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Prevalence of Diastolic Dysfunction in an Asymptomatic Young and Middle Aged Individuals Attending a Tertiary Care Hospital.

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ABSTRACT

Background: Left ventricular (LV) diastolic dysfunction is increasingly recognized as an important cause of heart failure, providing prognostic information that is incremental to systolic function. Symptomatic DD can occur in association to left ventricular (LV) systolic dysfunction or be a determinant of heart failure with preserved systolic function (ejection fraction >50%), which is responsible for 51% of the heart failure cases. We sought to examine the relationship between atrial volume indexed to body surface area (LAVi) and clinical and Doppler echocardiographic parameters in randomly selected participants. **Methods:** The Present study included 1021 subjects of both gender. Two-dimensional and color Doppler imaging were performed to screen for valvular stenosis or regurgitation. Diastolic function was graded as normal, abnormal relaxation (Grade I), pseudonormal (Grade II), and restrictive (Grade III). **Results:** Mean LAVi and the prevalence of LA enlargement increase with worsening diastolic function grade. Distribution of diastolic function and the associated mean LAVi. Atrial size, as measured by LAVi, increases progressively with increasing DD (r <0.20; p<0.01). The prevalence of LA enlargement also increases with increasing severity of DD. After controlling for age, gender, EF, and LAVi, diastolic function grade was associated with all-cause mortality. Adjusting for age, gender, EF, and diastolic function grade, LAVi was not associated with all-cause mortality. **Conclusion:** This study in Indian population suggests that DD contributes to left atrial remodeling and LAVI increase is an expression of DD severity. LAVI increase determinants in this sample with preserved or slightly reduced mean ejection fraction and no significant valvular heart disease are partly related to age, left ventricular hypertrophy, increased filling pressure and decreased LV systolic function.

Keywords: Diastolic dysfunction, Arterial function, Arterial volume.

INTRODUCTION

Left ventricular (LV) diastolic dysfunction is increasingly recognized as an important cause of heart failure, providing prognostic information that is incremental to systolic function.[1] Diastolic dysfunction (DD) is very common, especially in the elderly, and is considered an important prognostic indicator of various cardiac diseases.[2] It is a major cause of heart failure and has been associated to atrial fibrillation development.[3] The prevalence of asymptomatic DD is approximately 25% to 30% of the individuals older than 45 years in the general population.[4] Symptomatic DD can occur in association to left ventricular (LV) systolic dysfunction or be a determinant of heart failure with preserved systolic function (ejection fraction >50%), which is responsible for 51% of the heart failure cases.[5,6]

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Hypertension, ventricular hypertrophy, and other cardiovascular (CV) diseases could potentially lead to diastolic dysfunction (DD), elevation of filling pressures, and atrial remodeling from chronic pressure overload. Indeed, LA volume has been suggested as a marker of the severity and duration of DD, perhaps obviating the need for more complex characterization of diastolic function and filling pressures with Doppler echocardiography.[7,8]

During diastole, the LA is directly exposed to LV pressure that increases with worsening LV diastolic dysfunction. Consequently, LA pressure increases in order to maintain adequate LV filling.[9] This results in increased LA wall tension and dilatation of the LA. Previous study has shown a strong association of LA volume with LV diastolic function grade.[10]

We sought to examine the relationship between atrial volume indexed to body surface area (LAVi) and clinical and Doppler echocardiographic parameters in randomly selected participants. Further, we examined the predictive characteristics for use of LAVi to detect DD as defined by Doppler. Lastly, we examined the relative prognostic implications of DD and LA remodeling in the population.

MATERIALS AND METHODS

This cross sectional type of study was conducted in the departments of General Medicine, ESIC medical college and PGIMSR, Chennai, from April 2018 to September 2018. Present study included 1021 subjects of both gender. The study population included 18 to 60 years subjects of both gender.

Each subject's medical record was reviewed by trained nurse abstractors using established criteria for hypertension,[11] myocardial infarction and congestive heart failure.[12,13] In addition, a clinical diagnosis of coronary artery disease, diabetes mellitus, and history of atrial dysrhythmias were recorded. All six of these diagnoses are combined and used as a single variable: CV disease.

Two-dimensional and color Doppler imaging were performed to screen for valvular stenosis or regurgitation. Participants were labeled as having valve disease if they had more than moderate regurgitation or stenosis. Left ventricular (LV) mass (M-mode) was calculated according to the American Society of Echocardiography guidelines.[14] The LA dimension was measured by two-dimensional guided M-mode echocardiography obtained in the parasternal short-axis view at the base of the heart according to American Society of Echocardiography recommendations.[15]

Mitral inflow was assessed from the apical 4-chamber view with pulsed wave Doppler by placing a 1–2 mm sample volume between the tips of the mitral leaflets during diastole. From the mitral inflow profile, the E- and A-wave velocity, E-deceleration time (DT), A-wave duration, and E/A velocity ratio were measured. Pulmonary venous velocities were obtained from the same window with the sample volume placed 1 cm into the right upper PV. The flow velocities were recorded, the ratio of systolic to diastolic flow (S/D ratio) was calculated and duration of atrial reversal flow was measured. Doppler tissue imaging was used to measure E0 and A0 velocities by placing a 1–2 mm sample volume in the septal and lateral mitral annulus. LV diastolic function was determined using standard echocardiographic parameters including E/A velocity ratio, E-DT, PV atrial reversal velocity and duration, PV S/D ratio, and mitral E/E0 ratio. Diastolic function was graded as normal, abnormal relaxation (Grade I), pseudonormal (Grade II), and restrictive (Grade III). Pseudonormal (Grade II) is differentiated from normal by having (i) PV atrial reversal duration longer than mitral A duration by 30 ms; or (ii) peak PV atrial reversal velocity .35 cm/s; or (iii) mitral E/E0.[10] (lateral annulus) or.[15] (septal annulus).

This study was approved by the ethical committee of medical college and hospital, All the participants gave written informed consent.

Statistical methods.

Continuous variables are summarized as mean values ± SD and categorical data as a percent of the group total. The association of natural log LAVi with clinical and echocardiographic variables was examined in stages using linear regression. The log transformation of LAVi was used to satisfy the assumptions necessary for the modelling. All the Statistical analysis was done by SPSS software (version 13.0).

RESULTS

From the overall populations of 1021, LA volume could not be measured in 72 subjects, and in 131 subjects the diastolic assessment was inconclusive. This left a total of 828 subjects with data for LAVi and in whom diastolic function was able to be graded.

Table 1: Predictive Characteristics of LAVi in diastolic dysfunction patients within the Study Population

	AUC (CI)	Partition LAV i (ml/m2)	Sensitivity	Specificity
Any DD (gr I-IV)	0.66 (0.59-0.68)	23.6	0.53	0.65
Moderate to severe DD (gr II, III or IV)	0.85 (0.79-0.88)	26.4	0.7	0.79
Severe DD (gr III or IV)	0.99 (0.92-1.03)	34.7	0.94	0.95

Table 2: Predictive Characteristics of LAVi in diastolic dysfunction patients with normal diastolic dysfunction subjects

	AUC (CI)	Partition LAV i (ml/m2)	Sensitivity	Specificity
Mild (gr I)	0.59 (0.54-0.61)	22.2	0.62	0.54
Moderate (gr II)	0.87 (0.82-0.89)	24.5	0.76	0.71
Severe (gr III or IV)	1.02 (0.97-1.05)	31.6	1.04	0.96

Participant demographics. The characteristics of these 828 participants are presented in

Table 3: Basic characteristics of the participants

Male gender	
Age (Yrs) (mean ± SD)	54 ± 17
Height (m) (mean ± SD)	164 ± 10
Weight (Kg) (mean ± SD)	77 ± 16
BSA m2 (mean ± SD)	1.93 ± 0.35
LV mass (mean ± SD)	99 ± 35
Ejection fraction (%)	66 ± 8
Hypertension (%)	231 (28%)
CAD (%)	83 (10%)
Diabetes (%)	58 (7%)
MI (%)	34 (4%)
H/O arterial fibrillation (%)	24 (3%)
Arterial fibrillation (%)	2 (0.2%)
CHF (%)	8 (1%)

Mean LAVi and the prevalence of LA enlargement increase with worsening diastolic function grade. [Table 3] demonstrates the distribution of diastolic function and the associated mean LAVi. Atrial size, as measured by LAVi, increases progressively with increasing DD (r <0.20; p<0.01). The prevalence of LA enlargement also increases with increasing severity of DD.

Table 4: LAVi according to diastolic function grade

Diastolic grade	N	% of population	LAV i (ml/m2)	% Meeting criteria for LAE
Normal	612	73	25 ± 7	7
Grade I	157	19	28 ± 9	9
Grade II	59	7	32 ± 8	48
Grade III to IV	6	1	50 ± 11	100

We defined the strength of the association between LAVi and DD before and after controlling for pertinent covariates [Table 4].

Age, LV mass index (LVMi), and grades I, II, and III to IV DD all had a positive association with LAVi, whereas female gender and higher EF were inversely related to LAVi. In multivariate models, age, gender, LVMi, and DD grade were independently associated with LAVi. We constructed specific models to examine the additive contribution of variables to a model predicting atrial size.

Table 5: Determinants of LAVi

	Bivariate nalysis		Adjusted Analysis	
	Effect	p value	Effect	p value
Age	+9%	<0.01	+6%	<0.01
Female	-7%	<0.01	-5%	<0.01
Ejection fraction (%)	-4%	<0.01	-2%	>0.05
LV mass index (g/m2)	+12%	<0.01	+8%	<0.01
Gr I DD	+8%	<0.01	+2%	>0.05
Gr II DD	+39%	<0.01	+23%	<0.01
Gr III to IV DD	+99%	<0.01	+73%	<0.01

After controlling for age, gender, EF, and LAVi, diastolic function grade was associated with all-cause mortality. Adjusting for age, gender, EF, and diastolic function grade, LAVi was not associated with all-cause mortality.

Table 6: Multivariate Analysis of Predictors of All-Cause Mortality

	Chi Square	Hazard ratio	p value
Age (per yr)	22.5	1.08	<0.01
Female gender	0.09	1.09	>0.05
Ejection fraction (per 1%)	9.76	0.96	<0.01
Mild DD (grade I DD vs. normal diastolic function)	10.31	3.74	<0.01
Moderate DD (grade II DD vs. normal diastolic function)	9.06	4.32	<0.01
Severe DD (grade III or IV DD vs. normal diastolic function)	8.15	7.39	<0.01
LAVi (quartile 2 vs. quartile 1)	1.03	0.58	>0.05
LAVi (quartile 3 vs. quartile 1)	0.03	1.08	>0.05
LAVi (quartile 4 vs. quartile 1)	0.02	0.93	>0.05

DISCUSSION

This was one of the first studies based on the Indian population to demonstrate progressive increase in left atrial volume with worsening diastolic dysfunction in adults with relatively preserved systolic function and representative occurrence of cardiovascular disease risk factors. Additionally, we were able to verify in this series the independent predictors of LAVI increase, related to known risk factors such as age and LV hypertrophy and systolic dysfunction.

LA volume as an index of atrial remodeling. Studies using LA dimension measured by M-mode echocardiography to assess LA remodeling have demonstrated that LA enlargement occurs in persons with CV disease and that LA remodeling predicts CV events.[16-18] Because the LA may become less spherical as it remodels, LA volume is proposed as a better index of LA remodeling, and indeed we have previously reported that LA volume displays a somewhat stronger association with the presence of CV disease in the general population.[19] Tsang et al 20 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 LA dimension and may provide superior prognostic information.

Our main finding was the demonstration of the direct influence DD exerts on left atrial remodeling, as previously observed.[10] These results reinforce the concept of the prognostic role of left atrial dilation as cardiovascular event marker (as exemplified by atrial fibrillation and heart failure), associated to other risk factors traditionally linked to bad prognosis.[10,11]

Various methods of LA volume measurement have been described: the biplane or single plane area-length method,[14] the biplane or single plane Simpson's disc method,[15,16] the prolate-ellipsoid method,[17] and the elliptical model.[13] We used the elliptical method that does not require endocardial tracing. Instead, this method incorporates two short-axis and one long-axis measurement and has been previously validated.[13]

Left atrial remodeling can be seen in various cardiac diseases, resulting from volumetric or pressoric hemodynamic overload. DD represents an additional component to left atrial remodeling. In DD, abnormal LV relaxation and reduced LV compliance occur as a consequence of modifications in the interaction between actin and myosin, increased collagen deposition and cardiac viscoelastic properties changes. 21 On the initial DD phases (grade I), there is only increased participation of left atrial active contraction, which becomes more vigorous in order to surpass the relaxation difficulty, leading to A wave increase in mitral Doppler, without evident structural alterations in this chamber. With the progression of DD, this compensatory mechanism fails and the total atrial filling capacity is compromised, leading to atrial remodeling. Left atrial pressure increases to maintain adequate left ventricular filling, leading to increasing tension at the atrial walls, chamber dilation and atrial myocardial stretching. LAVI increase reflects, thus, the chronic exposure of the left atrium to high LV filling pressures and DD severity.[22]

We found that LA remodelling is present in patients with LV diastolic dysfunction. Indexed LA Volmax has a strong and graded relation to the severity of LV diastolic function grade. In addition, it is also able to discriminate pseudonormal from normal LV diastolic filling patterns with a high degree of accuracy. The role of LA size as a marker of LV diastolic function is well-known and accordingly, we found a strong relation between indexed LA Volmax and LV diastolic function grade.[23-25] Tsang et al,[18] had previously also demonstrated that LA Volmax reflects the severity of LV diastolic dysfunction. During diastole, the LA is directly exposed to LV pressure, which increases with increasing severity of LV diastolic dysfunction. Consequently, LA pressure increases in order to maintain adequate LV filling. This causes an increase in LA wall tension, resulting in stretching and dilatation of the LA. Thus, LA volume probably reflects chronic exposure of the LA to abnormal LV diastolic function and the resultant increased LA filling pressure.

The Doppler echocardiographic assessment of diastolic function reflects the combined influence of impairment in LV relaxation (grade I DD) and impairment in LV relaxation with elevation in filling pressures (grade II DD). When filling pressures are very high, restrictive physiology (grades III and IV DD) is present either because of a decrease in operant compliance (upward shift on the same LV enddiastolic 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] 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, whereas LAVi adds no incremental prognostic value beyond that provided by DD. These findings suggest that, at least in a population-based setting, LAVi is not an adequate surrogate for comprehensive Doppler assessment of DD. We speculate that 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.

CONCLUSION

This study in Indian population suggests that DD contributes to left atrial remodeling and LAVI increase is an expression of DD severity. LAVI increase determinants in this sample with preserved or slightly reduced mean ejection fraction and no significant valvular heart disease are partly related to age, left ventricular hypertrophy, increased filling pressure and decreased LV systolic function.

REFERENCES

1. Xie GY, Berk MR, Smith MD, Gurley JC, DeMaria AN. Prognostic value of Doppler transmitral flow patterns in patients with congestive heart failure. J Am Coll Cardiol 1994;24:132–9.
2. Grossman W. Defining diastolic dysfunction. Circulation. 2000;101(17):2020-1.
3. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol. 2002;90(12):1284-9.
4. Lester SJ, Tajik AJ, Nishimura RA, Oh JK, Khandheria BK, Seward JB. Unlocking the mysteries of diastolic function: deciphering the Rosetta Stone 10 years later. J Am Coll Cardiol. 2008;51(7):679-89.
5. Gottdiener JS, McClelland RL, Marshall R, Shemanski L, Furberg CD, Kitzman DW, et al. Outcome of congestive heart failure in elderly persons: influence of left ventricular systolic function. The cardiovascular Health Study. Ann Intern Med. 2002;137(8):631-9.
6. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss C, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. J Am Coll Cardiol. 1999;33(7):1948-55.
7. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol 2002;90:1284 –9.

8. Tsang TS, Gersh BJ, Appleton CP, et al. Left ventricular diastolic dysfunction as a predictor of the first diagnosed nonvalvular atrial fibrillation in 840 elderly men and women. J Am Coll Cardiol 2002;40:1636–44.
9. Greenberg BH, Chatterjee K, ParmleyW,Werner J, Holly A. The influence of left ventricular filling pressure on atrial contribution to cardiac output. Am Heart J 1979;98:742–51.
10. Tsang TS, Barnes ME, Gersh BJ, Bailey K, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol 2002;90:1284–9.
11. The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413– 46.
12. Gillum RF, Fortmann SP, Prineas RJ, Kottke TE. International diagnostic criteria for acute myocardial infarction and acute stroke. Am Heart J 1984;108:150–8.
13. McKee PA, Castelli WP, McNamara PM, Kannel WB. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971;285:1441– 6.
14. Park SH, Shub C, Nobrega TP, Bailey KR, Seward JB. Twodimensional echocardiographic calculation of left ventricular mass asrecommended by the American Society of Echocardiography: correlation with autopsy and M-mode echocardiography. J Am Soc Echocardiogr1996;9:119 –28.
15. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
16. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation 1994;89:724 –30.
17. Benjamin EJ, D'Agostino RB, Belanger AJ, Wolf PA, Levy D. Left atrial size and the risk of stroke and death. The Framingham Heart Study. Circulation 1995;92:835– 41.
18. Tsang TS, Barnes ME, Bailey KR, et al. Left atrial volume: important risk marker of incident atrial fibrillation in 1655 older men and women. Mayo Clinic Proc 2001;76:467–75.
19. Pritchett AM, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Left atrial volume as an index of left atrial size: a population-based study. J Am Coll Cardiol 2003;41:1036–43.
20. Tsang TS, Barnes ME, Gersh BJ, et al. Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography. J Am Coll Cardiol 2003;42:1199–205.
21. Dent CL, Bowman AW, Scott MJ, Allen JS, Lisauskas JB, Janif M, et al. Echocardiographic characterization of fundamental mechanisms of abnormal diastolic filling in diabetic rats with a parameterized diastolic filling formalism. J Am Soc Echocardiogr. 2001;14(12):1166-72.
22. Nishimura RA, Tajik AJ. Evaluation of diastolic filling of left ventricle in health and disease: Doppler echocardiography is the clinician's Rosetta Stone. J Am Coll Cardiol 1997;30:8–18.
23. Simek CL, Feldman MD, Haber HL, Wu CC, Jayaweera AR, Kaul S. Relationship between left ventricular wall thickness and left atrial size: comparison with other measures of diastolic function. J Am Soc Echocardiogr 1995;8:37–47.
24. Appleton CP, Galloway JM, Gonzalez MS, Gaballa M, Basnight MA. Estimation of left ventricular filling pressure using two dimensional and Doppler echocardiography in adult patients with cardiac disease: additional value of analyzing left atrial size, left atrial ejection fraction and the difference in duration of pulmonary venous and mitral inflow velocity at atrial contraction. J Am Coll Cardiol 1993;22:1972–82.
25. Matsuda M, Matsuda Y. Mechanism of left atrial enlargement related to left ventricular diastolic impairment in hypertension. Clin Cardiol 1996;19:954–9.
26. Douglas PS. The left atrium: a biomarker of chronic diastolic dysfunction and cardiovascular disease risk. J Am Coll Cardiol 2003;42:1206–7.

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