Noninvasive Estimation of the Instantaneous First Derivative of Left Ventricular Pressure Using Continuous-Wave Doppler Echocardiography

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Background. The complete continuous-wave Doppler mitral regurgitant velocity curve should allow reconstruction of the ventriculoatrial (VA) pressure gradient from mitral valve closure to opening, including left ventricular (LV) isovolumic contraction, ejection, and isovolumic relaxation. Assuming that the left atrial pressure fluctuation is relatively minor in comparison with the corresponding LV pressure changes during systole, the first derivative of the Doppler-derived VA pressure gradient curve (Doppler dP/dt) might be used to estimate the LV dP/dt curve, previously measurable only at catheterization (catheter dP/dt).

Methods and Results. This hypothesis was examined in an in vivo mitral regurgitant model during 30 hemodynamic stages in eight dogs. Contractility and relaxation were altered by inotropic stimulation and hypothermia. The Doppler mitral regurgitant velocity spectrum was recorded along with simultaneously acquired micromanometer LV and left atrial pressures. The regurgitant velocity profiles were digitized and converted to VA pressure gradient curves using the simplified Bernoulli equation. The instantaneous dP/dt of the VA pressure gradient curve was then derived. The instantaneous Doppler-derived VA pressure gradients, instantaneous Doppler dP/dt, dP/dtmax, and −dP/dtmax were compared with corresponding catheter measurements. This method of estimating dP/dtmax from the instantaneous dP/dt curve was also compared with a previously proposed Doppler method of estimating dP/dtmax using the Doppler-derived mean rate of LV pressure rise over the time period between velocities of 1 and 3 m/sec on the ascending slope of the Doppler velocity spectrum. Both instantaneous Doppler-derived VA pressure gradients (r=0.95, p<0.0001) and Doppler dP/dt (r=0.92, p<0.0001) correlated well with corresponding measurements by catheter during systolic contraction and isovolumic relaxation (pooled data). The Doppler dP/dtmax (1,266±701 mm Hg/sec) also correlated well (r=0.94) with the catheter dP/dtmax (1,200±573 mm Hg/sec). There was no difference between the two methods for measurement of dP/dtmax (p=NS). Although Doppler −dP/dtmax was slightly lower than the catheter measurement (961±511 versus 1,057±540 mm Hg/sec, p<0.01), the correlation between measurements by Doppler and catheter was excellent (r=0.93, p<0.0001). The alternative method of mean isovolumic pressure rise (896±465 mm Hg/sec) underestimated the catheter dP/dtmax (1,200±573 mm Hg/sec) significantly (on average, 25%; p<0.001).

Conclusions. The present study demonstrated an accurate and reliable noninvasive Doppler method for estimating instantaneous LV dP/dt, dP/dtmax, and −dP/dtmax. (Circulation 1991; 83:2101–2110)

The changing rate of left ventricular pressure (dP/dt) during the cardiac cycle is an important parameter in the assessment of myocardial systolic (e.g., dP/dtmax) and diastolic (e.g., −dP/dtmax) function. Conventionally, dP/dt is derived from the left ventricular (LV) pressure curve obtained at cardiac catheterization using micromanometer catheter recording.

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Mitral regurgitation is commonly found in patients with a variety of cardiac conditions.\textsuperscript{2-10} Continuous-wave Doppler echocardiography is able to record the complete velocity spectrum of regurgitant flow through the mitral valve during systole and isovolumic diastole. By using the simplified Bernoulli equation, the continuous-wave Doppler mitral regurgitant velocity curve can be converted to a pressure gradient curve.\textsuperscript{11,12} Therefore, it follows that, by using the complete mitral regurgitant velocity profile during systole and isovolumic relaxation, it should be possible to reconstruct a left ventriculoatrial pressure gradient curve and to derive dP/dt from the reconstructed pressure curve. If the left atrial (LA) pressure were constant during systole, the first derivative of the left ventriculoatrial pressure gradient curve would be identical to that of the LV pressure curve. Unfortunately, there is always a V wave of varying amplitude on the LA pressure tracing during systole. But if the LA pressure fluctuation is relatively minor in comparison with corresponding LV pressure changes during systole, this fluctuation should not result in a significant difference between the first derivative of the left ventriculoatrial pressure gradient curve and that of the LV pressure curve. Under these conditions, we can hypothesize that the Doppler-derived instantaneous dP/dt determined from ventriculoatrial gradients could be used to estimate true LV instantaneous dP/dt. From the Doppler-derived dP/dt curve it should be possible to obtain dP/dt\textsubscript{max} - dP/dt\textsubscript{max}, and other early systolic parameters, such as dP/dt corrected by developed pressure or instantaneous LV pressure.\textsuperscript{1} Thus, noninvasive Doppler assessment of LV dP/dt would be an attractive clinical and research tool.

Recent studies\textsuperscript{2-5} have attempted to assess LV dP/dt\textsubscript{max} noninvasively using Doppler echocardiography. It has been demonstrated that the mean rate of Doppler-derived LV pressure rise (RPR) during early systole (determined by the 1- and 3-m/sec velocity points on the rising segment of the continuous-wave mitral regurgitation velocity curve) correlated well with peak dP/dt obtained from LV pressure curves at catheterization.\textsuperscript{2-5} However, because this method uses an average slope, it may underestimate the true peak dP/dt.

To explore the possibility of noninvasive assessment of instantaneous LV dP/dt by Doppler echocardiography, we conducted an in vivo study using a canine model of mitral regurgitation to examine 1) the accuracy of the pressure gradient curve derived from continuous-wave Doppler mitral regurgitant velocity as compared with micromanometer catheter measurements and 2) the reliability of estimation of the first derivative of the LV pressure curve by the first derivative of the left ventriculoatrial pressure gradient curve using continuous-wave Doppler mitral regurgitant velocity curves.

\textit{Animal Preparation}

The study conformed to the guiding principles of the American Heart Association guidelines for animal research. Eight adult dogs (25–34 kg) were anesthetized with 30 mg/kg i.v. sodium pentobarbital, intubated, and ventilated with a respirator (Harvard Apparatus, South Natick, Mass.). The concentration of inspired oxygen and the ventilation rate were adjusted to keep blood gases within the physiological range.

A left thoracotomy was performed with the dog supine. The pericardium was left open throughout the experiment. The pressure catheters were inserted in the following manner: a micromanometer-tipped catheter (Millar Mikro-tip, Millar Instruments, Houston) and a fluid-filled catheter connected to a pressure transducer (Statham P23DB, Statham Instruments, Oxnard, Calif.) were inserted through the LV apex to record LV pressure. A second micromanometer-tipped catheter was inserted from a pulmonary vein into the LA to record LA pressure. A third micromanometer-tipped catheter was inserted from the internal mammary artery into the aortic root to record aortic pressure.

Great care was taken to ensure the accuracy of the pressure measurements. Fluid-filled transducers were balanced at atmospheric pressure and calibrated against a mercury column. Micromanometer-tipped catheters were calibrated against the zero and mean pressures recorded by the fluid-filled transducers. All pressure measurements and a single electrocardiographic lead were continuously recorded on an eight-channel strip-chart recorder (model 7700, Hewlett-Packard Co., Waltham, Mass.). Paper speed was increased to 100 mm/sec when data for each experimental stage were formally recorded.

The dogs were placed on right heart bypass. All venous return was drained from the superior and inferior vena cavae and coronary sinus. The venous blood was filtered, warmed and oxygenated, and then pumped by calibrated roller pump back into the dog through a wide-bore cannula inserted into the right atrium. With a second calibrated roller pump, blood could also be pumped into or removed from the systemic arterial circuit through cannulas inserted into the femoral arteries. This maneuver allowed LV systolic pressure, used as an index of afterload, to be controlled independent of preload.\textsuperscript{13}

To create mitral regurgitation, a grommet with a 2.8–4.5-mm diameter was inserted into the anterior mitral leaflet. The peak mitral regurgitant flow rate, calculated as the product of effective orifice area and peak velocity, varied from 21.5 to 87.5 ml/sec (41.8±18.2 ml/sec). The effective orifice areas were determined individually in an in vitro model as the ratio of flow rate and peak orifice velocity. For the grommets studied, the coefficient of contraction (ratio of effective to anatomic orifice area) ranged between 0.68 and 0.75.
FIGURE 1. Panel A: Continuous-wave Doppler recordings showing mitral regurgitant velocity spectrum (left). Horizontal white dots represent time scale (time period between two dots = 200 msec); vertical white dots represent velocity amplitude scale (amplitude between two dots = 1 m/sec). Upper right graph shows systolic and isovolumic diastolic left ventriculoatrial pressure gradient curve determined by continuous-wave Doppler mitral regurgitant velocity spectrum using the simplified Bernoulli equation. Lower right graph is $dp/dt$ curve derived from Doppler-determined pressure gradient curve. Panel B: Simultaneous left atrial pressure (LAP) and left ventricular pressure (LVP) recording (left) using a Millar catheter. Upper right graph is systolic and isovolumic diastolic pressure gradient curve determined by simultaneous Millar catheter atrial and ventricular pressure recordings. Lower right graph is $dp/dt$ curve derived from Millar catheter–recorded left ventricular pressure curve.
To simulate chronic mitral regurgitation, the LA was enlarged by attaching a skin graft or prosthesis to the posterior wall of the atrium in five dogs. This allowed a less dramatic elevation in LA pressure during systole, thereby simulating LA pressure fluctuations seen in chronic mitral regurgitation. In two dogs, acute mitral regurgitation was simulated by not surgically enlarging the LA, thereby allowing a more prominent rise (V wave) in LA pressure during systole. In the eighth dog, the LA was not enlarged at the first stage but was enlarged at subsequent stages.

**Experimental Protocol**

In the first phase of the experiment, arterial pressure was altered by manipulating roller pump flow into or out of the femoral artery. By use of this maneuver, systolic arterial pressure ranged from 65 to 145 mm Hg. In the second stage of the experiment, intravenous calcium (1 g) or propranolol (5 mg) was used to alter systolic and diastolic function. Finally, hypothermia was induced by cooling blood through the bypass, thereby allowing more dramatic alterations in diastolic (−dP/dt\text{max}) and systolic (dP/dt\text{max}) function.\(^4\) A total of 30 hemodynamic stages was obtained in the eight dogs. In each experimental stage, the Doppler velocity profile, electrocardiogram, and LA, LV, and aortic pressures were recorded simultaneously.

**Doppler Echocardiography**

For echocardiographic examination, the heart was stabilized in a pericardial cradle. Two-dimensional, continuous-wave color Doppler echocardiographic data were acquired using a Hewlett-Packard 72020 ultrasound imaging system. The mitral regurgitant velocity curves were obtained either using an apical approach (three dogs) or an LA site (five dogs). In each case, the continuous-wave Doppler ultrasound beam was aligned as parallel as possible to the color Doppler mitral regurgitant jets, or if a blind continuous-wave Doppler transducer was used, then the maximal and most clearly delineated velocity envelopes were recorded. All two-dimensional images and Doppler spectral velocity profiles were recorded at a speed of 100 mm/second on \(\frac{1}{2}\)-in. videotape for further analysis.

**Data Analysis**

The continuous-wave Doppler mitral regurgitant profile was traced manually beginning at the initial part of the QRS wave and ending at the zero crossover point and digitized at 5-msec intervals using a Bitpad (Summagraphics Corp., Seymour, Conn.) interfaced with a customized software written for the ASYST programming environment (Macmillan, Inc., New York). The instantaneous pressure drop between the LV and LA was calculated from the modified Bernoulli equation: \(\Delta p = 4v^2\), where \(\Delta p\) is the pressure gradient (in millimeters mercury) and \(v\) is the instantaneous regurgitant jet velocity (in meters per second). The pressure gradient curve was then reconstructed for each traced cardiac beat (Figure 1A). The instantaneous LV dP/dt throughout systole and early diastole (isovolumic relaxation period) was determined from this reconstructed pressure curve by differentiating the data at 5-msec intervals (Figure 1A).\(^1\) dP/dt\text{max} and −dP/dt\text{max} were then obtained. For comparison purposes, RPR in the LV during early systole was also calculated using two points on the initial ascending segment of the continuous-wave mitral regurgitant velocity curve as proposed by Bargiggia et al.\(^2\) The first point was selected at 1 m/sec=4 mm Hg, and the second point was selected at 3 m/sec=36 mm Hg; the time interval

![Figure 2. Graph comparing Doppler-derived left ventriculo-atrial pressure gradient curve (CW Doppler) with gradient curve derived from Millar catheter-recorded simultaneous left atrial and ventricular pressures.](http://circ.ahajournals.org/)

![Pressure gradients (mmHg) vs. Time from beginning of QRS (ms)](http://circ.ahajournals.org/)

**Figure 2.** Graph comparing Doppler-derived left ventriculo-atrial pressure gradient curve (CW Doppler) with gradient curve derived from Millar catheter-recorded simultaneous left atrial and ventricular pressures.
(dt) between these two points was measured. The RPR was calculated as 32 mm Hg/dt.2

Simultaneous Millar catheter–recorded LA and LV pressures were similarly traced and digitized at 5-msec intervals beginning at the initial part of the QRS wave and ending at the LA and LV pressure crossover (Figure 1B). The instantaneous left ventricular aortic pressure gradient was calculated from the digitized LV and LA pressure curves, and the instantaneous LV dp/dt was determined from the LV pressure curve (Figure 1B). dp/dt_{max} at the early systolic phase and −dp/dt_{max} at the early diastolic phase were obtained from the instantaneous dp/dt curve. For each hemodynamic stage, the velocity and pressure data from three cardiac cycles were analyzed, and the values were averaged for further comparison.

Variability Study

To determine intraobserver variability, a single cardiac beat was chosen for examination from each of 10 hemodynamic stages. For each beat, the Doppler-derived and Millar catheter-derived instantaneous pressure gradients and the instantaneous dp/dt were measured by one examiner (C.C.) on two separate days and then paired for statistical comparison. The correlation coefficient of linear regression analysis between the two measurements was 0.96±0.02 for instantaneous pressure gradients (10 separate correlations, p<0.0001 for all cases), 0.94±0.03 for instantaneous dp/dt (10 separate correlations, p<0.0001 for all cases), 0.93 for dp/dt_{max} (p<0.0001), and 0.92 for the −dp/dt_{max} (p<0.0001).

Statistical Analysis

Data are expressed as mean±SD. In each case, the Doppler-derived instantaneous pressure gradients and the instantaneous dp/dt were correlated with temporally corresponding Millar measurements using linear regression analysis. Comparisons of dp/dt_{max} and −dp/dt_{max} between Doppler measurements and catheterization measurements were performed using univariate linear regression analysis and paired Student’s t test. If there was a significant difference between the two measurement approaches, peak LV pressure, peak systolic (V wave) LA pressure, and dp/dt_{max} determined from Millar catheter recordings were correlated to this difference to examine the possible factors affecting the accuracy of Doppler measurement of dp/dt. The comparative accuracy with which Doppler-derived instantaneous dp/dt_{max} and mean RPR predicted the Millar catheter–derived peak dp/dt was tested by analysis of covariance. In addition, the relative accuracy of the mean and instantaneous estimates of peak dp/dt were assessed by the method of Bland and Altman.15 For this approach, the difference between the Doppler and hemodynamic measurements of dp/dt were plotted against the hemodynamic measurement. Mean±SD of this error were compared for the two Doppler methods.

Results

Pressure Gradients Between Left Ventricle and Atrium

The peak LV pressure recorded by Millar catheter was 105±28 (62–141) mm Hg. The mean LA pressure was 13±6 (6–30) mm Hg with a peak systolic (V wave) LA pressure of 17±9 (9–35) mm Hg. The calculated peak pressure drop between LV and LA was 89±19 (53–128) mm Hg from Millar catheter recordings.

The instantaneous Millar catheter–derived pressure gradients between LA and LV correlated well (r=0.91–0.97) with instantaneous continuous-wave

FIGURE 3. Graph comparing dp/dt curve determined by Doppler mitral regurgitant velocity spectrum (CW Doppler) with dp/dt curve derived from Millar catheter–recorded left ventricular pressure curve.
Doppler-derived pressure gradients for each case (Figure 2). For pooled data, the correlations between Doppler- and catheter-derived pressure gradients were excellent, with a correlation coefficient of 0.95 (p<0.0001) and slope of 0.92. The intercept of the regression line was not different from zero (p=NS). Although Doppler-derived mean pressure gradients (67±16 mm Hg) tended to be smaller than Millar catheter-derived mean gradients (69±14 mm Hg), this difference was not statistically significant (p=NS).

**Instantaneous Left Ventricular dP/dt**

Simultaneously recorded Millar catheter-derived dP/dt and continuous Doppler-derived dP/dt were correlated for each case (Figure 3). The correlation coefficient varied from 0.85 to 0.98 (0.92±0.038), and the slope of the regression line ranged from 0.87 to 1.20 (1.01±0.11). The intercept of the regression line (-14±13) was not significantly different from zero (p=NS). For pooled data, the correlation between Doppler- and catheter-derived dP/dt was similarly excellent (r=0.92, p<0.0001) with a slope of 0.93. The intercept was not significantly different from zero. The values of dP/dt from pooled data for all cases were not different for Doppler and catheter measurement (p=NS). To test whether higher LA pressure would affect the accuracy of the measurements, the data were divided into two groups. Group 1 consisted of nine hemodynamic stages in which the mean LA pressure was less than 13 mm Hg, and group 2 consisted of hemodynamic stages in which the LA pressure was 13 mm Hg or greater. No difference was found in the correlation coefficients between group 1 and group 2 (0.92±0.04 versus 0.93±0.03, p=NS), suggesting that Doppler-derived dP/dt is not significantly affected by a mean LA pressure ranging from 6 to 30 mm Hg.

**Maximal dP/dt**

Maximal dP/dt in early systole was 1,200±573 (447–2,935) mm Hg/sec for Millar measurements and 1,266±701 (415–3,231) mm Hg/sec for Doppler-derived measurements (p=NS). The correlation between both methods was strong, with an r value of 0.97 (Figure 4, filled circles; p<0.001). The regression line is not different from the line of identity.

**Mean Early Systolic Changing Rate of Ventricular Pressure**

We compared the relative accuracy of our Doppler-derived method of measuring dP/dtmax to the earlier method of estimating dP/dtmax by the mean rate of pressure rise using the arbitrarily selected time period between 1 and 3 m/sec of the regurgitant velocity profile; these two methods were compared with the Millar catheter-derived dP/dtmax (Figure 4). The mean RPR correlated well (r=0.94, p<0.001) with the catheter-derived dP/dtmax (Figure 4, open squares). However, the slope of the regression line was significantly different from the slope achieved by our Doppler method when compared against catheter-derived dP/dtmax (1.18 versus 0.77, p<0.01). The mean early systolic RPR (896±465 [320–2,133] mm Hg/sec) was found to significantly underestimate dP/dtmax measured by Millar catheter (1,200±573 mm Hg/sec, p<0.01). The difference between dP/dtmax and mean RPR correlated significantly with peak systolic pressure (r=0.48, p<0.01) and with dP/dtmax (r=0.67, p<0.001). For all the stages, the aortic diastolic pressure was more than 36 mm Hg above the LA pressure. Thus, the mean RPR data corresponded in all cases to ventricular pressure rise occurring before aortic valve opening.

Figure 5 displays the discrepancy between the Doppler and hemodynamic measurements of peak dP/dt for the instantaneous Doppler method (panel...
A) and the mean method (panel B). Shown on each graph are the average error and the 95% confidence intervals. On average, the instantaneous method overestimated the true (hemodynamic) $dP/dt$ by 59.3 mm Hg/sec with a standard deviation (variability) of ±185.8 mm Hg/sec. The average error was not statistically different from zero. By contrast, the two-point estimation significantly underestimated true peak $dP/dt$ by 303.1 mm Hg/sec ($p<0.00001$) with a standard deviation of ±196.6 mm Hg/sec.

**Maximal Negative $dP/dt$**

Doppler-derived and Millar catheter-derived measurements of $-dP/dt_{\text{max}}$ correlated well ($r=0.93$, $p<0.001$), as shown in Figure 6. $-dP/dt_{\text{max}}$ derived from Doppler velocity profiles (961±511 [252–2,272] mm Hg/sec) was slightly (mean, −95.4±193.1 mm Hg/sec; an average of 8.5% of the true value) but significantly ($p<0.02$) lower than that obtained by Millar catheter measurements (1,057±540 [245–2,369] mm Hg/sec) ($p<0.01$). The difference between $-dP/dt_{\text{max}}$ measured by Doppler and that measured by Millar catheter tended to correlate with peak systolic (V wave) LA pressure ($r=0.35$) but did not reach statistical significance ($p=0.07$).

**Discussion**

The present study demonstrates that Doppler-determined instantaneous left ventriculooatrial pressure gradients correlate well with simultaneous Millar catheter-measured gradients. More importantly, the first derivative of the Doppler-derived pressure gradient curve could also be used to reliably estimate the first derivative of the LV pressure curve during systole and early isovolumic diastole, as determined by Millar catheter recordings. This has important clinical and research applications, because the instantaneous $dP/dt$ curve permits accurate noninvasive determination of
systolic \((dP/dt_{max})\) and diastolic \((-dP/dt_{max})\) parameters of LV function. Although our results confirmed previous reports\(^2\)\(^-\)\(^5\) of good correlation between Doppler-derived mean rate of early systolic LV pressure rise (RPR) and the true \(dP/dt_{max}\) by Millar catheter, the mean RPR underestimated the true \(dP/dt_{max}\) significantly \((p<0.01)\).

**Accuracy and Feasibility of Measurements of Systolic Ventriculoatrial Pressure Gradients by Continuous-Wave Doppler Mitral Regurgitant Velocity Spectrum**

Using the simplified Bernoulli equation, the pressure gradient between two cardiac chambers can be derived from the velocity of blood flow across these chambers by Doppler echocardiography. The clinical accuracy and reliability of the Doppler determination of pressure gradients across stenotic lesions, such as aortic, pulmonary, and mitral stenoses, have been repeatedly demonstrated.\(^1\)\(^1\)\(^1\)\(^-\)\(^1\)\(^9\) Continuous-wave Doppler echocardiography is also an accurate method of measuring peak pressure gradients across regurgitant orifices including the tricuspid,\(^2\)\(^0\)\(^-\)\(^2\)\(^1\) pulmonary, aortic,\(^1\)\(^2\) and mitral valves.\(^1\)\(^2\) Comparing continuous-wave Doppler-determined pressure gradients between LA and LV with simultaneous catheter-derived pressure gradients, Nishimura and Tajik\(^1\)\(^2\) found a close linear correlation for mean gradient \((r=0.94, \text{SEE}=6 \text{ mm Hg})\) and for maximal systolic instantaneous gradient \((r=0.98, \text{SEE}=8 \text{ mm Hg})\) in patients with mitral regurgitation. However, in this study there were a time delay and a whip artifact from the fluid-filled catheters used to record LV and LA or pulmonary wedge pressures, making accurate instantaneous temporal comparisons between Doppler and catheter measurements difficult.\(^1\)\(^2\) Since currently available continuous-wave Doppler equipment typically analyzes the input signal in 5-msec windows,\(^2\)\(^3\) it is not clear whether the temporal resolution (5 msec) of continuous-wave Doppler echocardiography is able to reflect accurately the instantaneous pressure gradient changes during systole. Clarification of this issue, however, is of importance when attempting to use Doppler-determined pressure gradient curves to derive time-related changing parameters such as the first derivative of the pressure curve. Our study, by correlating the instantaneous pressure gradients measured by Millar catheter with those derived from Doppler velocity data, demonstrates that continuous-wave Doppler echocardiography can determine instantaneous pressure gradient changes with adequate accuracy in both amplitude and phase in this in vivo mitral regurgitation model.

**Temporal Derivative of Ventriculoatrial Pressure Gradient**

Having demonstrated accurate determination of ventriculoatrial pressure gradient curves using continuous-wave Doppler mitral regurgitant velocity profiles, we then calculated the first derivative of these curves. The results showed that for systole and early isovolumic diastole the Doppler-derived \(dP/dt\) curves correlated well \((r=0.85-0.98)\) with \(dP/dt\) from LV pressure curves simultaneously recorded by Millar catheter. There was no difference in absolute values between the two methods \((p=\text{NS})\) for all pooled data. The regression line for the correlation between values measured by the two methods was very close to the line of identity \((b=0.85-1.08)\), suggesting that the true first derivatives of LV pressure curve can be accurately estimated from the first derivative of the ventriculoatrial pressure gradient curve.

For the purpose of clinical applicability, we selected Doppler-derived \(dP/dt\) at individual time points in the cardiac cycle such as \(dP/dt_{max}\) and \(-dP/dt_{max}\) to compare with the true Millar catheter measurements. Our study demonstrated that \(dP/dt_{max}\) of the LV pressure curve during early systole can be accurately estimated from \(dP/dt_{max}\) of the Doppler-derived pressure gradient curve. However, there was a minor but significant difference in measurement of \(-dP/dt_{max}\) by the Doppler and Millar catheter methods. Doppler-derived \(-dP/dt_{max}\) was on average 8.5% less than Millar catheter–derived \(-dP/dt_{max}\). Nevertheless, the correlation between Doppler- and catheter-derived \(-dP/dt_{max}\) was excellent, suggesting that continuous-wave Doppler echocardiography can be used to reliably estimate and assess changes in direction of the true \(-dP/dt_{max}\). The reason for the Doppler underestimation of \(-dP/dt_{max}\) is unclear. It may be related to LA pressure fluctuation (V wave) during ventricular contraction at the time of \(-dP/dt_{max}\). The V wave of the LA pressure usually begins to decline while LV pressure is declining. As observed in this study (Figure 1B), this decline of LA pressure occurs at or near the point of \(-dP/dt_{max}\). The simultaneously decreasing LA and LV pressures may result in a fall in changing rate of ventriculoatrial pressure gradients during this phase. This may account for the underestimation of \(-dP/dt_{max}\) by the Doppler echocardiographic method.

**Estimation of Maximal \(dP/dt\) by Mean Rate of Left Ventriculoatrial Pressure Gradient Rise**

Bargiggia et al\(^2\) have estimated \(dP/dt_{max}\) using the Doppler-derived mean RPR at early systole. This mean RPR is determined by arbitrarily selecting the time period on the initial slope of the mitral regurgitant velocity curve between 1 m/sec (corresponding to 4 mm Hg of ventriculoatrial pressure gradient) and 3 m/sec (corresponding to 36 mm Hg of the pressure gradient). Although this noninvasive calculation of mean RPR during early systole correlated well with \(dP/dt_{max}\), our study shows that it significantly underestimates the true \(dP/dt_{max}\) (on average, \(-303\) mm Hg/sec, or 25% of the hemodynamic peak \(dP/dt\)). The degree of this underestimation is dependent on the peak systolic LV pressure and \(dP/dt_{max}\). Using RPR in rapidly changing \(dP/dt\) may result in greater errors than in a slower changing rate of pressure rise.
The mean RPR actually measures the rate of pressure change between developed pressures of 4 and 36 mm Hg (developed pressure=pressure rise from the end-diastolic LV pressure). However, the time point of dP/dt\textsubscript{max} on the LV pressure curve has been shown to depend in part on the peak systolic LV pressure attained.\textsuperscript{1,24} Thus, the peak dP/dt tends to occur at higher developed LV pressure when high peak LV pressures are present and at lower developed LV pressure when low peak ventricular pressures are attained.\textsuperscript{1,24} Thus, the accuracy of mean RPR using a fixed developed pressure interval (between 4 and 36 mm Hg) is significantly influenced by different systolic peak pressures. Our results may provide an explanation for discrepancies between the mean rate of pressure rise and true dP/dt\textsubscript{max} in various patient subgroups reported previously. For example, in patients with congestive cardiomyopathy, a correlation coefficient of 0.84 and a slope of 0.55 have been reported,\textsuperscript{4} whereas in populations with coronary or rheumatic heart disease, a correlation coefficient of 0.87 with a slope of 1.05 has been observed.\textsuperscript{2,3} The higher slope of 1.05 for correlation between the catheter-derived dP/dt\textsubscript{max} and the Doppler-derived RPR may also be due to the underestimation of dP/dt\textsubscript{max} by the fluid-filled catheter used in the previous study.\textsuperscript{2} Although the study of Bargiggia et al\textsuperscript{2} did not report underestimation of dP/dt\textsubscript{max} by RPR during early systole, there was a tendency toward a more reduced slope of regression line for correlation between Doppler RPR and dP/dt\textsubscript{max} derived from fluid-filled catheter recordings than for the correlation between Doppler RPR and dP/dt\textsubscript{max} derived from Millar catheter recordings, as shown in Figure 3 of their study.\textsuperscript{2} This is most likely related to the damping effect of the fluid-filled catheters used in their study.\textsuperscript{2}

**Clinical Implications**

The maximum rate of rise (dP/dt\textsubscript{max}) and decline (−dP/dt\textsubscript{max}) of LV pressure are among the oldest and most widely used measures of ventricular contractility and relaxation, respectively.\textsuperscript{1} Although both measurements are altered by loading conditions,\textsuperscript{1,24} these changes are usually small (<10%), in the physiological range of moderate increase in preload or afterload (25–30 mm Hg of systolic artery blood pressure).\textsuperscript{1} In the presence of mitral regurgitation, the validity of isovolumic indexes as indicators of contractility has been challenged. However, various studies\textsuperscript{25–27} have demonstrated that mitral regurgitation has little effect on the accuracy of determination of dP/dt derived from isovolumic indexes. Furthermore, in addition to dP/dt, more complex indexes have been introduced in an attempt to obtain a purer contractility index, less dependent on loading conditions. These indexes include the maximum value of (dP/dt)/P, dP/dt/PD, and V\textsubscript{max}, where P is the LV pressure, PD is the developed LV pressure, and V\textsubscript{max} is the extrapolated value of (dP/dt)/P versus P when P=0.\textsuperscript{1} The present study demonstrates accurate determination of instantaneous dP/dt and correspondingly derived pressure gradients and thus suggests that these complex isovolumic systolic indexes may also be derived from Doppler data in patients with mitral regurgitation. Since mitral regurgitation is common in patients with congestive heart failure and other cardiac disorders,\textsuperscript{6–10} serial noninvasive assessment of dP/dt in these conditions may be used to study the effect of disease course or interventions on myocardial function. It is also possible to combine Doppler-derived dP/dt or pressure gradient curves with two-dimensional or M-mode echocardiographic measurements to obtain end-systolic pressure-volume relations\textsuperscript{28} and the rate of increase in wall stress during systole, which have been shown to account for changes in LV geometry and mass.\textsuperscript{28–30}

**Limitations**

There are several potential limitations of this noninvasive method to derive instantaneous pressure gradients and the systolic LV dP/dt. A complete, well delineated velocity spectral envelope from mitral regurgitation is mandatory to derive accurate measurements of instantaneous pressure gradients, which are then used to derive the dP/dt curve during systole and early isovolumic diastole. It may be difficult to obtain the complete regurgitant spectral envelope in patients with trace mitral regurgitation.\textsuperscript{2} Eccentric mitral regurgitant jets may complicate the acquisition of complete regurgitant velocity spectral envelopes.\textsuperscript{31} However, in this canine model of mitral regurgitation, we were able to clearly record complete velocity curves from eccentric regurgitant jets using apical views. As with any Doppler velocity measurement, the ultrasound beam must be aligned parallel to the velocity vectors at the regurgitant orifice to prevent underestimation of the pressure gradients. Careful scanning is necessary to obtain maximal velocity spectra by blind Doppler transducer or by image-directed continuous-wave Doppler transducers.

We have demonstrated the accuracy of this method in a canine model of moderate to severe mitral regurgitation (a regurgitant flow rate of 41.8±18.2 ml/sec), both in enlarged (increased compliance) and normal-sized (low compliance) LAs and with LA pressures ranging from 9 to 35 mm Hg. It is possible that a higher V wave on the LA pressure tracing in patients with mitral stenosis or acute severe mitral regurgitation may affect the accuracy of this noninvasive determination of dP/dt. Further studies will be necessary to evaluate this method in such patient subgroups.

**Conclusions**

This in vivo canine study demonstrated that the instantaneous systolic gradient between the LV and LA can be accurately determined from the continuous-wave Doppler mitral regurgitant velocity spectrum and that the first derivative of the pressure gradient curve can be used to estimate the true LV dP/dt curve during systole and early isovolumic diastole. Thus, Doppler echocardiography provides an
accurate and reliable noninvasive approach for deriving the dP/dt\textsubscript{max} and \(-dP/dt\textsubscript{max}\) of the LV.

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