

THE RELATIONSHIP BETWEEN DIASTOLIC DYSFUNCTION AND LEVEL OF BLOOD PRESSURE IN BLACKS

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Introduction and Objective: Patients with essential hypertension are predisposed to impaired left ventricular relaxation, and consequently, diastolic dysfunction. Because diastolic dysfunction is an early marker of the pathological effects of hypertension on the heart, evaluating the relationship between the development of diastolic dysfunction and the level of blood pressure becomes pertinent. The aim of our study was to evaluate this relationship.

Patients and Methods: Between November 1998 and January 2000, 692 consecutive hypertensive patients, all Blacks, attending the medical outpatient and cardiac clinics of the University of Nigeria Teaching Hospital, Enugu, Nigeria were screened for the study. One hundred five of them, divided into 3 groups of 35 each according to levels of blood pressure, met the inclusion criteria. Thirty-five age and sex-matched normotensives were used in the control group. Clinical parameters, including systolic and diastolic blood pressures, and echocardiographic indices, were measured.

Results: A definite positive relationship between diastolic dysfunction and the level of the blood pressure was established, with the degree of diastolic dysfunction proportionate to increasing level of blood pressure ($P < .001$). A significant difference between the mean values of the diastolic dysfunction index (A/E ratio) in the hypertensive groups was evident ($P < .05$). While there was virtually no correlation found between normotensives and diastolic dysfunction ($r = 0.07$), direct relationships existed between moderate and severe hypertensives and diastolic dysfunction ($r = 0.24$ and 0.39 respectively).

Conclusion: This study has demonstrated that diastolic dysfunction was significantly and progressively higher in the hypertensive groups when compared to the normotensive control group. Further studies, with a large number of patients, are recommended to determine population-based data on diastolic dysfunction and its other confounding variables in our environment, independent from the level of blood pressure. (*Ethn Dis.* 2003;13:463-469)

Key Words: Relationship, Diastolic Dysfunction, Blood Pressure

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INTRODUCTION

Left ventricular filling during diastole is a crucial phase of the cardiac cycle. Diastole is the period of the cardiac cycle separating 2 consecutive contraction intervals, and from a clinical point of view can be further divided into the isovolumic relaxation period and 3 filling phases.

In patients with essential hypertension, increased left ventricular afterload, myocardial ischemia, regional asynchrony and left ventricular hypertrophy, alone, or in combination, predispose these patients to impaired left ventricular relaxation. Decreased left ventricular diastolic distensibility (compliance) that results from increased diastolic pressure at any level of diastolic volume also arises from myocardial fibrosis or increased muscle mass (left ventricular hypertrophy).¹⁻¹⁰

Left ventricular diastolic dysfunction has been documented as an early marker of the pathological effects of hypertension on the heart.^{2,11-17} Bonow and Udelson,¹ in a review, upheld the opinion that hypertension appears to be an important underlying factor in many patients with heart failure on the basis of diastolic mechanisms, considering the prevalence of hypertension in the general population. Trevi et al,¹⁸ in a related study, also noted that in hypertensive patients, symptoms and signs of heart failure could be manifested in the absence of myocardial hypertrophy, and

might be exclusively due to diastolic dysfunction. Though mortality due to heart failure from systolic impairment is higher than that due to diastolic dysfunction, morbidity from the latter, is much higher.¹⁹ Hemodynamic studies have shown that diastolic dysfunction plays a significant role in the abnormal exercise response in hypertension.²⁰⁻²²

Of all the complex interplay of factors responsible for diastolic dysfunction, only a few, such as blood pressure, left ventricular hypertrophy, age and heart rate, can be appreciably measured in a clinical setting and, of these factors, blood pressure is most prominent.

In consideration of the significant pathophysiological and morbidity burden, the authors decided to evaluate the relationship between the development of diastolic dysfunction and the level of blood pressure, especially as found in Blacks in Africa. Nigeria has a population of 120 million, mostly Blacks, the largest of such communities in Africa.

SUBJECTS AND METHODS

Subjects

One hundred five (105) patients with essential hypertension (BP $\geq 160/$

Left ventricular diastolic dysfunction has been documented as an early marker of the pathological effects of hypertension on the heart.^{2,11-17}

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Table 1. Clinical characteristics of study populations

Parameter	Normotensive Subjects (N)	Hypertensive Patients			ANOVA		
		Mild (I)	Moderate (II)	Severe (III)	P Value	F	R ²
Number	35	35	35	35			
Sex (M/F)	17/18	17/18	17/18	18/17			
Age (years)	43.46 (14.96)	51.37 (14.96)	54.23 (12.46)	52.17 (10.37)	.5618	0.6969	0.0695
BSA (m ²)	1.81 (0.18)	1.79 (0.18)	1.74 (0.19)	1.75 (0.19)	.3073	1.214	0.0261
BMI (kg/m ²)	26.7 (5.07)	27.43 (5.56)	26.24 (4.14)	26.14 (5.23)	.6959	0.4812	0.0105
HR (beats/min)	78.06 (11.12)	81.46 (11.46)	78.34 (10.84)	86.34 (13.40)	.4109	0.9658	0.0209
SBP (mm Hg)	123 (13)	159 (21)	172 (15)	194 (23)	<.0001	50.75	0.5282
DBP (mm Hg)	74 (7)	99 (2)	109 (2)	124 (8)	<.0001	508.0	0.9181

Table 2. Doppler data according to gender*

Parameters	Controls		Group I		Group II		Group III	
	M (17)	F (18)	M (17)	F (18)	M (17)	F (18)	M (18)	F (17)
E (cm/s)	63.71 (21)	59.94 (17)	58 (18)	49.28 (15)	52.34 (17)	56.89 (18)	53.56 (8)	50 (19)
A (cm/s)	53.47 (16)	53.56 (18)	62.71 (19)	60.78 (14)	61.80 (14)	66 (16)	69.72 (14)	64 (16)
A/E ratio	0.98 (1)	0.90 (0.30)	1.14 (0.35)	1.32 (0.46)	1.27 (0.45)	1.25 (0.54)	1.31 (0.26)	1.35 (0.4)
IVRT (sec)	0.07 (0.04)	0.06 (0.02)	0.08 (0.04)	0.07 (0.03)	0.07 (0.04)	0.08 (0.05)	0.07 (0.03)	0.08 (0.03)
FVI (cm)	11.25 (5)	11.51 (3)	9.69 (4)	7.04 (3)	8.46 (4)	9.44 (4)	9.23 (3)	8.77 (4)

* P value is not significant in all variables.

Table 3. Echocardiographic measurements of study population

Parameters	Normotensive Subjects (N)	Hypertensive Patients			ANOVA		
		I	II	III	P Value	F	R ²
LVEDD (mm)	48.11 (7.45)	47.63 (10.25)	49.26 (7.58)	48.46 (8.7)	.8781	0.2261	0.005
LVEDS (mm)	28.17 (6.59)	27.77 (8.16)	30.63 (7.84)	28.71 (7.98)	.4170	0.9531	0.0206
IVST (mm)	9.31 (1.93)	10.30 (3.17)	9.85 (2.51)	11.66 (3.43)	.0016	5.362	0.1058
LVMl (gm/m ²)	102.40 (5.63)	116.8 (5.73)	124 (5.61)	144 (6.28)	.0268	3.159	0.0651
LVEDV (cm ³)	85.37 (31.84)	92.69 (46.90)	91.54 (33.94)	116.70 (70.8)	.0398	2.850	0.0592
LVESV (cm ³)	34.06 (16.82)	38.43 (27.87)	36.83 (18.40)	45.91 (28.02)	.1657	1.721	0.0363
LAD (mm)	35.54 (6.08)	35.86 (6.03)	35.94 (6.45)	35.31 (7.04)	.9688	0.0838	0.0018
FS (%)	41.54 (8.93)	41.80 (9.33)	38.09 (10.19)	40.54 (11.31)	1.008		0.0218
EF (%)	60.10 (24.33)	58.54 (37.43)	59.77 (26.17)	60.66 (49.41)	.0525		0.0012

Table 4. Doppler indices of diastolic function in study population

Parameter	Normotensive Subjects (N)	Hypertensive Patients			ANOVA		
		I	II	III	P Value	F	R ²
(E) (cm/s)	61.77 (18.82)	53.51 (16.88)	52.34 (16.69)	52.29 (14.14)	.4938	0.8038	0.0174
(A) (cm/s)	53.51 (16.78)	61.71 (16.15)	61.80 (14.09)	66.97 (14.83)	.0048	4.507	0.0904
A/E ratio	0.94 (0.49)	1.23 (0.41)	1.27 (0.45)	1.33 (0.33)	.0008	5.894	0.1151
(IVRT) (sec)	0.06 (0.03)	0.08 (0.04)	0.07 (0.04)	0.07 (0.04)	.1325	1.900	0.0405

Table 5. Chi-square analysis of diastolic dysfunction across the hypertensive groups (using 2×Y contingency table)

Sources of Variation	Sum of Squares	Mean of Squares	Degree of (Freedom (df)	F Ratio	P Value
Between groups	118.27	59.13	2	47.13	<.05
Intra-groups	133.64	1.310	102		

Note: χ^2 (odds ratio)=33.49; *df*=3; *P* value=.00000025.

95 mm Hg) were recruited from the six hundred ninety two (692) volunteers for the study. Thirty-five healthy normotensive control subjects, matched for age and sex were also enrolled. All subjects were Black and informed consent was obtained from each participant.

Between November 1998 and January 2000, consecutive healthy subjects and essential hypertension patients were studied in the medical outpatient and cardiac clinics of our hospital. Participants met the following criteria:

- a) previously received no treatment or receiving no antihypertensive medication for at least 2 weeks prior to presentation;
- b) absence of clinical echocardiographic evidence of secondary hypertension, valvular, congenital, and ischemic heart diseases, as well as diabetes mellitus, heart failure, and renal diseases;
- c) normal hematological and biochemical indices.

Method

Essential hypertension was diagnosed in subjects fulfilling criteria (a–c mentioned above) and was diagnosed in subjects showing clinic diastolic blood pressure values ≥ 95 mm Hg—using the World Health Organization (WHO) classification criteria^{23,24} and the Nigerian Non-communicable Diseases Expert Survey cut-off point,²⁵ prevailing at the time the study was conducted.

A standard mercury sphygmomanometer, with appropriate cuff, was used. Blood pressure was measured in the mornings (between 9AM–12noon)

after bladder emptying, and after 30 minutes rest in a lying position. Blood pressure was taken on 3 separate occasions on different hospital visits and the average of the 3 readings was used for the study.

According to the prevailing WHO classification criteria, these were divided and then^{23,24} further divided into 3 separate groups consisting of 35 participants each:

Group I—mild hypertension with diastolic blood pressure 95–104 mm Hg;

Group II—moderate hypertension with diastolic blood pressure 105–114 mm Hg;

Group III—severe hypertension with diastolic blood pressure 115 mm Hg and above.

Healthy normotensives consisted of voluntary subjects chosen from medical students, hospital staff, and other subjects undergoing a clinical check-up and found to be healthy.

Doctors enlisted volunteers in attendance at the clinics. The authors, as consulting cardiologists, recruited 105 patients and 35 normotensive control subjects who satisfied the criteria.

Echocardiography

Each patient underwent M-mode, 2 dimensional and Doppler echocardiography, with a Siemens Sonoline CD echocardiographic machine, equipped with a 3.5 MHz transducer, a video recorder and print out processor. Left parasternal and the apical 4 chamber views were used as indicated.

Performance and reading of the

Table 6. One-way analysis of variance comparison of the mean values of A/E ratio in the hypertensive groups

Group	A/E Ratio ≥ 1	A/E Ratio < 1	Total
Normal	12	23	35
Mild	26	9	35
Moderate	28	7	35
Severe	33	2	35
Total	99	41	140

echocardiograms were done by one of the authors and another consultant cardiologist/echocardiographer to control for intra-observer bias.

Statistical Analysis

Data was expressed as mean and standard deviation. Where appropriate, comparisons between groups were performed by use of the analysis of variance or chi-square contingency analysis. *P* values less than .05 were regarded as significant. Linear and multiple regression analyses were used to assess the relationship between the variables affecting diastolic dysfunction.

Ethical Approval

Clearance was obtained from the Ethical Committee of the University of Nigeria Teaching Hospital, Enugu.

RESULTS

Subjects included 69 males and 71 females, aged 18 to 85 years. The clinical characteristics of the subject groups showed no statistically significant difference in age (*P*=.56; ANOVA) and body mass index (*P*=.70 by One Way Analysis of Variance). However, the systolic and diastolic blood pressures differed very significantly across the groups as a result of, and in keeping with, the BP selection criteria (*P*<.0001) (Table 1).

Table 2 lists important diastolic filling measurements in all study subjects subdivided by gender. No statistically significant difference was found between

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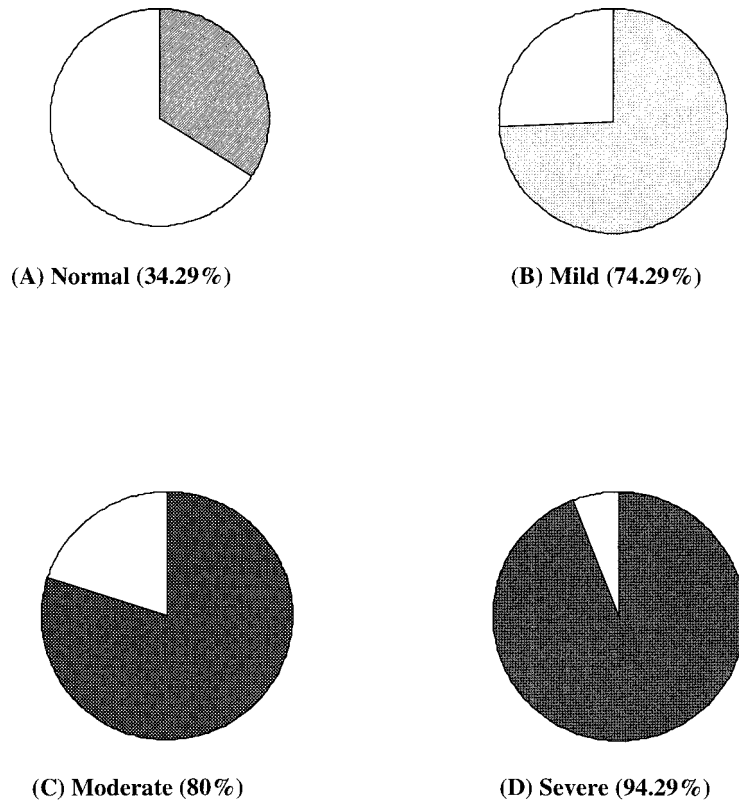


Fig 1. Proportion of each hypertensive group with diastolic dysfunction

males and females in any Doppler parameter (particularly A/E ratio—diastolic dysfunction index) considered ($P>.05$).

Table 3 shows that systolic function was maintained in part across all the groups. The fractional fibre shortening (FS) was more than 38% in all the groups, while ejection fraction (EF) re-

mained at between 58% to 60% in all of the subjects. As previously noted, FS values more than 25% and EF values more than 50% depict intact systolic function.

Table 4 reveals that the A/E ratio (diastolic dysfunction index) was significantly different across all the groups ($P<.005$; ANOVA). The statistical dif-

ference in A ($P=.0048$) contrasted against none in E ($P=.49$) may be due to the fact that the atrial filling characteristics (A) account more for the diastolic filling abnormalities than the early filling isovolumic phase (E).

In Table 5, a statistically significant difference was shown in diastolic dysfunction indices (A/E ratio ≥ 1) across the groups with P value $<.0001$. The number of subjects with diastolic dysfunction was significantly and progressively higher in the hypertensive groups when compared to the normotensive control groups.

A significant statistical difference is also observed between the mean values of diastolic dysfunction index of A/E ratio across the 3 hypertensive groups (One Way Analysis of Variance: $P<.05$; $F=47.13$) (Table 6).

Figure 1 displays the proportion of diastolic dysfunction (A/E ratio ≥ 1) in each study group. The range spans from 34.29% in the normotensive control groups to 94.29% in the severe hypertensive group.

By linear regression, virtually no correlation ($r=0.07$; Table 7) was found between normal blood pressure and diastolic dysfunction. However, a direct relationship existed between mild ($r=0.11$), moderate ($r=0.24$), and severe ($r=0.39$), hypertensives and diastolic dysfunction (Tables 8–10). The strength of the correlation increased with increasing level of blood pressure.

Table 7. Regression analysis of factors that correlate with A/E: normotensives

Variable/Parameter	Intercept	Y	Y ²	95% CI	B Coefficients			F
					Mean	Partial r	SE	
Simple linear								
Diastolic blood pressure (DBP)	73.18	0.07		-0.27<R<0.40	0.93	1.02	2.47	0.17
Left ventricular mass index (LVMI)	102.52	0.00		-0.33<R<0.33	0.93	-0.09	20.17	0.00
Age	24.03	0.62		0.36<R<0.79	0.93	20.69	4.57	20.49
Pulse	69.01	0.42		0.10<R<0.66	0.93	9.63	3.62	7.09
Multiple linear								
Diastolic blood pressure (DBP)			0.01	-0.01-0.03	74.14	0.01	0.01	1.68
Left ventricular mass index (LVMI)	-2.16		0.00	-0.001-0.003	102.44	0.001	0.001	0.35
Age			0.38	0.01-0.02	43.46	0.02	0.004	18.18
Heart rate			0.18	0.01-0.03	78.06	0.02	0.006	8.49

Table 8. Regression analysis of factors that correlate with A/E: mild hypertensives

Variable/Parameter	Intercept	Y	Y ²	95% CI	B Coefficients			
					Mean	Partial r	SE	F
Simple linear								
Diastolic blood pressure (DBP)	99.55	0.11		0.43<R<0.23	1.24	-0.562	0.89	0.40
Left ventricular mass index (LVMI)	84.45	0.19		-0.15<R< 0.49	1.24	26.20	23.62	1.23
Age	25.48	0.58		0.31<R<0.77	1.24	20.97	5.11	16.85
Heart rate	68.76	0.37		0.04<R<0.63	1.24	10.28	4.46	5.31
Multiple linear								
Diastolic blood pressure (DBP)			0.01	-0.05-0.07	98.86	0.01	0.03	0.14
Left ventricular mass index (LVMI)	-1.80		0.04	-0.001-0.002	116.80	0.0004	0.001	0.11
Age			0.34	0.01-0.02	51.37	0.02	0.004	13.65
Heart rate			0.14	0.001-0.023	81.46	0.012	0.006	4.24

A rising trend, proportionate to the blood pressure level group in the independent relation with diastolic dysfunction, was found utilizing multivariate analysis ($r^2=0.01, 0.01, 0.06, 0.15$ respectively in Tables 7-10). This finding was particularly evident in the moderate and severe hypertensive groups (Tables 9 and 10) and explains the strength of the relationship between diastolic dysfunction and level of blood pressure, independent of other variables. These other variables, which include left ventricular mass index, age, and heart rate (comparatively shown in Tables 7-10), are the subject of other publications emanating from this study.

DISCUSSION

This study has shown some correlation between diastolic blood pressure

and diastolic dysfunction. The strength of this correlation, as an independent determinant, tended to rise as blood pressure levels became more severe. Some studies, such as Fouad et al,²⁶ Smith et al²⁷ and Verdecchia et al²⁸ have demonstrated a correlation between peak filling rate and high blood pressure in hypertension. The study by Verdecchia et al²⁸ showed ambulatory blood pressure as a major independent predictor of diastolic function abnormality.

Some other studies, however, notably those of Inouye et al,¹¹ Nakashima et al,¹⁷ Dianzumba et al,²⁹ as well as Gardin et al,³⁰ demonstrated no correlation between the level of blood pressure and diastolic dysfunction.

According to the Dianzumba et al²⁹ study, the lack of relationship between diastolic dysfunction and blood pressure was attributed to the comparatively

small patient population of 37. Additionally, these patients had relatively lower blood pressure levels (clinic blood pressure of 152/98 mm Hg) that fell only within the mild hypertensive group, in the classification used in this current work. The work by Gardin and his colleagues also found relatively low blood pressures in the hypertensive group they studied (clinic blood pressure: 147.9/95.8 mm Hg) and their finding confirmed an absence of correlation between diastolic dysfunction and blood pressure.³⁰ In a related study involving patients with diabetes, Balogun et al³¹ inferred that the lack of correlation between blood pressure variables and indices of diastolic function observed in patients could be attributed to the filling abnormalities, which were due to changes in myocardial relaxation rather than load changes.

Table 9. Regression analysis of factors that correlate with A/E: moderate hypertensives

Variable/Parameter	Intercept	Y	Y ²	95% CI	B Coefficients			
					Mean	Partial r	SE	F
Simple linear								
Diastolic blood pressure (DBP)	107.42	0.24		-0.10<R<0.53	1.27	1.13	0.81	1.99
Left ventricular mass index (LVMI)	107.30	0.10		-0.24<R<0.42	1.27	13.14	21.71	0.37
Age	33.96	0.57		0.30<R<0.76	1.27	15.99	3.97	16.19
Heart rate	79.89	-0.05		-0.38<R<0.29	1.27	-1.22	4.21	0.08
Multiple linear								
Diastolic blood pressure (DBP)			0.06	-0.03-0.09	108.86	0.04	0.03	1.15
Left ventricular mass index (LVMI)	-3.45		0.01	-0.002-0.003	123.96	0.001	0.001	0.29
Age			0.33	0.01-0.03	54.23	0.02	0.005	13.01
Heart rate			0.00	0.02-0.01	78.34	0.003	0.006	0.18

Table 10. Regression analysis of factors that correlate with A/E: severe hypertensives

Variable/Parameter	Intercept	Y	Y ²	95% CI	B Coefficients			
					Mean	Partial r	SE	F
Simple linear								
Diastolic blood pressure (DBP)	111.01	0.39		0.07<R<0.64	1.33	9.45	3.84	6.05
Left ventricular mass index (LVMI)	116.63	0.11		-0.23<R<0.43	1.33	20.90	32.96	0.40
Age	26.53	0.61		0.35<R<0.79	1.33	19.28	4.33	19.83
Heart rate	68.81	0.32		-0.10<R<0.59	1.33	13.18	6.70	3.87
Multiple linear								
Diastolic blood pressure (DBP)			0.15	-0.002-0.02	123.57	0.01	0.01	2.50
Left ventricular mass index (LVMI)	-1.22		0.01	<0.001-0.001	144.42	0.0001	0.001	0.03
Age			0.38	0.01-0.03	52.17	0.02	0.004	17.97
Heart rate			0.11	-0.003-0.011	86.34	0.004	0.004	1.22

Several possible explanations exist for abnormal left ventricular diastolic filling (diastolic dysfunction) in arterial hypertension. In the presence of chronic pressure overload, the myocardial contents of collagen may increase, not only when hypertrophy has developed,³² but even before it.³³ Equally, in hypertension, with or without cardiac hypertrophy, structural and functional abnormalities in the large and small coronary vessels could contribute to inhibiting left ventricular diastolic filling.³⁴ Myocardial adenosine triphosphate (ATP) levels can be depressed by a pressure overload, with consequent impaired relaxation due to reduced calcium uptake by the sarcoplasmic reticulum.³⁵

Furthermore, an increase in afterload at the early filling phase has a deleterious effect on ventricular relaxation.³⁶ Non-uniform distribution of relaxation could also prolong its overall duration.³⁷

This study demonstrated that diastolic dysfunction was significantly more prevalent in the hypertensive groups, when compared to the normotensive control groups.

CONCLUSION

This study demonstrated that diastolic dysfunction was significantly more prevalent in the hypertensive groups, when compared to the normotensive control groups. This prevalence was higher with increasing levels of blood pressure. A positive relationship between diastolic dysfunction and the level of blood pressure was established.

Further studies with a large number of patients should be undertaken to determine population-based data on diastolic dysfunction and other confounding variables in our environment (such as left ventricular hypertrophy, age, and heart rate), aside from the level of blood pressure.

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Manuscript draft: Ike, Onwubere
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