Prevalence of left ventricular diastolic dysfunction in newly diagnosed Nigerians with systemic hypertension: a pulsed wave Doppler echocardiographic study

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Abstract

Background: Systemic hypertension is a common cause of left ventricular diastolic dysfunction. However, its prevalence in Nigerians with untreated systemic hypertension is unknown.

Objective: To determine the prevalence of left ventricular diastolic dysfunction in newly diagnosed Nigerians with systemic hypertension using Doppler transmitral inflow and pulmonary venous flow velocities.

Methods: Two-dimensional echocardiography including Doppler was performed on 150 newly diagnosed cases of systemic hypertension and 150 normotensive controls. They were divided into hypertensives without left ventricular hypertrophy and those with left ventricular hypertrophy based on echocardiographically determined left ventricular mass index. Pulsed Doppler transmitral inflow and the pulmonary venous flow waves were used to categorise the patterns of diastolic dysfunction.

Results: The hypertensives and the normotensive controls were comparable in their baseline characteristics. The E/A ratio differed significantly between hypertensives with and without left ventricular hypertrophy and controls (1.00+0.30, 1.04±0.42, 1.33±0.27, $p < 0.001$). Left ventricular diastolic dysfunction occurred in 62% of systemic hypertension and 11.3% of the controls. Impaired relaxation was the commonest pattern (84.9%) of diastolic dysfunction.

Conclusion: Our study showed that left ventricular diastolic dysfunction is prevalent in Nigerians with newly diagnosed systemic hypertension and effort should be made to routinely screen for them.

Key words: Nigerians, Diastolic dysfunction, Echocardiography, Systemic hypertension

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Introduction

Systemic hypertension (SH) is a major public health problem and an important cause of morbidity and mortality.[1-2] The prevalence of SH in adult Nigerians is estimated to be 10 – 20%.[3] SH is also globally recognized as the most prevalent cardiovascular risk factor.[4]

Uncontrolled Blood Pressure (BP) will lead to morphologic changes and functional alterations in the myocardial structure.[5] Diastolic dysfunction is the commonest of these functional alterations.[6-9] and is commoner in Blacks than Whites,[10] and in elderly women than men.[11] The clinical significance of Left Ventricular Diastolic Dysfunction (LVDD) as a cause of heart failure with normal systolic function in patients with SH is well recognised.[12-14]

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Early recognition of diastolic dysfunction may assist in additional risk stratification and subsequently guide the introduction of appropriate pharmacological interventions. The enhanced regression of left ventricular mass, relative wall thickness and relative septal thickness by these drugs may lead to normalization of several diastolic filling parameters and improvement in overall prognosis.[15,16] Diastolic dysfunction can be assessed by several methods.[17] Doppler echocardiography is an important non-invasive and an easily reproducible method of evaluating and follow-up of hypertensives with diastolic dysfunction. The parameters of diastolic function obtained by pulsed Doppler echocardiography have been found to correlate well with the other methods used in assessing diastolic function.[17]

Most of the studies of LV diastolic dysfunction in Nigerian hypertensives have been on chronic hypertensives on treatment.[8,9] We therefore used pulse-wave Doppler transmitral inflow and pulmonary venous flow velocity parameters to determine the prevalence of left ventricular diastolic function in newly diagnosed Nigerians with SH.

Methods

One hundred and fifty newly diagnosed cases of SH aged between 35 years and 74 years whose BP were greater than or equal to 140/90 mmHg seen at the Cardiology Clinic of University of Ilorin Teaching Hospital were prospectively studied between January 2005 and December 2006. One hundred and fifty age-and-sex-matched normotensive individuals served as the controls. Those patients with SH and concomitant diabetes mellitus, congestive cardiac failure, chronic renal failure, ischaemic heart disease, thyrotoxic cardiomyopathy, moderate to severe obesity were excluded from the study.

Others excluded were pregnant women, patients with pericardial diseases and atrial fibrillation. The BP were measured with the mercury (Accoson's) sphygmomanometer in the consulting room in sitting position after about 5-10 minutes of rest according to standard guidelines.[18] Systolic BP (SBP) and diastolic BP (DBP) were taken as Korotkoffs sounds I and V, respectively. Those individuals with an average SBP greater than or equal to 140 mmHg and/or the DBP of greater than or equal to 90 mmHg on three separate hospital visits at one week interval were considered to be hypertensive. All the patients have not been commenced on treatment as at the time of enrolment. The study protocol was approved by the local Ethical Review Committee, and a written informed consent was obtained from all those that participated in the study.

Echocardiography

All transthoracic examinations were performed with a commercially available cardiac ultrasound machine (ESAOTE SPA Megas CVS, Italy) equipped with a 2.5 MH_Z transducer. Conventional Two-dimensional echocardiography including M-mode were performed on all patients according to the ASE recommendations.[19] The pulsed-wave Doppler of the transmitral inflow and pulmonary venous flow velocities in diastole were obtained by the use of the apical 4-and 5-chamber views in the partial left lateral decubitus position. The sample volume was placed at the tip of the opened mitral leaflets parallel to the flow as possible so as to record the maximal velocity during diastole. The maximal velocity of three consecutive cardiac cycles were manually traced and averaged. The parameters measured were: peak velocity of early filling (E-wave), peak velocity of atrial contraction (A-wave), and the E/A ratio. The E-wave of the deceleration time (DT) was measured as the interval from the peak of E-wave velocity to its extrapolation to baseline. Isovolumic relaxation time (IVRT) was taken as the interval between the aortic valve closure to the beginning of the mitral inflow with the simultaneous visualisation of the aortic and mitral flows[17].

The pulmonary venous flow velocities were obtained from an apical 4–chamber view with the pulsed-wave Doppler by placing the cursor 1-2 cm into the right upper pulmonary vein close to the interatrial septum occasionally with the help of colour flow Doppler. The peak systolic (S wave), diastolic (D wave) flow velocities and the peak atrial reversal (Ar) were recorded and the ratio of S/D was calculated. They were only satisfactorily measured in 88% of patients with SH and in 93% of the controls. LV hypertrophy (LVH) was calculated using the modified Devereux formula[20] and the Left Ventricular Mass Index was calculated by indexing the LVH to the body surface area[21]. LVH was said to be present if LVMI is more than 134g/m^2 in males and 110g/m^2 in females.[21] Measurement of relative wall thickness and relative septal thickness was obtained as twice the posterior wall thickness or the interventricular wall thickness divided by the LV dimension in diastole (2PWd/LVDd, 2IVSd/LVDd). The value of more than 0.44 was considered abnormal[20]. According to the LVMI, hypertensive patients were divided into two groups: The first one without LVH and the second one with LVH and the normotensive controls without LVH constituted the third group.

The patterns of LV diastolic function were categorised using the model proposed by Yamamoto et al[22]; Normal LV diastolic function was identified as E/A ratio between 1 and 2, IVRT of 80-110 ms and DT between 150-240 ms, pulmonary venous flow velocity S/D ratio > 1 and Ar < 35 ms. Impaired relaxation was identified by prolonged IVRT (> 110 ms) and DT (> 240 ms) and a reduced E/A ratio (< 1); pseudonormal pattern was recognised by E/A between 1 and 2, normal IVRT of 80-110 ms, and DT between 150 and 220 ms as well as pulmonary venous flow velocity S/D ratio < 1 and Ar > 35ms and restrictive pattern was identified as E/A ratio > 2 and reduced DT (< 150 ms).

Data analysis

Data were analysed using the SPSS Software Version 11.0 for Windows (SPSS Inc, Chicago, Illinois). Continuous variables are expressed as the mean (SD)

while dichotomous data as percentages. Categorical variables were compared by Chi-square analysis and continuous data by Student's *t* test for independent samples and two way analysis of variance to evaluate differences between different groups, as indicated. For all tests, $p < 0.05$ was considered significant.

Results

Demographic and baseline clinical characteristics

There were fifty six patients without LVH and ninety four patients with LVH. All the controls had no LVH. They were aged between 35 and 74 years and 49.3%. The baseline demographic and clinical characteristics are shown in Table 1. There was no statistically significant difference between groups in mean age, Body Mass Index (BMI) and waist/hip ratio ($p > 0.05$).

Table 1: Demographic and clinical characteristics of the study population

Variables	Systemic hypertension cases (n=150)	Normotensive controls (n=150)	P-value
Age (years)	52.74±9.81	52.59±9.58	NS
Sex: Male	74 (49.3%)	74 (49.3%)	NS
Female	76 (50.7%)	76 (50.7%)	NS
BMI (kg/m^2)	27.82±4.23	27.25±3.97	NS
WHR	0.91±0.05	0.90±0.05	NS
SBP (mmHg)	162.00±20.88	115.51±10.61	<0.001*
DBP (mmHg)	98.33±13.12	73.80±7.82	<0.001*
HR (bpm)	73.12±6.20	73.27±9.33	NS
Pulse Pressure (mmHg)	63.37±19.59	41.37±11.01	<0.001*

*B*MI-Body mass index, DBP-Diastolic blood pressure, SBP-Systolic blood pressure, HR-Heart rate, BPM-Beat per minute, Plus-minus values are means ±SD, NS-Not significant
*Statistical significance

Echocardiographic Parameters

The interventricular septum in diastole (IVSd), left ventricular diameter in diastole (LVDd) and the LVMI were higher in the newly diagnosed hypertensives. The ejection fraction, a measure of systolic function of all the patients and controls was more than or equal to 55%. Left ventricular diastolic filling parameters in the study groups

Table 2: Echocardiographic variables of the study population

Variables	Hypertensives without LVH (n=56)	Hypertensives with LVH (n=94)	Controls (n=150)	ANOVA P value
IVSd (cm)	1.17±0.3	1.98±0.3	1.01±0.2	<0.001*
LVDd (cm)	4.41±0.6	4.75±0.6	4.60±0.5	<0.001*
PWd (cm)	0.98±0.2	1.17±0.3	0.93±0.2	<0.001*
LVDs (cm)	2.99±0.6	3.10±0.6	3.08±0.5	NS
EF (%)	61.7±8.6	63.0±8.0	64.2±9.3	NS
FS (%)	33.0±7.3	34.7±7.3	33.3±5.5	NS
LAD (cm)	3.31±6.6	3.13±0.6	3.19±0.4	NS
ARD (cm)	2.97±0.4	3.13±0.5	2.88±0.4	<0.001*
RST	0.54±0.2	0.62±0.2	0.45±0.1	<0.001*
RWT	0.48±0.1	0.51±0.2	0.41±0.1	<0.001*
LVMI(g/m^2)	104.6±17.1	160.9±42.0	97.3±16.2	<0.001*

IVSd- Interventricular Septal thickness in diastole, LVDd-Left ventricular dimension in diastole, LVDs- Left ventricular dimension in systole, PWd-Posterior wall thickness in diastole, EF-Ejection fraction, FS-Fractional shortening, LVH- Left ventricular hypertrophy, LAD-Left atrial dimension, ARD-Aortic root dimension, RST-Relative septal thickness, RWT-Relative wall thickness, LVH- Left ventricular hypertrophy, LVMI-Left ventricular mass index, plus-minus values are means ± SD; NS- not significant, * Statistical significance

Table 3 depicts the Doppler findings among the groups. The mean peak mitral E-wave and the E/A ratio were greater in the normotensive controls (68.42±115.63 and 1.33±0.27) than in the hypertensives without LVH (57.1±13.2, 1.00±0.30) and hypertensives with LVH (57.9±14.0, 1.04±0.40) $p < 0.001$. There was no significant difference between the mean of the peak mitral A-wave in the hypertensives and the normotensives. There was significant difference between the mean S-wave of the pulmonary venous flow between the hypertensives with and without LVH and controls ($p < 0.001$).

Table 3: Left ventricular diastolic function indices of the study population

Variables	Hypertensives without LVH n =56	Hypertensives with-LVH n=94	Controlsn =150	ANOVA P value
Peak mitral E-wave (ms)	57.1±13.2	57.9±14.0	68.4±115.6	<0.001*
Peak mitral A-wave (ms)	60.8±18.1	59.9±15.6	56.2±143.4	NS
E/A ratio	1.00±0.30	1.04±0.4	1.33±0.3	<0.001*
IVRT (ms)	95.8±26.2	96.6±28.7	83.83±16.0	<0.001*
Deceleration time (ms)	163.7±57.8	157.0±60.1	177.5±40.7	<0.007*
Peak PVF S-wave (ms)	85.3±10.6	34,7±10.4	40.6±11.2	<0.001*
Peak PVF S-wave (ms)	31.0±9.0	32.9±9.4	33.7±10.3	NS
Ar (ms)	22.6±6.1	22.6±4.9	22.4±5.1	NS
S/D ratio	1.17±0.3	1.07±0.3	1.26±0.4	<0.001*

*IVRT-Isovolumic relaxation time, Ar-Atrial reversal, PVF-Pulmonary venous flow, S/D-Systolic and diastolic wave ratio, plus-minus values mean ±SD, NS-not significant, LVH- Left ventricular hypertrophy, * Statistical significance*

Pattern of left ventricular diastolic filling in the hypertensive and normotensive controls

Table 4 shows the different patterns of diastolic dysfunction seen in the three groups. The prevalence of LV diastolic dysfunction in the newly diagnosed hypertensives was 62% and 11.3% in the normotensives controls. The commonest type of diastolic dysfunction noted in the study, both in the systemic hypertensives and normotensives was the impaired relaxation pattern, 84.9% and 8.7% respectively. Ninety four (63%) of the hypertensives were hypertensives with LVH. The pseudonormal pattern of diastolic dysfunction was found in (12)12.9% of the hypertensives with diastolic dysfunction and in 4 (2.6%) of the normotensives. Restrictive pattern of LV diastolic dysfunction was found in 2 (2.2%) of the hypertensives, however none of the controls demonstrated the restrictive pattern of LV diastolic dysfunction.

Table 4: Pattern of left ventricular diastolic function in the hypertensive and normotensive control groups

Pattern	Hypertensives without LVH (n=56)	Hypertensives with LVH (n=94)	Controls(n=150)	ANOVA P value
Normal	19 (33.9%)	38(40.4%)	133 (88.7%)	0.001
1 – Impaired relaxation	28 (50%)	51 (54.2%)	13 (8.7%)	0.009
II – Pseudonormal	8 (14.3%)	4 (4.3%)	4 (2.6%)	ns
III – Restrictive	1 (1.8%)	1(1.1%)	0	ns

LVH- Left ventricular hypertrophy

Discussion

The main findings of the study are; Firstly, abnormalities of LV diastolic function are common in Nigerians with untreated cases of systemic hypertension in whom the left ventricular systolic performance is still normal. Secondly, the prevalence of LV diastolic dysfunction was 62% in the newly diagnosed cases of SH with most of the hypertensives been those with LVH and 11.3% in the controls. Lastly the use of several Doppler indices including the Doppler pulmonary venous flow velocity helped in distinguishing the different patterns

of LV diastolic dysfunction that would have been otherwise difficult to classify. The prevalence of LV diastolic dysfunction in hypertensives in this study was 62% (93 out of the 150). However, the prevalence in the normotensive controls was 11.3% (17 out of 150). This prevalence is almost similar to that of Kingue et al[23] in a study in Black African untreated hypertensive population in Cameroon (67%). Balogun et al[8] .reported a lower prevalence of 46% in their study on hypertensives. The selection and the characteristics of those patients might have accounted for the lower prevalence in their study. A similar study by Ike et al[9] deposed a prevalence of 82.86%, which was much higher than in this study. This may be explained by the fact that the enrolled patients in the study by Ike et al were hypertensives that were already on medications.

Recent studies in Asia on the prevalence of DD by Masliza et al[24] found a lower incidence of 18.6% (32 out of 198) in their newly diagnosed with systemic hypertensives and 6 (3.4%) among the controls. Balogun et al[8] and Oyati et al[25] had each alluded to the fact that the poor state of the economy is among the factors militating against hypertensives presenting early for cardiac evaluation. It is also an established fact that untreated SH and its complications are more severe in Blacks than in the other races.[10]

Diastolic dysfunction is a continuum and it is made up of three different pathologic filling patterns aside from the normal pattern of filling.[20] It begins with the impaired relaxation and progresses to the restrictive pattern through the pseudonormal form. These patterns evolve from one to another in a single individual, with changes in hypertensive heart disease evolution, loading conditions and treatment.[13, 17, 22] The use of several Doppler indices assisted in demonstrating these patterns in this study. The impaired relaxation pattern is the commonest detectable abnormality of LV filling in hypertensives.[8,17,23] The result of the study agrees with the finding of the above studies where the impaired relaxation pattern was found in more than two third (84.9%) of the hypertensives with diastolic dysfunction. It was observed that most of the hypertensives with diastolic dysfunction were hypertensives with LVH (60.2%) with only 39.8% being hypertensives without LVH. The study by Snider et al[12] in children with systemic hypertension emphasized the presence of diastolic dysfunction even in the absence of LVH. This may suggest that the increased tension placed on the myocardium by SH may lead to an increase in the left ventricular diameter with subsequent prolongation of relaxation even before the development of LVH.[13]

The pseudonormal pattern is the moderate stage of diastolic dysfunction and was found in 12 (12.9%) of the hypertensives with diastolic dysfunction, most of whom were hypertensives without LVH and a small proportion of them had concentric remodelling pattern of LVH. The addition of the Doppler pulmonary venous flow indices like S/D ratio and IVRT and DT of the transmitral inflow velocity assisted in the characterization of the pattern of diastolic dysfunction. However, none of the normotensive controls showed either the pseudonormal or the restrictive patterns. The restrictive pattern was seen in 2 (2.2%) of the hypertensives with diastolic dysfunction.

In any case, it is to be noted that the presence of diastolic dysfunction and LVH may imply a higher mortality[26] and the finding of associated complications may lead to frequent hospitalization and a higher morbidity.[27] Since the study was hospital-based, it may not represent the actual prevalence of LV diastolic dysfunction in hypertensives.

Furthermore, as it is common to all Doppler modalities used in assessing LV diastolic function, a high signal-noise-ratio and marked angle dependency might also affect the result. Ideally, the addition of tissue Doppler imaging or flow propagation methods that are less load dependent would have contributed more information in clearly differentiating the normal from the pseudonormal pattern.

Lastly, the exclusion of hypertensives with moderate to severe obesity, atrial fibrillation and individuals with long duration of hypertension might have omitted those with severe forms of LV diastolic dysfunction.

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Conclusion

The study has shown that LV diastolic dysfunction is common in newly diagnosed Nigerians with systemic hypertension, and effort should be made to screen for them routinely.

LV diastolic dysfunction occurred in hypertensives without LVH, hence its early detection may lead to

additional risk stratification and may guide the choice of antihypertensive drugs.

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