CONTRIBUTION OF CHAMBER COMPLIANCE AND LEFT VENTRICULAR MINIMUM PRESSURE TO ABNORMAL LEFT VENTRICULAR FILLING DYNAMICS

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AND TAKENOBU KAMADA, M.D.

This study was designed to clarify whether changes in transmitral flow velocity patterns in left ventricular (LV) dysfunction are determined primarily by changes in left atrial (LA) pressure and LV relaxation, and, if not, to determine the contribution of changes in other parameters. Two levels of acute LV dysfunction were produced in 11 dogs by coronary microembolization, and pulsed Doppler transmitral flow velocity patterns and hemodynamic parameters were recorded. The mean ratio of peak early diastolic filling velocity (E) to peak late diastolic filling velocity decreased with mild LV dysfunction (LV end-diastolic pressure of between 12 and 17 mmHg), and redistribution of diastolic filling to early diastole was observed with severe LV dysfunction (LV end-diastolic pressure of ≥18 mmHg). Changes in E correlated best with those in the LA-LV pressure gradient integral. Multiple linear regression analysis of the changes in possible determinants of the pressure gradient integral, i.e., LA to LV crossover pressure, LV time constant, LV minimum pressure, and LA and LV chamber compliance, yielded a highly significant correlation with the changes in E. However, analysis of only the changes in the crossover pressure and the time constant showed a very poor correlation. Thus, changes in chamber compliance and LV minimum pressure, in addition to the changes in LA pressure and LV relaxation, may significantly affect the changes in E that are associated with LV dysfunction.

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Pulsed Doppler transmitral flow velocity patterns change characteristically in heart failure. In mild heart failure, decreased peak early diastolic filling velocity (E), increased peak late diastolic filling velocity (A) and a decreased ratio of E to A are observed. In patients with severe heart failure, “normalization” of E, A and the ratio of E to A is frequently observed. These changes may be due, at least in part, to an interaction between left atrial (LA) pressure and left ventricular (LV) relaxation, since previous studies have shown that transmitral flow velocity patterns are significantly influenced by these 2 factors in normal hearts. A recent theoretical study suggested that other hemodynamic parameters, which may be dramatically altered in heart failure, also affect flow velocity patterns, and it may be inadequate to interpret the changes in the flow velocity patterns associ-

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- Left ventricular filling
- Heart failure
- Doppler echocardiography
- Chamber compliance
- Left ventricular minimum pressure

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ated with heart failure solely in terms of the interaction between LA pressure and LV relaxation.

Little attention has been paid to Doppler echocardiographic parameters other than E and A, although a few previous clinical studies have shown that deceleration time changes in a consistent direction in heart failure. Thus, it may be helpful to consider changes in other parameters when assessing the hemodynamic profile of heart failure.

The aims of this animal study were 1) to clarify whether changes in LA pressure and LV relaxation are the main determinants of changes in transmirtal flow velocity patterns in LV dysfunction, 2) if not, to identify other contributors to changes in transmirtal flow velocity patterns in LV dysfunction, and 3) to clarify whether information obtained by the analysis of changes in E and A is complemented by measuring changes in other Doppler parameters when assessing the hemodynamic profile in LV dysfunction.

METHODS

Animal Preparation and Data Collection

This study conforms to the guiding principles of Osaka University School of Medicine with regard to animal care and to the “Position of the American Heart Association on Research Animal Use”. Eleven mongrel dogs (12 to 35 kg) were sedated with morphine sulfate (3 mg/kg, subcutaneously) 30 min before induction of general anesthesia with \( \alpha \)-chloralose (50 mg/kg, intravenously). After the induction of general anesthesia, intravenous infusion of \( \alpha \)-chloralose (30 mg/kg/h) was continued until the end of the experiment. Each dog was intubated and artificially ventilated with a Harvard type respirator (R-60, Aika, Tokyo, Japan) in the supine position. The pericardium was incised only around the right atrium through a midline sternotomy, and the right atrial appendage was paced to keep heart rate constant after the sinus node was crushed. An 8F high-fidelity manometer-tipped catheter (Sentron, Roden, Netherlands) was introduced into the LV through the left carotid artery. A 6F high-fidelity manometer-tipped catheter (Millar Instruments, Houston, TX) was introduced into the LA through the left pulmonary vein. The manometers were calibrated relative to atmospheric pressure before introduction of the catheters into the cardiac chambers. A 7F flow-directed pulmonary artery catheter (Gould, Cleveland, OH), whose fluid-filled lumen was connected to a fluid-filled pressure transducer (Model TP-400T, Nihon Kohden, Tokyo, Japan) positioned at the midthoracic level, was advanced into the right ventricle via the right jugular vein. A 5F Judkins left coronary catheter (Schneider Inc., Minneapolis, MN) was advanced into the left coronary ostium under echocardiographic guidance through the right femoral artery. A small amount of hand-agitated saline was injected into the left coronary artery to verify the appropriate positioning of the catheter by observing a homogeneous staining of the LV wall in contrast echocardiograms. Continuous lead II electrocardiographic tracing, LA and LV pressures, right ventricular pressure and the first derivative of LV pressure (dP/dt) were displayed on the 8 channel recorder (Nihon Kohden, Tokyo, Japan), and all recordings were made at a paper speed of 100 mm/s.

A commercially available echocardiograph (SSH-65A, Toshiba, Tokyo, Japan) was used to record pulsed Doppler transmirtal flow velocity patterns and M-mode echocardiograms of the LA and LV cavities. These were recorded simultaneously with high-fidelity LA and LV pressure signals transmitted from the 8 channel recorder.

Pulsed Doppler transmirtal flow velocity patterns were obtained using a transoesophageal two-dimensional phase array echocardiographic 3.75 MHz transducer with pulsed Doppler capabilities (ESB-37SR, Machida, Tokyo, Japan). The probe was adjusted to obtain a modified four-chamber view. After a stable two-dimensional image of the mitral valve inflow was obtained, the sample volume was placed at the tip of the mitral valve leaflets so that the maximum velocity across the mitral valve would be measured.

Two-dimensional targeted M-mode echocardiograms of the LA and LV cavities were obtained with a 5 MHz transducer. To obtain an M-mode echocardiogram of the LA, the transducer was placed near the outflow tract of the right ventricle so that a B-mode view similar to a parasternal long axis
view could be obtained. The orientation of the transducer was adjusted to make the ultrasound beam transect the aorta and the aortic valve and to obtain a good recording of the anteroposterior LA diameter. An M-mode echocardiogram of the LV was obtained at the midpapillary muscle level.

Pressures were monitored with and without the transducer placed on the heart to ensure that transducer manipulation had little or no effect on the measurements. All Doppler and M-mode echocardiographic recordings were obtained at a paper speed of 100 mm/s using a strip chart recorder (LSR-20B,
TABLE I CHANGES IN DOPPLER ECHOCARDIOGRAPHIC AND M-MODE ECHOCARDIOGRAPHIC PARAMETERS

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>96 ± 10</td>
<td>96 ± 10</td>
<td>96 ± 10</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>59 ± 14</td>
<td>47 ± 13</td>
<td>47 ± 16</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>38 ± 12</td>
<td>41 ± 8</td>
<td>33 ± 7</td>
</tr>
<tr>
<td>E/A</td>
<td>1.7 ± 0.5</td>
<td>1.2 ± 0.4*</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>TVI-E (cm)</td>
<td>8.7 ± 2.4</td>
<td>6.2 ± 2.3**</td>
<td>5.3 ± 2.2**</td>
</tr>
<tr>
<td>TVI-A (cm)</td>
<td>1.6 ± 0.7</td>
<td>1.6 ± 0.4</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Diastolic TVI (cm)</td>
<td>10.2 ± 2.9</td>
<td>7.7 ± 2.4**</td>
<td>6.5 ± 2.3**</td>
</tr>
<tr>
<td>Acceleration time (ms)</td>
<td>89 ± 23</td>
<td>84 ± 17</td>
<td>80 ± 13</td>
</tr>
<tr>
<td>Acceleration (cm/s²)</td>
<td>691 ± 197</td>
<td>583 ± 199</td>
<td>587 ± 181</td>
</tr>
<tr>
<td>Deceleration time (ms)</td>
<td>155 ± 15</td>
<td>123 ± 25*</td>
<td>95 ± 18**†</td>
</tr>
<tr>
<td>Deceleration (cm/s²)</td>
<td>382 ± 91</td>
<td>381 ± 62</td>
<td>499 ± 146†</td>
</tr>
<tr>
<td>LAD₁ (mm)</td>
<td>19 ± 7</td>
<td>24 ± 7**</td>
<td>29 ± 8**††</td>
</tr>
<tr>
<td>LAD₂ (mm)</td>
<td>17 ± 7</td>
<td>22 ± 8**</td>
<td>26 ± 8**††</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>22 ± 6</td>
<td>31 ± 7**</td>
<td>35 ± 8**</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>33 ± 5</td>
<td>38 ± 6**</td>
<td>41 ± 5**</td>
</tr>
<tr>
<td>LAC (mm/mmHg)</td>
<td>1.71 ± 0.89</td>
<td>1.18 ± 0.70*</td>
<td>0.87 ± 0.39**</td>
</tr>
<tr>
<td>LVC (mm/mmHg)</td>
<td>1.60 ± 0.75</td>
<td>0.92 ± 0.41**</td>
<td>0.53 ± 0.36***</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD. *p<0.05 vs Control, †p<0.05 vs Mild LV dysfunction, **p<0.01 vs Control, ††p<0.01 vs Mild LV dysfunction.
Abbreviations: A=peak late diastolic filling velocity; diastolic VTl=the sum of the time-velocity integral of the early and late diastolic filling waves; E=peak early diastolic filling velocity; E/A=the ratio of E to A; HR=heart rate; LAC=left atrial compliance; LAD₁=left atrial diameter at mitral valve opening; LAD₂=left atrial diameter before atrial contraction; LVC=left ventricular compliance; LVEDD=left ventricular end-diastolic diameter; LVESD=left ventricular end-systolic diameter; TVI-A=time-velocity integral of the late diastolic filling wave; TVI-E=time-velocity integral of the early diastolic filling wave.

Toshiba, Tokyo, Japan).

Before each recording, the manometric LV pressure was aligned with the pressure measured by the fluid-filled lumen of the catheter connected to a TP-400T transducer positioned at the midthoracic level, and the difference between manometric LA and LV pressures during mid-diastole of long diastolic cycles was recorded. All measurements were made during the end-expiratory portion of the respiratory cycle.

Experimental Protocol
First, Doppler echocardiographic, M-mode echocardiographic and hemodynamic parameters were obtained at control. Plastic microspheres (49±2 μm in diameter, 3M, St. Paul, MN) were then injected into the left coronary artery to induce acute ischemic LV dysfunction, as described previously. The microspheres were continuously agitated in saline suspension and injected every 5 to 10 min as a bolus of 5 ml (24000 microspheres/ml). A sequence of injections was made to first produce mild LV dysfunction (LV end-diastolic pressure of 12 to 17 mmHg) followed by severe LV dysfunction (LV end-diastolic pressure of ≥18 mmHg). After 10 to 15 min of stability under each of these conditions, ultrasound studies and hemodynamic measurements were performed.

Data Analysis
A personal computer system (NEC, Tokyo, Japan) was used to digitize pressure tracings and pulsed Doppler transmural flow velocity patterns. Transmural flow velocity patterns were traced along the darkest portion of the velocities to obtain E and A, mean acceleration and deceleration rates of the early diastolic filling wave, acceleration and deceleration times of the early diastolic filling wave, and time-velocity integrals of the early and late diastolic filling waves (Fig. 1). Acceleration and deceleration times of
the early diastolic filling wave were defined as twice the interval between the point at peak velocity and that at half of the peak velocity during the acceleration and deceleration phases, respectively. The time-velocity integrals of the early and late diastolic filling waves were taken as the areas under the traced transmitral velocity profiles during the early and late diastolic filling periods, respectively. When the early and late diastolic filling waves overlapped, the integral of the early diastolic filling wave was measured to the onset of the late diastolic filling wave, and the residual area was measured as the integral of the late diastolic filling wave.\textsuperscript{11,12}

Simultaneous tracings of high-fidelity LA and LV pressures were digitized for measurements of LA to LV crossover pressure, peak instantaneous difference of LA and LV pressures in early diastole, LA-LV pressure gradient integral in early diastole, LV minimum pressure in early diastole, LV end-diastolic pressure and LV systolic pressure. The difference between LA and LV pressures during mid-diastole of long diastolic cycles was subtracted from the recorded LA pressure to adjust LA and LV pressures to a common baseline when LA and LV pressures were reconstructed on the computer system\textsuperscript{7} Right ventricular pressure was traced to obtain right ventricular end-diastolic pressure. LV and right ventricular end-diastolic pressures were defined as LV and right ventricular pressures at the R wave of electrocardiogram. LV systolic pressure was defined as maximal LV pressure. LV relaxation was assessed by the least-square method, using pressure points from the time of peak-dP/dt until 5 mmHg above LV end-diastolic pressure based on a model of exponential decay with a variable asymptote:

\[ P(t) = PA exp (-t/T_D) + PB, \]

where \( P(t) \) is LV pressure, \( t \) is time, and \( PA \), \( PB \) and \( T_D \) are constants determined by the data. \( T_D \) was computed from this formula as a time constant of isovolumic pressure decrease.\textsuperscript{13,14} The LA-LV pressure gradient integral in early diastole was defined as the area of the forward transmitral pressure gradient (LA pressure > LV pressure) that was circumscribed by the LA and LV pressure signals in early diastole (Integral \( \Delta P \) in Fig. 1).

LA diameter at the mitral valve opening (LAD\textsubscript{1}) was measured at the crossover pressure. LA diameter just before atrial contraction (LAD\textsubscript{2}) was measured at the onset of the “a”-wave of LA pressure. LA compliance was calculated as follows\textsuperscript{7}:

\[ \frac{(LAD_2 - LAD_1)(LAP_2 - XP)}{LAP_2 - XP} \]

where XP is the crossover pressure, and LAP\textsubscript{2} is LA pressure at LAD\textsubscript{2}. LV end-diastolic diameter (LVEDD) was measured at the R wave of the electrocardiogram. LV end-systolic diameter was measured at the peak downward motion of the interventricular septum.

LV compliance was calculated as follows\textsuperscript{7}: 
TABLE II  CHANGES IN HEMODYNAMIC PARAMETERS

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDP (mmHg)</td>
<td>8 ± 3</td>
<td>14 ± 2**</td>
<td>22 ± 3**t</td>
</tr>
<tr>
<td>LV minP (mmHg)</td>
<td>3 ± 1</td>
<td>8 ± 1**</td>
<td>12 ± 2**t</td>
</tr>
<tr>
<td>XP (mmHg)</td>
<td>8 ± 2</td>
<td>12 ± 2**t</td>
<td>17 ± 3**t</td>
</tr>
<tr>
<td>Peak ΔP (mmHg)</td>
<td>3 ± 1</td>
<td>5 ± 1</td>
<td>3 ± 1</td>
</tr>
<tr>
<td>Integral ΔP (mmHg·ms)</td>
<td>282 ± 88</td>
<td>180 ± 51*</td>
<td>190 ± 90*</td>
</tr>
<tr>
<td>LVSP (mmHg)</td>
<td>132 ± 18</td>
<td>128 ± 19</td>
<td>125 ± 22</td>
</tr>
<tr>
<td>peak + dP/dt (mmHg/s)</td>
<td>2969 ± 522</td>
<td>2213 ± 376**</td>
<td>1980 ± 377**</td>
</tr>
<tr>
<td>peak − dP/dt (mmHg/s)</td>
<td>2432 ± 492</td>
<td>1674 ± 359**</td>
<td>1385 ± 275**</td>
</tr>
<tr>
<td>T_D (ms)</td>
<td>39 ± 6</td>
<td>57 ± 10**</td>
<td>71 ± 8**t</td>
</tr>
<tr>
<td>RVEDP (mmHg)</td>
<td>8 ± 4</td>
<td>11 ± 3*</td>
<td>13 ± 4**t</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD. *p<0.05 vs Control, †p<0.05 vs Mild LV dysfunction, **p<0.01 vs Control, ‡p<0.01 vs Mild LV dysfunction.

Integral ΔP=left atrial-left ventricular pressure gradient integral in early diastole; LVEDP=left ventricular end-diastolic pressure; LV minP=left ventricular minimum pressure in early diastole; LVSP=left ventricular systolic pressure; Peak ΔP=peak instantaneous difference of left atrial and left ventricular pressure in early diastole; T_D=time constant of left ventricular isovolumic pressure fall; XP=left atrial to left ventricular crossover pressure.

(LVEDD−LVDD1)/(LVEDP−LV minP)

where LVDD1 is LV diameter at LV minimum pressure (LV minP), and LVEDP is LV end-diastolic pressure.

Averaged values of three consecutive cardiac cycles were used for the quantitative analysis.

Statistical Analysis

Values are expressed as the mean ± SD. The statistical significance of the differences between data under different conditions, i.e., at control, at mild LV dysfunction, and at severe LV dysfunction, was tested with an analysis of variance (ANOVA) and Scheffe's F test. Bivariate correlations between the changes in Doppler echocardiographic parameters and those in hemodynamic parameters were performed with simple least-squares linear regression analysis. Multiple linear regression analysis was performed to identify the contribution of changes in several hemodynamic parameters to changes in E. Specifically, we considered changes in E as dependent variables in a multiple regression with the changes in the crossover pressure and the time constant, or those in the crossover pressure, the time constant, LV minimum pressure and LA and LV chamber compliance, as independent variables. To examine whether the associated regression coefficient was significantly different from zero and whether it contributed significantly to the multiple regression, the t-value of each variable was calculated as

\[ t = \text{the associated regression coefficient of each variable/the standard error of the coefficient} \]

Results were considered significant at a probability value of less than 0.05. All calculations were performed with the STATVIEW II (Abacus Inc., Berkeley, CA) statistical program.

RESULTS

Changes in Doppler Echocardiographic Parameters (Table I)

Representative recordings are shown in Fig. 1. In this case, E decreased and A increased at mild LV dysfunction. E increased, A decreased, and deceleration time was shortened at severe LV dysfunction. The mean value of the ratio of E to A decreased at mild LV dysfunction (p<0.05) but increased at severe LV dysfunction. Mean values of E and A were comparable at the different levels of LV function. Mean values of changes in E and A were also not significantly different at the various levels of

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LV function, but changes in these parameters varied widely among the dogs (Fig. 2). Deceleration time was progressively shortened with a depression of the level of LV function.

**Changes in M-mode Echocardiographic Parameters** (Table I)

All of the LA diameters at mitral valve opening and just before atrial contraction, and the LV end-systolic and end-diastolic diameters, increased with a depression of the level of LV function. LA and LV compliance progressively decreased with the depression of the level of LV function.

**Changes in Hemodynamic Parameters** (Table II)

LV end-diastolic pressure, LV minimum pressure, LA to LV crossover pressure and right ventricular end-diastolic pressure progressively increased as the level of LV function was depressed. The time constant also increased as the level of LV function was depressed. The LA-LV pressure gradient integral in early diastole was lower at mild and severe LV dysfunction than at control.

**Correlations between Changes in Doppler Echocardiographic Parameters and Those in M-mode Echocardiographic and Hemodynamic Parameters** (Table III)

Changes in M-mode echocardiographic and hemodynamic parameters associated with the depression of the level of LV function were compared to those in Doppler
### TABLE IV

**RESULTS OF MULTIPLE LINEAR REGRESSION ANALYSIS RELATING THE CHANGES IN PEAK EARLY DIASTOLIC FILLING VELOCITY (n=22)**

<table>
<thead>
<tr>
<th>Variables</th>
<th>t-value</th>
<th>Probability (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV minP</td>
<td>−6.088</td>
<td>0.0001</td>
</tr>
<tr>
<td>XP</td>
<td>4.952</td>
<td>0.0002</td>
</tr>
<tr>
<td>LAC</td>
<td>−4.811</td>
<td>0.0002</td>
</tr>
<tr>
<td>LVC</td>
<td>3.292</td>
<td>0.0049</td>
</tr>
<tr>
<td>Tdo</td>
<td>3.023</td>
<td>0.0086</td>
</tr>
</tbody>
</table>

Abbreviations are the same as those in Tables I and II.

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**DISCUSSION**

In this study, 2 levels of acute ischemic LV dysfunction were produced by stepwise injection of plastic microspheres into the left coronary artery. These results indicated that the changes in LA and LV chamber compliance and LV minimum pressure, as well as those in LA pressure and LV relaxation, significantly affect the changes in E, particularly in LV dysfunction.

**Peak Early Diastolic Filling Velocity (E)**

Courtois et al.\(^5\) showed that a close relation exists between E and the LA to LV pressure gradient, and this relation is maintained even with changes in the preload or afterload.\(^4\,16\,17\) This study showed that the changes in E correlate with those in the LA to LV pressure gradient even if LV function is altered. As determinants of the LA to LV pressure gradient, LA pressure and LV relaxation have been considered to be important in animals with normal LV function.\(^4\,5\) However, none of the changes in these 2 parameters, i.e., the LA to LV crossover pressure and the LV time constant, corrected with those in E in dogs with LV dysfunction, and multiple linear regression analysis of the changes in E and the changes in these 2 parameters resulted in a poor correlation coefficient. Himura et al.\(^19\) suggested that changes in LV systolic function alter the relation between indexes of transmitial flow velocity patterns and hemodynamic parameters. Courtois et al.\(^20\) also showed that E is affected by LV systolic function and is not necessarily determined by LA pressure and LV relaxation. Thus, a poor correlation between the changes in E and those in the crossover pressure and the time constant in dogs with LV dysfunction may be due to changes in other LV or LA characteristics.

In addition to the crossover pressure and the time constant, LA and LV chamber compliance and LV elastic recoil have been considered to be parameters which affect the LA to LV pressure gradient.\(^5\,21\) When the level of LV function is depressed, chamber compliance and LV elastic recoil also markedly decrease, and the contribution of these factors, if present, would be expected to be much larger than in normal hearts. In our dogs, LA and LV chamber compliance

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decreased, and LV minimum pressure increased as the level of LV function decreased. Because the changes in LV minimum pressure correlated with those in LV end-systolic diameter \( (r=0.52, p<0.05) \), the increase in LV minimum pressure may partially reflect the impaired LV elastic recoil associated with depressed LV systolic function. Multiple linear regression analysis of the changes in \( E \) and the changes in the crossover pressure, LA compliance, the time constant, LV compliance and LV minimum pressure, showed a significant correlation, and all 5 of these parameters significantly contributed to the relation (Table IV). Given such a complex contribution and complex changes in \( E \), it is no wonder that the simple linear regression analysis of the changes in \( E \) and those in each of these 5 hemodynamic parameters showed a poor correlation coefficient (Table III). The poor correlation may have also been due to the simultaneous changes in these hemodynamic parameters and does not preclude the possibility that the changes in these hemodynamic parameters may significantly affect the changes in \( E \). The simultaneous changes in these hemodynamic parameters may also be responsible for the unexpected t-value of the time constant (Table IV). To our knowledge, there should be an inverse correlation between \( E \) and the time constant. However, the t-value of the time constant was positive in this study. In this study, the time constant was increased with the elevation in LA pressure during the production of LV dysfunction, and this elevation in LA pressure should increase \( E \). In addition, other parameters, such as chamber compliance and LV elastic recoil, changed to decrease \( E \), and the effects of the changes in these parameters on the decrease in \( E \) may have been larger than those of the changes in the time constant, as expected from the t-values of these parameters. This may account for the positive t-value of the time constant. If parameters other than the time constant had been controlled during interventions, the time constant might have been inversely correlated with \( E \).

Considering the complex relations, it is impossible to speculate on changes in the severity of LV dysfunction solely by observing changes in \( E \). An increase in \( E \) in patients with congestive heart failure may not necessarily indicate an elevation of crossover pressure associated with the progression of LV dysfunction. Likewise, a decrease in \( E \) associated with some therapeutic interventions may not necessarily indicate a decrease in the crossover pressure. An increase in cardiac performance induced by administration of some drugs may well improve LV elastic recoil and LV relaxation to increase \( E \). Administration of vasodilators may reduce interventricular interaction and a constraining force of the pericardium, in addition to preload (crossover pressure), which would also increase \( E \). A decrease in \( E \) associated with some therapeutic interventions may result from a decrease in the crossover pressure as well as from changes in the LA and LV compliance, LV relaxation and/or LV elastic recoil. Thus, it may be misleading to assess the outcome of therapeutic interventions by only observing changes in \( E \) in patients with heart failure.

Deceleration Time of the Early Diastolic Filling Wave

In this study, deceleration time was shortened as level of LV function was depressed. Shortening of the deceleration time of the early diastolic filling wave is not usually observed in patients with mild heart failure. Thus, questions arise regarding why deceleration time was shortened with mild LV dysfunction in this study, but not in patients with mild heart failure. The difference may be explained by the difference in the changes in LA compliance. A previous animal study suggests that the LA chronically adapts to loading and that LA compliance may increase if LA pressure is not extremely elevated. In contrast, LA compliance was lower with mild LV dysfunction than under control conditions in this study. The directions of the changes in the time constant, the crossover pressure and the LV end-diastolic pressure associated with the mild depression of LV function in our dogs may be similar to those observed in patients. Considering the significant correlation between the changes in LA compliance and the changes in deceleration time, the decrease in deceleration time with acute-onset mild LV dysfunction in this study may have been due to an associated decrease in LA compliance.
Deceleration time is markedly shortened in patients with severe heart failure. This earlier finding is consistent with our present results. The shortening of deceleration time observed in subjects with severe heart failure may also be explained by decreased LA chamber compliance. In subjects with severe heart failure, LA pressure is increased markedly, and the slope of LA pressure-volume relation during early diastole may be steep at high LA pressure because of the concave curvilinearity of the relation.

A positive correlation was observed between the changes in LV compliance and those in deceleration time, and an inverse correlation was observed between the changes in LV minimum pressure and those in deceleration time. If LV compliance is decreased, a steep increase in LV pressure from the nadir to the end of the early diastolic filling wave occurs, which may facilitate a reversal of the transmitial pressure gradient. An increase in the LV minimum pressure may also promote the reversal of the transmitial pressure gradient. Previous studies showed that deceleration of the early diastolic filling velocity was steepened with an increase in the magnitude of the reversed transmitial pressure gradient. Thus, a decrease in LV compliance and an increase in LV minimum pressure may also be responsible for the shortening of deceleration time in severe heart failure.

**Study Limitations**

Several limitations are noted. First, LA and LV diameters were used instead of their volumes. LA and LV diameters have been shown to correlate with their respective volumes and LV compliance and contractility have been calculated using LV diameter. However, since acute LV dysfunction was produced by injection of plastic microspheres into the left coronary artery, LV dysfunction may have been produced in a segmental manner. This may have compromised the accuracy of the calculation of the chamber compliance from the chamber diameters although qualitative similarities may be expected.

Second, a progression of mitral regurgitation and an enlargement of mitral annular area associated with a progression of LV dysfunction may have affected the changes in the Doppler parameters of transmitral flow velocity patterns. However, color flow jets on Doppler echocardiograms were small, and a giant "v"-wave of LA pressure was not observed throughout our experiment. Thus, the effects of mitral regurgitation may be negligible. Therefore, changes in the mitral annular area may not have been large enough to affect our results.

Third, the crossover pressure, the time constant, LA compliance, LV compliance and LV minimum pressure were used as independent variables in the multiple linear regression analysis. However, these parameters partially depend on one another, and the interrelation among the parameters may very well change with an alteration of the severity of LV dysfunction. These 5 parameters changed simultaneously when the level of LV function was depressed in this study. The t-value of the time constant in the multiple linear regression analysis was positive (Table IV), although a negative value is expected based on the data in the literature. This may be due in part to the interdependence of the hemodynamic parameters.

Fourth, LV pressure was measured at one site in the LV in each dog. Courtois et al showed that there is a pressure gradient in the LV, and thus, absolute values of indexes obtained from LV pressure tracings may differ according to the site where LV pressure was measured. In this study, the intraindividual changes in the indexes that were associated with the production of LV dysfunction were used to assess the correlation among the indexes. Therefore, the effects of measuring LV pressure at different sites in different dogs may be small if present.

**Clinical Implications**

Changes in E associated with interventions or with a progression of LV dysfunction have been considered to be significantly affected by changes in the interaction between LA pressure and LV relaxation. This study showed that it is necessary to consider at least 3 additional factors, i.e., LA and LV compliance and LV elastic recoil, when interpreting the changes in E. For example, findings of transmitral flow velocity patterns in patients with severe heart failure include increased E and decreased A. Because the crossover pressure is likely to be elevated...

in patients with severe heart failure, the increase in E in these patients has been considered to be due to an elevation of the crossover pressure. However, the value of the increased E in such patients is not necessarily as high as expected from their markedly elevated LA pressure. Considering our results, this previous finding may reflect an association of the impaired LV elastic recoil and/or the decreased LA and/or LV chamber compliance with the elevated LA pressure.

This study showed that the changes in E are affected by the changes in hemodynamic parameters in a complex fashion, and also that the changes in the deceleration time reflect the changes in LV diastolic function and loading conditions differently than the changes in E. Thus, an assessment of deceleration time may provide complementary information. Changes in other Doppler echocardiographic parameters, such as A, may also reflect changes in hemodynamic parameters differently, although the results of this study cannot show a clear relation between A and indexes of LV function or loading conditions. Pulmonary venous flow velocity patterns can also be observed with pulsed Doppler echocardiography, and have recently been shown to provide additional information which can not be obtained only by analysis of transmirtal flow velocity patterns. Thus, pulsed Doppler echocardiography appears to have clinical potential that deserves further investigations in assessing LV diastolic function and loading conditions.

REFERENCES


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