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Gender Differences in Left Ventricular Size and Geometric Pattern of Hypertension Subjects

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Abstract: Left Ventricular Hypertrophy (LVH) and Left Ventricular (LV) geometric pattern are known risk factors for increased burden of cardiovascular morbidity and mortality in patients with hypertension, but the influence of gender on these parameters remains unclear. Two-dimensional and M-mode echocardiograms were recorded in 676 newly presenting hypertensive adults and 162 normal controls. Left ventricular mass was estimated using M-mode echocardiography and indexed by body surface area. Relative Wall Thickness (RWT) and Left Ventricular Mass Index (LVMI) were used to classify LV geometric patterns according to gender. The left ventricle of females had a greater fractional shortening (30.6±10.4 versus 26.4±11.6), smaller end diastolic chamber size (48±9.0 versus 51.6±10.6) and higher ejection fraction (56.5±16.4 versus 53.7±17.7) than males. Ninety (22.5%) hypertensive males against 68 (24.7%) females had normal LV geometry (p = 0.49). Incidence of concentric remodelling was similar (p = 0.86) between females and males (23.3% versus 22.7%, respectively). LVH occurred in 54.8% of males versus 52% of females, p = 0.46. Eccentric LVH was commoner (p = 0.01) in males but more (p = 0.04) females had concentric LVH. LVMI in the 2 groups, septal thickness in males, posterior wall thickness and weight in females were predictors of LV geometric pattern, respectively.

Key words: Gender, systemic hypertension, echocardiography, left ventricular geometry

INTRODUCTION

System Hypertension (SH) affects about 1 billion people world-wide and it is a major cause of cardiovascular morbidity and mortality in Black Africans in whom the disease presents early and runs a rapid course (Frazier *et al*., 2005; Rahman *et al*., 1997). It is a common cause of heart failure, stroke and chronic kidney failure in Nigerian populations (Kadiri, 2000). LVH as determined by echocardiography has been shown to be a strong predictor of adverse prognosis in patients with cardiovascular diseases (Levy *et al*., 1990). LVH can be characterized by geometric subtypes, based on LV mass indexed for body size and RWT which further refines cardiovascular risk assessment (Muiesan *et al*., 2004; Aje *et al*., 2006). Patients with increased RWT and LVMI (concentric LVH) have been shown to have the worst cardiovascular outcomes compared with other subtypes of LV geometric patterns (Koren *et al*., 2002). Epidemiological studies particularly in Caucasians and Africans in Diaspora have suggested that gender may influence compensatory changes in left ventricle in response to chronic pressure overload (Villari *et al*., 1995; Krumholz *et al*., 1993). Racial differences in LV adaptation to hypertension have also been reported (Koren *et al*., 1993). This study aimed at determining the influence of gender on LV dimensions and patterns of LV remodelling in Nigerian hypertensive subjects.

MATERIALS AND METHODS

Six hundred and seventy-six (401 males and 275 females) consecutive newly presenting adult hypertensive patients referred for echocardiography at our laboratory between May 2004 and May 2008 were cross-sectionally studied. They were compared with 162 (81 males and 81 females) apparently healthy normotensive individuals. Echocardiographic assessment of cardiac function is 1 of the initial investigations in hypertensive patients in our centre. All the subjects were selected if they were 18 years and above, did not have structural heart lesions such as congenital heart disease, rheumatic valvular heart disease, intra-cardiac masses and diabetes mellitus. The patients' age, sex, anthropometric

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measurements such as weight, height, Body Mass Index (BMI) and blood pressure were recorded. Echocardiograms were performed using Esaote Megas CVX machine (2003 model) which has facilities for 2 Dimensional (2D), m-Mode and colour flow, pulsed and continuous wave Doppler. A long Parasternal 2D-guided m-Mode echocardiogram was obtained from each patient and LV dimensions were taken according to the recommendations of the American Society of Echocardiography (ASE) (Schiller *et al*., 1989). Parameters recorded included: LV Internal Dimension in diastole (LVIDd), LV Internal Dimension In systole (LVIDs), Interventricular Septal thickness in diastole (IVSd), Interventricular Septal thickness in systole (IVSs), Posterior Wall thickness in diastole (PWd), Posterior Wall thickness in systole (PWs), LV Ejection Fraction (EF) and Fractional Shortening (FS). Others include Right Ventricular dimension in diastole (RVd), Aortic Dimension (AOD) and Left Atrial Dimension (LAD). LV Mass (LVM) was calculated using the formula (Devereux *et al*., 1986):

$$0.8\times \{1.04\times [(LVIDd + IVSd + Pwd)^3-(LVIDd)^3] \} + 0.6$$

Left Ventricular Mass Index (LVMI) was determined using formula:

LVM/BSA

where:
BSA = The body surface area

Left Ventricular Hypertrophy (LVH) was considered present if LVMI was ≥119.6 g m^{-2} in females and ≥168.8 g m^{-2} in males (2 standard deviations above the mean values for LVMI of control subjects). Relative Wall Thickness (RWT) was calculated by the formula (Savage *et al*., 1987):

$$2 \times PWd/LVIDd$$

The pattern of LV remodelling was determined using LVMI and RWT. Increased RWT was present if RWT was ≥0.45 (Savage *et al*., 1987). LV geometric pattern was classified using RWT and LVMI as follows:

Normal geometry = Normal LVMI and RWT
Concentric remodelling = Normal LVMI and RWT ≥0.45
Eccentric LV hypertrophy = Increased LVMI and RWT<0.45
Concentric LV hypertrophy = Increased LVMI and RWT ≥0.45

Statistical analysis: Statistical analysis was performed using the SPSS Version 15 and the numerical values were presented as mean±standard deviation. Student t-test was used to compare means of continuous variables, while chi-square test was used to compare means of proportions. Test of correlation was done using the Spearman's Rank correlation method. Stepwise regression analysis using 0.05 as entry probability and 0.10 as removal probability was used to determine predictors of LV geometry. A statistically significant association was taken at $p<0.05$.

RESULTS

The demographic and echocardiographic data of the patients and control subjects are shown in Table 1. Although, the mean age and height of the patients and controls were similar, body weight of the patients was significantly higher ($p = 0.045$) than that of the controls. However, the mean BMI was not different between the two groups. Mean Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were significantly higher in the patients when compared with the controls. LV dimensions, PWd, IVSd, AOD, LAD and LVMI were higher in the patients than in the controls. LVMI of the female control subjects ranged from 58-135 g m^{-2} with a mean of 89.4±15.1 g m^{-2}, while that of the male controls ranged from 65-173 g m^{-2} with mean of 109.8±29.5 g m^{-2}. The demographic and echocardiographic parameters of hypertensive subjects by gender are presented in Table 2. Mean ages of the male and female hypertensive subjects were similar. Although, the mean body weights were similar ($p = 0.07$) between the 2 groups, males were taller ($p = 0.02$) but females had higher BMI ($p = 0.03$). SBP and DBP profiles were not different between the 2 groups. LV cavity sizes (LVIDd and LVIDs) were higher in males and similarly the PWd was thicker in males than females. However, the EF and FS were better in the females than

Table 1: Characteristics of the study group

Variable	Patients	Control	p-value
Number	676	162	
Age (years)	55.9±12.9	52.8±11.5	0.23
Height (meters)	1.7±0.09	1.68±0.08	0.5
Weight (kg)	75.3±12.4	71.2±13.9	0.045*
BMI (kg m^{-2})	26.6±8.5	25.7±7.9	0.4
SBP (mmHg)	158±28.6	121±19.2	0.001*
DBP (mmHg)	105.9±13.6	82.3±10.4	0.001*
LVDd (mm)	50.1±20.4	45.6±6	0.001*
LVDs (mm)	35.6±12.5	29.7±4.6	0.001*
PWd (mm)	11.2±3.8	9.3±2.3	0.001*
IVSd (mm)	14.2±7	10.5±3.5	0.001*
EF (%)	54.9±17.2	64.8±8.8	0.001*
FS (%)	29.8±11	35.5±7	0.001*
AOD (mm)	34.3±13	29.7±4.6	0.001*
LAD (mm)	37.5±15.4	31.5±4.7	0.001*
LVMI (g m^{-2})	167.8±84.2	99.2±25.2	0.001*

BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, LVDd: Left Ventricular Dimension in diastole, LVDs: Left Ventricular Dimension in systole, PWD: Posterior Wall in Diastole, IVSd; Inter-Ventricular Septum in diastole, EF: Ejection Fraction, FS: Fractional Shortening, AOD: Aortic root Dimension, LAD: Left Atrial Dimension, LVMI: Left Ventricular Mass Index; *Statistically significant

Table 2: Demographic and echocardiographic characteristics of hypertensive subjects by gender

Variable	Males	Females	p-value
Number	401	275	
Age (years)	56.2±12	55.4±14	0.4
Height (m)	1.74±0.09	1.63±0.07	0.02*
Weight (kg)	73.4±13.6	76.1±12.9	0.07
BMI (kg m^{-2})	24.7±4.4	27.9±3.8	0.03*
SBP (mmHg)	159±19.8	157±18.5	0.9
DBP (mmHg)	105.6±12	103.3±15.9	0.8
LVDd (mm)	51.6±10,6	48.0±9.0	0.027*
LVDs (mm)	37.4±12.4	33.0±12	0.01*
PWd (mm)	11.6±4.2	10.7±3.2	0.01*
IVSd (mm)	14.5±6.5	13.8±7.6	0.3
EF (%)	53.7±17.7	56.5±16.4	0.035*
FS (%)	26.4±11.5	30.6±10.4	0.032*
AOD (mm)	35.3±16.3	29.3±3.5	0.001*
LAD (mm)	37.6±11.6	37.3±19.7	0.8
LVMI (g m^{-2})	182.2±88.2	148.6±74.7	0.001*
RWT	0.45±0.14	0.48±0.19	0.04*

BMI: Body Mass Index, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, LVDd: Left Ventricular Dimension in diastole, LVDs: Left Ventricular Dimension in systole, PWd: Posterior Wall in diastole, IVSd: Inter-Ventricular Septum in diastole, EF: Ejection Fraction, FS: Fractional Shortening, AOD: Aortic root Dimension, LAD: Left Atrial Dimension, LVMI: Left Ventricular Mass Index, RWT: Relative Wall Thickness; *Statistically significant

Table 3: Shows pattern of left ventricular geometry in male and female hypertensive subjects

Geometric pattern	Males frequency (%)	Females frequency (%)	Total No. (%)	p-value
Normal	90 (22.5)	68 (24.7)	158 (23.4)	0.49
Concentric remodelling	91 (22.7)	64 (23.3)	155 (22.9)	0.86
Eccentric LV hypertrophy	139 (34.7)	69 (25.1)	208 (30.8)	0.01*
Concentric LV hypertrophy	81 (20.1)	74 (26.9)	155 (22.9)	0.04*
Total	401 (100)	275 (100)	676 (100)	

LV: Left Ventricle; *Statistically significant

males. Although, the LVMI was higher in males, the RWT was significantly higher in females than male hypertensive subjects. Mean LAD, which is a reflection of LV filling pressure was not different between the 2 groups. Table 3 shows left ventricular geometric patterns in the male and female hypertensive subjects. Ninety (22.5%) males against 68 (24.7%) females had normal LV geometry ($p = 0.49$). Incidence of concentric remodelling in female and male patients (23.3% versus 22.7%, respectively) was similar ($p = 0.86$) between the 2 groups. Although, the prevalence of LVH was similar in the 2 groups (54.8% in males versus 52% in females, $p = 0.46$), LV geometric pattern differs between males and females with LVH. Occurrence of eccentric LVH was significantly higher ($p = 0.01$) in males than females. However, concentric LVH was commoner ($p = 0.04$) in female patients.

Correlates of LV geometry are presented in Table 4. LV geometric pattern showed significant positive correlation with age, PWd, IVSd, LVMI and RWT in both males and females. However, significant negative correlation was seen between LV geometric pattern and EF only in male hypertensive subjects. On the other hand,

Table 4: Correlates of left ventricular geometry

	Males		Females	
Parameters	R	p-value	R	p-value
Age and LVG	0.158	0.012*	0.191	0.007*
Weight and LVG	0.167	0.01*	0.380	0.001*
Height and LVG	0.114	0.065	0.074	0.62
SBP and LVG	0.242	0.001*	0.231	0.001*
DBP and LVG	0.280	0.001*	0.230	0.01*
LVDd and LVG	0.119	0.053	0.037	0.598
LVDs and LVG	0.148	0.059	0.097	0.29
PWd and LVG	0.230	0.001*	0.350	0.0001*
IVSd and LVG	0.360	0.001*	0.270	0.01*
EF and LVG	-0.131	0.034*	-0.130	0.86
FS and LVG	-0.116	0.065	-0.010	0.9
LVMI and LVG	0.414	0.0001*	0.488	0.0001*
LAD and LVG	0.056	0.38	0.181	0.12*
RWT and LVG	0.330	0.001*	0.370	0.0001*

LVG: Left Ventricular Geometry, LVDd: Left Ventricular Dimension in diastole, LVDs: Left Ventricular Dimension in systole, PWd: Posterior Wall in diastole, IVSd: Inter-Ventricular Septum in diastole, EF: Ejection Fraction, FS: Fractional Shortening, LAD: Left Atrial Dimension, LVMI: Left Ventricular Mass Index, RWT: Relative Wall Thickness; *Statistically significant

LV geometry correlated positively with LAD and body weight in the female subjects. LV dimensions (LVIDd and LVIDs) did not show significant correlation with LV geometry in both sexes. LVMI was an independent predictor of LV geometric pattern in both sexes ($R^2 = 0.379$, $F = 66.5$, $p = 0.0001$ in females and $R^2 = 0.263$, $F = 51.7$, $p = 0.0001$ in males). While, IVSd predicted ($R^2 = 0.354$, $F = 39.4$, $p = 0.0001$) LV geometry in males, Pwd and weight were predictors ($R^2 = 0.518$, $F = 58.1$, $p = 0.0001$ for PWd and $R^2 = 0.557$, $F = 30.8$, $p = 0.003$ for weight) of LV geometry in females.

DISCUSSION

LV adaptation to chronic pressure overload is a complex process and it is characterized by changes in ventricular size, shape and function (Duprez, 2004). Because of the prognostic importance of LVH, much attention has been focused on its determinants. Recently, there has been a renewed interest on the influence of gender on LV geometric pattern and by extension outcome of LV dysfunction in SH (Deschepper and Llamas, 2007; Weinberg *et al*., 1999). The old belief that pre-menopausal women have low risk of developing major cardiovascular complication because of effects of oestrogen which appears to have cardio-protective effect has been challenged by current body of evidence (Krumholz *et al*., 1993; Vriz *et al*., 1997; Verdecchia *et al*., 1992). Some studies have shown that the heart of men and women respond in different ways to SH (Krumholz *et al*., 1993; Verdecchia *et al*., 1992). Elderly women with isolated systolic hypertension have been found to be more prone to concentric LVH and men to eccentric LVH (Krumholz *et al*., 1993).

Our study showed that most clinical and echocardiographic parameters were deranged in the hypertensive subjects when compared with the controls (Table 1). The differences between the subjects and the controls may be due to compensatory structural changes in left ventricle and neuro-hormonal alterations in SH (Weber *et al*., 1994; Frohlich, 1999).

The results of our study also showed that LV dimensions were higher in the males than females. However, the females had greater EF and FS than males. The pattern described above is consistent with available literature on patients with chronic pressure overload (Carroll *et al*., 1992; Aurigemma and Gaasch, 1995). Although, LVMI was higher ($p = 0.001$) in males, RWT was significantly higher ($p = 0.04$) in females (surrogate for concentric LVH) than in men. LV geometric pattern associated with highest incidence of cardiovascular complications (concentric LVH) occurred more ($p = 0.04$) in women than in men. Previous studies to determine the role of gender on LV geometric pattern gave inconsistent results. It is known that concentric remodelling even in the absence of LVH confers an additional risk for poor cardiovascular outcome (Koren *et al*., 2002). Our findings concur with that of Weinberg *et al*. (1999) who observed that hypertensive women had greater degree of increase in LV wall thickness and concentric LVH. In the Framingham Heart Study (Vasan *et al*., 2004), serum aldosterone was positively associated with concentric LVH in women but not in men. This finding suggests possible interactions between signalling effects of oestrogen and aldosterone receptor in the myocardium, contributing to gender differences in LV remodelling. Experimental study (Douglas *et al*., 1989) involving aortic banding in rats had shown females having more concentric LVH while males had eccentric LVH. On the other hand, Kurata *et al*. (2005) reported association between concentric LVH and serum uric acid (higher risk profile) in male Japanese hypertensive subjects but not in females.

Age correlated positively with LV geometric pattern of our patients in both sexes. This concurs with results of earlier studies, which associated abnormal LV structure and function with ageing (Sumimoto *et al*., 1995; Slotwiner *et al*., 2001). The effect of body weight on LV remodelling appears to be more in females than males as weight was a predictor of LV geometric pattern in our subjects. However, in our patients, LVMI independently predicted geometric pattern in both sexes. In the Losartan Intervention For End Point Reduction in Hypertension (LIFE) Study (Wachtell *et al*., 2002), antihypertensive treatment reduces the prevalence of LVH and concentric LVH. In that cohort, patients with concentric LVH at baseline often had either eccentric LVH or normal geometry after 1 year of treatment. This implies that early intervention with appropriate treatment of hypertensive subjects will reduce LVH and abnormal LV geometric patterns.

CONCLUSION

Gender differences exist in LV geometric pattern of hypertensive Nigerians with females having more of concentric and males eccentric LVH. Future studies to determine the prognostic significance of gender and LV geometric patterns in Nigerian patients are warranted.

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