



LEFT ATRIAL VOLUME AS AN INDEPENDENT PREDICTOR OF HEART FAILURE WITH NORMAL EJECTION FRACTION

Cardiology

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ABSTRACT

Introduction- In approximately 30-50% of the individuals who develop congestive cardiac failure the systolic function as assessed by left ventricular (LV) ejection fraction is either normal or relatively normal.

Aim- Study the relationship between left atrial (LA) volume and LV diastolic dysfunction and LV hypertrophy. Correlate LA volume with cardiovascular risk factors.

Methodology- A total of 60 patients was included in the study. These patients underwent a screening echocardiography to diagnose left ventricular hypertrophy and diastolic dysfunction.

Result- There is a significant correlation between left ventricular hypertrophy and diastolic dysfunction. 79% patients with evidence of diastolic dysfunction by tissue Doppler had a higher left atrial volume.

Conclusion- Increased left ventricular mass is associated with increasing severity of diastolic dysfunction. Increased left ventricular mass is also associated with increased left atrial volume indexed to body surface area. Left atrial volume correlates with the duration of diabetes mellitus. Increasing severity of left ventricular diastolic dysfunction correlates significantly with left atrial volume indexed to body surface area. At milder degrees of diastolic dysfunction, left atrial enlargement may not be the best predictor of severity. But with increasing severity of diastolic dysfunction in left ventricular hypertrophy, left atrial volume indexed to body surface area may be a sensitive and easy marker for assessment of severity and thus the long-term prognosis in terms of atrial fibrillation, stroke and mortality.

KEYWORDS

diastolic dysfunction, hypertrophy, Doppler, echocardiography

INTRODUCTION

In approximately 30-50% of the individuals who develop congestive cardiac failure the systolic function as assessed by left ventricular (LV) ejection fraction is either normal or relatively normal¹⁻⁸. Diastolic dysfunction is an important cause of morbidity in patients with heart disease.⁹ Diastolic dysfunction may be caused by abnormalities of ventricular relaxation, increased ventricular stiffness or a combination of both.¹⁰

The gold standard for evaluation of diastolic dysfunction has been the direct measurement of left ventricular pressure with simultaneous left ventricular volume estimation.¹¹ This allows us to construct pressure-volume curves and determine the exact relationship between these parameters. Unfortunately, this requires an invasive procedure of placing of intraventricular catheters with sophisticated micro manometers, which makes this method unsuitable for routine use.^{12,13} Echocardiography is now the most commonly used method for assessment of diastolic function.^{14,16} In addition to high-resolution 2-D images; Doppler flow velocity offers important information about the dynamics of ventricular filling. Pulsed wave Doppler of the mitral valve and of the pulmonary veins is used for routine assessment of left ventricular diastolic function. Similarly, Doppler investigation of the tricuspid valve and hepatic veins is used to evaluate right ventricular diastolic function. An important limitation of the spectral Doppler assessment of diastolic function is its dependence on loading conditions.^{14, 15} Two new technologies, color M-mode¹⁶ and Doppler Tissue echocardiography¹⁷, have emerged as investigations in complementing the information provided by Doppler echocardiography and may allow us a more complete evaluation of diastolic function. Increased left atrial volume (LAV), which is an indicator of chronic diastolic dysfunction, is an independent marker of cardiovascular risk. Epidemiological studies have observed that in healthy subjects, LAV indexed for body size does not increase with age.^{9, 18-20} Increased LAV is a morphological expression of chronic diastolic dysfunction²¹ and a measure of cardiovascular risk burden.

Increased left atrial size has been shown to be highly predictive of atrial fibrillation (AF) and stroke in the community, and superior to ejection fraction (EF) in the prediction of mortality in patients with myocardial infarction (MI) and dilated cardiomyopathy.¹⁵⁻¹⁷

Aim of this study to determine LA volume by 2D Echo and to correlate LA volume with LV diastolic dysfunction. Study the relationship between LA volume LV diastolic dysfunction and LV hypertrophy and to correlate LA volume with cardiovascular risk factors.

MATERIALS AND METHODS

The study was conducted at the N M WADIA INSTITUTE OF CARDIOLOGY, PUNE. Permission from ethical committee was taken. A total of 60 patients were included in the study. These patients had undergone a screening echocardiography to diagnose left ventricular hypertrophy and diastolic dysfunction.

The echo was performed on Agilent Sonus 4500 2D Echo machine department of cardiology. Left atrial volume was measured using biplane area – length method. The area of the LA was measured by planimetry in the apical two & four chamber views. Then a linear dimension or length was measured from the center of the mitral annulus to the superior border of the chamber. LA volume was calculated as: $LAV = (0.85 * A1 * A2) / L$. This left atrial volume will be indexed to body surface area (LAVi). The body surface area (BSA) was calculated from the height and weight of the patient as follows: $BSA = \text{square root of } \{(\text{height in cm} \times \text{weight in kg}) / 3600\}$. $LAVi = LAV / BSA$. LV mass (M mode) was calculated according to American Society of Echocardiography guidelines by computerized methods.

Pulse wave Doppler examination of mitral inflow was studied for measurement of the early (E) and late (A) diastolic filling velocities. The ratio of E/A was calculated from these values. The deceleration time and the isovolumic relaxation time were also measured using the same pulse wave Doppler examination. Tissue Doppler imaging of

the mitral annulus on the septal leaflet was performed for measurement of the early (E') and late (A') diastolic wall motion. The parameters used were as follows: E wave, A wave, E', A', E/A ratio, E'/A' ratio, Isovolumic relaxation time (IVRT), Deceleration time (DT), Mitral inflow velocity profile. The statistical tests like ANOVA test, Pearson's correlation with SPSS software were applied for correlation between LAVi, LV mass and diastolic dysfunction.

RESULT

The study included 60 patients. The mean age of these patients was 59 years. The maximum number of patients was in the age groups of 50 to 59 years and 60 to 69 years which was 19 in each of the groups. These 60 patients included 49 males and 11 female patients. The patients were categorized according to their duration and presence or absence of hypertension.

33 patients were not hypertensive. 19 patients had hypertension for the duration of less than 5 years. 6 patients had hypertension for more than 6 and less than 10 years. 2 patients had hypertension for more than 10 years. 54 out of the 60 patients did not have diabetes and 6 patients were diabetic. The patients' electrocardiograms were also evaluated for left ventricular hypertrophy. 39 out of 60 patients had evidence of left ventricular hypertrophy on their electrocardiogram. 21 patients did not show evidence of left ventricular hypertrophy on their electrocardiogram.

The left atrial volumes of these patients were calculated by echocardiographic assessment and the patients were divided into four groups based on their left atrial volumes. 16 patients had a left atrial volume of less than 28 ml/m². The maximum number of patients was in the group with left atrial volume index more than 40 ml/m². This group included 38 patients. The geometric mean of the group was 146.94±1.30. The geometric mean was used instead of the arithmetic mean so as to include outliers in giving the group mean. The ratio of E and A velocities was calculated. These were then divided into four groups with a ratio of less than 1, 1 to 1.5, 1.6 to 2.5 and more than 2.5.

The maximum number of patients had E' velocity of less than 8. 35 patients were included in this group. 3 patients had an E' of more than 10. 20 patients had an E' between 8 and 10. 2 patients had an E' of less than 5 indicating diastolic dysfunction. The ratio of E/E' was calculated. On the basis of this ratio patients were divided into 4 groups with a ratio of less than 15, 16 to 19, 20 to 25 and more than 25 respectively. Patients were divided into 3 groups based on their deceleration times (DT). The groups were based on a DT of less than 160 msec, 160 to 240 msec and more than 240 msec. The patients were also divided into three groups according to their isovolumic relaxation times (IVRT). These three groups were based on an IVRT of less than 70(39 subjects), 70 to 90(10 subjects) and more than 90 msec (11 subjects).

50 out of 60 patients had a left ventricular mass index of more than 125 gm/m². 10 patients had a left ventricular mass index of less than 125 gm/m². The geometric mean of LV mass index was 42.14±1.60. 76% of patients with a left ventricular mass of more than 125 gm/m² had a left atrial volume index of more than 28 ml/m² whereas only 24% patients with a left ventricular mass index of more than 125 gm/m² had a left atrial volume of less than 28 ml/m². 96% patients with a left ventricular mass index more than 125 gm/m² had an E/E' of more than 15 indicating diastolic dysfunction, whereas only 50% patients with LV mass index of less than 125 gm/m² had diastolic dysfunction. 42 patients with an E/E' more than 15 had a left atrial volume of more than 28 ml/m², i.e 79% patients with diastolic dysfunction had an elevated left atrial volume. Patients with more severe diastolic dysfunction have a higher LA volume as compared to those with a milder diastolic dysfunction. No patient with severe diastolic dysfunction had a normal LA volume.

Table 1: Distribution of left atrial volume index according to severity of diastolic dysfunction

SEVERITY	Mean LAVi	No. of subjects	Std. Deviation
Mild	25.02	11	4.87
Moderate	48.03	34	15.68
Severe	59.44	15	26.41
Total	46.67	60	20.90

As observed in table 1, it shows that severe diastolic dysfunction has most mean LAVi and standard deviation than moderate and mild

dysfunction.

Table 2: Multiple Parameters according to severity of diastolic dysfunction.

Normal	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Severe (Grade 4)
DT (ms)*	160–240	>240	160–240	<160
E/A*	0.9–1.5	<0.9	0.9–1.5	>2.0
E' (cm/s)	10	<10	<8	<5
E/E' (septal)	1–14	15	15	20
LAVi (ml/m ²)	22 ± 6	>28	>28	>35
IVRT (ms)	70–90	>90	<90	<70

Table 3: ANOVA OF MEAN LAVI

	Variable	N	Mean LAVI	ANOVA	
				F	P
E/E'	15	9	23.52	7.097	0.010*
	15	51	50.75		
LVMI	125	11	37.36	1.895	0.174
	125	49	48.75		

As observed from table 3, the ANOVA of mean LAVi correlates significantly with E/E' which is the best marker for diastolic dysfunction. It did not correlate significantly with LV mass index.

Table 4: DISTRIBUTION OF PATIENTS ACCORDING TO SEVERITY OF DIASTOLIC DYSFUNCTION

SEVERITY	Mean	N	Std. Deviation
Mild	25.02	11	4.87
Moderate	48.03	34	15.68
Severe	59.44	15	26.41
Total	46.67	60	20.90

Table 4 shows standard deviation of patients with mild, moderate, severe diastolic dysfunction. According to table severe diastolic dysfunction had most standard deviation.

Table 5: MULTIPLE ANALYSES BETWEEN VARIOUS GRADES OF DIASTOLIC DYSFUNCTION

		Mean Difference	Std. Error	Significance	95% Confidence Interval	
SEVERITY	SEVERITY				Lower Bound	Upper Bound
MILD	MODERATE	-23.02	6.18	0.001	-38.27	-7.76
	SEVERE	-34.42	7.08	0.000	-51.87	-16.96
MODERATE	MILD	23.02	6.18	0.001	7.76	38.27
	SEVERE	-11.40	5.53	0.131	-25.03	2.23

* The mean difference is significant at the 0.05 level.

Table 6: CORRELATION OF LAVi TO OTHER VARIABLES

	Pearson's correlation	p value
AGE	-0.192	0.141
HT	0.018	0.889
DM	0.436**	<0.001
LVMAS index	0.349**	0.006
E/A	0.557**	<0.001
E/E'	0.379**	0.003

** Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

The study included 60 patients who were selected on the basis of their echocardiographic parameters. These patients were subjected to a detailed echocardiographic examination. Tissue Doppler studies and left atrial volumes were assessed for all these patients. Barnes et al²² studied a population of elderly individuals and demonstrated the importance of LAV as an independent predictor of the first ischaemic stroke or AF.

As seen in the table 6, the left atrial volume indexed to body surface area was correlated with various patient factors, i.e. age, duration of

hypertension, duration of diabetes, left ventricular mass indexed to body surface area, E/A and E/E'. The left atrial volume indexed to body surface area was found to correlate significantly with the duration of diabetes mellitus, left ventricular mass indexed to body surface area, E/A and E/E'. 76% of patients with LV mass index more than 125 mg/m² had a higher LAVi.

In this study, the left atrial volume indexed to body surface area is increased in patients with left ventricular hypertrophy, although the association was not found to be significant. Cioffi et al²³ studied the connection between left ventricular geometry and LA dimension in patients with systemic arterial hypertension and verified that the concentric left ventricular hypertrophy is associated with a higher left atrial volume, thus indicating a higher degree of diastolic dysfunction. This study shows that 96% of patients with a higher left ventricular mass index had diastolic dysfunction. The mean LV Mass index in the group with E/E' < 15 is 123.94 and that in the group with E/E' > 15 is 157.79. The correlation co-efficient for LV Mass index with E/E' > 15 is 0.431, and p value is 0.001 which means that there is a significant correlation between left ventricular hypertrophy and diastolic dysfunction. Coucolo et al²⁴ studied that the severity of left ventricular hypertrophy is a factor which contributes to severity of diastolic dysfunction. Left ventricular mass index correlates significantly with indices of diastolic filling at rest.

This study shows that 79% patients with evidence of diastolic dysfunction by tissue Doppler had a higher left atrial volume. Various tests of significance were applied to left atrial volume indexed to body surface area and E/E'. The correlation coefficient was 0.379 with a p value of 0.003, showing a significant correlation.

As observed in table 2, it was found that LAVi was significantly increased in case of deteriorating diastolic function. E/A and E/E' were found to be strong predictors of diastolic dysfunction and also to correlate with LAVi. Lee et al²⁵ studied the relation between left atrial volume and diastolic function and found that left atrial volume is a useful and easy diagnostic tool for evaluating left ventricular diastolic function.

As showed in table 5, using multiple analysis it was found that there is a significant difference in the mean LAVi between groups with mild versus moderate severity and groups with mild versus severe diastolic dysfunction. Thus in this study it was found that at milder degrees of diastolic dysfunction, left atrial enlargement may not be the best predictor of severity. But with increasing severity of diastolic dysfunction in left ventricular hypertrophy, left atrial volume indexed to body surface area may be a sensitive and easy marker for assessment of severity and thus the long term prognosis in terms of atrial fibrillation, stroke and mortality. It was also found that increasing left ventricular mass index correlates significantly with increasing severity of diastolic dysfunction. Since this was a cross sectional study, long term follow up of these patients for future cardiac events was not done.

The Doppler echocardiographic assessment of diastolic function reflects the combined influence of impairment in LV relaxation (grade I or mild DD) and impairment in LV relaxation with elevation in filling pressures (grade II or moderate DD). When filling pressures are very high, restrictive physiology (grades III and IV or severe DD) is present either because of a decrease in operant compliance (upward shift on the same LV end diastolic pressure-volume relationship) or as a result of a true decrease in LV compliance (upward and leftward shift of the LV end-diastolic pressure-volume relationship). Although these Doppler patterns have been validated with invasive hemodynamic measurements and have been demonstrated to have prognostic value, like any diagnostic test, sensitivity and specificity are imperfect. Further, the comprehensive assessment needed to optimally define diastolic function and filling pressures is technician dependent, requires informed interpretation, and is not routinely performed in all laboratories. Finally, such an assessment provides information about a single point in time and may not reflect the severity of DD over time. Thus, it has been suggested that LAVi may provide a superior and more easily measured index of CV risk.²⁶ However, it was found that although LAVi is highly sensitive and specific for the detection of severe (grade III or IV) DD, it is not a robust marker of mild or moderate DD. Mild, moderate, and severe DD all have prognostic importance within the population as a whole. Chronic and severe elevation of filling pressures is needed to induce significant atrial remodeling and that the minimal or milder degree of atrial pressure

elevation likely associated with grade I or II DD is insufficient to induce clearly abnormal LA volume. In contrast, severe elevation of atrial pressures indicated by advanced (grade III or IV) DD is more likely to have induced significant atrial remodeling making LA volume relatively sensitive for the detection of advanced DD.²⁷

Tsang et al^{22,28} reported that LA volume was more predictive of future atrial fibrillation and other CV events than LA dimension in variable clinical populations. Thus, LA volume may be a more sensitive index of LA remodeling than any other LA dimension and may provide superior prognostic information.

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