Reversible Cardiac Failure
During Angina Pectoris

Hemodynamic Effects of Atrial Pacing
in Coronary Artery Disease

By John O. Parker, M.D., J. Rodney Ledwich, M.B.,
Roxroy O. West, M.D., and Robert B. Case, M.D.

SUMMARY
Left ventricular end-diastolic pressure and left ventricular stroke work were measured during a 10-min period of atrial pacing in 10 normal subjects and 30 patients with coronary artery disease. The normal subjects and the patients with coronary artery disease who did not experience angina during pacing reacted similarly with a fall in left ventricular end-diastolic pressure from 8 to 2 mm Hg returning to control values on cessation of pacing. The average left ventricular end-diastolic pressure during pacing in the 21 patients who developed angina was similar to control values although this pressure rose to abnormal levels in four patients. On cessation of pacing the left ventricular end-diastolic pressure rose abruptly to an average value of 22 mm Hg. This lack of elevation of filling pressure during pacing and the rise to abnormal levels on termination of pacing can best be explained by relating left ventricular end-diastolic pressure to left ventricular stroke work. Analyzed in this fashion it is evident that the ischemic ventricle is operating on a depressed ventricle function curve. This depression of function is reversible following cessation of pacing and can be prevented by the prior administration of nitroglycerin.

Additional Indexing Words:
Ventricular function curve
Left ventricular stroke work
Nitroglycerin

Angina Pectoris, precipitated by exercise or occurring spontaneously, is generally, but not always, associated with an elevation of left ventricular filling pressure. Our investigations have consistently shown a high left ventricular end-diastolic pressure during exertional angina, averaging 34 mm Hg. This was not accompanied by an increase in left ventricular stroke work and we have interpreted these changes as evidence of left ventricular failure during myocardial ischemia. Recent reports have shown that angina can be readily produced by increasing heart rate with atrial pacing, although angina produced in this manner is associated with normal or only slightly elevated left ventricular filling pressure. This is in sharp contrast to the gross abnormalities observed during exertional or spontaneous angina. In view of this seeming paradox, we have assessed left ventricular performance during myocardial ischemia utilizing the technic of right atrial pacing. The effect of nitroglycerin on the clinical and...
hemodynamic consequences of pacing was also evaluated. The precipitation of angina solely by increase in heart rate also makes it possible to examine left ventricular function without the changes in cardiac output, oxygen consumption, and circulating catecholamines that accompany exercise.

Methods

Hemodynamic investigations with subsequent selective cine-coronary arteriography and left ventriculography were performed in 42 patients with known or suspected coronary artery disease without cardiomegaly, arrhythmias, or clinical evidence of cardiac failure. None of the patients was receiving digitalis or diuretics at the time of the study. Ten patients had systolic pressure exceeding 140 mm Hg, in two of whom it exceeded 170, but only four had diastolic pressure exceeding 90 mm Hg. None had been treated for arterial hypertension or exhibited hypertensive retinopathy exceeding grade 1 in severity.

The patients were brought to the laboratory the day prior to the study so they would be familiar with the surroundings and the nature of the procedure. Resting minute ventilation was recorded and a period of supine leg exercise carried out on a bicycle ergometer. This allowed us to observe the patient's response to stress and to estimate the pacing rate that would be required to produce angina. In general, the heart rate required to produce pain with atrial pacing was 20 beats/min more than that coincident with the onset of angina during exercise.

Patients were studied in the fasting state without premedication. Under local anesthesia the brachial artery and two veins were isolated in the right antecubital fossa. The tip of a no. 6 bipolar pacing catheter was placed either in the midportion of the coronary sinus or against the lateral wall of the right atrium. A no. 9 double lumen Courmand catheter was passed into the right heart so the tip lay in the pulmonary artery and the proximal lumen in the right ventricle. A no. 8 Sones catheter was inserted into the left ventricle from the right brachial artery and the left brachial artery was cannulated with a Courmand needle. Lead II of the electrocardiogram and pressures from the pulmonary artery, right ventricle, brachial artery, and left ventricle were recorded at 5-min intervals during a 15-min control period (control I). The cardiac output was measured in duplicate during the final 3 min by the dye-dilution technic using indocyanine green. A 9 to 10-min period of pacing was then carried out during which the electrocardiogram and pressures were measured during the first, fourth, sixth, and ninth minutes. The cardiac output determination was repeated during the final 3 min of pacing. Oxygen consumption was measured and brachial and pulmonary arterial blood withdrawn for analysis of pH, pO₂, pCO₂, and oxygen saturation, with both cardiac output determinations. Continuous recordings of brachial artery and left ventricular pressures were made during the termination of pacing. In later studies, pacing was interrupted for 15 sec at 2-min intervals to determine the effect of sudden reduction in heart rate.

Twenty minutes after pacing was terminated hemodynamic measurements, including the cardiac output (control II) were made in 20 patients. Following this a 0.5-mg tablet of nitroglycerin in a lactose base (glyceryl trinitrate*) was chewed, and these parameters were measured again between the sixth and tenth minute following drug administration (control NG), and then a second period of pacing was carried out at a rate identical to that of the first study.

Pressures were measured with P 23Db Statham strain gauges from a zero reference level 5 cm below the angle of Louis and were recorded on a photographic recorder.* Pressures were measured over at least two respiratory cycles and the mean pressures in the brachial and pulmonary arteries were obtained electronically. Recording speed was normally 25 mm/sec, but for determination of ventricular end-diastolic pressure a high sensitivity was employed with a speed of 100 mm/sec. Expired air was collected in a Tissot spirometer and analyzed for carbon dioxide and oxygen by the micro-Scholander technic.

The left ventricular stroke work index in g-m/m² was calculated using the formula:

\[
LVSWI = \frac{SI \times (BAm - LVEDP) \times 13.6}{1,000}
\]

where SI = stroke index in ml/m²; BAm = brachial artery mean pressure in mm Hg, and LVEDP = left ventricular end-diastolic pressure in mm Hg. A modified tension-time index was calculated as the product of peak left ventricular systolic pressure and heart rate. This modification is based on the fact that peak systolic pressure is a more important determinant of myocardial oxygen consumption than the total area under the left ventricular systolic pressure curve.15 The maximum rate of rise of left ventricular pressure (dp/dt) was obtained by an electronic differentiator.* There are theoretical objections to measurement of dp/dt using a fluid-filled catheter and external transducer but direct in vivo

*Burroughs Wellcome & Co. (Canada) Ltd.
‡Electronics for Medicine, White Plains, New York.
cardiac failure during angina pectoris

In comparison with a catheter tip transducer at rates of 75 to 150/min has shown that the two methods of measurement correspond closely up to a value of 2,000 mm Hg/sec. The pH, pCO2, and pO2 were measured on a pH/gas analyzer* and the oxygen saturation measured with a hemoresector.† Following the completion of these hemodynamic studies, selective cine-coronary arteriography and left ventriculography were carried out in all patients. Twelve patients were found to have normal coronary arteriograms and left ventriculograms and had no hemodynamic or electrocardiographic evidence of heart disease and were placed in the normal group. The remaining 30 patients had major obstructive lesions in one or more coronary vessels. The left ventriculograms show minor local impairment of contractility in some patients, but none had evidence of ventricular aneurysm.

Results

Twenty-one of the 30 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. In no case was it necessary to discontinue pacing prematurely. After pacing was terminated, pain frequently stopped within 30 sec, was generally absent by 2 min, but in the occasional patient pain subsided slowly over a 5 to 6-min period. For purposes of analysis, three groups will be considered: (a) angina group—21 patients with coronary artery disease who developed pain with pacing, (b) non-angina group—nine patients with coronary artery disease who did not experience pain with pacing, (c) normal group—12 patients free of cardiac disease.

*Instrumentation Laboratories, Inc.
†American Optical Co.

Figure 1

Left ventricular stroke work index (LVSWI) showing a decrease in each of the three groups of patients during the pacing period.

Figure 2

Left ventricular end-diastolic pressure (LVEDP) in the three groups of patients before and during pacing, and in the immediate post-pacing period. The LVEDP falls during pacing in the normal and non-angina groups but shows little change in the angina patients. In the post-pacing period it returns to control in the normal and non-angina group but rises to abnormal levels in the angina patients.

Circulation, Volume XXXIX, June 1969
Summary of Hemodynamic Effects of Atrial Pacing

<table>
<thead>
<tr>
<th></th>
<th>BAm (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>PAm (mm Hg)</th>
<th>(\dot{V}O_2) (ml/min/m²)</th>
<th>HR (beats/min)</th>
<th>CI (L/min/m²)</th>
<th>SI (ml/m²)</th>
<th>SERI (g/sec/m²)</th>
<th>LVSWI (g-m/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>101 ± 14.5</td>
<td>8.0 ± 3.2</td>
<td>12.7 ± 2.7</td>
<td>137 ± 13.5</td>
<td>78 ± 12.3</td>
<td>2.92 ± 0.55</td>
<td>38 ± 7.0</td>
<td>116 ± 19.3</td>
<td>47.2 ± 8.6</td>
</tr>
<tr>
<td>Pace</td>
<td>119 ± 22.7</td>
<td>9.2 ± 6.0</td>
<td>20.1 ± 7.5</td>
<td>160 ± 22.5</td>
<td>144 ± 10.9</td>
<td>3.03 ± 0.88</td>
<td>21 ± 6.9</td>
<td>83 ± 21.3</td>
<td>32.7 ± 11.6</td>
</tr>
<tr>
<td>Post-pace</td>
<td>21.6 ± 6.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>95 ± 4.9</td>
<td>9.5 ± 2.9</td>
<td>12.3 ± 1.7</td>
<td>147 ± 23.1</td>
<td>79 ± 16.5</td>
<td>3.03 ± 0.22</td>
<td>40 ± 5.9</td>
<td>126 ± 15.7</td>
<td>46.7 ± 8.7</td>
</tr>
<tr>
<td>Pace</td>
<td>102 ± 8.7</td>
<td>3.2 ± 2.2</td>
<td>13.6 ± 2.7</td>
<td>153 ± 17.4</td>
<td>140 ± 6.8</td>
<td>3.18 ± 0.42</td>
<td>23 ± 3.8</td>
<td>91 ± 11.5</td>
<td>31.2 ± 6.3</td>
</tr>
<tr>
<td>Post-pace</td>
<td>12.7 ± 2.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>90 ± 11.0</td>
<td>8.7 ± 2.6</td>
<td>11.8 ± 2.2</td>
<td>130 ± 21.3</td>
<td>72 ± 10.2</td>
<td>2.87 ± 0.41</td>
<td>40 ± 5.1</td>
<td>121 ± 14.1</td>
<td>44.9 ± 10.1</td>
</tr>
<tr>
<td>Pace</td>
<td>93 ± 11.5</td>
<td>2.3 ± 1.9</td>
<td>14.5 ± 2.0</td>
<td>143 ± 22.8</td>
<td>142 ± 6.0</td>
<td>3.11 ± 0.71</td>
<td>22 ± 5.0</td>
<td>88 ± 23.0</td>
<td>26.8 ± 7.0</td>
</tr>
<tr>
<td>Post-pace</td>
<td>9.8 ± 2.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Angina group (n = 21)

Non-angina group (n = 9)

Normal group (n = 12)

Abbreviations: control = sinus rhythm; pace = atrial pacing; post-pace = immediately following pacing; BAm = brachial artery mean pressure; LVEDP = left ventricular end-diastolic pressure; PAm = pulmonary artery mean pressure; \(\dot{V}O_2\) = oxygen consumption (STPD); HR = heart rate; CI = cardiac index; SI = stroke index; SERI = systolic ejection rate index; LVSWI = left ventricular stroke work index; TTI = modified tension-time index; dp/dt = first derivative of left ventricular systolic pressure curve; pCO₂ = partial pressure of carbon dioxide; pO₂ = partial pressure of oxygen; sat = oxygen saturation. Values shown are means and standard deviations.

Table 1 shows a summary of the control, pacing, and post-pacing hemodynamic data for all patients. Table 2 shows the significance of change in any measured parameter during the initial study period. The average heart rates were similar in each group during the control period. The pacing rate chosen for the group which developed angina varied from 125 to 160 and averaged 140. The average rate for the non-angina group was 140 and for the normal subjects 142. The cardiac index during the control period was similar in each group and did not change significantly during the period of pacing. Consequently the stroke index fell by approximately 45% in each group during the period of pacing. The mean brachial artery pressure was similar in the normal and non-angina groups during the control period. There was a small but significant rise in mean brachial artery pressure in the non-angina group during pacing, but no change in the normal subjects during the control period and rose during pacing from 101 to 119 mm Hg. The left ventricular stroke work index fell during pacing by 40% in the normal group and by 31% and 33% in the angina and non-angina groups (fig. 1).

There was no significant difference in left ventricular end-diastolic pressure during the control period among the three groups (fig. 2). The mean value in each group was between 8 and 9 mm Hg although one patient in the angina group and one in the non-angina group exceeded normal (12 mm Hg). In the non-angina and normal groups, the mean left ventricular end-diastolic pressure showed an immediate decline at the onset of pacing from an average value of about 9 mm Hg to between 2 and 3 mm Hg where it remained for the duration of the pacing period (fig. 3). In the angina group the initial fall in left ventricular end-diastolic pressure was less marked reaching 5 mm Hg in the early pacing period. This subsequently rose progressively throughout the period of pacing reaching an average of 9.5 mm Hg at the end of pacing. In four patients it exceeded normal. The large standard error in the angina group indicates
considerable variability in left ventricular end-diastolic pressure during the pacing period, the range during the final minute of pacing being 3 to 27 mm Hg. These variations appeared to be unrelated to the site of pacing.

On interruption of pacing at any time the left ventricular end-diastolic pressure increased rapidly reaching a stable level in two or three beats and was measured over the next two respiratory cycles. The mean value for the left ventricular end-diastolic pressure during interruption at intervals throughout the pacing period is shown in figure 3. In the normal group the filling pressure during interruption returned to control values. Similar results were seen in the non-angina group although these values were slightly greater than the control values. In contrast the angina group showed a rise to abnormal levels during interruption even within the first 2 min of pacing, usually before the onset of pain. The pressures during interruption continued to rise throughout the period of pacing reaching 21.7 mm Hg at the termination of pacing. The highest post-pacing pressures were observed in those patients who exhibited an abnormally elevated left ventricular end-

### Table 2

**Summary of Significance of Changes (P Values) During Pacing Study**

<table>
<thead>
<tr>
<th>Angina group: C-P*</th>
<th>Non-angina group: C-P*</th>
<th>Normal group C-P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAm</td>
<td>&lt;0.001</td>
<td>0.02</td>
</tr>
<tr>
<td>LVEDP</td>
<td>NS</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(p&lt;0.001†)</td>
<td>(0.01†)</td>
<td>(NS†)</td>
</tr>
<tr>
<td>PM,</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>VO2</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
<tr>
<td>HR</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CI</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>SI</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERI</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVSWI</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TTI</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>dp/dt</td>
<td>&lt;0.001</td>
<td>0.05</td>
</tr>
</tbody>
</table>

* C-P = significance of change between control and pacing periods.
† Values for C-PP = significance of change between control and immediate post-pacing periods.
For other abbreviations see footnote of Table 1.
diastolic pressure during pacing. The abnormal rise in left ventricular end-diastolic pressure during interruption of pacing is shown in figure 4. Following cessation of pacing this pressure remained elevated for periods varying from 20 sec to 6 min. When the pressure elevation persisted for more than 1 min, it was usually accompanied by continued pain and S-T segment depression (fig. 5). The dp/dt rose 29% to 42% during pacing, but there was no significant difference among the three groups. The tension-time index rose in all groups, but this was greatest in the angina group and is related to the abnormal rise in systemic pressure during pacing. In the angina and non-angina groups during pacing there was an increase in arterial blood pH, pO₂, and oxygen saturation and a decrease in pCO₂. This pattern of respiratory alkalosis, probably due to hyperventilation, was not seen in the normal group.

The 20 patients studied after administration of nitroglycerin consisted of six patients in the angina group, seven in the non-angina group, and seven normal subjects. During pacing after nitroglycerin, only one of the angina group developed pain. Table 3 shows the data from both study periods in these patients and table 4 shows the significance of change in any measured parameter during these studies. The pertinent observations are summarized in figures 6 to 8. The average values for heart rate, cardiac index, left ventricular end-diastolic pressure, and left ventricular stroke work index correspond closely in the three groups during the initial control period (control I) and before administration of nitroglycerin (control II). Following nitroglycerin (control NG) heart rate rose and cardiac index, systemic pressure, left ventricular end-diastolic pressure, and left ventricular stroke work index declined in each group, but these changes were not always of statistical significance. Following nitroglycerin there was a fall in left ventricular end-diastolic pressure of approximately 50% in all groups.

During pacing there was a further decline in left ventricular end-diastolic pressure in all groups to approximately 2 mm Hg. This is in

Figure 3
The average left ventricular end-diastolic pressure (LVEDP) and standard error are shown for each of the three groups during the control period, at intervals throughout the pacing period and at points of interruption. In the normal and non-angina groups, the LVEDP falls during the early pacing period and remains low throughout the period of pacing. At points of interruption the LVEDP returns to near control values. In the angina group there is a small initial decrease in LVEDP, but this gradually returns to control values. The LVEDP during periods of interruption is abnormal throughout the pacing period.
Figure 4

Left ventricular end-diastolic pressure (LVEDP) in a patient experiencing angina during pacing. The LVEDP is normal during pacing but rises quickly during interruption to abnormal levels and falls with reinitiation of pacing.

Figure 5

Left ventricular end-diastolic pressure (LVEDP) during pacing and at intervals during the post-pacing period when the patient was still experiencing angina. The LVEDP is still abnormal 6 min after cessation of pacing.

Contrast to the initial pacing period where there was no fall in left ventricular end-diastolic pressure in the angina group. On cessation of pacing the mean values in each group rose to approximate the control values. Only one patient of any group exceeded normal values during the post-pacing period, and this was the single patient who developed angina despite the prophylactic administration of nitroglycerin, where the post-pacing left ventricular end-diastolic pressure reached 30 mm Hg. The left ventricular stroke work index
Table 3

Summary of Hemodynamic Effects of Atrial Pacing Before and After Nitroglycerin

<table>
<thead>
<tr>
<th></th>
<th>BAm (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>PAm (mm Hg)</th>
<th>VO2 (ml/min/1.73 m²)</th>
<th>HR (beats/min)</th>
<th>CI (L/min/m²)</th>
<th>SI (ml/m²)</th>
<th>SERI (ml/sec/m²)</th>
<th>LVSWI (g-m/m²)</th>
<th>TTI (min X 10⁻¹)</th>
<th>dp/dt (mm Hg/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control I</td>
<td>107 ± 12.3</td>
<td>8 ± 2.1</td>
<td>13.5 ± 2.2</td>
<td>130 ± 8.19</td>
<td>75 ± 4.8</td>
<td>2.67 ± 0.318</td>
<td>36 ± 3.2</td>
<td>109 ± 9.3</td>
<td>48.0 ± 8.0</td>
<td>1128 ± 138</td>
<td>1090 ± 500</td>
</tr>
<tr>
<td>Pace I</td>
<td>130 ± 21.9</td>
<td>8.5 ± 3.2</td>
<td>18.8 ± 3.6</td>
<td>157 ± 33.1</td>
<td>144 ± 10.3</td>
<td>2.74 ± 0.467</td>
<td>19 ± 4.3</td>
<td>77 ± 9.4</td>
<td>31.9 ± 10.0</td>
<td>2378 ± 670</td>
<td>1306 ± 666</td>
</tr>
<tr>
<td>Post-pace I</td>
<td>20.2 ± 5.3</td>
<td>7.3 ± 2.1</td>
<td>12 ± 1.9</td>
<td>130 ± 1.7</td>
<td>74 ± 4.7</td>
<td>2.6 ± 0.130</td>
<td>35 ± 3.0</td>
<td>103 ± 6.1</td>
<td>48.4 ± 9.0</td>
<td>1156 ± 162</td>
<td>1061 ± 134</td>
</tr>
<tr>
<td>Control NG</td>
<td>108 ± 11</td>
<td>3.5 ± 1.5</td>
<td>9.3 ± 1.8</td>
<td>127 ± 4.0</td>
<td>78 ± 10.7</td>
<td>2.3 ± 0.26</td>
<td>30 ± 4.0</td>
<td>94 ± 12.9</td>
<td>41.9 ± 8.5</td>
<td>1102 ± 203</td>
<td>1153 ± 205</td>
</tr>
<tr>
<td>Pace II</td>
<td>108 ± 20</td>
<td>2.2 ± 1.5</td>
<td>11.5 ± 3.6</td>
<td>146 ± 11.8</td>
<td>144 ± 9.2</td>
<td>2.4 ± 0.29</td>
<td>17 ± 2.9</td>
<td>72 ± 9.1</td>
<td>23.8 ± 5.1</td>
<td>1908 ± 639</td>
<td>1400 ± 307</td>
</tr>
<tr>
<td>Post-pace II</td>
<td>10.0 ± 4.9</td>
<td>7.7 ± 5.6</td>
<td>10.3 ± 2.6</td>
<td>153 ± 45.7</td>
<td>139 ± 9.3</td>
<td>2.97 ± 0.33</td>
<td>21 ± 2.8</td>
<td>98.7 ± 2.8</td>
<td>26.9 ± 4.4</td>
<td>1679 ± 211</td>
<td>1542 ± 343</td>
</tr>
<tr>
<td>Non-angina group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control I</td>
<td>96 ± 5.1</td>
<td>10.4 ± 2.6</td>
<td>12.3 ± 1.8</td>
<td>151 ± 27.9</td>
<td>73 ± 8.2</td>
<td>3.0 ± 0.24</td>
<td>42 ± 3.8</td>
<td>130 ± 14.8</td>
<td>48.9 ± 7.5</td>
<td>969 ± 92</td>
<td>1357 ± 463</td>
</tr>
<tr>
<td>Pace I</td>
<td>105 ± 6.5</td>
<td>3.3 ± 1.1</td>
<td>13.9 ± 2.7</td>
<td>156 ± 19.7</td>
<td>139 ± 7.7</td>
<td>3.3 ± 0.38</td>
<td>24 ± 3.4</td>
<td>94 ± 10.5</td>
<td>33.6 ± 4.8</td>
<td>1781 ± 105</td>
<td>1709 ± 309</td>
</tr>
<tr>
<td>Post-pace I</td>
<td>13.9 ± 1.8</td>
<td>7.9 ± 6.0</td>
<td>12.0 ± 0.6</td>
<td>136 ± 38.9</td>
<td>73 ± 8.8</td>
<td>2.99 ± 0.25</td>
<td>41 ± 6.7</td>
<td>124 ± 22.9</td>
<td>48.7 ± 10.7</td>
<td>1002 ± 130</td>
<td>1189 ± 240</td>
</tr>
<tr>
<td>Control NG</td>
<td>92 ± 12.5</td>
<td>5.7 ± 2.7</td>
<td>9.1 ± 2.7</td>
<td>146 ± 23.4</td>
<td>79 ± 9.6</td>
<td>2.79 ± 0.39</td>
<td>36 ± 5.4</td>
<td>116 ± 21.6</td>
<td>42.2 ± 9.3</td>
<td>964 ± 184</td>
<td>1297 ± 361</td>
</tr>
<tr>
<td>Pace II</td>
<td>95 ± 10.7</td>
<td>1.9 ± 1.5</td>
<td>10.3 ± 2.6</td>
<td>153 ± 45.7</td>
<td>139 ± 9.3</td>
<td>2.97 ± 0.33</td>
<td>21 ± 2.8</td>
<td>98.7 ± 2.8</td>
<td>26.9 ± 4.4</td>
<td>1679 ± 211</td>
<td>1542 ± 343</td>
</tr>
<tr>
<td>Post-pace II</td>
<td>7.7 ± 2.6</td>
<td>7.5 ± 2.6</td>
<td>10.3 ± 2.6</td>
<td>153 ± 45.7</td>
<td>139 ± 9.3</td>
<td>2.97 ± 0.33</td>
<td>21 ± 2.8</td>
<td>98.7 ± 2.8</td>
<td>26.9 ± 4.4</td>
<td>1679 ± 211</td>
<td>1542 ± 343</td>
</tr>
<tr>
<td>Normal group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control I</td>
<td>91 ± 13.3</td>
<td>9.1 ± 2.9</td>
<td>12.9 ± 1.8</td>
<td>127 ± 22.0</td>
<td>72 ± 10.8</td>
<td>2.94 ± 0.51</td>
<td>41 ± 5.6</td>
<td>120 ± 14.2</td>
<td>46.1 ± 12.5</td>
<td>924 ± 176</td>
<td>1200 ± 263</td>
</tr>
<tr>
<td>Pace I</td>
<td>93 ± 12.7</td>
<td>1.6 ± 1.8</td>
<td>14.9 ± 2.34</td>
<td>138 ± 24.9</td>
<td>142 ± 5.3</td>
<td>3.32 ± 0.83</td>
<td>24 ± 5.6</td>
<td>96 ± 23.6</td>
<td>29.4 ± 7.1</td>
<td>1682 ± 223</td>
<td>1417 ± 271</td>
</tr>
<tr>
<td>Post-pace I</td>
<td>9.6 ± 3.6</td>
<td>9.0 ± 2.6</td>
<td>13.1 ± 3.0</td>
<td>138 ± 19.9</td>
<td>72 ± 9.9</td>
<td>2.91 ± 0.53</td>
<td>40 ± 4.0</td>
<td>119 ± 12.9</td>
<td>46.4 ± 7.7</td>
<td>941 ± 175</td>
<td>1073 ± 234</td>
</tr>
<tr>
<td>Control NG</td>
<td>84 ± 15.8</td>
<td>4.6 ± 4.4</td>
<td>9.0 ± 2.58</td>
<td>143 ± 19.7</td>
<td>79 ± 10.4</td>
<td>2.72 ± 0.68</td>
<td>34 ± 7.6</td>
<td>109 ± 21.6</td>
<td>36.7 ± 9.7</td>
<td>908 ± 104</td>
<td>1184 ± 238</td>
</tr>
<tr>
<td>Pace II</td>
<td>91 ± 16.2</td>
<td>2.0 ± 2.1</td>
<td>12.4 ± 3.69</td>
<td>149 ± 15.1</td>
<td>140 ± 5.3</td>
<td>3.08 ± 0.82</td>
<td>22 ± 5.6</td>
<td>87 ± 21.2</td>
<td>26.6 ± 8.4</td>
<td>1623 ± 246</td>
<td>1468 ± 389</td>
</tr>
<tr>
<td>Post-pace II</td>
<td>7.1 ± 4.4</td>
<td>7.1 ± 4.4</td>
<td>10.3 ± 2.6</td>
<td>153 ± 45.7</td>
<td>139 ± 9.3</td>
<td>2.97 ± 0.33</td>
<td>21 ± 2.8</td>
<td>98.7 ± 2.8</td>
<td>26.9 ± 4.4</td>
<td>1679 ± 211</td>
<td>1542 ± 343</td>
</tr>
</tbody>
</table>

Abbreviations: control I = sinus rhythm; pace I = first period of atrial pacing; post-pace I = immediately following pacing; control II = sinus rhythm 10 min after pacing completed; control NG = sinus rhythm 10 min after administration of nitroglycerin; pace II = second period of atrial pacing; post-pace II = immediately following second pacing period; BAm = brachial artery mean pressure; LVEDP = left ventricular end-diastolic pressure; PAm = pulmonary artery mean pressure; VO2 = oxygen consumption (STPD); HR = heart rate; CI = cardiac index; SI = stroke index; SERI = systolic ejection rate index; LVSWI = left ventricular stroke work index; TTI = modified tension-time index; dp/dt = first derivative of left ventricular systolic pressure curve.
was similar in all groups during control I and II but fell following administration of nitroglycerin. During pacing after nitroglycerin there was a further fall in left ventricular stroke work index. The left ventricular stroke work index was lower than during the initial pacing period in the angina and non-angina groups but not significantly different in the normal subjects.

**Discussion**

It is not immediately apparent why left
ventricular end-diastolic pressure should not rise during angina induced by pacing as earlier work in man has repeatedly shown myocardial ischemia to be associated with elevated left ventricular filling pressure and impaired left ventricular contractility. Similar observations have also been reported in animals with experimental myocardial ischemia. The problem, however, may be resolved when left ventricular end-diastolic pressure and left ventricular stroke work are examined together (fig. 9). In the normal subjects the cardiac output was unchanged during pacing and there was subsequently a decline in stroke volume and stroke work of approximately 40%. In accordance with the Starling relationship, there was a decrease in left ventricular end-diastolic pressure. The values obtained during the control and pacing period describe a different type of ventricular function curve in which left ventricular stroke work is varied by rate change alone, as contrasted to the usual methods involving blood volume changes, exercise, or drug administration. This type of ventricular function curve in addition to the Starling mechanism includes the Bowditch phenomenon wherein an increase in myocardial contractility results from an increase in heart rate, but this factor is common to all groups studied in this manner. When left ventricular stroke work is increased by the
CARDIAC FAILURE DURING ANGINA PECTORIS

Figure 8

Left ventricular stroke work index (LVSWI) for patients studied before and after nitroglycerin. The LVSWI declines after administration of nitroglycerin and decreases further during pacing in the angina and non-angina groups.

cessation of pacing, the left ventricular end-diastolic pressure returns along the previously established curve. In the non-angina group, the control, pacing, and post-pacing points follow along this line previously described by the normal subjects. On the other hand, the angina patients in spite of a similar decrease in left ventricular stroke work during pacing do not exhibit a decrease in left ventricular end-diastolic pressure. This pressure, even though within an apparently normal range, is actually elevated for the reduced left ventricular stroke work. This abnormal relationship is illustrated by the dotted line showing the movement to a depressed ventricular function curve. This concept is supported by the marked elevation of left ventricular end-diastolic pressure that occurs as left ventricular stroke work is suddenly increased by the abrupt fall in heart rate at the cessation of pacing and this second point outlines the upper portion of the depressed ventricular function curve. The gradual return of left ventricular end-diastolic pressure to normal indicates that depressed left ventricular function is a reversible phenomenon accompanying myocardial ischemia. All points during control and pacing periods were obtained from hemodynamic data. The post-pacing points were however constructed assuming

Figure 9

Relationship between the left ventricular end-diastolic pressure (LVEDP) and the left ventricular stroke work index (LVSWI) in the three groups of patients during the control (C), pacing (P), and post-pacing (PP) periods. In the normal and non-angina groups the decrease in LVSWI accompanying the increase in heart rate is associated with a reduction in LVEDP according with the Starling relationship. The patients in the angina group, however, show no change in LVEDP with the decrease in LVSWI and thus change from a normal to an abnormal ventricular function curve when ischemia develops. Depression of ventricular function persists for a variable time during the post-pacing period.
Figure 10

Relationship between the left ventricular end-diastolic pressure (LVEDP) and the left ventricular stroke work index (LVSWI) in the three groups of patients during sinus rhythm before (C II) and after (C NG) nitroglycerin, during pacing (PP2) and in the post-pacing period (PP2). All groups now are on the normal ventricular function curve. The one patient who experienced angina during this second pacing period again showed depressed ventricular performance and is not included in this figure.

that the cardiac output in the immediate post-pacing period was equal to that during the control and pacing periods. This assumption of a constant cardiac output seems justified in view of our present findings and other reports indicating that cardiac output is not significantly affected by changes in rate over the ranges used.12,29,30 This may, however, not be the case in the early post-pacing period in the angina group. The imposition of a sudden volume load on the ischemic ventricle might well result in a fall in cardiac output in the early post-pacing period. This would imply an even more depressed ventricular function curve than is represented.

Results during the nitroglycerin studies support the concept that left ventricular function is depressed during myocardial ischemia and that the elevation of the post-pacing left ventricular end-diastolic pressure is subsequent to decreased ventricular contractility resulting from myocardial ischemia. Five of the six patients of the angina group did not experience pain during pacing after nitroglycerin and displayed a relationship between left ventricular end-diastolic pressure and stroke work during control, pacing, and post-pacing periods similar to the normal and the non-angina groups (fig. 10). The one patient who experienced angina during pacing despite the administration of nitroglycerin continued to show depression of ventricular function during the pacing and post-pacing periods. This return from a depressed ventricular function curve to a normal one by the administration of nitroglycerin indicates that abnormal left ventricular filling pressures during angina are not due to chronic alterations in ventricular compliance as previously suggested.7 These observations do not rule out temporary, reversible change in ventricular compliance during myocardial ischemia, but changes in ventricular performance seem more likely.

References


Reversible Cardiac Failure During Angina Pectoris: Hemodynamic Effects of Atrial Pacing in Coronary Artery Disease

JOHN O. PARKER, J. RODNEY LEDWICH, ROXROY O. WEST and ROBERT B. CASE

_Circulation_. 1969;39:745-757
doi: 10.1161/01.CIR.39.6.745

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1969 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/39/6/745

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/