Left Ventricular Pressure-Volume Alterations and Regional Disorders of Contraction During Myocardial Ischemia Induced by Atrial Pacing

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SUMMARY

Left ventricular function, pressure-volume relationships, and wall motion were studied by sequential cineventriculography during acute myocardial ischemia, induced by atrial pacing, in 10 subjects. Observations made in this group were contrasted to data obtained during atrial pacing in a smaller normal group.

An acute alteration in the pressure-volume relation occurred in five subjects during ischemia with an elevation of the left ventricular end-diastolic pressure, associated with a declining end-diastolic volume.

A deterioration in ventricular function, as manifested by a rightward shift of the ventricular function curve, was also observed in eight of the angina group. A more severe instance of myocardial failure was seen in one patient, who, during angina, demonstrated a marked increase of both left ventricular end-diastolic pressure and end-diastolic volume.

Asynergy of left ventricular contraction occurred acutely during angina and was usually manifested by regional akinesis or hypokinesis. Diminished wall motion was often found in more than one region, reflecting multiple vessel involvement. We were generally able to correlate the dynamic alteration in wall motion with deteriorating ventricular function.

Additional Indexing Words:
Angina pectoris Ventricular function Regional motion of left ventricular wall

VENTRICULAR end-diastolic compliance

ALTHOUGH alterations in hemodynamics, metabolism, and the electrocardiogram have been extensively studied during angina pectoris, induced by exercise and atrial pacing, relatively little is known concerning the volume changes and characteristics of ventricular wall motion during angina.

The association of angina and an elevation of the left ventricular end-diastolic pressure, seen consistently with exercise and occasionally with atrial pacing, has led to an interpretation that angina is a reversible state of heart failure. Support of this interpretation can be readily found in animal experimentation where tangible evidence of impaired myocardial contractility appears when left ventricular ischemia is produced.

However, with myocardial ischemia in man, the accompanying increases in cardiac output, mean systolic ejection rate, stroke work, and left ventricular dp/dt are not typical of the hemodynamic responses seen in heart failure. Therefore, an alternate explanation of the increased ventricular filling pressure has been proposed. It has been suggested that a reduction in diastolic compliance occurs during myocardial ischemia. Our investigation was directed toward clarification of the
left ventricular pressure-volume relationship during angina pectoris. To this end, sequential single plane angiography and left ventricular pressure determinations were obtained prior to and during angina pectoris precipitated by atrial pacing.

An additional feature of the study is the angiographic technic which permits analysis of ventricular wall motion during angina.

Several observations have been made in both the experimental animal\textsuperscript{11, 12} and man\textsuperscript{13} which demonstrate the frequency in which the contractility of regional myocardial areas are depressed by an acute coronary occlusion. Herman and associates,\textsuperscript{14} in an extensive study of myocardial contraction in patients with coronary artery disease, presented evidence of chronic abnormalities of regional ventricular morphology. The left ventricular angiograms in our patients point up the magnitude and frequency of regional dynamic disorders of ventricular wall motion which can be seen acutely during angina pectoris and are apparently reversible.

Methods

The study was performed in 11 male and two female patients, whose ages ranged from 25 to 68 years. Three of the subjects were considered normal by standard hemodynamic measurements and coronary arteriography. Each of these patients was studied for evaluation of chest pain. For the remaining 10 patients, a typical history of angina pectoris was obtained. A history of a myocardial infarction and confirmatory electrocardiographic evidence of a transmural infarction was obtained in nine of these 10 patients. All were potential candidates for coronary artery surgery and were studied for that purpose. Symptoms or signs of congestive heart failure were elicited in only one patient (H.L.). All patients were in sinus rhythm.

The patients were brought to the laboratory in the fasting postabsorptive state, following premedication with oral pentobarbital (100 mg). Under local anesthesia (lidocaine, 1%), the right brachial artery and vein were isolated. Retrograde left heart catheterization was performed with a Statham SF-1 catheter-tip micromanometer to permit recording of the pressures with high fidelity.

Observations of pulmonary artery pressure, left ventricular (LV) pressure, brachial artery pressure, and cardiac output were made during a 20-min control period with the patient in a supine position. Left ventricular end-diastolic pressure was determined from high amplification pressure tracings. The zero reference pressure was set at midchest level. The first derivative of the left ventricular pressure curve (LV dp/dt) was measured by an R/C differentiating circuit.\textsuperscript{*} The other pressures were measured with Statham strain-gauge transducers (P23Db series). Cardiac output determinations were made by the dye-dilution technic, with injection of indocyanine green into the pulmonary artery. Cineventriculography was performed through multiple-hole, closed-tip catheters with injection of 50 to 60 ml of methylglucamine diatrizoate (Renograin-76) into the pulmonary artery. During the ventriculogram, left ventricular pressure, brachial artery pressure, LV dp/dt, and the electrocardiogram were recorded simultaneously at 200 mm/sec on a photographic recorder\textsuperscript{*} and also directly on the cine-film using the cine-tracing system.\textsuperscript{*} To minimize the effects of contrast material on ventricular function, the earliest systoles providing adequate visualization of the left ventricular cavity were analyzed.

A no. 5 or no. 6 bipolar electrode catheter was positioned at the lateral wall of the right atrium. Heart rates were gradually increased in increments of 10 to 20 beats/min until the appearance of angina or marked ST-segment changes. With either manifestation of myocardial ischemia, pressure measurements and cardiac output were repeated. To insure the same relationship between the long and short axes, the patient was rotated to the same right anterior oblique position, using a calibrated mechanical rotating cradle, and a repeat ventriculogram was obtained. All ventriculograms were obtained at end-inspiration and as a consequence of our own observations and those of others,\textsuperscript{14, 15} an interval of 25 to 30 min was allowed between ventriculograms to permit normalization of the hemodynamic state. Selective cineangiography of the right and left coronary arteries was then performed in multiple projections by the Sones technic.

Calibration of all measurements in each ventriculogram to actual dimensions was done by positioning a grid with 1-cm markings at the level of the cardiac apex so that a single factor (f) could be calculated to correct for magnification and distortion.

The silhouette of the left ventricular end-diastolic cavity was drawn in outline. The area (A) within the left ventricular outline was obtained by planimetry. The long axis (L) from apex to mid-plane of the mitral valve was

\textsuperscript{*} Electronics for Medicine, Inc., White Plains, New York.

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measured directly. Average width (W) or short axis was then calculated from the equation for the area of an ellipse, where

\[ W = \frac{4A}{\pi L}. \]

Left ventricular end-diastolic volume was calculated from the single plane cine picture, using the ellipsoid model and method as described in detail by Greene and co-workers. The formula used in each instance is:

\[ V = \frac{\pi}{6} \cdot \frac{1}{f^2} \cdot L \cdot W^2 \]

where \( V \) = volume; \( f \) = magnification factor; \( L \) = long axis, and \( W \) = short axis.

Original validation of the angiographic technic was done by Dodge and Tannenbaum using a biplane technic. Later studies by Greene and associates as well as Hermann and Bartle demonstrated a high degree of correlation between the single plane and biplane angiographic technic. Regardless, it was not our purpose to present absolute data on ventricular volume but to reflect as accurately as possible the relative changes in volume during myocardial ischemia.

The stroke volume was calculated by dividing the dye-dilution cardiac output determination by the heart rate. It was elected not to use the stroke volume as determined by the angiographic technic because of our own and other authors' observations of difficulties in the measurement of end-systolic volume. Mitchell's group as well as Davila and Sanmarco have aptly characterized the problem; the cavity does not retain its ellipsoid shape during ejection, and also there is a significant underestimation of the end-systolic chamber silhouette due to small amounts of dye in the deep trabeculations of the ventricle. As a result, Davila and Sanmarco suggested that parallel measurement of a dye-dilution cardiac output for stroke volume and end-diastolic volume by angiography may provide the most reproducible data for estimation of ejection fraction. The ejection fraction was determined by dividing the dye solution stroke volume by the angiographic end-diastolic volume. The ejection fraction, so determined, will usually be less than the ejection fraction calculated solely by the angiographic technic. An equivalence between the dye-dilution and angiographic method is not implied. The dye-dilution stroke volume was used because of its demonstrated reproducibility.

Ventricular wall motion was analyzed by constructing perpendiculars to the long axis, at quarter length intervals. Each of these perpendiculars was divided into two parts (the anterior wall hemiaxis and the posterior wall hemiaxis) by the long axis. The hemiaxes were then measured at end diastole and end systole and the difference recorded as percent change (fig. 1). For ease of analysis, the percent changes in the three hemiaxes of the anterior and posterior walls were averaged and summarized in table 1 as a single factor. The percentage change was measured at rest and during myocardial ischemia induced by atrial pacing. A similar analysis of apical wall motion was carried out. The point of reference for this measurement was the transverse diameter at the midpoint of the long axis.

Finally, the pressure-volume relationship of the left ventricle was examined at a single point in the cardiac cycle, that is, end diastole. We have taken the ratio LVEDV:LVEDP at this point and

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**Figure 1**

*Normal left ventricular contraction at rest and during atrial pacing. The percent of inward motion depicted at each hemiaxis represents the ratio of the wall movement during systole to the radius at end diastole. Atrial pacing reduced the end-diastolic volume while the degree of wall motion increased in the majority of regions in the ventricle.*

*Circulation, Volume XLII, December 1970*
Table 1
Hemodynamic and Angiographic Data Obtained from the Normal and the Angina Patients

<table>
<thead>
<tr>
<th>Pt. &amp; BSA</th>
<th>Age &amp; sex</th>
<th>State</th>
<th>HR</th>
<th>CI</th>
<th>SI</th>
<th>EDV</th>
<th>EF (%)</th>
<th>LV dp/dt</th>
<th>LVSP</th>
<th>LVEDP</th>
<th>Motion (% Δ)</th>
<th>Ant. wall</th>
<th>Post. wall</th>
<th>Apex</th>
<th>LV compliance</th>
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<td>T.L.</td>
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<td>84</td>
<td>3.7</td>
<td>44</td>
<td>116</td>
<td>38</td>
<td>900</td>
<td>125</td>
<td>6</td>
<td>26</td>
<td>31</td>
<td>10</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>1.94</td>
<td>52 M</td>
<td>Rest</td>
<td>115</td>
<td>3.7</td>
<td>32</td>
<td>85</td>
<td>38</td>
<td>1340</td>
<td>130</td>
<td>3</td>
<td>27</td>
<td>47</td>
<td>7</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>R.A.</td>
<td>46 M</td>
<td>Rest</td>
<td>75</td>
<td>3.2</td>
<td>43</td>
<td>93</td>
<td>46</td>
<td>1740</td>
<td>120</td>
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<tr>
<td>1.78</td>
<td>52 M</td>
<td>Pacing</td>
<td>70</td>
<td>3.0</td>
<td>44</td>
<td>100</td>
<td>44</td>
<td>900</td>
<td>120</td>
<td>7</td>
<td>37</td>
<td>52</td>
<td>23</td>
<td>27</td>
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</tr>
<tr>
<td>F.H.</td>
<td>52 M</td>
<td>Pacing</td>
<td>115</td>
<td>3.8</td>
<td>32</td>
<td>43</td>
<td>74</td>
<td>1200</td>
<td>120</td>
<td>3</td>
<td>55</td>
<td>65</td>
<td>50</td>
<td>27</td>
<td></td>
</tr>
</tbody>
</table>

- **Normal group**
  - C.N. | 40 M | Rest | 96 | 4.5| 47 | 118 | 40     | 1800     | 120   | 9     | 13        | 0        | 10         |
  - 1.97 | Pacing| 150 | 4.5| 30 | 103| 29   | 2100   | 135   | 20    | 13       | 2        | 0          |
  - 1.98 | Pacing| 66  | 3.9| 59 | 134| 44   | 1560   | 120   | 16    | 40       | 24       | 21         |
  - J.S. | 41 M | Rest | 80 | 2.9| 36 | 88  | 41     | 1320    | 100   | 12    | 22       | 44       | 8          |
  - 1.96 | Pacing| 110 | 1.5| 14 | 163| 9    | 1270   | 170   | 40    | 9        | 13       | 0          |

- **Angina group**
  - 1.94 | Pacing| 130 | 2.4| 18 | 36 | 50   | 1200   | 130   | 6     | 36       | 37       | 20         |
  - J.G. | 39 F  | Rest | 110| 2.9| 26 | 89  | 30     | 1080    | 105   | 10    | 26       | 23       | 4          |
  - R.K. | 41 M | Rest | 66 | 3.5| 53 | 105 | 50     | 1200    | 140   | 16    | 45       | 57       | 29         |
  - 1.81 | Pacing| 90  | 4.0| 44 | 91 | 48   | 1380   | 140   | 25    | 35       | 33       | 17         |
  - F.L. | 48 M | Rest | 55 | 2.3| 42 | 81  | 51     | 1050    | 190   | 15    | 55       | 30       | 8          |

<table>
<thead>
<tr>
<th>Pt. &amp; BSA</th>
<th>Age &amp; sex</th>
<th>State</th>
<th>HR</th>
<th>CI</th>
<th>SI</th>
<th>EDV</th>
<th>EF (%)</th>
<th>LV dp/dt</th>
<th>LVSP</th>
<th>LVEDP</th>
<th>Motion (% Δ)</th>
<th>Ant. wall</th>
<th>Post. wall</th>
<th>Apex</th>
<th>LV compliance</th>
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<td>Rest</td>
<td>75</td>
<td>2.2</td>
<td>30</td>
<td>69</td>
<td>50</td>
<td>1770</td>
<td>160</td>
<td>21</td>
<td>19</td>
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<tr>
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<td>Pacing</td>
<td>138</td>
<td>2.7</td>
<td>20</td>
<td>36</td>
<td>55</td>
<td>1925</td>
<td>135</td>
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</tr>
<tr>
<td>H.L.</td>
<td>68 M</td>
<td>Rest</td>
<td>70</td>
<td>2.9</td>
<td>42</td>
<td>174</td>
<td>24</td>
<td>1000</td>
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<td>15</td>
<td>8</td>
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</tr>
<tr>
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<td>Pacing</td>
<td>120</td>
<td>2.6</td>
<td>22</td>
<td>163</td>
<td>13</td>
<td>1100</td>
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<td>9</td>
<td>0</td>
<td>6</td>
<td></td>
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</tbody>
</table>

**Abbreviations:** BSA = body surface area (m²); HR = heart rate (beats/min); CI = cardiac index (L/min/m²); SI = stroke index (mL/m²); EDV = end-diastolic volume (mL/m²); EF = ejection fraction (%); LV dp/dt = left ventricular first derivative (mm Hg/sec); LVSP = left ventricular systolic pressure (mm Hg); LVEDP = left ventricular end-diastolic pressure (mm Hg); Ant. wall = anterior wall motion (% change); Post. wall = posterior wall motion (% change); Apex = apical wall motion (% change); LV compliance = left ventricular compliance (units; EDV/LVEDP).
expressed it as left ventricular end-diastolic compliance. This determination was made for the resting state and during atrial pacing.

In circulatory physiology, the term "compliance" has generally referred to the volume change for a given change in pressure \( \Delta V / \Delta P \). Dodge and Tannenbaum,\(^1\) in the course of construction of pressure-volume loops from angiographic data analyzed diastolic compliance in the traditional manner, while other investigators\(^{21-23} \) have studied pressure-volume changes by simply relating end-diastolic volume or circumference to end-diastolic pressure. Recognizing that we are not expressing true diastolic compliance of the left ventricle, we nevertheless feel that this ratio provides a useful means of expressing the relationship of pressure and volume at this specific phase in diastole.

For the purpose of statistical analysis, individual data were converted to percent change and comparisons between the two groups were performed using an unpaired t test.

**Results**

The effects of atrial pacing on the normal group and on those patients who developed myocardial ischemia are summarized in table 1.

In the normal group, atrial pacing failed to elicit any chest pain or electrocardiographic changes; whereas, in the patients with demonstrated coronary artery disease, angina was elicited in seven and marked ST-segment changes in the other three.

The coronary arteriograms were, of course, normal in the normal group. In the angina group, the two female patients demonstrated single vessel involvement, while in the eight remaining male subjects, either two of the three or all three vessels were significantly (>75%) obstructed.

**Hemodynamics**

The average heart rate increased from 76 to 117 beats/min with atrial pacing in the normal patients and from 80 to 128 beats/min in the group with angina. In both groups, the mean cardiac index and systolic pressure remained unchanged during pacing, and the stroke index also failed to demonstrate any significant change between the normal (44 to 30 ml/m\(^2\)) and angina (39 to 23 ml/m\(^2\)) groups (fig. 2).

Left ventricular end-diastolic pressure (LVEDP) fell from 8 to 3 mm Hg during atrial pacing in the normal subjects, whereas in the angina group, an increase occurred in four patients, no change in one, and in the remaining five, a reduction was found (15 to 9 mm Hg). However, when compared to the group of normal subjects (fig. 2), there was no significant difference.

The left ventricular dp/dt increased in all subjects of both normal and abnormal groups. In the normal patients, the average change was 440 mm Hg/sec while in the angina group, the average increase was significantly less \((P < 0.05)\), increasing only 250 mm Hg/sec during atrial pacing.

**Left Ventricular End-Diastolic Volume (LVEDV)**

In the normal group, the average LVEDV was 103 ml/m\(^2\) which fell to 62 ml/m\(^2\) during atrial pacing. In the patients with angina, the LVEDV at rest was somewhat less (98 ml/m\(^2\)) than in the normal group. In nine of 10 patients, atrial pacing resulted in a fall (81 ml/m\(^2\)) in end-diastolic volume (fig. 2). The magnitude of this reduction was significantly
A patient who developed overt heart failure during angina. Angina has resulted in a marked increase in end-diastolic pressure and a fall in stroke work.

Figure 3

(P < 0.05) less than that seen in the normals. In one patient (fig. 3), however, angina pectoris induced by atrial pacing was accompanied by a marked increase in the LVEDV (65 to 163 ml/m²).

Ejection Fraction

In the normal subjects, the mean resting ejection fraction was calculated as 43%. With atrial pacing, an average but nonsignificant change in the ejection fraction occurred, increasing from 43 to 53%. Analysis of the effect of atrial pacing on the ejection fraction of the normal group revealed that no change occurred in two of the subjects while in the third patient, the ejection fraction rose from 44 to 74%, accounting entirely for the mean increase.

In the group with angina, atrial pacing resulted in a decline in the ejection fraction in eight patients and remained essentially unchanged in the other two subjects. The overall average decline in the 10 patients was from 41 to 32% (fig. 4), which was significantly (P < 0.05) different from the normal group.

In one of the patients (J. L.) with angina, the reduction was severe (from 38 to 9%) and was associated with a marked increase in both LVEDV and LVEDP, indicative of gross deterioration of left ventricular function.

Left Ventricular End-Diastolic Compliance

The left ventricular end-diastolic compliance in the normal group during the control period averaged 27 units and increased to 35 units during atrial pacing.

In the group with angina, resting left ventricular end-diastolic compliance (12 units) was less than the normal group and declined during myocardial ischemia to 10 units. The change demonstrated in the angina group was significantly different (P < 0.01) from the normal subjects.

In five patients, an abnormal decline in end-

Figure 4

Mean values of left ventricular end-diastolic compliance and ejection fraction. In contrast to normals, the patients with pacing-induced ischemia demonstrate a significant (P < 0.05) reduction in compliance and the ejection fraction.
diastolic compliance resulted from acute myocardial ischemia. In one of these five, angina resulted in a precipitous increase of both the filling pressure and volume, concurrent with a decline in stroke work. This latter response is representative of changes usually described in left ventricular failure (fig. 5). Of the other four demonstrating an abnormal reduction in end-diastolic compliance, the left ventricular end-diastolic volume declined during atrial pacing in all, while the filling pressure increased in three and was unchanged in one (fig. 5).

The other five subjects responded normally to atrial pacing in spite of the appearance of angina. In each of these five, both ventricular diastolic volume and pressure diminished during pacing.

**Patterns of Ventricular Contraction**

In the normal patients, the left ventricular wall moved inward in a concentric fashion during systolic ejection (fig. 1). A quantitative analysis of contraction in the anteroposterior axes and base-apex axis demonstrated a variable degree of contraction within the left ventricle and between different ventricles. The sum of three regions of the anterior wall motion ranged from 26 to 51%, while the posterior wall contraction ranged from 31 to 55%. At the apex a lesser degree of contraction was observed, ranging from 10 to 23%.

In the group with angina pectoris, abnormal patterns of ventricular contraction were seen in five patients in the resting state. The other five exhibited a normal pattern of ventricular wall motion. Of the five with asynergy, regional akinesis was found in two patients, a ventricular aneurysm was present in one, antero-apical dyskinesis in one, and in the fifth, regional hypokinesis was observed in the basal section of the posterior wall. Both the aneurysm and regional hypokinesis were confirmed during subsequent surgery.

During atrial pacing, the sequence or degree of myocardial contraction, in the normal group, was not altered in any significant fashion. In general, the normal patients tended to increase the degree of wall motion during atrial pacing, whereas, in eight of the patients with myocardial ischemia during atrial pacing, gross regional alterations in ventricular wall motion were observed. Five of the patients showed diminution of ventricular wall motion in two separate regions (fig. 6), and in the other three patients, regional hypokinesis was observed in a single region. In each instance, an associated narrowed coronary artery, supplying the affected region, could be demonstrated. In the two patients with no observed decline in wall motion, the ejection fraction remained at normal levels during atrial pacing. Quantitation of the changes in wall movement was carried out. The reductions found during myocardial ischemia ranged from 7 to 35%, with an 18% overall decline in the regions affected (fig. 7).

**Discussion**

The technic of atrial pacing, as described by Sowton and associates\(^{24}\) was used to elicit acute reversible myocardial ischemia, manifested by either angina pectoris or severe ST-segment depression. During this period of myocardial ischemia, an analysis of volume

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**Figure 5**

Pressure-volume changes which occurred during atrial pacing in individual subjects. A single patient demonstrated typical heart failure with elevation of left ventricular end-diastolic pressure and volume, while four of the group exhibited alteration in end-diastolic compliance during pacing-induced ischemia. The remainder, three normal subjects and five of the patients with angina, responded in a normal manner to the tachycardia with a decline in both end-diastolic pressure and volume.
changes, ventricular motion, and hemodynamic alterations was undertaken.

In a group of three normal patients, the effects of atrial pacing were studied and contrasted to the results obtained in the angina group by statistical analysis. The small number in the normal group is an acknowledged deficiency in the study, which presents some difficulties in analysis of the effects of pacing in the angina group. The inclusion of stress hemodynamics as an integral part of most catheterizations may account for our infrequent encounter with normal patients. Fortunately, the hemodynamic and volume data obtained in our few normals is similar to results reported by others during pacing. Cardiac output remains stable, while a decline in arterial pressure, stroke volume, and left ventricular end-diastolic pressure is observed.

Atrial pacing to heart rates between 115 and 120 beats/min produced a 40% reduction in end-diastolic volume, so that, in spite of a 32% decline in stroke volume, the ejection fraction increased by 10%. This change was accounted for solely by a marked increase in one of the subjects while the remaining two were unchanged. Bristow and associates using a thermodilution technic in dogs, found an

Figure 6
These two patients show a diminution of wall contraction during atrial pacing-induced ischemia. In both patients, anterior and posterior walls show diminished motion. The irregular outline in patient C.N. represents an anterolateral aneurysm.

Figure 7
Regional hypokinesis was a frequent occurrence during tachycardia-induced ischemia. The frequent reduction in the percentage of regional wall motion contrasts with the mean augmentation in contraction found in normal subjects.
unchanged ejection fraction (equal decline in stroke and end-diastolic volume) at increase in the heart rate comparable to that in our normals. Tsakiris’ group27 estimated volumes in animals with an angiographic technic during induced tachycardia. Their results in three animals calculated at heart rates under 150 beats/min demonstrated a slight average decline in ejection fraction from 40% down to 38%.

In the patients with tachycardia-induced angina, hemodynamic changes likewise did not differ from previous reports.5–7 During the tachycardia, stroke volume and work fell, left ventricular dp/dt increased, and cardiac output remained stable. The degree and direction of change of the left ventricular end-diastolic pressure were variable. In four of our subjects, an increase was observed. Although such an increase is inconstant during pacing-induced angina, it is a consistent finding during exertional angina.1,2 The increased left ventricular filling pressure during exertional angina has been interpreted as heart failure by some authors5,7,28 and as a diminished diastolic compliance by others.2,5,6 The several observations of gross myocardial deterioration, during both graded ischemia and complete coronary artery occlusion9,29 in animals, have given considerable substantiation to the impression that heart failure occurs during angina.

Braunwald30 and more recently, Rackley and associates,31 have discussed the difficulties inherent in the assumption that increases in diastolic pressure represent increases in myocardial fiber length. Discrepancies have been frequently demonstrated between end-diastolic volumes and pressures, particularly in diseased hearts.

Several other observations have suggested that an acute alteration in compliance occurs rather than heart failure. Increases in cardiac output, stroke work, mean systolic ejection rate, and LV dp/dt, although subnormal, are measured during exertional angina, whereas, these parameters usually decline during exertional stress in those subjects who exhibit classical “congestive” heart failure.10 Animal experiments by Bianco and associates32 have also directed attention to a reduction in left ventricular compliance following a coronary occlusion. In addition, Kasparian and Winer38 have presented recent data with a thermodilution technic in human subjects supporting the concept of an acute alteration of pressure-volume relationships during transient ischemia.

Observations from our studies suggest that both interpretations are valid, since both a change in end-diastolic compliance and a shift of the ventricular function curve to the right were observed. An abnormal pressure-volume relationship in the left ventricle was found during angina in five of the patients. In four, an increasing or stable filling pressure was associated with a declining end-diastolic volume (fig. 5).

Does the faster heart rate (increase of 11 beats/min) achieved in the angina group account for the difference in the pressure-volume response to atrial pacing? Mitchell and associates34 demonstrated increases in ventricular end-diastolic pressure with a declining end-diastolic volume at very rapid heart rates. They attributed the change to incomplete ventricular relaxation. Such changes in left ventricular end-diastolic pressure have not been observed in normal subjects at paced heart rates under 150 beats/min.5,7 Therefore, it does not seem likely that the somewhat more rapid heart rate accounts for the observed difference between groups, and indeed, the induced heart rate was 120 beats/min or less in three of the five patients with a demonstrated alteration in end-diastolic compliance.

Ventricular function, as expressed by the relationship between stroke work and end-diastolic volume, deteriorated during angina pectoris, that is, the ventricular function curve was observed to shift to the right (fig. 8). The stroke volume diminished in a normal fashion during the tachycardia, but the volume decline was less than expected. It would appear that compensatory mechanisms are operative in the ischemic left ventricle during pacing, wherein a greater-than-expected fiber length is achieved to maintain an appropriate
stroke volume. Unfortunately, the presence of a pre-existing infarction in nine of our 10 patients prevents a clear-cut analysis of this change. The presence of a larger-than-expected filling volume during tachycardia-induced angina could be related to either the residual infarction or the acutely ischemic myocardium. To clarify this point, further volume studies should be carried out during angina on patients who do not have residual infarctions. However, in one patient, gross left ventricular deterioration occurred during angina and was rapidly reversed with cessation of pacing. In this subject, we observed a considerable increase of both filling pressure and volume with a striking reduction in stroke volume. It is clear from this one patient that overt left ventricular failure can occur during angina pectoris.

Since stroke volume and end-diastolic vol-

ume are the two determinants of the ejection fraction, this factor also aptly characterizes the direction and degree of change of ventricular function. As might be expected, a significant difference was found between the normal and angina group. In the normal group, an observed but not significant increase in the ejection fraction was shown during atrial pacing while a decline in ejection fraction was noted during angina.

Regional disturbances of myocardial contraction have been extensively studied by Herman and co-workers in patients with residual infarction. Similar analysis of myocardial regions has been carried out during acute ischemia, usually secondary to a coronary occlusion. In these studies, myographic measurements of segment length showed systolic lengthening and reduced contractility of the infarcted myocardium shortly after the onset of ischemia.11, 12, 35 In patients with an acute infarction or angina, several authors, using kinetocardiographic and kymographic technics, have shown that an area of ischemia may exhibit reduced contractility or even a systolic bulge.

Left ventricular wall motion was studied during a period of acute myocardial ischemia and compared to wall motion in normals during pacing. In the three normal subjects, anterior and posterior ventricular wall shortening during systole ranged from 26 to 62% while apical inward movement was somewhat less (10 to 23%). At most regions, the degree of wall motion was substantially unchanged, and in a few regions, an increase was observed during atrial pacing. Abnormal regional disturbances of contraction were found in eight of 10 patients with acute ischemia. Asynergy of multiple regions was a common observation, and this may simply reflect the presence of multiple vessel involvement in a large percentage of our patients.

The appearance of akinesia in a previously contracting region was observed in several patients. However, the most frequent alteration during angina was a reduction in the degree of wall motion (hypokinesis). It is of some interest that in the two patients without

Figure 8

During atrial pacing, normal subjects exhibit a concurrent decline in stroke work and end-diastolic volume. The angina group, during ischemia, failed to demonstrate an appropriate decline in end-diastolic volume for the observed decrease in stroke work which occurred with institution of atrial pacing. This resulted in a shift from a normal to an abnormal function curve consistent with depression of ventricular function.
observed changes in wall movement, stroke volume, end-diastolic volume, and ejection fraction changed in a normal fashion during pacing-induced angina.

Maintenance of cardiac output in the presence of a dynamic regional asynchrony during ischemia reflects the capacity of a nonaffected myocardium to augment its performance. Attention was directed toward this phenomenon particularly in patients in whom only single regions were affected. The opposite wall was frequently observed to increase its degree of contraction during ischemia, but the changes we observed were no greater than those changes found in normal subjects during induced tachycardia. It is possible that areas not adequately visualized during angiography (that is, lateral wall or septum) may be performing super-normally. There are supporting metabolic and physiologic studies of the normal myocardium during focal ischemia which suggest that a compensatory improvement in the function of nonaffected regions occurs in order to maintain an adequate stroke output.

This study emphasizes the multifaceted picture of angina pectoris. A single view of this disorder will not provide an adequate explanation of all the observed clinical and physiologic alterations. The degree of ischemia, the number of diseased vessels and the reserve capacity of nondiseased myocardium are a few of the many factors which determine the overall response of the heart to stress. Caution should be exercised not to extrapolate these data to explain changes occurring during exer-tional angina. Increased venous return occurring during exercise as well as increased sympathetic tone may induce different alterations in wall motion and volume.

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