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# Tissue Doppler as Non Invasive Method for Prediction of Left Ventricular End Diastolic Pressure (LVEDP)

RANDA ALY, MD; AYMAN HEIKAL, MD; ASHRAF WADIE, MD

The left ventricular end diastolic pressure (LVEDP) is an important parameter which reflects volume status in critically ill patients. Noninvasive assessment by Doppler echocardiography provides a safe and reproducible investigation comparable with invasive pressure monitoring.

***Aim:*** This study was designed to evaluate the role of tissue Doppler imaging (TDI) variables in the assessment of LVEDP.

***Methods:*** Patients scheduled for cardiac catheterization were studied with Doppler echocardiography immediately before the procedure. Early and late mitral inflow velocity (E, A wave respectively) and peak diastolic velocity from medial and lateral mitral annulus (Ea medial, Ea lateral) were obtained. Invasive measurement of LVEDP was obtained with a fluid filled pigtail catheter. The results were blinded to the interpreter.

***Results:*** There were 50 patients (mean age 53.6±9.7 years, mean ejection fraction [EF] 57.7±11.9%). Significant coronary lesions were found in 84% of this group. The correlation between LVEDP and E, Ea medial or Ea lateral were significant ($r$=0.20, $p$=0.0001: $r$=–0.7, $p$<0.0001 and $r$=–0.4, $p$=0.01 respectively). The ratio of E/Ea medial had the strongest correlation with LVEDP ($r$=0.8, $p$<0.0001). E/Eamedial >10 accurately predicted LVEDP >15mmHg with 77% sensitivity and 88.7% specificity. In patients with EF >50%, the correlation between E/Eamedial and LVEDP was still significant ($r$=0.7, $p$<0.0001).

***Conclusion:*** E/Ea medial correlates well with LVEDP and can be used to estimate LVEDP in coronary artery disease patients even in patients with normal LVEF.

***Key Words:*** *Tissue Doppler – LVEDP.*

## Introduction

Left ventricular end diastolic pressure (LVEDP) is an important parameter that should be evaluated during management of patients with heart disease. This is particularly true in critically ill patients. Doppler echocardiography has become the non-invasive and reproducible method for the assessment of systolic and diastolic function of the left ventricle and also of the left ventricular filling pressure **[1,2]**.

Mitral inflow velocities [Early mitral inflow velocity (E wave) and late mitral inflow velocity (A wave)], measured by pulsed Doppler echocardiography, are used to evaluate left ventricular diastolic performance. By this method, diastolic filling patterns are classified into four patterns **[3]**.

The Department of Critical Care, Cairo University.

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***Address for Correspondence:*** *Dr. Randa Aly, The Department of Critical Care, Cairo University.*

Normal and abnormal relaxation patterns can have normal left atrial pressure (LAP), while restrictive filling pattern is associated with elevated LAP and LVEDP. Restrictive pattern of mitral valve inflow predicts high LVEDP (pre-A >15 mmHg) with a sensitivity of approximately 10-40% and specificity of 100% **[1]**.

There was limitation of mitral inflow velocities to predict left ventricular filling pressure because it depends on ventricular preload status, left ventricular relaxation, atrial and ventricular compliance **[4,5]**.

Tissue Doppler imaging (TDI) of mitral annular motion has been proposed to evaluate diastolic filling function and detect pseudonormalization of mitral valve inflow **[6,7]**.

There are several reports about using TDI parameters such as peak early diastolic velocity of mitral annulus (Ea), peak late diastolic velocity of mitral annulus (Aa), and E/Ea, to predict left ventricular filling pressure. However, there were no

correlation between TDI intervals (duration, acceleration time and DT) and LVEDP **[8]**.

Combining transmitral flow velocity with annular velocity (E/Ea) has been proposed as the best single Doppler predictor for evaluating left ventricular filling pressure **[6,8,9]**. Until now, there are several inconclusive issues to resolve before using these parameters in different populations such as those with good LV systolic function **[8]**, patients with coronary artery disease 14 and aging patients. Almost all previously published studies used pulmonary capillary wedge pressure (PCWP) as alternative parameter for LVEDP **[6,10]**.

The cut off point of E/Ea to predict high LV filling pressure was still uncertain, varying between 10-15 for E/Ea medial and 8-12 for E/Ea lateral **[5-10]**.

The purpose of this study is to evaluate sensitivity and specificity of E/Ea >10 for prediction of LVEDP >15mmHg in patients with coronary artery disease undergoing left heart catheterization.

## Methods

### *Population:*

After local ethical committee approval and guardian oral and written consent, the study was conducted. The study was designed as a prospective study and the population consisted of 50 patients who were scheduled for elective left heart catheterization (between the year 2008 and 2010) in critical care department at Cairo University. Subjects 18 years old or older with sinus rhythm were eligible. Exclusion criteria were severe valvular heart disease, complete left bundle branch block or complete right bundle branch block, pacemaker dependence, atrial fibrillation and post mitral valve replacement.

### *Echocardiography measurements:*

All patients were examined by trans-thoracic Doppler echocardiography within 2 hours of catherization by an operator who was blinded to the patient's history and hemodynamic data. An ATL 5000 with S3 probe was used to perform echocardiography using the following protocol.

1- Mitral valve inflow assessment by Pulsed wave Doppler, sampling volume (1-2mm) placed between the mitral leaflet tips, parallel with the mitral inflow, as determined by color flow Doppler echocardiography in apical four chamber view. Doppler variables were recorded from the velocity tracing as early mitral inflow peak velocity (E), deceleration time of E wave (DT), peak velocity of late mitral inflow (A) and isovolumic relaxation time (IVRT).

2- Tissue Doppler imaging (TDI) measurements of the mitral annulus were obtained from the apical four chambers view. Tissue Doppler mode was selected, at a rate of 100-133 color Doppler frames/sec using a velocity range of 0.1-16 cm/sec. A 1.5mm sampling volume was placed sequentially at the medial and lateral mitral annulus.

Analysis was performed for the early (Ea) and late (Aa) diastolic peak velocity of medial and lateral mitral annulus. These variables were analyzed individually, and as the average of the medial and lateral annulus. All measurements must be averaged from at least three beats. To determine intra-observer variability of Doppler echocardiographic measurements, variables in randomly selected patients were analyzed on two different occasions.

### *Cardiac catheterization:*

After complete echocardiographic examination, left ventricular catheterization was performed via the femoral approach, using 6-8 French sheaths. Left ventricular diastolic pressure was directly measured by fluid filled pigtail catheter attached to a pressure transducer (model P23XL or P10EZ, Becton Dickinson, Critical Care Systems, Singapore).

The Fourth intercostal spaces between the A-P diameter of the chest wall measured as Zero level. All hemodynamic data were recorded before the left ventriculogram was performed. The left ventricular end diastolic pressure (LVEDP) was obtained by computer recording.

Results from at least 5 beats were averaged. After that, standard technique coronary angiography was performed. Demographic data including age, sex, underlying disease, risk factors for coronary artery disease, drug administration and indications for catheterization were recorded.

### *Statistical analysis:*

Data were summarized using mean Data. They were collected, verified, revised and edited on PC. They were then analyzed statistically using SPSS statistical package version 11.5. The data were

presented as mean and standard deviation for continuous variables, independent samples *t*-test for normally distributed quantitative variables while quantitative variables that were not normally distributed were compared using non-parametrical Mann-Whitney test & Wilcoxon signed rank test. Percentages were compared using Chi-square test or Fisher's exact test. Logistic regression was used for assessment of single independent factor relation to binary factors. Pearson's correlation coefficient was used for correlation of continuous variables and LVEDP. The predictive accuracy for LVEDP >15mmHg was assessed from receiver operating characteristic curves (ROC). Intra-observer variation was presented by means of absolute percent differences between two sampling. A *p*-value of <0.05 was accepted as statistically significant.

## Results

Fifty patients participated in this study. The mean age was 53.6±9.7 years and 66% were men. The underlying disease, coronary risk factors, indication for cardiac catheterization and current medication within two months are presented in Table (1). The mean ejection fraction (EF) measured by modified Simpson's rule was 57.7±11.9%.

Forty two patients (84%) had significant coronary artery disease (Table 2). The patients with significant coronary artery disease (CAD) had higher prevalence of hypertension (23/42 versus 3/8 but the *p*-value was not significant 0.4) and there was no significant difference in the use of nitrates. Mean LVEDP was 17.6±6mmHg in patients with significant coronary artery disease versus 15.7±5.1mmHg in non significant CAD and *p*-value was 0.4.

Twenty three patients (46%) had LVEDP <15mmHg and 27 (64%) had LVEDP >15mmHg. The Doppler echocardiographic parameters are shown in (Table 3). There were minor intraobserver variations; 1.00±2.39% for E/Ea derived from medial mitral annulus and 2.64±0.35% for E/Ea derived from lateral mitral annulus.

**Table 1:** Demographic data.

| Characteristics | Overall N (50) | Non significant CAD N (8) | Significant CAD N (42) | *p*-value |
|---|---|---|---|---|
| Age | 53.6±9.7 | 54.6±10.7 | 53.4±9.7 | 0.76 |
| Sex (male) | 33 (66%) | 4/8 | 29/42 | 0.4 |
| *Underlying disease:* | | | | |
| Diabetes mellitus | 20 (40%) | 2/8 | 18/42 | 0.45 |
| Hypertension | 26 (52%) | 3/8 | 23/42 | 0.5 |
| Dyslipidemia | 20 (40%) | 1/8 | 19/42 | 0.12 |
| Smoking | 27 (54%) | 3/8 | 24/42 | 0.44 |
| *Indication for catheterization:* | | | | |
| IHD | 27 (54%) | 5/8 | 22/42 | |
| Post MI | 18 (36%) | 2/8 | 16/42 | 0.7 |
| CHF | 5 (10%) | 1/8 | 4/42 | |
| *Medications used within 2 months:* | | | | |
| BB | 38 (76%) | 5/8 | 33/42 | 0.3 |
| ACEI | 17 (34%) | 4/8 | 13/42 | 0.4 |
| ARBS | 5 (10%) | 0/8 | 5/42 | 0.6 |
| Statins | 37 (74%) | 5/8 | 32/42 | 0.4 |
| Calcium blockers | 9 (18%) | 3/8 | 6/42 | 0.14 |
| Nitrates | 40 (80%) | 7/8 | 33/42 | 0.5 |
| Diuretics | 11 (22%) | 1/8 | 10/42 | 0.66 |
| ASA | 47 (96%) | 8/8 | 39/42 | 0.58 |
| Clopidogrel | 40 (80%) | 3/8 | 37/42 | 0.008* |
| *Hemodynamic values:* | | | | |
| SBP mmHg | 123.9±19.15 | 127.5±29.6 | 123.2±16.9 | 0.70 |
| DBP mmHg | 76.2±10.8 | 74.4±15.9 | 76.5±9.8 | 0.71 |
| HR b/min | 74.5±13.9 | 73.9±16 | 74.6±13.7 | 0.90 |
| LVEDP mmHg | 17.3±6.6 | 15.7±5.1 | 17.6±6.8 | 0.4 |

**Table 2:** Angiographic data.

| Profile | Numbers | % |
|---|---|---|
| Coronary angiogram | 50 | 100 |
| No significant CAD | 8 | 16 |
| Significant CAD | 42 | 84 |
| • Lt Main | 4/50 | 8 |
| • 3 vessel disease | 12/50 | 24 |
| • 2 vessel disease | 8/50 | 16 |
| • 1 vessel disease | 18/50 | 36 |

**Table 3:** Echocardiographic data.

| | Overall (50) | No significant CAD | Significant CAD | *p* value |
|---|---|---|---|---|
| E | 69.6±21.6 | 55.7±10.9 | 72.3±22.2 | 0.004 |
| A | 64.7±23.6 | 68.4±20.4 | 63.9±24.3 | 0.59 |
| E/A | 1.3±0.9 | 0.9±0.2 | 1.4±0.9 | 0.002 |
| DT | 176.4±53.8 | 168.0±51.8 | 178.0±54.6 | 0.63 |
| IVRT | 88.9±25.8 | 94.1±28.9 | 87.9±25.5 | 0.59 |
| Ea medial | 8.3±3.9 | 10.4±3.6 | 7.9±3.9 | 0.10 |
| Ea lateral | 9.8±3.4 | 9.6±2.6 | 9.8±3.5 | 0.83 |
| Ea mean | 9.0±3.1 | 9.9±2.8 | 8.9±3.1 | 0.32 |
| Aa medial | 9.5±2.5 | 11.2±1.6 | 9.2±2.5 | 0.01 |
| Aa lateral | 10.6±3.5 | 12.5±1.6 | 10.2±3.7 | 0.009 |
| Aa mean | 10.0±2.8 | 11.8±1.4 | 9.7±2.8 | 0.004 |
| E/Ea medial | 10.9±6.4 | 8.3±3.5 | 11.4±6.7 | 0.004 |
| E/Ea lateral | 8.5±6.8 | 6.3±2.4 | 8.9±7.3 | 0.07 |
| E/Ea mean | 9.6±6.4 | 7.3±2.8 | 10.1±6.8 | 0.06 |
| EF% | 57.7±11.9 | 64.7±8.4 | 56.4±12.2 | 0.03 |

### *Doppler echocardiographic parameters and correlation with LVEDP:*

The correlations of LVEDP with Doppler variables are shown in Table (5). The mitral inflow velocity (E) had a significant positive correlation with LVEDP (*r*: 0.7, *p*<0.0001) while (A) had an insignificant weak correlation (*r*: –0.2, *p* NS) and E/A is yet significantly correlated to LVEDP (*r*: 0.6, *p*<0.0001).

Tissue Doppler variables (Ea, Aa) show weak but still significant negative correlation with LVEDP. When we combine variables derived from mitral inflow velocity and Tissue Doppler variables, E/Ea ratio shows moderate to good correlation with LVEDP. The best echocardiographic parameter that can be correlated with LVEDP was E/Ea measured from medial mitral annulus [*r*=0.8, *p*<0.0001] (Table 4).

The Scatter plots between LVEDP versus E/Ea are shown as Figs. (1,2).

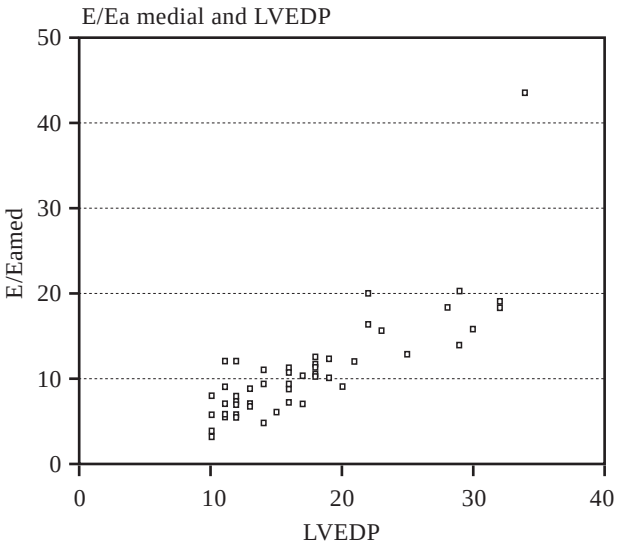


**Figure 1:** LVEDP versus E/Ea (*r*=0.8, *p*<0.0001).

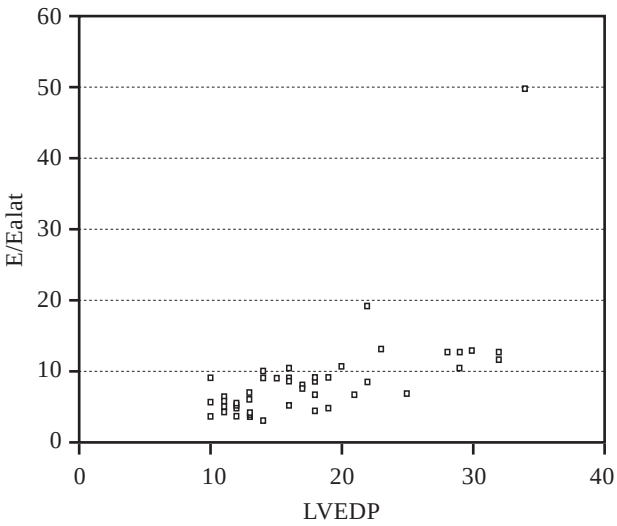


**Figure 2**

To evaluate the accuracy of E/Ea for predicting high LV filling pressure, the ROC analysis of LVEDP >15mmHg was performed as shown in Figs. (3,4). The area under the curves was 0.9 (*p*<0.0001) and 0.8 (*p*<0.0001) for E/Ea derived from the medial and lateral mitral annulus respectively.

According to the ROC curve, the cut off point of E/Ea for predicting LVEDP higher than 15mmHg was from medial mitral annulus >10 (sensitivity 77%, specificity 87%; *p*<0.0001) and from lateral mitral annulus >8 (sensitivity 70%, specificity 83%; *p*<0.0001).

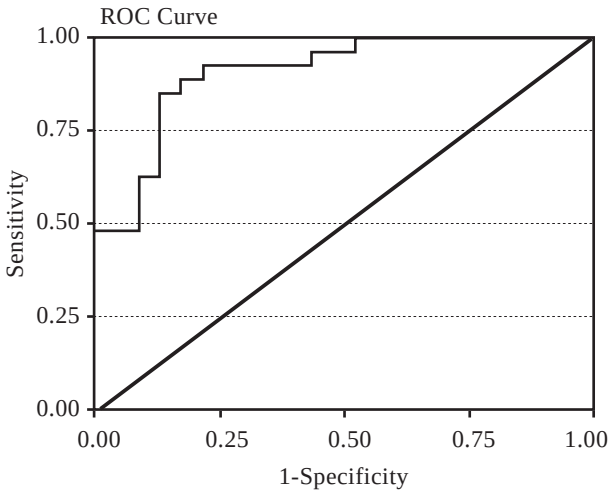


**Figure 3:** ROC curve for prediction of LVEDP >15 using E/Ea medial area under the curve is 0.9 (sensitivity 77% and specificity 87%).

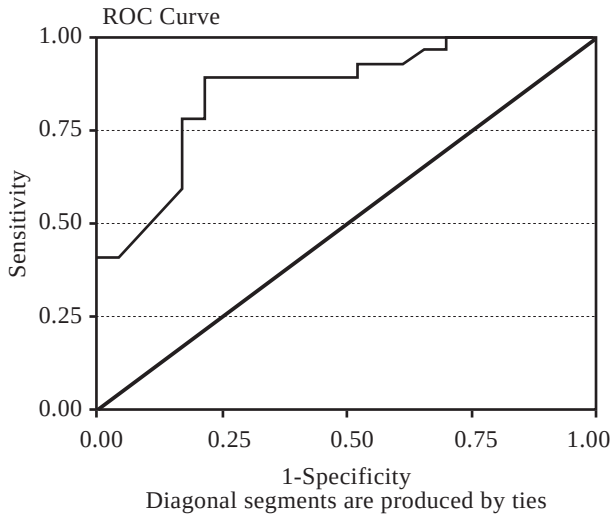


**Figure 4:** ROC curve for prediction of LVEDP >15 using E/Ea lateral area under the curve is 0.8 (sensitivity 70% and specificity 83%).

**Table 4**

| Profile | Total (50) | | No significant CAD (8) | | Significant CAD (42) | |
|---|---|---|---|---|---|---|
| | *r* | *p* | *r* | *p* | *r* | *p* |
| E | 0.75 | 0.0001 | 0.6 | 0.08 | 0.77 | 0.0001 |
| A | 0.2 | 0.17 | 0.3 | 0.4 | –0.2 | 0.12 |
| E/A | 0.67 | 0.0001 | 0.39 | 0.33 | 0.69 | 0.0001 |
| DT | –0.34 | 0.01 | –0.15 | 0.7 | –0.38 | 0.012 |
| IVRT | 0.2 | 0.13 | 0.5 | 0.2 | 0.18 | 0.2 |
| Ea medial | –0.7 | 0.0001 | –0.7 | 0.02 | –0.7 | 0.0001 |
| Ea lateral | –0.4 | 0.004 | –0.5 | 0.15 | –0.39 | 0.01 |
| Aa medial | –0.34 | 0.015 | 0.13 | 0.7 | –0.36 | 0.017 |
| Aa lateral | –0.2 | 0.15 | 0.5 | 0.2 | –0.2 | 0.14 |
| E/Ea medial | 0.8 | 0.0001 | 0.89 | 0.0001 | 0.8 | 0.0001 |
| E/Ea lateral | 0.6 | 0.0001 | 0.7 | 0.05 | 0.6 | 0.0001 |
| E/Ea mean | 0.75 | 0.0001 | 0.8 | 0.003 | 0.75 | 0.0001 |

**Table 5**

| Group of patients | Prediction of LVEDP >15 mmHg | | *p*-value |
|---|---|---|---|
| | Sensitivity | Specificity | |
| | Total (50) | | |
| E/Ea medial (cut off at 10) | 77% | 87% | 0.0001 area 0.9 |
| E/Ea lateral (cut off at 8) | 70% | 83% | 0.0001 area 0.8 |
| | Non significant CAD (8) | | |
| E/Ea medial (cut off at 10) | 75% | 98% | 0.02 area 0.98 |
| E/Ea lateral (cut off at 8) | 50% | 98% | 0.01 area 0.9 |
| | Significant CAD (42) | | |
| E/Ea medial (cut off at 10) | 74% | 85% | 0.0001 area 0.88 |
| E/Ea lateral (cut off at 8) | 69% | 79% | 0.0001 area 0.83 |
| | EF ≤50% (13) | | |
| E/Ea medial (cut off at 10) | 81% | 100% | 0.049 area 0.95 |
| E/Ea lateral (cut off at 8) | 81% | 99% | 0.048 area 0.95 |
| | EF >50% (37) | | |
| E/Ea medial (cut off at 10) | 75% | 86% | 0.0001 area 0.86 |
| E/Ea lateral (cut off at 8) | 62% | 81% | 0.002 area 0.8 |

**Table 6**

| Cut off point in different studies | | | | Sensitivity | Specificity |
|---|---|---|---|---|---|
| Nagueh 1997 | 125 | Mean PCWP >15 | E/Ea lateral >10 | 97% | 78% |
| Ommen 2000 | 100 | Mean LVDP >12 | E/Ea medial >15 | 48% | 100% |
| | | Mean LVEDP <12 | E/Ea medial <8 | 45% | 85% |
| Poerner 2003 | 98 | LVEDP >15 | E/Ea lateral >10 | 76% | 76% |
| Rivas – Gotz 2003 | 109 | MeanPCWP >15 | E/Ea medial >10,EF >50% | 79% | 80% |
| | | | E/Ea medial >11, EF <50% | 85% | 82% |
| Manrencal 2004 | 32 | Pre-AP >15 | E/Ea lateral >9 | 69% | 93% |
| Surat Tongyoo 2006 | 138 | LVEDP >15 | E/Ea medial >10 | 82% | 84% |
| | | | E/Ea lateral >8 | 76% | 65% |
| Present study | 50 | LVEDP >15 | E/Ea medial >10 | 77% | 87% |
| | | | E/Ea lateral >8 | 60% | 83% |

***Impact of coronary artery disease:***

The correlation between E/Ea and LVEDP was more or less similar in the group of patients with or without significant coronary artery disease, as shown in Table (4). The sensitivity and specificity of E/Ea to predict elevation of LVEDP in different subgroups are presented in Table (5).

***Influence of left ventricular ejection fraction:***

There were 37 patients who had the ejection fraction evaluated by modified Simpson's rule >50%, and only 13 patients with EF ≤50%.

Among the group with good LV systolic function, E/Ea from medial mitral annulus was also correlated to LVEDP [$r$=0.7, $p$<0.0001]. E/Ea ratio >10 can thus be used as a cut off point to predict elevation of LVEDP with high sensitivity and specificity (Table 5).

## Discussion

This study supports that E/Ea is the best Doppler echocardiographic parameter to estimate LVEDP. The early peak mitral inflow velocity is measured by placing pulse wave Doppler sampling volume between the mitral leaflet tips in the apical 4 chambers view, while Ea can be measured by sampling annulus velocity from either medial or lateral portion of mitral valve. Ommen, et al **[8]** reported that the correlation of mean-left ventricular diastolic pressure with the medial annulus TDI were consistently equivalent or better than the lateral annulus or the combinations of the medial and lateral annulus.

However, the lateral mitral annulus velocity was chosen by Nagueh, et al **[6]** to evaluate the correlation with pulmonary capillary wedge pressure (PCWP). This is because the lateral mitral annulus velocities were slightly higher than the septal velocities and were often easier to quantify.

According to our study, we found that the measurement of medial mitral annulus velocities was easier and had higher successful examination rate than the lateral mitral annulus measurements. E/Ea derived from medial mitral annulus correlated better with LVEDP than E/Ea derived from the lateral mitral annulus. Regarding to the ROC curve, E/Ea from medial mitral annulus with value more than 10 is the best cut off point to predict LVEDP higher than 15mmHg.

Cut off points of E/Ea to predict elevation of left ventricular filling pressure from previous studies are presented in Table (6). When subgroup analysis was performed to evaluate the correlation of E/Ea and LVEDP in patients with significant coronary artery stenosis, the cut off point of E/Ea for predicting high LVEDP was also the same as in overall group. Previous studies have shown the accuracy of E/Ea for predicting elevation of left ventricular filling pressure in patients with reduced ejection fraction (EF) with a limited role in patients with normal EF **[8,10,11]**.

In this study, 37 patients had EF >50%. Analysis of this subgroup confirms that E/Ea is also correlated to LVEDP and that E/Ea ratio greater than 10 can be used to predict LVEDP >15mmHg with high sensitivity and high specificity.

The cut off points in different studies were demonstrated in 1997 by Nagueh et al, who conducted a study on 125 cardiac patients and found a cutoff point of E/Ea lateral >10 which could predict PCWP >15 with a sensitivity of 97% and a specificity of 78% **[2]**.

There was renewal of that interest in 2000 by Ommen et al, who conducted a limited study on 100 patients with ischemic heart disease but failed to show high sensitivity of E/Ea medial >15 and E/Ea lateral >8 to predict LVEDP >12 although showing 100% specificity of E/Ea medial in prediction of the target **[8]**.

Rivas-Gotz et al, has conducted a study similar to our study and has divided his study population by LVEF <50% and >50%. He found that the best cutoff point of E/Ea medial in prediction of mean PCWP >15 is slightly different in subgroups, that was 10 in patients with LVEF >50% and 11 in those who had their LVEF <50% with a sensitivity of (79%, 85%) and a specificity of (80%, 82%), respectively **[10]**.

Comparable to our study, Stuart Tongyoo has designed and conducted a larger study on 138 patients and found that E/Ea medial ratio of 10 gives a sensitivity of 82% and a specificity of 84% to predict LVEDP >15 in all studied population subgroups regardless to LVEF whether it is more or less than 50%. For E/Ea lateral >8, it showed a sensitivity of 76% and a specificity of 65% **[12]**. The following table shows a summary of our and previous studies for cutoff points of E/Ea medial and lateral (Table 6).

## Conclusion

E/Ea significantly correlated with LVEDP in the population with high prevalence of coronary artery disease. The value derived from the medial mitral annulus is better than those from the lateral to predict LVEDP. The LVEDP >15mmHg is predicted if E/Ea from medial annulus is >10 with high sensitivity and specificity. This cut off point can also be used to predict elevated LVEDP in patients with good LVEF.

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