aorta to the leading edge of the posterior wall of the left atrium at end systole. Left atrial enlargement (LAE) was defined as LAD > 40mm. The end diastolic measurements of the interventricular septal thickness (IVSd), LV internal diameter (LVIDd) and posterior wall thickness in diastole (PWTd) at the QRS peak using the Penn convention were obtained. The LVM was calculated according to the Devereux ASE cube and indexed to body surface area (BSA) to obtain the LVMI. Subjects with LVMI > 134g/m² in males and > 110g/m² in females were classified as having left ventricular hypertrophy (LVH). Relative wall thickness (RWT) was calculated as 2X(PWTd)/(LVIDd). Increased RWT was present when this ratio was ≥ 0.45. The LV geometric classification was based on the evaluation of the LVMI and RWT as follows: Normal geometry was present when the LVMI and RWT were normal. Increased RWT and normal LVMI were classified as concentric remodelling, increased LVMI but normal RWT identified eccentric hypertrophy and increases in the two variables identified concentric hypertrophy.

**Statistical Analysis**

Data was analysed using the Statistical Packages for Social Sciences (SPSS) version 20 statistical software. Continuous variables were expressed as mean and standard deviation and
RESULTS

Demographic and Echocardiographic Characteristics of the Study Population

There were one hundred and sixty one (161) subjects recruited for the study. Eighty one (81) subjects were hypertensive consisting of 46 males and 35 females. Eighty (80) were non hypertensive control subjects consisting of 41 males and 39 females. There was no significant difference between the ages of the two groups, however, the weight, BMI, BSA, LAD, IVSd, LVIDd, LVM, LVMI (LVM/BSA) were significantly higher in the hypertensive group than the control subjects. This is shown in table 1.

Table 1: Demographic and echocardiographic characteristics of the hypertensives and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypertensive (n=81) mean (SD)</th>
<th>Non-hypertensive (n=80) mean (SD)</th>
<th>t-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.44 (9.03)</td>
<td>43.11 (8.58)</td>
<td>0.24</td>
<td>0.81</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>75.38 (15.79)</td>
<td>66.86 (8.11)</td>
<td>4.30</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66 (0.09)</td>
<td>1.70 (0.09)</td>
<td>-2.99</td>
<td>0.003*</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.37 (5.57)</td>
<td>23.07 (1.57)</td>
<td>6.65</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.85 (0.21)</td>
<td>1.77 (0.15)</td>
<td>2.77</td>
<td>0.006*</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>40.39 (8.32)</td>
<td>33.27 (5.69)</td>
<td>6.32</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IVSd (mm)</td>
<td>13.7 (3.81)</td>
<td>9.56 (2.47)</td>
<td>8.19</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>54.07 (13.11)</td>
<td>45.36 (3.87)</td>
<td>5.70</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVPWTD (mm)</td>
<td>11.24 (2.85)</td>
<td>10.49 (2.86)</td>
<td>1.64</td>
<td>0.102</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>290.92 (130.26)</td>
<td>147.31 (51.34)</td>
<td>9.18</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVM/BSA (g/m²)</td>
<td>158.08 (73.22)</td>
<td>83.37 (28.91)</td>
<td>8.50</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>RWT</td>
<td>0.45 (0.18)</td>
<td>0.42 (0.09)</td>
<td>1.14</td>
<td>0.26</td>
</tr>
</tbody>
</table>

*Statistically significant
BMI = Body Mass Index
BSA = Body Surface Area
LAD = Left Atrial Dimension
IVSd = Interventricular Septal thickness in diastole
LVIDd = Left Ventricular Internal Diameter in diastole
LVPWTD = Left Ventricular Posterior wall thickness in diastole
LVM = Left Ventricular Mass
LVM/BSA = Left Ventricular Mass indexed to body surface area
RWT = Relative wall thickness

The hypertensive subjects were divided into two groups: Those with LVH and those with no LVH. The LVH group were 52 in number and the no LVH group were 29 in number. There was no significant difference in the ages of the LVH and the no LVH group. However, the BMI, LAD, IVSd, LVIDd, LVM, LVMI were significantly higher in the LVH group than the no LVH group. This is shown in table 2.

Table 2: Demographic and echocardiographic characteristics of hypertensives with LVH and no LVH

<table>
<thead>
<tr>
<th>Variable</th>
<th>LVH n=52 mean (SD)</th>
<th>No LVH n=29 mean (SD)</th>
<th>t-test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.35 (9.07)</td>
<td>45.41 (8.78)</td>
<td>-1.48</td>
<td>0.144</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.04 (14.78)</td>
<td>79.56 (16.93)</td>
<td>-1.81</td>
<td>0.074</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.67 (0.08)</td>
<td>1.64 (0.85)</td>
<td>1.30</td>
<td>0.197</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.22 (5.00)</td>
<td>29.43 (6.01)</td>
<td>-2.57</td>
<td>0.012*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.83 (0.20)</td>
<td>1.90 (0.23)</td>
<td>-1.30</td>
<td>0.198</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>42.68 (7.63)</td>
<td>36.25 (8.00)</td>
<td>3.57</td>
<td>0.001*</td>
</tr>
<tr>
<td>IVSd (mm)</td>
<td>14.57 (4.00)</td>
<td>12.17 (2.92)</td>
<td>2.83</td>
<td>0.006*</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>59.37 (12.30)</td>
<td>44.57 (8.36)</td>
<td>5.77</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVPWTD (mm)</td>
<td>11.79 (3.03)</td>
<td>10.24 (2.11)</td>
<td>2.42</td>
<td>0.018*</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>353.19 (118.74)</td>
<td>179.27 (51.83)</td>
<td>7.48</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVM/BSA (g/m²)</td>
<td>194.08 (66.91)</td>
<td>93.53 (21.01)</td>
<td>7.86</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>RWT</td>
<td>0.48</td>
<td>0.42</td>
<td>-1.48</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*Statistically significant
BMI = Body Mass Index
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LAD = Left Atrial Dimension
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RWT = Relative wall thickness

Prevalence of Left Atrial Enlargement in the Hypertensive Population
The prevalence of LAE in the hypertensive population was 50.6%. It was more prevalent in males than females with rates of 58.5% versus 41.5% but the difference was not statistically significant (χ² = 0.103, p=0.748). LAE was more prevalent in the LVH than in the no LVH group with rates of 80.5% versus 19.5% and this was statistically significant (χ² = 9.586; p=0.002). With respect to age, the prevalence of LAE in hypertensives < 50 years with LVH was 58.5% versus 41.5% but the difference was not statistically significant (χ² = 0.22). Figure 1 is a documented case of LAE.

Figure 1: Left atrial enlargement in 60 year old man with long standing hypertension. The patient also had sinus bradycardia.

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Correlation between Left Atrial Dimension and Demographic/Echocardiographic Parameters

Bivariate correlation showed that LA size correlated positively with IVSd, LVIDd, LVM, LVM/BSA all (p <0.001). It also correlated with weight, BMI and BSA (p = 0.006, p = 0.011 and p = 0.016 respectively). There was no correlation between LA size and age. This is shown in table 3.

Table 3: Correlation between left atrial dimension, demographic and echocardiographic parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Gender</th>
<th>R</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>M (n=87)</td>
<td>0.136</td>
<td>0.085</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.214</td>
<td>0.006*</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>M (n=87)</td>
<td>0.190</td>
<td>0.016*</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.190</td>
<td>0.016*</td>
</tr>
<tr>
<td>BMI(kg/m²)</td>
<td>M (n=87)</td>
<td>0.190</td>
<td>0.016*</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.190</td>
<td>0.016*</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>M (n=87)</td>
<td>0.565</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.565</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVM/BSA (g/m²)</td>
<td>M (n=87)</td>
<td>0.550</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.550</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>M (n=87)</td>
<td>0.354</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.354</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IVSd (mm)</td>
<td>M (n=87)</td>
<td>0.032</td>
<td>0.090</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.032</td>
<td>0.090</td>
</tr>
<tr>
<td>RWT (mm)</td>
<td>M (n=87)</td>
<td>0.097</td>
<td>0.220</td>
</tr>
<tr>
<td></td>
<td>F (n=74)</td>
<td>0.097</td>
<td>0.220</td>
</tr>
</tbody>
</table>

*Statistically significant M=male F=female
BMI = Body Mass Index
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RWT = Relative wall thickness

LV Geometric Pattern amongst Hypertensive Patients with LAE

The LV geometric pattern amongst subjects with LAE was as follows: 2.4% of subjects with LAE had normal geometry, 9.8% had concentric remodelling, 53.7% had eccentric hypertrophy and 34.1% had concentric hypertrophy. Amongst hypertensive patients without LAE, 32.5% had normal geometry, 30% had concentric remodelling, 17.5% had eccentric hypertrophy and 20% had concentric hypertrophy. Eccentric hypertrophy was therefore the most prevalent LV geometric pattern in hypertensive subjects with LAE.

DISCUSSION

The present study has demonstrated that LAE is a feature of long standing hypertension. It has also shown that the strongest correlate of LA size is LVM followed by LVIDd. Other correlates include IVSd, weight, BMI and BSA. LAE was significantly more prevalent in the LVH than the no LVH group. The most prevalent LV geometric pattern in subjects with LAE was eccentric hypertrophy. There was no correlation between LAE and age in this study and it was not significantly associated with gender.

The findings in this study are similar to the findings of the Losartan Intervention For Endpoint Reduction in hypertension (LIFE) study which found independent correlates of LA size in middle aged and older hypertensives to include : LVH and eccentric geometry, higher BMI and systolic blood pressure. However the LIFE study differed from ours in finding an association between age and female gender with LAE.

One of the early findings that LA size was significantly related to LVM is in accordance with previous findings in older patients with isolated systolic hypertension. Long standing hypertension leads to changes in left ventricular structure and function evident as increased LVM, LVH and LV diastolic dysfunction. By altering diastolic function, these adaptive changes in the LV facilitate the development of LAE. LVH and distinct LV geometric patterns are independent predictors of cardiovascular (CV) morbidity and mortality with the worst prognosis associated with concentric hypertrophy followed by eccentric hypertrophy.

Our study showed that the prevalence of LAE was significantly higher in the LVH than no LVH group. Echocardiographically determined LAE has been established as a prognostic marker for adverse CV as well as overall clinical outcomes. LAE is viewed as a marker of chronicity and severity of diastolic function and exposure to abnormal filling pressure which is influenced by several pathologic factors among which LVH plays an important role. There was correlation between LAE and LVIDd in our study. LV dilatation may be a precursor to LV failure in hypertensive heart disease. Although molecular triggers of the transition from concentric hypertrophy to LV failure have been the subject of intense investigation, there are no previous large studies in humans demonstrating that this progression occurs frequently. LV dilatation reflects adverse ventricular remodelling and may be associated with an increased risk of arrhythmias and sudden death. Eccentric Hypertrophy was the LV geometric pattern most prevalent in patients with LAE in our study. It has been noted above that this agrees with the findings of the LIFE study. However other reports of investigation of the relationship...
between LV geometry and LAE have drawn different conclusions. Cioffi et al, in a cohort of 336 patients with essential hypertension found that concentric hypertrophy (CH) was associated with greater LA size than eccentric hypertrophy. There was no correlation between LAE and age in our study. Though LAE was more prevalent in hypertensive patients with LVH and older than 50 years than in those with LVH and less than 50 years, this was however not statistically significant. Tedesco et al. had a different finding in his study which showed a significant association of LAE with age and LVM. Significant correlation with age was also noted in the LIFE study. The body mass index showed significant correlation with LA size in our study. Obesity has previously been thought to mediate the relation between LA size and LVM in previous studies. However the LIFE study found an independent association of both obesity and LVH with LAE. The mechanism by which overweight leads to LAE is unclear, but a relation to hemodynamic changes seen in obese patients including increased intravascular volume and cardiac output has been suggested.

CONCLUSION

The present study has demonstrated that LAE is associated with increased LVM and LVH in long standing hypertensive patients. Eccentric hypertrophy was the most prevalent type of LV geometric pattern seen in patients with LAE in this study.

Recommendation

The findings of this study emphasize the need for early institution of drugs that inhibit LVH to forestall its development and subsequent LAE in hypertensive patients. This will go a long way to prevent sudden death and frequent hospitalizations in this group of individuals.

Limitation

The hypertensive patients were already on drug treatment at the time of the study. This may have affected the outcome of the study. In addition, our study lacks Doppler echocardiographic indices or tissue Doppler imaging assessment of mitral annulus motion to determine diastolic function. This may have provided further explanation for our findings.

Conflict of Interest

None declared

REFERENCES

incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study). The American Journal of Cardiology. 2001; 87(9): 1051 – 1057.


