

## LVMI: A detrimental paradigm shift of left ventricular geometry and function in accidentally detected hypertensives

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### Abstract

**Introduction:** Left ventricular hypertrophy (LVH) is an important predictor of mortality and morbidity in hypertension, leading to hypertensive heart disease (HHD). Left ventricular mass (LVM), therefore, chiefly determines the geometrical reorientation of LV in hypertensives and these geometrical patterns are useful determinant of severity and prognosis of congestive heart failure (CHF). Studies on the geometrical assessment of LV in hypertensive patients involving large number of patients are limited in India. 2-D Echocardiography, is a non-invasive, cost effective, and a gold standard technique in the early detection of LV hypertrophy in hypertensive patients.

**Aims and Objectives:** To determine the structural and functional integrity of LV in accordance with the variability of the LV geometry and function in recently detected hypertensive patients by 2D- Echocardiography and Colour Doppler.

**Material and Methods:** 2D-Echocardiography and colour Doppler was done in 1000 randomly selected patients in OPD with accidentally detected hypertension. LV geometrical patterns were determined by using Echocardiographic parameters chiefly left ventricular mass (LVM), left ventricular mass index to the power 2.7 of ht. (LVMI) and relative wall thickness (RWT) were recorded according to American society of Echocardiography convention (ACE).

**Results and Observations:** Four patterns of LV geometry were noted i.e. concentric hypertrophy (CH) (22.9%), eccentric hypertrophy (EH) (9.7%), and concentric remodeling (CR) (50%) and normal geometry (NG) (17.4%).

In this study, we observed that patients with concentric hypertrophy were significantly (<0.0001) older than the normal geometry and had significantly elevated pressures SBP (.0130), DBP (0.0363), MAP (.0038) and PP (0.0217) higher than in normal geometry. Diastolic dysfunction was detected in hypertensive patients with concentric hypertrophy and eccentric hypertrophy, abnormal LV patterns observed in our study.

LV systolic function was significantly lower in patients with eccentric hypertrophy and some degree of diastolic dysfunction was present in abnormal geometry.

**Conclusion:** The study determines that if there are regular screenings of the high blood pressure, then early steps can be taken to detect the establishment of LV hypertrophy.

**Keywords:** LV hypertrophy, 2D-Echocardiography, LV mass, Hypertension.

### Introduction

Hypertension is a potential risk factor for the cardiovascular disease (CVD) and stroke. It is a deterring factor in the process of initiation of the various events leading to left ventricular hypertrophy (LVH).<sup>1,2</sup> Hypertension leads to LV structural and functional reorientation in different planes leading to early heart failure and rise in mortality morbidity.

At some point of time in the natural history of hypertension, when the compensatory increase of left ventricular mass (LVM) ceases to be beneficial, then the Left ventricular hypertrophy becomes a preclinical disease.<sup>3</sup>

LVH is defined as abnormal increment in the LV mass either due to pressure or volume overburden or overload, which is the end point of the organic processes resulting from the sustained elevation of blood pressure in hypertensive patients.<sup>1,2</sup> LVH is widely documented as an individual risk factor and predictor of cardiovascular mortality.<sup>1,2</sup>

Various other factors associated with increased LVM include age, diet,<sup>4</sup> high salt intake, gender,

genetics, chronic stress, increase BMI, physical inactivity, rise in blood viscosity,<sup>5</sup> ageing and obesity<sup>6</sup> etc.

Concentric hypertrophy of LV ultimately precipitates early left heart failure. Pathologically LVH is denoted by liberation of fibrogenic cytokines and neurohumoral factors, notably angiotensin II, which favour interstitial collagen deposition and perivascular fibrosis.<sup>7</sup> Hypertension, Diabetes mellitus and Obesity are implicated as most important determinants of increased LVM.

Cardiac maladaptive process has four differing LV geometrical patterns, notably Concentric hypertrophy (CH), Eccentric hypertrophy (EH), Concentric remodeling (CR) and Normal geometry (NG). Furthermore, LVMI shows the index of severity of maladaptive process in LV geometry. Structural classification of LV geometry provides useful and additional prognostic information.<sup>9,10</sup>

LV mass is more closely related to mean 24-hour blood pressure.<sup>11</sup> Each of the four LV geometrical patterns is found to be associated with different

triggering patterns and distinct combination of pressure and volume stimuli, contractile efficiency and prognosis (worst with concentric hypertrophy and best with normal geometry).<sup>12</sup>

Studies with large number of hypertensive patients in India are rare and there is very little information of how the LV geometrical patterns behave in recently detected hypertension.

Therefore, we decided to undergo an intricate analysis of these hypertensive patients routinely attending OPD clinics in SRMS-IMS Bareilly (UP), India. This study will further add facets about the LV structural and functional aspect in the academic database.

### Materials and Methods

**Defining Hypertensive Case:** Patients were defined to be hypertensive when they had SBP $\geq$ 140 mmHg and DBP $\geq$ 90 mmHg according to JNC-7 criteria.<sup>13</sup>

**Inclusion Criteria:** Patients between 25 -70 years of age of both the genders were included.

**Exclusion Criteria:** Patient with coronary heart disease, cardiac failure, stroke, End stage renal failure, endocrinal disorders, locomotor disorders and neurological disorders were excluded.

**Methodology:** The study was conducted with the joint efforts of Dept of Medicine, Dept. of Cardiology, and Dept. of Physiology in Sri Ram Murti Smarak Institute of Medical Sciences (SRMS-IMS), Bareilly a tertiary health care facility and research centre in Uttar Pradesh.

For the present study, patients were selected between age group of 25 to 70 years of both the genders. 1000 patients were considered for the study who are ignorant about their blood pressure profile, attending medicine OPD for their other minor illnesses, accidentally detected to be SBP $>$ 140mmHg and DBP $>$ 90mmHg. History taking and general examination was done before going for 2D-Echocardiography.

Demographic data of all the patients under study was collected and analysed. BP was recorded by Diamonds mercurial type sphygmomanometer. Echocardiography and Color Doppler has become integral to the diagnostic workup and treatment strategy in hypertensive LVH, as recommended by the European Society of Hypertension (ESH) and European Society of Cardiology (ESC).<sup>14</sup> Echocardiography is a non invasive, cost-effective, tool generally considered ideal for serial mass and functional assessment of LV.

LV mass is calculated from the LV interventricular septum and posterior wall thicknesses and internal diameter using the Penn or American Society of Echocardiography (ASE) formulas.<sup>8,12</sup> Values obtained using different formulas have given superimposable results.<sup>15</sup> Trans-thoracic Echo by Siemens Sonline G50s. Echocardiographic parameters were recorded by a cardiologist in accordance with American society of

echocardiography convention (ASE). LVM was determined by Devereux modified formula.<sup>12</sup>

**LVM=0.80[1.04 (LVIDD+PWT+IVSD) 3-LVIDD]+0.6g/BSA:** All the Echocardiographic parameters were calculated according to ACE convention.<sup>16</sup> Ejection fraction is automatically calculated following acquisition of the LV volumes using the Simpson biplane method.

**Left Ventricular Systolic Function:** All the parameters were adjusted for size by dividing with body surface area. Height based adjustment was done by dividing LVM by height.<sup>2,7</sup>

1. Ejection fraction (EF%)=  $\frac{LVIDD^3 - LVIDS^3}{LVIDD^3} \times 100$
2. Fractional fiber shortening (FS)=  $\frac{LVIDD - LVIDS}{LVIDD} \times 100$

**Left Ventricular Diastolic Function:** maximum velocity of passive mitral filling (E), maximum velocity of active mitral filling (A), ratio of passive to active velocity (E/A). The left atrial diameter was measured using M mode in the parasternal long axis view.<sup>16,17</sup>

**LV Geometric Pattern:** Left ventricular hypertrophy (LVH) is recognised as an independent predictor of morbidity and mortality.<sup>18,19</sup> The prevalence in hypertensive patients ranges from 36% to 41%. LVH is essentially an increase in left ventricular (LV) mass.<sup>12</sup> Methods to measure LV mass include Devereux's formula and the area length method.<sup>16</sup> Relative wall thickness (RWT) allows further classification of LV mass increase as either concentric hypertrophy (RWT  $>$ 0.42) or eccentric hypertrophy (RWT  $\leq$ 0.42):  $RWT = \frac{2 \times PWT}{LVID}$ .

The pattern of LV remodeling was determined using LVMI and RWT. Subjects were stratified according to quantile of RWT and also according to LV geometric pattern. The RWT and LVMI were used to categorize subjects as having

1. Normal geometry –normal RWT and normal LVMI
2. Concentric remodeling- increased RWT and normal LVMI
3. Eccentric hypertrophy- normal RWT and increased LVMI
4. Concentric hypertrophy- increased RWT and increased

Partition values for LVMI (g/m) and RWT were: Indian Asian males -118/0.50 and Indian Asian females- 107/0.47.<sup>20</sup>

### Statistical Analysis

SPSS software version 16.0 (SPSS inc, Chicago, IL, USA) was used for statistical analysis. Variables in different categories were expressed as proportions and percentages whereas continuous variables were expressed as mean $\pm$  SD.

Categorical variables were compared using chi square test. Analysis of variance (ANOVA) was used to determine the significant differences of the studied

parameters among the four groups of LV geometrical patterns, multiple comparisons between the 4 groups were performed by one way analysis of variance with the Duncan post hoc test. The level of statistical significance was  $\leq 0.05$ .

## Results

In the present study, population of study subjects were the recently detected hypertensive patients without having any symptoms of raised blood pressure, just attended the OPD for their other ailment and accidentally detected to be hypertensives.

**Table 1: Profile of hypertensive patients in various LV geometrical patterns**

| Variable                 | Normal<br>N=174 | Concentric<br>hypertrophy<br>N=229 | Eccentric<br>hypertrophy<br>N=97 | Concentric<br>remodeling<br>N=500 | P- value |
|--------------------------|-----------------|------------------------------------|----------------------------------|-----------------------------------|----------|
| AGE(Yrs)                 | 54.47±12.60     | 59.65±12.78                        | 58.98±12.22                      | 55.80±11.56                       | 0.0001** |
| HEIGHT(m)                | 1.66±0.08       | 1.67±0.07                          | 1.66±0.07                        | 1.68±0.07                         | 0.1826   |
| WEIGHT(kg)               | 68.70±15.6      | 68.55±15.66                        | 69.22±15.77                      | 68.56±13.60                       | 0.9240   |
| BMI (kg/m <sup>2</sup> ) | 26.50±5.80      | 26.23±5.81                         | 24.80±5.59                       | 28.98±3.55                        | 0.6440   |
| SBP(mmHg)                | 144±22.30       | 149.55±22.0                        | 141.88±22.0                      | 141.56±22.65                      | 0.0130*  |
| DBP(mmHg)                | 88.22±12.12     | 91.0±13.90                         | 88.32±11.90                      | 89.32±13.60                       | 0.0363*  |
| PP(mmHg)                 | 55.0±16.20      | 59.71±16.0                         | 52.80±15.87                      | 55.00±15.87                       | 0.0038 * |
| MAP(mmHg)                | 105.32±13.78    | 108.53±13.9                        | 103.39±12.88                     | 107.21±13.66                      | 0.0217*  |

**BMI:** Body mass index, **SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure, **BSA:** Body surface area, **PP:** Pulsepressure, **MAP:** Mean arterial pressure. \*significant, \*\*highly significant.

Table 1 shows the relative comparison of the demographic profile of the hypertensive subjects with the variable cardiac geometrical profile with the LV geometrical patterns. 229 (22.9%) of the subjects had concentric hypertrophy (CH), 97 (9.7%) had eccentric

hypertrophy, 174 (17.4%) had normal geometry and the rest 500 (50%) of the study subjects had concentric remodeling. Patients with concentric hypertrophy were older than the eccentric hypertrophy and concentric remodelling. These patients also had relative increased SBP, DBP, PP, MAP those with normal geometry.

**Table 2: Basic demographic and blood pressure parameters in hypertensive patients**

| Variables                | Hypertensive (n=1000) |
|--------------------------|-----------------------|
| Age (yrs)                | 56.87± 11.80          |
| Sex- males               | 560                   |
| Females                  | 440                   |
| Height (meters)          | 1.65±0.09             |
| Weight (kg)              | 71.45±14.88           |
| BMI (Kg/m <sup>2</sup> ) | 26.06± 4.45           |
| SBP (mmHg)               | 144.45±20.45          |
| DBP (mmHg)               | 88.23± 11.89          |
| BSA (mmHg)               | 1.78±5.33             |
| PP (mmHg)                | 56.00±15.99           |
| MAP(mmHg)                | 107.22±13.4           |

**BMI:** Body mass index, **SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure, **BSA:** Body surface area, **PP:** Pulse pressure, **MAP:** Mean arterial pressure. \*significant, \*\*highly significant.

It can be appreciated in Table 1 that out of 1000 hypertensive patients 560 were male and 440 were female patients. The mean age was 56.87±11.80. The demographic profile of the study subjects is shown in

table 2. The average body mass index (BMI) of the patient was 26.06±4.45 and mean SBP was 144.45±2.45 and mean DBP was 88.23±11.89 respectively.

**Table 3: Echocardiography parameters of hypertensive patients in LV geometrical patterns**

| Variables  | Normal<br>N=174 | Concentric<br>hypertrophy<br>N=229 | Eccentric<br>hypertrophy<br>N=97 | Concentric<br>remodelling<br>N=500 | P-value  |
|------------|-----------------|------------------------------------|----------------------------------|------------------------------------|----------|
| LVIDd (mm) | 46.77± 5.00     | 46.74±6.99                         | 56.86±7.77                       | 40.56±6.00                         | 0.9617   |
| IVSD (mm)  | 10.11±2.23      | 13.89±2.88                         | 10.99±2.07                       | 12.08±2.05                         | 0.0001** |
| PWD (mm)   | 8.88±1.32       | 15.34±7.99                         | 10.56±1.79                       | 12.06±1.55                         | 0.0001** |
| LAD (mm)   | 33.45±5.55      | 38.90±17.67                        | 37.89±7.98                       | 34.33±18.10                        | 0.0001** |

|                                  |              |              |              |              |          |
|----------------------------------|--------------|--------------|--------------|--------------|----------|
| <b>EF%</b>                       | 66.70±12.32  | 69.00±11.80  | 556.76±17.66 | 71.10±10.99  | 0.0579*  |
| <b>FFS%</b>                      | 31.22±9.56   | 33.7±10.99   | 26.34±10.99  | 34.88±7.89   | 0.0182*  |
| <b>RWT (mm)</b>                  | 0.34±0.06    | 0.60±0.35    | 0.37±0.054   | 0.55±0.10    | 0.0001** |
| <b>LVM</b>                       | 157.34±16.88 | 210.00±65.23 | 154.01±7.99  | 167.43±27.66 | 0.0001** |
| <b>LVMI (gm/m<sup>2.7</sup>)</b> | 50.76±14.98  | 42.88±1.15   | 36.40±4.99   | 41.22±6.99   | 0.0001** |
| <b>E-wave (m/s)</b>              | 66.34±20.65  | 65.66±17.87  | 72.33±24.87  | 62.22±15.56  | 0.7238   |
| <b>A-wave (m/s)</b>              | 69.32±15.60  | 76.21±18.95  | 68.67±24.67  | 70.45±17.23  | 0.0001** |
| <b>E/A velocity</b>              | 1.04±0.43    | 0.95±0.32    | 1.54±0.67    | 0.94±0.23    | 0.0164*  |
| <b>DT (m/s)</b>                  | 201.20±49.55 | 212.56±53.88 | 199.22±59.89 | 212±47.66    | 0.0306** |
| <b>IVRT (m/s)</b>                | 93.89±25.66  | 107.11±32.00 | 106.33±33.00 | 97.00±25.00  | 0.0001** |

**LVIdD:** left ventricular internal dimension in diastole, **IVSD:** Internalseptal dimension, **PWD:** Posterior wall dimension, **LAD:** left atrial internal dimension, **EF%:** Ejection fraction of LV, **FFS%:** fractional fibre shortening, **RWT:** relative wall thickness, **LVM:** Left ventricular mass, **LVMI:** left ventricular mass index, **A velocity:** active velocity of mitral filling, **E velocity:** passive velocity of mitral filling, **DT:** deceleration time, **IVRT:** Interventricular relative transport. \*-significant, \*\*highly significant.

Various cardiac various LV geometrical patterns are shown in Table 3. The internal LV dimension was relatively more in concentric hypertrophy as compared to the other variables. The left atrial dimension was also higher in concentric hypertrophy and eccentric hypertrophy as compared to the other types.

Patients with eccentric hypertrophy had lower indices of LV function in terms of Ejection fraction (EF%) and Fractional fibre shortening(FFS%) as compared to other variables.

Color Doppler imaging showed a lesser degree of diastolic dysfunction in hypertensive patients with abnormal geometrical profile. These parameters included the E-velocity & A-velocity across the mitral valve, deceleration time (DT).

Left ventricular mass (LVM) and Left ventricular mass index (LVMI) was significantly higher in case of hypertensive abnormal geometry especially in concentric and eccentric hypertrophy rather than normal geometry and concentric remodeling as depicted in table 3.

## Discussion

In our study, patients with concentric hypertrophy were significantly older than those with normal geometry, which is similar to the findings of previous studies.<sup>21,22</sup>

In the present study we found no significant alteration in terms of height, weight and BMI, which would have altered the geometry of left ventricle. Each LV geometrical pattern carries a different risk profile for major adverse cardiovascular events.<sup>23</sup> LV hypertrophy is a powerful independent predictor of morbidity and mortality in hypertensive patients.<sup>24</sup> We also observed enhanced longitudinal LV function and augmented EF with increasing degrees of concentric remodelling as earlier reported in London by Chahal et al.<sup>20</sup>

Two main definitions of echocardiography LVH based on prognostic data are in current use: (i) LV mass indexed to height (m<sup>2.7</sup>) ≥51 g in both genders<sup>22</sup> and

(ii) LV mass indexed to body surface area (m<sup>2</sup>) >125 in both genders.

Echocardiography is also useful in assessing the different types of LV geometric adaptation to increased cardiac load.<sup>25</sup> The characteristics of concentric hypertrophy increases in both mass and relative wall thickness, whereas those of eccentric hypertrophy are increased mass and a relative wall thickness < 0.45.

Remodelling is said to be concentric when thickness increases with respect to radius, but without an increase in LV mass. Concentric hypertrophy appears to carry the highest risk and eccentric hypertrophy an intermediate risk, while concentric remodelling is probably associated with a smaller, albeit noteworthy risk.

Our result showed that concentric remodelling was the most common LV geometric pattern, next to concentric hypertrophy which is also elucidated by Wang et al and Fox et al. A study conducted at USA (Texas) the most common LV geometrical pattern was eccentric hypertrophy with or without any evidence of coronary artery disease Environmental factors do play a role in ethnic differences and genetic variability.<sup>26</sup>

LV systolic performance can be measured both at the endocardium by fractional shortening, reflecting chamber function, and at the midwall, where circumferential fiber contraction makes a greater contribution to stroke volume.<sup>27</sup>

Midwall fractional shortening has important prognostic significance.<sup>15,22</sup> Video densitometry in hypertensive patients with LVH, and diabetes indicate that this technique can complement clinical evaluation by revealing preclinical end-organ damage.<sup>28,29</sup>

In several studies the adjusted risk of cardiovascular morbidity associated with baseline LVH ranges from 1.5 to 3.5 with a weighted risk ratio of 2.3 for all studies combined,<sup>1,15,18</sup> the adjusted risk of all-cause mortality associated with baseline LVH ranges from 1.5 to 8, with a weighted mean risk ratio of 2.5 for all studies combined.<sup>30</sup>

In our study we found disproportionate increment in the LVM, LVMI & RWT in hypertensive patients

because of the structural remodeling of cardiomyocytes, non-myocytes, and fibroblasts that occurs in cardiac hypertrophy contributes to perivascular fibrosis, initially around intramural coronary arteries and thereafter in the interstitial space.<sup>31</sup>

Increase in fibrillar collagen types I and III lead to progressive abnormalities of diastolic ventricular filling and relaxation. LV systolic function depends closely on myocardial afterload. LV fractional shortening or ejection fraction, measured at the endocardium, reflects chamber dynamics, but does not necessarily provide a direct measure of myocardial fiber shortening.<sup>32</sup> Circumferential end-systolic stress reveals that myocardial chamber function is often overestimated in hypertension, particularly if LV wall thickness is increased.<sup>15</sup> Several studies have shown that LV midwall function is commonly reduced by 15% to 20% in hypertensive patients. Low midwall fractional shortening has proved an independent predictor of cardiovascular morbidity and mortality in hypertensive patients, as well as in healthy elderly subjects and American Indians.<sup>28,29,32,33</sup>

Diastolic dysfunction may be observed early in the natural history of hypertension and also in the normotensive children of hypertensive parents.<sup>34</sup> It becomes more frequent in the presence of hypertensive LVH, and is influenced by advancing age, high heart rate and obesity. LV diastolic dysfunction has been increasingly diagnosed in asymptomatic hypertension by Echo.<sup>35</sup>

Other study have also demonstrated that hypertensive patients may have diastolic dysfunction, regardless of the differences in their structural geometries.<sup>36,37</sup> Also diastolic dysfunction differed in various LV geometrical patterns in hypertensives.

The PIUMA study showed an association between E/A ratio changes and significant increases in cardiovascular events in a cohort of 1839 middle-aged hypertensives.<sup>38</sup> The frequency of congestive heart failure increased dramatically with the severity of diastolic dysfunction.<sup>39</sup>

## Conclusion

Indeed, it is true that diastolic heart failure in hypertensive patients is found in one third of the cases but the mortality rate is lower than other forms of heart failure, and morbidity is high.

Therefore, it is categorically advocated that early recognition and appropriate therapy should be instituted to prevent progression of diastolic heart failure. LVH and failure are frequently associated with coronary artery disease, and hypertension is a major risk factor for coronary atherosclerosis.

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