The Validity of Pulse Wave Tissue Doppler Imaging in Predicting Elevated left Ventricular end Diastolic Pressure in Patients with Coronary Artery Disease

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ABSTRACT:

BACKGROUND:

Elevated left ventricular filling pressures are the main physiological consequence of diastolic dysfunction and carry a prognostic significance in different cardiovascular diseases including coronary artery diseases, and cardiomyopathies. Filling pressures are considered elevated when the mean pulmonary capillary wedge pressure is >12mmHg or when the left ventricular end diastolic pressure is ≥ 16 mm Hg. a reliable noninvasive method for the estimation of LVEDP is needed.

OBJECTIVE:

The aim of this study was to evaluate the correlation between the Tissue Doppler Imaging derived E/é ratio, and Left Ventricular End Diastolic Pressure (measured during left ventricular catheterization) in patients with significant Coronary artery Disease, and to identify the optimal cutoff value of the E/é ratio to predict elevated LVEDP.

PATIENTS AND METHODS:

This study included 87 patients scheduled for elective coronary angiography at Ibn-Albitar Hospital catheterization laboratory between December 2012 and April 2013.Transthoracic echocardiography was performed to all patients within 2 hours before left heart catheterization, using Philips echocardiography system & S5-1 probe. Mitral valve inflow velocities were assessed by Pulsed-wave Doppler performed in the apical 4-chamber view. Ejection fraction (EF) was measured with biplane Simpson's method from the apical 4-chamber view. PW TDI was performed in the apical 4-chamber view to measure mitral annular velocities from the medial and lateral mitral annuli.

RESULTS:

The mitral inflow velocities (E, and A) were not correlated to LVEDP while the E/A ratio had a weak positive and the DT of the E wave had a weak negative correlations with LVEDP. E/é ratio showed intermediate to good positive correlation with LVEDP especially those derived from the medial mitral annulus.

The correlation between E/é ratio and LVEDP was similar in the patients with or without significant CAD. The ROC curve showed that the cutoff point of E/ é ratio for predicting LVEDP higher than 15mm Hg was from medial mitral annulus > 15 (sensitivity 77.5 % , specificity 84.6%; P<0.001) and from lateral mitral annulus >10 (sensitivity 79 %, specificity 80.3 %; P < 0.001).

On subgroup classification according to EFs, the E/é medial showed significant but weaker correlation with LVEDP in patients with EF ≥ 50%, as compared to patients with EF < 50 %. E/é lateral and E/é average had poor correlation with LVEDP in patients with EF ≥ 50 %, while they have intermediately significant correlation in patients with EF < 50%.

CONCLUSION:

The TDI derived E/é ratio is better than mitral inflow doppler velocities and intervals for predicting elevated LVEDP in patients with or without significant CAD, especially in patients with reduced EF.

The E/é medial > 15 and E/é lateral > 10, predict LVEDP > 15 mm Hg with good sensitivity and specificity.

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INTRODUCTION:

Elevated left ventricular filling pressures are the main physiological consequence of diastolic dysfunction and carry a prognostic significance

in different cardiovascular diseases including coronary artery diseases, and cadiomyopathies
Filling pressures are considered elevated when the mean pulmonary capillary wedge pressure is>12mmHg or when the left ventricular end diastolic pressure is ≥ 16 mm Hg [1.2,3].

Tissue Doppler Imaging mitral annular diastolic velocities:

Another method to estimate LV relaxation and filling pressure is by using Tissue Doppler Imaging which enables measurement of high amplitude, low frequency Doppler shifts caused by myocardial motion. As cardiac structures move in a velocity range 0.06 to 0.24 m/s, some 10 times slower than myocardial blood flow, and have an amplitude approximately 40 decibels higher, it is possible to obtain images of tissue Doppler motion of high resolution without significant artifact originating from the blood pool[4,5,6].

Because the longitudinal contraction and relaxation velocities of the LV myocardium are greatest in the basal segments and decrease progressively toward the apex, the sample volume of the PW TDI is placed at the septal and lateral borders of the mitral annulus. During systole, the annulus descends towards the apex, whereas it recoils back toward the base in early and late diastole. TDI measurements of mitral annular velocities include the systolic (S), early diastolic (é), and late diastolic (a') velocities [7,8,9,10].

Hemodynamic determinants of Tissue Doppler Mitral annular diastolic velocities :

The hemodynamic determinants of e´ velocity include LV relaxation, preload, systolic function, and LV minimal pressure. A significant association between e´ and LV relaxation was observed[11,12,13]. In the presence of impaired LV relaxation and irrespective of LA pressure, the e´ velocity is reduced and delayed, such that it occurs at the LA-LV pressure crossover point. On the other hand, mitral E velocity occurs earlier with PNF or restrictive LV filling. Accordingly, the time interval between the onset of E and e´ is prolonged with diastolic dysfunction[14].

For preload, LV filling pressures have a minimal effect on e´ in the presence of impaired LV relaxation. On the other hand, with normal LV relaxation, preload increases é. Therefore, in patients with cardiac disease, e´ velocity can be used to correct for the effect of LV relaxation on mitral E velocity, and the E/e´ ratio can be applied for the prediction of LV filling pressures[15,16,17,18].

Because septal e´ is usually lower than lateral e´ velocity, the E/e´ ratio using septal signals is usually higher than the ratio derived by lateral e´, and different cutoff values should be applied according to e´ location[16] .

Clinical application of Tissue Doppler Imaging mitral annular diastolic velocities:

Since é velocity is less load dependent compared to mitral inflow Doppler velocities, It can be used along with E velocity (E/é) to predict LV filling pressures, especially in conditions where conventional mitral and pulmonary venous flow velocities are poor indicators of LV filling pressures, like patients with sinus tachycardia[17], hypertrophic cardiomyopathies[8].

The E/é ratio is highly predictive of adverse events after acute myocardial infarction, HF, hypertensive heart disease, severe secondary mitral regurgitation, atrial fibrillation, and cardiomyopathic disorders[16].

AIM OF THE STUDY:

The aim of this study was to evaluate the correlation between the Tissue Doppler Imaging (TDI) derived E/é ratio, and Left Ventricular End Diastolic Pressure (LVEDP) in patients with significant Coronary artery Disease , and to identify the optimal cutoff value of the E/é ratio for predicting elevated LVEDP.

PATIENTS AND METHODS:

Patient population:

This study included patients scheduled for elective coronary angiography at Ibn-Albitar Hospital catheterization laboratory for ten months period Patients 18 years or older with sinus rhythm were eligible.

Exclusion criteria

complete left and right bundle branch block Pacemaker dependence , Atrial fibrillation , Significant mitral annular calcification , Surgical mitral rings , Mitral stenosis , Moderate to severe mitral regurgitation, Prosthetic mitral valves. All patients were examined clinically. Demographic data including age, sex, underlying major risk factors for coronary artery disease, cardiovascular drugs, and clinical data including blood pressure and heart rate were recorded.

Conventional Echocardiography:

Transthoracic echocardiography was performed by single operator for all patients within 2 hours before left heart catheterization using Philips CX50 echocardiography machine, USA with a 1.5-3.6 MHz S5-1 Philips Ultrasound Transducer, USA. The machine settings during PW Doppler were frequency 45 Hz, gain 50%, and sweep speed 50 to 100 mm/s, and during TDI were frequency 71 Hz, gain 30 %, and sweep speed 50 to 100 mm/s. Mitral valve inflow velocities were assessed by Pulsed-wave Doppler performed in the apical 4-chamber view. Color flow imaging was used for optimal alignment of the Doppler beam. A 1mm-3mm sample volume was placed between mitral leaflet tips. Variables measured include the peak early diastolic filling (E-wave) and late diastolic filling (A-wave) velocities, and the (DT) of early filling velocity. Mitral inflow velocities were obtained at end-expiration, and averaged over 3 consecutive cardiac cycles. E/A ratio was calculated, and IVRT was measured by placing the cursor of pulse-wave (PW) Doppler in the LV outflow tract to simultaneously display the end of aortic ejection and the onset of mitral inflow (19,20,21)..

Cardiac catheterization:

Left ventricular catheterization was performed via femoral artery approach using seildenger technique and 6 or 7 French femoral sheaths. Left ventricular end diastolic pressure was measured by fluid filled 5 or 6 French pigtail catheters attached to Argon model P2202-1 pressure tranducer. The Fourth intercostal space in the mid-axillary line was considered as Zero level..

Statistical analysis:

Baseline characteristics are expressed as the mean value ± SD and compared between patients group with and without CAD, using Independent-Samples t test. Categorical data are presented as percentages and compared using Chi square.Correlations between Echocardiographic variables and LVEDP were calculated using the Pearson correlation coefficient (r).The predictive accuracy for LVEDP > 15 mm Hg was assessed using receiver operating characteristic curves (ROC).IBM SPSS version 20 was used for all statistical analysis.Significance was set at $P \leq 0.05$.

RESULTS:

Eighty seven patients were included in this study. The mean Age was 56.13 ± 7.19 years and 52 % were males. Patients with significant CAD constitute 80 % of the population of this study while the remaining 20 % have either no or non significant CAD. When comparing baseline characteristic between patients with significant CAD and those without significant CAD there was no significant difference in cardiovascular risk factors and cardiac drugs used before catheterization between the two groups. No significant difference was found in HR, SBP, or DBP between the two groups (Table 1).Patients with significant CAD had higher mean LVEDP (P=0.014) and lower EF (P=0.008) in comparison to those patients without significant CAD. (Table 1)

The Correlations of Doppler Echocardiography variables with LVEDP are shown in Table 2. The mitral inflow velocities (E, A) were not correlated to LVEDP while the E/A ratio had a weak positive and the DT of the E wave had a weak negative correlations with LVEDP.Combined variables derived from early diastolic mitral inflow velocity (measured by pulse wave Doppler) and early diastolic mitral annular velocity (measured by TDI), E/é ratio, showed intermediate to good significant positive correlation with LVEDP, especially those derived from the medial mitral annulus.The correlation between E/é ratio and LVEDP was similar in the patients with or without significant CAD. (Table 2)

On subgroup classification of patients with significant CAD into patients with preserved LV systolic function (EF ≥ 50%), and patients with LV systolic dysfunction (EF < 50 %), the E/é medial showed significant but weaker correlation with LVEDP in patients with EF ≥ 50 %, as compared to patients with EF < 50 %. E/é lateral and E/é average had poor correlation in patients with EF ≥ 50 %, while they have intermediately significant correlation with LVEDP in patients with EF < 50 % (Table 3)

Table 1: Baseline characteristics.

Variables	No CAD (n=17)	Significant CAD (n=70)	P value
Age: mean± SD	53.4±9.6	57.3±6.9	٠.06
Sex: male	47 %	54 %	٠.59
CAD risk factors			
Hypertension	58 %	61 %	٠.52
Diabetes mellitus	23 %	37 %	٠.22
Dyslipedemia	27 %	29 %	٠.53
Smoking	22 %	27 %	٠.82
Drugs			
Beta blocker	37 %	31 %	٠.22
ACEI or ARB	35 %	30 %	٠.67
Calcium Channel blocker	17 %	18 %	٠.61
Diuretics	13 %	17 %	٠.51
Nitrate	60 %	70 %	٠.30
Statin	58 %	65 %	٠.39
Systolic blood pressure mm Hg	140.8±23.8	142±20.8	٠.77
Diastolic blood pressure mm Hg	86.9±13.8	89.2±14.1	٠.54
Heart rate (beat/min)	80.1±9.8	77.4±10.6	٠.32
LVEDP mm Hg	14.8±5.1	18.5±5.9	٠.014
EF %	58.94 ± 6.58	53.54 ± 7.54	0.008

Table 2: Correlation of Echocardiographic variables with LVEDP.

Echocardiographic Variables	No significant CAD n=17			Significant CAD n=70		
	Mean ± SD	r	p	Mean ± SD	r	p
E cm/s	77.05 ± 11.96	0.36	0.156	79.16 ± 7.36	0.12	0.308
A cm/s	62.98 ± 12.10	-0.40	0.107	64.13 ± 8.55	-0.04	0.696
E/A	1.29 ± 0.41	0.35	0.03	1.27 ± 0.24	0.24	0.041
DT cm/s	199.41 ± 36.78	-0.33	0.04	198.14± 29.12	-0.24	0.04
IVRT ms	83.68 ± 8.62	-0.024	0.627	85.72 ± 9.16	-0.19	0.133
E/é Medial	11.15 ± 5.33	0.76	<0.001	14.19 ± 2.84	0.68	<0.001
E/é Lateral	8.25 ± 3.32	0.54	<0.001	9.97 ± 1.91	0.54	<0.001
E/é Average	9.14 ± 4.19	0.60	<0.001	11.66 ± 2.20	0.63	<0.001

r value indicates Pearson correlation coefficient.

Table 3: Correlation of E/é ratio measured from medial, lateral, and the average of medial and lateral mitral annulus velocity in patients with significant coronary artery disease classified according to their ejection fraction.

	EF ≥ 50% n=45			EF < 50% n=25		
	mean±SD	r	P	mean±SD	r	P
E/é Medial	12.97±2.59	0.41	0.005	16.37±1.79	0.67	<0.001
E/é Lateral	9.29±1.71	0.26	0.04	11.13±1.68	0.44	0.02
E/é average	10.79±1.94	0.35	0.016	13.24±1.73	0.53	0.007

DISCUSSION:

Tissue Doppler imaging has been well validated to estimate left ventricular filling pressure in the general population and in patients with specific heart diseases[8, 21]. The most accurate tool for this estimation is the mitral inflow to mitral annulus velocities ratio (E/é). However, this method should be thoroughly evaluated in patients with CAD before its utilization for prediction of the LV filling pressures, because in patients with chronic or acute ischemia, a wall motion abnormality may be present and this might interfere with the accuracy of the recorded velocities.This study showed that E/é ratio have good correlation with LVEDP measured during LV catheterization in patients with significant CAD and that it's the best noninvasive echocardiographic variable for predicting elevated LV filling pressure (Table 2) .

The current study confirmed that E/é ratio is a valid tool for predicting an elevated LVEDP in patients with CAD similar to the patient group without significant CAD. E/é derived from medial mitral annulus correlated better with LVEDP than E/é derived from the lateral mitral annulus. According to the ROC curve, cut off points of E/é to predict LVEDP > 15 mm Hg in this study were E/é from medial mitral annulus more than 15 (sensitivity 77.5%, specificity 84.6%; P < 0.001) and E/é from lateral mitral annulus more than 10 (sensitivity 79 %, specificity 80.3 %; P < 0.001). (Figure 8 and 9).Previous studies had examined the correlation of E/é ratio with LV filling pressure, Ommen, et al[22], reported that the E/é ratio was the single best parameter for predicting mean LV Diastolic Pressure more than 12 mm Hg (cut off point of E/é medial > 15, sensitivity 48 %, specificity 100 %). This study revealed that the correlation of mean LV diastolic pressure with the medial mitral annulus TDI was consistently equivalent or better than the lateral annulus or the combination of the medial and later al annuli.Nagueh, et al[23], chose the lateral mitral annulus velocity to evaluate the correlation with PCWP measured by pulmonary artery catheters, because the lateral mitral annulus velocities were slightly higher than the septal velocities and were often easier to quantify. This study revealed that E/é related significantly with mean PCWP, with r value of 0.87, P < 0.001. An E/é lateral > 10 predicted a mean PCWP > 15 mm Hg, with a sensitivity of 97 % and a specificity of 78 %.Dokainish H, et al[24], showed that mitral E/é ratio as the average of the septal and lateral annuli é velocities, had the best correlation with PCWP (r =0.69, P <0.001), the optimal cutoff for E/é to predict PCWP > 15 mmHg was > 15 (sensitivity 85 %, specificity 88 %).

In subgroup analysis, patients with EF < 50 %, the optimal cutoff for E/é was > 15 (sensitivity 92 %, specificity 90 %). While in patients with EF ≥ 50, the optimal cutoff for E/é was > 11 (sensitivity 78 %, specificity 80 %).Tongyoo S, et al[25], revealed that E/é measured from the medial mitral annulus is the best Doppler echocardiographic parameter to estimate LVEDP in patients with significant CAD (r=0.55, P < 0.001). The optimal cutoff points of E/é to predict LVEDP > 15 mmHg, were > 10 from septal annulus (sensitivity 88 %, specificity 81.3%; P < 0.001) and > 8 from lateral mitral annulus (sensitivity 81.2 %, specificity 66.7 %; P < 0.001).All These studies agreed that E/é is the best echocardiographic variable to predict elevated LV filling pressures. There were discrepancies between the studies in the strength of the correlation of the E/é ratio with LV filling pressures (r value), the optimal cutoff point of the E/é ratio, and the sensitivity and specificity of that cutoff point to predict elevated LV filling pressure. These discrepancies were likely the result of the following differences. First,

Different parameters were used to represent the LV filling pressures like PCWP, LVEDP, pre-A pressure, and mean LV diastolic pressure. Second, studies used the medial, lateral, or the average of medial and lateral mitral annular velocities to calculate the E/é ratio. Third, the possibility that regional wall motion abnormalities may affect the accuracy of E/é velocities.

On subgroup analysis of the patients with significant CAD according to EF, patients with significant CAD and reduced EF in the current study showed a good and significant correlation between E/é medial and LVEDP (Table 3), while E/é lateral and E/é Average had a moderate correlation with LVEDP. The group of patients with CAD and preserved systolic function (EF ≥ 50 %) showed a significant intermediate correlation between E/é medial and LVEDP and a significant but weak correlation between each of E/é lateral and E/é Average and LVEDP.Ommen, et al[22], showed that correlation between E/é medial and Mean-LV diastolic pressure was better in patients with EF < 50 % (r=0.60) than in patients with EF > 50 % (r=0.47).Tongyoo S, et al[25], showed that among patients with preserved LV systolic function, E/é medial correlates well with LVEDP (r=0.52, P=<0.001), and that E/é medial > 10 can be used as a cutoff point to predict elevation of LVEDP with high sensitivity and specificity (79.4%, and 85.2% respectively).Mansencal N, et al[26], showed that the correlation between E/é lateral and Pre-A-wave pressure was strong in patients with LVEF < 50% (r=0.76, P=<0.001), whereas In patients with LVEF > 50 %, no correlation was found (r=0.18, P=0.44).Kasner M, et al[27], showed a good correlation between E/é lateral and LVEDP (r=0.71, P=0.001) in patients with HFNEF.The difference noticed between these studies could be attributed to the enhanced positive effect of preload on é in patients with preserved or normal systolic function and normal relaxation, whereas in patients with reduced EF, this effect is negligible[33]. This may affect the accuracy of E/é ratio in patients with normal systolic function. In spite of that, the European Association of Echocardiography and the American Society of Echocardiography recommended that for estimation of LV filling pressures in patients with normal EF, the E/é ratio should be calculated[34].

Study limitations:

The main limitation of our study is the small number of patients. Because of the critical importance of time during the daily work in the catheterization laboratory and the difficulty in obtaining good quality recordings suitable for pulmonary venous flow measurements by Doppler echocardiography in many patients included in this study, the correlation of this echocardiographic parameter with LVEDP was not recorded in this study.The use of fluid filled catheters, not solid conductance catheters, is another limitation, because of the potential for overdampening in fluid filled catheters.

CONCLUSION:

The TDI derived E/é ratio is better than mitral inflow doppler velocities and intervals for predicting elevated LVEDP in patients with or without significant CAD, especially in patients with reduced EF.The E/é medial > 15 and E/é lateral > 10, predict LVEDP > 15 mm Hg with good sensitivity and specificity.

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