Diastolic Myocardial Wall Stiffness and Ventricular Relaxation during Partial and Complete Coronary Occlusions in the Conscious Dog


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SUMMARY. Seven dogs were instrumented with a left ventricular micromanometer, pairs of ultrasonic crystals to measure wall thickness in normal and ischemic regions, as well as both short and long axes of the left ventricle; and cuff occluders were placed around the left circumflex coronary artery and the inferior vena cava. Left ventricular volume, mass, circumferential wall stress, midwall strain, and strain rate were calculated at rest, at 1 and 2 minutes of partial and complete coronary occlusion, and 1, 2, and 10 minutes after release of partial and complete coronary occlusions. Reference values at zero pressure were obtained during inferior vena cava occlusion. Relaxation was assessed from the exponential fall of left ventricular pressure and from the exponential fall of left ventricular stress (myocardial relaxation) of the control and the ischemic wall regions. Passive diastolic pressure, the left ventricular short axis increased from 35 to 37 mm during complete coronary occlusion, but remained unchanged during partial occlusion. One minute after release of partial and complete occlusion, left ventricular short axis decreased significantly compared to control and returned to control 10 minutes after release of coronary occlusion. The rate of ventricular pressure fall increased during complete coronary occlusions, whereas myocardial relaxation of the control wall region increased and of the ischemic wall region decreased during both partial and complete occlusions. Passive diastolic wall stiffness increased significantly from 22 to 27 (23% increase) at 2 minutes of complete coronary occlusion, but was unchanged during partial occlusion. One minute after release of both partial and complete coronary occlusion, wall stiffness decreased significantly. The diastolic pressure-volume relationship of the left ventricle was shifted significantly upward during complete coronary occlusion without inferior vena cava occlusion, but no shift was observed during partial occlusion or in the experiments with inferior vena cava obstruction. It is concluded that: (1) myocardial wall stiffness is normal during coronary stenosis when systolic wall thickening is reduced but maintained, whereas it is increased during complete coronary occlusion when there is systolic wall thinning. (2) Resting muscle length at zero diastolic pressure is increased during complete coronary occlusion or ischemia. (3) Regional relaxation parameters show a decrease in the rate of relaxation of the ischemic wall but an increase in that of the nonischemic wall during partial and complete coronary occlusions. (4) The upward shift of the diastolic pressure-volume curve during complete coronary occlusion is prevented by inferior vena cava obstruction and could be due to reductions in right ventricular pressure and volume (ventricular interaction).

(Myocardial ischemia is accompanied by regional wall motion abnormalities, a decrease in left ventricular systolic function, and an increase in left ventricular end-diastolic pressure and volume or dimensions (Parker et al., 1969; McCans and Parker, 1973; Theroux et al., 1974; Mann et al., 1979). The effects of acute ischemia on the diastolic properties of the left ventricle have been studied in patients with coronary heart disease (Dwyer, 1970; Barry et al., 1974; Grossman and McLaurin, 1976; Mann et al., 1979), and the increase in left ventricular end-diastolic pressure appears to be higher than would be expected, since the end-diastolic volume shows only a small increase or no change (Dwyer, 1970; Barry et al., 1974), suggesting increased chamber stiffness. In these clinical studies and a recent experimental study (Serizawa et al., 1980), a parallel upward shift of the diastolic pressure-volume curve was also observed during acute myocardial ischemia. This shift occurred even in experiments in which the pericardium was removed (Serizawa et al., 1980). In other experimental studies, performed without the pericardium, left ventricular chamber stiffness during acute coronary occlusion or ischemia has been reported to be unchanged (Palacios et al., 1976) or to decrease (Forrester et al., 1972; Tyberg et al., 1974; Wong et al., 1978). Previous studies in this laboratory, both in open-chest (Theroux et al., 1974) and conscious dogs (Theroux et al.,...
1976), have indicated that the regional diastolic pressure-length relation in the ischemic zone is shifted to the right and steepened during acute coronary occlusion, suggesting increased segment stiffness. Hood and coworkers (1970) have described decreased chamber stiffness several days after coronary occlusion, and decreased segment stiffness has also been reported at that time in conscious dogs (Theroux et al., 1977).

Several mechanisms which might contribute to the increases in ventricular end-diastolic pressure observed during acute myocardial ischemia have been proposed, such as altered diastolic myocardial stiffness, impaired left ventricular relaxation, changes in coronary artery perfusion, alterations of intrapericardial pressure, and altered right ventricular loading conditions (Templeton et al., 1972; Grossman and McLaurin, 1976; Glantz and Parmley, 1978; Ross, 1979; Mirsky and Rankin, 1979). The purpose of the present study was to examine in detail the sequential effects of both partial and complete coronary occlusions on diastolic myocardial stress-strain relations, left ventricular relaxation, and the diastolic pressure-volume properties of the left ventricle in a conscious animal preparation in which the pericardium was removed. The preparation also permitted determination of the zero pressure intercept of the diastolic pressure-volume relation, and observations on the ventricular pressure-volume curve in the presence or absence of obstruction to right and left heart filling.

Methods

Seven mongrel dogs weighing 16–44 kg (average 30.3 kg) underwent left thoracotomy in the 5th intercostal space under sodium pentobarbital anaesthesia (25 mg/kg, iv). The pericardium was widely opened, a high-fidelity micromanometer (Koenigsberg P-22) was inserted into the left ventricle through a stab incision at the ventricular apex, and a Tygon tube was also positioned in the left ventricular chamber through a stab incision at the ventricular apex, and a Tygon tube was also positioned in the left ventricular chamber using pairs of ultrasonic crystals (Rankin et al., 1976). Left ventricular wall thickness was measured near the anterior and posterior epicardial walls to obtain the maximum transverse external diameter in the plane of the left ventricular short axis. A pair of epicardial wires and tubing were passed subcutaneously to the back of the dog and brought through the skin between the scapulae.

Experimental Protocol

Experiments were begun 10–14 days postoperatively, with the dog resting quietly on its right side on the floor during spontaneous sinus rhythm. Control recordings of pressure and dimensions were made for 5–10 minutes. An IVC obstruction then was performed over a period of 60 seconds to obtain zero pressure during diastolic filling. The degree of IVC obstruction was adjusted by gradually inflating the water-filled cuff occluder until the lowest diastolic pressure reached zero mm Hg (Fig. 1). Usually, mild IVC obstruction was required during control to obtain zero pressure, whereas—during coronary occlusion—complete obstruction was performed to obtain zero pressure. Partial coronary occlusion of the left circumflex coronary artery was induced by gradually inflating the water-filled hydraulic occluder with a screw-driven syringe (Theroux et al., 1976). The partial occlusion was fixed when systolic thickening of the ischemic wall had decreased to a level about 40% of control. After a stable partial coronary artery constriction had been achieved (average time 3.2 minutes; range 1.0 to 5.8 minutes), measurements of pressure and dimensions were performed for 2.5 minutes with IVC obstructions lasting 30 seconds at 1 and 2 minutes of partial coronary occlusion. Then the coronary cuff was completely released, and the subsequent reactive hyperemia was recorded for 10 minutes with IVC obstruction at 1, 2, and 10 minutes. After a second control run of 5 to 10 minutes, the left circumflex coronary artery was completely and abruptly occluded by the cuff occluder, and pressure and dimension measurements were performed for 2.5 minutes, with IVC obstructions at 1 and 2 minutes of complete coronary occlusion. Then the occluder was again completely released and reactive hyperemia was recorded for 10 minutes with IVC obstructions at 1, 2, and 10 minutes (Fig. 1).

For the assessment of the hemodynamic effects of IVC obstruction, the entire experiment with partial and complete coronary occlusion was repeated a few days after the first experiment without IVC obstruction. From 18 to 63 days (average 45 days) postoperatively, the experiment was terminated by an overdose of sodium pentobarbital, iv, and autopsies were performed to verify the position of the ultrasonic crystals. In each experimental animal, the crystals of each pair were confirmed to be in proper alignment. The epicardial crystals of the long and short left ventricular axes were found to be properly seated in all dogs studied, and the inner wall thickness crystals of both control and ischemic walls were found to lie within the inner one-third of the left ventricular wall in every dog reported. An eighth animal that was instrumented was excluded from the study because the inner wall thickness crystal of the ischemic region was diagonally positioned in the middle third of the left ventricular wall. No infarction or scar was visible on gross examination of the left ventricle in any of the seven dogs studied. After excision of the adjacent right ventricular muscle, valvular tissue, and fat, the left ventricle and septum were weighed in all dogs.

Data Analysis

All data were recorded during the experiment on an eight-channel Brush chart recorder and a Hewlett-Packard magnetic tape recorder (model HP 3955 D). The taped data
CONTROL RUN  |  1 MIN. COR. OCCL. |  1 MIN. AFTER COR. OCCL.

**LV PRESSURE**

- CONTROL WALL (mm)
- ISCHEMIC WALL (mm)
- LONG AXIS (mm)
- SHORT AXIS (mm)
- PLEURAL PRESSURE (mmHg)

**Calculations**

All analog data were digitized at a 200 Hz rate. Calibrations were performed for each channel separately, and at the end of the calibration procedure the left ventricular high-fidelity pressure was matched to the left ventricular catheter pressure to correct for drift. This pressure match was repeated several times during each experiment to exclude changes in diastolic pressure due to drift of the pressure gauge. After the calibration, 10–20 heart cycles were digitized and averaged to compensate for small beat-to-beat variations in pressure and dimensions. Peak dP/dt served as a reference signal for the computer, and all beats 100 msec longer or shorter than the mean RR-interval were rejected. It is obvious that variations in heart rate during the digitization procedure might have affected the systolic and diastolic portions of the cardiac cycle. However, the average change in heart rate during the digitization procedure was usually small (Table 1) because only stable runs were selected for the digitization procedure. The averaging interval was 5 msec, and all data of the averaged beats stored on a floppy disc for further computation, display on an oscilloscope, and plotting. The averaged beats used for
The mathematical analysis of left ventricular systolic and diastolic function included between 11 and 18 beats for the two runs with partial and complete coronary occlusion (Table 1). The changes in pleural pressure during cardiac cycles were minimal after beat averaging and ranged between -0.3 and -1.1 mm Hg for both studies (Fig. 1). Since the changes in pleural pressure were small and statistically not significantly different, pleural pressure was not subtracted from left ventricular pressure to obtain transmural left ventricular pressure. Thus, the reference data in the present paper refer to an intracavitary pressure of zero mm Hg, as widely used in clinical applications of diastolic function calculations (Forrester et al., 1972; McCans and Parker, 1973).

The following variables were calculated in each animal at 5-msec intervals:

- **LV internal long axis:** $L = L_{\text{ext}} - h_v$ (1.1)
  
  (Rankin et al., 1976)

- **LV internal short axis:** $S = S_{\text{ext}} - (h_v + h_h)$

- **LV volume:** $V = \frac{\pi}{6} L S^2$ (Dodge et al., 1966)

- **LV muscle mass:** $M = \left(\frac{\pi}{6} L_{\text{ext}} S_{\text{ext}} - \text{EDV}\right) + 1.05$
  
  (Rackley et al., 1964)
Circumferential wall stress using

Control wall: $\sigma = \frac{P \cdot S}{2h_c} \left(1 - \frac{S^2}{L^2}\right)$

(Mirsky, 1976, 1979)

Ischemic wall: $\sigma = \frac{P \cdot S}{2h} \left(1 - \frac{S^2}{L^2}\right)$

Midwall circumference using

Control wall: $l_c = \pi (S + h_c)$

Ischemic wall: $l_c = \pi (S + h_i)$

Midwall strain using

Control wall: $\varepsilon_c = \ln \frac{l_c}{l_{o}}$

Ischemic wall: $\varepsilon_i = \ln \frac{l_i}{l_{o}}$

Midwall strain rate, which was digitally differentiated from midwall strain using a least square procedure as proposed by Savitzky and Golay (1964):

Control wall: $\dot{\varepsilon}_c = \frac{d\varepsilon_c}{dt}$

Ischemic wall: $\dot{\varepsilon}_i = \frac{d\varepsilon_i}{dt}$

where $L$: left ventricular long axis (mm); $L_e$: external left ventricular long axis (mm); $h_c$: control wall thickness (mm); $S$: left ventricular short axis (mm); $S_e$: external left ventricular short axis (mm); EDV: left ventricular end-diastolic volume (ml); $P$: left ventricular pressure (mm Hg); $h_i$: ischemic wall thickness (mm); $l_c$: left ventricular midwall circumference using $h_c$ (mm); $l_i$: left ventricular midwall circumference using $h_i$ (mm); $l_j$: at zero diastolic pressure (mm); the units of the circumferential wall stress data are g/cm².

It is clear that the control wall or ischemic wall segment does not extend entirely around the left ventricle, especially during myocardial ischemia; for theoretical reasons, however, left ventricular wall stress ($\sigma$), midwall circumference ($l$), midwall strain ($\varepsilon$), and midwall strain rate ($\dot{\varepsilon}$) were determined, using the control or the ischemic wall thickness to evaluate wall stress and strain of the control and ischemic region during control and myocardial ischemia.

Validation of the left ventricular muscle mass calculation was performed by comparing the calculated muscle mass and that measured at autopsy. The correlation between these two variables was excellent (correlation coefficient 0.979), although a slight underestimation of the true left ventricular mass was found at small masses and a slight overestimation at large masses (calculated muscle mass = 1.033 X measured mass -14.20).

Left ventricular systolic function was assessed by the degree of systolic thickening of the control and ischemic walls, the extent of shortening of the left ventricular long and short axes, and the left ventricular ejection fraction defined as the ratio of the systolic stroke volume to the end-diastolic volume multiplied by 100 (Dodge et al., 1966).

Left Ventricular Relaxation

The isovolumic relaxation phase was defined as the interval between end-systole and the time at which left ventricular pressure on the descending portion of the pressure curve corresponded to the left ventricular end-diastolic pressure (Kumada et al., 1979). From this interval, the time constants of the fall in left ventricular pressure ($T$) and the ischemic ($T_i$) and nonischemic wall stress ($T_c$) were calculated from pressure and $-dP/dt$ data at 5-msec intervals using the equation $dP/dt = a \cdot P + b$ (Raff and Glantz, 1981) and $da/dt = a' \cdot a + b'$ and $da/dt = a'' \cdot a + b''$, respectively.* All pressure ($P$) and stress data of the control ($\sigma_c$) and the ischemic wall region ($\sigma_i$) were fitted to a linear regression equation between LV pressure and $-dP/dt$, and between LV stress and $-dP/dt$. The regression analysis was started 5 msec after maximum $dP/dt$ (dP/dt min) and 5 msec after $da/dt_{min}$ as originally described by Craig and Murgo (1980) and Weisfeldt et al. (1980). $dP/dt_{min}$ and $da/dt_{min}$ usually occurred at the same time, since the left ventricular pressure is the main determinant of the left ventricular wall stress during isovolumic relaxation when dimensional changes are small. The average correlation coefficient was 0.99 (range: 0.96-1.00) for $T$, 0.96 (range: 0.91-0.99) for $T_c$, and 0.96 (range: 0.91-1.00) for $T_i$ (Fig. 2).

Left Ventricular Diastolic Function

Diastolic myocardial function was evaluated by fitting the diastolic stress-strain data from zero pressure to end-diastole to a viscoelastic model incorporating a parallel elastic and a parallel viscous element (Rankin et al., 1977; Hess et al., 1979; Edwards et al., 1981):

$$
\sigma = \alpha (e^\beta - 1) + \eta \dot{\varepsilon}
$$

where $\alpha$ = the nonlinear elastic constant, $\beta$ = the constant of passive myocardial wall stiffness, and $\eta$ = the constant of myocardial viscosity. Diastolic strain was normalized to minimum diastolic length at zero pressure.

The viscoelastic stress-strain model was used in the present study because it had been demonstrated (Rankin et al., 1977) that deviation from the monoexponential stress-strain relationship occurs during rapid filling in early diastole and with changes in muscle fiber length (Pouleur et al., 1979). For calculation of the nonlinear elastic constants, $a$, $\beta$, and $\eta$, a computer program for a nonlinear curve fit (Metzler et al., 1974) was used. The best curve fit was determined by an iteration procedure. The number of performed iterations is given in Table 4.

Statistics

Statistical comparisons (Hammond-software, STATS-11 statistical package, 1980) of data during control, ischemic, and reperfusion conditions were performed using an analysis of variance for repeated measures (Winer, 1971). In all tables the significant differences between the control group and the other five groups are given. Data are reported as mean values ± SEM.

Results

Original tracings illustrating the variables measured are shown in Figure 1. Changes in cardiac dimensions and pressure during partial and complete coronary occlusion are summarized in Table 1. Heart rate, left ventricular end-diastolic and peak systolic pressures, and systolic thickening of the control wall remained normal during partial coronary occlusion, whereas, during complete coronary occlusion, heart rate increased significantly. Systolic wall thickening in the
ischemic zone decreased significantly from 28% to 10% during partial and from 28% to -4% (systolic thinning) during complete coronary occlusion. Left ventricular ejection fraction fell from 54% to 43% during partial and from 53% to 33% during complete occlusion. Left ventricular end-diastolic thickness in the ischemic region increased significantly after release of partial and complete coronary occlusion. Pleural pressure showed only minor changes during all experiments after beat averaging (Table 1; Fig. 1).

The left ventricular end-diastolic short axis remained unchanged during partial and complete coronary occlusion, but decreased significantly after release of partial and complete occlusion (Table 1). Systolic shortening of the left ventricular short axis decreased significantly during partial or complete coronary occlusions. The left ventricular long axis showed no significant changes during both partial and complete coronary occlusions.

The left ventricular end-diastolic volume did not change significantly during partial and complete coronary occlusion, and decreased significantly after release of partial and complete coronary occlusions. The left ventricular ejection fraction returned to normal after release of both occlusions.

**Left Ventricular Relaxation (Table 2)**

\( \frac{dP}{dt_{\text{min}}} \) decreased significantly during partial coronary occlusion and remained depressed 1 and 2 minutes after release of partial coronary constriction, whereas the changes during complete coronary occlusion were not statistically significant. The time constant of LV pressure fall (T_p) did not change significantly during partial occlusion, but increased significantly during complete occlusion and returned to normal during reperfusion (Fig. 2).

The control and the ischemic wall thickness showed significantly different behavior during isovolumic relaxation, when the control wall thickness showed wall thinning, and the ischemic wall thickness, wall thickening (Table 2), during acute myocardial ischemia (Kumada et al., 1979). The time constants of the left ventricular stress fall for both the control wall (T_c) and the ischemic wall (T_i) regions are shown in Table 2. The time constant of LV stress fall of the control wall region (T_c) decreased slightly but not significantly during partial and complete coronary occlusions, whereas the time constant of LV stress fall of the ischemic wall region (T_i) increased slightly, but also insignificantly, during partial as well as during complete coronary occlusion (Fig. 2).

**Diastolic Reference Values (Table 3)**

Wall thickness at zero pressure remained unchanged in the control zone during partial and complete coronary occlusions, but increased significantly, 1, 2, and 10 minutes after release of complete coronary occlusion. Wall thickness at zero pressure in the ischemic zone did not change during partial coronary occlusion, but decreased significantly during complete coronary occlusion, and it increased significantly after release of both partial and complete coronary occlusion (reactive hyperemia). This increase was observed even 10 minutes after release of both partial and complete coronary occlusions. Control wall thickness also showed a significant increase up to 10 minutes after complete coronary occlusion.

The left ventricular short axis at zero pressure remained normal during partial occlusion but increased significantly during complete coronary occlusion (Fig. 3). One minute after release of both occlusions, the left ventricular short axis decreased signifi-
cantly. However, the decrease in short axis length lasted up to 10 minutes after complete occlusion, whereas the short axis was back to control in 2 minutes after partial occlusion (Fig. 3). The left ventricular long axis at zero pressure remained normal during partial and complete occlusion, but decreased significantly 1 minute after release of complete occlusion.

The left ventricular diastolic volume at zero pressure remained unchanged during partial occlusion (Fig. 3), but increased significantly during complete coronary occlusion. One minute after release of both occlusions (Fig. 2), the diastolic volume at zero pressure decreased significantly and was back to control 10 minutes after partial, but was still decreased 10 minutes after complete occlusion.

The calculated left ventricular muscle mass remained constant during partial and complete coronary occlusion.

### Table 2

<table>
<thead>
<tr>
<th>Relaxation Parameters</th>
<th>Partial coronary occlusion</th>
<th>Complete coronary occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>max dp/dt (mm Hg/sec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>min dp/dt (mm Hg/sec)</td>
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<td></td>
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<tr>
<td>T (msec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (msec)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (msec)</td>
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<tr>
<td>C</td>
<td>3135 ± 180</td>
<td>2397 ± 157</td>
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<td>C₁</td>
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<tr>
<td>C₂</td>
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<tr>
<td>P₁</td>
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<tr>
<td>P₂</td>
<td>2813 ± 177†</td>
<td>1841 ± 11.3‡</td>
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<td>P₃</td>
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<tr>
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<tr>
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<tr>
<td>P₁</td>
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</tr>
<tr>
<td>P₂</td>
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<td>2119 ± 205</td>
</tr>
<tr>
<td>P₃</td>
<td>2567 ± 125†</td>
<td>1919 ± 123†</td>
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</table>

C = control; C₁ = 1 minute of coronary occlusion; C₂ = 2 minutes of coronary occlusion; P₁ = 1 minute after coronary occlusion; P₂ = 2 minutes after coronary occlusion; P₃ = 10 minutes after coronary occlusion; max. dp/dt = maximal rate of left ventricular pressure rise; min. dp/dt = maximal rate of left ventricular pressure fall (mm Hg/sec); T = time constant of left ventricular pressure fall (mm Hg/sec); T₀ = time constant of left ventricular control wall stress fall; T₀ = time constant of left ventricular ischemic wall stress fall.

* P < 0.05; †P < 0.01; ‡P < 0.001; given are mean values ± 1 SEM.

### Table 3

<table>
<thead>
<tr>
<th>Reference Values</th>
<th>Partial coronary occlusion</th>
<th>Complete coronary occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>11.7 ± 1.0</td>
<td>11.8 ± 1.0</td>
</tr>
<tr>
<td>C₁</td>
<td>11.8 ± 1.0</td>
<td>11.7 ± 1.0</td>
</tr>
<tr>
<td>C₂</td>
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<td>13.4 ± 1.3</td>
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<tr>
<td>P₁</td>
<td>12.0 ± 1.0</td>
<td>15.3 ± 1.5‡</td>
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<tr>
<td>P₂</td>
<td>11.8 ± 1.0</td>
<td>14.7 ± 1.3†</td>
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<tr>
<td>P₃</td>
<td>12.1 ± 1.1</td>
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<td>12.0 ± 1.2</td>
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<tr>
<td>P₃</td>
<td>11.9 ± 1.1*</td>
<td>14.3 ± 1.3*</td>
</tr>
</tbody>
</table>

C = control; C₁ = 1 minute of coronary occlusion; C₂ = 2 minutes of coronary occlusion; P₁ = 1 minute after coronary occlusion; P₂ = 2 minutes after coronary occlusion; P₃ = 10 minutes after coronary occlusion; CWW = left ventricular control wall thickness at zero pressure; LW = left ventricular ischemic wall thickness at zero pressure; S₀ = left ventricular short axis at zero pressure; L₀ = left ventricular volume at zero pressure; M₀ = left ventricular muscle mass at zero pressure.

* P < 0.05; †P < 0.01; ‡P < 0.001; given are mean values ± 1 SEM.
occlusion, and there was no increase in calculated muscle mass during reactive hyperemia after release of either partial or complete coronary occlusion.

Left Ventricular Diastolic Function (Table 4)

The end-diastolic wall stress of the control (σc) and ischemic (σi) regions behaved in a similar fashion, with no increase in wall stress at end-diastole during partial as well as during complete coronary occlusions. Wall stress of both the control and ischemic regions decreased significantly at 1 and 2 minutes, respectively, after release of coronary occlusions (Table 4). The end-diastolic midwall strain of the control (εc) and the ischemic (εi) regions also showed no significant change during partial, but a significant decrease in both control and ischemic wall regions during 1 and 2 minutes of complete, coronary occlusions. Furthermore, control and ischemic wall thickness showed wall thinning of a similar degree during diastolic filling (from zero diastolic pressure to end-diastole; Fig. 1 and 3) ranging from -10 to -15% for the control wall and from -8 to -18% for the ischemic wall. Thus, diastolic stress-strain data demonstrated a similar behavior in the control and ischemic wall regions during myocardial ischemia and reperfusion, in contrast to the changes during isovolumic relaxation when control wall thickness showed wall thinning and ischemic wall thickness showed wall thickening during ischemia. Therefore, the stress-strain data of the control wall region were used for calculating the other diastolic properties of the left ventricle (Table 4).

During partial coronary occlusion, the diastolic stress-strain relations showed no significant change in myocardial wall stiffness (β) (Fig. 4), but wall stiffness decreased significantly 1 and 2 minutes after release of partial coronary constriction (Fig. 4). ε showed a significant increase during 2 minutes of partial occlusion and returned to normal during reperfusion.

During complete coronary occlusion, diastolic myocardial wall stiffness (β) increased significantly (average increase at 1 minute 27%) (Fig. 4; Table 4).
Myocardial stiffness showed a significant decrease 1 and 2 min. after release of complete occlusion (Fig. 4). The nonlinear elastic constant ($\alpha$) remained essentially unchanged during partial and complete coronary occlusions. The viscous constant ($\eta$) showed a significant increase during complete coronary occlusion and returned to normal after release of coronary occlusion.

**Comparison of Systolic and Diastolic Function with and without IVC Obstruction (Table 5)**

The changes in heart rate, peak systolic pressure, lowest diastolic pressure ($P_{min}$), diastolic reference volume at zero pressure ($V_{min}$), left ventricular end-diastolic volume, and ejection fraction were not statistically significantly different in the two groups, with
or without IVC obstruction, during partial and complete coronary occlusions. During partial coronary occlusion, $P_{min}$ remained unchanged in both groups, with or without IVC obstruction. However, the lowest diastolic pressure increased significantly during complete coronary occlusion in the group without IVC obstruction but not in the group with IVC obstruction (Fig. 5). During partial coronary occlusion, the end-diastolic pressure remained unchanged in both groups, with or without IVC obstruction. The left ventricular end-diastolic pressure increased significantly during complete coronary occlusion in the group without IVC obstruction but remained unchanged in the group with IVC obstruction (Fig. 5). Thus, the pressure-volume curves in the seven dogs without IVC obstruction showed a significant upward shift during complete coronary occlusion, (which was not seen during partial coronary occlusion), and this shift was prevented by IVC obstruction during complete coronary occlusion (Fig. 5).

**Discussion**

The present study was performed to determine the sequential effects of both partial and complete coronary occlusions on left ventricular relaxation and diastolic properties in the conscious animal. The techniques employed provided accurate and continuous monitoring of myocardial dimensions and pressure, allowing determination of wall stress and strain without appreciable constraining effects on the myocardium. A major goal of the study was to examine the diastolic mechanical properties of the left ventricle at a common preload produced by adjusting the venous return, using IVC obstruction (Rankin et al., 1976).

Changes in left ventricular systolic function during acute coronary occlusion have been well established (Tennant and Wiggers, 1935; Prinzmetal et al., 1949; Tatrooles and Randall, 1961; Theroux et al., 1974), and systolic expansion of the ischemic wall, as well as impairment of overall systolic performance of the left ventricle, has been described by a number of investigators. In the present study, partial coronary occlusion was accompanied by a significant decrease in systolic thickening of the ischemic wall (without systolic expansion) and a slight decrease in left ventricular ejection fraction, whereas complete coronary occlusion was accompanied by systolic thinning of the ischemic wall and a significant decrease in the ejection fraction. In contrast to most clinical studies, the left ventricular end-diastolic pressure remained unchanged during partial and complete coronary occlusion because IVC obstruction prevented a significant increase in end-diastolic pressure (Table 5). However, in the experiments without IVC obstruction, a significant increase in left ventricular end-diastolic pressure occurred (average 10 to 16 mm Hg) during complete coronary occlusion (Table 5).

**Left Ventricular Relaxation**

The assessment of global left ventricular relaxation has been performed by calculating left ventricular $dP/dt_{min}$ and the time constant of left ventricular pressure fall (Weisfeldt et al., 1978; Weiss et al., 1976), and it has been demonstrated that these parameters are affected during acute myocardial ischemia (Mann et al., 1979, Kumada et al., 1979). Analogous to the time constant $T_c$, we also calculated the time constant of left ventricular stress fall in the control ($T_c$) and the ischemic wall region ($T_i$), in order to obtain an index of regional relaxation. Furthermore, we used a linear regression analysis between left ventricular pressure and $-dP/dt$ and left ventricular stress and $-dσ/dt$ for the calculation of the time constant $T_c$ and $T_i$, respectively, since it has been demonstrated recently (Craig and Murgo, 1980) that the exponential curve fit between $ln P$ and time for the calculation of the time constant $T$ is accurate.

The change in $dP/dt_{min}$ suggested a delayed relaxation during partial coronary occlusion, whereas $dP/dt_{min}$ remained unchanged during complete coronary occlusion without IVC obstruction.

**TABLE 5**

Left Ventricular Function With and Without Partial Obstruction of the Inferior Vena Cava (IVC)

<table>
<thead>
<tr>
<th></th>
<th>HR  (beats/min)</th>
<th>LVEDP (mm Hg)</th>
<th>LVSP (mm Hg)</th>
<th>$P_{min}$ (mm Hg)</th>
<th>$V_{min}$ (ml)</th>
<th>EDV (ml)</th>
<th>EF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>90 ± 6</td>
<td>10 ± 1</td>
<td>125 ± 3</td>
<td>1 ± 1</td>
<td>1 ± 1</td>
<td>66 ± 8</td>
<td>56 ± 4</td>
</tr>
<tr>
<td>Partial CO</td>
<td>103 ± 6</td>
<td>11 ± 1</td>
<td>123 ± 4</td>
<td>2 ± 1</td>
<td>46 ± 7</td>
<td>68 ± 9</td>
<td>46 ± 5</td>
</tr>
<tr>
<td>Complete CO</td>
<td>126 ± 10‡</td>
<td>16 ± 2‡</td>
<td>122 ± 5</td>
<td>7 ± 1I</td>
<td>53 ± 8‡</td>
<td>69 ± 8</td>
<td>34 ± 5</td>
</tr>
<tr>
<td>1 minute after complete CO</td>
<td>103 ± 8</td>
<td>11 ± 2</td>
<td>127 ± 6</td>
<td>3 ± 1</td>
<td>34 ± 5*</td>
<td>62 ± 9‡</td>
<td>57 ± 5</td>
</tr>
</tbody>
</table>

HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVSP = left ventricular peak systolic pressure; $P_{min}$ = left ventricular lowest diastolic pressure; $V_{min}$ = left ventricular volume at $P_{min}$; EDV = left ventricular end-diastolic volume; EF = left ventricular ejection fraction.

* $P < 0.05$; ‡$P < 0.01$; †$P < 0.001$; given are mean values ± 1 SEM.
occlusion. In contrast, the time constant of left ventricular pressure fall ($T$) indicated normal relaxation during partial, but delayed relaxation during complete, occlusion. These contradictions in the results observed in $dP/dt_{min}$ and the time constant of left ventricular pressure fall can be explained by the fact that $dP/dt_{min}$ is sensitive to changes in heart rate, inotropic state, and loading conditions, all of which change during ischemia. Thus, $dP/dt_{min}$ is not a valid measure of left ventricular relaxation (Karliner et al., 1977) during myocardial ischemia, and the decrease in $dP/dt_{min}$ known to occur with left ventricular ischemia (Theroux et al., 1976) might have been counterbalanced by the increase in heart rate during complete coronary occlusion. The time constant of left ventricular pressure fall has been reported to be less sensitive to changes in loading conditions and to reflect direct effects on the relaxing system better (Weiss et al., 1976; Karliner et al., 1977), suggesting that the observed changes in $T$ during complete coronary occlusion represent true changes in left ventricular relaxation, whereas relaxation remains normal during partial coronary occlusion. However, recent studies (Raff and Glantz, 1981) demonstrated that the time constant of left ventricular pressure fall is also dependent on loading conditions; therefore, the observed changes in relaxation during complete coronary occlusion might have been due to altered loading conditions, as well as to changes in inotropic state. On the other hand, evaluation of regional relaxation parameters suggested enhanced relaxation in the non-ischemic zone ($T_c$) and delayed relaxation in the ischemic zone ($T_i$). Although the differences in $T_c$ and $T_i$ were not statistically significant, $T_c$ decreased by more than 15% and $T_i$ increased by 10-15% during partial and complete coronary occlusions. Movements of
Thus, loss of basic contractile tone rendered the isch-

emic muscle fibers particularly vulnerable to sarco-
mere elongation (Crozatier et al., 1977). An increase in
resting length of ischemic segments during coro-
nary occlusion was observed by Theroux et al. (1974)
and elongation of the major and minor left ventricular
axes was noted by Edwards and co-workers (1981).
During partial coronary occlusion, we were not able
to demonstrate any changes in resting length of the
left ventricular short axis, probably due to the fact
that persistent (although reduced) systolic thickening
of the ischemic wall prevented systolic overstretch of
the muscle fibers, and therefore no diastolic thinning
of the ischemic region occurred. Interestingly, a de-
crease in resting muscle length was observed follow-
ning release of complete coronary occlusion. The na-
ture of this phenomenon is not clear, but increased
myocardial blood flow during early reperfusion could
have been responsible for the significant increase in
diastolic wall thickness with a decrease in resting
length of the left ventricular short axis and reduced
volume. The nature of these changes in resting length
is not clear; the effect, however, might be due to
rearrangement of muscle fibers during ischemia, to an
increase in sarcomere length caused by the systolic
overstretch of the ischemic muscle fibers, or to acute
fiber slippage during coronary occlusion. In the study
by Crozatier and co-workers (1977), sarcomere
lengths in the ischemic myocardium were signifi-
cantly longer than in the nonischemic regions, and it
was suggested that the increase in sarcomere length
during ischemia was due to sarcomere overstretch
during systole. This increase in sarcomere length in
the ischemic myocardium might cause the sarcomeres
to operate at a higher point on the sarcomere pressure-
length relationship than normal, so that they require
a higher filling pressure for diastolic lengthening. This
increase in operating sarcomere stiffness might be
responsible for the observed increase in myocardial
wall stiffness in the ischemic zone.

Regional myocardial wall stiffness was calculated
from an ellipsoidal model, assuming that the ischemic
segment extended entirely around the left ventricle.
This is not strictly true, but the use of control or
ischemic wall thickness for the calculation of wall
stress showed no major differences for the determi-
nation of myocardial wall stiffness (Table 4). This
observation probably relates to our finding that there
was little difference in diastolic wall thicknesses be-
tween the two regions, and the fact that the short axis
is used for the calculation of stresses and strains in
both regions. The study of Edwards and co-workers
(1981), using left ventricular ischemic wall thickness,
and left ventricular long or short axis for the deter-
mination of left ventricular chamber stiffness, showed
a similar increase in chamber stiffness to that which
we observed during coronary occlusion. In addition to
the findings of their study, we were able to dem-
strate no change in myocardial wall stiffness (\(B\))
during partial coronary occlusion, whereas myocar-
dial wall stiffness increases significantly during com-
plete occlusion. After release of both partial and

Left Ventricular Diastolic Function

Our assessment of left ventricular diastolic myo-
cardial function is based on the diastolic stress-strain
relationship of the left ventricle (Mirsky, 1976). Since
it had been demonstrated that diastolic stress-strain
relations are characterized more precisely by a visco-
elastic than a simple elastic model (Rankin et al., 1977;
Hess et al., 1979), we employed such a model for the
evaluation of left ventricular diastolic properties. Im-
paired left ventricular relaxation could play a role in
determining left ventricular diastolic passive elastic
properties (Papisoularides et al., 1980) and might
account for some of the observed changes in early
diastolic filling (Pouleur et al., 1979). It seems unlikely
that—in our experiments—incomplete relaxation
played the primary role, however, since the changes in
T were small, although significant; the possibility
also exists that myocardial viscous forces were influ-
enced by delayed left ventricular relaxation during
complete coronary occlusion. Thus, parallel to the
increase in the time constant of left ventricular pres-
sure fall, a significant increase in the viscous constant
\(\eta\) occurred during complete coronary occlusion. The
viscous constant also increased during partial coro-
nary occlusion, whereas the time constant T remained
unchanged. Changes in viscous resistance might relate
to changes in heart rate like those known to occur in
normal hearts (Pouleur et al., 1979). These changes
might also be related to alterations in left ventricular
relaxation, with delayed deactivation of the heart
muscle leading to higher viscous resistance during
early diastolic filling.

For interindividual comparisons of diastolic me-
chanical properties, normalization of the diastolic
stress-strain relationship to a common preload is im-
portant, especially when diastolic filling pressures
show considerable variations during interventions
such as coronary occlusion (Serizawa et al., 1980).
Therefore, IVC obstruction was used (Rankin et al.,
1977) to adjust the venous return mechanically in
order to maintain a constant preload throughout all
measurements. Using IVC obstruction, we obtained
diastolic reference data at zero filling pressure when
no load was acting on the muscle fibers. These ref-
ence data were used for the calculation of normal-
ized short axis strain (Mirsky, 1976) and served as a
reference point for the assessment of changes in rest-
ing muscle length.

Systolic overstretch of the ischemic muscle fibers
was probably responsible for the diastolic thinning of
the ischemic wall and the increase in resting muscle
length observed during complete coronary occlusion.
Thus, loss of basic contractile tone rendered the isch-
complete coronary occlusion, myocardial wall stiffness decreased significantly and returned to normal 10 minutes later. These data suggest that the changes in myocardial wall stiffness are dependent on the degree of myocardial ischemia and the presence or absence of changes in resting muscle length.

Diastolic Pressure-Volume Relationship

The mechanism of the upward shift of the diastolic pressure-volume curve during acute myocardial ischemia (Serizawa et al., 1980) remains unclear. A decrease in the speed of relaxation, increased myocardial wall stiffness, loss of diastolic suction, ventricular interaction, and changes in myocardial perfusion have all been suspected of causing this upward shift of the diastolic pressure-volume curve. Since we performed our experiments with and without vena caval obstruction, we were able to determine the effect of reducing venous return on the left ventricular diastolic pressure-volume curves (Table 5; Fig. 5). During partial coronary occlusion, there was no significant difference in left ventricular pressure-volume curves with or without caval obstruction (Fig. 5). During complete coronary occlusion, however, there was a marked upward shift of the pressure-volume curve without caval obstruction, which was prevented by mechanically reducing the venous return using vena caval obstruction (Fig. 5). These findings show that the upward shift of the pressure-volume curve during myocardial ischemia is dependent on the extent of ischemia, since the upward shift was seen only during complete coronary occlusion. That the shift of the pressure-volume curve could be prevented by caval obstruction suggests that the underlying mechanism for the curve shift may be related to a change in right ventricular loading conditions with altered interaction between the right and left ventricles (Mirsky and Rankin, 1979), rather than to increased left ventricular myocardial wall stiffness, left ventricular relaxation, or pericardial constriction (the pericardium had been removed in the present study). However, changes in left ventricular geometry due to right ventricular interaction could not be detected, since the changes in left ventricular long and short axes were not significantly different with or without obstruction of the inferior vena cava.

In summary, our data indicate that myocardial wall stiffness (β) is normal during partial, but increased during complete, coronary occlusion, and that resting muscle length at zero diastolic pressure is increased only during complete coronary occlusion; the latter measure is decreased during reperfusion when regional hyperemia of the ischemia wall occurs. Regional relaxation of the ischemic wall is prolonged, but relaxation of the nonischemic wall is enhanced during partial, as well as during complete, coronary occlusion. These changes suggest that both systolic overstretch of the ischemic region and the upward shift of the diastolic pressure-volume curve of the left ventricle depend on the extent of myocardial ischemia, occurring in this study only during complete coronary occlusion, and its prevention by IVC obstruction suggests that right ventricular loading conditions with altered ventricular interaction may play a role in this phenomenon.

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Diastolic myocardial wall stiffness and ventricular relaxation during partial and complete coronary occlusions in the conscious dog.

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