**Original Research Article**

**Tissue doppler imaging for estimation of left ventricular filling pressure in patients with systolic and diastolic heart failure: a comparative simultaneous doppler catheterization study**

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**ABSTRACT**

**Background:** Noninvasive assessment of diastolic filling by Doppler echocardiography provides important information about left ventricular (LV) status in selected subsets of patients. This study was designed to assess whether the lateral mitral annular velocity as assessed by tissue Doppler imaging is associated with invasive measures of diastolic LV performance in patients with diastolic and systolic heart failure. Aim of the study was to compare the diagnostic accuracy of lateral mitral annular E/E′ as an estimate of LV filling pressure with invasive LVEDP measurement in subjects with systolic or purely diastolic heart failure.

**Methods:** Total 100 patients were studied, 50 patients with diastolic heart failure and 50 patients with systolic heart failure in patients undergoing diagnostic coronary angiogram. Detailed 2D Echocardiography, Trans mitral Doppler and Tissue Doppler velocities of lateral mitral annulus was obtained. The ratio of peak mitral velocity (E) to lateral mitral annular velocity (E′) by TDI (E/E′) was calculated.

**Results:** The ratio of E/E′ in diastolic group was 13.4±4.9 and in systolic group it was 13.7±5.2. The mean LVEDP in diastolic heart failure patients was 14.3±4.5 and 14.2±4.9 in systolic heart failure patients. The ratio of E/E′ showed a better correlation with LVEDP. E/E′ <8 accurately predicted normal LVEDP, and E/E′ >15 identified increased LVEDP ≥15mmHg.

**Conclusions:** E/E′ is a reliable estimate of LV filling pressures in subjects with systolic and diastolic heart failure. In subjects with diastolic heart failure, E/E′ seems helpful to identify those with truly elevated LV filling pressures. In patients with diastolic heart failure and normal E/E′, a search for other causes of symptoms (pulmonary disease, obesity and so forth) may be warranted.

**Keywords:** Diastolic heart failure, Left ventricular end diastolic pressure, Lateral mitral annular velocity, Peak mitral velocity, Receiver-operating characteristic curves

**INTRODUCTION**

Tissue Doppler imaging is a robust and reproducible echocardiographic tool which has permitted a quantitative assessment of both global and regional function and timing of myocardial events. Most published studies have examined the long-axis function of the heart by TDI from apical views.

In diastole, potentially important prognosticators include peak myocardial early diastolic velocity measured at the lateral mitral annulus (E′) as well as measurement of trans-mitral to TDI of early diastolic velocity ratio (E/E′).
These myocardial velocity measurements with TDI have been shown to be useful in various diseases, including heart failure (HF), hypertension, acute myocardial infarction (MI) and in patients undergoing stress echocardiography for suspected coronary heart disease.3

Diastolic dysfunction is common in cardiac disease and contributes to the signs and symptoms of heart failure. Doppler echocardiography is widely used for the noninvasive assessment of diastolic filling of the left ventricle (LV).4 Analysis of the mitral inflow velocity curve has provided useful information for determination of filling pressures and prediction of prognosis in selected patients. However, mitral flow is dependent on multiple interrelated factors, including the rate and extent of ventricular relaxation, suction, atrial and ventricular compliance, and left atrial pressure.4,5 These factors may have confounding effects on the mitral inflow; thus, it has not been possible to determine diastolic function from the mitral flow velocity curves in many subsets of patients.4,5

To overcome these limitations of the mitral inflow parameters, combinations of the mitral flow velocity curves with other Doppler parameters have been used. These include the pulmonary venous velocity curves, color M-mode propagation velocity, and the response of the mitral inflow to altered loading conditions.6,7 Tissue Doppler imaging (TDI) of mitral annular motion has been proposed to correct for the influence of myocardial relaxation on trans-mitral flows. This has been shown to be an excellent predictor of diastolic filling in subsets of patients.18-28

The present study compares the diagnostic accuracy of E/E’ with invasive LVEDP as an estimate of LV filling pressure in subjects with systolic and pure diastolic heart failure.

METHODS

Total 100 patients were studied between July 2007 to March 2008, 50 patients (22 coronary artery disease, 28 hypertensive) with diastolic heart failure (defined by heart failure signs and symptoms but with preserved ejection fraction) and 50 patients (48 coronary artery disease, 26 dilated cardiomyopathy) with systolic heart failure (heart failure signs and symptoms and reduced ejection fraction) in patients who underwent clinically indicated cardiac catheterization in the admitted patients to the hospital (Sri Jayadeva Institution of Cardiology, Bangalore, India.) and who were able provide written informed consent.

The Patients with systolic and diastolic heart failure aged between 21 to 80 years who underwent clinically indicated cardiac catheterization were included. Patients with mitral stenosis, Patients with prothestic valves, Patients with arrhythmias/heart blocks during study, Patients with mitral annular calcification and Patients with permanent pacemaker implantation were excluded.

Data are expressed as mean values±SD. Comparison between the diastolic and systolic variables were using non paired Student’s t test. For dichotomous variables, chi-square analysis was used for comparison. Statistical significance was set at p <0.05. Statistical relations between conventional Doppler echo/TDI variables and LV end-diastolic pressures were assessed by simple linear regression analysis. Receiver-operating characteristic (ROC) curves analysis was generated for the E/E’ ratio to predict a LV end-diastolic pressure ≥15 mm Hg. Linear regression analysis was used to assess statistical relations between E/E’ and hemodynamic variables.

Patients underwent Echocardiographic examination in the catheterization laboratory just before case was taken for coronary angiography. LV end diastolic pressure was estimated by pigtail catheter before doing left ventriculogram.

The 2D Echocardiography and evidence of impaired LV relaxation or filling, that is, abnormal age dependent isovolumic relaxation time, mitral E/A ratio, deceleration time and thus met the criteria for diastolic heart failure (diastolic heart failure group). Twenty (50) patients had systolic dysfunction with EF <50% (systolic heart failure group).

Images were taken ≤2 hours before cardiac catheterization according to the guidelines of the American Society of Echocardiography using a PHILIPS EnVisor machine.90 For TDI recordings from the apical window, a 5-mm sample volume was located at the septal and lateral sites of the mitral annulus in the 4-chamber view.31 Peak systolic (S’), early (E’), and late (A’) diastolic velocities were obtained at each site and average values of these measurements were calculated for each patient. The mitral E/E’ ratio was subsequently derived (Figure 2).31

Figure 1: E, A, IVRT and deceleration time was derived from pulse-wave doppler recordings of the mitral inflow.
RESULTS

Coronary artery disease was the most common cause for heart failure in patients with systolic and diastolic heart failure; whereas dilated cardiomyopathy was only present in the systolic heart failure group (Table 1).

Table 1: Clinical data of the study participants.

| Variable                                | Heart failure          |
|-----------------------------------------|------------------------|
|                                         | Diastolic(n=50) | Systolic(n=50) |
| Age (years)                             | 51±8 | 51±9 |
| Men/women                              | 40/10 | 42/8 |
| Coronary artery disease                 | 22 (44%) | 48 (96%) |
| Previous myocardial infarction          | 6 (12%) | 48 (96%) |
| Dilated cardiomyopathy                  | – | 2 (4%) |
| Systemic hypertension                   | 28 (56%) | 26 (52%) |
| Body surface area (m²)                  | 1.76±0.2 | 1.72±0.3 |
| Systolic blood pressure (mm Hg)         | 132±16 | 128±17 |
| Diastolic blood pressure (mm Hg)        | 81±1 | 87±23 |
| Heart rate (beats/min)                  | 73±8 | 76±9 |

Patients with systolic heart failure were in a worse New York Heart Association functional (NYHA) class than patients with diastolic heart failure. In patients with systolic heart failure, LV dimensions and volumes were increased, but ejection fraction and fractional shortening were reduced compared with the diastolic heart failure group (Table 2).

Table 2: Baseline Echocardiographic Variables among participants.

| Variable                          | Heart failure          |
|-----------------------------------|------------------------|
|                                   | Diastolic | Systolic | p value |
| LV diastolic diameter (cm)        | 3.7±1.1   | 5.7±1.6  | 0.62    |
| LV systolic diameter (cm)         | 2.1±0.8   | 4.3±1.6  | 0.82    |
| LV diastolic volume (ml)          | 89±21     | 114±23   | 0.97    |
| LV systolic volume (ml)           | 37±10     | 74±17    | 0.66    |
| LA diameter (cm)                  | 2.8±1.5   | 3.2±1.4  | 0.15    |
| Fractional shortening (%)         | 32±8      | 18±9     | 0.60    |
| Ejection fraction (%)             | 58±2.6    | 35±4.7   | 0.65    |

In the diastolic heart failure group, deceleration time and isovolumic relaxation time were prolonged, and the E/A ratio was reduced compared with the systolic heart failure group (Table 3).

Table 3: Conventional Doppler and TDI-derived variables.

| Variable                          | Heart failure          |
|-----------------------------------|------------------------|
|                                   | Diastolic | Systolic | p value |
| E (cm/s)                          | 73±13     | 84±11.5  | 0.001   |
| A(cm/s)                           | 71±19     | 39±6.4   | 0.79    |
| E/A ratio                         | 1.2±0.5   | 2.2±0.3  | 0.23    |
| Deceleration time (ms)            | 179±32    | 159±27   | 0.39    |
| Isovolumic relaxation time (ms)   | 77±15     | 72±11    | 0.15    |
| Systolic mitral annular velocity (S') (cm/s) | 7.0±1.1   | 4.3±1.3  | 0.67    |
| Early diastolic lateral mitral annular velocity (E') (cm/s) | 6.5±3.2   | 7.1±2.8  | 0.41    |
| Late diastolic lateral mitral annular velocity (A') (cm/s) | 9.0±2.1   | 6.0±2.6  | 0.95    |
| E/E'                              | 13.4±4.9  | 13.7±5.2 | 0.46    |

TDI analysis of mitral annulus velocity was readily obtained in all study subjects. S' and A' were significantly reduced in the diastolic heart failure group compared with the systolic heart failure group, but E' and E/E' did not differ significantly between groups.
In the diastolic heart failure group, the LV end-diastolic pressure was similar to systolic group (14.3±4.5 Vs 13.7±4.3 mm Hg). In patients with diastolic heart failure, E/E’ was significantly related to the LV end-diastolic pressure (r=0.79, p <0.0001) (Figure 3).

In patients with systolic heart failure, E/E’ also correlated significantly with LV end-diastolic pressure (r =0.79, p <0.0001) (Figure 4).

Figure 3: The relation between LV end-diastolic pressure (LVEDP) and E/E’ in the diastolic heart failure group.

Figure 4: The relation between LV end-diastolic pressure (LVEDP) and E/E’ in the systolic heart failure group.

In the diastolic heart failure group, an E/E’ >15 derived from ROC analysis, (Figure 5) identified patients with a LV end-diastolic pressure ≥15 mm Hg with a sensitivity of 87% and a specificity of 90% (AUC-area under the curve, 0.78) positive predictive value, 90%; negative predictive value, 84%.

Figure 5: ROC curve analysis for prediction of LV end-diastolic pressure >15 mm Hg in the diastolic heart failure group. The area under the curve (AUC) was 0.80 for E/E’.

In patients with systolic heart failure, E/E’ >15 derived from ROC analysis, (Figure 6) for the prediction of LV end-diastolic pressure ≥15 mm Hg had 87% sensitivity and 90% specificity (AUC-area under the curve, 0.78); positive predictive value, 90%; negative predictive value, 84%.

Figure 6: ROC curve analysis for prediction of LV end-diastolic pressure >15 mm Hg in the systolic heart failure group. The area under the curve (AUC) was 0.78 for E/E’.

DISCUSSION

Study confirms that the mitral E/E’ ratio is a reliable estimate of LV filling pressures in subjects who have diastolic heart failure, as evidenced by heart failure symptoms but preserved LV systolic performance. Our results confirm previous work that indicates that E/E’ readily identifies elevated LV filling pressures in subjects with reduced LV systolic performance. Results was comparable with the study done by Christian Bruch et al,
in both systolic and pure diastolic heart failure. E/E' also seems an appropriate tool to exclude elevated LV filling pressures in subjects presenting with heart failure symptoms. E/E' is reproducibly obtained so that a widespread clinical application of this ratio seems feasible.

Within the last 30 years, the number of patients affected by chronic heart failure has increased dramatically in the Western population. In 2/3 of such patients, systolic and diastolic dysfunction coexist; whereas in 1/3, signs and symptoms are attributable to purely diastolic heart failure. Elevated LV filling pressures have long been identified as the hallmark of diastolic heart failure. However, even in patients with a reduced ejection fraction, exercise limitation is determined by the increase in filling pressures, irrespective of the degree of systolic dysfunction. Thus, in patients with heart failure with or without systolic dysfunction, noninvasive estimation of filling pressures is desirable.

Using echocardiography, LV filling pressures have been estimated by using equations that incorporate ≥1 mitral or pulmonary vein-flow-derived variable. Rossvoll and Hatle have shown that combined trans mitral and pulmonary vein flow variables provide valuable information about filling pressures. However, the feasibility of this approach has been questioned, mainly because mitral and pulmonary vein flow variables are known to change with age, heart rate, and loading conditions. Those limitations seem to have been partly overcome with the introduction of TDI.

The mitral annular E' velocity decreases with worsening diastolic function, suggesting a role of E' as an index of LV relaxation. In addition, the mitral E/E' ratio was proposed as an estimate of LV filling pressures, and this ratio was properly validated in subjects who were admitted to an intensive care unit, most of whom had underlying cardiac disease and reduced systolic performance. Those findings were confirmed by Ommen et al, who studied 100 patients during left-sided cardiac catheterization. In these previous studies, however, patients with diastolic heart failure were not separately evaluated, and the diagnostic accuracy of E/E' in this important diastolic heart failure patient's population was not addressed.

Study has few limitations that are LVEDP was the only invasive measure of LV diastolic function. Relatively small sample of population who had LVEDP >15 mmHg may have weakened the potential correlation between LVEDP and E/E'.

CONCLUSION

Our results confirm that E/E’ is a reliable estimate of LV filling pressures in subjects with systolic and diastolic heart failure. In subjects with diastolic heart failure, E/E’ seems helpful to identify those with truly elevated LV filling pressures. In patients with diastolic heart failure and normal E/E’, a search for other causes of symptoms (pulmonary disease, obesity and so forth) may be warranted.

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