Peak Early Diastolic Velocity Rather Than Pressure Half-Time Is the Best Index of Mechanical Prosthetic Mitral Valve Function

Valerian Fernandes, MD, Leopoldo Olmos, MD, Sherif F. Nagueh, MD, Miguel A. Quinones, MD, and William A. Zoghbi, MD

Reliable screening of mechanical prosthetic mitral valve (PMV) dysfunction by transthoracic echocardiography (TTE) is mandatory because transesophageal echocardiography (TEE) cannot be routinely used. However, acoustic shadowing seriously hampers detection of PMV dysfunction with TTE, particularly regurgitation. To identify TTE indexes that can detect PMV dysfunction (regurgitation or obstruction), 134 patients (age 60 ± 12 years, 64 men) with PMV who underwent TTE and TEE within 3 ± 5 days were assessed. There were 73 normal and 61 dysfunctional valves (40 regurgitant, 21 obstructive). By multivariate analysis, peak E velocity was the best predictor of a dysfunctional valve. Both peak E velocity (E > 1.9 m/s; sensitivity 92%, specificity 78%) and the ratio of velocity-time integrals of flow through the prosthesis to that of the left ventricular outflow (VTIpmv/VTI lvo > 2.2; sensitivity 91%, specificity 74%) were successful in detecting PMV dysfunction. Although pressure half-time (PHT) readily identified PMV obstruction, it did not detect regurgitation. Logistic models including peak E velocity and VTIpmv/VTI lvo or PHT were equally successful in detecting PMV dysfunction. However, all 3 variables were needed to best distinguish among normal, obstructed, and regurgitant valves. A peak E velocity > 1.9 m/s and VTIpmv/VTI lvo ratio > 2.2 predicted valve regurgitation in 83% of valves when PHT was < 130 ms, and valve stenosis in 95% when PHT was > 130 ms. Importantly, a peak E velocity < 1.9 m/s, VTIpmv/VTI lvo ratio < 2.2, and a PHT < 130 ms had a predictive accuracy for a normal valve of 98%. Thus, TTE Doppler indexes can be used as screening parameters of PMV dysfunction and help select patients for further diagnostic evaluation with TEE. ©2002 by Excerpta Medica, Inc.

Ttransthoracic echocardiography (TTE) is currently the modality of choice for serial evaluation of prosthetic valve function.1,2 Assessment of prosthetic mitral valves (PMV), however, has remained a challenge, particularly for mechanical valves. Although evaluation of PMV obstruction with transthoracic Doppler is quite reliable using pressure half-time (PHT) and a mean gradient or the continuity equation, the detection of PMV regurgitation is seriously hampered by acoustic shadowing and attenuation.1,5,7-10 Despite this handicap, the presence of significant PMV regurgitation has recently been assessed by transthoracic Doppler indexes that do not rely on recording of the regurgitant jet, using peak early E velocity and the ratio of the velocity time integral of mitral inflow to the velocity time integral in the left ventricular outflow (VTIpmv/VTI lvo ) ratio.11

To date, there have been no studies identifying an accurate screening tool using TTE for evaluation of PMV dysfunction (i.e., obstruction or regurgitation). Because flow velocity across the PMV should increase in either stenosis or regurgitation, we postulated that this could be used as the first screening parameter for any PMV dysfunction. Other Doppler parameters may further refine the distinction between stenosis and regurgitation. The purpose of this study was therefore to test the accuracy of this hypothesis and to identify Doppler indexes that can be used in an algorithm to facilitate evaluation of prosthetic valve function with the transthoracic approach. Such an evaluation could increase the accuracy of identifying normal prosthetic valves and alert the physician to unsuspected prosthetic valve dysfunction.

METHODS

One hundred sixty-four consecutive patients with mechanical PMVs who underwent TTE and transesophageal echocardiography (TEE) were evaluated for inclusion in the study. Patients with significant aortic regurgitation (n = 7), LVO tract obstruction (n = 2), technically inadequate TTE (n = 4), or time between TTE and TEE > 2 weeks (n = 17) were
TTE and TEE studies were performed within 3 days of the initial echocardiographic examination. The Doppler study was performed in all patients from multiple windows, using both color flow and stand-alone continuous-wave Doppler. In all cases, pulsed Doppler recording of blood velocity in the LVO from the apical window was performed. An attempt at detecting and recording mitral regurgitation (MR) was performed.6 Recording of the tricuspid insufficiency jet, when present, was attempted from the parasternal and apical windows with color and continuous-wave Doppler.

### Quantitation of transthoracic 2-dimensional/Doppler parameters:
A single observer, blinded to the TEE studies and clinical data, performed analysis of the TTE studies with the use of an off-line station (Digisonics EC 500, Houston, Texas). Measurements are shown in Table 1. Left ventricular volumes and ejection fraction were calculated by the multiple diameter method.13,14 From recordings of PMV inflow by continuous-wave Doppler, the following parameters were measured as previously described:6,11: peak inflow (E) velocity (meters per second), mean gradient (mm Hg), PHT (milliseconds), and VTI (centimeters). The VTI of pulsed Doppler was determined. The ratio of VTI to VTI of pulsed Doppler, which relates mitral flow to systemic flow, was then derived. Isovolumic relaxation time was measured as previously described.12 When a tricuspid regurgitant jet was recorded, the highest velocity was used, denoting the least ultrasound angulation with flow. All results represent the average of 2 to 3 beats in sinus rhythm and 5 beats in atrial fibrillation.

### Transesophageal echocardiography:
TEE was performed using a 5-MHz phased-array transducer with the same ultrasound equipment. The PMV was carefully inspected for thrombus, pannus, vegetation, and paravalvular dehiscence or abscesses. In addition, valve mobility, leaflet excursion, and transvalvular velocities were evaluated for signs of obstructive dysfunction. Significant PMV obstruction (moderate or severe) was defined as an alteration in valve structure and function.
mobility, thrombus formation, or pannus) that was usually accompanied by a valve area by PHT of $2 \text{ cm}^2$ and a mean gradient $5 \text{ mm Hg}$. When MR was detected by color flow, the positions of the probe and imaging planes were adjusted to obtain maximum visualization of the MR jet within the field. Physiologic or normal prosthesis leakage backflow was defined as a jet $2 \text{ cm}$ long and $1 \text{ cm}$ wide in the left atrium, originating from the valve leaflets with a typical pattern. Pathologic MR jets were more extensive, turbulent, and frequently crescent shaped. The direction of the MR jet was noted and the maximal area of the jet was quantitated by tracing the contour of the turbulent high-velocity mosaic. Each pulmonary vein was assessed with pulsed Doppler to assess flow patterns. Severity of MR was assessed as previously described. In the case of central MR jets, the severity of MR was assessed based on the maximal area of the MR jet and graded as trace (physiologic), mild (jet area 1.5 to 4 cm²), moderate (4 to 7 cm²), or severe (>7 cm²) and corroborated with the pulmonary venous flow pattern, as previously described. With eccentric jets, MR was considered moderate or severe if the jet ran into the left atrial wall, changing its direction and turning around within the cavity along with reduced (moderate MR) or reversed (severe MR) systolic pulmonary vein velocity. Significant PMV regurgitation was defined as moderate or severe MR.

**Statistical analysis:** The primary aim of this study was to identify a set of TTE-Doppler indexes that could be used as reliable screening parameters of PMV dysfunction. Therefore, patients were classified in 3 groups based on the results of TEE studies: normal, regurgitant (moderate or severe), and obstructed (moderate or severe). The aim was accomplished in 2 steps. Step 1 involved univariate testing (analysis of variance) to determine which conventional 2-dimensional and Doppler indexes distinguished between those groups. Step 2 involved using stepwise and multinomial logistic regression to develop models capable of predicting which patients would and would not have PMV dysfunction. The Pearson chi-square test was used to assess the fit of each of the models. The predictive ability of the final models was compared utilizing the area under the receiver-operating characteristic curves (AUC). The AUC was determined using the trapezoidal rule. The test used for the comparison of the AUC for the respective models was developed by Hanley and McNeil. A p value $<0.05$ was considered significant for all statistical analyses.

**RESULTS**

One hundred thirty-four patients (64 men and 70 women; mean age $60 \pm 12$ years) met the inclusion and exclusion criteria and constituted the study population. There were 73 normal PMVs, and 40 regurgitant and 21 obstructed valves. The PMVs with mixed obstructive and regurgitant lesions ($n = 4$) were assigned to the dominant category. Valve size ranged between 23 and 33 mm. Fifty-nine patients

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**TABLE 2** Doppler Model and Multivariate Predictors of Prosthetic Mitral Valve Dysfunction

<table>
<thead>
<tr>
<th>Doppler Models</th>
<th>Odds Ratio</th>
<th>p Value</th>
<th>95% Confidence Intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>E Vel + VTI_{pmv}/VTI_{lvo} (AUC: 0.97)</td>
<td>2.58</td>
<td>$&lt;0.0001$</td>
<td>1.59–4.18</td>
</tr>
<tr>
<td>E Vel</td>
<td>5.93</td>
<td>0.003</td>
<td>1.83–19.20</td>
</tr>
<tr>
<td>E Vel + PHT (AUC: 0.96)</td>
<td>3.03</td>
<td>$&lt;0.0001$</td>
<td>1.90–4.84</td>
</tr>
<tr>
<td>PHT</td>
<td>1.27</td>
<td>0.015</td>
<td>1.05–1.54</td>
</tr>
</tbody>
</table>

AUCs were not statistically different ($p = 0.73$). Odds ratios were calculated for every 10 cm/s increments of peak E velocity or 10-ms increments in PHT.

E vel = peak E velocity; MV = mitral valve.

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**FIGURE 1.** Receiver-operating characteristic curves for detection of prosthetic mitral valve dysfunction using TTE Doppler variables. These receiver-operating characteristic curves were used to select index values slightly favoring sensitivity over specificity, as is preferred clinically.
PMV dysfunction:
For the total population, left ventricular systemic stroke volume in the LVO was lower in diastolic and systolic diameters and volumes. The ever, no differences were detected in left ventricular significantly higher in regurgitant PMV (Table 1). How-
variables, left ventricular ejection fraction was signif-
ically among all patient groups. Regarding 2-dimensional
valve size, blood pressure, and heart rate were similar
more important predictor. One set adds the VTIpmv/
VTI lvo ratio and increases the sensitivity of the model
to detect PMV regurgitation. Another set includes
PHT and makes the model sensitive for the detection
of valve obstruction (Table 1).

Multivariate analysis and prediction of any PMV dys-
function: When univariate predictors (Doppler vari-
ables) of any PMV dysfunction were included in a stepwise logistic model, the best multivariate predic-
tor was peak E velocity (Table 2). The best models
could be fitted to identify any dysfunction of the
valve included 1 of 2 additional independent predic-
tors: VTIpmv/VTI lvo ratio or PHT (Table 2). The pre-
dictive power of both models was similar (AUC 0.97
vs 0.96; p = 0.73). Cut-off values for multivariate
predictors were derived from receiver-operating char-
acteristic curves to construct Doppler indexes of PMV
dysfunction (obstruction and regurgitation) (Figure 1,
Table 3). The cut-off values chosen slightly favored
sensitivity of detection of valvular dysfunction over
specificity, as would be preferred clinically. Mean
gradient was not an independent predictor of PMV
dysfunction. A mean gradient ≥5 mm Hg had a sen-
sitivity of 92% and a specificity of 62% (Figure 1).

Multivariate analysis and distinction between regur-
gitant and obstructive PMVs: The distinction between
regurgitant and obstructive PMVs was explored using
a multinomial logistic approach. Two different sets of
variables were needed to differentiate these condi-
tions, including peak E velocity as both a common and
more important predictor. One set adds the VTIpmv/
VTI lvo ratio and increases the sensitivity of the model
to detect PMV regurgitation. Another set includes
PHT and makes the model sensitive for the detection
of valve obstruction (Table 4).

Decision tree analysis: A decision tree was con-
structured to evaluate the conditional probabilities of valve
dysfunction using the 3 multivariate TTE predictors:
peak E velocity, VTIpmv/VTI lvo ratio, and PHT (Figure
2). The probability (in percentages) of any signi-
cant valve dysfunction is depicted at the end of every path of
the tree, along with the probability for signi-
cant regurgitation jet in only 9 of the 40
patients (22.5%) with significant
MR. PHT was only predictive of PMV obstruction
(Table 4).

were in sinus rhythm, 52 in atrial fibrillation, and the
remaining 23 had paced or junctional rhythm.

Univariate analysis of TTE variables predictive of
PMV dysfunction: For the total population, left ventric-
ular ejection fraction averaged 52 ± 15% (range 13%
to 80%) and mean heart rate was 80 ± 17 beats/min
(range 50 to 169). Determination of VTI lvo was not
feasible in 4 patients and PHT could not reliably be
measured in 1 patient because of a very short diastolic
filling period. Table 1 shows the comparison of clinical,
2-dimensional, and Doppler parameters among
normal, regurgitant, and obstructed valves. Age and
valve size, blood pressure, and heart rate were similar
among all patient groups. Regarding 2-dimensional
variables, left ventricular ejection fraction was sig-
ificantly higher in regurgitant PMV (Table 1). How-
ever, no differences were detected in left ventricular
diastolic and systolic diameters and volumes. The
systemic stroke volume in the LVO was lower in
patients with prosthetic insufficiency.

The following Doppler variables allowed distinc-
tion between normal and dysfunctional (regurgitant or
obstructive) prostheses: peak E velocity, VTIpmv,
mean and peak gradient, and tricuspid regurgitant jet
(Table 1). The values for all these prosthetic inflow
variables were higher in obstructive compared with
regurgitant valves (Table 1). Other calculated Doppler
indexes were also highly predictive of valve dysfunc-
tion: VTIpmv/VTI lvo and stroke volume/VTI pmv ratios
(Table 1). The VTIpmv/VTI lvo ratio was higher in
obstructive compared with regurgitant valves. Ste-

| TABLE 3 | Sensitivity, Specificity, Positive (PPV) and Negative (NPV) Predictive Values of Various Doppler Indexes for Identifying Dysfunctional Prosthetic Mitral Valves* |
| Index | Sensitivity | Specificity | PPV | NPV |
| Peak E velocity ≥1.9 m/s | 92% | 78% | 83% | 90% |
| VTIpmv/VTI lvo ≥2.2 | 91% | 74% | 80% | 87% |
| PHT ≥130 ms | 38% | 99% | 96% | 57% |

*Cut-off values were selected from the receiver-operating characteristic.

| TABLE 4 | Multivariate Predictors of Type of Prosthetic Valve Dysfunction |
| Valve Status | Odds Ratio | p Value | 95% Confidence Intervals |
| PMV regurgitation | | | |
| E Vel | 2.45 <0.0001 1.49-4.02 |
| VTIpmv/VTI lvo | 5.15 0.020 1.29-20.58 |
| PMV obstruction | | | |
| E Vel | 3.51 0.001 1.62-7.57 |
| PHT | 2.63 0.012 1.24-5.57 |

Relative risk ratios were calculated for every 10-unit increments of peak E velocity (cm/s) or PHT (ms).
Abbreviation as in Table 2.
When PHT was ≥130 ms, the probability of dysfunction was very high (100%); most of the dysfunctional valves were obstructed (95%). When PHT was <130 ms, most of the dysfunctional valves were regurgitant (80%). The sensitivity of this algorithm to detect a dysfunctional valve was 92%, with a specificity of 85%. The accuracy of a simplified algorithm using only 2 of the variables was also tested: peak E velocity to screen for valve dysfunction and PHT to discriminate obstruction from regurgitation (Figure 3). This model was still able to separate dysfunctional from normal valves, although its ability to stratify PMV dysfunction in patients with normal PHT was less. Furthermore, a slightly higher percentage of regurgitant valves were missed (5%) when E was <1.9 m/s and PHT was <130 ms (Figure 3) compared with the model with 3 variables (Figure 2).

DISCUSSION

The present study demonstrates for the first time that the comprehensive use of Doppler indexes from TTE can differentiate normal from dysfunctional mechanical PMVs. The single most accurate index to evaluate PMV function is the mitral peak E velocity. The addition of VTI ratios and PHT can further refine the distinction between normal, regurgitant, and stenotic valves.

Doppler parameters of PMV function: Evaluation of mechanical PMV function with TTE has been most challenging, particularly in evaluating MR. Assessment of PMV function has traditionally involved measurement of mean gradient and valve area by PHT. Peak E velocity in normal mechanical valves has averaged between 1.2 and 2.0 m/s, and is dependent on flow rate, valve type, and size. In an early study by Nellessen et al., the value of peak E velocity and mean gradients in diagnosing PMV dysfunction in 15 patients with bioprostheses was demonstrated, but no differentiation between obstruction and regurgitation was feasible. More recently, we showed that peak E velocity is a helpful discriminator between normal and regurgitant valves.11 Because flow velocity across the PMV increases in either stenosis or regurgitation, we postulated that peak E velocity might be a good screening parameter for valve dysfunction. In the present study, peak E velocity was the most accurate single parameter to identify prosthetic valve dysfunction. The cut-off value for peak E velocity was ≥1.9 m/s, similar to that previously evaluated in a small series of regurgitant prosthetic valves.11 Although in this study, peak E velocity was significantly higher in obstructive compared with regurgitant valves, individual data overlapped considerably, precluding a good distinction between these 2 factors with this parameter alone. However, peak E velocity was the main multivariate predictor of valve dysfunction.

The VTI pmv/VTI lvo ratio was almost as powerful as
E velocity in identifying valvular dysfunction and was elevated in both PMV regurgitation and stenosis. In valvular regurgitation, the higher flow through the mitral valve and the reduced systemic flow in the LVO both contributed to the increased ratio. In contrast, in valvular stenosis, the increased ratio was mostly because of high velocities through the prosthesis secondary to a small effective orifice area. In this study, the most advantageous cut-off value for the VTImv/VTIivo ratio was \( \geq 2.2 \). Although this parameter and peak E velocity may provide some redundant information, their combination improves the accuracy of distinction of normal from dysfunctional valves, particularly regurgitant valves, as shown in this and a study from our institution.\(^{11}\) Although extremes of flow (high or low output) affect E velocity directly, the VTImv/VTIivo ratio corrects for this situation, because velocities through both the mitral valve and ventricular outflow are influenced in the same direction.

PHT was the least effective in screening for valve dysfunction. Its value was in discriminating PMV obstruction from regurgitation when indexes of mitral inflow velocity or VTI ratio were increased. The prolongation of PHT in native and prosthetic mitral stenosis has been well documented.\(^1^,2\) Previously suggested PHT cut-off values have ranged anywhere from 100 to 200 ms. In this study, the best cut-off value, based on receiver-operating characteristic curves, was 130 ms, with a sensitivity of 38% and a specificity of 99% in predicting dysfunction. However, sensitivity increased to 95% when identifying obstruction. The lowest PHT in obstructed valves in this series was 125 ms. PHT has been shown to be affected by ventricular relaxation, ventricular and atrial compliance, and heart rate in addition to the effective orifice area of the valve.\(^{6,23,24}\) In a small percentage of patients, PHT may not be prolonged despite the presence of valve obstruction.\(^6\) In these instances, an increase in peak E velocity and/or the VTI ratio may alert the echocardiographer to valvular dysfunction, prompting further evaluation with TEE.

**Clinical implications:** The algorithms in Figures 2 and 3 provide a guide for the evaluation of PMV function based on the logistic analysis. We propose that sonographers first determine the peak E velocity, as it is the most accurate, easiest parameter to measure, and alerts the observer to valvular dysfunction, if present. The other 2 indexes are needed to better distinguish between normal, and PMV obstruction and regurgitation (Figure 2). Although one can forego the determination of the VTI ratio (Figure 3), particularly in severely obstructed valves, it is preferable that determination of the VTI ratio be performed more routinely, as it improves the confidence of the abnormalities detected and the predictive accuracy for a normally functioning valve. With the on-line capabilities of measuring VTIs, which are currently performed in most laboratories for calculation of cardiac output and mean gradients, the derivation of this ratio is rather simple. An elevated E velocity \( \geq 1.9 \) and VTImv/VTIivo ratio \( \geq 2.2 \) is practically diagnostic (89% probability) of valve dysfunction: there is a 83% probability of dysfunction, mostly regurgitation if PHT is normal, and 100% probability if PHT is \( >130 \) ms, with most of the valves (95%) showing obstruction. In cases of discordance between peak E velocity and the VTI ratio, the probability for significant MR is intermediate (25% to 29%; Figure 2). Further evaluation with TEE may be needed in this situation. A high PHT, with an elevated E velocity or VTI ratio is indicative of prosthetic valve obstruction (>95% probability). None of the valves with obstruction had a normal VTI ratio (Figure 2). Importantly, in patients where all 3 Doppler parameters were normal (E velocity <1.9 m/s, VTI ratio <2.2, and PHT <130 ms), the likelihood of having a normal valve was very high (98%).

All of the prosthetic valves evaluated were mechanical, with predominance of bileaflet prostheses. Therefore, the usefulness of the present parameters, particularly the actual cut-off values, may not be applicable to bioprosthesis valves or ball and cage valves. Patients with significant aortic insufficiency should not be evaluated with the VTImv/VTIivo ratio because increased flow through the LVO will overestimate this parameter. PHT is also less accurate in this condition. As in any other valve position, knowledge of valve type and particularly size, remains important because small valves can simulate valve obstruction. Finally, in the appropriate clinical setting and with echocardiographic and Doppler parameters pointing to valvular regurgitation and/or obstruction, TEE would be required to detail the mechanism and severity of the dysfunction and to ultimately guide patient management.

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