Noninvasive Measurement of Rate of Left Ventricular Relaxation by Doppler Echocardiography
Validation With Simultaneous Cardiac Catheterization

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Background. The instantaneous pressure gradient between the left ventricle and left atrium during systole can be calculated from the mitral regurgitation Doppler velocity curve. The purpose of our study was to determine the accuracy of measuring the time constant of relaxation (TAU) derived from the Doppler mitral regurgitation signal by comparing it with simultaneous high-fidelity left ventricular pressure measurements in humans.

Methods and Results. Twenty-five patients had continuous-wave Doppler mitral regurgitation recordings performed with simultaneous high-fidelity left ventricular pressure measurements. Fifteen of these patients had measurements of six to eight beats at various RR intervals. Doppler velocity curves were converted to left ventricular pressure curves by different methods through application of the modified Bernoulli equation at 3-msec intervals. The correlation between catheter-derived and Doppler-derived TAU was best when a zero asymptote and knowledge of the left ventricular end-diastolic pressure were used. A less optimal but acceptable method used the addition of 20 mm Hg to the Doppler-derived ventriculoatrial gradient. Use of a nonzero asymptote for calculation of TAU yielded poor correlation between catheter and Doppler measurements. The correlation of percentage change in Doppler-derived TAU plotted against percentage change in catheter-derived TAU was poor.

Conclusions. The descending limb of the Doppler-derived mitral regurgitation velocity signal can be used as a semiquantitative estimate of the rate of ventricular relaxation. This method requires knowledge of left atrial pressure and may not be sufficiently accurate for detecting small changes in the rate of relaxation on a beat-to-beat basis. (Circulation 1993;88:146-155)

KEY WORDS • Doppler echocardiography • mitral regurgitation • time constant of relaxation • ventricular relaxation

In heart muscle disease, abnormalities of diastolic function play a major role in producing the signs and symptoms of heart failure.1,2 Because of the complex sequence of interrelated events that constitute diastolic filling of the heart, it has been difficult to detect and to measure abnormalities of diastolic function in clinical practice.1,2 Although global filling patterns can now be assessed noninvasively with radionuclide angiography3,4 and Doppler echocardiography,5,6 a more detailed evaluation of the individual events has been possible only with invasive, sophisticated techniques that measure such variables as wall stress and wall strain.7,8 One of these events is the rate of left ventricular relaxation, in which various monoexponential or biexponential equations are fitted to the decrease in left ventricular pressure that occurs during isovolumic relaxation, i.e., the method for determining the time constant of relaxation (TAU).7 There are many limitations inherent in this measurement,7,8 but the measurement of TAU remains the most accepted method for determining the rate of left ventricular relaxation in humans. The widespread use of the measurement of TAU has been limited because invasive high-fidelity, manometer-tipped catheters are required.

Doppler echocardiography has emerged recently as a powerful noninvasive method for determination of hemodynamics.9 Intracardiac pressures, valve gradients, and volumetric flow can be determined accurately with Doppler echocardiography by measurement of blood flow velocities across valves and through great vessels. In mitral regurgitation, the instantaneous pressure gradient between the left ventricle and the left atrium can be derived by applying the modified Bernoulli equation (pressure gradient=4×[velocity]2) to the mitral regurgitation velocity signal.10 As a measurement of systolic contractility, the rate of increase of left ventricular pressure has been derived from the rate of increase of the velocity of mitral regurgitation. This measurement has been validated in the animal model11 and in humans.12,13 The rate of increase of left ventricular pressure derived from the Doppler mitral regurgitation signal has proved to be clinically important as an

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independent index of systolic contractility in patients with mitral regurgitation before mitral operation.\textsuperscript{13}

It has been proposed that examination of the rate of decrease of the velocity curve of mitral regurgitation may provide insight into the rate of left ventricular relaxation. In the animal model, the rate of decrease in velocity has been correlated with peak negative dP/dt derived from high-fidelity left ventricular pressure measurements.\textsuperscript{11} The actual derivation of TAU from the velocity curve of mitral regurgitation has been demonstrated recently in the animal model.\textsuperscript{14} It is unclear whether the rate of decrease in the velocity curve of mitral regurgitation can be used for measurement of the rate of ventricular relaxation in humans. As opposed to the period of isovolumic contraction, there are unknown variables during isovolumic relaxation that may affect the rate of decrease in the velocity curve of mitral regurgitation, such as changing left atrial pressure and variable pressure at mitral valve opening.

The purpose of our study was to determine the accuracy of measuring TAU derived from the Doppler mitral regurgitation signal by comparing it with high-fidelity pressure measurements made simultaneously.

\textbf{Methods}

\textbf{Patient Population}

The study group consisted of patients referred to the cardiac catheterization laboratory with a diagnosis of mitral regurgitation. All had undergone a comprehensive two-dimensional and Doppler echocardiographic examination, which confirmed there was at least moderate mitral regurgitation.\textsuperscript{9} Immediately before catheterization, interrogation of mitral regurgitation velocity was made with a small, nonimaging, continuous-wave Doppler transducer. Patients were selected for the study if the spectral display of mitral regurgitation showed a sharp, distinct border of the descending limb of the curve. The study was approved by the Mayo Clinic Institutional Review Board, and informed consent was obtained from all the patients.

Twenty-five patients formed the study group: All had mitral regurgitation Doppler signals adequate for analysis. The mean age of these 25 patients was 49 years (range, 22 to 80 years); they had a mean body surface area of 1.9 m\textsuperscript{2} (range, 1.6 to 2.3 m\textsuperscript{2}). The cause of the mitral regurgitation, based on two-dimensional echocardiography, was prolapse in 15 of the patients, rheumatic heart disease in 3, dilated annulus in 5, and ischemic heart disease in 2. The rhythm was normal sinus in 15 patients and atrial fibrillation in 10.

\textbf{Methodology}

All patients were lightly sedated with either intravenously administered diazepam or fentanyl before catheter insertion. An intravenous infusion of dextrose in water was begun at a rate of <10 mL/hr. All patients were heparinized with 2500 U of heparin after femoral arterial puncture. An 8F pigtail or Rodriguez fluid-filled catheter was inserted retrogradely across the aortic valve into the left ventricle and positioned at the base of the heart 2 to 3 cm distal to the mitral valve. A 3F, high-fidelity, manometer-tipped catheter was balanced to atmospheric pressure and then inserted through a hemostasis valve into the lumen of the fluid-filled catheter to its distal end, as previously described.\textsuperscript{15,16} The pressure measurements obtained with the high-fidelity manometer-tipped catheter were calibrated against the pressure measured simultaneously with the fluid-filled catheter at end diastole. Measurements of both the high-fidelity and fluid-filled catheter pressures were made at periodic intervals; no electronic "drift" was present in the pressure tracings obtained with the high-fidelity manometer-tipped catheters. All measurements were made before injection of any contrast material.

Simultaneous Doppler interrogation of the mitral regurgitation velocity jet was made from the apical window in all patients by using a small, nonimaging, continuous-wave transducer (1.8 to 2.5 mHz) with either a Hewlett-Packard or Acuson echocardiographic instrument. Small changes were made in the position and angulation of the Doppler beam until the signal with the cleanest spectral display was obtained. The pressure measurements obtained with the high-fidelity manometer-tipped catheter and the simultaneous Doppler signal were recorded on a hard-copy strip chart at 100 mm/sec (Fig 1).

To examine changes in the rate of left ventricular relaxation in individual patients, 6 to 8 different cardiac cycles were recorded at various RR intervals in 15 of the 25 patients (total, 120 beats). Atrial fibrillation with irregular ventricular response was present in five patients. In the eight other patients, premature ventricular contractions were induced by causing ventricular irritation with a catheter in either the left or right ventricle.

\textbf{Analysis}

Both the left ventricular pressure curve and the simultaneous mitral regurgitation velocity curve were digitized at 3-msec intervals by using an off-line Jandel Scientific Tablet. Five different pressure curves were generated from the Doppler velocities for each baseline cycle from each of the 25 patients. The Doppler velocities at each 3-msec interval (V\textsubscript{n}) were converted to a pressure gradient by using the modified Bernoulli equation (Eq 1). The final pressure at each 3-msec interval (P\textsubscript{n}) was calculated with the following equations.

\begin{equation}
\text{Pn(0)} = 4(V\text{n})^2
\end{equation}

\begin{equation}
\text{Pn(10)} = 4(V\text{n})^2 + 10
\end{equation}

\begin{equation}
\text{Pn(20)} = 4(V\text{n})^2 + 20
\end{equation}

\begin{equation}
\text{Pn(LVEDP)} = 4(V\text{n})^2 + \text{LVEDP}
\end{equation}

\begin{equation}
\text{Pn(VA)} = 4(V\text{n})^2 + VA
\end{equation}

LVEDP equals the left ventricular end-diastolic pressure from the high-fidelity pressure curve measured at the beginning of the rapid rise of left ventricular pressure after the atrial wave (ie, pressure at mitral valve closure). VA is a value calculated to obtain left atrial pressure from the Doppler velocity curve. It was derived by applying the modified Bernoulli equation to the measured peak velocity of the Doppler mitral regurgitation curve (ie, the maximum left ventricular/left atrial gradient during systole). This maximum ventriculatoarial
The high-fidelity pressure was then subtracted from the simultaneous peak left ventricular pressure measured by high-fidelity pressure manometers, resulting in a calculated left atrial pressure. It was possible to derive this calculated left atrial pressure in only 16 patients, because peak systolic velocities on the mitral regurgitation velocity curve could not be measured in the 9 other patients. For the 15 patients in whom 6 to 8 separate cycles at various preceding RR intervals were recorded, \( P_n \) (LVEDP) was calculated from the digitized Doppler velocities for all the cycles (total, 120 cycles).

The data files were transferred to an IBM PC on which a data analysis program was used as described previously.\(^{16} \) Each of the high-fidelity pressure or Doppler-derived pressure contours was analyzed blindly in random order. The following measurements were then obtained: peak positive \( \frac{dP}{dt} \) (+dP/dt), peak negative \( \frac{dP}{dt} \) (−dP/dt), LVEDP, peak systolic blood pressure (SBP), and TAU. TAU (T) was calculated by two methods. The first method was the semilogarithmic model that used a zero asymptote:

\[
P_0 = \frac{P_a}{e^{-t/T}}
\]

where \( P = \) pressure and \( t = \) time. \( P_a \) is equivalent to \( P_t \) (pressure at beginning of isovolumic relaxation) when a true exponential decay is approximated starting at peak \(-dP/dt\) and ending at 5 mm Hg above the LVEDP for the high-fidelity pressure. For the converted pressure curves from the digitized Doppler velocities, the exponential decay was approximated starting at peak \(-dP/dt\) and ending at the time when the Doppler velocity curve reached zero baseline (at mitral valve opening). Five calculations of TAU from the Doppler velocities were performed for each patient: TAU-0, from \( P_n(0) \); TAU-10, from \( P_n(10) \); TAU-20, from \( P_n(20) \); TAU-EDP, from \( P_n(LVEDP) \); and TAU-VA, from \( P_n(VA) \). The \( P_a \) and \( T \) variables were estimated from a linear least squares fit on \( \ln P = -t/T + \ln P_b \).\(^{17} \)

The second method (TAU-NZ)\(^{18} \) allowed the pressure to decay to a nonzero asymptote \( P_b \):

\[
P(t) = P_a e^{-t/T} + P_b
\]

A nonlinear least squares technique\(^{19} \) was used to estimate the parameters \( P_b \) and \( T \). For the high-fidelity pressure curve, the nonlinear least squares fit was begun at peak \(-dP/dt\) and ended at 5 mm Hg above the LVEDP. The nonlinear least squares fit was applied to the converted pressure points of the Doppler velocity curve without an added pressure \( (P_n[0]) \) from peak \(-dP/dt\) to zero baseline.

For determination of intraobserver variability of the measurement technique, one cycle was randomly selected from each of the 15 patients, and a second digitization of the Doppler velocity curve was blindly performed.

The time from 3 m/sec to 1 m/sec was measured directly off the descending limb of the Doppler mitral regurgitation velocity curve \([V_{0\cdots1}]\) (Fig 1).

**Statistical Analysis**

Doppler-derived measurements of the rate of pressure (or velocity) decrease were compared with catheter-derived measurements by linear regression analysis. To examine further the comparison of two methods of clinical measurements (Doppler-derived and pressure-derived TAU), the method of Bland and Altman\(^{20} \) was
TABLE 1. Comparison of Catheter-Derived and Doppler-Derived Variables for 120 Beats in 15 Patients

<table>
<thead>
<tr>
<th>Catheter-derived variables</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDP (mm Hg)</td>
<td>22±10.2</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>132±36.0</td>
</tr>
<tr>
<td>TAU (msec)</td>
<td>58±22.0</td>
</tr>
<tr>
<td>TAU-NZ (msec)</td>
<td>89±68.0</td>
</tr>
</tbody>
</table>

| Doppler-derived variables (msec) |
|-------------------------------|---------|
| TAU-EDP                       | 62±26.0 |
| TAU-VA                        | 75±43.0 |
| TAU-NZ                        | 106±84.0|
| TAU-0                         | 24±6.0  |
| TAU-10                        | 43±12.0 |
| TAU-20                        | 58±18.0 |
| $V_{m-1}$                     | 48±17.0 |

LVEDP, left ventricular end-diastolic pressure; SBP, systolic blood pressure; TAU, time constant of relaxation (zero asymptote); NZ, nonzero asymptote; EDP, end-diastolic pressure; VA, ventriculoatrial; $V_{m-1}$, time interval from $3 \text{ m/sec}$ to $1 \text{ m/sec}$ as measured from the descending limb of the mitral regurgitation Doppler velocity curve. Other variables are defined in the text.

used. The analysis of the change in rate of relaxation in an individual patient was made by comparing the percentage change of the Doppler-derived and the pressure-derived parameters by linear regression. The percentage change was calculated for a given variable $(x)$ by Equation 3:

\[ \% \text{ change} = \frac{x_2 - x_1}{x_1} \]

where $x_1$ is the first beat analyzed (a beat that was either a normal sinus beat or, in patients with atrial fibrillation, the preceding RR interval was approximately the average RR interval) and $x_2$ is the second to eighth beat.

Results

For all 25 patients, the mean±SD for LVEDP, SBP, TAU (using zero asymptote), and TAU-NZ (using nonzero asymptote) measured from the high-fidelity pressure curves are shown in Table 1. The mean±SD for the Doppler measurements of $V_{m-1}$, TAU-0, TAU-10, TAU-20, TAU-EDP, TAU-VA, and TAU-NZ are shown in Table 1.

The relation of each Doppler-derived TAU to the catheter-derived TAU for the 25 patients is outlined in Table 2. Fig 2 illustrates the Doppler-derived and catheter-derived values for TAU when adding a measured variable (EDP) or a calculated variable (VA) to the Doppler-derived pressures. The zero asymptote TAU, derived from addition of the measured LVEDP to the Doppler-derived pressure ($P_n[LVEDP]$), was the method that correlated most closely with the catheter-derived TAU ($r=.84$; standard error of estimate, 15), with a mean difference of catheter-derived minus Doppler-derived TAU of $-4±28 \text{ m/sec}$ (mean±2 SD). Fig 3 illustrates several examples in which $P_n[LVEDP]$ was used to calculate TAU. The zero asymptote TAU derived from the calculated VA gradient from the peak mitral regurgitation velocity ($P_n[VA]$) had a poorer correlation, with a mean difference of catheter-derived minus Doppler-derived TAU of $-15±65 \text{ m/sec}$ (mean±2 SD).

Fig 4 illustrates the relation of the Doppler-derived TAU to the catheter-derived TAU when a fixed left atrial pressure was added to the Doppler-derived pressure ($0 \text{ mm Hg}, 10 \text{ mm Hg}, 20 \text{ mm Hg}$). There was a consistent underestimation of the catheter-derived TAU when 0 and 10 mm Hg were used as the fixed left atrial pressure. The use of 20 mm Hg as the fixed left atrial pressure produced the smallest mean difference of the catheter-derived TAU minus Doppler-derived TAU of $0±34 \text{ m/sec}$ (mean±2 SD) for these three fixed values.

The relation of Doppler-derived TAU to the catheter-derived TAU using a nonzero asymptote is shown in Fig 5. There was no significant correlation seen when using this method for calculation of TAU.

To determine whether a simplified Doppler measurement could be used, the relation of the time interval from $3 \text{ m/sec}$ to $1 \text{ m/sec}$ on the descending limb of the mitral regurgitation velocity curve ($V_{m-1}$) was plotted against the catheter-derived TAU (Fig 6). A direct relation was present but with a wider scatter than with the other methods.

Intraobserver variability was calculated for Doppler-derived TAU. The absolute mean difference between the two measurements was $10.2±7.4 \text{ m/sec}$. The percent difference between the two measurements was $17±7\%$.

Fig 7 illustrates several different beats in the same patient at different loading conditions and at different levels of contractility caused by premature contractions. The Doppler-derived TAU closely followed the catheter-derived TAU on a beat-to-beat basis. However, when the percentage change in Doppler-derived TAU was plotted against the percentage change in catheter-derived TAU for all 15 patients, there was wide scatter (Fig 8).

Discussion

Doppler echocardiography has emerged as a powerful modality for measurement of hemodynamic variables. It is used widely for determining valve gradients, intracardiac pressures, and volumetric flow. Recently, there has been interest in using Doppler echocardiography to evaluate diastolic filling of the heart by examining mitral and tricuspid flow velocities and inflow.
velocities from the pulmonary and caval veins.\textsuperscript{5,6,21} Although these findings have greatly enhanced our understanding of diastolic function, they are only an indirect assessment of overall filling and cannot separate out the various events of diastole, such as relaxation and compliance.

Ventricular relaxation, an important determinant of diastolic function,\textsuperscript{1,2,22} is a complex process that is the result of cessation of the excitation-contraction coupling and the removal of calcium ions by the calcium export mechanism. It is influenced by a triple-control mechanism of decay of active force generation, ventricular load, and nonuniformity\textsuperscript{22} and is a major contributor to the pathophysiology of many myocardial disease states.\textsuperscript{1,2} Previously, measurement of the rate of relaxation was limited to analyzing isovolumic relaxation from pressure recordings obtained with invasive techniques, i.e., high-fidelity manometer-tipped catheters. This precluded its widespread application in clinical practice.\textsuperscript{1,2,7,8}

Abnormalities of relaxation may be recognized indirectly on noninvasive Doppler evaluation by a long isovolumic relaxation time and a low E-to-A ratio, with prolongation of deceleration time on the mitral flow velocity curve.\textsuperscript{21} However, these measurements are influenced by changes in loading conditions of the heart and cannot be used to reliably determine left ventricular relaxation. For example, lowering of preload in a normal heart produces a mitral flow velocity curve similar to that of abnormal relaxation.\textsuperscript{21,23,24} Conversely, prolonged relaxation may be present with a normal mitral velocity curve if there is significant increase in filling pressures.\textsuperscript{21,24,25} A direct measurement of the rate of decrease of left ventricular pressure would provide a valuable addition to evaluation of diastolic filling of the heart.

The application of the modified Bernoulli equation to Doppler velocity curves has been used to measure intracardiac pressures.\textsuperscript{9,10} This has been shown to determine accurately an instantaneous pressure gradient in valvular lesions on both the left and right sides of the heart.\textsuperscript{10,26,27} The mitral regurgitation velocity curves represent the instantaneous pressure gradient between the left ventricle and left atrium during systole.\textsuperscript{10} By converting instantaneous velocities at small intervals to a pressure gradient by the Bernoulli equation, a left ventricular pressure contour can be reconstructed if the left atrial pressure is assumed to be constant.\textsuperscript{10,11} This
tau \textsuperscript{(C)}

\begin{align*}
\text{TAU} & = & \text{tau} \\
\text{TAU} & = & \text{tau} \\
\text{TAU} & = & \text{tau}
\end{align*}

Doppler velocity curve by the zero asymptote method. The best correlation occurred when the actual left atrial V wave pressure was added to the Doppler-derived pressure curve, although the addition of an arbitrary value of 10 mm Hg to the Doppler-derived gradient yielded accurate estimates of TAU in this animal model of mitral regurgitation.

The accuracy of calculating in humans the rates of left ventricular pressure decrease directly from a Doppler mitral regurgitation signal without knowledge of the left atrial pressure or its contour has not been validated previously. Theoretically, the use of the Doppler-derived mitral regurgitation velocity curve for derivation of instantaneous left ventricular pressure might be less accurate during isovolumic relaxation as opposed to the

**Figure 3.** Simultaneous Doppler mitral regurgitation velocity curve and high-fidelity left ventricular pressure curve are shown for three different patients (panels A, B, and C) with the respective calculated time constants of relaxation (TAU). TAU (C), TAU derived from catheter pressure curve; TAU (D), TAU derived from digitized Doppler velocity curve using the final pressure of left ventricular end-diastolic pressure. Pressure calibrations in millimeters of mercury are shown at the left of each panel; Doppler velocity calibrations are shown in meters per second.
isovolumic contraction period because left atrial pressure is not constant during the former time period. The height of the V wave varies significantly from patient to patient as well as in an individual patient under differing loading conditions.

The results of our study provide insight into using Doppler mitral regurgitation velocity curves as a measure of ventricular relaxation in humans. Several methods have been proposed for calculating TAU from high-fidelity pressure measurements.8,17-19,28 Two of the accepted methods include the use of a monoeponential fit to the decrease in pressure during isovolumic relaxation to either an arbitrary asymptote (nonzero) or a zero asymptote. Because the use of a zero asymptote requires knowledge of the absolute left ventricular pressure, a nonzero asymptote TAU would be ideal when using Doppler-derived data.18 However, the calculation of a nonzero asymptote TAU has significant variability when applied to high-fidelity pressure curves.29 As shown in our study, the variability produced an unacceptable error in the calculation of TAU from the mitral regurgitation Doppler velocity curve even when applying a nonlinear least squares fit.19

The optimal method for calculation of TAU from the mitral regurgitation Doppler velocity curve would be to use the ventriculotropic pressure gradients derived from the modified Bernoulli equation added to the pressure at mitral valve opening and applied to the zero asymptote method. Because a direct measurement of the pressure at mitral valve opening was not available, the measured LVEDP (ie, pressure at mitral valve closure) was added to the ventriculotropic pressure gradient from the Doppler mitral regurgitation velocity curves to reconstruct the left ventricular pressure curve beginning at the onset of systole. This resulted in a measurement of TAU that correlated reasonably well with TAU from the simultaneous high-fidelity pressure curves and produced the best correlation of all methods examined in this study. This correlation was not as close as has been shown for measurement of +dP/dt,11-13,15 which may be

**Figure 4.** The relation of Doppler-derived time constant of relaxation (TAU) to catheter-derived TAU when a fixed left atrial pressure is added to the Doppler-derived ventriculotropic pressure gradient. Panel A: Scattergram demonstrating the relation of catheter-derived TAU to Doppler-derived TAU at three different assumed left atrial pressures: 0 mm Hg (4v^2), 10 mm Hg (4v^2+10), and 20 mm Hg (4v^2+20). Panel B: Mean vs the difference between catheter-derived TAU and Doppler-derived TAU when using the uncorrected ventriculotropic pressure gradient. Panel C: Mean vs the difference between catheter-derived TAU and Doppler-derived TAU when adding a constant of 10 mm Hg to the derived ventriculotropic pressure gradient. Panel D: Difference of the correlation of the mean vs the difference between catheter-derived TAU and Doppler-derived TAU when using a constant of 20 mm Hg added to the calculated ventriculotropic pressure gradient. In panels B, C, and D, solid line is mean difference; dashed lines are 2 SD of mean difference.
related to a changing left atrial pressure during isovolumic relaxation as well as to the unknown difference between the pressure at mitral valve closure and the pressure at mitral valve opening. In addition, the calculation of TAU by this method requires knowledge of the absolute left ventricular pressure as opposed to the measurement of +dP/dt, which examines relative rate of change of left ventricular pressure.

The use of an uncorrected ventriculoatrial gradient derived from the mitral regurgitation velocity curve led to a gross underestimation of TAU, as shown previously in the animal model. However, addition of an arbitrary value of 10 mm Hg to the ventriculoatrial gradient, which produced accurate estimates of TAU in the animal model, yielded consistent underestimation of TAU in our study. It was the addition of 20 mm Hg to the ventriculoatrial gradient that produced a closer estimation of TAU than 0 or 10 mm Hg in our study, although there was wider scatter than when the actual measured LVEDP was used. These findings support the concept that even minor shifts of the pressure curve in respect to the zero line substantially alter the measurement of TAU.

The use of a left atrial pressure calculated from the difference between the maximum mitral regurgitation systolic velocity and the SBP failed to produce an acceptable method for calculation of TAU. Although this velocity can accurately determine the maximum ventriculoatrial gradient at peak systole, there may be a significant difference between left atrial pressure at the time of the maximum ventriculoatrial gradient and that at mitral valve opening. Also, the actual measured left ventricular systolic pressure was used in our study; thus, further errors would be present if a blood pressure measured by sphygmomanometer was used as a noninvasive parameter that may not reflect central aortic pressure. It also appears that a simple measurement of the time interval from 3 m/ sec to 1 m/ sec directly from the velocity curve does not accurately reflect TAU. Digitization of the entire downslope of the mitral regurgitation velocity curve is required for measuring left ventricular relaxation.

Even with the use of a measured LVEDP, the accuracy of the Doppler-derived TAU may not be sufficient to allow determination of small changes in individual patients. This inability to determine changes accurately on a beat-to-beat basis may be due partly to differences between left atrial pressure at end diastole and pressure at mitral valve opening.

There are limitations to our study. Only patients with chronic mitral regurgitation were included in our study, and the same analysis may not be applicable to patients with more acute onset of mitral regurgitation and differing left atrial compliance. Patients without adequate delineation of the mitral velocity curves cannot be analyzed. This was the case for 60% of patients who were considered to be candidates for the study.

Finally, there is still controversy about the optimal method for calculation of TAU. Disadvantages may be associated with the use of a mathematical description of the rate of decline in pressure to assess myocardial relaxation. The decrease in pressure does not always fit a monoeponential fit, and it does not take into account the time of onset of relaxation. Also, the zero asymptote method used in our study is based on a nonphysiological factor, that is, the assumption that left ventricular pressure will approach 0 mm Hg. Because TAU is calculated by using left ventricular cavity pressure and not transmural pressure, this parameter is altered by changes in pericardial pressure when myocardial relaxation remains unchanged. Although the nonzero asymptote method may overcome this problem, it could not be applied to the Doppler velocity signal as demonstrated herein. The definition of isovolumic relaxation (peak -dP/dt to 5 mm Hg above left
Simultaneous Doppler mitral regurgitation velocity curve and high-fidelity left ventricular pressure curve from (panel A) a patient in whom premature ventricular contractions had been induced and (panel B) in a patient in atrial fibrillation. There are a range of RR intervals and a range of time constants of relaxation (Tau) in each patient. Doppler-derived Tau (D) (using final pressure of left ventricular end-diastolic pressure) follows closely catheter-derived Tau (C) on a beat-to-beat basis. Tau is shown in milliseconds.

ventricular end-diastolic pressure) may not accurately define the true isovolumic relaxation period. In patients with mitral regurgitation, the measurement period is not truly isovolumic. Nonetheless, the method of calculating Tau used in this study has been well accepted for describing left ventricular relaxation in humans.

In summary, with the use of a hand digitization process, the descending limb of the Doppler-derived mitral regurgitation velocity signal can be used as a semiquantitative estimate of the rate of ventricular relaxation. By using a zero asymptote, Tau can be derived from the Doppler velocities, but it does require direct measurement of left atrial pressure. Additional studies are required to determine whether this method is feasible using noninvasive estimates of left atrial pressure calculated from Doppler interrogation of mitral and pulmonary venous inflow.24,32-34 The addition of

![Graph](http://circ.ahajournals.org/)

**FIG 8.** Percentage change in Doppler-derived time constant of relaxation (TAU) is plotted against the percentage change in catheter-derived TAU (pressure). The final pressure of left ventricular end-diastolic pressure and zero asymptote method are used for Doppler-derived TAU.
the value 20 mm Hg to the Doppler ventriculoatrial gradient produces a less optimal but acceptable method for calculation of TAU. This method may not be sufficiently accurate for detecting small changes in the rate of relaxation on a beat-to-beat basis in individual patients. Future investigations examining a large number of patients noninvasively with this technique are needed to determine the clinical usefulness of measuring TAU.

References


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