ORIGINAL ARTICLE

LEFT ATRIAL TO LEFT VENTRICULAR END DIASTOLIC DIAMETER RATIO IN LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

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Background: Diastolic dysfunction (DD) is difficult to diagnose and characterize despite many techniques. It is known that left atrial diameter (LAD) increases and left ventricular internal end diastolic diameter (LVIDD) remains the same in moderate to severe diastolic dysfunction (grade II and above) but a ratio between these two (LAD/LVIDD) has never been used to assess diastolic dysfunction. This study aims to analyze the relationship between the ratio, left atrial diameter/ left ventricular internal end diastolic diameter (LAD/LVIDD) and diastolic dysfunction (grade II and above). This study also aims to give a statistical model based upon this relationship that is able to help in diagnosing diastolic dysfunction. **Methods:** This case control analytical study was carried out at the Department of Cardiology, Holy Family Hospital, Rawalpindi, from Jan 2014 to Jan 2016. On the basis of echocardiographic findings, 226 patients were identified as normal healthy control group whereas 226 patients were identified as having diastolic dysfunction of grade II and above and were categorised as disease group. Doppler diastolic function parameters were used to assess diastolic function in all of these 452 patients. Appropriate statistical methods were then applied on the data by using IBM statistical package for social sciences (SPSS). **Results:** LAD/LVIDD was correlated to diastolic dysfunction at r=0.858 (p<0.01). A binary logistic regression model using age, sex and LAD/LVIDD gave an accuracy of 96.9% in diagnosing diastolic dysfunction. LAD/LVIDD in the model had an odds ratio of 2.678×10^{24}. A Receiver Operation Characteristic curve between diastolic dysfunction and LAD/LVIDD yielded a specificity of 93.8% and sensitivity of 99.1% at the cut-off value of 0.7268. **Conclusion:** A new parameter, left atrial diameter (LAD) to left ventricular internal end diastolic diameter (LVIDD) ratio (LAD/LVIDD), is significantly correlated to diastolic dysfunction (grade II and above). It is also a significant predictor for diastolic dysfunction.

Keywords: Diastolic dysfunction, atrial, ventricular, echocardiography, atrio-ventricular diameter ratio, cardiac,

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INTRODUCTION

Cardiac diastolic dysfunction (DD) refers to inadequate or restricted filling of the ventricles mainly the left ventricle during diastole because of hardening or stiffening of the ventricles and could be the result of sustained hypertension, aortic stenosis and advanced age.[1,2] Diastolic dysfunction is difficult to characterize in clinical practice and many question its diagnosis.[3] Nevertheless, heart failure with preserved or nearly preserved ejection fraction is diagnosed as diastolic dysfunction.[4] The usual symptoms of left diastolic heart failure (DHF) or dysfunction remain similar to that of the systolic heart failure like dyspnoea, fatigue, exercise intolerance, and pulmonary oedema. However, pulmonary oedema is more common in diastolic dysfunction and symptoms of low cardiac output like fatigue and exercise intolerance are predominant in systolic dysfunction.[5] Due to thickening and stiffening of left ventricle, the diameter of ventricular cavity decreases (increased 'left ventricular mass/volume'). The thickened wall relaxes slowly in diastole and thus offers a greater resistance to inflow of the blood from the left atrium which causes a rise in the filling pressures.[6] Diastolic dysfunction differs considerably from systolic dysfunction/ failure in mechanism, patho-physiology, causes, prognosis and diagnosis despite their almost similar symptoms.[2,6]

Diastolic dysfunctions are diagnosed in patients with symptoms of heart failure with a near normal ejection fraction (>50%). These patients have increased diastolic pressures and impaired filling.[1,7,8] Trans-mitral inflow, pulmonary inflow, deceleration time and intra ventricular filling patterns can be observed by Doppler Echocardiography and are used to diagnose diastolic dysfunction and its severity.[9] Trans mitral inflow velocities which are E/A ratio (E is the velocity of blood during early phase of diastole and A is the velocity during atrial phase of diastole) can easily be found using echocardiography and are used to diagnose diastolic dysfunction. In normal healthy individuals, E/A ratio is slightly greater than 1.[6,10] E/e′ (E is velocity of blood during early phase of diastole and e′ is early diastolic mitral valve annular velocity) and deceleration time (time required for flow velocities to decline during early diastole) are also used in categorizing diastolic dysfunction.[10]

Diastolic Dysfunction can be divided into four grades[7]:

- Grade I is characterised by a reversal of E/A ratio (E/A<0.8). E/e′ is less than 8. This is the mildest form of diastolic dysfunction and is usually without any symptoms.
- Grade II has a pseudo normal filling dynamics and have a near normal E/A ratio (1–2) and E/e′=9–12. This is a moderate diastolic dysfunction with raised filling pressures.
- Grade III and Grade IV will have a greatly increased E/A ratio (E/A>2) and E/e′>13. These will have a restrictive filling dynamic and are the severest form of diastolic dysfunction.

Left atrial diameter enlargement is a well documented feature in left ventricular diastolic dysfunction, concentric hypertrophy and in hypertension in which the diameter increases 2 to 5 mm depending upon the severity and is due to restricted filling of the left ventricle which causes blood to pool in the left atrium.[11–14] The left ventricle, in some studies, decreases in its internal end diastolic diameter (LVIDD) but the overall consensus regarding LVIDD is that it remains the same in diastolic dysfunctions of all grades, hypertension, and concentric left ventricular hypertrophy.[11–15] So a ratio between these two diameters might have some predictive capacity to diagnose diastolic dysfunction in moderate to severe cases.

The present study aims to utilize a new parameter 'Left atrial diameter to Left ventricular internal end diastolic diameter (LAD/LVIDD) ratio' to diagnose moderate to severe diastolic dysfunctions (grade II-IV). When done in combination with other diagnostic indices (E/A ratio, E/e′ ratio, deceleration time etc), this new parameter might improve diagnosis and/or prognosis in patients with diastolic dysfunction since left atrial enlargement itself is a predictor of heart failure, atrial fibrillation and ischemic stroke.[13] The Doppler indices (E/A ratio, E/e′ ratio etc) indicate filling pressures and dynamics at the time of measurement, left atrial diameter or volume reflects the overall effects of filling pressures over time.[7]

MATERIAL AND METHODS

This cross-sectional analytical study spanned over two years from January 2014 to January 2016 and included 452 patients who arrived at the department of cardiology, Holy Family Hospital, Rawalpindi. The study population was divided into control and disease groups having the following inclusion criteria.

Control Group (n=226)

- Patients were essentially normal on echocardiography
- Patients had normal left ventricular geometry
- Patients had an ejection fraction of 60% or above
- Patients had an E/A ratio around one, E/e′ ratio of less than 8 and a normal deceleration time

Disease Group (n=226)

- Patients showed signs of diastolic dysfunction of grade II and above
- Patients had concentric left ventricular (LV) remodelling or concentric LV hypertrophy with DD of grade II and above
- Patients had an ejection fraction of 50% or above
- Patients had E/A ratio between 1–2 and E/e′ ratio of greater than 10 and an abnormal deceleration time

The following were excluded from the study:

- Valvular abnormalities like mitral stenosis, mitral regurgitation and aortic regurgitation
- Pericardial effusion and pericarditis
- Mild diastolic dysfunction or grade-I diastolic dysfunction

All 452 patients had a Doppler echocardiography. The measurements of left ventricular internal end diastolic diameter (LVIDD) and left atrial diameter (LAD) were performed as per the guidelines.[16] Diastolic function was characterized by using early diastolic filling velocity and atrial diastolic filling velocity (E/A ratio) and by early diastolic filling velocity and diastolic mitral annulus velocity (E/e′ ratio) as per published guidelines.[7,8] Statistical analysis was performed on SPSS-19, and $p<0.05$ was considered significant.

RESULTS

Among the four variables, LAD/LVIDD had the highest correlation with diastolic dysfunction, followed by left atrial diameter. Left ventricular internal end diastolic diameter was negatively correlated with diastolic dysfunction (Table-1).

The LAD/LVIDD was far more successful in modelling diastolic dysfunction than age or sex as evident by their coefficients and odds ratio. Sex was insignificant in diagnosing diastolic heart failures. Overall the model had an accuracy of 96.9% in diagnosing diastolic dysfunction (Table-2, 3).

Receiver operation characteristics determined the sensitivity and specificity of a particular cut off point in LAD/LVIDD. The best specificity and sensitivity combination was found at 0.7286 with 99.1% sensitivity and 93.8% specificity (Table-4).

Figure-1 shows difference in LAD/LVIDD among healthy and diastolic dysfunctional hearts. The ratio is more to the left in diastolic dysfunctional hearts than healthy hearts. Figure-2 demonstrates an increase in probability of diastolic dysfunction when LAD/LVIDD is raised.

Table-1: Characteristics and correlations of DD with variables among the study population (Mean±SD)

Character	Control Group (n=226)	Disease group with grade II and above (n=226)	Spearman Correlation *r*	*p*
Gender	Male=115 Female=111	Male=133 Female=93	---	0.397
Age	36.87±16.487	59.74±15.590	0.581	<0.001
LAD (mm)	28.49±2.689	42.32±9.529	0.814	<0.001
LVIDD (mm)	44.86±3.603	40.2±4.608	-0.498	<0.001
LAD/LVIDD	0.638±0.069	1.065 ±0.269	0.858	<0.001

Table-2: Binary logistic regression model for DD

Variable	Regression Coefficients (B)	Odds ratio (Exp B)	95% CI	*p*
LAD/LVIDD	56.247	2.678×10^{24}	7.148×10^{16}–1×10^{32}	<0.001
Age	0.062	1.064	1.023–1.106	0.02
Sex	1.314	3.722	---	>0.05

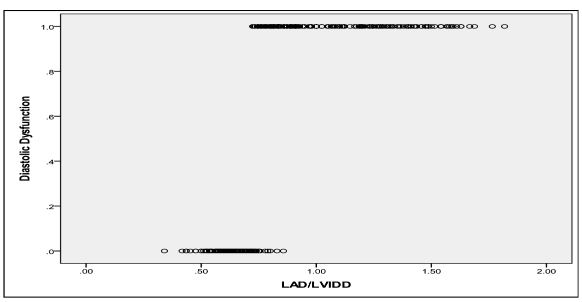
Accuracy of the null model (all patients being positive for DD)=50%. Regression Equation is logit (prediction)=ln (p/1-p)= -45.914+56.247 (LAD/LVIDD)+0.062 (Age)+1.314 (Sex). Nagelkerke R^2=0.948. (Sex is taken as 0=female and 1=male)

Table-3: Predictive capacity of binary logistic regression model for DD

Regression model for DD	Observed	Predicted		
		Present	Not present	% Correct
DD Present	226	218	8	96.5
DD Not present	226	6	220	97.3
Overall correct percentage				96.9

Table-4: Receiver operation characteristics

Area under the curve	*p*	95% CI	Selected cut-off value of LAD/LVIDD	Sensitivity for cut-off value	Specificity for cut-off value
0.995	<0.001	0.991–0.999	0.7286	99.1%	93.8%



0=Normal control group 1=Disease group

Figure-1: Difference in LAD/LVIDD among healthy normal control group and disease group

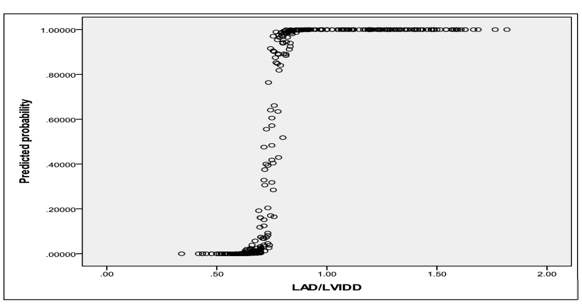


Figure-2: Graph based on binary logistic model showing an increased probability of DD when LAD/LVIDD is increased

DISCUSSION

Diagnosis of diastolic dysfunction is complex and confusing. Differentiation between systolic and diastolic dysfunctions cannot be made on the basis of history, physical examination, ECG or chest radiography as markers for both of these occur with same relative frequencies. Traditional basis for diagnosing diastolic dysfunction involve trans-mitral velocities (E/A, E/e´) on Doppler echocardiography. These parameters have many shortcomings and offer limited interpretability. The precise pattern of early and late diastolic trans-mitral flow velocities depend on factors that govern instantaneous left atrial and left ventricular pressures before and after mitral valve opening and the resultant atrial-ventricular pressure gradient (filling load). Thus interventions or pathological conditions that increase left atrial pressure increase early trans-mitral flow velocities, whereas interventions that reduce left atrial pressure reduce early filling velocities. To correctly interpret changes in trans-mitral flow velocities, concomitant changes in filling load must be considered. On the other hand, left atrial and left ventricular diameters reflect gross changes in filling pressures/loads over time.[5] Many studies showed a significant correlation between left ventricular mass and diameter with trans-mitral velocities. Hence, left atrial and left ventricular diameters can supplement trans-mitral velocities in diagnosing diastolic dysfunction.[13]

Left ventricular and left atrial geometrical changes occur in all patients with moderate to severe diastolic dysfunction (grade II and above).[5] In the present study, left atrial diameters were greater in the patients as compared to controls while left ventricular diameters were less in patients as compared to the control group. This change in left atrial diameter is in agreement with other studies. This study also reports a decrease in left ventricular diameter which is contrary to some research that showed no change. [5,17]

Many studies have shown that left atrial diameter is a sensitive and specific marker for diastolic dysfunction in grade IV. Upon comparison with other researchers, our study shows that a ratio of left atrial to left ventricular diastolic diameter is more specific and sensitive than just left atrial diameter and it also has acceptable sensitivity and specificity in grade II, III and IV.[18,19] Pritchet *et al* in their study found that the sensitivity and specificity of just left atrial diameter alone was 69% and 77% respectively at AOC (area under the curve) of 0.81 to diagnose moderate to severe diastolic dysfunction.[19] The present study in contrast shows that using a ratio between left atrial diameter and left ventricular internal end diastolic diameter can raise the sensitivity and specificity to 99.1% and 93.8% respectively at AOC of 0.99. The left ventricular diastolic diameter alone was not a strong marker for diastolic dysfunction in our study and this is in agreement with other researchers as well.[18] However, in combination with left atrial diameter, the diagnostic capability of LAD/LVIDD increased many folds.

CONCLUSION

A new parameter left atrial diameter (LAD) to left ventricular internal end diastolic diameter (LVIDD) ratio (LAD/LVIDD) is a strong parameter to diagnose moderate to severe diastolic dysfunction (grade II and above).

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