Evaluation of Left Ventricular Diastolic Function When Mitral E and A Waves Are Completely Fused: Role of Assessing Mitral Annulus Velocity

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Mitral inflow parameters have been used most widely in the evaluation of left ventricular (LV) diastolic function. However, when the mitral E and A waves are completely fused, mitral inflow parameters cannot provide information about the LV diastolic function. LV filling pressure, mitral inflow, mitral annulus velocity, and tau (tau) were measured in 59 patients with sinus rhythm when mitral E and A waves were completely fused with right atrial pacing. When mitral E and A waves were completely fused, tau correlated with the peak fused mitral annulus velocity ($r = -0.60, P < .001$), and peak fused mitral annulus velocity of less than 12.5 cm/s best discriminated prolonged (≥ 50 ms) from normal tau, with a sensitivity of 78% and specificity of 69%. The peak fused mitral inflow velocity to peak fused mitral annulus velocity ratio correlated with LV filling pressure ($r = 0.62, P < .001$). A ratio of at least 8, could predict elevated LV filling pressure (≥ 15 mm Hg) with a sensitivity of 65% and specificity of 74%. In conclusion, even when mitral E and A waves are completely fused, mitral annulus velocity can be used in the evaluation of LV diastolic function. (J Am Soc Echocardiogr 1999;12:203-8.)
with symptoms of congestive heart failure. In the evaluation of LV diastolic function, Doppler mitral inflow parameters are most widely used. However, these parameters cannot be used if mitral E and A waves are completely fused.

Load dependency of the mitral inflow parameters has been well recognized. Increased driving pressure at the mitral valve opening, increases the E velocity and shortens the deceleration time (DT). When mitral E and A waves are completely fused, atrial contraction superimposed on the early diastolic filling period increases driving pressure at the mitral valve opening. Therefore fused mitral inflow tends to show high peak velocity and short deceleration time, even in the presence of relaxation abnormality. Mitral annulus velocity was reported to be less load-dependent than mitral inflow parameters, and we hypothesized that atrial contraction superimposed on the early diastolic filling period would affect the fused mitral annulus velocity less than the fused mitral inflow.

METHODS

Study Subjects

Simultaneous LV pressure measurements and Doppler examinations were performed on 59 patients who were undergoing clinically indicated left ventriculography or coronary angiography. Patients with valvular stenosis, significant valvular regurgitation, unstable angina, regional wall motion abnormality at the basal septum, or apical dyskinesis were excluded. Fifty-nine patients (40 male, 19 female) were enrolled; mean age was 60 ± 11 years (range 18 to 74 years). Clinical indications for the invasive studies were as follows: atypical chest pain (13 patients), angina (32), myocardial infarction (12), and follow-up study after coronary artery bypass surgery (2). LV function was normal (ejection fraction >50%) in 37 patients and depressed in 22 patients, with the mean ejection fraction of 53.6% ± 11.9%.

Echocardiography

Echocardiograms were obtained with a 2.5-MHz transducer (128XP/10, Acuson, Mountain View, Calif). After 2-dimensional and Doppler examinations, heart rate was increased gradually with right atrial pacing until mitral E and A waves were completely fused.

A 2-mm sample volume of the pulsed wave Doppler was placed between the tips of the mitral leaflets on the apical 4-chamber view. Peak velocity (EA) and DT of fused mitral inflow were obtained.

Pulsed wave Doppler tissue imaging (DTI) was performed by activating the DTI function in the same machine. Sample volume was located at the septal side of the mitral annulus, and peak fused mitral annulus velocity (EA) was measured.

Doppler echocardiograms were recorded on a strip chart with the sweep speed of 100 mm/s, and mean values of 3 different cardiac cycles were obtained.

Cardiac Catheterization

Left heart catheterization was performed through the femoral approach. Study was performed before left ventriculography or coronary angiography. Pacing electrode was placed in the high right atrium. A 3F Millar transducer (Millar instruments, Houston, Tex) located within an 8F pigtail catheter or a 7F Millar transducer with a single lumen was introduced into the left ventricle. Care was taken to avoid premature ventricular contraction. Pressure waveform was recorded with a digital audio tape recorder (Sony, Tokyo, Japan) with the sampling rate of 600 Hz for the later analysis; it was recorded simultaneously into the echocardiographic machine while obtaining Doppler signals.

LV pressure after pacing did not show a discrete pressure increment with atrial contraction, and LV end-diastolic pressure was measured to represent LV filling pressure.

tau was calculated according to the method proposed by Weiss et al, fitting the time course of the isovolumic pressure fall beginning at the time of negative peak dP/dt and lasting through the mitral valve opening. The exponential function of time was calculated as follows.
\[ P(t) = P_0 e^{\frac{-t}{T}} \quad (A) \]

where \( P_0 \) is pressure at the time of negative peak \( dP/dt \), \( t \) is time after negative peak \( dP/dt \), and \( T \) is time constant of isovolumic pressure decay (tau). In previous studies, timing of the mitral valve opening is regarded as the point when LV pressure reaches 5 mm Hg above the minimal LV diastolic pressure. We adopted an objective criterion in the detection of the mitral valve opening point for our study. With a new data sample, we calculated the derivative of \( P(t) \) and checked whether the negative peak point of \( dP/dt \) had been reached. If negative peak \( dP/dt \) was detected, the following calculation steps were repeated for each new data sample until the mitral valve opening point was identified.

1. By taking the natural logarithm of the new data sample, we calculated \( T \) from the slope \((-1/T)\) of the regression line between \( \log_e P(t) \) and \( t \).
2. With the calculated \( T \) from step 1, \( P(t) \) was reconstructed with equation A.
3. Mean square error between the measured pressure data samples and the reconstructed \( P(t) \) was calculated.
4. Mean square error was compared with the preset criterion to determine the mitral valve opening point.

Because equation A is no longer valid, the error is supposed to increase abruptly at this point.

**Statistics**

Statistical analysis was performed with the use of the statistical package, SAS (SAS, Cary, NC). Results are reported as the mean value ± SD, and sensitivity and specificity were calculated with the standard formula. Statistical relations were assessed by linear regression analysis. A \( P \) value less than .05 was considered statistically significant.

**RESULTS**

**Hemodynamic Change After Pacing**

At the baseline, \( T \) was 55.2 ± 8.9 ms and became significantly shortened to 50.8 ± 9.3 ms after pacing when mitral E and A waves were completely fused (\( P < .001 \)). LV systolic pressures were not significantly different between baseline and after pacing (146.8 ± 24.4 vs 142.5 ± 24.8 mm Hg, \( P = \) not significant). At the baseline, LV diastolic pressure before atrial contraction was 11.8 ± 4.0 mm Hg and LV end-diastolic pressure was 17.4 ± 6.0 mm Hg. LV end-diastolic pressure after pacing was 13.5 ± 6.4 mm Hg.

**Mitral Annulus Velocity in the Prediction of Relaxation Abnormality**

Among EA, DT, and EA, DT and EA correlated with \( T \) after pacing when mitral E and A waves were completely fused. The correlation coefficient of DT was weaker (\( r = -0.33, \ P < .05 \))(Figure 1) than that of EA (\( r = -0.60, \ P < .001 \))(Figure 2).
Moreover, because of the narrow range of variation in DT (80 to 130 ms), discrimination of prolonged (≥50 ms) from normal tau was limited. EA of less than 12.5 cm/s was associated with most optimal sensitivity (23/30, 78%) and specificity (20/29, 69%) in predicting a tau greater than 50 ms after pacing when mitral E and A waves were completely fused.

**Mitral Annulus Velocity in the Prediction of Elevated LV Filling Pressure**

EA/E'A' correlated with LV filling pressure ($r = 0.62$, $P < .001$) after pacing when mitral E and A waves were completely fused (Figure 3).
An EA/EA velocity ratio of at least 8 could predict elevated LV filling pressure ($\geq 15$ mm Hg) with a sensitivity of 65% (11/17) and specificity of 74% (31/42). EA and DT did not correlate with LV filling pressure after pacing when mitral E and A waves were completely fused.

**DISCUSSION**

It is not uncommon to encounter a situation where mitral E and A waves are completely fused. In such a case, carotid sinus massage is sometimes helpful to slow the heart rate for the evaluation of LV diastolic function; however, carotid sinus massage is not without hazard and often is not effective.

**Mitral Annulus Velocity and LV Relaxation**

In the previous studies, tau correlated with early diastolic mitral annulus velocity and early diastolic velocity of the posterior wall, which represent rate of volume changes that occur immediately after the mitral valve opening in the long and short axis, respectively. This phenomenon could be explained by the fact that early mitral annulus velocity is determined by the rate of relaxation immediately after the mitral valve opening, and this rate, in turn, is predominantly determined by the rate of relaxation during isovolumic relaxation period (tau). Our study results indicate that this relationship is valid even when atrial contraction occurs during the early diastolic filling period (Figure 4).
Fig. 4. Upper panel, Fused mitral inflow. Lower panel, fused mitral annulus velocity. A, Fused mitral annulus velocity of 15 cm/s in patient with normal tau (39 ms). B, In patients with a prolonged tau of 62 ms, fused mitral annulus velocity showed lower value (9.2 cm/s) than that shown in A. C, In patients whose rate of relaxation was 78 ms, fused mitral annulus velocity was only 5 cm/s. DT, Deceleration time; tau (τ), time constant of left ventricular pressure decay.

Prolonged relaxation (τ ≥ 50 ms) when mitral E and A waves were completely fused could reasonably (sensitivity 78%, specificity 69%) be predicted by the EA.

The right atrial pacing used in our study predominantly has the pure effect of an increase in heart rate. Decrease in τ with the increased heart rate was documented both in animal models and in human subjects. In our study, the mean τ after pacing was significantly shorter than at baseline. However, 10 (17%) patients showed prolongation of τ after pacing, and τ did not change in 7 (12%) patients. Changes in τ did not correlate with baseline τ, implying that the rate of relaxation at the time of tachycardia cannot be predicted by the relaxation property at rest. Thus estimating the relaxation property at the time of tachycardia is more informative clinically, and this could be done by assessing mitral annulus velocity.

Estimation of Filling Pressure

Rate of relaxation is one of the parameters used in the evaluation of diastolic function; however, complex interactions with other factors operate in the production of elevated LV filling pressure. Simplistically, relaxation abnormality could be the cause, whereas elevated LV filling pressure is the direct cause of symptoms of heart failure.

Because it is noninvasive, Doppler technique is the ideal way to clinically estimate elevated LV filling pressure. Various Doppler parameters have been suggested for this purpose, but all have had limitations, including age dependency and a tendency to be helpful only in patients with reduced LV systolic function. Moreover, when mitral E and A waves are completely fused, mitral inflow parameters cannot be used, and applicability of pulmonary venous flow parameters is not adequately validated.

Based on the hypothesis that correcting the E wave velocity for the influence of relaxation will improve its relation with left atrial pressure, the ratio of E wave velocity to the propagation velocity has been proposed as the index that could estimate well the mean capillary wedge pressure. In the report by Nagueh et al., correction of the influence of relaxation could also be accomplished with the E velocity, and the E/E ratio correlates well with the mean capillary wedge pressure. Even when mitral E and A waves are completely fused, our study showed that EA/EA correlates with LV filling pressures. An EA/EA velocity ratio of at least 8 best discriminated elevated LV filling pressure (≥ 15 mm Hg) with a sensitivity of 65% and specificity of 74%.
Fig. 5. A Patient with normal left ventricular filling pressure of 10 mm Hg. Fused mitral inflow to fused mitral annulus velocity ratio is 6. B Patient with elevated left ventricular filling pressure of 20 mm Hg. Fused mitral inflow to fused mitral annulus velocity ratio is 11. EA, Fused mitral inflow velocity; EA, fused mitral annulus velocity.

When a cutoff value of at least 7 was used, sensitivity increased to 88% and specificity decreased to 52%.

**Study Limitations**

It could be argued that our results may not extend to physiologic tachycardia. Pacing-induced tachycardia might show different tau, LV filling pressure, and Doppler parameters from physiologic tachycardia, even when heart rate is the same in both conditions. However, relations between tau, LV filling pressure, and Doppler parameters would not be very different between the two conditions. If the relations derived from pacing-induced tachycardia are limited, results from physiologic tachycardia would have the same limitations.
as tau. LV filling pressure and Doppler parameters might differ even in the physiologic tachycardia of the same heart rate, according to the causes.

**Conclusions**

Even when mitral E and A waves are completely fused, the rate of myocardial relaxation can be predicted from the EA, and LV filling pressure can be estimated from the EA/EA ratio. Thus evaluation of mitral annulus velocity is useful in the evaluation of LV diastolic function when mitral E and A waves are completely fused.

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Abstract
