Left Ventricular Pressure-Volume Relationships During Myocardial Ischemia in Man

By John L. McCans, M.D., and John O. Parker, M.D.

SUMMARY

It has been shown in man that myocardial ischemia, whether precipitated by exercise or pacing-induced tachycardia, is associated with abnormalities of left ventricular end-diastolic pressure. There has been controversy as to whether this relationship is due to decreased myocardial compliance or to an increase in left ventricular volume as a manifestation of left ventricular failure. Simultaneous measurements of left ventricular pressure and left ventricular volume using ultrasonic techniques were carried out in five normal subjects and 21 patients with coronary artery disease. In the normal subjects a decrease in left ventricular end-diastolic pressure during pacing was associated with a decrease in left ventricular end-diastolic volume, and during interruption of pacing, pressures and volumes returned to normal. In nine patients with coronary artery disease who did not develop angina, a similar response was seen. In 12 patients with coronary artery disease who developed angina during pacing, the reduction in left ventricular end-diastolic volume during pacing was less marked than the other groups and during periods of interruption the increase in diastolic pressure to 26 mm Hg was accompanied by an increase in left ventricular end-diastolic volume to 24% above control values. The end-systolic volume showed a similar increase during myocardial ischemia.

These data suggest that the changes in left ventricular filling pressure seen during myocardial ischemia are related to increase in left ventricular volume but do not exclude the possibility that there may be accompanying changes in left ventricular diastolic compliance.

Additional Indexing Words:
Left ventricular volume
Left ventricular compliance
Ultrasound
Echocardiography
Left ventricular end-diastolic pressure

The hemodynamic changes during myocardial ischemia have been examined intensively, and there is now general agreement as to the abnormalities that occur.1-9 Opinions differ however as to the pathophysiologic mechanisms involved. Some investigators interpret the elevation of left ventricular filling pressure seen during myocardial ischemia as evidence of a transient decrease in left ventricular compliance5-6-10 while others consider that reversible left ventricular failure occurs with an associated increase in left ventricular volume.3-4-7 Only limited information is available in man concerning changes in left ventricular volume and compliance during myocardial ischemia.11-18 Until recently volume measurements have been made largely using angiographic techniques, but these methods are difficult to employ during interventions to create ischemia and in themselves alter ventricular function.14 Measurements of left ventricular volume by pulsed-reflected ultrasound have been shown to agree closely with those determined angiographically.15-17 This technique has the advantage of being noninvasive and readily repeatable while not altering left ventricular function. The present study was carried out to investigate the effect of pacing-induced tachycardia on left ventricular volume in man and to study the relationship between ventricular volume and filling pressure during myocardial ischemia.

Methods

Twenty-six patients with known or suspected coronary artery disease were studied at the time of diagnostic cardiac catheterization. Twenty-one patients were subsequently shown to have significant occlusive coronary artery disease on the basis of selective coronary arteriography and five were found not to have cardiac disease. All patients were free of cardiac failure at the time of study, and none was receiving digitalis,
diuretics, or antihypertensive medications. Informed consent was obtained from each patient, and there were no complications related to the investigation.

Studies were carried out in the fasting, postabsorptive state. Under local anesthesia the brachial artery and an accompanying vein were isolated in the right antecubital fossa. A No. 8 Gorlin catheter was positioned in the midportion of the coronary sinus and a No. 8 Sones catheter was placed in the left ventricle. A Teflon cannula was placed in the left brachial artery percutaneously. Following a 10 min control period, atrial pacing was initiated at a constant rate which varied from 132 to 155 beats/min in individual patients. Pacing was interrupted for 15 sec intervals, 30 sec after initiation of pacing, and also at a point between 45 and 10 min of pacing. The periods immediately before and during interruption at 30 sec of pacing will be designated as the early pacing (P1) and early interruption (I1) periods respectively and those immediately before and during the interruption between 45 and 10 min of pacing as the late pacing (P2) and late interruption (I2) periods respectively. A modified lead II of the electrocardiogram was recorded throughout the study. Brachial arterial and left ventricular end-diastolic pressures and left ventricular dimensions were recorded using ultrasound during the control period and during the early and late pacing and interruption periods. Cardiac output was measured in duplicate by the dye dilution technique during the control period and after 5 min of pacing. Blood was withdrawn simultaneously from the coronary sinus and brachial artery during the control period and after 7 min of pacing. The blood samples were centrifuged within 30 min, the plasma separated and stored at 

-30°C. Lactate concentration was determined by an automated fluorometric technique.18

The ultrasonic examinations were performed with an ultrasonoscope* utilizing a 2.25 MHz 14 mm diameter transducer with a repetition rate of 1000 impulses/sec and constructed to focus at 5 cm. The ultrasonoscope was interfaced with a photographic recorder equipped with a channel which provided a time-motion display of the echocardiographic patterns.† Tracings of the electrocardiogram and left ventricular pressure at high sensitivity were recorded on the same photographic paper as the echocardiograms allowing comparisons of simultaneous left ventricular pressures and dimensions.

The technique described by Feigenbaum et al.15 was followed in recording the echocardiograms. The patient was examined recumbent in 20° right anterior oblique position. A water miscible gel was used to ensure an air-free contact between the transducer and the skin. The transducer was placed on the chest in the fourth or fifth intercostal space at the left sternal edge and directed posteriorly. Scanning movements were made by tilting the transducer until the characteristic echoes of the mitral valve leaflets were obtained with maximum clarity. The transducer was then directed inferiorly and laterally until the mitral echo became indistinct and the echoes from the intraventricular septum and posterior left ventricular wall were obtained. The transducer position was further adjusted and the damping devices of the ultrasonoscope manipulated so that clear continuous echoes from the endocardium of both septum and posterior wall were obtained. This position was maintained by holding the transducer manually for the duration of this portion of the study. The echocardiogram, electrocardiogram, and left ventricular pressure trace were recorded at a paper speed of 50 mm/sec.

Left ventricular dimensions just before the onset of atrial systole (LVD pre-a), at end-diastole (LVDed), and end-systole (LVDes) were measured from the endocardial echo of the posterior left ventricular wall to the corresponding echo of the left side of the intraventricular septum using the simultaneously recorded electrocardiogram and left ventricular pressure trace as references (fig. 1). LVDed was measured at the peak of the R wave of the electrocardiogram and LVDes was taken at the point when the ventricular walls were in closest apposition. Calibration was performed in each study by recording a grid of lines which were spaced to represent distances of 1 cm.

Left ventricular dimensions were averaged over a complete respiratory cycle during control and pacing periods and over as many beats as were available during periods of interruptions, usually between five and ten cardiac cycles. The dimension of the left ventricle obtained with ultrasound approximates but does not coincide precisely with the short axis of the ventricle. Despite this, a formula has been derived by which left ventricular volume can be calculated using the dimension obtained with ultrasound.15,16 The formula is a modification of that used for estimation of left ventricular volume using angiographic techniques which considers the left ventricle to be a prolate ellipse,19,20 the volume of which is expressed by the formula \[ V = \pi \times D_1 \times D_2 \times L \], where \( V \) = ventricular volume in ml, \( D_1 \) and \( D_2 \) are the minor axes of the ventricular chamber at right angles to each other in mm and \( L \) = the major axis of the ventricle in mm. It has been shown that \( D_1 \) and \( D_2 \) are virtually identical21 and that \( L \) bears a constant relation to \( D \) throughout the cardiac cycle, being approximately twice the minor axis.15,22 Thus the formula may be simplified to \[ V = \pi \times 2D^3 \], where \( D = \) the minor axis of the ventricle. By substituting the dimension obtained with ultrasound into this formula left ventricular volumes can then be obtained. Close agreement between volume estimations with ultrasound and those with angiography has been documented.15-17 Stroke volume is given by the difference between the volume at end-diastole and at end-systole and the contribution of atrial systole to ventricular filling is given by the difference between the volume of the left ventricle prior to and following atrial systole.

Pressures were measured with P23 Db Statham strain gauges from a zero reference level 5 cm below the angle

*Cekline 20, Smith-Kline Instruments, Inc., Palo Alto, California.
†DR12 Electronics for Medicine, White Plains, New York.
Simultaneous left ventricular pressure and echocardiogram during sinus rhythm and following the initiation of atrial pacing. The left ventricular posterior wall and septum are shown demonstrating the abrupt reduction in left ventricular volume associated with the increase in heart rate. Top trace from modified lead II ECG.

Results

Twelve of the 21 patients with coronary artery disease developed angina during the period of atrial pacing. This developed within 1 to 5 min and persisted, usually with increasing severity, until pacing was terminated at the end of 9 to 10 min of pacing. In one patient severe chest pain necessitated termination of pacing after 4 min. After pacing was terminated pain was generally gone within a period of 2 min. Ischemic ST-segment changes were observed in all patients who developed angina. The presence of myocardial ischemia was documented by the demonstration of myocardial lactate production in all patients. For purposes of analysis three groups will be considered.

a) Normal group consisting of five patients subsequently shown to be free of cardiac disease.

b) Nonangina group consisting of nine patients with coronary artery disease who did not experience pain and had no metabolic evidence of ischemia during pacing.

c) Angina group consisting of 12 patients with coronary artery disease who developed angina during pacing and who showed biochemical evidence of myocardial ischemia at this time.

* DR12 Electronics for Medicine, White Plains, New York.
The coronary arteriographic abnormalities were similar in the angina and nonangina groups, all having at least 75% luminal narrowing of one major coronary artery and the majority having significant disease in two or three coronary arteries. In the nonangina group, eight of the nine patients had satisfactory left ventriculograms. Four patients had normal left ventriculograms while four had mild to moderate enlargement of the left ventricle with reduced ejection fractions. One had diffuse hypokinesis, one demonstrated akinesis of the inferior wall and two had apical akinesis. In the angina group, five patients showed normal left ventriculograms while seven had moderate enlargement of the left ventricle and reduced ejection fraction. One showed diffuse hypokinesis, four akinesis of the apex, and one of the inferior wall. No patient in either group showed dyskinesis and none had mitral regurgitation.

**Hemodynamics During Sinus Rhythm and Atrial Pacing**

A summary of the hemodynamic data during the control, pacing, and pacing interruption periods for the three groups is shown in table 1.

**Heart Rate**

The average values for heart rate during the control period were similar in the three groups--81 beats/min in the normal subjects and in the nonangina patients and 76 beats/min in the angina group. The pacing rates chosen for the patients who developed angina varied from 138 to 154 beats/min and averaged 145 beats/min. The average rate for the normal and nonanginal groups was 148 and 147 beats/min respectively.

In the angina group the average sinus rate was 75 beats/min both during I₁ and I₂. These rates were similar to the average heart rate during the control period of sinus rhythm. Likewise, in the nonangina group, the rates during the interruptions were 80 and 79 beats/min and were similar to the control value. In the normal patients the rates for I₁ and I₂ were 77 and 86 beats/min and were not significantly different from the control value.

**Cardiac Index**

The average values for cardiac index in the normal subjects were similar during control and pacing, being 3.0 and 3.3 liters/min/m² respectively. In the nonangina group the cardiac index was somewhat lower than in the normal group: 2.4 liters/min/m² during control and increased to 2.7 liters/min/m² during pacing (P < 0.05). In the angina group the cardiac index during control and pacing-induced angina was 2.4 and 2.6 liters/min/m² respectively (NS). The stroke index decreased during pacing in every patient, this fall

### Table 1

<table>
<thead>
<tr>
<th>Summary of Hemodynamic Data</th>
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<tbody>
<tr>
<td><strong>HE</strong></td>
</tr>
<tr>
<td>beats/min</td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>P₁</td>
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<tr>
<td>I₁</td>
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<tr>
<td>P₂</td>
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<tr>
<td>I₂</td>
</tr>
<tr>
<td><strong>Non-Angina Group N = 9</strong></td>
</tr>
<tr>
<td>C</td>
</tr>
<tr>
<td>P₁</td>
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<tr>
<td>I₁</td>
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<tr>
<td>P₂</td>
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<tr>
<td>I₂</td>
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<td><strong>Angina Group N = 12</strong></td>
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<tr>
<td>C</td>
</tr>
<tr>
<td>P₁</td>
</tr>
<tr>
<td>I₁</td>
</tr>
<tr>
<td>P₂</td>
</tr>
<tr>
<td>I₂</td>
</tr>
</tbody>
</table>

Abbreviations: HE = heart rate; CI = cardiac index; SI = stroke index; BAm = brachial arterial mean pressure; LVEDP = left ventricular end-diastolic pressure; C = control; P₁ = early pacing; I₁ = early interruption; P₂ = late pacing; I₂ = late interruption.

Values shown are mean ± standard error.
was 33% in the normals, 38% in the nonangina group and 43% in the angina group.

**Brachial Arterial Mean Pressure**

In the normal group brachial arterial mean pressure averaged 90 mm Hg during the control period and 95 mm Hg during pacing (NS). In the nonangina group this pressure increased from 108 to 118 mm Hg ($P < 0.005$), and a similar change was observed in the angina group in which brachial arterial mean pressure rose from 96 mm Hg during control to 107 mm Hg during pacing-induced angina ($P < 0.002$).

**Left Ventricular Diastolic Pressure**

In the normal group left ventricular diastolic pressure at the onset of atrial systole (LVP pre-a) was 5 mm Hg during the control period and during both I₁ and I₂. Left ventricular end-diastolic pressure (LVEDP) was 9 mm Hg during the control period and fell to 4 mm Hg during P₁ and P₂. This pressure returned to control values during I₁ and I₂ (fig. 2).

In the nonangina group LVP pre-a was 5 mm Hg during the control period and 6 mm Hg during I₁ and I₂. LVEDP in this group was 9 mm Hg during the control period and fell to 3 and 2 mm Hg during P₁ and P₂ ($P < 0.001$). LVEDP returned to approximate control values during I₁ and I₂.

In the angina group LVP pre-a was 7 mm Hg during the control period, 9 mm Hg during I₁ and 15 mm Hg during I₂. LVEDP was 14 mm Hg during the control period and fell to 7 mm Hg during P₁ ($P < 0.001$). This increased to 17 mm Hg during I₁ ($P < 0.005$). During P₂ when angina had developed LVEDP was 11 mm Hg, a value significantly lower than the control value ($P < 0.02$) but higher than during P₁ ($P < 0.005$). During I₂ when angina was present LVEDP rose to an average value of 26 mm Hg. This was greater than either that during control ($P < 0.001$) or during I₁ ($P < 0.005$).

**Left Ventricular Volume During Sinus Rhythm and Atrial Pacing**

The average data for left ventricular volumes and pressures during the control, pacing, and pacing interruption periods are shown in table 2.

![diagram](image)

**Figure 2**

Left ventricular end-diastolic pressure (LVEDP) in the three groups of patients. The left panel shows the change in LVEDP between the early and late pacing periods. The group with angina show higher pressure during late pacing when ischemia is present. The right panel shows the value for LVEDP during the control period and during sinus rhythm at periods of interruption. The increase in LVEDP during myocardial ischemia is apparent.
Table 2

<table>
<thead>
<tr>
<th></th>
<th>LVV pre-a ml</th>
<th>LVVed ml</th>
<th>LVVes ml</th>
<th>LVP pre-a mm Hg</th>
<th>LVEDP mm Hg</th>
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<tr>
<td>C</td>
<td>65 ± 11</td>
<td>87 ± 11</td>
<td>25 ± 4</td>
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<td>P1</td>
<td>60 ± 6</td>
<td>80 ± 11</td>
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<tr>
<td>I1</td>
<td>67 ± 11</td>
<td>89 ± 11</td>
<td>22 ± 4</td>
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<tr>
<td>P2</td>
<td>62 ± 7</td>
<td>88 ± 11</td>
<td>25 ± 3</td>
<td>5 ± 1</td>
<td>9 ± 1</td>
</tr>
<tr>
<td>I2</td>
<td>68 ± 12</td>
<td>88 ± 11</td>
<td>25 ± 3</td>
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<td>Nonangina Group N = 9</td>
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<tr>
<td>C</td>
<td>76 ± 13</td>
<td>109 ± 14</td>
<td>43 ± 10</td>
<td>5 ± 1</td>
<td>9 ± 2</td>
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<td>P1</td>
<td>78 ± 13</td>
<td>122 ± 18</td>
<td>41 ± 12</td>
<td>6 ± 1</td>
<td>10 ± 2</td>
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<td>83 ± 14</td>
<td>119 ± 16</td>
<td>44 ± 12</td>
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<td>P2</td>
<td>73 ± 10</td>
<td>110 ± 22</td>
<td>68 ± 17</td>
<td>6 ± 1</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>I2</td>
<td>80 ± 12</td>
<td>178 ± 26</td>
<td>78 ± 20</td>
<td>15 ± 2</td>
<td>26 ± 3</td>
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Angina Group N = 12

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<tr>
<th></th>
<th>LVV pre-a ml</th>
<th>LVVed ml</th>
<th>LVVes ml</th>
<th>LVP pre-a mm Hg</th>
<th>LVEDP mm Hg</th>
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<tr>
<td>C</td>
<td>103 ± 20</td>
<td>136 ± 22</td>
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<td>P1</td>
<td>95 ± 20</td>
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<td>61 ± 16</td>
<td>9 ± 1</td>
<td>17 ± 2</td>
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<tr>
<td>I1</td>
<td>111 ± 21</td>
<td>110 ± 22</td>
<td>68 ± 17</td>
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<tr>
<td>P2</td>
<td>138 ± 29</td>
<td>178 ± 26</td>
<td>78 ± 20</td>
<td>15 ± 2</td>
<td>26 ± 3</td>
</tr>
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</table>

Abbreviations: LV pre-a = left ventricular volume prior to atrial systole; LVVed = left ventricular volume at end diastole; LVVes = left ventricular volume at end systole; LVP pre-a = left ventricular pressure before atrial systole; LVEDP = left ventricular end-diastolic pressure; C = control; P1 = early pacing; I1 = early ischemia; I2 = late pacing; P2 = late pacing.

Left Ventricular Diastolic Volume

In the normal group left ventricular volume at the onset of atrial systole (LVV pre-a) was 65 ml and was similar during I1 and I2. Left ventricular volume at end-diastole (LVVed) averaged 87 ml during the control period and decreased significantly to 80 ml during P1 (P < 0.01), and 62 ml during P2 (P < 0.01). During I1 and I2 LVVed increased to 89 and 88 ml respectively (fig. 3). Changes in ventricular size followed promptly any change in rate such that the volume stabilized within two or three beats after either abrupt increases or decreases in heart rate (fig. 1).

In the nonangina group LVV pre-a averaged 76 ml during the control period. During I1 and I2 LVV pre-a was similar, at 83 and 80 ml respectively. LVVed averaged 109 ml during the control period, 122 ml during I1 and 119 ml during I2, values which were not significantly different. During pacing LVVed fell significantly to 78 ml during P1 (P < 0.025) and 73 ml during P2 (P < 0.05).

In the angina group LVV pre-a was 103 ml during the control period, 111 ml during I1 but rose significantly during I2 when ischemia was present to 138 ml (P < 0.001). LVVed during the control period was 136 ml and during P2 decreased to 95 ml (P < 0.001). During I1 this volume averaged 143 ml. During P2, after angina had developed, LVVed was 110 ml. Although this was significantly less than the control volume (P < 0.02) and the volume during I1 (P < 0.005), it represented a 14% increase from that recorded during P1 (P < 0.005). During I2 when ischemia was present the average LVVed was 178 ml. This value was 24% greater than control (P < 0.001) and 20% greater than during I1 (P < 0.005). Thus, during myocardial ischemia left ventricular volume was greater during both sinus rhythm and pacing-induced tachycardia.

Left Ventricular End-Systolic Volume

Left ventricular end-systolic volume (LVVes) in the normal group averaged 25 ml during control, 23 ml during P1 and 22 during P2 (NS), and approximated control levels during I1 and I2 (fig. 4).

In the nonangina group LVVes was 43 ml during control and fell to 33 ml during P1 (P < 0.01) and returned to control values during I1. Similar results were obtained during P2 and I2.

In the angina group LVVes was 59 ml during the control period, 55 ml during P1 (NS) and 61 ml during I1. During P2 when angina had developed LVVes averaged 68 ml, a volume significantly greater than during P1 (P < 0.005). During I2 LVVes increased to 78 ml and at this time was significantly greater than that recorded during
LV PRESSURE-VOLUME DURING ISCHEMIA

L.V.V.e.d., change from $P_1$ (ml)  L.V.V.e.d., change from $C$ (ml)

![Graph showing LV pressure-volume changes](image)

**Figure 3**

*Left ventricular volume at end diastole (LVV ed) in the three groups of patients. The left panel shows the change from early to late pacing in the three groups of patients. The increase in end-diastolic volume during myocardial ischemia is apparent in the angina group. The right panel shows the volume changes during periods of sinus rhythm. In the late interruption period in the angina group there is a significant increase in end-diastolic volume.*

the control period ($P < 0.001$) or during $I_1$ ($P < 0.001$).

**Stroke Volume Estimated by Ultrasound**

Stroke volume estimated by ultrasound averaged 61 ml/beat during the control period in the normal subjects. By the dye dilution technique the average stroke volume was 65 ml/beat. Estimations of stroke volume during pacing by the two methods were similar—36 ml/beat by ultrasound and 37 ml/beat by dye dilution. Values for stroke volume derived by ultrasound were similar during $P_1$ and $P_2$ and during $I_1$ and $I_2$ returned promptly to near control values.

In the nonangina group the control stroke volume recorded by ultrasound averaged 66 ml/beat and fell to 41 ml/beat during pacing. The corresponding values as estimated by the dye dilution technique were 52 and 33 ml/beat. The average values by ultrasound were significantly higher than those obtained by dye dilution both during control and pacing ($P < 0.005$). Stroke volumes by ultrasound were similar during $P_1$ and $P_2$ and during $I_1$ and $I_2$.

In the angina group stroke volume measured by ultrasound averaged 77 ml/beat in the control state and fell to 41 ml/beat during $I_1$. During $P_2$ in the presence of angina the average stroke volume was similar to that during $P_1$—43 ml/beat—and during $I_2$ rose to 102 ml/beat. This was significantly greater than during either control ($P < 0.01$) or $I_1$ ($P < 0.05$). Although estimations of stroke volume were somewhat greater by ultrasound than by dye dilution both during control and pacing, the differences were not statistically significant.

**Discussion**

The hemodynamic changes observed during atrial pacing in the normal subjects and in patients with coronary artery disease are in close agreement with those previously reported.\(^{6-9}\) Cardiac output did not change significantly during pacing, and there were only minor changes in systemic pressure.
and thus left ventricular stroke work decreased. This should be associated with a decrease in left ventricular filling pressures. This response was seen in the normal and in the nonangina group where LVEDP decreased sharply. During pacing in the angina group, LVEDP fell initially but subsequently increased as myocardial ischemia developed. The filling pressures did not however exceed those observed during the control period. This level of LVEDP, although within the normal range, does in fact represent an abnormal response during atrial pacing. When pacing is stopped, heart rate and stroke work return abruptly to normal, and LVEDP in the normal and nonangina groups rose immediately to normal levels. In the angina group, however, when pacing was interrupted during myocardial ischemia, LVEDP rose to levels clearly above those seen during the control period and during early interruption of pacing prior to the development of ischemia. This pattern of abnormal ventricular function during pacing-induced ischemia has been attributed to transient left ventricular failure but there have been no simultaneous measurements of left ventricular volume to indicate whether the pressure changes were due to changes in ventricular volume or to alterations in left ventricular diastolic compliance.

Figure 5 shows the simultaneous changes in left ventricular end-diastolic pressure and end-diastolic volume during the various phases of the study. It is evident that changes in volume induced by altering heart rate are accompanied by directional changes in filling pressure. Furthermore, during myocardial ischemia, elevations of filling pressure were seen to be associated with increased ventricular end-diastolic volume. These data suggest that the elevation of left ventricular end-diastolic pressure during myocardial ischemia is due at least in part to the increase in left ventricular volume.

Determination of left ventricular volume by means of echocardiography is dependent on the measurement of one ventricular dimension. Thus if the ventricular configuration is abnormal the calculated volume, assuming the ventricle to be a prolate ellipse, would be invalid. In coronary artery disease it is recognized that localized contraction abnormalities are frequently manifest during systole, and this is particularly so during episodes of ischemia. This phenomenon may be responsible for the disparity seen between stroke volume measurements by the dye dilution method and the ultrasonic technique in some of our patients with coronary artery disease. Such abnormalities are however systolic events and measurements of ventricular volume during diastole should not be affected significantly by ischemia. We thus feel that
LV PRESSURE-VOLUME DURING ISCHEMIA

Percent change from control for left ventricular end-diastolic volume (LVVed) and left ventricular end-diastolic pressure (LVEDP) for the three groups of patients. During pacing LVVed and LVEDP fall in each of the three groups and return to near control values with interruption of pacing. During late pacing, when ischemia has developed in the angina group, the fall in LVVed is less than during early pacing. During late interruption the normal and nonangina groups return to normal levels of LVVed and LVEDP but in the angina group LVVed and LVEDP are above control levels.

In previous studies of the alterations in left ventricular volume during myocardial ischemia, measurements in the control state were not made at heart rates comparable to those when ischemia was present. Thus a direct comparison of these results with the present study is difficult. However, Dwyer, using angiographic methods, did show that left ventricular end-diastolic volume fell less during pacing in nine patients experiencing angina than in a group of normal subjects. In one patient left ventricular end-diastolic volume was greater during pacing-induced ischemia than during sinus rhythm in the control period. Eubanks et al. measured left ventricular volume angiographically at rest and during supine leg exercise in 15 patients with coronary artery disease. They were able to demonstrate a greater increase in end-diastolic volume in the patients who developed ischemia than in those who did not. On the other hand Kasperian and Weiner, employing a thermodilation technique, reported a decrease in ventricular volume during angina induced by exercise and atrial pacing. These workers did not however state how many patients developed angina during pacing; a reduction in left ventricular volume is to be expected when heart rate increases.

Several investigators have reported decreased ventricular compliance in patients with coronary artery disease. The curvilinear nature of the pressure-volume relationships of the left ventricle however makes comparison of data from ventricles of different size difficult. Ventricular compliance has been estimated by relating the change in volume occurring as a result of atrial systole to the concomitant change in pressure (ΔV/ΔP). When the volume and pressure data from the present study during the control period were analyzed in this fashion some patients with coronary artery disease had values for ventricular compliance that were clearly below the average for the normal group. There was considerable range however and the averages for the three groups were not significantly different. The individual values for ΔV/ΔP did not appear to be related to ventricular volume or to the presence or absence of ventricular contraction abnormalities.

It has been suggested that the elevation of left ventricular end-diastolic pressure during angina pectoris is a reflection of a transient fall in left ventricular compliance related to myocardial ischemia. In figure 6 the average left ventricular pressure in the angina group before and following atrial systole during sinus rhythm and at end diastole during pacing are plotted against the corresponding values for ventricular volume. In this method of presentation a shift upward and to the left would indicate a decrease in compliance. When the data obtained prior to the onset of angina are compared to that occurring during ischemia, no clear shift in the pressure-volume curve is apparent. Thus the elevation of left ventricular end-diastolic pressure during myocardial ischemia appears to be due largely to the increase in left ventricular volume and not to a decrease in compliance.

The increase in left ventricular volume is likely the result of the following chain of events. Myocardial ischemia is precipitated by an increase in oxygen requirements over the available supply, and metabolic alterations produced by ischemia.

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result in asynergy of the ischemic area. With the functional loss of a portion of the ventricular muscle, ventricular ejection falls and an increase in residual volume occurs. Venous return and ventricular filling remain essentially unchanged, however, and thus left ventricular end-diastolic volume increases with an accompanying rise in left ventricular end-diastolic pressure. The nonischemic portions of the left ventricle are now at an increased fiber length and because of the Frank-Starling mechanism are able to contract more forcibly and to compensate, at least in part, for the ischemic regions of ventricular muscle.

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JOHN L. McCANS and JOHN O. PARKER

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