Clinical Utility of Doppler Echocardiography and Tissue Doppler Imaging in the Estimation of Left Ventricular Filling Pressures
A Comparative Simultaneous Doppler-Catheterization Study
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Background—Noninvasive assessment of diastolic filling by Doppler echocardiography provides important information about left ventricular (LV) status in selected subsets of patients. This study was designed to assess whether mitral annular velocities as assessed by tissue Doppler imaging are associated with invasive measures of diastolic LV performance and whether additional information is gained over traditional Doppler variables.

Methods and Results—One hundred consecutive patients referred for cardiac catheterization underwent simultaneous Doppler interrogation. Invasive measurements of LV pressures were obtained with micromanometer-tipped catheters, and the mean LV diastolic pressure (M-LVDP) was used as a surrogate for mean left atrial pressure. Doppler signals from the mitral inflow, pulmonary venous inflow, and TDI of the mitral annulus were obtained. Isolated parameters of transmitral flow correlated with M-LVDP only when ejection fraction $<50\%$. The ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/E$'$) showed a better correlation with M-LVDP than did other Doppler variables for all levels of systolic function. E/E$'$ $<8$ accurately predicted normal M-LVDP, and E/E$'$ $>15$ identified increased M-LVDP. Wide variability was present in those with E/E$'$ of 8 to 15. A subset of those patients with E/E$'$ 8 to 15 could be further defined by use of other Doppler data.

Conclusions—The combination of tissue Doppler imaging of the mitral annulus and mitral inflow velocity curves provides better estimates of LV filling pressures than other methods (pulmonary vein, preload reduction). However, accurate prediction of filling pressures for an individual patient requires a stepwise approach incorporating all available data. (Circulation. 2000;102:1788-1794.)

Key Words: diastole • echocardiography • pressure

Diastolic dysfunction is common in cardiac disease and contributes to the signs and symptoms of heart failure. Doppler echocardiography is widely used for the noninvasive assessment of diastolic filling of the left ventricle (LV).$^1$ Analysis of the mitral inflow velocity curve has provided useful information for determination of filling pressures and prediction of prognosis in selected patients. However, mitral flow is dependent on multiple interrelated factors, including the rate and extent of ventricular relaxation, suction, atrial and ventricular compliance, mitral valve inertia, and left atrial pressure.$^1,2$ These factors may have confounding effects on the mitral inflow; thus, it has not been possible to determine diastolic function from the mitral flow velocity curves in many subsets of patients.$^3,4$

To overcome these limitations of the mitral inflow parameters, combinations of the mitral flow velocity curves with other Doppler parameters have been used. These include the pulmonary venous velocity curves,$^3-10$ color M-mode,$^{11,12}$ and the response of the mitral inflow to altered loading conditions.$^{13,14}$ Tissue Doppler imaging (TDI) of mitral annular motion has been proposed to correct for the influence of myocardial relaxation on transmitral flows. This has been shown to be an excellent predictor of diastolic filling in subsets of patients.$^{15-22}$

The purpose of this study was to evaluate critically the usefulness and limitations of TDI for the evaluation of diastolic filling with direct simultaneous high-fidelity measurement of LV pressure. Additionally, we sought to compare the results of TDI with other techniques currently available for the assessment of diastolic function.

Methods

Invasive Measurements
One hundred consecutive patients in sinus rhythm referred for clinically indicated left heart catheterization made up the study.

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group. High-fidelity, micromanometer-tipped catheters were placed in the LV chamber and calibrated as previously described. Rapid-acquisition (5-ms intervals) digital records were obtained. Measurements were taken from 3 to 5 end-expiratory cycles. The mean LV diastolic pressure (M-LVDP), measured from the time of mitral valve opening to mitral valve closure, is a better surrogate of mean left atrial pressure than the pre–A-wave pressure and can be measured from the digitized pressure tracings as previously described. An elevated LV filling pressure was defined a priori as M-LVDP ≥12 mm Hg. The time constant of relaxation (τ) was calculated by use of a zero asymptote method as described by Weiss et al.

Ejection fraction (EF) was visually estimated with 2-dimensional echocardiography, as is done routinely in our laboratory. To validate this commonly used measure of systolic function, 55 patients also had quantitative measurement with biplanar Simpson’s rule from the apical 2- and 4-chamber views. The correlation coefficient between the 2 methods was r=0.91. The visually estimated EF is used in the remainder of this article.

Conventional Doppler Measurements
Doppler echocardiography was performed simultaneously with the invasive recordings with an Acuson 128XP/10. A single investigator (S.R.O.), who had performed Doppler echocardiography for >2 years and had achieved level 3 training in echocardiography, performed all Doppler recordings. Mitral inflow and pulmonary venous curves were recorded as previously described. The peak Doppler velocities of early (E) and late diastolic flow (A), the deceleration time (DT), the E/A ratio, and the duration of the late diastolic flow (a-dur) were measured (Figure 1).

Pulmonary vein systolic (PVs), diastolic (PVd), and atrial reversal (PVa), as well as the duration of flow at atrial contraction (a-dur), were recorded (Figure 1). The difference between the pulmonary a-dur and mitral a-dur (PVa – MVA) was calculated. There was a strong correlation between the PVs/PVd velocity ratio and the septal annulus (r=0.71) and a similar association with M-LVDP in 20 randomly selected patients. The PVs/PVd ratio is used as a surrogate for the pulmonary venous systolic filling fraction.

The mitral inflow pattern was also recorded during the strain phase of the Valsalva maneuver with real-time 2-dimensional echocardiography to ensure that the placement of the sample volume and angle of interrogation were unchanged with respect to the baseline measurements. Patients were required to forcefully exhale into an analog manometer to achieve an intrathoracic pressure of ≥30 mm Hg. Patients unable to achieve this level did not have their signals analyzed. Because of the relative tachycardia seen during the Valsalva maneuver, slight fusion of the mitral E and A waves can occur. In those instances, the late diastolic velocity was determined by subtracting the velocity at the fusion point (E at A) from the measured A velocity (Figure 1).

Tissue Doppler Measurements
TDI of the mitral annulus was obtained from the apical 4-chamber view. A 1.5-mm sample volume was placed sequentially at the lateral and medial mitral annulus. Analysis (Figure 1) was performed for the early (E′) and late diastolic velocity (A′); peak velocity (E′, A′), time to peak velocity (E′ at, A′ at), DT (E′DT, A′DT), and duration of velocity profile (E′dur, A′dur). These variables were analyzed individually, as the average of the medial and lateral annulus, and as the maximum of the medial and lateral annulus.

All Doppler signals were recorded with a chart recorder set at 100 mm/s. The average of 3 end-expiratory cycles was used.

Data were presented as mean±SD. Linear regression was used to assess whether the Doppler variables were associated with the invasive variables. Receiver-operating characteristic (ROC) curves were constructed for the individual Doppler variables for the prediction of M-LVDP >12 mm Hg. Comparisons between patient groups were assessed with t tests. Statistical significance was defined as P<0.05.

Results
Baseline Characteristics
The baseline characteristics are presented in Table 1. The patients were 63.3 years old, and 61% were men. Seventy-
three patients were referred for evaluation of angina (11 of whom had no epicardial coronary artery disease [CAD]); the remainder were referred for symptoms of congestive heart failure. Of the latter group, 6 had LV dysfunction on the basis of CAD. No patients studied were having an acute coronary syndrome. Thirty-six patients had EF <50%.

### Technical Success Rate of Obtaining Doppler Signals

Mitral inflow and TDI signals were recorded in all patients. The mitral signal was fused in 6 patients (94% available for analysis), and the TDI signal was fused in 3 (97% available). Twenty TDI signals were remeasured by a second observer; the mean difference in velocity between the 2 observers was 0.001±0.002 m/s (P=NS).

Pulmonary venous signals were adequate in 73%, whereas 61% had adequate Valsalva recordings. The Valsalva recordings were felt to be inadequate in 10 patients (10%) because of poor effort, in 20 patients because of fusion of the signal, and in the remainder because of inadequate or loss of signal during the strain phase of the maneuver.

### Conventional Doppler Parameters and Correlation With M-LVDP

The correlations of M-LVDP with Doppler variables are shown in Table 2. Among patients with EF <50%, there was a significant correlation between DT and M-LVDP (r=0.60) but not in those with EF >50% (r=0.17). Likewise, the E/A ratio was better correlated with M-LVDP when EF was <50% (r=0.46) than when EF was >50% (r=0.28).

### Tissue Doppler Correlation With Invasive Parameters

The correlations with the medial annulus TDI were consistently equivalent or better than the lateral annulus or the combinations of the medial and lateral annulus (Table 2). The ROC curves for prediction of elevated M-LVDP from the E/E ratios are shown in Figure 2. The areas under the curves were 0.82 and 0.75 for the medial and lateral annulus, respectively. The medial annulus signals were obtained in a higher proportion of patients and thus are used in the remainder of this article. None of the TDI intervals (dura-
tions, acceleration times, and DTs) showed a strong relationship to LV filling pressures (Table 2).

There was a correlation between the time constant of relaxation and E' (r=0.46), but scatter was present (Figure 3). The correlation was worse in patients with normal (r=0.28) versus abnormal (r=0.42) systolic function. The best TDI parameter correlating with M-LVDP was the E/E' ratio (r=0.64). This correlation was better in patients with EF <50% (r=0.60) than in those with EF >50% (r=0.47). The medial E/E' ratio performed as well when the analysis was confined to those patients with documented CAD (medial r=0.65, lateral r=0.54).

Comparison of Doppler Methods

The Doppler variables were tested to determine the accuracy of each variable in identifying M-LVDP >12 mm Hg on the basis of previously published criteria. The prediction of elevated M-LVDP was based on mitral E/A >2,29,30 DT <130 ms,29 a decrease in E/A with the Valsalva maneuver of ≥0.5, 14 PVd >PVs, PVa duration ≥30 ms longer than MVa dur,9 or E/E' >10.18 The percentage of patients correctly identified by each variable is shown in Figure 4. The E/E' ratio had the highest predictive accuracy when all patients were analyzed (71%) or when only those patients with interpretable signals (76%) were considered. The ROC curves for all measured Doppler parameters are shown in Figure 5. The largest area was 0.82 for E/E' compared with 0.75 for E/A ratio, 0.68 for DT, 0.77 for the Valsalva maneuver, and 0.67 for PVa/MVa.

The ROC analysis was repeated with M-LVDP >15 mm Hg used as the definition of elevated filling pressure. The areas under the respective ROC curves were 0.81 (septal E/E'), 0.80 (Valsalva maneuver), 0.78 (E/A ratio), 0.76 (DT), and 0.67 (PVa-MVa). As with the cutoff value of M-LVDP >12 mm Hg, the septal E/E' had the best ROC curve and was the most readily obtained. E/E' >15 had 86% specificity (64% positive predictive value) for M-LVDP >15 mm Hg (97% negative predictive value for E/E' <8).

**TABLE 2. Correlation (r) of TDI Variables With M-LVDP**

<table>
<thead>
<tr>
<th>Variable</th>
<th>EF &gt;50%</th>
<th>EF &lt;50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>E/A</td>
<td>0.59</td>
<td>0.25</td>
</tr>
<tr>
<td>DT</td>
<td>0.48</td>
<td>0.17</td>
</tr>
<tr>
<td>PVd/PVs</td>
<td>0.31</td>
<td>0.03</td>
</tr>
<tr>
<td>PVa-MVadur</td>
<td>0.29</td>
<td>0.39</td>
</tr>
<tr>
<td>Change in E/A</td>
<td>0.43</td>
<td>0.36</td>
</tr>
<tr>
<td>E' medial</td>
<td>0.36</td>
<td>0.04</td>
</tr>
<tr>
<td>E' lateral</td>
<td>0.23</td>
<td>0.05</td>
</tr>
<tr>
<td>E' maximum</td>
<td>0.26</td>
<td>0.12</td>
</tr>
<tr>
<td>E' mean</td>
<td>0.31</td>
<td>0.06</td>
</tr>
<tr>
<td>E' at</td>
<td>0.27</td>
<td>0.09</td>
</tr>
<tr>
<td>E' DT</td>
<td>0.32</td>
<td>0.08</td>
</tr>
<tr>
<td>E' duration</td>
<td>0.32</td>
<td>0.03</td>
</tr>
<tr>
<td>A' medial</td>
<td>0.50</td>
<td>0.34</td>
</tr>
<tr>
<td>A' lateral</td>
<td>0.31</td>
<td>0.08</td>
</tr>
<tr>
<td>A' maximum</td>
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</tr>
<tr>
<td>A' mean</td>
<td>0.42</td>
<td>0.24</td>
</tr>
<tr>
<td>A' at</td>
<td>0.12</td>
<td>0.30</td>
</tr>
<tr>
<td>A' DT</td>
<td>0.03</td>
<td>0.08</td>
</tr>
<tr>
<td>A' duration</td>
<td>0.04</td>
<td>0.28</td>
</tr>
<tr>
<td>E'/A'</td>
<td>0.17</td>
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</tr>
<tr>
<td>E'/E' medial</td>
<td>0.64</td>
<td>0.47</td>
</tr>
<tr>
<td>E'/E' lateral</td>
<td>0.51</td>
<td>0.40</td>
</tr>
<tr>
<td>E'/E' maximum</td>
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<td>0.40</td>
</tr>
<tr>
<td>E'/E' mean</td>
<td>0.62</td>
<td>0.45</td>
</tr>
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</table>

**Figure 2.** ROC curve for prediction of M-LVDP >12 mm Hg using E/E' at both septal and lateral annulus. Area under the curve (AUC)=0.82 (septal) and 0.75 (lateral).

**Figure 3.** Scatter plot of peak early diastolic mitral annular velocity (E') versus τ. ● indicates patients with EF <50%; ○, patients with EF >50%.

**Figure 4.** Accuracy of single Doppler variables for classifying M-LVDP as normal or elevated. Open bars represent predictive accuracy for patients in whom technique was available; closed bars, predictive accuracy for entire population, including patients in whom adequate Doppler parameters could not be obtained.
Clinical Application of Doppler Methods for Determining LV Filling Pressure

The E/E’ ratio was the single best parameter for predicting M-LVDP and was obtained most readily. With use of the ROC curve, patients were divided into 3 groups. Of the 27 patients with E/E’ <8, normal M-LVDP was found in 23 (85%). All patients with E/E’ >15 had elevated M-LVDP. This scheme remains accurate whether patients with preserved or reduced systolic function are assessed (Figure 6).

Fifty-one patients had indeterminate M-LVDP (8 E/E’ ≥9, E/E’ <8). Figure 7 displays the incremental utility of the conventional Doppler data in this group. Patients with Valsalva maneuver (change in E/A >0.5) and/or PVa–MVa >30 ms tended to be those with the highest filling pressures. There was no incremental benefit of using the conventional Doppler variables (Valsalva mitral inflow pattern or pulmonary vein velocities) among patients with E/E’ <8 or >15.

Discussion

The noninvasive assessment of LV filling pressures can be an important clinical tool. In diseased ventricles, progressive shortening of the transmitral DT and increasing E/A ratio can be seen with decreasing ventricular compliance and increasing left atrial pressure. Transmitral parameters have been shown to be useful in patients with LV systolic dysfunction. The present study confirms that DT and the E/A ratio correlate with LV filling pressure when EF <50%. However, healthy ventricles that maintain early diastolic suction forces may also manifest a relatively short DT and high E/A ratio. Thus, as shown in this study and others, transmitral parameters alone do not correlate with LV filling pressure in patients with preserved systolic function. Attempts to overcome this limitation have involved altering the loading conditions during the Doppler assessment or combining the transmitral variables with pulmonary venous signals.

TDI of the mitral annulus during diastole has been proposed as a new method for assessing cardiac function. With systolic contraction, there is long-axis shortening of the LV manifest by mitral annular descent toward a relatively fixed apex. In patients in sinus rhythm, the annulus ascends in 2 phases. Pulsed-wave TDI provides the velocity profile of these movements. The velocity of the earliest diastolic motion may reflect the rate of myocardial relaxation, and these velocities may not be as dependent on pressure gradients as is blood flow. TDI has been applied to several subsets of patients to show a correlation with systolic and diastolic cardiac function. Combining transmitral flow velocity with annular velocity (E/E’) has been proposed as a tool for assessing LV filling pressures. In the present study, this combined variable was the best single Doppler predictor of elevated filling pressures. However, there remains significant scatter with E/E’, particularly with intermediate values of E/E’. The annular velocity should not be viewed as a direct measure of myocardial relaxation because the correlations between E’ and τ that have been reported here (r=0.46) and elsewhere are modest at best. Nonuniformity of LV relaxation, particularly in patients with CAD, may further confound the direct relationship between the annular velocities and a global measurement of myocardial relaxation.

TDI is easier to obtain and, in the present study, more accurate than other methods in determining LV filling pressures. Signals adequate for analysis during the Valsalva maneuver or from the pulmonary venous flow were obtained in 61% and 73%, respectively. By comparison, the tissue signals were obtained in 97%.

We would propose that the E/E’ ratio be used as the initial measurement for estimation of LV filling pressures, particularly in those patients with preserved systolic function.
Patients with E/E’ >15 can be classified as having elevated filling pressure. An E/E’ <8 suggests normal filling pressure. In the range of E/E’ of 8 to 15, other information must be applied. With high-specificity cutoff points for A-wave duration (PVa 30 ms longer than MVa) and a change in mitral E/A ratio during the Valsalva maneuver (reduction >0.5), further characterization of the intermediate E/E’ group is possible. Prior investigations also point out the importance of considering left atrial size in assessing filling pressures.30

Study Limitations
The motion of the mitral annulus is not entirely due to myocardial contraction but rather is the summation of contraction, rotation, and translation. The effects of each of these may vary from patient to patient. The use of the apical transducer position to sample the mitral annulus is an attempt to minimize the translational and rotational effects and focus on long-axis excursions of the LV cavity. We have not accounted for differences in the length of the long axis, which may inherently be related to total annular plane displacement. Nor was any adjustment made for regional wall motion abnormalities, although there was clearly more data scatter in patients with known CAD. The septal annulus appeared more sensitive to this heterogeneity, although there was a strong correlation between the septal and lateral annulus velocities.18

The effects of regional dysfunction on the motion of the annular plane are not yet known, and we did not examine the anterior or posterior annulus motion. Measurements of the medial annulus demonstrated a better correlation with LV filling pressures than did measurements of the lateral annulus or combinations of the two. We sought to examine an “unselected” group of patients who would be representative of a broader patient population. However, all patients were referred for clinically indicated left heart catheterization and as such represent a group of patients with a high prevalence of cardiac disease. The relatively low technical success of pulmonary venous flow and Valsalva maneuver may be explained in part by the fact that these patients were studied in the supine position in the catheterization laboratory. There were also stringent criteria for acceptance of adequate Valsalva maneuver, which limits the overall success of obtaining these signals. Using optimal patient positioning, more advanced echocardiographic equipment, and/or contrast enhancement may potentially increase the success of obtaining these signals. However, the percentage of these Doppler parameters that were adequate for analysis in this study may well represent the type of data obtained in most echocardiographic laboratories.

Conclusions
Overall, the E/E’ ratio was the single best predictor of LV filling pressure but did not have adequate discriminatory power to be used in isolation. All available information, including systolic function, chamber dimensions, and all Doppler variables, must be considered in the analysis of individual patients.

References
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