Clinical Validity of Measuring Time Difference Between Onset of Mitral Inflow and Onset of Early Diastolic Mitral Annulus Velocity in the Evaluation of Left Ventricular Diastolic Function

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**OBJECTIVES**

This study was performed to validate the clinical usefulness of measuring the time difference between onset of mitral inflow and onset of early diastolic mitral annulus velocity (TE\(\rightarrow\)E) for the evaluation of left ventricular (LV) diastolic function.

**BACKGROUND**

In recent studies, TE\(\rightarrow\)E correlated well with the time constant of LV pressure decay (tau), and the ratio of IVRT/TE\(\rightarrow\)E, where IVRT is isovolumic relaxation time, was useful in the prediction of elevated LV filling pressure.

**METHODS**

Simultaneous left heart catheterization and Doppler echocardiography were performed in 40 patients.

**RESULTS**

The TE\(\rightarrow\)E was evaluated in the same cardiac cycle and in the same hemodynamic status in 31 patients. Despite the wide range of tau (31 to 70 ms), there was no delay in the onset of mitral annulus velocity compared with the onset of mitral inflow (TE\(\rightarrow\)V = 0) in 27 patients and, therefore, TE\(\rightarrow\)E did not correlate with tau. Only three patients showed prolongation in TE\(\rightarrow\)E, and all three showed tau >50 ms and pre-A-wave pressure ≥18 mm Hg. In one patient, mitral annulus velocity began earlier than the onset of mitral inflow. Because TE\(\rightarrow\)E was 0 in the majority of patients, the LV filling pressure could not be predicted by the previously suggested index of IVRT/TE\(\rightarrow\)E.

**CONCLUSIONS**

In contrast to previous studies, TE\(\rightarrow\)E did not correlate with tau, and IVRT/TE\(\rightarrow\)E could not be applied in the prediction of filling pressure, because of the limitation of a zero denominator. However, prolongation of TE\(\rightarrow\)E might suggest an elevated filling pressure in the setting of prolonged tau. (J Am Coll Cardiol 2004;43:2097–101) © 2004 by the American College of Cardiology Foundation

Early diastolic mitral annulus velocity (E') evaluated by tissue Doppler imaging (TDI) is a relatively load-independent parameter useful in the assessment of left ventricular (LV) relaxation (1,2), and the ratio of early diastolic mitral inflow velocity (E) over E' (E/E') has been suggested as an index representing LV filling pressure (3–5). However, in the absence of cardiac disease, E' is reported to be affected by the loading conditions, and E/E' is not accurate in the estimation of LV filling pressure (6,7). Recently, the time interval between the onsets of mitral inflow and mitral annulus velocity (TE\(\rightarrow\)E) was proposed as a new index representing LV relaxation (8,9), and LV filling pressure can be predicted from IVRT/TE\(\rightarrow\)E, where IVRT indicates isovolumic relaxation time. Compared with the E/E', LV filling pressure estimated from IVRT/TE\(\rightarrow\)E has been suggested to be more accurate in patients without cardiac diseases (9). This study was performed to validate this new index and test the feasibility of applying it in clinical practice.

**METHODS**

Study subjects. Simultaneous LV pressure measurements and Doppler examinations were performed in 40 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 dyskinesia were excluded. Nine patients were excluded from the analysis; eight because exactly the same cardiac cycle length between mitral inflow and mitral annulus velocity tracing could not be obtained, and one owing to different systolic blood pressure at the time of mitral inflow and mitral annulus velocity tracing. Remaining for analysis were 31 patients, 19 male and 12 female, with a mean age of 51 ± 13 years (range 20 to 69 years). Left ventricular function was normal (≥50%) in 26 patients and depressed in the other 5 patients with a mean ejection fraction of 56.4 ± 10.9%.

**Echocardiography.** Echocardiograms were obtained using Acuson XP/10 (Siemens, Mountain View, California) with a 2.5-MHz transducer. Sample volume (2 mm size) of the pulsed wave Doppler was placed between the tips of the mitral leaflets on the apical four-chamber view. Pulsed wave TDI was performed by activating the TDI function in the same machine. Sample volume was located at the septal side of the mitral annulus.

Doppler echocardiograms were recorded on a strip chart with a sweep speed of 100 mm/s, and at least 10 cardiac cycles were recorded in both the mitral inflow and the mitral...
annulus velocity recording. One pair of mitral inflow and mitral annulus velocity recordings with exactly the same cardiac cycle length on the basis of electrocardiogram signals was selected for analysis. Early mitral inflow velocity (E), late mitral inflow velocity, deceleration time of E, early diastolic mitral annulus velocity (E’), and late diastolic mitral annulus velocity were obtained.

Cardiac catheterization. Left heart catheterization was performed through the femoral approach. The study was performed before left ventriculography or coronary angiography. Seven-French Millar transducers (Millar Instruments, Inc., Houston, Texas) with single lumen were introduced into the LV, and the pressure wave form was recorded in the digital audio tape-recorder (Sony Co., Tokyo, Japan) with a sampling rate of 600 Hz for the later analysis of the time constant of LV pressure decay (tau). Tau was calculated according to the method described previously (10).

Statistics. Statistical analysis was performed with the use of the statistical package SPSS 10.0 (SPSS Inc., Chicago, Illinois). Statistical relationships were assessed by linear regression analysis. Differences in the cardiac cycle lengths between patients with simultaneous and delayed onset of mitral annulus velocity at different cycle lengths were compared using Mann-Whitney U test. A value of p < 0.05 was considered statistically significant.

RESULTS

Correlation between $T_{E^{-}E}$ and tau. Despite the wide range of tau (31 to 70 ms), there was no delay in the onset of mitral annulus velocity compared with the onset of mitral inflow ($T_{E^{-}E} = 0$) in 27 patients and, therefore, $T_{E^{-}E}$ did not correlate with tau.

$T_{E^{-}E}$ in two extreme cases. In the patient with highest tau value (70 ms) included in our study, the LV pre–A-wave pressure was 8 mm Hg, and this patient showed simultaneous onset of mitral inflow and mitral annulus velocity (Fig. 1). In another patient with the highest LV pre–A-wave pressure included in this study, tau was 35 ms, and this patient also showed simultaneous onset of mitral inflow and mitral annulus velocity (Fig. 2).

$T_{E^{-}E}$ and LV filling pressures. In our study, the previously suggested index of IVRT/$T_{E^{-}E}$ could not be applied because of the limitation of dividing by zero. Three patients showed prolongation of $T_{E^{-}E}$ (Fig. 3), all of whom showed both tau ≥50 ms and pre–A-wave pressure ≥18 mm Hg (Fig. 4).

Effect of different cardiac cycle length in the estimation of $T_{E^{-}E}$. Among the 10 patients with simultaneous onset of mitral inflow and mitral annulus velocity ($T_{E^{-}E} = 0$) at the same cardiac cycle lengths, $T_{E^{-}E}$ was measured at different cardiac cycle lengths between the mitral inflow and mitral annulus velocity tracing. Four patients showed differences between the onset of mitral inflow and mitral annulus velocities. The magnitude of differences in the cardiac cycle lengths was not different between these four patients and the remaining six who showed simultaneous onset even at different cardiac cycle lengths (48.3 ± 24.8 ms vs. 35.0 ± 19.1 ms, p = NS).

DISCUSSION

In previous reports, $T_{E^{-}E}$ correlated well with tau, and the LV filling pressure was predicted from the ratio of IVRT/$T_{E^{-}E}$. We could not reproduce these results in our study. The majority of patients (27 of 31, 87%) showed simultaneous onset of mitral inflow and mitral annulus velocities despite the wide range of tau. We cannot suggest a clear explanation for this discrepancy; however, several aspects should be considered.

The peak velocity of E’ is determined by the elongation in the LV long axis. However, in our opinion, the beginning of E’ might be attributed to a decrease in the dimension of the left atrium as well as elongation in the LV long axis. In
our experience, certain patients show double peaks in early diastolic mitral annulus velocity, and this phenomenon can be explained by the mitral annulus velocity resulting from the decrease in left atrial volume as the first peak and the increase in LV long axis as the second peak (Fig. 5). Therefore, even if the beginning of the elongation in the LV
long axis is delayed, the beginning of $E'$ and of mitral inflow might occur simultaneously.

**Practical limitation of measuring $T_{E'-E}$**. Theoretically, the onsets of mitral inflow and mitral annulus velocities should be compared at the same cardiac cycle lengths. However, with the current technology, mitral inflow and mitral annulus velocities need to be obtained separately for the comparison. In our study, exactly the same cardiac cycle lengths in mitral inflow and mitral annulus velocity tracings could not be obtained in eight patients (8 of 40, 20%). As there are larger differences in the diastolic periods than in the systolic periods at different cardiac cycle lengths, it could be interpreted that slight differences in cardiac cycle lengths might be permissible in the measurements. However, when $T_{E'-E}$ was measured at different cardiac cycle lengths between mitral inflow and mitral annulus velocities in the 10 patients with simultaneous onset of mitral inflow and mitral annulus velocities ($T_{E'-E} = 0$) at the same cardiac cycle lengths, four patients showed a difference in the onsets ($T_{E'-E} \neq 0$). Moreover, these erroneous results of $T_{E'-E}$ measurement, resulting from different cardiac cycle lengths, could not be predicted from the magnitude of the difference in cardiac cycle lengths.

The measurement of $T_{E'-E}$ can also lead to an erroneous result when hemodynamics are not the same during two separate measurements. One patient was excluded in our study owing to a significant increase in systolic blood pressure during mitral annulus velocity measurement. In this patient, the onset of mitral annulus velocity appeared to be delayed compared with the onset of mitral inflow at the same cardiac cycle lengths. However, LV pressures at the onsets of mitral inflow and mitral annulus velocities were the same, and $T_{E'-E} > 0$ resulted from the delay in reaching mitral valve opening pressure as the systolic pressure was increased when mitral annulus velocity was obtained (Fig. 6). Finally, the previously suggested index of IVRT/$T_{E'-E}$ for the prediction of LV filling pressure could not be applied when mitral inflow and mitral annulus velocity started simultaneously because of the mathematical limitation of dividing by zero. In a previous report (9), IVRT/$T_{E'-E}$ could be obtained in all patients with positive values, indicating that $T_{E'-E} > 0$ in all patients. In the measurement of $T_{E'-E}$, they used different methodology. Instead of matching cardiac cycle length, they measured the difference

**Figure 4.** Time constant of left ventricular pressure decay (tau) and pre-A-wave pressure in patients with time interval between the onsets of mitral inflow and mitral annulus velocity ($T_{E'-E}$) of $> 0$, $= 0$, and $< 0$.

**Figure 5.** Two peaks in the early diastolic mitral annulus velocity.
between the interval from the peak of the R-wave to the onset of E velocity and the interval from the peak of the R-wave to the onset of E'. They measured Tₑ₋ₑ' at four areas of the mitral annulus, and averages of these velocities were used. In our study, a majority of the patients showed Tₑ₋ₑ' of 0; therefore, this index could not be applied in the prediction of LV filling pressure. When Tₑ₋ₑ' is <0, which has been noted in normal subjects (11) and also in one patient included in our study, these patients might erroneously be classified as having high LV filling pressure when this index is used.

CONCLUSIONS

In contrast to previous studies, Tₑ₋ₑ' did not correlate with tau, and IVRT/ Tₑ₋ₑ' could not be applied in the prediction of filling pressure. Obtaining two separate measurements at the same cardiac cycle lengths and hemodynamic status in effect limits the application of this index in clinical practice. However, the prolongation of Tₑ₋ₑ' might suggest an elevated filling pressure in the setting of prolonged tau.

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