ORIGINAL RESEARCH PAPER

General Medicine

ASSESSMENT OF THE RELATION OF CHANGES IN LEFT VENTRICULAR MASS WITH DIASTOLIC DYSFUNCTION IN UNTREATED HYPERTENSIVES

KEY WORDS: Diastolic Dysfunction Left Ventricular Hypertrophy, Untreated Hypertensives, Left Ventricular Mass

Dr. Koushik Reddy. T* — 3rd Year Post Graduate, General Medicine, Meenakshi Medical College Hospital And Research Institute, Kanchipuram *Corresponding Author

Dr. Manu Reddy. S — 2nd Year Post Graduate, General Medicine, Meenakshi Medical College Hospital And Research Institute, Kanchipuram

Dr. Srinivasagalu. K — Professor Of General Medicine, Meenakshi Medical College Hospital And Research Institute, Kanchipuram

ABSTRACT

BACKGROUND AND OBJECTIVES : Assessment of the relation of changes in left ventricular mass with diastolic dysfunction in untreated hypertensives

METHODOLOGY:100 cases of untreated hypertensives included in the study after taking into account all the inclusion and exclusion criteria. Echocardiography was done for all to access the relation of left ventricular mass index and diastolic dysfunction

RESULTS : Out of 100 patients, 62 patients have grade 1 diastolic dysfunction with increased left ventricular mass, 26 have grade 2 diastolic dysfunction with increased left ventricular mass, and 12 have grade 3 and 4 diastolic dysfunction.

CONCLUSION : The early diastolic filling impaired in hypertensive patients with increased left ventricular mass. The patient having a normal architecture or concentric remodeling have a normal diastolic function. Those with concentric hypertrophy with or without eccentric remodeling will demonstrate diastolic dysfunction

INTRODUCTION

Systemic hypertension affects 1.4 billion worldwide and remains the most readily identifiable and reversible risk factor for myocardial infarction, heart failure, peripheral arterial disease, aortic dissection, stroke, and atrial fibrillation. As we entered into the age of the inactivity and obesity, increasing obesity and population aging in developing and developed countries, the global burden of hypertension was also increasing and projected to affect more than 1.6 billion persons by the year 2025[1]. In 2016, out of 40.5 million or 71% of deaths due to noncommunicable diseases globally, cardiovascular disease with hypertension accounted for 17.9 million or 44% of deaths. Still, hypertension remains a leading risk factor of death and significant public health problems worldwide.

Hypertension is a significant risk factor not only for CAD but also for heart failure and LVH. In hypertensive patients, LVH is an independent predictor of morbidity and mortality, predisposing to heart failure, ischemic stroke, atrial fibrillation, ventricular tachyarrhythmia, and stroke.

In the hypertrophied hypertensive heart, coronary blood flow will be normal at rest, but vasodilator reserve becomes impaired when myocyte mass outstrips the blood supply. The combination of subendocardial ischemia and cardiac fibrosis impairs diastolic relaxation leading to exertional dyspnoea and diastolic heart failure[2]. As about 30% of patients with heart failure have a preserved LVEF, Diastolic function assessment should be an integral part of an evaluation of cardiac function. Currently, echocardiography is the best non-invasive way to evaluate the diastolic function and to estimate filling pressure.M-mode,2D, and Doppler echocardiography are all helpful in evaluating diastolic function

MATERIALS AND METHODS

1. SOURCE OF DATA:

This study conducted from 2017- 2019 at Meenakshi medical college and research institute, Kanchipuram. Patients included in the study after Informed consents.

2. SELECTION CRITERIA:

100 patients in age ranging from 26 - 55 years who newly detected for high blood pressure (> 140/90 mm of Hg) on routine checkup included in the study. The subjects are taken randomly irrespective of the sex.

INCLUSION CRITERIA

1)Patients of age group 26 -55 years (men and women) with blood pressure above 140 /90 mm of Hg at least twice during three consecutive visits at a 1-week interval.Blood pressure measured in the sitting position with a standard mercury sphygmomanometer at least 3 times at each visit.

2) Patients with no previous antihypertensive treatment

EXCLUSION CRITERIA

1) Patients with antihypertensive treatment
2) Patients were having a history of previous myocardial infarction.
3) Patients who have diabetes.
4) Patients having a history of significant alcohol consumption
5) Patients with rheumatic heart disease.
6) Patients who are an anemic and retroviral disease.

Two-dimensional and Doppler echocardiography:

After completing three consecutive visits, all patients underwent two-dimensional directed M-mode and pulsed Doppler echocardiography examinations at rest

By using Penn's convention formula, the left ventricular mass index calculated:

LVM = 1.04 [(LVIDd + PWT + IVST)3– LVIDd3] – 14 gm.

LVMI = LVM/BSA.

[LVM = left ventricular mass; LVIDd = left ventricle internal dimension in end diastole; PWT = posterior wall thickness; IVST = interventricular septal thickness; LVMI= left ventricular mass index; BSA=body surface area]

The normal left ventricular mass index for the Indian population[3] is :

1.Females :110g/m2

2.Males : 121g/m2

Any value more than this was considered as left ventricular hypertrophy.

By pulsed doppler echocardiography following parameters of diastolic filling were measured:

Peak velocity of the early filling(E); Peak velocity of the late filling(A); and their ratio (E/A).

E/A less than 1 is taken as an indicator of diastolic dysfunction. The parameters like Haemoglobin, Total count, Differential count, Erythrocyte Sedimentation Rate, Blood Urea, Creatinine, Liver function test, Random Blood Sugar, ECG, Chest X-Ray, HIV test (by ELISA), Pulsed Doppler Echocardiography, Two dimensional directed M-Mode Echocardiography recorded at baseline, 3 months and 6 months

STATISTICAL ANALYSIS:

Data were expressed as means ± S.D as where it was appropriate. Statistical correlation between indexes performed with linear regression analysis as appropriate.A statistically significant difference between means of different groups determined by use of the student 't' test. P-value <0.05 was considered statistically significant, <0.01 highly significant and <0.001 very highly significant.

RESULT

Of 100 hypertensive patients, 20 subjects are within the age group of 26–35years,32 subjects within 36-45 years, and 48 subjects within 46-55years. Among them, 68 were males, and 32 were females.

In the present study,82 (82%) belonged to grade I or mild hypertension group, 7 (7%) belonged to grade II or moderate hypertension group and the remaining 11 (11%) belonged to grade III or severe hypertension group

Among 100 patients 62 patients are grade I diastolic dysfunction,26 patients are grade II diastolic dysfunction,12 patients are grade III and grade IV diastolic dysfunction(Table 1)

TABLE 1: TOTAL NUMBER OF PATIENTS WITH VARIOUS GRADES OF DIASTOLIC DYSFUNCTION

Diastolic dysfunction Grading	male	female	total	percentage
Grade I	41	21	62	62%
Grade II	19	7	26	26%
Grade III and Grade IV	8	4	12	12%

TABLE 2. CLINICAL CHARACTERISTICS AND ECHOCARDIOGRAPHIC MEASUREMENTS:

Parameters	Mean Value with Standard Deviation
BMI	20.1±1.9
BSA (m2)	1.64±0.14
SBP (mm of Hg)	154.5±28.8+
DBP (mm of Hg)	96.6±15.4+
LVIDd	46.2±10
LVPWd	10.8±1.8**
RWT	0.49±0.18
IVS (mm)	12.3±2.8+
LVEDV (ml)	106.2±37.2*
LVESV(ml)	42.5±20.7*
EF	61.6±9.3
LVMI (gm/m2)	134.53±51.9**
E (cm/sec)	66.6±7.1
E/A	0.99±1.17*

DBP = Diastolic blood pressure,SBP = Systolic blood pressure ,* P<0.05= significant

** P<0.01=highly significant,+ P<Q.001= very highly significant.

There was no statistically significant differences in age, sex, BSA, and BMI. There was no significant difference in the E velocity also (table 2)

Patients with hypertension further divided into four subgroups.

Subgroup A- patients with normal LVMI and RWT.

Subgroup B- patients with normal LVMI but increased RWT. They showed concentric remodeling.

Subgroup C- patients with increased LVMI and RWT. They, therefore, had concentric hypertrophy.

Subgroup D- patients with concentric hypertrophy with eccentric hypertrophy, i.e., they had normal RWT but increased LVMI.

Of 100 hypertensive patients in this study, Subgroup A had 20 patients (20), Subgroup B had 20 patients (20%), Subgroup C had 32 patients (32%), and Subgroup D had 28 patients (28%)(Table 3)

TABLE3: CLINICAL CHARACTERISTICS AND ECHOCARDIOGRAPHY MEASUREMENTS WITH LEFT VENTRICULAR HYPERTROPHIC PATTERNS

	A	B	C	D
No. of Patients	20	20	32	28
Age (yrs)	30.5±6.4	47.5±3.5+	48.3±2.9+	44.6±7.7+
Sex (M/F)	16:6	12:8	22:10	18:8
BSA (m2)	1.59±0.01	1.55±0.07	1.63±0.16+	1.72±0.18+
BMI	19.7±0.6	20.5±0.4	18.7±1.4	19.6±0.8
SBP (mm of Hg)	138±1.4	146±8.4+	156±15.1+	171.6±5.1+
DBP (mm of Hg)	90±1.4	94±5.7+	96.6±3.1+	106.6±28.9+
LVPWd	8±1.4	11.5±0.7**	12.3±1.6**	10.3±1.2**
LVIDd	42.5±2.1	36±5.6°	45.3±1.1*	56.3±6.1**
IVS (mm)	9.5±2.1	14±2.8**	14.3±3.2**	10.6±1.5**
RWT	0.38±16.3	0.62±0.09**	0.57±0.15**	0.36±0.06
LVESV (ml)	28.5±4.9	15±7.1°	45.6±5.1**	66.6±5.8**
LVEDV (ml)	85.5±16.3	55±20.5°	126.6±30**	133.6±7.1**
EF (%)	66.5±0.7	73±2.8*	61.3±8.1	51.3±1.2
LVMI (gm/m2)	82.52±18.3	87.38±5.4	171.47±49.5**	163.68±35**
E (cm/sec)	69±1.4	73±2.8	59±1.7°	66.6±5.8
E/A	1.10±0.07	1.14±0.06	0.79±0.16	0.98±0.05

+ Group mean > 2 S.D. of Group A means,* Group mean > 1 S.D. of average mean

** Group mean > 2 S.D. of normal mean,° Group mean < 1 S.D. of average mean

°° Group mean < 2 S.D. of normal mean

The hypertensives with alterations in ventricular structure belonged to an older Age group. There was no marked difference in body surface area (BSA) and body mass index (BMI) between the groups A and B, although subgroups C and D had a Slightly higher BSA. Both systolic and diastolic blood pressures were higher in patients with concentric remodeling and concentric hypertrophy alone or combination with eccentric hypertrophy, as compared to group A. The LVPWd and IVS increased in all the subgroups except group A. The the maximum increase has seen the patients with concentric hypertrophy.

TABLE 4: CORRELATION BETWEEN THE LEFT VENTRICULAR MASS INDEX AND ECHOCAR DIOGRAPHY INDICES AND BLOOD PRESSURE:

	LVMI (gm/m2)	P-value
E (cm /sec)	-0.481	<0.05
E/A	-0.409	<0.05
EF (%)	-0.631	<0.01
LVPWd (mm)	0.788	<0.01
LVIDd (mm)	0.681	<0.01

SBP (mm of Hg)	0.705	<0.001
DBP (mm of Hg)	0.763	<0.001

The RWT was within normal limits in patients with eccentric hypertrophy. However, it increased in patients with concentric hypertrophy and concentric remodeling. The LVIDd increased in patients with concentric hypertrophy, and eccentric hypertrophy, with the highest increase in the last group. However, in patients with concentric remodeling, LVIDd was low. Both the LVEDV and LVESV increased in the concentric hypertrophy and eccentric hypertrophy groups, with the highest increase in the last group. Both the LVEDV and LVESV showed a decrease in patients with concentric remodeling. The EF was markedly diminished in the group with eccentric hypertrophy, though it was above the level for systolic dysfunction. It was increased in patients with concentric remodeling, while in the other two groups, it did not differ much. The lowest E velocity recorded in the concentric hypertrophy group- The ratio E/A was less than 1 in groups with concentric hypertrophy and with eccentric hypertrophy. A significant negative correlation exists between LVMI with E velocity, the ratio E/A and EF. LVMI also showed a significant positive correlation with LVPWd, LVIDd, systolic, and diastolic blood pressures.

DISCUSSION

Diastolic dysfunction is a significant cause of heart failure, early in the course of hypertension. In the present day, diastolic dysfunction assumed a much greater significance, where appropriate potent anti-hypertensive drugs can delay heart failure from systolic dysfunction[4]. The left ventricular function assessment is an essential component for the evaluation of the hypertensive patient. Anatomic validity of echocardiographic methods of determining left ventricular hypertrophy using the Penn and American society of echocardiography measurements was demonstrated in 2 independent correlation studies, using the sex-specific criteria, which showed a high sensitivity of 97% and specificity of 96%.

GRADE 1 DIASTOLIC DYSFUNCTION(IMPAIRED RELAXATION)

An early abnormality of diastolic filling is abnormal myocardial relaxation. During this stage of diastolic dysfunction, an adequate diastolic filling period is critical to maintaining normal filling without increasing filling pressure. As long as LA pressure remains normal, the pressure crossover between the LV and LA occurs late, and the early transmitral pressure gradient decreased. Subsequently, IVRT is prolonged. Mitral E velocity decreased, and A velocity is increased, producing an E/A ratio of less than 1, with prolonged DT. Pulmonary vein diastolic forward flow velocity (PVD) parallelled mitral E velocity and decreased with compensatory[5]increased flow in systole. The duration and velocity of pulmonary vein atrial flow reversal (PVA) are usually normal. Ea and mitral flow propagation velocity reduced, usually less than 7 cm/sec (at septal annulus) and less than 50 cm/sec, respectively. In most patients with the described mitral inflow velocity pattern, diastolic filling pressure not increased, and E/Ea is ≤ 8. This pattern has been designated as grade 1a diastolic dysfunction to emphasize that filling pressure increased while there is a standard grade 1 mitral inflow velocity pattern.

GRADE 2 DIASTOLIC DYSFUNCTION

This stage is pseudo-normalized mitral flow filling pattern, and it represents a moderate stage of diastolic dysfunction.[6] As diastolic function worsens, the mitral inflow pattern goes through a phase resembling a regular diastolic filling pattern, that is, E/A ratio of 1 to 1.5 and standard DT (160 to 240msec). This is the result of a moderately increased LA pressure superimposed on delayed myocardial relaxation.

GRADE 3-4 DIASTOLIC DYSFUNCTION OR SEVERE DIASTOLIC DYSFUNCTION

This stage is restrictive filling and can be present in any cardiac abnormality or in a combination of abnormalities that produce decreased LV compliance and markedly increased LA pressure. Examples include decompensated congestive systolic heart failure, advanced restrictive cardiomyopathy, severe coronary artery disease, acute severe aortic regurgitation, and constrictive pericarditis. Early rapid diastolic filling into a less complaint LV causes a rapid increase in early LV diastolic pressure, with rapid equalization of LV and LA pressures producing a shortened DT. Atrial contraction increases LA pressure, but A velocity and duration shortened because LV pressure increases even more rapidly. When LV diastolic pressure markedly increased, there may be diastolic mitral regurgitation during mid-diastole or with atrial relaxation. Therefore restrictive filling with severe diastolic dysfunction is characterized by increased E velocity, decreased A velocity (<<E) with E/A ratio greater than 2 and shortened DT (< 160 ms) and IVRT (< 70 ms). Systolic forward flow velocity in the pulmonary vein is decreased because of increased LA pressure and decreased LA compliance.[7] Because of myocardial relaxation impaired in patients with a restrictive filling pattern, mitral annulus Ea is reduced (< 7 cm/sec). E/Ea is usually higher than 15. Flow propagation velocity may not be reduced in the restrictive filling when the LV cavity is small and systolic function well preserved.

The Valsalva maneuver may reverse the restrictive filling pattern to a grade 1 to 2 pattern, indicating the reversibility of high filling pressure (grade 3 diastolic filling). However, even if the restrictive filling pattern does not change with the Valsalva maneuver, reversibility cannot be excluded because the Valsalva maneuver may not be adequate or filling pressure is too high to be altered by the Valsalva maneuver.

For the diagnosis of LVH, left ventricular wall thickness and left ventricular mass utilized. Following recordings are required to obtain them.[8]

1. Interventricular septal wall thickness (ST)
2. Posterior wall thickness (PWT)
3. Left ventricular internal dimensional (LVIdD)
4. Left Ventricular Mass.

Penns's Conventional Formula calculates it

LVM = 1.04 [(LVIdD + PWT + IVST) 3 – LVIdD3] - 14 gram

(LVM = Left ventricular mass ; LVIdD = Left ventricular internal diameter at end-diastole ; PWT = Posterior wall thickness ; IVST = Interventricular septal thickness)

Left ventricular wall thickness for detecting LVH, achieved lower specificity than sex-specific LVH among normotensive individuals and hypertensive subjects.[9]The overall presence of left ventricular hypertrophy in hypertension as defined by sex-specific reference standard is reported to be 25 to 30%. With 97% specificity by Devereux RB et al., Martinez et al[10] reported LVH to be 26% in hypertension. In similarity to other studies left ventricular hypertrophy detected by 2D – echocardiography in this study is 26% with a specificity of 88%.

In the present study group of 100 patients, 68 males and 32 females. Male are more affected than female patient. In a study by **H. S. Chirmus et al**[11] reported a more significant proportion of left ventricular hypertrophy in men than women

In this study 46-55 years, aged patients are more associated with increased left ventricular mass index and diastolic dysfunction. **Hammond et al**[12]**.** also showed that increased age is associated with increased left ventricular mass.

In this study, it also noted that irrespective of the stage of hypertension most of the patients have type 1 diastolic dysfunction, i.e., impaired relaxation pattern which is found to be the most common except during the later stages of the disease. In most of the studies on diastolic dysfunction in hypertensives, an increase in left ventricular mass seems to be an important factor responsible for impaired diastolic function.[13]

In the present study, the early left ventricular filling index, the ratio E/A, was significantly reduced in patients with hypertension. This occurred early in the evolution of disease when ejection fraction was still normal. The left ventricular mass index showed a significant negative correlation with early diastolic filling (E/A ratio) and ejection fraction. The rise in blood pressure, both systolic and diastolic, showed a significant favorable influence on the increase in ventricular mass.

In the concentric hypertrophic group, both LVEDV and LVESV were increased remarkably, (>2 S.D) thereby representing a volume overload state. Despite increased LV mass, the EF was within normal limits, which probably represents depressed myocardial contractility.

The patients with eccentric hypertrophy had increased LVEDV and LVESV (>2 S.D) also, decreased EF (<2 S.D), thus most probably representing a state with volume overload with grossly depressed contractility. Both these latter groups are unfavorably suited to hypertensive state. They are also the groups showing diastolic dysfunction. In addition to the hypertrophy, volume overload may play a role in the genesis of diastolic dysfunction in these cases.

In the other two groups, the absence of a grossly Increased LV mass, and probablyabsence of volume overload contributed to the maintenance of normal diastolic function. As mentioned earlier, several studies showed the presence of diastolic dysfunction inhypertensives with normal LV mass. The plausible explanations for this phenomenonmay be as follows

1. Effect of treatment, which decreases wall stress and hence the myocyte size.
2. Alteration in neurohumoral adjustments can shift loading factor on myocardium from late to early ejection period, thereby delaying the relaxation
3. Expression of genes, producing calcium sequestration abnormalities. The hypertrophic response of these genes may be compensated by other factors like volume underloading so that the LV mass remains normal.

CONCLUSION

We conclude that early diastolic filling impaired in hypertensives with increased left ventricular mass. In terms of left ventricular adaptation patterns, the patients having concentric hypertrophy with or without eccentric hypertrophy will demonstrate dysfunction. Those with normal architecture or concentric remodeling have a normal diastolic function. Thus, the identification of subgroups with adverse adaptation patterns will help Further in optimizing the anti-hypertensive treatment. Those patients with concentric hypertrophy or eccentric hypertrophy will require more aggressive treatment. On the other hand; patients having a normal architecture or concentric remodeling may manage with non-pharmacological therapy.

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