



CORRELATION OF ECHOCARDIOGRAPHY ASSESSMENT OF MITRAL INFLOW AND PULMONARY VENOUS PARAMETERS WITH INVASIVE MEASUREMENT OF LEFT VENTRICULAR RELAXATION PROPERTIES IN CASES OF HEART FAILURE WITH PRESERVED EJECTION FRACTION

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ABSTRACT Heart failure is a global problem and HFpEF constitutes a major group of patients with HF. Most of these patients have diastolic dysfunction. This study was conducted to evaluate the usefulness and association of mitral inflow and pulmonary venous flow parameters by Doppler echocardiography for the evaluation of diastolic function, with same-day direct measurement of LVEDP and PCWP to find out any standardized correlation between invasive and non-invasive procedure.

METHODOLOGY: It was a prospective study done in NRS Medical College between January 2018 to December 2018. Patients who were admitted with congestive heart failure and were diagnosed to have HFpEF were included in this study. In addition to basic blood tests, echocardiography and left heart catheterization were performed on same day for evaluation of LVEDP.

RESULTS: There was a weak correlation between mitral inflow parameters like peak E velocity, peak A velocity, IVRT, Mitral DT, pulmonary venous peak systolic and diastolic flows to LVEDP, but the relationship was not statistically significant. However, there was a good positive correlation between elevated LVEDP and Ard-Ad ($p < 0.001$).

CONCLUSION: Our study suggests that mitral inflow parameters alone might not be sufficient to precisely predict LVEDP, thereby assessing LV diastolic function. Additional parameters like Ard-Ad and tissue Doppler parameters might need to be evaluated to diagnose LV diastolic dysfunction. Among the parameters studied in our study, Ard-Ad had statistically significant relationship with LVEDP.

KEYWORDS : Heart failure (HF), HFpEF – Heart failure with preserved ejection fraction, echocardiography, LVEDP – Left ventricular end diastolic pressure, PCWP – pulmonary capillary wedge pressure

INTRODUCTION

Heart failure (HF) is a clinical syndrome consisting of important symptoms (e.g. breathlessness, ankle swelling, fatigue) which may be accompanied by certain signs (e.g. elevated jugular venous pressure (JVP), pulmonary crackles, and peripheral edema), caused due to a structural and/or functional abnormality of the heart, resulting in decreased cardiac output and/or elevated intracardiac pressures^[1]. Based on left ventricular ejection fraction (LVEF), HF is divided into three phenotypes (Table 1)^[1,2].

The overall incidence of HF is increasing, probably due to ageing and better treatment and salvage of patients with acute myocardial infarctions earlier in course, though age-adjusted incidence of HF may be falling in developed countries^[3,4]. In Europe, the incidence of HF is about 3/1000 person-years (all age-groups) or about 5/1000 person-years in adults^[1,5]. Low and middle income countries (LMIC) including India present an additional set of challenges. On one hand, there is double burden of HF due to persistence of diseases like rheumatic heart disease (RHD) and untreated congenital heart diseases (CHD) in addition to modern day diseases like ischemic heart disease (IHD), and on other hand there is sparse data and poor characterization. The data from available regional HF registries in India show that HF patients are younger by 10-years and the majority of the burden lies below 65 years of age^[6]. The incidence of HF in India is estimated to be at least between 0.5 and 1.7 cases per 1000 person per year, for a total of 492,000 to 1.8 million new cases per year^[7]. Prevalence of HF appears to be 1 - 2% of adults^[1,8,9]. Based on studies in hospitalized patients, 50% of patients have HFrEF and about 50% have HFmrEF/HFpEF^[10,11]. Female constitute more than 50% of HF patients^[1].

Patients with HFpEF may have somewhat better prognosis than HFrEF, though the difference is negligible^[12]. These patients are elderly and more often females with high incidence of co-morbidities like hypertension, obesity, diabetes, CKD, anemia and atrial fibrillation (AF)^[13]. These patients were noted to have myocardial hypertrophy and interstitial fibrosis associated with increased ventricular stiffness and prolonged ventricular relaxation^[14]. In many of these cases, signs of pure diastolic left ventricular dysfunction have been reported^[15]. It has been suggested that Doppler measurements of transmitral blood flow velocities might be useful for assessing left ventricular diastolic function, thereby assessing ventricular relaxation, chamber compliance and filling pressures; though invasive measurements of left ventricular end-diastolic pressure (LVEDP) and/or pulmonary capillary wedge pressure (PCWP) still remain the gold standard^[16]. In this study we have studied the mitral inflow

parameters of patients with HFpEF and correlated them with invasive measurement of left ventricular relaxation properties, done on the same day.

Table 1

Type of HF	HFrEF	HFmrEF	HFpEF	
CRITERIA	1.	Symptoms ± Signs ^c	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2.	LVEF < 40%	LVEF 41 - 49% ^b	LVEF > 50%
	3.	-	-	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c

HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LV = left ventricle; LVEF = left ventricular ejection fraction.

a Signs may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.

b For the diagnosis of HFmrEF, the presence of other evidence of structural heart disease (e.g. increased left atrial size, LV hypertrophy or echocardiographic measures of impaired LV filling) makes the diagnosis more likely.

c For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.

MATERIAL AND METHODS

Patients who fulfilled the criteria of HFpEF were included in the study. We evaluated the patients with the features of congestive heart failure as per Framingham criteria, who were admitted in Nil Ratan Sircar Medical College, Kolkata 14 from January 2018 to December 2018. Hemodynamically unstable patients were excluded from the study. Patients underwent baseline blood and urine tests, Brain Natriuretic peptide (BNP), chest X-ray, electrocardiography, echocardiography and left heart catheterization for invasive LVEDP measurement.

Patients were first optimized with anti-failure therapy and echocardiography for left ventricular diastolic function was performed. Patients were examined by M-mode, 2D & Doppler echocardiography within 3 h before cardiac catheterization. An ultrasonographic instrument with a 2.5-MHZ Doppler transducer (SIEMENS, ACUSON-CV70, Germany) was used with a multi frequency phased array transducer and pulsed wave Doppler tissue imaging technique was used. Standard echo views were obtained as per American society of Echocardiography and different measurements were made as per the standard protocol. Ejection fraction was derived from Simpson's modified single plane method using the apical 4-chamber view.

From the transmitral flow, the peak early (*E*) and late atrial (*A*) diastolic velocities, *E* wave deceleration time (DT) and isovolumic relaxation time (IVRT) were all measured. Transmitral flow during Valsalva was noted. Color M-mode Doppler flow propagation velocity of LV inflow (*V_p*) in all consecutive beats as the slope of the first aliasing velocity (45 cm/s) during early filling, from the mitral valve plane to 4 cm distally into the LV cavity, was noted. Tissue Doppler echocardiography (TDE) was used to measure left ventricular longitudinal myocardial wall motion from the apical 4- and 2-chamber views using 1-2 mm sample volume. Peak *e'* and *a'* were measured and *E/e'*, *e'/a'*, and *E/V_p* ratios were calculated for the four segments.

OBSERVATIONS

A total of 28 patients were evaluated with a mean age of 61.13 ± 12.91 years. 17 (60.7 %) patients were male and 11 (39.3 %) were female. Severity of HF was evaluated as per NYHA functional class and 14 (50 %) patients were in NYHA class II, 10 (35.7 %) in class III, and 4 (14.3 %) patients in class IV. Other baseline characteristics were as in Table 2

Table 2

Patient's Anthropometric Data	Mean ± SD	Range
Age (years)	61.13 ± 12.91	40-75
Female/Male (no.)	11 (39.3%)/17 (60.7%)	
Height (in cm)	176 ± 10	152-193
Weight (in kg)	84 ± 18	52-117
BMI	26 ± 8	19-34
Systolic blood pressure (mm Hg)	150.09 ± 22.20	130-184
Diastolic blood pressure (mm Hg)	98 ± 13	80-111
Heart rate (beats/min)	88 ± 22	70-115
NYHA Class I, II, III and IV	0/14(50%)/10 (5.7%)/4 (14.3%)	

Approximately 71 % of patients had a history of hypertension, 36% had a history of IHD, and 43% had diabetes. 23 percent of patients had a GFR ≤ 40 ml/min. Multiple co-morbidities were present in 24 out of 28 (85 %) patients. Anemia was present in 66% patients, 34% had hypoalbuminemia and BNP level was elevated in all the patients. Other biochemical parameters tested were as in table 3.

Table 3

Variable	Values
Hemoglobin	9.95 ± 2.75 g/dL
Total Protein	6.39 ± 0.91 g/dL
Serum Albumin	3.43 ± 0.63 g/dL
CRP	2.37 ± 4.67 mg/dL
CPK-MB	6.26 ± 25.61 µg/L
Trop-I	1.00 ± 4.77 µg/L
BNP	795.39 ± 352.70 pg/mL
Serum LDL	132.13 ± 46.70 mg/dl
Blood urea	39 ± 16 mg/dl
Serum creatinine	1.6 ± 0.9 mg/dl
Serum sodium	124 ± 11 mEq/L
Serum potassium	3.7 ± 1.2 mEq/l.

Echocardiography of the patients was performed in all patients which revealed LVEF ≥ 50%. Other echo parameters were as in table 4. LVEDP, measured invasively was > 20 mm Hg in 63% of the patients. There was a weak correlation, though not statistically significant, between peak *E* velocity, peak *A* velocity, IVRT, Mitral DT, pulmonary venous peak systolic and diastolic flows to LVEDP (Table 5). However, there was a good positive correlation between elevated LVEDP and Ard-Ad (*p*<0.001).

Table 4

LA and LV Dimensions and Function	Mean ± SD	Range
Left atrial diameter (mm)	36 ± 9	27-57
LV septal wall thickness, diastole (mm)	14.6 ± 6.8	9.4-29.0
LV posterior wall, diastole (mm)	12.6 ± 3.4	9-19
LV diastolic diameter (mm)	42 ± 10	36-54
LV systolic diameter (mm)	26 ± 17	17-40
LV fractional shortening (%)	37 ± 11	26-40
LV ejection fraction (%)	56 ± 18	50-78
LV Mass	194.14 ± 44.90	149.24-239.04
LA Volume index (ml/m ²)	39 ± 15	24-54
LVEDVI (mL/m ²)	61 ± 10	51-71
<i>E</i> (cm/s)	71 ± 47	25-266
<i>A</i> (cm/s)	65 ± 66	15-335
Mitral <i>E/A</i> ratio	1.6 ± 1.0	0.2-4.1
Mitral IVRT (ms)	93 ± 49	20-220
Mitral DT (ms)	167 ± 65	80-350
Ard-Ad (ms)	36 ± 10	26-46
LVEDP (mm Hg)	22 ± 6	16-30

LA: Left atrium, LV: Left ventricle, LVEDVI: Left ventricular end-diastolic volume index, *E* = early diastolic; *A* = atrial diastolic; IVRT = isovolumic relaxation time; DT = deceleration time; LVEDP = Left ventricular end-diastolic pressure.

Table 5

Spectral Doppler	Mean ± SD	Range	Correlation to LVEDP
MF <i>E</i> , cm/s	71 ± 47	25-266	<i>r</i> =0.14, <i>p</i> =0.631
MF <i>A</i> , cm/s	65 ± 66	15-335	<i>r</i> =0.67, <i>p</i> =0.593
<i>E/A</i>	1.7 ± 0.3	1.4-2.0	<i>r</i> =0.57, <i>p</i> =0.162
MF IVRT, ms	93 ± 49	20-220	<i>r</i> =-0.35, <i>p</i> =0.178
MF DT, ms	167 ± 65	80-350	<i>r</i> =-0.06, <i>p</i> =0.842
PVF systole cm/s	34 ± 16	13-76	<i>r</i> =-0.02, <i>p</i> =0.966
PVF diastole cm/s	48 ± 14	25-79	<i>r</i> =0.47, <i>p</i> =0.201
Ard-Ad (ms)	36 ± 10	26-46	<i>r</i> =0.77 <i>P</i> =0.001

DISCUSSION

There has been an increase in HF deaths despite advances in treatment, likely due to increasing numbers owing to ageing, and better treatment and salvage of patients with acute MI earlier in life. It is generally believed that, of those with HF, about 50% have HF_rEF and 50% have HF_pEF/HF_{mr}EF^[1,17]. HF_pEF differs from HF_rEF and HF_{mr}EF in that HF_pEF patients are older and more often female^[1]. In our study we found a male preponderance and high incidence of hypertension and multiple risk factors of heart failure. Proper diagnosis of these patients is of paramount importance for their proper and timely treatment.

Doppler echocardiography is a rapid and non-invasive method for the evaluation of cardiac function. Most of the recommended echocardiographic parameters for evaluation of diastolic function were observed and then these were correlated with LVEDP measured by cardiac catheterization.

Invasive measurement of left ventricular end-diastolic pressure (LVEDP) and/or pulmonary capillary wedge pressure (PCWP) is the gold standard but invasive measurements are not suitable for all patients due to cost and the risk of complications. So the project was undertaken to get the best approximate of LVEDP by various echo parameters and to see which of the suggested criteria may correlate closely with elevated LVEDP.

There was weak correlation between peak *E* velocity, peak *A* velocity, IVRT, Mitral DT, pulmonary venous peak systolic and diastolic flows to LVEDP, but the relationship was not statistically significant. However, there was a good positive correlation between elevated LVEDP and Ard-Ad (*p*<0.001). Our study suggests that mitral inflow parameters alone might not be sufficient to precisely predict the LVEDP, thereby assessing LV diastolic function. These parameters might need to be supplemented by additional parameters like Ard-Ad and tissue Doppler parameters to precisely predict diastolic function of LV.

The limitations of the present study include its relatively small sample size, and LVEF was measured by the biplane Simpson's method, which might be a poor tool for detecting longitudinal systolic dysfunction.

CONCLUSION

Our study suggests that mitral inflow parameters alone might not be sufficient to precisely predict LVEDP, thereby assessing LV diastolic function. Additional parameters like Ard-Ad and tissue Doppler parameters might need to be evaluated to diagnose LV diastolic dysfunction. Among the parameters studied in our study, Ard-Ad had statistically significant relationship with LVEDP.

Conflict of Interest

None.

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