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Correlation of Invasively Estimated Left Ventricular End Diastolic Pressure with Acceleration of E' Wave by Tissue Doppler Imaging of Mitral Annulus

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Abstract

Background: There is no single noninvasive index that provides a direct measure of LV filling pressure. However, invasive measuring of LV end diastolic pressure (LVEDP) provides reliable assessment of LV diastolic dysfunction, but its invasive nature limits its use in daily practice. Accurate noninvasive assessment of LV diastolic dysfunction is highly desirable, and the relationship between the degree of LVEDP and acceleration of E' wave obtained by tissue Doppler imaging (TDI) of mitral annulus is not clearly assessed; here in our study we aimed to assess the relation between the degree of LVEDP and the acceleration rate of E' wave of mitral annular Doppler tissue. **Patients and Methods:** The study included 60 patients divided equally into 3 groups according to the degree of LVEDP, group I (Normal): <10 mmHg, group II (Grey zone): 10 - 14 mmHg, and group III (Elevated): ≥15 mmHg. All participants underwent Electrocardiographic examination (ECG), standard two-dimensional echocardiography, mitral Doppler flow and tissue Doppler imaging of mitral annulus including E/E' ratio and E' wave acceleration rate. Coronary angiography and left sided heart catheterization and measuring LVEDP were performed for correlating E' wave acceleration rate with invasively estimated LVEDP. **Results:** There was significant progressive decrease in E' acceleration rate (E' Acc rate) with progressive increase in LVEDP from I to III (P 0.001), while there was significant progressive increase in E/E' ratio with progressive increase in LVEDP from I to III (P 0.003). Peak E' acceleration rate had a significant negative correlation with LVEDP in all three groups, with p value of 0.003, 0.044 and 0.021 respectively in group I, II & III. Regarding E/E' ratio there was a significant positive correlation in predicting normal and elevated LVEDP with p value (0.001 and 0.006) respectively while there was a non-significant correlation between E/E' and LVEDP within grey zone group. **Conclusion**: E' acceleration rate could be used as a reliable index to assess LVEDP.

Keywords

LV End Diastolic Pressure, E Annular Wave Acceleration

1. Introduction

The assessment of left ventricular (LV) diastolic function should be an integral part of a routine examination, particularly in patients presenting with dyspnea or heart failure. About half of patients with new diagnoses of heart failure have normal or near normal global ejection fractions (EFs). These patients are diagnosed with "diastolic heart failure" or "heart failure with preserved EF" [1]. Technical advances in the noninvasive imaging modalities have allowed the assessment of LV mechanics which has resulted in the development of novel parameters that can play a promising role in the quantification of LV diastolic function [2]. In some patients, elevated filling pressure is observed only during exercise; therefore, normal filling pressure at rest does not exclude clinically significant diastolic dysfunction. There is no single noninvasive index that provides a direct measure of relaxation, restoring forces, compliance, or LV filling pressure [3] [4].

The aim of this study is to assess the relation between the degree of invasively measured LVEDP and the acceleration rate of E' wave of mitral annular Doppler tissue.

2. Patients and Methods

The study was conducted on 60 consecutive patients scheduled for coronary angiography and left-sided heart catheterization to measure LVEDP in cardiology department, Menoufia University Hospital from Augustus 2017 to October 2018; Patients were enrolled in the study after their informed consent and approval by the Committee of Ethics of Menoufia University Hospital were obtained. Patients with acute myocardial infarction, significant coronary artery disease proved by coronary angiography, atrial fibrillation, left bundle branch block, mitral and/or aortic prosthesis, mitral stenosis, annular mitral calcification, more than mild primary valvular regurgitation, pericardial diseases, and contraindications to dye were excluded from the study. All patients underwent detailed history taking, thorough physical examination and 12-lead ECG.

2.1. Cardiac Catheterization

LVEDP was directly measured by fluid-filled 6 F pigtail catheter introduced retrogradly via femoral artery into the cavity of LV. The Fourth intercostal spaces between the A-P diameters of the chest wall measured as Zero level. Pressure values were averaged as mean value of three consecutive sinus cycles. The left ventricular end diastolic pressure (LVEDP) was obtained by computer recording. Included patients were classified into three groups according to LVEDP as follow:

Group I (Normal): include 20 patients with normal LVEDP < 10 mmHg, Group II (Grey zone): include 20 patients with mild increase LVEDP 10 - 14 mmHg and Group III (Elevated): include 20 patients with elevated LVEDP ≥ 15 mmHg.

2.2. Conventional Echocardiography

Transthoracic echocardiographic examination was done using a commercially available echo machine (vivid E9, GE Medical Systems, Milwaukee,) according to the American Society of echocardiography recommendations [5] [6]. Conventional Echocardiography measuring: left atrial, LV end diastolic and systolic dimensions, EF, Septal and Posterior wall thickness. Mitral inflow was analyzed where E/A ratio and E/E' ratio were measured. Continuous-wave Doppler was used to estimate systolic pulmonary artery pressure from the tricuspid regurgitation velocity. All Doppler values represent the average of 3 consecutive beats.

2.3. Tissue Doppler Imaging (DTI)

In the apical 4 chamber view, a 4 - 5 mm sample volume was placed at the septal and lateral margins of the mitral annulus and the cursor was oriented so that it is parallel to the direction of mitral annular motion. Velocities of early (E') and late (A') diastolic waves and peak systolic (S) wave were recorded and E'/A' ratio was calculated and averaged from both annular sites. Myocardial isovolumic relaxation time (IVRT) was measured from the end of S wave to the onset of E' wave. Acceleration time of E' wave (E' Acc time) was measured from onset to peak of E' wave and acceleration rate of E' wave (E' Acc rate) was calculated as peak E' velocity divided by E' Acc time.

Statistical analysis:

Data were analyzed using SPSS software. Quantitative data expressed as mean and standard deviation Chi square test student t test, Mann whiney U test, Kruskal Walls test and correlation coefficient test.

3. Results

The study included 60 patients, that were further classified according to LVEDP into three groups, group I (Normal), group II (grey zone) and group III (Elevated) with mean age for each group (46.5 ± 5.5, 52.1 ± 5.9 and 58.4 ± 1.9 years) respectively. Elevated LVEDP was noticed in males, older, hypertensive and diabetic patients, while there were no statistically significant differences regarding dyslipidemia and smoking (P > 0.05) between groups (**Table 1**). There was no significant difference between groups as regards conventional echocardiographic parameters, as LV end systolic & diastolic dimension also EF. EDV, ESV and SV,

Table 1. Demographic criteria and risk factors of study population.

Items	Normal (<10) mmHg (No = 20)		Gray Zone (10 - 14) mmHg (No = 20)		Elevated (≥15) mmHg (No = 20)		Test of sig. and P value
	No	%	No	%	No	%	
Gender							
Male	12	60	10	50	20	100	$X^2 = 6.7$ P = 0.036
Female	8	40	10	50	0	0	
Age							
Mean ± SD	46.5 ± 5.5		52.1 ± 5.9		58.4 ± 1.9		F = 15.5 P = 0.001
Diabetes Mellitus							
Yes	6	30	6	30	18	90	$X^2 = 9.6$ P = 0.008* (≤0.05)
No	14	70	14	70	2	10	
Hypertension							
Yes	6	30	6	30	20	100	$X^2 = 10.8$ P = 0.004* (≤0.05)
No	14	70	14	70	0	0	
Dyslipidemia							
Yes	12	60	14	70	14	70	$X^2 = 0.30$ P = 0.86 (>0.05)
No	8	40	6	30	6	30	
Smoking							
Yes	10	50	12	60	16	80	$X^2 = 2.01$ P = 0.37 (>0.05)
No	10	50	8	40	4	20	

while there was a highly significant progressive increase in LAD, TR velocity and PASP from group I to group III.E wave peak velocity and E/A ratio were maximum in group III and lowest in group II (Table 2).

Regarding TDI parameters, there was significant progressive decrease in E' acceleration rate and E' peak velocity from group I to group III while there was significant progressive increase in E/E' ratio and E' acceleration time from group I to group III. IVRT is maximum in group II and lowest in group I (Table 3, Figures 1-3).

According to peak E' acceleration rate there was a significant negative correlation between E' acceleration rate and LVEDP in all three groups, with p value of (P 0.003, 0.044 and 0.021 respectively) (Tables 4-6, Figures 1-3).

Regarding E/E' ratio it was noticed that There was a significant positive correlation in predicting normal and elevated LVEDP with p value (0.001 and 0.006) respectively while there was a non-significant correlation between E/E' and LVEDP within grey zone group (p value = 0.138) (Tables 4-6).

By analysis of ROC curve; the cutoff point of E' acceleration rate to identify patients with elevated LVEDP was 132 cm/s^2 that had 42% sensitivity and 93% specificity while cut off point of E/E' was 9.81 and had 87% sensitivity and 21% specificity to identify patients with elevated LVEDP (Table 7).

Table 2. Comparison between studied groups as regarding conventional echocardiographic parameters.

Parameter Mean ± SD	Normal <10 mmHg (No = 20)	Gray Zone 10 - 14 mmHg (No = 20)	Elevated ≥15 mmHg (No = 20)	Test of sig. & P value
LVIDd (cm):	5.01 ± 0.27	5.02 ± 0.19	5.3 ± 0.35	P = 0.06
LVIDs (cm):	3.5 ± 0.29	3.4 ± 0.23	3.6 ± 0.36	P = 0.67
EDV (ml):	106.1 ± 17.5	104.0 ± 19.4	114.2 ± 14.7	P = 0.39
ESV (ml):	44.1 ± 8.8	40.7 ± 9.4	43.1 ± 7.2	P = 0.07
SV (ml):	62.1 ± 10.2	63.3 ± 13.1	71.1 ± 10.9	P = 0.18
EF (%):	62.9 ± 3.4	60.2 ± 1.7	61.2 ± 1.6	P = 0.07
AO (cm):	3.4 ± 0.35	3.6 ± 0.47	3.7 ± 0.65	P = 0.38
LA (cm):	3.7 ± 0.18	3.8 ± 0.33	4.4 ± 0.26	P = 0.001
E (cm/s):	91 ± 7.4	66.5 ± 11.7	100.2 ± 9.3	P = 0.04
A (cm/s):	54.2 ± 8.3	73.5 ± 12.2	59.1 ± 17.7	P = 0.04
E/A (ratio):	1.2 ± 0.31	0.91 ± 0.19	1.7 ± 0.54	P = 0.027
TR (m/s):	1.9 ± 0.14	2.5 ± 0.26	3.1 ± 0.30	P = 0.001
PASP (mmHg):	24.8 ± 2.02	35.5 ± 5.3	48.8 ± 7.5	P = 0.001

Table 3. Comparison between studied groups as regarding TDI parameters.

Parameter to be estimated	Normal <10 mmHg (No = 20)	Gray Zone 10 - 14 mmHg (No = 20)	Elevated ≥15 mmHg (No = 20)	Test of sig. & P value
E' (cm/s): Mean ± SD	8.7 ± 1.8	6.3 ± 1.5	4.9 ± 0.69	F = 17.8 P = 0.001
A' (cm/s): Mean ± SD	7.3 ± 0.55	7.8 ± 1.2	6.03 ± 1.1	Kruskal Wallis H = 11.3 P = 0.004
E'/A' (ratio): Mean ± SD	1.2 ± 0.22	0.82 ± 0.08	0.81 ± 0.07	Kruskal Wallis H = 9.8 P = 0.07
E/E' (ratio): Mean ± SD	7.2 ± 1.02	11.01 ± 3.1	15.4 ± 2.5	Kruskal Wallis H = 20.6 P = 0.003
IVRT (ms): Mean ± SD	72.8 ± 3.5	108.8 ± 3.4	83.6 ± 23.1	F = 18.3 P = 0.001
E' Acceleration time (ms): Mean ± SD	37.8 ± 1.8	39.0 ± 2.9	41.4 ± 2.9	Kruskal Wallis H = 7.9 P = 0.019
E' Acceleration rate (cm/s^2): Mean ± SD	230.6 ± 55.7	164.2 ± 48.6	121.1 ± 25.4	Kruskal Wallis H = 15.1 P = 0.001

EF: *Ejection fraction*; LA: *left atrium*; TR: *Tricuspid Regurgitation*; PASP: *Pulmonary artery systolic pressure*; Acc: *Acceleration*.

Table 4. Correlations between E/E', E' acceleration rate, and LVEDP within normal group of LVEDP (<10 mmHg).

		E/E'	E' acceleration rate	LVEDP
E/E'	Pearson Correlation		0 - 0.749	0.772
	Sig. (2-tailed)		0.002	0.001
E' acceleration rate	Pearson Correlation	−0.749		−0.728
	Sig. (2-tailed)	0.002		00.003

Table 5. Correlations between E/E’, E’ acceleration rate, and LVEDP within grey zone group of LVEDP (10 - 14 mmHg).

		E/E’	E’ acceleration rate	LVEDP
E/E’	Pearson Correlation		−0.595	0.679
	Sig. (2-tailed)		0.213	0.138
E’ acceleration rate	Pearson Correlation	−0.595		0 - 0.823
	Sig. (2-tailed)	0.213		0.044

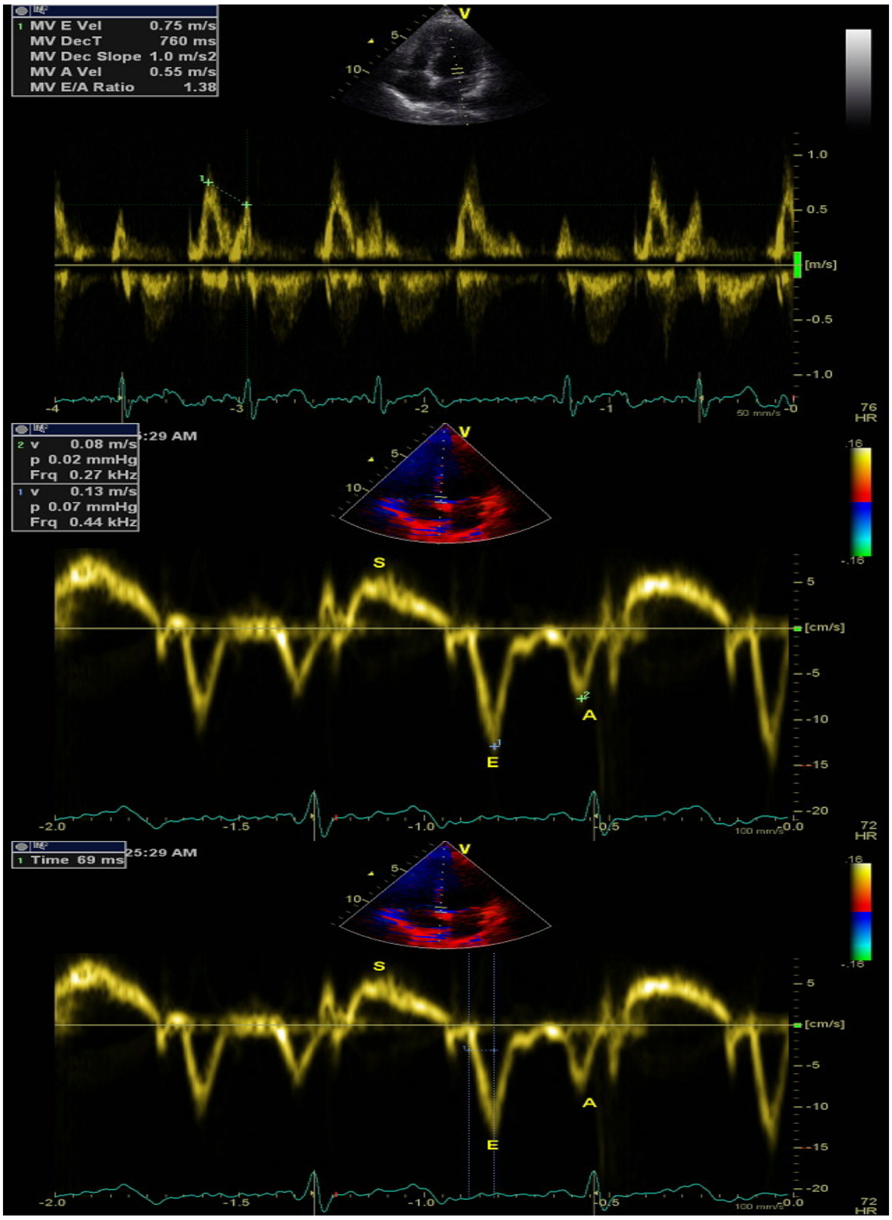

Figure 1. Mitral flow and DTI from patient in group (I). Pulsed wave Doppler of mitral inflow (*upper image*) and Pulsed wave tissue Doppler tissue Imaging from the medial mitral annulus in apical 4 chamber view (*middle image*). Note the normal peak E’ velocity (13 cm/s) with peak E’ *acceleration rate* (188 cm/s^2) as E’ *acceleration time* is (69 ms) (*lower image*) in normal subject.

Table 6. Correlations between E/E', E' acceleration rate, and LVEDP within elevated group of LVEDP (≥15 mmHg).

		E/E'	E' acceleration rate	LVEDP
E/E'	Pearson Correlation		−0.870	0.790
	Sig. (2-tailed)		0.001	0.006
E' acceleration rate	Pearson Correlation	−0.870	.	−0.710
	Sig. (2-tailed)	0.001		0.021

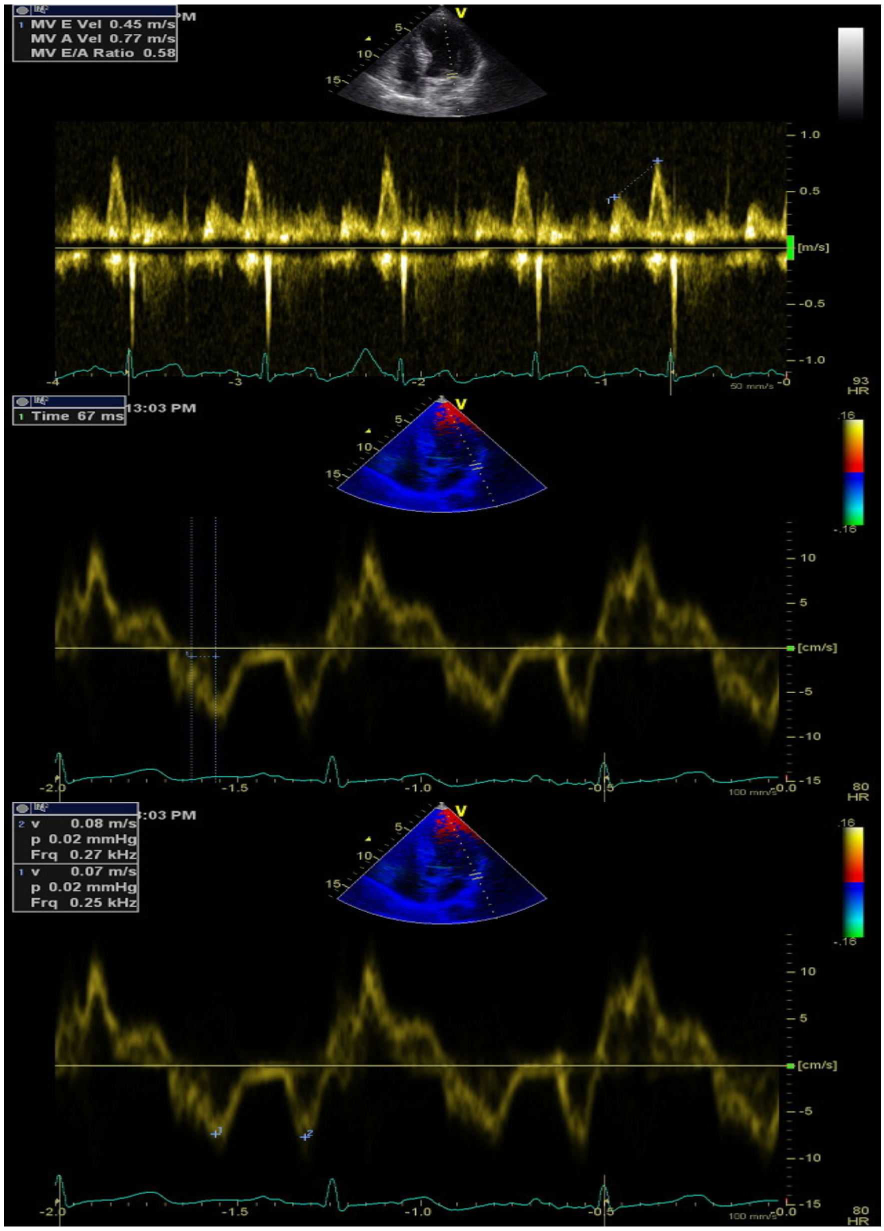

Figure 2. Mitral flow and DTI from patient in group (2). Pulsed wave Doppler of mitral inflow (*upper image*) and Pulsed wave tissue Doppler Imaging from the apical 4 chamber view sampling from the lateral mitral annulus (*middle image*). Note the reduced peak E' velocity (7 cm/s) with peak E' acceleration rate (104 cm/s^2) as E' *acceleration time* is (67 ms) (*lower image*) in patient with impaired relaxation (IR) pattern.

Table 7. Analysis of ROC curve between E/E' and E' acceleration rate as regard LVEDP.

Test Result Variable(s)	Area Under the Curve AUC	Cut off point	Sensitivity	Specificity	R	P value
E/E'	0.991	9.82	87%	21%	**0.95**	**0.001**
E' acceleration rate	0.054	132	42%	93%	**−0.87**	**0.001**

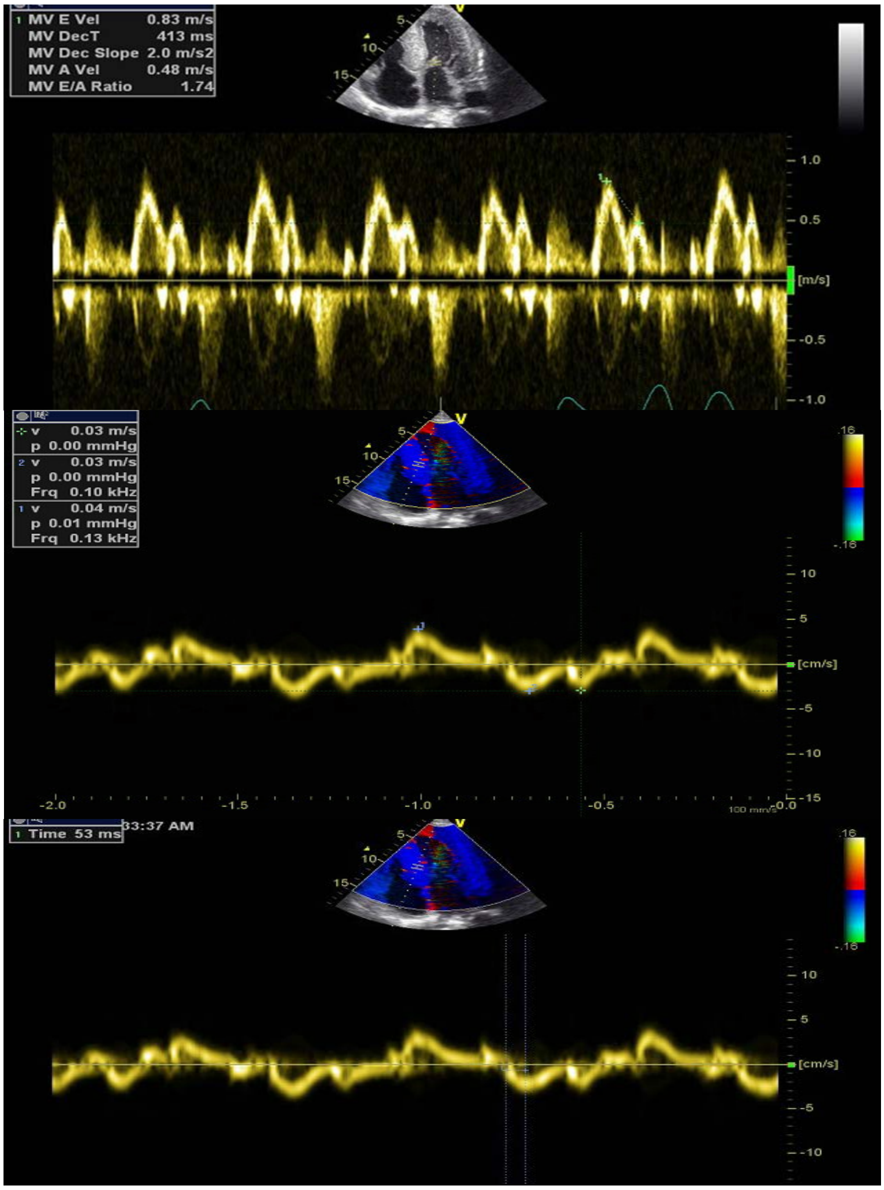

Figure 3. Mitral flow and DTI from patient in group (3). Pulsed wave Doppler of mitral inflow (*upper image*) and Pulsed wave tissue Doppler Imaging from the apical 4 chamber view sampling from the medial mitral annulus (*middle image*). Note the reduced peak E' velocity (3 cm/s) with peak E' *acceleration rate* (56 cm/s^2) as E' *acceleration time* was (53 ms) (*lower image*) and in patient with pseudonormal (PN) pattern denoting elevated LAP.

4. Discussion

The major findings of this study were first: there was a highly significant progressive decrease in E' acceleration rate from group I to group III and there was a significant negative correlation between E' acceleration rate and LVEDP in all three groups. Second: there was significant progressive increase in E/E' ratio from group I to group III and there was a significant positive correlation in predicting normal and elevated LVEDP while there was a non-significant correlation between E/E' and LVEDP within grey zone group. Third: There were highly significant progressive increases in LAD, TR velocity and PASP from group I to group III.

4.1. E' Acceleration Rate in Patients with Diastolic Dysfunction

In our study, similar to peak E' velocity, peak acceleration rate of E' was significantly lower in patients with elevated LV filling pressure (group III) compared to other two groups of LVEDP (P value ≤ 0.001) and there was significant negative correlation between E' acceleration rate and LVEDP, consistent with the result of Qinyun Ruan, *et al.* [7] study which reported that the peak acceleration rate of E', at either side of the mitral annulus, in patients with impaired LV relaxation (IR, PN, and Res groups) was significantly lower than in the age-matched control group. Overall its accuracy in identifying patients with impaired relaxation and elevated filling pressures was similar to peak E' velocity [7].

4.2. E/E' Ratio in Patients with Diastolic Dysfunction

In our study we found that (E/E') showed a statistically significant higher values in elevated group of LVEDP compared to other two groups and there was positive correlation between E/E' and LVEDP but there was a non-significant correlation within grey zone group (p value = 0.138)., S.F. Nagueh, *et al.* [8] suggests that the mitral E/E' ratio is of supportive value for the non-invasive prediction of the LVEDP. Arteaga *et al.* [9], Kasner M *et al.* [10] and Yu, *et al.* [11] reported that the ratio between transmitral E and E' (E/E') correlates well with LV filling pressure or pulmonary capillary wedge pressure (PCWP). Ommen SR *et al.* [12] also reported that Patients with E/E' < 8 can be classified as normal filling pressure and if there is a normal left atrial size, normal diastolic function can be diagnosed. Those with E/E' > 15 have raised filling pressure. But in contrast to many studies that reported weak correlations between E/E' ratio and LV filling pressure. Oleg F *et al.* [13] reported there was no clear or sufficient evidence to support that E/E' can reliably estimate LVFP in preserved EF as the diagnostic accuracy of E/E' to identify/exclude elevated LVFP and DD/HFpEF is limited and requires further validation in a well-designed prospective clinical trial. Mario Previtali *et al.* [14] suggested that the mitral E/E' ratio is of limited value for the non-invasive prediction of the LVEDP in the individual patients.

Lindqvist *et al.* [15], found a weak correlation between E/E' and PCWP at, septal and lateral walls ($r = 0.43$ - 0.44, $p < 0.05$). Similarly, Hadano *et al.* [16] reported poor correlation between E/E' Lateral and LVEDP ($r = 0.33$, $p < 0.001$) among 140 patients referred for cardiac catheterization.

5. Conclusion

TDI derived E' peak acceleration rate was found to be a useful index to assess LVEDP especially in patients with advanced LV diastolic dysfunction.

Limitations

The sample size was small and we are in need for larger study with different category of patients (normal versus depressed LV systolic function) to validate this parameter.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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