LEFT ATRIUM VOLUME AS A SURROGATE MARKER OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION

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Date Received:
October 15, 2015
Date Revised:
November 28, 2015
Date Accepted:
December 26, 2015

ABSTRACT

Objective: To determine correlation between left atrial volume and left ventricular diastolic dysfunction.

Methodology: This was a single center observational study conducted at Lady Reading Hospital, Peshawar. Patients above 18 years of both genders, who were in sinus rhythm and having no significant systolic dysfunction or significant mitral insufficiency on echocardiography, were included in the study, using purposive non-probability sampling technique. A total 339 patients underwent transthoracic echocardiography from July 2013 to June 2014. Detailed cardiac echocardiography was performed to determine left atrial volume, ejection fraction, E and A velocities, deceleration time and e'velocity, E/e.'

Results: A total of 339 patients were studied. Male were 61.9%. Mean age of study population was 58.42 ±10.48 years. Baseline characteristics of patients having some degree of diastolic dysfunction were; mean age 65.5 ±12.3, mean body mass index 25.2 ±2.5 kg/m2, mean ejection fraction 55.1 ±7.5%, hypertension 48.6%, diabetes mellitus 10.1% and left ventricular hypertrophy 38.6%. Echocardiographic findings in diastolic dysfunction patients were as follow: mean left atrial volume was 65.3 ±10.1ml, E/A 1.4 ±0.6, TDI e' was 6.7 ±1.3 m/sec and TDI E/e' was 12.7 ±2.1. Increasing left atrial volume was well correlated with increasing severity of left ventricular diastolic dysfunction (γ = +0.8, Spearman rank correlation).

Conclusion: Increase in left atrial volume is directly correlated with severity of diastolic dysfunction. Severity of diastolic dysfunction increases with increased left atrial volume.

Key Words: Left atrial size, Left ventricular diastolic dysfunction

This article may be cited as: **Hadi A, Iqbal MA, Ahmad F, Ikramullah, Ashraf A, Hafizurehman. Left atrium volume as a surrogate marker of left ventricular diastolic dysfunction. J Postgrad Med Inst 2016; 30(1): 84-8.**

INTRODUCTION

Left ventricular impaired relaxation (LVIR) or left ventricular diastolic dysfunction (LVDD), is common, especially in the elderly. It is considered an important prognostic indicator of various cardiac diseases[1]. Relaxation abnormality is one of the earliest manifestations of cardiac dysfunction and has been associated with the development of atrial fibrillation. Prevalence of asymptomatic LVDD in general population is approximately 25% to 30% among individuals older than 45. Symptomatic LVDD (ejection fraction >50%) is responsible for nearly 51% of heart failure patients[2]. Recent studies showed that advanced diastolic dysfunction is strongly associated with increased mortality[3].

In medical practice, left ventricular relaxation (LVR) can be assessed indirectly by estimating early diastolic filling. LVR has been identified in a simple and innocuous matter by echo-doppler-cardiography (Echo) and characterized by the analysis of the mitral diastolic flow by pulsatile doppler and the study of the mitral ring velocity by tissue Doppler[4-6].

In diastolic dysfunction (DD), abnormal LV relaxation and reduced LV compliance occur as a consequence of modifications in the interaction between actin and myosin[7]. 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[8-10].

Thus LAV increase reflects, the chronic exposure of the left atrium to high LV filling pressures and DD severity[6,11].

Left atrium (LA) is a reservoir for the LV during systole, a conduit [for blood to flow from pulmonary veins (PVs) to the LV] during early diastole and an active contractile chamber in late diastole. It contributes up to 30% of LV output. During diastole, 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. This results in increased LA wall tension and dilatation of the LA[1,12-14]. More recently Left Atrial Volume (LAV) measured by bi dimensional echo was proposed as more accurate index for the detection of left atrial dilation, superior than the simple antero-posterior diameter derived by the M-mode echo. LAV has been suggested as a marker of the severity and duration of LVDD, as well as predictor of cardiac events such as atrial fibrillation, heart failure and embolic stroke[15,16].

International studies reported correlation between increased LAV to LVDD severity[10,11]. Authentic national data is not available on the subject. This study was, therefore conducted to correlate LAV with LVDD in our population looking for the relationship between LAV and the various LVDD grades in a series of outpatients with preserved or slightly reduced systolic function; and to identify the clinical and echocardiographic variables independently associated to LAV increase in this subset of patients.

METHODOLOGY

Research was approved by the hospital Ethics Committee and all patients signed an informed consent document. This study was conducted in echocardiography laboratory (Echo Lab) of Department of Cardiology, Lady Reading Hospital, Peshawar. Study population was patients referred for two- dimensional transthoracic echocardiogram (TTE) for various indications. A total 373 patients underwent echocardiography during the study period. Patients of age 18 years or above from both genders who were having normal systolic function on TTE were included from the study. Patients with arrhythmia, significant valvular heart disease, congenital heart disease, or permanent pacemaker implantation were also excluded, because inadequate mitral diastolic flow pattern (n-34) on echocardiography was not measurable in them.

Medical record of study population was reviewed for baseline patient's characteristics including diabetes, hypertension, dyslipidaemia. Present and past history was taken for diabetes, hypertension and dyslipidemia. Height, weight, heart rate and blood pressure were measured on the day of echocardiography. Random blood sugar and blood cholesterol measured to determine diabetes and dyslipidemia.

Complete two-dimensional, M-mode, and Doppler echocardiogram was performed by experienced sonographers according to a standardized protocol using echocardiography machine Acusen CV70, available in Echo lab. LV end-diastolic and end- systolic dimensions and subsequent ejection fraction were determined using the biplane Simpson method of disks.

Mitral inflow was assessed from the apical 4-chamber view with pulsed wave doppler by placing 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), and E/A velocity ratio were measured. Doppler tissue imaging was used to measure e' and a' velocities by placing 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 and mitral E/e' ratio. Diastolic function was graded as normal, abnormal relaxation (Grade I), pseudonormal (Grade II), and restrictive (Grade III). Pseudonormal (Grade II) was 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/E'.10 (lateral annulus) or 0.15 (septal annulus).

Left atrial volume was measured in apical four chamber view at end of LV systole, i-e; just before opening of mitral valves, by tracing inner borders of LA and excluding area under mitral valve annulus and pulmonary veins inlet[12]. All the details were recorded on a predetermined profroma

Following operational definitions were used: Hypertension; systolic levels ≥ 140 mmHg and/or diastolic levels ≥ 90 mmHg on at least two occasions or using antihypertensive medications. Diabetes mellitus; fasting glucose levels >126 mg/dl or taking medications for diabetes. Dyslipidemia was defined as total cholesterol levels >200 mg/dl and/or LDL cholesterol >130 mg/dl or using hypelipidemic agents. Individuals who smoked on the day of echocardiography study were considered smokers. Obesity; Body mass index ≥30.

SPSS version 16.0 statistical package was used for data analysis. All values were expressed as mean±SD. Correlation between indexed LA volume and LV diastolic function grades was measured using the Spearman rank correlation coefficient (γ).

RESULTS

Total 339 patients were included in the study. Mean age was 58.42 ±10.48 years (35–80). Male patients were 61.9% (n-210) and females were 38.1% (n-129). Indications for echocardiography were as follow: dyspnea/pe-

ripheral edema/congestive heart failure 28% (96), cerebrovascular accident 11% (36), preoperative assessment 14% (48), coronary artery disease 14% (48), and others 33% (111).

The demographic and clinical characteristics of the sample, according to different grade of DD, are shown in table 1. Diastolic function was normal in 64% (n-218). Grade I diastolic dysfunction (DD)-Impaired relaxation, was present in 25% (n-82) patients, Grade II DD (Pseudo normal) and Grade III(restrictive physiology) were present in 9% (n-32) and 2% (n-7) patients respectively.

Age was higher in the DD groups as compared to the normal function group. Hypertension, smoking and LV hypertrophy were more prevalent in the DD group in comparison to the group with normal diastolic function, and having positive correlation (γ = +0.8). The ejection fraction was markedly reduced only in the grade III DD group (ventricular filling restriction pattern). Details are given in table 1.

Echocardiographic findings varies according to DD group. LA Volume progressively increased with DD increased: 39.3 ±9.3ml (absent DD), 48.2 ±14.7ml (DD Grade I), 64.7 ±11ml (DD Grade II) and 88.9 ±12.5ml (DD Grade III). There was a relative decrease of the E-wave and E/A ratio, and an increase of the mitral deceleration time in the grade I DD groups (altered relaxation) in comparison to the group with normal diastolic function; the opposite was observed in the group with grade III DD (restrictive pattern). The e' wave was significantly smaller in all DD grades, in comparison to the group with preserved diastolic function. Progressive increase of the E/e' ratio was observed with worsening DD. Detail is given in table 2.

DISCUSSION

This was the first study conducted locally, which looked into the correlation between left atrial volume with worsening diastolic dysfunction in adults with relatively preserved systolic function.

We found that DD directly influence left atrial remodeling. 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 poor prognosis (age, LV hypertrophy, LV dysfunction and increased E/e' ratio) as previously observed [9].

It was established in our study that LAVI values are associated with DD grades with high accuracy. This same observation has been reported by other international studies as well. Pritchett et al[2] in his study on 2042 subjects, and the study by Tsang et al[6], showed that LAVI is having good sensitivity and specificity in the identification of intermediate (II) and severe (III) grade DD. This finding was according to our observation, although the values were inferior as compare to our findings. Differences in the selection of cases may justify the differences. These observations suggest that LAVI can be used, in addition to other variables, of mitral diastolic flow pattern for DD analysis in day today practices.

Table 1: Baseline demographic and clinical characteristics of normal and different diastolic dysfunction groups

Parameters	Normal 64% (n-218)	DD G-I 25% (n-82)	DD G-II 9% (n-32)	DD G-III 2% (n-7)	Total 100% (n-339)
Age (years)	45.1±13.8 (35-68)	64.4±10.6 (37-72)	60.2±10.9 (37-73)	70.6±15.3 (40-80)	
Men % (n)	12.3% (n-42)	15.1% (n-52)	20.2% (n-70)	14.3% (n-46)	61.9% (n-210)
Women % (n)	5.3% (n-14)	10.8% (n-34)	12.1% (n-55)	9.9% (n-26)	38.1% (n-129)
Weight (Kg)	65.5±12	67.8±13	69.4±15	68±12	
Height (m)	1.64±0.9	1.68±0.8	1.61±0.9	1.68±0.7	
BMI (Kg/m2)	24.3±3.8	24.1±2.9	26.7±2.5	24.3±3.6	
Smokers%(n)	2.1% (n-8)	5.3% (n-18)	6.3% (n-22)	2.1% (n-6)	15.8% (n-56)
Hypertension (%)	7.3% (n-24)	17.3% (n-59)	21.2% (n-72)	10.1% (n-35)	55.9% (n-190)
Diabetes Millets (%)	4.8% (n-16)	2.0% (n-7)	6.1% (n-21)	2.0% (n-7)	14.9% (n-51)
LVH (%)	10.2% (n-36)	15.3% (n-54)	12.2% (n-41)	11.1% (n-37)	48.8% (n-168)
EF(%)	70.7 ± 5.5	69.1 ± 6.4	68.8± 7.4	43.8 ± 15.9	

Table 2: Mean values of LVDD parameters as assessed by 2D Echo, Doppler and TDI

Variable	Normal 64% (n-218)	DD Grade I 25% (n-82)	DD Grade II 9% (n-32)	DD Grade III 2% (n-7)
LAV(ml)	39.3 ± 9.3	48.2 ± 14.7	64.7 ± 11	88.9 ±12.5
LVDD(cm)	5.0 ± 0.5	5.2 ± 0.5	5.4 ± 0.8	6.5 ± 1.2
LVSD(cm)	3.1 ± 2.1	3.2 ± 0.5	3.3 ± 0.6	5.0 ± 1.4
IVS(cm)	1.0 ± 0.9	1.1 ± 0.2	1.2 ± 0.3	1.9± 2.7
LVPW(cm)	1.0 ± 0.9	1.2 ± 1.1	1.1 ± 0.1	2.0 ± 2.9
Mitral E(m/s)	79 ± 18	58.8 ± 11.6	82.7 ± 13.9	98.6 ± 32.1
Mitral A(m/s)	64.7 ± 17	87.3 ± 18.4	74.3 ± 18	50.9 ± 16
E/A	1.29 ± 0.5	1.3 ± 7.4	1.16 ± 0.2	2.1 ± 0.8
DT(m/s)	156 ± 25	226 ± 34	172 ± 20	137 ± 12
TDI e'(m/s)	11.5 ± 4.1	7.4 ± 7.1	7.2 ± 1	5.9 ± 1.2
TDI E/e'	7.1 ± 2	8.8 ± 2.1	11.3 ± 2.5	16.1 ± 2.6

Spearman Rank Correlation (γ) for LAV and Severity of LVDD is +0.8

We have identified, that age, LV hypertrophy (left ventricular mass and relative wall thickness), E/e' ratio and LV ejection fraction as the determinant factors for LAVI increase in this population. Left Ventricular DD prevalence increases with age and advanced age is admittedly associated to more severe DD presentation[13,14], justifying this finding. LV hypertrophy is also admittedly a factor intimately related to DD[15]. These elements may have had greater participation in the most severe DD presentations (grades II and III), associated to systolic dysfunction and left ventricular remodeling with higher filling pressures[16].

The study of the transmitral flow and mitral annulus velocities by pulsed doppler, associated to LAV measurement, could better differentiate the most advanced stages of DD, especially grade II dysfunction or the so-called pseudo normal left ventricle filling pattern. We have identified, that age, LV hypertrophy, E/e' ratio and LV ejection fraction increase in this population, as the determinant factors for LAV.

STUDY LIMITATIONS

Data is not applicable to patients with atrial fibrillation, as only patients with sinus rhythm were included in this study. Patients with significant mitral insufficiency were excluded from the study, so it is unlikely that mitral insufficiency could have affected our findings. The fact that we have included only outpatients with less severe cardiac disease and smaller prevalence of severe DD can be considered a limitation of this study. However, it is in accordance with the natural occurrence of milder DD without significant systolic dysfunction, as seen in daily practice.

CONCLUSION

Diastolic dysfunction contributes to left atrial remodeling and LAV increase is an expression of DD severity. LAV increase in our local population with relatively preserved systolic functions and with no significant mitral insufficiency is partly related to age, left ventricular hypertrophy, increased filling pressure and decreased LV systolic function.

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CONTRIBUTORS

AH conceived the idea, planned the study, and drafted the manuscript. MAI, FA, I and H helped acquisition of data and did statistical analysis. AA drafted the manuscript and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.