Prevalence of Echocardiographic Indices Of Diastolic Dysfunction in Patients with Hypertension at a Tertiary Health Facility in Nigeria

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Abstract

Background: Hypertension is the commonest of the cardiovascular risk factors. The prevalence in Nigeria is between 10-20%.It is the leading cause of various cardiovascular diseases including heart failure, stroke and renal failure in Nigeria. It can result into diastolic and/ or systolic dysfunction in the heart. Echocardiography was used to assess the prevalence of diastolic abnormalities in a population of hypertensive subjects.
Objectives: To determine the prevalence of diastolic abnormalities using Doppler echocardiographic parameters in a population of hypertensive patients.
Patients and Methods: One hundred consecutive hypertensive patients were recruited (50 each with Stage 1 and 2 hypertension) and fifty controls . They were investigated with 2-D, M-mode and Doppler Echocardiography. The demographic parameters including age, sex, body surface area, systolic and diastolic blood pressure were taken.
Results: Diastolic dysfunction was detected in 85.0% of 100 hypertensive patients. 76.0% had early diastolic dysfunction while 9% shows late diastolic dysfunction. Only 15.0% of these patients are likely to have normal diastolic function.
Conclusion: There is a high prevalence of diastolic function abnormalities among patients with essential hypertension. This calls for early detection with Doppler echocardiography and early therapeutic intervention to reduce the burden of diastolic heart failure in the nearest future.
This study further buttresses the need for aggressive intervention in the black population with essential hypertension as they are more prone to developing heart failure and other complications due to hypertension.

ABBREVIATION

BMI Body mass index
BSA Body surface area
DBP Diastolic blood pressure
DT Deceleration time
FS Fractional shortening
IVRT Isovolumic relaxation time
LVM Left ventricular mass
LVMI Left ventricular mass index
PP Pulse pressure
RWT Relative wall thickness
SBP Systolic Blood pressure

INTRODUCTION

Hypertension is defined as persistent elevation of blood pressure ≥ 140/90 mmHg in an adult. [1] . The Seventh National Council on Detection, Evaluation, and Treatment of High blood pressure introduced the new classification called pre-hypertension which hopes to raise the awareness and early interventional strategies to control this disease. [2]

Hypertension remains a major cardiovascular risk factor worldwide causing heart failure, coronary artery disease, kidney failure, strokes etc. [3] The prevalence of hypertension is between 10-20%. Uncontrolled hypertension leads to a number of structural changes in the heart which eventually cumulates into interstitial fibrosis, myocardial wall thickness and functional alteration such as diastolic dysfunction.

The diastolic function of the heart consist of the early diastolic filling, late diastolic filling and isovolumic relaxation time (IVRT) which is the time interval between the closure of aortic valve and the opening of the mitral valve. Left ventricular diastolic dysfunction has been

reported to be the first manifestation of heart disease manifested in patients with hypertension. [4,5]

One of the investigative modalities used in the evaluation of diastolic function and dysfunction is Doppler echocardiogram. [6,7,8]

Pulse Doppler transmitral echocardiography can detect left ventricular diastolic filling abnormalities in patients with hypertension even before any clinical or electrocardiographic abnormalities are present. [9,10] The early inflow velocity of the mitral valve opening reaches a peak at the E point. Flow then decelerates until atrial systole at which time the left atrial pressure rises above the left ventricular pressure and flow again passes through the mitral valve with the depiction of the A wave. The two waves almost move at the same velocity in a normal person. [11]

Alteration in left ventricular diastolic function may reduce the amplitude of the E wave and increase that of the A wave and usually accompanied by prolongation of the isovolumic relaxation time and deceleration time. [8,12,13] Other pathologic abnormality seen is the reverse with a tall E wave and a short A wave accompanied by short isovolumic relaxation time and deceleration time which tend to occur late in the disease progression. [11]

The prevalence of left ventricular diastolic dysfunction has been well documented in the Caucasians ranging from 46%-68% of the Hypertensive population. [14,15,16,17] In Nigeria, There are few reports on the prevalence of diastolic dysfunction among hypertensive subjects in Nigeria. 82.6% has been documented in a study carried out at the University of Nigeria Teaching Hospital. [18]

Diastolic impairment is associated with significant morbidity and mortality. [18] 20 – 50% of patients with clinical heart failure have been shown to have preserved left ventricular systolic function and have thus been referred to as having diastolic heart failure. [19] There are various definitions of Diastolic heart failure. The Definition by the Working group of European Society of Cardiology proposed the following criteria. [20]

1. Presence of signs and symptoms of congestive heart failure
2. Presence of normal or only mildly abnormal left ventricular left ventricular systolic function and
3. Evidence of abnormal left ventricular relaxation, filling or diastolic distensibility.

Hypertension is the number one of the causes of heart failure in our environment. [21,22] It is therefore imperative to identify the proportion of the patients being managed for hypertension who already have diastolic dysfunction and who may need aggressive interventions to prevent the development of diastolic heart failure

Echocardiography is an alternative technique to cardiac catheterization in the evaluation of patients with diastolic dysfunction which include M-mode, 2-D and Doppler echocardiography studies. [21,22] An increased relationship of left atrial size and stage of diastolic dysfunction has been described. [23] The basic parameters of the transmitral flow vary with age and within the spectrum of diastolic filling. [24,25]

The normal E/A ratio is usually greater than 1. In diastolic dysfunction, it passes from a reversed E/A ratio through a “pseudo-normal” pattern (E/A ratio greater than 1) to the most abnormal restrictive pattern.

Therefore it is difficult to use this single parameter to evaluate correctly diastolic dysfunction. An increased pulmonary atrial reversal flow, reversal velocity or width and valsalva manouvre may aid to differentiate pseudo-normal from normal diastolic function corresponding to elevated left atrial or left ventricular diastolic pressures. [23,26,27]

Four stages of diastolic abnormalities have been described and have been shown to correlate with diastolic impairment and symptom class. [28] The normal pattern seen in normal people with E/A ratio greater than 1, mitral valve deceleration time is between 150-220ms. The fist stage of diastolic dysfunction is the delayed relaxation phase seen in patients with delayed left ventricular relaxation but with relatively normal compliance and filling pressures. [29] E/A ratio is less than 1, deceleration time prolonged (more than 220ms) and isovolumic relaxation time greater than 100ms. This pattern is seen in the aged, [24,30] ischaemia, [31] hypertrophic cardiomyopathy, [31] and secondary hypertrophy, and obese diabetic. [32]

The second stage is the pseudo-normal stage which is difficult to recognize because it is similar to the normal pattern. Abnormalities of relaxation and compliance and

elevated filling pressures are present. Transmitral E/A ratio is between 1-2, a deceleration time between 150-220ms and IVRT between 60-100ms. The left atrial size is usually increased and left ventricular function may be impaired or wall thickness increased.

Restrictive filling pattern stage III is seen in the presence of severely reduced left ventricular compliance and elevated filling pressures and ongoing delayed relaxation. E/A ratio is usually greater than 2, deceleration time is less than 150ms and IVRT less than 60ms. The restrictive filling pattern (Stage IV) is associated with a poor prognosis. Additional prognostic information can be obtained in patients with restrictive filling patterns evaluated under different haemodynamic conditions. Patients are graded into mild, moderate and severe diastolic abnormalities in accordance with the pattern of diastolic dysfunction demonstrated in them.

SUBJECTS AND METHODS

One hundred subjects (50 each with stage 1 and 2 hypertension according to JNC VII classification of hypertension) with hypertension were consecutively recruited from the medical outpatient clinic of our teaching hospital and studied. 50 normotensive control subjects recruited among hospital staff and patient relatives were also studied. Stage 1 hypertension includes SBP of 140-159 and DBP of 90-99mmHg while stage 2 hypertension includes SBP ≥160mmHg and DBP≥ 100mmHg.

The demographic data including age, sex (gender),weight, height, body surface area, were taken as well as diastolic and systolic blood pressure, mitral E point, mitral A point, deceleration time and isovolumic relaxation time. mitral E/A ratio were evaluated.

The blood pressures were recorded in the left arm after an average of five to ten minutes rest with Accosson's sphygmomanometer in the sitting position according to standardized protocols. Hypertension was defined as sitting Blood pressure ≥ 140/90mmHg taken twice at least two weeks interval or a patients already taking antihypertensive therapy. They were subjected to 2D guided Doppler echocardiogram to evaluate the heart after informed consent (both verbal in local language and written). Echocardiographic parameters obtained include left ventricular internal diastolic dimension (LVIDD), left ventricular end systolic dimension (LVSD), left atrial dimension (LAD), Aortic root dimension, aortic cusp separation (ACS), posterior wall thickness (PWTd), Interventricular septal thickness in diastole(IVSd), transmitral E- wave velocity, A wave velocity and E wave deceleration time. Echocardiography was performed using a SUIS APOGEE 16.4.4 and 3.5MHz probe according to ASE criteria [35] with appropriate use of valsalva manouvre in patients with seeming normal diastolic function to see whether there will be reversal of mitral E/A ratio.

LVM was calculated using the ASE formula,

$$LVM_{ASE}\ (g) = 0.8 \times 1.04((IVSd + LVIDd + LVPWd)^3 - (LVIDd)^3) + 0.6$$ [35]

Transmitral flow is assessed in the apical 4-chamber view with the pulsed Doppler volume (1-2mm) at the leaflet tip along a laminar flow stream into the left ventricular cavity and the peak velocities (E and A points taken and the E/A ratio and the deceleration time calculated. Isovolumic relaxation time is measured by placing the pulse wave Doppler beam between the left ventricular inflow and the outflow tract to measure the time from the aortic valve closure to the mitral valve opening. By placing the pulse Doppler volume at the tip of the mitral valve leaflets in the apical four chamber view. Isovolumetric relaxation time of the left ventricle was obtained by placing the Doppler probe inbetween the left ventricular inflow and outflow tracts and the time between aortic valve closure and mitral valve opening taken.

Patients with reversed E/A ratio and /or abnormalities in the isovolumic relaxation time and deceleration time are grouped as early diastolic dysfunction while patients with restrictive abnormalities in stage III and IV are grouped as late diastolic dysfunction.

Values were expressed as means ± standard deviation. Proportions were expressed as percentages. Comparism between groups was done using analysis of variance (ANOVA). Analysis was by the Statistical package for Social Science (SPSS) Chicago 15.0. Statistical significance was taken as $P<0.05$.

RESULTS

A total of 100 consecutive patients with hypertension were selected from the medical outpatient clinic. There were 65 males (65%) and 35 (35%) females with the age range between 21-86 years. The Clinical and demographic characteristics of the study groups are shown in Table 1. There is no statistical difference in the ages and gender of

the three groups. The systolic blood pressure, diastolic blood pressure, pulse pressure, fractional shortening, left ventricular mass, left ventricular mass index and relative wall thickness was statistically different among the two groups. Interestingly, subjects with stage I hypertension had a higher fractional shortening, left ventricular mass and left ventricular mass index than those with stage 2 disease. Hypertensive patients with stage 2 disease had a higher SBP, DBP and relative wall thickness than those with stage 1 hypertension.

Figure 1

Table 1: showing the clinical and demographic parameters of study participants.

Parameter	Normotensives	Grade 1 Hypertension	Grade 2 Hypertension	ANOVA	
				F	P value
Age(years)	52.39±11.24	57.60±13.13	57.46±13.67	1.22	0.30
Sex (M/F)	28/22	34/16	31/19		0.582
SBP (mmHg)	118.0±10.16	145.26±6.75	172.34±15.62	188.55	<0.001
DBP (mmHg)	76.43±8.18	84.98±9.12	100.86±11.69	56.66	<0.001
BMI (kg/m²)	25.16±4.54	27.69±6.34	27.42±5.56	2.29	0.105
PP (mmHg)	41.57±9.46	47.54±12.07	71.48±13.87	69.1	<0.001
FS (%)	39.05±5.24	47.58±9.26	45.59±5.36	364.93	<0.001
BSA(m²)	1.74±0.13	1.78±0.18	1.79±0.17	1.19	0.307
LVM (g)	152.54±28.72	220.0±76.37	212.12±56.98	9.98	<0.001
LVMI (g/m²)	87.58±15.5	123.82±40.79	118.57±30.38	9.91	<0.001
RWT	0.43±0.07	0.50±0.18	0.53±0.11	3.79	0.025

Figure 3

Table 3: Showing the prevalence of diastolic dysfunction among study participants.

Parameter	Stage 1	Stage 2	Normal controls	ANOVA	
				F	P value
Mitral E(mm/s)	68.22±19.70	70.58±24.39	66.78±15.01	0.301	0.741
Mitral A (mm/s)	62.24±17.01	73.06±16.72	56.39±15.70	9.52	<0.001
E/A ratio	1.24 ±0.31	1.05±0.59	1.24±0.31	1.254	0.289
DT(msec)	148.02±27.07	211.60±54.25	148.02±27.07	13.47	<0.001
IVRT (msec)	82.0±9.59	101.6±27.26	82.0±9.59	2.364	0.10

The mean value for mitral E wave, mitral A wave, deceleration time and IVRT are higher among those subjects with stage 2 hypertension, although only that of mitral A wave and deceleration time achieved statistical significance.

{image:3}

The prevalence of diastolic dysfunction is as shown in table 3. 36 (72%) of the patients with stage 1 hypertension had early diastolic dysfunction with any of the abnormalities of a reversed E/A ratio, abnormal deceleration time and/ or isovolumic relaxation time. Whereas 6 (12%) of stage 1 hypertensive patients had late diastolic dysfunction and only 3(6%) of those hypertensive subjects with stage 2 hypertension had late diastolic dysfunction. None of the normotensive subjects had late diastolic dysfunction although 18 (36%) of them has early diastolic dysfunction.

DISCUSSION

Diastolic function is determined by the passive elastic properties of the left ventricle and by the process of active relaxation. Abnormal passive elastic properties generally are caused by a combination of increased myocardial mass and alteration of extramyocardial collagen network.

The prevalence of diastolic dysfunction in this study was 85.0%. This is in agreement with similar report from another region of the Nigeria where a prevalence of 82.86% has been reported. [18] It is however higher than what is reported among the European populations where a prevalence of between 46-48% have been reported. [14,15] This may be attributable to the higher prevalence of left ventricular hypertrophy among the black hypertensives which may be responsible for more cases of early diastolic dysfunction seen among the participants in this study. Blacks have also been known to have more severe forms of hypertension than in the comparable Caucasian population. [17]

The prevalence of diastolic dysfunction increases with age as has been demonstrated in several studies. [17,22,23] Increased left ventricular mass and left ventricular mass index is associated with development of diastolic dysfunction as left ventricular hypertrophy leads to abnormal relaxation and increased filling pressures of the heart. The burden of left ventricular hypertrophy is suggested by the increased pulse pressure, left ventricular mass and left ventricular mass index among subjects with stage 2 hypertension than those with stage 1 hypertension. Many of the patients in this study in stage 2 hypertension were in the lower region of the blood pressure demarcation for that group. Many of them would have been classified as Stage 2 in the JNC VI 3-staged-classification. This probably account for the higher mean LVM and LVMI among subjects with Stage 1 hypertension in this study.

The higher prevalence of hypertension in Nigeria may herald a higher frequency of occurrence of diastolic heart failure among subjects with systemic hypertension although there is at present a dearth of information on the contribution of diastolic heart failure among patient with symptoms and signs of heart failure.

Majority of the subjects in this study has early diastolic dysfunction. Late diastolic dysfunction was rare among the study population .This might be due to the fact that many of the subjects were recently diagnosed and their blood pressures were not severely elevated. The duration of

hypertension may determine the diastolic function abnormalities in a patient. The prevalence rate for the subjects with stage 1 hypertension was less than those with stage 2 hypertension (72% vs. 80 %) This is in agreement with previous studies that have documented increased prevalence of diastolic dysfunction with higher blood pressures. [17,18]

There is need for a follow up study on the cohorts of subjects with diastolic dysfunction to evaluate the likelihood of developing diastolic and or systolic heart failure in the future and the impact of antihypertensive therapy on them.

One limitation of this study is that Doppler studies are an indirect measure of diastolic function. Tissue Doppler imaging would have been a better index of diastolic function. A certain percentage of our patients in this study may actually be in the pseudo-normalization phase and could have been missed despite the manouvres such as valsava manouvre done to assess for reversal of mitral E/A ratio in this study. Therefore a certain percentage of subjects with normal diastolic dysfunction could have had a mild diastolic dysfunction thereby increasing the prevalence of diastolic dysfunction in these patients.

CONCLUSIONS

The result of this study shows a very high prevalence of diastolic dysfunction among patients with essential hypertension. This therefore calls for concerted effort at appropriate diagnosis of diastolic dysfunction in patients with essential hypertension to prevent future upsurge in the incidence of diastolic heart failure among these group of patients with its attendant increase in morbidity, mortality, economic and productivity loss to a developing economy like Nigeria. The use of appropriate antihypertensive agents such as Angiotensin converting enzyme inhibitor

(ACE-I)Inhibitors and /or Angiotensin converting enzyme inhibitors, calcium channel blockers, diuretics etc may reduce the burden of diastolic function abnormalities among these patients.

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