

# Non-Invasive Assessment of Left Ventricular End-Diastolic Pressure in Patients with Chronic Aortic Regurgitation, Comparison of the Sensitivity and Specificity of CW Doppler Echocardiography with Angiography

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**Background:** Left ventricular end diastolic pressure could be estimated collectively using various measures of mitral valve and pulmonary venous flow velocities. In patients with aortic regurgitation, the AR velocity reflects the diastolic pressure difference between the aorta and the left ventricle. We sought to predict the left ventricular end diastolic pressure by a new Doppler index as aortic regurgitation peak early to late diastolic pressure gradient ratio.

**Patients and Methods:** Fifty three patients with at least moderate aortic regurgitation were enrolled in this study. Physical examination, electrocardiography and echocardiography were performed one day before cardiac catheterization. The severity of AR was graded according to the recommendations of American society for echocardiography. The pressure half time, aortic regurgitation early diastolic velocity, aortic regurgitation early diastolic pressure gradient, aortic regurgitation end diastolic velocity, aortic regurgitation end diastolic pressure gradient, and early diastolic to end diastolic pressure gradient ratio of averaged three beats were measured and recorded. The results from cardiac catheterization and echocardiography were compared.

**Result:** The early diastolic to end diastolic pressure gradient ratio was very accurate (80%) for determining the left ventricular end diastolic pressure ( $P=0.01$ ). An early diastolic to end diastolic pressure gradient ratio of 1.5 has a sensitivity of 96% and a specificity of 32% for left ventricular end diastolic pressure  $\leq 12$  mmHg. The best cutoff value of early diastolic to end diastolic pressure gradient ratio for the prediction of left ventricular end diastolic pressure  $>12$  mmHg was higher than 2.0, with a sensitivity of 71% and specificity of 96%. We found no significant correlation between the left ventricular end diastolic pressure with either left ventricular ejection fraction or aortic regurgitation severity in cardiac catheterization ( $P=0.5$ ).

**Conclusion:** Doppler echocardiography is a viable alternative of cardiac catheterization for determination of the left ventricular end diastolic pressure. The early diastolic to end diastolic pressure gradient ratio is a simple, easy and new method for assessment of the LVEDP in patients with severe chronic aortic regurgitation.

**Key words:** Aortic Regurgitation Left Ventricular End Diastolic Pressure, Doppler Echocardiography

## Introduction

Deciding when to operate on a patient with chronic aortic regurgitation (AR) may be

extremely difficult. The timing of surgery requires consideration of the etiology and pathophysiology of the aortic regurgitation. The asymptomatic patient who has moderate to severe aortic regurgitation may not have symptoms for many years, so functional class (FC) assessment cannot be used to accurately define underlying left ventricular (LV) performance

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or hemodynamics in an individual patient with chronic aortic insufficiency.<sup>1-4</sup> Therefore, periodic quantitative evaluation of left ventricular function is necessary in patients with moderate to severe aortic regurgitation. The AR velocity reflects the diastolic pressure difference between the aorta and the LV. In patients with chronic AR, we sought to predict the left ventricular end diastolic pressure (LVEDP) using a new Doppler derived index as an aortic regurgitation peak early to late diastolic pressure gradient ratio.

### Patients and Methods

From July 2006 to October 2008, 53 consecutive patients with at least moderate AR were prospectively enrolled into the study. Exclusion criteria included patients with significant mitral regurgitation, aortic stenosis, coronary artery disease, systemic hypertension and severe left ventricular dysfunction (LVEF<30%).

All the participants underwent a clinical examination, 12-lead electrocardiography (ECG), complete transthoracic echocardiography one day before cardiac catheterization. Cardiac catheterization was done with at least 6 hours fasting. Oral sedation (5 mg diazepam and 25 mg promethazine) was administered to all patients. Hemodynamic measurements were done before angiocardiography. Left ventricular end-diastolic pressure was obtained using a fluid-filled pig-tail catheter. The severity of AR was generally graded by visual assessment determining the relative amount of radiographic contrast medium that opacified the left ventricle and classified as the Sellers classification.

Standard transthoracic 2D and Doppler

echocardiography were performed in the left lateral decubitus position using a commercially available system (Vivid 3; General Electric Company, Norway) equipped with a 2.5-3.5 MHz transducer in the parasternal and apical views.

The severity of AR was graded according to the recommendations of American society for echocardiography. The pressure half time (PHT), aortic regurgitation early diastolic velocity (ARErDV), aortic regurgitation early diastolic pressure gradient (ARErDPG), aortic regurgitation end diastolic velocity (ARErDV), aortic regurgitation end diastolic pressure gradient (ARErDPG), (ARErDG/ARErDG ratio) of averaged three beats were measured and recorded. The LVEDP was measured using previously suggested formula  $[DBP-(ARErDV)^2 \times 4]$ <sup>3</sup> followed by calculating the ratio of aortic regurgitation early diastolic pressure gradient to aortic regurgitation late diastolic pressure gradient (ARErDG/ARErDG).

The left ventricular ejection fraction (LVEF) and LVEDP were also assessed during cardiac catheterization and the results were compared with ARErDG/ARErDG ratio to predict the LVEDP. Those performing noninvasive determinations were blinded to catheterization results.

### Statistical Analysis

Statistical analysis was conducted using SPSS software package (SPSS 13 Inc. Chicago, IL, USA) for Windows. Continuous variables were presented as mean± standard deviations (SD) and categorical data are expressed as frequencies and proportions. The sensitivity and specificity of different cut points

of AREdG/AREdG ratio for identification of the LVEDP > 12 mmHg were calculated. Positive and negative predictive values were also computed accordingly. The comparison of the differences was performed using the paired samples t-test. The multiple comparisons were performed with the ANOVA, and the comparison of the difference between LVEDP which is estimated by echocardiography and that measured by cardiac catheterization was performed

**Table 1.** Baseline characteristics of the patients (n=53)\*

<b>Age (year)</b>	44.13±13.6
<b>Gender (% men)</b>	32 (60.4)
<b>SBP<sub>R</sub> / SBP<sub>L</sub> (mmHg)</b>	130.2±19.4 / 127.6±18.0
<b>DBP<sub>R</sub> / DBP<sub>L</sub> (mmHg)</b>	56.9±11.0 / 53.3±9.4
<b>Other Valvular Heart Disease(%)</b>	
Mitral Stenosis	66
Mitral Regurgitation	16.5
Aortic Stenosis	5.5
Tricuspid Regurgitation	11
<b>AF/NSR</b>	7/46
<b>HR (BPM)</b>	73±10
<b><sup>e</sup>LVEF (%)</b>	44.62 ±9.24
<b><sup>e</sup>LVEF (%)</b>	42.73 ±8.22
LVEF >55%	27.95
45% < LVEF < 55%	33.99
35% < LVEF < 45%	33.99
LVEF < 35%	3.7
<b>AR severity (%)<sup>a</sup></b>	
Moderate	32.1
Moderate to severe, Severe	67.9
<b>AR severity (%)<sup>b</sup></b>	
+2	7.5
+3	39.6
+4	52.9

\*Plus-minus values are means ± standard deviation, **SBP<sub>R</sub>**: right arm systolic blood pressure, **SBP<sub>L</sub>**: left arm systolic blood pressure, **AF**: atrial fibrillation, **NSR**: normal sinus rhythm, **HR**: heart rate, **LVEF**: left ventricular ejection fraction, **AR**: aortic regurgitation, <sup>a</sup>aortic regurgitation severity by echocardiography, <sup>b</sup>aortic regurgitation severity by cardiac catheterization.

**Table 2.** Doppler echocardiography parameters of the patients (n=53)\*

<b>PHT (msec)</b>	359.94±111.70
PHT < 250 msec (%)	16.98
250 < PHT < 450 (%)	62.26
PHT > 450 (%)	22.6
<b>ARErDV (m/sec)</b>	4.27± 0.52
<b>ARErDG (mmHg)</b>	74.53±17.2
<b>AREdV (m/sec)</b>	3.01±0.59
<b>AREdG (mmHg)</b>	38.05±14.1
<b>ARErDG/AIEdG ratio</b>	2.10±0.57
<b>LVEDP (mmHg)<sup>a</sup></b>	17.47±7.29
<b>LVEDP (mmHg)<sup>b</sup></b>	14.9±4.5
<b>LVEDP &gt; 12 mmHg (%)<sup>b</sup></b>	50.9

\*Plus-minus values are means ± standard deviation, **PHT**: pressure half time, **ARErDV**: aortic regurgitation early diastolic velocity, **ARErDPG**: aortic regurgitation early diastolic pressure gradient, **AREdV**: aortic regurgitation end diastolic velocity, **AREdPG**: aortic regurgitation end diastolic pressure gradient, **ARErDG/AIEdG ratio**: the ratio of aortic regurgitation early diastolic pressure gradient to aortic regurgitation late diastolic pressure gradient, <sup>a</sup>**LVEDP**: left ventricular end diastolic pressure estimated by subtraction of diastolic blood pressure and aortic regurgitation late diastolic gradient, <sup>b</sup>**LVEDP**: left ventricular end diastolic pressure measured during cardiac catheterization.

with the independent samples t-test. A difference was considered significant when the P value was < 0.05.

## Results

Baseline characteristics of the patients are summarized in Tables 1, 2. Thirty four percent of patients had multivalvular heart disease. The most common associated valvular heart disease was mitral stenosis. More than two-third of patients had significant AR, one half had increased LVEDP, two-third had mild and moderate LV dysfunction (50% < LVEF > 40%).

There was a close relation between mean ±SD of LVEF (44.62 ±9.24 versus 42.73 ±8.22%,  $r = 0.74$ ) and LVEDP which is estimated by echocardiography and that measured

**Table 3:** Comparison of mean  $\pm$ SD of LVEDP in patients with aortic regurgitation measured by cardiac catheterization.

AR severity	LVEDP (mmHg)*
+2 (n=4)	11.00 $\pm$ 3.36
+3 (n=21)	14.42 $\pm$ 8.34
+4 (n=28)	14.53 $\pm$ 4.54

\*Plus-minus values are means  $\pm$  standard deviation, LVEDP: left ventricular end diastolic pressure. P value not significance

by cardiac catheterization (17.47 $\pm$ 7.29 versus 14.9 $\pm$ 4.5 mmHg,  $r=0.76$ ).

In this study, no relation was found between LVEDP and either LVEF or severity of AR (Tables 3). The receiver operating characteristic (ROC) curve showed that ARErDG/AREdG ratio was highly accurate (AUC= 0.81 $\pm$ 0.39) compared to cardiac catheterization for prediction of LVEDP ( $PV<0.01$ ). An ARErDG/AREdG ratio of about 1.5 has a sensitivity of 96% and a specificity of 32% for prediction of LVEDP  $\leq$ 12 mmHg. Table 4 shows that ARErDG/AREdG ratio higher than 2.0 had 71% sensitivity and 96% specificity for prediction of patients with increased LVEDP (> 12 mmHg).

Using logistic regression analysis in patients with chronic AR, LVEDP could be predicted using underlying formula:

$$\text{LVEDP} = [\text{DBP} - \text{AREdG} \times 0.64] + 1.47$$

Where DBP is diastolic blood pressure, AREdG is end diastolic gradient of AR flow measured using continuous wave Doppler echocardiography.

## Discussion

Our study showed that echocardiography is highly sensitive (96%) and specific (64%) method for diagnosis of AR severity. The results

**Table 4:** Comparison of sensitivity and specificity of different cutoff values for ARErDG/AREdG ratio

Positive if Greater than of Equal to <sup>a</sup>	Sensitivity	Specificity
1.32	1.00	.05
1.43	1.00	.14
<b>1.50</b>	<b>.96</b>	<b>.32</b>
1.55	.93	.41
1.57	.93	.46
1.59	.93	.50
1.64	.90	.55
1.69	.90	.64
1.73	.90	.69
1.78	.87	.73
1.81	.87	.78
1.83	.87	.82
1.87	.87	.91
1.94	.83	.91
<b>2.00</b>	<b>.77</b>	<b>.91</b>
2.07	.71	.96
2.16	.67	.96

<sup>a</sup>ARErDG/AREdG ratio: The ratio of aortic regurgitation early diastolic pressure gradient to aortic regurgitation late diastolic pressure gradient, **a**: the smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

are similar to the study by Kramer et al who found a sensitivity of 92% for detection of AR.<sup>5</sup> In contrast to the study by Yousof et al, we did not find a significant relation between LVEDP and LVEF.<sup>6</sup> This might have been secondary to the small number of our patients with very low LVEF or be partly related to our policy for patients' selection at an earlier time, before significant LV dysfunction had occurred. The clinical evaluation of the best time for the surgical treatment of chronic AR was assessed by Dallo et al. They proposed the index of left ventricle end systolic diameter to left ventricular normalized velocity of posterior wall (LVESD/ LVPWNV)

to determine the LVEDP ( $r = 0.92$ ).<sup>7</sup> They showed that LV performance parameters had no significant relation with AR severity, so the whole clinical information together with echocardiographic parameters is necessary for identification of the most appropriate time for surgical treatment before the phase of myocardial damage.<sup>7</sup> The results were consistent with our study, in which there was no significant relation between LVEDP with either LVEF or the severity of AR.

Finally to our knowledge the present study is the first to evaluate the accuracy of AR-ERDG/AREDG ratio for noninvasive assessment of LVEDP. Neumann et al. evaluated the accuracy of the mitral regurgitation (MR) velocity at the time of aortic valve opening for the noninvasive estimation of LVEDP.<sup>8</sup> In this study LVEDP was calculated as diastolic blood pressure-  $[4 \times (\text{MR velocity at aortic opening})^2]$ . In patients with a LVEDP greater than 15 mm Hg the yield was 65%.<sup>8</sup> The results of our study showed that LVEDP could be estimated using diastolic blood pressure and the AR end diastolic gradient  $[\text{LVEDP} = (\text{DBP} - \text{AREDG} \times 0.64) + 1.47]$ . We found a good and specific (96%) relation between ARErDG/AREDG ratio higher than 2 with LVEDP > 12 mmHg. The present study we examines the validity of a

new Doppler derived index with invasive hemodynamic measurement for prediction of the LVEDP in patients with chronic AR in order to obtain the accurate criteria for prospective prediction of LV systolic dysfunction.

However, our study suffers from a few limitations. Firstly, the total number of patients evaluated in the current study was small. Secondly, patients with mild degree of AR were not included in our study. Thirdly, invasive measurements were performed by multiple operators, in contrast to echocardiography which were done by single operator and rechecked by supervisor medical staff.

Our results demonstrated that Doppler echocardiography is a good alternative to cardiac catheterization for determination of the LVEDP. The ARErDG/AREDG ratio is a simple, easy, and accurate new method for non-invasive assessment of the LVEDP in patients with severe chronic AR.

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