The Effect of Left Ventricular Chamber Compliance on Early Diastolic Filling during Coronary Reperfusion

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This study was designed to assess the changes in left ventricular (LV) diastolic filling and to evaluate the dynamic determinants of LV diastolic filling during coronary reperfusion after acute myocardial ischemia. We examined LV diastolic pressure-volume relations (D-PVRs) using the conductance catheter technique with a high-fidelity micromanometer, and the transmirtal flow using transesophageal pulsed Doppler echocardiography in 9 open-chest anesthetized dogs with the pericardium opened. We measured early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), the ratio of peak E to peak A (E/A), operational chamber compliance at the minimum LV pressure [(dV/VdP) nadir], and the time constant of LV relaxation (TC). Acute regional myocardial ischemia was produced by occluding the proximal portion of the left anterior descending coronary artery. Data were acquired at baseline, 10 min after acute myocardial ischemia, and after 15 and 90 min of reperfusion under left atrial pacing at 100 beats/min. During myocardial ischemia, D-PVRs shifted upward and rightward on the same curvilinear relationship compared with that at baseline (LV end-diastolic pressure (LVEDP) from 7.3 to 10.5 mmHg, LVEDV from 25 to 31 ml, both p<0.01), accompanied by a decrease in peak E and E/A (E from 41 to 25 cm/sec, E/A from 1.7 to 1.1, both p<0.01) and a prolongation of TC (from 25.4 to 30.3 msec, p<0.01). After coronary reperfusion, D-PVRs returned to baseline accompanied by an improvement in the peak E and E/A ratio. No significant changes in peak A were observed in any of the stages. There was no correlation between peak E and TC, however, a significant positive correlation was observed between peak E and (dV/VdP) nadir (r=0.76, p<0.01).

In conclusion, this study demonstrated that, using pulsed Doppler echocardiography, the improvement of diastolic filling after coronary reperfusion was based mainly on changes in early diastolic filling, and that LV operational chamber compliance at early diastole, rather than a LV relaxation property, might play an important role in determining early diastolic filling during coronary reperfusion.

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It is generally believed that brief myocardial ischemia is followed by sustained muscle hypofunction when coronary blood flow to the ischemic muscle is resumed. This phenomenon has been referred to as "stunned myocardium". While initial reports of stunned myocardium focused exclusively on systolic abnormalities of the previously ischemic myocardial wall, it has recently been emphasized that abnormalities in diastolic function of the heart might also play a

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Stunned myocardium
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role in producing cardiac dysfunction. The importance of left ventricular (LV) diastolic function in coronary heart disease and other heart diseases has been reported in both clinical and experimental studies. Abnormalities in diastolic function may precede abnormalities in systolic function in most cardiac diseases. In trying to understand these observations, we have learned that many factors can acutely affect LV filling and LV diastolic pressure-volume relations. However, changes in LV diastolic function during coronary reperfusion after acute myocardial ischemia have received little attention.

Therefore, in the present study, we investigated the time course of changes in LV diastolic function during coronary reperfusion in dogs with experimental acute myocardial ischemia. We also assessed the hemodynamic determinants of LV diastolic filling during coronary reperfusion, and propose that LV chamber compliance plays an important role in early diastolic filling.

MATERIALS AND METHODS

Nine healthy mongrel dogs weighing between 9 and 17 kg (mean 12.4 kg) were sedated with morphine sulfate (4 mg/kg body weight, sc) 30 min before induction of general anesthesia with α-chloralose (30 mg /kg, iv). After the induction of general anesthesia, intravenous infusion of α-chloralose (25 mg/kg per h) was continued until the end of the experiment. Autonomic reflexes were eliminated by intravenous administration of propranolol (2 mg). After endotracheal intubation, the dogs were ventilated with oxygen-enriched room air using a volume respirator (Harvard Apparatus, Bodine Electric Inc, Chicago, IL), and arterial blood gases were maintained within physiological limits. A left lateral thoracotomy was performed through the sixth intercostal space. The pericardium was opened and the heart was suspended in a pericardial cradle. After crushing the sinus node, the left atrial appendage was paced to keep the heart rate at 100 beats per min throughout the experiment. A 7F high-fidelity catheter-tip micromanometer with a side hole (PC484A, Millar Inc. Houston, Texas), was introduced into the LV through the left carotid artery. Another micromanometer was introduced into the left atrium (LA) through the LA appendage. The LV and LA pressure signals from the micromanometer were adjusted to match the pressure measured through the fluid channel of these catheters by means of a Statham P23ID transducer (Gould Inc, Oxnard, CA), and calibrated with a mercury manometer. The zero reference point was the right atrium. An 8-pole-electrode conductance (volume) catheter (Leycom, Netherlands) was introduced into the LV from the apex, guided by 2-dimensional transesophageal echocardiography, and positioned straight along the long axis with the distal tip beneath the subaortic valve. The catheter was connected to a stimulator/signal processor (Sigma 5, Leycom, Netherlands). This catheter placement required our examination of each segmental pressure-volume loop to confirm that each of the individual segments (sequential electrode pairs) were intracavitary and displayed normal counterclockwise pressure-volume resurgence. The conductance catheter technique, which is based on the fact that changes in blood conductance in the LV are proportional to changes in left ventricular volume, has been previously described in detail. A fluid-filled catheter was placed in the pulmonary artery to calibrate the volume signal. Calibration was performed by the hypertonic saline technique and saline was rapidly injected into the pulmonary artery with ventilation held at the end of expiration.

To measure regional LV segmental lengths, 2 pairs of miniature flat piezoelectric crystals (diameter 2 mm, frequency 5 MHz, Triton Technology, USA) were implanted at 2 sites in the endocardium of the LV: 1 in the anterior wall (ischemic region) adjacent to the left anterior descending coronary artery (LAD) and the other in the posterior wall (non-ischemic region) adjacent to the left circumflex coronary artery. The transmittal flow velocity was determined by transesophageal pulsed Doppler echocardiography. An Aloka (Japan) ultrasound system with a 5-MHz Doppler transducer was used. The sample volume was placed at the mitral valve orifice in the 4-chamber view. All Doppler echocardiographic recordings were made at a paper speed of 100 mm/sec using a strip chart
recorder with electrocardiogram and LA and LV pressure tracings.

Experimental Protocol

The experiments were started when LV pressure had reached a completely steady state after instrumentation. The ventilator was stopped at the end of expiration during data acquisition. The protocol consisted of 4 stages. First, a baseline recording was performed in the Control stage. After baseline recordings, the LAD was exposed proximal to the first major branch and an occluder was placed loosely around it. In the Ischemia stage, recordings were made after the LAD was occluded to produce 10 min of ischemia. The occluder was then completely released, and the stage at 15 min after reperfusion (REP-15) was examined. Finally, the same recordings were repeated at 90 min after reperfusion (REP-90).

Estimation of the percent risk area was performed as follows. After arrest by the intravenous injection of KCL, the hearts were removed and monas taylor blue was injected into the proximal LAD. Hearts were then fixed in formalin (10%) and sliced into 5 approximately 1-cm-thick short-axis sections. Each section was further divided into 16 equally spaced segments. Each segment was considered a risk area if it was stained with dye. The overall extent of the percent risk area was calculated as the sum total mass of all the dye-stained segments divided by the total left ventricular mass. Percent risk area was 35 ± 3% (n = 6) in this study.

Data Analysis

End-systole was defined as 20 msec before the peak negative first derivative of LV pressure (−dP/dt). End-diastole was defined as the rapid pressure upstroke (when LV + dP/dt exceeded 50 mmHg/sec). Electrocardiogram, LV and LA pressures, dP/dt of LV pressure, LV volume, and segment lengths in both the anterior and posterior wall were collected for 10 beats and simultaneously digitized at 5-msec intervals using an on-line A-D conversion (at 200 Hz) with custom software (the Codas, DATAQ Inc, Akron, Ohio) on a 32-bit microcomputer system (IBM PC/AT). The real-time pressure-volume loop was monitored with a 16-bit microcomputer system (PC-9801 EX, NEC, Japan). Data was stored on a removable hard disk for subsequent analysis.

We measured the following variables: LV peak systolic pressure (LVSP); LV end-diastolic pressure (LVEDP); LV minimum pressure (LVmin); LA pressure (LAP); LV end-diastolic volume (EDV); LV end-systolic volume (ESV); stroke volume (SV); ejection fraction (EF); LV peak positive and negative dP/dt; LV isovolumic pressure decay rate (TC) calculated by Weiss’s method; the maximum difference between LA and LV pressures during early diastole (max (LAP-LVP)); and LA pressure at the atrioventricular pressure crossover (MOP). The stiffness constant (K) and operational compliance at LV minimum pressure normalized by LV minimum volume (dV/dP) nadir were calculated as follows:

The exponential nature of the LV pressure (P)-volume (V) relation has been emphasized previously. Accordingly, the relation between diastolic pressure and volume in the present study was assumed to be exponential, and sequential data (from the point of the LV minimum pressure to end-diastole) were fit using an exponential equation: 

P = be^V

The least-squares method was used to calculate b and K, where K is the chamber stiffness constant (mm⁻¹), and b is the elastic constant. Volume distensibility (dV/dP) can be calculated as 1/KP at any given operating pressure if a value for K is obtained at each stage. Consequently, normalized operational compliance at the minimum pressure, (dV/dP) nadir, was obtained from K, LVSPmin and LV minimum volume. (dV/dP) nadir is a normalized index of distensibility at early diastole.

End-diastolic length (EDL), end-systolic length (ESL) and percent segment shortening of the LV (%SS = (EDL - ESL)/EDL × 100) were calculated at each steady state.

We measured the early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), and the ratio of E to A (E/A) using transesophageal pulsed Doppler echocardiography.

Statistical Analysis

All values are expressed as the mean ± standard deviation. A one-way analysis of variance (ANOVA) for repeated measures was used to test for significant differences.
between Control, Ischemia, REP-15 and REP-90. Fisher’s PLSD was used for multiple comparisons within the ANOVA. A p value of less than 0.05 was considered significant.

RESULTS

Influence of Reperfusion on Hemodynamic Indices

Hemodynamic data are summarized in Table I. No significant changes in heart rate or LVSP were observed throughout the study. LVEDP (from 7.3 to 10.5 mmHg, p<0.01), EDV (from 25 to 31 ml, p<0.01) and ESV (from 13 to 20 ml, p<0.01) were significantly increased and EF (from 51 to 36%, p<0.01) was significantly decreased in Ischemia compared to the respective Control values, and these data returned to the Control values after coronary reperfusion. During ischemia, LV peak positive and negative dP/dt were significantly decreased (+dP/dt: from 2014 to 1802 mmHg/sec, p<0.05; –dP/dt: from –1691 to –1848 mmHg/sec, p<0.05). At 15 min after reperfusion, LV negative dP/dt had returned to the baseline value, while LV peak positive dP/dt remained depressed at both 15 and 90 min after reperfusion (+dP/dt: 1754 and 1763 mmHg/sec, respectively, p<0.05).

Mean variables of segment length in non-ischemic and ischemic regions are shown in Table II. EDL in both non-ischemic and ischemic regions was significantly increased in Ischemia compared to the Control values. In REP-90, EDL in both ischemic and control regions returned to Control values.

### Table I: Hemodynamic Data at Control, During Ischemia, and After Reperfusion for 15 and 90 min

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Ischemia</th>
<th>Reperfusion 15 min</th>
<th>Reperfusion 90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>103 ± 7</td>
<td>103 ± 7</td>
<td>103 ± 7</td>
<td>103 ± 7</td>
</tr>
<tr>
<td>LVEDP (mmHg)</td>
<td>7.3 ± 2.5</td>
<td>10.5 ± 3.7*</td>
<td>7.8 ± 2.6*</td>
<td>7.7 ± 2.4*</td>
</tr>
<tr>
<td>LVSP (mmHg)</td>
<td>113 ± 22</td>
<td>112 ± 21</td>
<td>113 ± 19</td>
<td>110 ± 20</td>
</tr>
<tr>
<td>peak (+) dp/dt (mmHg/s)</td>
<td>2014 ± 532</td>
<td>1802 ± 405*</td>
<td>1754 ± 411*</td>
<td>1763 ± 533*</td>
</tr>
<tr>
<td>peak (−) dp/dt (mmHg/s)</td>
<td>−1828 ± 309</td>
<td>−1691 ± 226*</td>
<td>−1848 ± 256*</td>
<td>−1814 ± 420*</td>
</tr>
<tr>
<td>LVEDV (ml)</td>
<td>25 ± 10</td>
<td>31 ± 9*</td>
<td>26 ± 10*</td>
<td>26 ± 10*</td>
</tr>
<tr>
<td>LVESV (ml)</td>
<td>13 ± 6</td>
<td>20 ± 7*</td>
<td>15 ± 8*</td>
<td>15 ± 7*</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>13 ± 4</td>
<td>11 ± 3</td>
<td>11 ± 3</td>
<td>11 ± 3</td>
</tr>
<tr>
<td>EF (%)</td>
<td>51 ± 11</td>
<td>36 ± 3*</td>
<td>43 ± 11*</td>
<td>44 ± 10*</td>
</tr>
</tbody>
</table>

*p<0.05 vs baseline, *p<0.05 vs ischemia
Results are expressed as mean ± SD. HR: heart rate, LVEDP: left ventricular end-diastolic pressure, LVSP: left ventricular peak systolic pressure, (+) dp/dt: peak positive dp/dt, (−) dp/dt: peak negative dp/dt, LVEDV: left ventricular end-diastolic volume, LVESV: left ventricular end-systolic volume, SV: stroke volume, EF: left ventricular ejection fraction.

### Table II: Variables of LV Regional at Control, During Ischemia, and After Reperfusion for 15 and 90 min

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Ischemia</th>
<th>Reperfusion 15 min</th>
<th>Reperfusion 90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>control region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDL (mm)</td>
<td>10 ± 0</td>
<td>10.94 ± 0.32*</td>
<td>10.27 ± 0.03*</td>
<td>10.15 ± 0.34*</td>
</tr>
<tr>
<td>%SS (%)</td>
<td>20.1 ± 4.9</td>
<td>24.8 ± 4.2*</td>
<td>26.1 ± 4.1*</td>
<td>19.7 ± 4.3*</td>
</tr>
<tr>
<td>ischemic region</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDL (mm)</td>
<td>10 ± 0</td>
<td>11.93 ± 1.3*</td>
<td>10.88 ± 0.75*</td>
<td>10.50 ± 0.64*</td>
</tr>
<tr>
<td>%SS (%)</td>
<td>26.6 ± 10</td>
<td>−5.6 ± 2.9*</td>
<td>11.7 ± 7.6*</td>
<td>21.3 ± 9.2*</td>
</tr>
</tbody>
</table>

*p<0.05 vs baseline, *p<0.05 vs ischemia
Results are expressed as mean ± SD. EDL: End-Diastolic Length, SS: Segment Shortening.
TABLE III VARIABLE OF LV DIASTOLIC FUNCTION AT CONTROL, DURING ISCHEMIA, AND AFTER REPERFUSION FOR 15 AND 90 MIN

<table>
<thead>
<tr>
<th></th>
<th>control</th>
<th>ischemia</th>
<th>15 min</th>
<th>90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (msec)</td>
<td>25.4 ± 2.7</td>
<td>30.3 ± 3.8</td>
<td>27.3 ± 3.3&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>27.9 ± 4.7&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>MOP (mmHg)</td>
<td>7.2 ± 1.7</td>
<td>9.0 ± 2.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.6 ± 1.9&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7.8 ± 1.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>LVPmin (mmHg)</td>
<td>4.3 ± 2.3</td>
<td>6.6 ± 3.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.7 ± 2.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.6 ± 2.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>max (LAP-LVP)</td>
<td>2.2 ± 0.6</td>
<td>1.6 ± 0.7</td>
<td>1.8 ± 0.5</td>
<td>2.0 ± 0.7&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>K</td>
<td>0.112 ± .113</td>
<td>0.091 ± .038</td>
<td>0.088 ± .037</td>
<td>0.0857 ± .058</td>
</tr>
<tr>
<td>(dV/VdP) nadir</td>
<td>0.363 ± .434</td>
<td>0.105 ± .057&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.275 ± .328&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.301 ± .329&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>p<0.05 vs baseline, <sup>b</sup>p<0.05 vs ischemia

Result are expressed as mean ± SD. TC: time constant, MOP: left atrial pressure at the atrioventricular pressure crossover, LVPmin: left ventricular minimum pressure, max (LAP-LVP): maximal atrioventricular pressure difference during early diastole, K: stiffness constant, (dV/VdP) nadir: normalized operational compliance at left ventricular minimum pressure.

Fig.1. Examples of diastolic LV pressure-volume relations at 4 stages (Control, Ischemia, REP-15 and REP-90). Note the upward and rightward shift of the relation during acute ischemia. After coronary reperfusion, the relation returned toward the control values.

Open circles=control; closed circles=acute ischemia; open triangle=after 15 min of reperfusion; closed triangle=after 90 min of reperfusion.

%SS of the LV in the non-ischemic region was significantly increased in Ischemia compared with the Control value, and was significantly decreased (vs Ischemia) in REP-15 and REP-90. In contrast, %SS of the LV in the ischemic region was significantly decreased in Ischemia compared with the Control value, and was significantly increased in both REP-15 and REP-90 (vs Ischemia).

Table III shows mean values of LV diastolic hemodynamic data. During ischemia, TC was prolonged (from 25.4 to 30.3 msec, p<0.01). Although this value decreased significantly in REP-15 compared with Ischemia, it did not return to the Control value even after 90 min of reperfusion. MOP and LVPmin were both significantly increased, and max (LAP-LVP) and (dV/VdP) nadir were both significantly decreased in Ischemia compared with the respective Control values. These data returned to the Control values after reperfusion. No significant changes in K were observed in any of the stages.

Changes in Diastolic LV Pressure-Volume

TABLE IV  PARAMETERS OF TRANSMITRAL FLOW BY TRANSSESOPHAGEAL ECHOCARDIOGRAPHIC DATA

<table>
<thead>
<tr>
<th></th>
<th>control</th>
<th>ischemia</th>
<th>15 min</th>
<th>90 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>peak E (cm/sec)</td>
<td>41 ± 6</td>
<td>25 ± 6*</td>
<td>32 ± 7*</td>
<td>36 ± 7*</td>
</tr>
<tr>
<td>peak A (cm/sec)</td>
<td>28 ± 8</td>
<td>28 ± 7</td>
<td>26 ± 7</td>
<td>25 ± 6</td>
</tr>
<tr>
<td>E/A</td>
<td>1.7 ± 0.7</td>
<td>1.1 ± 0.4*</td>
<td>1.3 ± 0.3*</td>
<td>1.6 ± 0.5*</td>
</tr>
</tbody>
</table>

*p<0.05 vs baseline,  *p<0.05 vs ischemia
Results are expressed as mean ± SD. peak E: early diastolic peak flow velocity, peak A: late diastolic peak flow velocity.

Transmitral Flow by TEE

Fig.2. Examples of tracings of transmitral flow assessed by pulsed Doppler echocardiography during acute ischemia and reperfusion.
During acute ischemia, E was decreased and A was increased. After 90 min of reperfusion, E and A returned to baseline values.
E = early diastolic peak flow velocity, A = late diastolic peak flow velocity.

Relations (D-PVRs)

Fig.1 shows representative LV diastolic pressure-volume relations (D-PVRs) at baseline, during ischemia and after reperfusion. During ischemia, LVEDP and EDV increased (δLVEDP, 3.2 ± 3.7 mmHg, δEDV, 6 ± 9 ml, both p<0.01 vs baseline), and D-PVRs shifted up and to the right compared with the baseline on the same curvilinear relationship. However, after 15 and 90 min of reperfusion, D-PVRs had shifted back down and to the left.

Influence of Reperfusion on Transmitral Flow

Transmitral flow assessed by transesophageal Doppler echocardiographic analysis is summarized in Table IV. A typical example of transmitral flow is shown in Fig. 2. Cases of mitral regurgitation caused by papillary muscle dysfunction were eliminated from our present study. E was significantly decreased in Ischemia (from 41 to 25 cm/sec, p<0.01), but then returned to the baseline value in REP-90. In contrast, no significant changes in A were observed in any of the stages. Like E, the E/A ratio was significantly decreased in Ischemia, and returned to the baseline value in REP-90.

Correlation Between Early Diastolic Filling and Hemodynamic Indices

To assess the factors which determine E during coronary reperfusion, correlations between E and the following hemodynamic indices were examined by simple linear regression analysis: TC, LVPmin, and operational chamber compliance at the time of minimum LV pressure and at peak E. Each parameter

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was normalized by dividing with the control value (% change = stage value/control value). Fig. 3 (lower panel) shows a significant positive correlation between the change from baseline for E (%peak E) and the change from baseline for (dV/Vdp) nadir [% (dV/Vdp) nadir] (r=0.76, p<0.01). However, as shown in Fig. 3 (upper panel), there was no significant correlation between %peak E and the change from baseline for TC (%TC). In addition, %peak E was also correlated with the change from baseline for the LV operational chamber compliance at the time of E (r=0.62, p<0.01) and LVPmin (r=0.57, p<0.01).

**DISCUSSION**

1. **Diastolic LV Pressure-Volume Relations**

**During Acute Ischemia and Reperfusion**

It has been documented that the LVEDP is increased by regional ischemia. Several mechanisms have been proposed to explain this elevated diastolic pressure. In both pacing-induced angina and pacing-induced ischemia in experimental animals with critical coronary stenosis, the diastolic LV pressure-volume and pressure-length relationships were shifted upward. However, these results did not take into account pericardial disturbance, which may affect diastolic LV pressure-volume relationships. The diastolic properties of the LV are determined not only by the properties of the LV itself, but also potentially by the properties of the surrounding pericardium. Therefore, the stiffness of the pericardium may be an important determinant of the pressure-volume relationship. In addition, the interaction of left and right ventricular pressures through the pericardium may alter diastolic LV properties.

In the present study, in which there was no pericardial disturbance LVEDP and LVEDV were both increased during ischemia, and the D-PVRs shifted up and to the right on the same curvilinear relationship compared with the baseline values. The mechanism for this upward and rightward shift in acute ischemia may involve an increase in diastolic pressure, primarily resulting from increased diastolic volume, as the heart uses the Frank-Starling mechanism in an attempt to maintain cardiac output in the face of impaired overall systolic contractile performance. After reperfusion, D-PVRs shifted back down and to the left. No significant changes in the stiffness constant K were observed in any of the stages. Therefore, during ischemia and reperfusion, D-PVRs without pericardial disturbance may follow the same curvilinear relationship.

2. **Transmitral Flow Waveforms During Acute Ischemia and Reperfusion**

Recent studies using contrast ventriculography have suggested that diastolic LV abnormalities at rest may be improved after coronary bypass surgery (coronary angioplasty). In the present study, we examined whether transmitral flow velocity waveforms are influenced by changes in LV diastolic properties during coronary reperfusion after...
acute ischemia. The transmural flow velocity waveforms with diastolic dysfunction in coronary artery disease usually show a decreased early diastolic filling velocity, a slower deceleration of the early diastolic filling wave and an increased filling velocity at atrial contraction. However, only a few studies have investigated Doppler parameters after coronary reperfusion.

In our present study, E was significantly decreased during acute myocardial ischemia, and E returned gradually to the baseline value at 90 min after reperfusion. Similarly, E/A was also significantly decreased during acute ischemia, and returned to the baseline value in REP-90. These changes in E and E/A might be due to the improvement of LV diastolic properties. The results of the present study confirm previous clinical observations in patients with abnormal LV filling during PTCA, as evaluated from pulsed Doppler measurements of transmural velocity waveforms. Thus, monitoring E and E/A may be clinically useful for predicting whether or not coronary arteries are revascularized during ischemia.

3. Influence of Operational Chamber Compliance and the Time Constant of LV Relaxation on Early Diastolic Filling

In our study, no significant change in the LV stiffness constant was observed, while operational compliance changed significantly and correlated with the change in early diastolic filling. Accordingly, operational compliance may have a greater effect on diastolic filling than the LV stiffness constant.

Although the relationship between LV chamber compliance and TC has been examined in both clinical and experimental studies, it is still not fully understood. We found that, during coronary occlusion and reperfusion, early diastolic filling was significantly correlated with LV operational chamber compliance, especially at the mini LV pressure, but not with TC, which is independent of LV preload. The present results indicate that LV chamber compliance is a more important determinant of early diastolic filling than TC. This raises the question of why early diastolic filling did not correlate with TC. One possible explanation involves the differences in the time-course of recovery between operational chamber compliance and TC after coronary reperfusion.

In the present study, although both LV operational chamber compliance and TC changed with acute ischemia, only LV operational chamber compliance returned to the baseline value at 90 min after reperfusion. Many earlier studies have examined the time-course of the recovery of LV contractile function after various durations of ischemia and Paulus et al presented evidence regarding diastolic function which suggested that impaired calcium sequestration by sarcoplasmic reticulum in ischemic myocardium may be the mechanism which causes increased diastolic muscle stiffness. This suggests the persistence of postischemic diastolic abnormalities, long after the complete recovery of systolic function.

Another possibility is that TC and chamber compliance may change independently during coronary reperfusion after acute myocardial ischemia. The independence of the time constant of LV relaxation and chamber compliance has been reported in experimental studies using caffeine or and by comparing hypoxia and ischemia. These previous studies have suggested that TC might not change in parallel with chamber compliance during coronary reperfusion.

In conclusion, this study showed that the improvement of diastolic filling during coronary reperfusion was reflected mainly by changes in E and E/A, and that the improvement in early diastolic filling during coronary reperfusion after acute ischemia was determined mainly by the recovery of LV operational chamber compliance during LV early diastole, especially at minimum LV pressure.

Clinical Implications

Early thrombolytic therapy is now a standard modality for the treatment of patients with acute myocardial ischemia or infarction. The advent of Doppler echocardiography has allowed the non-invasive measurement of transmural flow velocities, and we have been able to easily evaluate diastolic properties. The present results suggest that by measuring LV early diastolic filling, especially changes in E and E/A of transmural flow, the effectiveness of coronary reperfusion may be evaluated non-invasively in a clinical setting.
Experimental Limitations

Several limitations should be considered. In the present study, myocardial viscoelasticity and engorgement of the coronary vasculature might play some role in determining the LV pressure-volume relation during diastole. Since autonomic reflex blockade might be insufficient, minor changes in contractility caused by baroreflex-mediated alterations in sympathetic discharge may not be able to be excluded.

Mitrail regurgitation may be caused by ischemia. However, mitrall regurgitation was not detected by transesophageal Doppler echocardiography in any of the dogs during ischemia induced by LAD occlusion.

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