



## **Impact of Left Ventricular Diastolic Dysfunction (Grade I) on Left Atrial Size assessed by 2D Echocardiography.**

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### **Abstract**

**Introduction:** Though LA enlargement is associated with diastolic dysfunction as the progression of DD may lead to an elevated LV filling pressure, this study is designed to see LA diameter in LV Diastolic Dysfunction (Grade I).

**Method:** This is retrospective, cross-sectional study conducted in 212 patients with LV diastolic dysfunction (Grade 1) with preserved LV Systolic function who were referred for clinically indicated two dimensional transthoracic echocardiogram (TTE) in Chitwan Medical College from 6<sup>th</sup> June 2020 to 8<sup>th</sup> August 2020.

**Result:** Out of total 212 patients, 107 (50.47%) were female and 105 (49.52%) were male. Age ranged from 33 to 87 years with the mean age of  $63.2 \pm 12.2$  years, female (34 to 86 years) with the mean age of  $62.9 \pm 10.8$  years and male (33 to 87 years) with the mean age of  $63.3 \pm 13.8$  years. Left atrial diameter varied from 18mm to 39mm with average diameter  $31.11 \pm 4.62$  mm which implies that the value of LA diameter tended to be within normal limits. In female, left atrial diameter ranged from 18mm to 39mm with average diameter  $30.34 \pm 4.58$ mm and in male it ranged from 19mm to 39mm with average diameter  $31.90 \pm 4.72$ mm. LA diameter of both male and female was under normal limit in LVDD (Grade I).

**Conclusion:** The result showed that LA diameter in LV Diastolic Dysfunction was within normal limits. So, LA enlargement was not independently associated with LV diastolic dysfunction (Grade 1).

**Keywords:** Echocardiography; Left ventricular diastolic dysfunction; Left atrial size.

## 1. Introduction

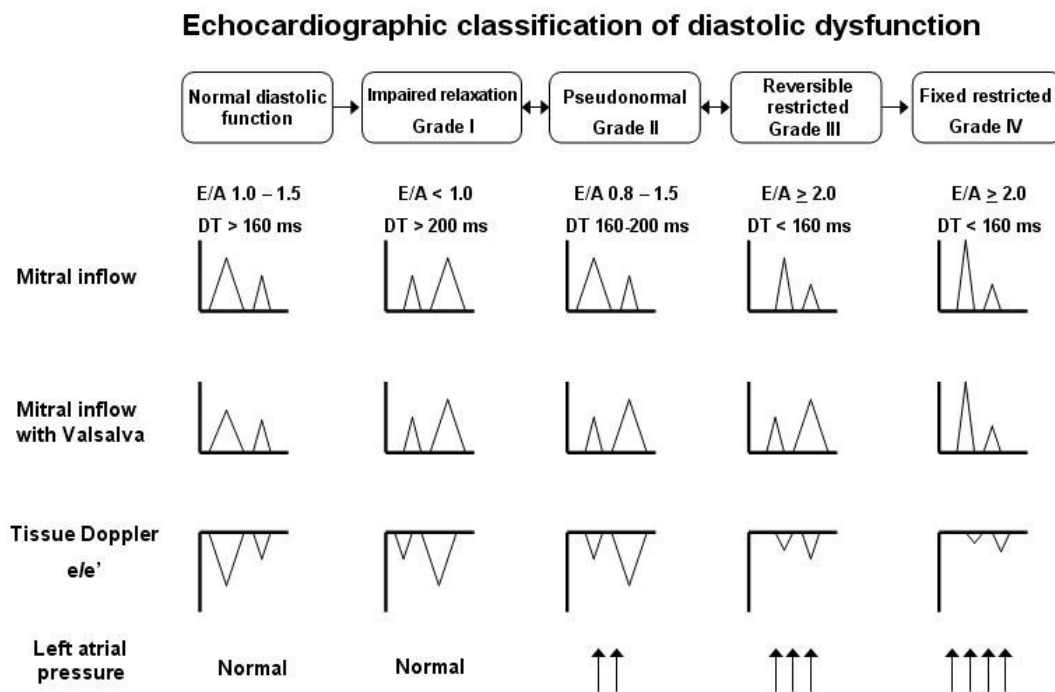
Left atrial (LA) enlargement can be easily assessed by echocardiography and is an important predictor of future cardiovascular events including stroke, atrial fibrillation, congestive heart failure, and death [1–4]. Thus, it is important to clarify the clinical factors that are associated with LA enlargement from the viewpoint of preventing LA remodeling. In the clinical setting, there are few reports on the factors that lead to atrial remodeling in the absence of mitral valve disease [2,3]. In contrast, experimental studies have shown that LA enlargement is associated with numerous signaling pathways, such as the renin–angiotensin–aldosterone system, transforming growth factor- $\beta$ 1, and oxidative stress [5,6]. Although the pathophysiology of LA enlargement is probably multifactorial, the clinical factors independently associated with LA enlargement have not been well defined. Especially, associations between LA enlargement and the factors that can cause congestive heart failure or atrial fibrillation have not been adequately investigated.

A previous study [7] showed a graded relationship between LA enlargement and the progression of left ventricular (LV) diastolic dysfunction (DD). An increased LA volume is generally accepted as an echocardiographic indicator of DD [8]. Thus, the current guidelines of the European Association of Echocardiography and American Society of Echocardiography recommend the use of LA volume measurements for grading DD (I to III). On the other hand, the current guideline also recommended that one should consider LA volume measurement in conjunction with patients' clinical status [8]. However, the question remains to what extent we should consider patients' clinical status in interpreting LA volume. For instance, when impaired relaxation (DD grade I) occurs, LA volume is unlikely to increase because LA pressure is not elevated at the stage of mild DD [9]. Moreover, some recent studies showed that LA volume might not increase with advancing age [10,11], despite the progression of DD with age [10,12].

These findings suggest there is a clinical necessity to elaborate how much each clinical status can influence dilation of LA volume. In other words, we questioned the extent to which LA enlargement could serve as a surrogate marker of DD.

We sought to determine the major independent clinical factors that are associated with LA enlargement in subjects without valvular disease or LV systolic dysfunction, and to clarify the associations between LA enlargement and DD.

Figure 1: Echocardiographic Classification of Diastolic Dysfunction

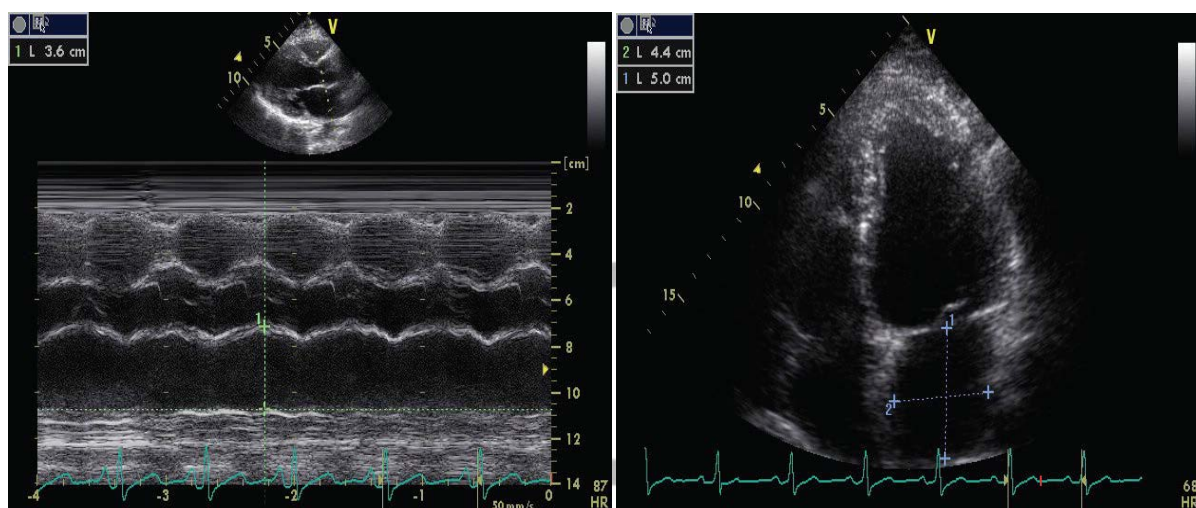


**Anatomy:** The LA is located in the mediastinum, oriented leftward and posterior to the right atrium (RA). LA structure is characterized by a pulmonary venous component, a lateral fingerlike appendage, an inferior vestibular component, which surrounds the mitral valve orifice, and a prominent body that shares the septum with the RA. The pulmonary venous component with venous orifices at each corner is situated posteriorly and superiorly, and directly confluent with the body. The walls of the LA can be described as superior (roof), posterior (inferoposterior), left lateral, septal, and anterior. The majority of the atrium is relatively smooth, whereas the appendage is rough with pectinate muscles. The walls are composed of one or more overlapping layers of differently aligned myocardial fibres, with marked regional variations in thickness. Circular fibres are more or less parallel to the atrioventricular valve plane, whereas

longitudinal fibres run nearly perpendicularly. Oblique fibres are those inclined between the two major axes [13].

Increased LA size is associated with adverse cardiovascular outcomes [14, 15]. LA size correlates with both LA and LV functions, and it is a strong predictor of cardiovascular death and morbidity. Relationships exist between increased LA size and the incidence of AF and stroke, risk of overall mortality after myocardial infarction, and risk of death and hospitalization in patients with dilated cardiomyopathy [16–19]. LA is a marker of both the severity and chronicity of diastolic dysfunction and magnitude of LA pressure elevation [14].

*Figure 2: LA Dimensions*



(a)

(b)

In above figure, LA Dimensions: anteroposterior diameter in parasternal long-axis view (a); longitudinal and transverse diameters in 4-chamber view (b).

## 2. Methods

This was retrospective, cross-sectional study conducted in 212 patients with LV diastolic dysfunction who were referred for clinically indicated two dimensional transthoracic echocardiogram (TTE) in Chitwan Medical College from 6<sup>th</sup> June 2020 to 8<sup>th</sup> August 2020. After approval of the study by the institutional ethical committee, informed consent was taken of all 212 patients. Only patients with normal LV systolic function were included. Patients with arrhythmia, valvular heart disease, congenital heart disease, or permanent pacemaker implantation were excluded has a strong influence on LA volume.

## Echocardiographic Imaging:

Complete M-mode, two-dimensional and Doppler echocardiogram was performed by myself according to a standardized protocol using Siemens ultrasound machine.

The LA size is measured at the end-ventricular systole when the LA chamber is at its greatest dimension, in long-axis view (anterior-posterior diameter) and in 4-chamber view (longitudinal and transverse diameters) [20] (Figure 1).

LV diastolic dysfunction using transmitral diastolic flow by pulsed-wave Doppler from an apical four-chamber view and pulsed-tissue Doppler imaging (TDI) of LV myocardial velocities was evaluated. Peak velocities of the early (E-wave) and late (A-wave) phase of the mitral inflow pattern from Doppler recordings were measured, and their ratio (E/A) was calculated. The peak systolic (S) and peak early diastolic (E') velocities of the septal mitral annulus by pulsed-TDI was measured. The ratio between the E and the E' waves (E/E') as a preload-independent index of LV filling pressure was calculated. Diastolic function was classified as normal or abnormal and then diastolic dysfunction (when it was present) was classified as: (i) E/A ratio <1.0, E/e' ratio <10 (grade I, impaired relaxation); (ii) E/A ratio 0.8 - 1.5 , E' velocity < 7 cm/s and E/e' ratio 10-14 (grade II, pseudo-normalized pattern); or (iii) E/A ratio  $\geq$  2.0, E' velocity < 7 cm/s E/e' ratio >14 and (grade III, Reversible restrictive pattern). ) E/A ratio  $\geq$  2.0 , E' velocity < 7 cm/s and E/e' ratio >14 (grade III, fixed restrictive pattern). For this study grade 1 diastolic dysfunction was taken to see whether LA size falls under normal range or not.

### 2.1. Statistical Analysis and Presentation:

Statistical analysis was performed using MS Excel. Descriptive statistical tools like mean, standard deviation, percentage and range were used for data analysis. Table and graph were used for data presentation.

## 3. Results

It is a retrospective cross-sectional study in total 212 patients of LV Diastolic Dysfunction (grade I) with preserved LV Systolic function who were assessed by 2D echocardiography. Among them, 107 (50.47%) were female and 105 (49.52%) were male. Age ranged from 33 to 87 years with the mean age of  $63.2 \pm 12.2$  years, female (34 to 86 years) with the mean age of  $62.9 \pm 10.8$  years and male (33 to 87 years) with the mean age of  $63.3 \pm 13.8$  years. Left atrial diameter varied from 18mm to 39mm with average diameter  $31.11 \text{mm} \pm 4.62$  mm which implies that the value of

LA diameter tended to be within normal limits. In female, left atrial diameter ranged from 18mm to 39mm with average diameter  $30.34\text{mm} \pm 4.58\text{mm}$ . In male, left atrial diameter ranged from 19mm to 39mm with average diameter  $31.90\text{mm} \pm 4.72\text{mm}$ . LA diameter of both male and female were under normal limit in LVDD (Grade I).

Figure 3: LA Diameter in Grade I LVDD

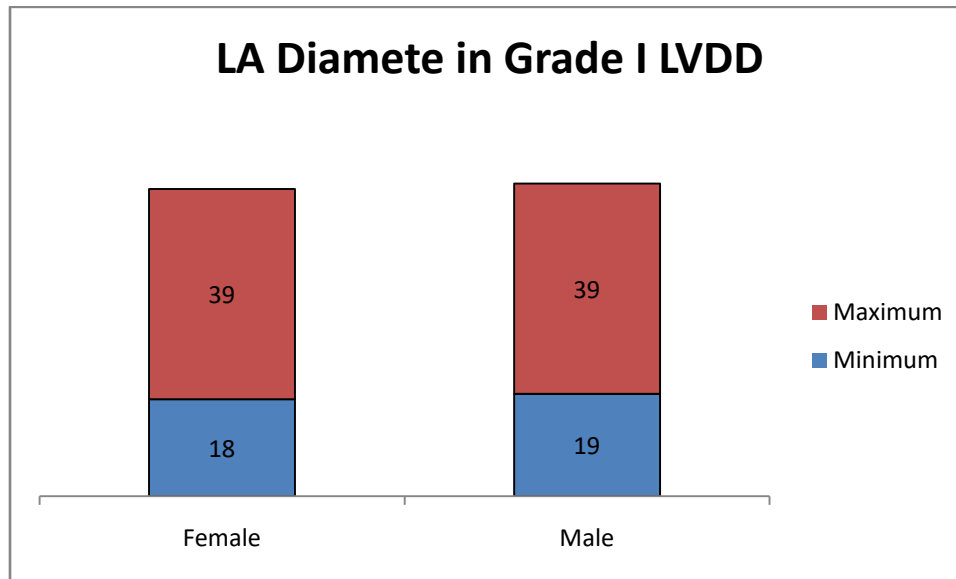


Table 1: LA Diameter in Grade I LVDD

Parameter	Male	Female
Average Age	63.5	62.9
LA Diameter Distribution	$31.90 \pm 4.72$	$30.34 \pm 4.58$
Maximum	39	39
Minimum	19	18

#### 4. Discussion

In this cross sectional study of 212 patients with preserved ejection fraction, we found Diastolic dysfunction(grade I) was not independently associated with LA enlargement among several clinical variables. LA enlargement is associated with Diastolic dysfunction as the progression of DD may lead to an elevated LV filling pressure. However, DD grade I (mild DD) was defined as the stage of abnormal LV diastolic function where there was normal LV filling pressure [8]. Pritchett et al. [3] have shown similar findings. They also demonstrated that DD grade I was not associated with LAVI in their adjusted analysis, while DD grade was independently associated

with LAVI [3]. Thus, our finding that DD grade I was not independently associated with LA enlargement seems reasonable.

## 5. Conclusion

The result showed that LA diameter was within normal limits. So, LA enlargement was not independently associated with LV diastolic dysfunction (grade I).

**Conflict of Interest:** None

**Acknowledgement:** None

## References

- [1] 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.
- [2] Gupta S, Matulevicius SA, Ayers CR, Berry JD, Patel PC, Markham DW, Levine BD, Chin KM, de Lemos JA, Peshock RM, Drazner MH. Left atrial structure and function and clinical outcomes in the general population. *Eur Heart J* 2013;34:278–85.
- [3] Pritchett AM, Mahoney DW, Jacobsen SJ, Rodeheffer RJ, Karon BL, Redfield MM. Diastolic dysfunction and left atrial volume: a population-based study. *J Am Coll Cardiol* 2005;45:87–92.
- [4] Kim TH, Shim CY, Park JH, Nam CM, Uhm JS, Joung B, Lee MH, Pak HN. Left ventricular diastolic dysfunction is associated with atrial remodeling and risk or presence of stroke in patients with paroxysmal atrial fibrillation. *J Cardiol* 2016;68:104–9.
- [5] Tan AY, Zimetbaum P. Atrial fibrillation and atrial fibrosis. *J Cardiovasc Pharmacol* 2011;57:625–9.
- [6] Yamamoto K. Beta-blocker therapy in heart failure with preserved ejection fraction: importance of dose and duration. *J Cardiol* 2015;66:189–94.
- [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] Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009;22:107–33.

[9] Redfield MM, Jacobsen SJ, Burnett Jr JC, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA* 2003;289:194–202.

[10] Daimon M, Watanabe H, Abe Y, Hirata K, Hozumi T, Ishii K, Ito H, Iwakura K, Izumi C, Matsuzaki M, Minagoe S, Abe H, Murata K, Nakatani S, Negishi K, et al. Gender differences in age-related changes in left and right ventricular geometries and functions. *Echocardiography of a healthy subject group. Circ J* 2011;75:2840–6.

[11] AlJaroudi W, Alraies MC, Halley C, Rodriguez L, Grimm RA, Thomas JD, Jaber WA. Effect of age, gender, and left ventricular diastolic function on left atrial volume index in adults without known cardiovascular disease or risk factors. *Am J Cardiol* 2013;111:1517–22.

[12] Munagala VK, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Association of newer diastolic function parameters with age in healthy subjects: a population-based study. *J Am Soc Echocardiogr* 2003;16:1049–56.

13. W. A. McAlpine, *Heart and Coronary Arteries: An Anatomical Atlas for Clinical Diagnosis, Radiological Investigation, and Surgical Treatment*, Springer, Berlin, Germany, 1975.

[14] T. S.M. Tsang, M. E. Barnes, B. J. Gersh, K. R. Bailey, and J. B. Seward, “Left atrial volume as a morphophysiological expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden,” *The American Journal of Cardiology*, vol. 90, no. 12, pp. 1284–1289, 2002.

[15] T. S. M. Tsang, M. E. Barnes, B. J. Gersh et al., “Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography,” *Journal of the American College of Cardiology*, vol. 42, no. 7, pp. 1199–1205, 2003.

[16] E. J. Benjamin, R. B. D'Agostino, A. J. Belanger, P. A. Wolf, and D. Levy, “Left atrial size and the risk of stroke and death: the framingham heart study,” *Circulation*, vol. 92, no. 4, pp. 835–841, 1995.



[17] T. S. M. Tsang, M. E. Barnes, B. J. Gersh, K. R. Bailey, and J. B. Seward, “Risks for atrial fibrillation and congestive heart failure in patients  $\geq 65$  years of age with abnormal left ventricular diastolic relaxation,” *The American Journal of Cardiology*, vol. 93, no. 1, pp. 54–58, 2004.

[18] T. S. M. Tsang, B. J. Gersh, C. P. Appleton et al., “Left ventricular diastolic dysfunction as a predictor of the first diagnosed nonvalvular atrial fibrillation in 840 elderly men and women,” *Journal of the American College of Cardiology*, vol. 40, no. 9, pp. 1636–1644, 2002.

[19] M. G. Modena, N. Muia, F. A. Sgura, R. Molinari, A. Castella, and R. Rossi, “Left atrial size is the major predictor of cardiac death and overall clinical outcome in patients with dilated cardiomyopathy: a long-term follow-up study,” *Clinical Cardiology*, vol. 20, no. 6, pp. 553–560, 1997.

[20] R. M. Lang, M. Bierig, R. B. Devereux et al., “Recommendations for chamber quantification: a report from the American society of echocardiography's guidelines and standards committee and the chamber quantification writing group, developed in conjunction with the European association of echocardiography, a branch of the European society of cardiology,” *Journal of the American Society of Echocardiography*, vol. 18, no. 12, pp. 1440–1463, 2005.