Doppler Estimation of Left Ventricular Filling Pressure in Sinus Tachycardia
A New Application of Tissue Doppler Imaging

Sherif F. Nagueh, MD; Issam Mikati, MD; Helen A. Kopenhren, RDMS; Katherine J. Middleton, RCT; Miguel A. Quiñones, MD; William A. Zoghbi, MD

Background—Doppler echocardiography is frequently used to predict filling pressures in normal sinus rhythm, but it is unknown whether it can be applied in sinus tachycardia, with merging of E and A velocities. Tissue Doppler imaging (TDI) can record the mitral annular velocity. The early diastolic velocity (Ea) behaves as a relative load-independent index of left ventricular relaxation, which corrects the influence of relaxation on the transmitral E velocity.

Methods and Results—We evaluated 100 patients 64±12 years old with simultaneous Doppler and invasive hemodynamics. Mitral inflow was classified into 3 patterns: complete merging of E and A velocities (pattern A), discernible velocities with A dominance (B), or E dominance (C). The Doppler data were analyzed at the mitral valve tips for E, acceleration and deceleration times of E, and isovolumic relaxation time. In patterns B and C, the A velocity, E/A ratio, and atrial filling fraction were derived. Pulmonary venous flow velocities were also measured, and TDI was used to acquire Ea and Aa. Weak significant relations were observed between pulmonary capillary wedge pressure (PCWP) and sole parameters of mitral flow, pulmonary venous flow, and annular measurements. These were better for patterns A and C. E/Ea ratio had the strongest relation to PCWP [r=0.86, PCWP=1.55+1.47(E/Ea)], irrespective of the pattern and ejection fraction. This equation was tested prospectively in 20 patients with sinus tachycardia. A strong relation was observed between catheter and Doppler PCWP (r=0.91), with a mean difference of 0.4±2.8 mm Hg.

Conclusions—The ratio of transmitral E velocity to Ea can be used to estimate PCWP with reasonable accuracy in sinus tachycardia, even with complete merging of E and A velocities. (Circulation. 1998;98:1644-1650.)

Key Words: tachycardia ■ diastole ■ pressure ■ echocardiography

The determination of ventricular function and filling pressures is important in patients with sinus tachycardia (ST) of various causes. Although invasive assessment is possible, it carries a certain risk and takes longer than noninvasive assessment by echocardiography. Doppler was successfully applied to estimate filling pressures in normal sinus rhythm1–4 and recently in atrial fibrillation.9,10 It is unknown whether it can be of value in ST because of the merging of mitral E and A velocities to various degrees. Furthermore, the utility of pulmonary venous flow is unknown, given the difficulty of its acquisition in the intensive care unit with transthoracic imaging.5

Tissue Doppler imaging (TDI) allows the recording of myocardial contraction and relaxation velocities.11–17 Compared with mitral inflow velocity, the early diastolic velocity at the mitral annulus (Ea) is less influenced by left atrial pressure.17 The ratio E/Ea can correct for the influence of relaxation on transmitral E and relates strongly to filling pressures.17 Whether the use of TDI will be helpful in ST is unknown. This investigation was undertaken to evaluate the role of conventional Doppler and TDI in the estimation of filling pressures in ST.

Methods

Patient Population
Patients with ST undergoing right heart catheterization at the Methodist Hospital (Houston, Tex) were screened. Patients with a heart rate ≥100 bpm and partial or complete merging of mitral E and A velocities were eligible. Those with mitral stenosis, prosthetic mitral valves (n=5), inadequate pressure tracings (n=3), poor echocardiographic windows (n=3), or atrial fibrillation (n=7) were excluded. Accordingly, 100 patients with ST (age, 64±12 years [range, 27 to 86 years]; 60 men; 31 on mechanical ventilation; Table 1) undergoing right heart catheterization in the intensive care unit (n=70) or catheterization laboratory (n=30) were consecutively enrolled. All patients (or next of kin) gave informed consent before participation.

Echocardiographic Studies
All patients, while in a supine position, had simultaneous right heart catheterization with echo-Doppler studies using an Acuson XP-128 equipped with a multifrequency transducer and the TDI program. Two-dimensional imaging was performed, followed by Doppler. For
Echocardiographic Analysis

A single investigator blinded to all data performed the analysis using an off-line station (Digisonics EC 500). Left ventricular ejection fraction (LVEF) was calculated with the multiple-diameter method. Doppler measurements were averaged over 5 consecutive cycles. Three inflow patterns were noted (Figure 1). Patients with pattern A exhibited a single waveform, with complete merging of E and A velocities. The A pattern was further divided into 2 categories: 1 with the velocity peaking in the first half of the diastolic filling period (A₁) and the other peaking in the second half (A₂). In patterns B and C, the E and A velocities could be identified. In B, the E velocity was lower than the A velocity, and the reverse was present in pattern C. The following Doppler parameters were measured in all patterns: peak E velocity, E/A, early diastolic (Eₐ) and late diastolic (Aₐ) velocities, and Eₐ/Aₐ ratio. The AT of E, and DT of E and A velocities.

Hemodynamic Measurements

Mean right atrial pressure, pulmonary artery pressure, and pulmonary capillary wedge pressure (PCWP) were measured with a pulmonary artery catheter. The wedge position was verified by changes in the waveform and when needed, with O₂ saturation (>95%). In the catheterization laboratory, fluoroscopy was also used. An investigator unaware of the echocardiographic data acquired the pressure measurements. All were an average of 5 cycles at end-expiratory apnea. Fluid-filled transducers were balanced before the study with the zero level at the midaxillary line. Cardiac output (average of 3 cycles with <10% variation) was derived by thermodilution.

Statistical Analysis

Continuous variables are presented as mean±SD. The χ² and the Fisher exact tests were used to compare the frequency of mean PCWP >12 mm Hg among the inflow patterns. ANOVA was used to compare LVEF, PR interval, and heart rate among the 3 patterns. Bonferroni correction was then applied for multiple comparisons. Linear regression analysis was used to correlate Doppler parameters, patterns, LVEF, heart rate, TDI velocities, and ratios to mean PCWP. Stepwise regression analysis was subsequently performed. On further analysis of the relation between PCWP and E/Eₐ, the 120 patients were divided into 2 groups: patients with E/Eₐ $\geq$ 3 and those with E/Eₐ < 3. Significance was set at P≤0.05.

Results

Doppler Patterns, Parameters, and Feasibility in ST

Hemodynamic data are presented in Table 2. Thirty-five patients had the A, 37 the B, and 28 the C pattern. Heart rate was similar among the 3 patterns (111±4 bpm in A, 112±7 bpm in B, and 110±6 bpm in C, P=0.37), as was IVRT. The PR interval, however, was longer with the A pattern (178±22 ms in A, 125±18 ms in B, and 131±25 ms in C, P<0.001). Recording of pulmonary venous flow was feasible in 38 patients (38%), with a higher success rate in the catheterization laboratory than in the intensive care units (60% versus 29%). By comparison, TDI acquisition of Eₐ and Aₐ was successful in all 100 patients. Distinct Eₐ and Aₐ velocities were recorded in all patients with patterns B and C and in 10 patients (29%) with pattern A.

Extrapolation of the peak E velocity to the baseline. In patterns B and C, this measurement was made if the E velocity decreased by $\geq$30% of its peak value before onset of the A wave. DT of the A wave was measured by linear extrapolation of peak A velocity to baseline. The atrial filling fraction and IVRT were obtained as previously described. To account for the influence of heart rate on A velocity in patterns B and C, a corrected A velocity was derived as peak A minus mitral velocity at onset of A. The square root of the RR interval was used to correct for the influence of heart rate on IVRT, AT of E, and DT of E and A velocities.

Pulmonary venous flow was analyzed for the peak velocity and time velocity integral of systolic (TVIₚ), diastolic (TVIₙ), and atrial reversal waves. The end of the T wave marked the end-systolic velocity. The ratio of the peak systolic to peak diastolic velocity and respective time velocity integrals were calculated. Systolic filling fraction was derived as SFF = TVIₛ/(TVIₛ+TVIₙ). The following measurements were made from the mitral annular velocity by TDI: early diastolic (Eₐ) and late diastolic (Aₐ) velocities and Eₐ/Aₐ ratio. With complete merging of Eₐ and Aₐ, the resulting velocity was taken as Eₐ.

Statistical Analysis

Continuous variables are presented as mean±SD. The χ² and the Fisher exact tests were used to compare the frequency of mean PCWP >12 mm Hg among the inflow patterns. ANOVA was used to compare LVEF, PR interval, and heart rate among the 3 patterns. Bonferroni correction was then applied for multiple comparisons. Linear regression analysis was used to correlate Doppler parameters, patterns, LVEF, heart rate, TDI velocities, and ratios to mean PCWP. Stepwise regression analysis was subsequently performed. On further analysis of the relation between PCWP and E/Eₐ, the 120 patients were divided into 2 groups: patients with E/Eₐ ≥ 3 and those with E/Eₐ < 3. Significance was set at P≤0.05.
Relation of Doppler Patterns and Parameters to PCWP

Pattern B was more frequently associated with a normal PCWP, whereas the A and C patterns were more frequent with elevated PCWP (*P=0.04 for A versus B and C versus B, Table 3). No significant difference in the prevalence of mean PCWP >12 mm Hg was seen between the A and C patterns. Within the A group, elevated PCWP was more prevalent in A1 than in A2 (*P=0.001). A significant overlap existed, however, among the patterns in the distinction of normal versus elevated PCWP.

Weak relations were present between the transmitral flow parameters and PCWP (Table 4). The DT of E velocity could be measured in 90 patients (90%) and atrial filling fraction in 100 patients (100% of B and C). No significant relations with PCWP were observed for A velocity, E at onset of A, corrected A velocity, or the ratio of E to corrected A velocity (*P=0.23, *P<0.001; AT, *P=0.14). Similarly, correction for the effect of heart rate did not improve the correlation of the time intervals with PCWP (DT of E, *P=0.37; DT of A, *P=0.4; AT, *P=0.4; and IVRT, *P=0.5). The PR interval had no significant relation with the DT of A velocity (*P=0.1, *P>0.2). In patients with satisfactory pulmonary venous flow recordings, SFF had the best correlation with PCWP (*P=0.53, *P=0.09). PCWP related weakly to Ea and Aa. However, the strongest relation

<table>
<thead>
<tr>
<th>Mitral Inflow Pattern</th>
<th>PCWP ≤12 mm Hg, n (%)</th>
<th>PCWP &gt;12 mm Hg, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pattern A</td>
<td>8 (24)</td>
<td>27 (40)</td>
</tr>
<tr>
<td>A1</td>
<td>2 (6)†</td>
<td>24 (36)†</td>
</tr>
<tr>
<td>A2</td>
<td>6 (18)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Pattern B</td>
<td>19 (58)*</td>
<td>18 (27)*</td>
</tr>
<tr>
<td>Pattern C</td>
<td>6 (18)</td>
<td>22 (33)</td>
</tr>
<tr>
<td>Total</td>
<td>33 (100)</td>
<td>67 (100)</td>
</tr>
</tbody>
</table>

*P<0.05 vs each of A and C.
†P<0.01 vs A2.

Effect of Inflow Pattern and Ejection Fraction on the Relationship of Doppler Parameters to Mean PCWP

Significant weak relations were noted between the transmitral flow variables and PCWP in all 3 patterns (Table 5). Overall, relations were worse for pattern B. LVEF was higher in pattern B (51±15% versus 36±16% and 39±15% for A and C, respectively; *P<0.001), which may explain in part the weaker relations in this group, as recently noted.

The E/Ea ratio had a good relation to PCWP, irrespective of the inflow pattern (Figure 3), even in the 25 patients with complete merging of E and Aa (*P=0.87, *P<0.001; PCWP, 7 to 28 mm Hg). Although transmitral variables had stronger relations with PCWP in patients with LVEF <45% (n=51, Table 6), E/Ea performed reasonably well in both groups.

**Table 3. Distribution of Mitral Inflow Patterns in Relation to PCWP in the Initial Population**

<table>
<thead>
<tr>
<th>Mitral Inflow Pattern</th>
<th>PCWP ≤12 mm Hg, n (%)</th>
<th>PCWP &gt;12 mm Hg, n (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

**Table 4. Correlation Between PCWP and Doppler Parameters in the Initial Group**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>0.86</td>
</tr>
<tr>
<td>DT of E</td>
<td>-0.36*</td>
</tr>
<tr>
<td>DT of A</td>
<td>-0.45†</td>
</tr>
<tr>
<td>E/A</td>
<td>0.40*</td>
</tr>
<tr>
<td>AFF</td>
<td>-0.4†</td>
</tr>
<tr>
<td>IVRT</td>
<td>-0.52*</td>
</tr>
<tr>
<td>TVI/TVIa</td>
<td>-0.41†</td>
</tr>
<tr>
<td>SFF</td>
<td>-0.53†</td>
</tr>
<tr>
<td>PSV</td>
<td>-0.41†</td>
</tr>
<tr>
<td>Ea</td>
<td>-0.37*</td>
</tr>
<tr>
<td>Aa</td>
<td>-0.28†</td>
</tr>
<tr>
<td>E/Ea</td>
<td>0.86*</td>
</tr>
</tbody>
</table>

E indicates peak early diastolic velocity; A, peak late diastolic velocity; TVI/TVIa, ratio of time velocity integral of systolic to diastolic wave; and PSV, peak velocity of systolic flow.

*P<0.001; †P<0.05.
The correlation remained strong in patients with LVEF \( \leq 30\% \) (n = 28, \( r = 0.88, P < 0.001 \)). Stepwise regression analysis revealed no increment in predicting filling pressures with inflow pattern or LVEF once E/Ea was introduced in the regression model.

**Prediction of Mean PCWP Prospectively**

The equation derived initially \([\text{PCWP} = 1.55 + 1.47(\text{E/Ea})]\) was tested prospectively in a separate population for the prediction of PCWP. Of 25 patients screened, 2 with atrial fibrillation and 3 with prosthetic mitral valves were excluded. Thus, 20 patients were included (age, 69 ± 8 years; 14 men; EF, 55 ± 15%). Tables 1 and 2 provide their clinical diagnoses and hemodynamics. Seven had the A pattern, 9 the B, and 4 the C. Mean PCWP related well with E/Ea \((R^2 = 0.83; \text{mean difference}, -0.4 \pm 2.8 \text{ mm Hg [range, } -5 \text{ to } 6]\) between Doppler and catheter PCWP). Figure 5 shows this relation in the prospective and total populations. The mean difference between Doppler and catheter PCWPs in the 120 patients was 0 ± 3.7 mm Hg (Figure 6).

The sensitivity and specificity of Doppler parameters for PCWP \( > 12 \text{ mm Hg} \) are shown in Table 7 (n = 120). With a receiver operator curve, E/Ea ratio \( > 10 \) had the best performance, with a sensitivity of 78\% and specificity of 95\%. A ratio \( > 8 \) had a higher sensitivity of 87\% (specificity, 70\%), whereas a ratio of 12 had a higher specificity, 96\% (sensitivity, 68\%). An E/Ea ratio \( > 10 \) had the highest sensitivity (85\%) and specificity (93\%) for detecting PCWP \( > 15 \text{ mm Hg} \).

**Reproducibility**

Ten studies were chosen at random and analyzed by another investigator and by the same investigator at a later time. The mean intraobserver and interobserver differences (mean ± SD) for E/Ea were \(-0.46 ± 1.3 \) (−2 to 0.75) and \(0 ± 1.9 \) (−2 to 1.5), respectively. The corresponding differences for the Doppler PCWP were \(-0.7 ± 1.9 \) (−4 to 1) mm Hg and \(0 ± 2 \) (−2 to 2) mm Hg, respectively.
**Discussion**

This is the first investigation to examine the utility of conventional Doppler and TDI velocities in the estimation of PCWP in ST, a clinical condition that challenges this methodology. Of the 3 inflow patterns, the A1 and C were most predictive of high filling pressures. Weak significant relations were noted for individual mitral and pulmonary venous flow and TDI variables. The strongest relation with PCWP was observed with E/Ea, which corrects for the influence of myocardial relaxation on the mitral E velocity. This relation remained strong irrespective of the inflow pattern and LVEF and performed equally well in a prospective population.

Transmitral Flow and Estimation of PCWP

Various degrees of merging of mitral E and A velocities occur during ST secondary to shortening of the diastolic filling period, adding complexity to the evaluation of filling dynamics and pressure. In this study, we have shown that for comparable heart rates, the degree of merging is determined in part by the PR interval, such that patients with a longer PR interval are more likely to have complete merging. We observed 3 inflow patterns. Patients with accelerated early filling (A1 and C) in ST, similar to normal sinus rhythm, were more likely to have elevated PCWP (83%). However, 44% of the patients with slow early filling (A2 and B) had elevated PCWP. The relations of all mitral inflow parameters to mean PCWP were also weaker in pattern B. This may be due in part to the stronger influence of impaired relaxation on the E velocity despite an elevated PCWP. With shortening of diastole due to tachycardia, the slow relaxation leaves these patients with a prolonged IVRT and thus an abbreviated filling time. Accordingly, although an impaired relaxation pattern in normal sinus rhythm usually denotes normal PCWP, this is not the case in ST, analogous to the recent report in hypertrophic cardiomyopathy.

Because heart rate influences the A velocity, we attempted to correct for the influence of atrial preload by using the mitral velocity at onset of A. The results were worse than with the conventional A velocity and E/A ratio. Peak E velocity and IVRT related best, but nevertheless weakly, with...
filling pressure. When these relations were further examined according to LVEF, much better correlations were identified in patients with depressed EF, similar to normal sinus rhythm and atrial fibrillation, further emphasizing the limitations of simple mitral inflow in the evaluation of filling pressures in patients with normal systolic function.

**Pulmonary Venous Flow**
The low yield of adequate pulmonary venous flow (38%) in this study is similar to our earlier observations with transthoracic echocardiography in the intensive care unit and is much lower than in ambulatory patients. This resulted from the inclusion of heavily instrumented patients and the high-frequency interference commonly present in the intensive care unit. Despite the small number analyzed, significant relations were present with PCWP, were best for SFF, and were directionally similar to patients in sinus rhythm. In our experience, the majority of ambulatory patients evaluated with echocardiography have normal heart rates, whereas critically ill patients in the intensive care units are usually tachycardic. Thus, the difficulty of acquisition of pulmonary venous flow in this study is a limitation for its use in several patients with ST.

**Tissue Doppler Imaging**
We observed weak but significant inverse relations between E, A, and PCWP. For E, this is probably related to the compensatory increase in left atrial pressure with impaired relaxation. For A, which reflects annular motion secondary to atrial contraction, a negative relation to filling pressures is expected, similar to the inverse relation of the transmitral A velocity to PCWP in sinus rhythm. E behaves as an index of LV relaxation that is reduced with impaired relaxation and is less influenced by left atrial pressure. Sohn et al demonstrated changes in the transmitral E velocity and DT with saline infusion and nitroglycerin, without a significant change in the E velocity at the septal corner of the mitral annulus. As such, E can partially correct for the influence of relaxation on the transmitral E velocity, as recently shown in our laboratory. The concept of correcting for the relaxation influence on transmitral E using E is similar to the approach with the color M-mode flow propagation velocity, reported in sinus rhythm and atrial fibrillation.

In this investigation, the E/E ratio provided the best index for the prediction of PCWP, irrespective of the filling pattern. Importantly, E/E performed well in patients with normal LVEF, the most problematic group for conventional Doppler. Furthermore, in patients with complete merging of E and A, E/E also performed well, highlighting the important role of TDI-derived velocities in ST. The equations we derived previously in patients with sinus rhythm (PCWP = 1.9 + 1.24 E/E) and with heart transplants (PCWP = 2.6 + 1.46 E/E) are very similar to the one derived in this study, further demonstrating the validity of this new approach in the estimation of filling pressures. In fact, the relation of E/E to PCWP was maintained if our initial 60 patients in normal sinus rhythm were combined with the 120 patients in ST (r = 0.87, Figure 7). There were minor differences between the equations derived for these 2 separate populations, and the addition of heart rate did not add to the predictive power of E/E in the stepwise regression analysis. Although the use of the specific equations may yield slightly more accurate prediction of PCWP, particularly for very high filling pressures, the unifying equation $PCWP = 2 + 1.3 E/E$ (180 patients combined) can be used for practical purposes in sinus rhythm, irrespective of heart rate. The sensitivity and specificity of different E/E values in predicting PCWP > 15 mm Hg (n = 180) are shown in Table 8. The best cutoff remains E/E > 10 (sensitivity, 92%; specificity, 80%).

**TABLE 7. Sensitivity and Specificity of Selected Doppler Parameters for PCWP > 12 mm Hg in ST**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, C patterns</td>
<td>68</td>
<td>73</td>
</tr>
<tr>
<td>E/A &gt; 1</td>
<td>48</td>
<td>77</td>
</tr>
<tr>
<td>IVRT ≤ 70 ms</td>
<td>59</td>
<td>79</td>
</tr>
<tr>
<td>DT of E ≤ 150 ms</td>
<td>74</td>
<td>40</td>
</tr>
<tr>
<td>SFF ≤ 0.4</td>
<td>67</td>
<td>88</td>
</tr>
<tr>
<td>E/Ea &gt; 10</td>
<td>78</td>
<td>95</td>
</tr>
</tbody>
</table>

Abbreviations as in other tables.

Figure 6. Bland-Altman plot of Doppler and catheter PCWP in total population with ST.

Figure 7. Plot of PCWP by catheter vs E/Ea in 180 patients combined: 60 with normal sinus rhythm and 120 with ST.
TABLE 8. Sensitivity and Specificity of Various E/Ea Cutoffs for PCWP >15 mm Hg in the 180 Patients Combined: Normal Sinus Rhythm\(^7\) (n=60) and ST (n=120)

<table>
<thead>
<tr>
<th>E/Ea</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;8</td>
<td>99</td>
<td>58</td>
</tr>
<tr>
<td>&gt;10</td>
<td>92</td>
<td>80</td>
</tr>
<tr>
<td>&gt;12</td>
<td>74</td>
<td>92</td>
</tr>
<tr>
<td>&gt;15</td>
<td>46</td>
<td>100</td>
</tr>
</tbody>
</table>

Limitations

We have few patients with the A\(_2\) subpattern. Our observations in this subgroup need further evaluation. We used the single annular velocity in lieu of the E\(_r\), with merging of E\(_r\) and A\(_r\). Although this may not always have been the true E\(_r\), when the data were analyzed for this group of patients, the correlation was as strong as that in patients with separate E\(_r\) and A\(_r\). We could not completely evaluate the utility of pulmonary venous flow in ST because of the low feasibility given the supine position of all our patients. It is important to note that, although E/E\(_a\) provided a reasonable estimate of PCWP, the 95% confidence limits are wide and should be considered in application of the regression equation. It is thus possible that, depending on the clinical setting and the estimated PCWP, one may need invasive measurements. However, for a Doppler estimate of PCWP \(\geq 22\) mm Hg, there is 95% certainty that the actual pressure is \(\geq 15\) mm Hg; conversely, an estimated pressure \(\leq 8\) mm Hg is indicative of PCWP \(\leq 15\) mm Hg. None of our patients had regional dysfunction at the lateral base. Accordingly, we cannot address the utility of TDI velocities at the lateral annular corner in patients with lateral wall abnormalities. Fortunately, this is an uncommon clinical occurrence.

Acknowledgments

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References

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