Abnormalities of Ventricular Motion Induced by Atrial Pacing in Coronary Artery Disease

By Andre Pasternac, M.D., Richard Gorlin, M.D., Edmund H. Sonnenblick, M.D., Jacob I. Haft, M.D., and Harvey G. Kemp, M.D.

SUMMARY
In order to study left ventricular performance and motion under ischemic stress, incremental atrial pacing was performed in 10 patients with angiographically proven coronary artery disease until angina pectoris or segmental S-T depression appeared. Single-plane left ventricular cineangio grams were obtained in both the resting and the transiently ischemic state induced by pacing.

Abnormal motion appeared with pacing in two of three patients with normal contraction at rest; in one of them, gross dyskinesis of the cardiac apex was noted. Seven patients had abnormal contraction at rest; six showed an increase in either the severity or the topographic distribution of abnormality, while one showed no change.

Left ventricular end-diastolic pressure and cardiac index were not altered significantly despite changes in the pattern of contraction. Left ventricular end-diastolic volume decreased irrespective of the development of asynergy, but ejection fraction decreased markedly in those patients in whom asynergy was induced de novo or increased.

Thus left ventriculography during pacing-induced ischemia may reveal segmental or generalized abnormalities of contraction not necessarily reflected in the usual hemodynamic parameters of function. Moreover, asynergy induced by pacing is associated with a decreased ejection fraction.

Additional Indexing Words: Asynergy, Left ventricular end-diastolic pressure, Left ventricular end-diastolic volume, Left ventriculography, Ejection fraction

Abnormalities of segmental contraction of the ventricle at rest have been defined and their contribution to ventricular dysfunction recognized. Whether these abnormalities are permanent or dynamic and whether they are dependent upon the moment-to-moment metabolic requirements of the myocardium is less well understood. If such changes do occur, it may be possible to elicit and define areas of the myocardium that are potentially subject to ischemia by stressing the heart. In some patients with extensive coronary disease, the left ventricle may contract uniformly during control studies since myocardial ischemia may not be present. Temporary ischemia may be provoked by interventions which increase mechanical activity of the heart and its energy requirements beyond the capacity to augment coronary blood flow.

The production of myocardial ischemia within a laboratory setting has posed both complex technical and physiologic problems. Currently, tachycardia induced by electrical
pacing of the heart has become the procedure of choice in preference to exercise or catecholamine infusion. With this approach, the number of variables is reduced while the stress state can also be terminated immediately as needed. Previous studies have sought to analyze ventricular motion during acute ischemia that has occurred with exercise, during anginal attacks, or immediately following myocardial infarction. However, in all of the studies indirect methods have been used, as kinetocardiography, and radarkymography. More recently left ventricular (LV) pressure and volume have been measured during angina induced by exercise or pacing, with demonstration of abnormal wall motion in the latter report.

It is the purpose of this study to utilize atrial-pacing tachycardia as a stress and during this state to measure LV pressure and volume, to observe the contraction pattern, and to determine if acutely induced regional myocardial ischemia leads to disordered local contraction.

Material and Methods

Ten patients (nine males and one female) aged 33 to 61 (mean 48.8 years) were studied. Coronary cineangiography was performed in six patients because of a history of chest discomfort alone, and in four patients it was performed because of chest pain and previous myocardial infarction. Myocardial infarction was considered certain when typical prolonged chest discomfort had occurred, together with enzyme changes, and/or evolution of the classical changes in the ST-T segments and Q waves of the ECG. Myocardial infarction was considered probable when enzyme changes occurred with nondiagnostic transient ECG changes. The mean duration of the symptoms was 4.3 years. All patients underwent complete clinical and electrocardiographic study. A double Master's test was also performed on seven patients utilizing specific criteria which give results comparable to other forms of exercise stress testing. Clinical signs of congestive heart failure were absent in all patients at the time of the study, but one had failure in the past. Cardiac size by roentgenogram was normal in eight patients while there was slight enlargement of the left ventricle in two patients (cases 2 and 8). Informed consent was obtained from all patients.

The studies were performed in the fasting state. Each patient was premedicated with pentobarbital sodium (50 mg im) and meperidine (50 mg im) 1 hour before the procedure. All patients underwent a right and left heart catheterization. Pressures were inscribed on a Sanborn 560 polybeam photographic recorder using a Statham P 23 Db transducer, connected directly to a cardiac catheter 100 cm in length. The zero reference level was set at two thirds of the anteroposterior chest diameter. Cardiac output was determined by dye-dilution technic using indocyanine green dye and a Gilford densitometer.

Selective coronary cineangiography was performed in all patients using the Sones technic. Multiple injections were performed of 75% sodium and meglumine diatrizoate in the left and right

<table>
<thead>
<tr>
<th>Pt</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Dur symptoms (yrs)</th>
<th>No. of MI</th>
<th>CHF</th>
<th>ECG</th>
<th>Control</th>
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<td>DMI</td>
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<td>M</td>
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<td>M</td>
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<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>48</td>
<td>4.0</td>
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<td>M</td>
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<td>2</td>
<td>1</td>
<td>DMI</td>
<td>ND</td>
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</table>

Table 1

Clinical Data

Abbreviations: MI = myocardial infarction; CHF = congestive heart failure; N = normal; NSp ST = nonspecific segmental ST-T changes; DMI = diaphragmatic myocardial infarction; ASMI = anteroseptal myocardial infarction; ND = not done.
Changes in ventriculographic patterns induced by atrial pacing. In patients 3 and 9, asynergy appeared de novo with pacing. In patients 1, 5, and 7, there was an increase in the severity of the abnormality, while in patients 2, 6, and 10 there was an increase in the topographic distribution of asynergy. The contraction pattern of patients 4 and 8 remained unchanged.

Anterior oblique positions and were recorded at 60 frames/sec on 16-mm Ilford Pan F films, with a 9-6 inch dual-field General Electric X-ray image amplifier. A no. 8 Eppendorf or Lehman catheter was then substituted, and after an interval of 20 min a left ventricular cineangiogram was recorded single plane at 60 frames/sec in a 30° right anterior oblique projection, using 40 ml of
Data Obtained in Patients during Pacing-Induced Tachycardia

<table>
<thead>
<tr>
<th>Pt</th>
<th>Vessels involved</th>
<th>%</th>
<th>Obstruction</th>
<th>Dominant system</th>
<th>Collaterals</th>
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<tr>
<td>1</td>
<td>RCA</td>
<td>50</td>
<td>Prior to marg</td>
<td>R</td>
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</tr>
<tr>
<td>2</td>
<td>LCF</td>
<td>&gt;75</td>
<td>Post marg</td>
<td>R</td>
<td>RCA → LCF</td>
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<tr>
<td>3</td>
<td>LAD</td>
<td>100</td>
<td>Prior to septal</td>
<td>R</td>
<td>RCA → LAD</td>
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<tr>
<td>4</td>
<td>LAD</td>
<td>&lt;75</td>
<td>Postdiagonal</td>
<td>R</td>
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<tr>
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<td>&gt;75</td>
<td>Origin</td>
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</tr>
<tr>
<td>6</td>
<td>LAD</td>
<td>&gt;50</td>
<td>Prior to diag</td>
<td>R</td>
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</tr>
<tr>
<td>7</td>
<td>LAD</td>
<td>50</td>
<td>Prior to diag</td>
<td>R</td>
<td>RCA → RCA</td>
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<tr>
<td>8</td>
<td>LAD</td>
<td>&gt;75</td>
<td>Prior to marg</td>
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<tr>
<td>9</td>
<td>LCF</td>
<td>50</td>
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<td>RCA → LAD</td>
</tr>
<tr>
<td>10</td>
<td>LAD</td>
<td>&gt;75</td>
<td>Prior to diag</td>
<td>L</td>
<td>LAD → RCA</td>
</tr>
</tbody>
</table>

Abbreviations: LAD = left anterior descending artery; RCA = right coronary artery; LCF = left circumflex artery; A = apicosuperior quadrant; B = basosuperior quadrant; C = basoinferior quadrant; D = apicoinferior quadrant; S = increase in severity; E = increase in extent; ak = akinesis; hypok = hypokinesis; and dysk = dyskinesis.

c contrast material, injected at 400 psi. The distance from X-ray tube to table top was measured. Distortion due to parallax exhibited only a 5% increase in the outer third of the field.1

Again to obviate the myocardial depression secondary to the administration of contrast material,20 a long recovery period averaging 40 min was allowed (range 27–60 min) after the first left ventriculogram. The recovery period was increased to 48–60 min whenever angina had been experienced by the patient during the coronary angiograms (patient 5) or after the left cineventriculogram (patient 9).

A no. 8 BE bipolar electrode catheter of the Goodale-Lubin type was then positioned in the coronary sinus. Left ventricular pressure, repeat cardiac output (in five cases), and lactate levels from the lateral coronary sinus site and the brachial artery were measured. Pacing was performed in all patients at rates of 100, 120, 130, 140, and 150 beats/min sequentially for 2 min at each rate. LV pressures and a complete ECG were obtained at each rate. The heart rate was not increased to a higher rate if the patient developed chest discomfort similar to previous anginal attacks, whenever the ECG showed significant segmental S-T depression (1 mm or more), or if a heart rate of 150 beats/min had been reached. When one of these states was obtained, cardiac output was measured in five cases and arterial and coronary sinus blood samples were again taken for lactate determination.

After completion of these observations, the pacing was discontinued providing a recovery period averaging 16 min (range 12–25 min). The pacemaker was then reactivated at the same rate that had induced chest pain and/or S-T change. When neither had occurred, a rate of 150 beats/min was used. After 3 to 4 min, a repeat left ventriculogram was obtained under exactly the same conditions as the initial pacing studies.

The following parameters of LV function were measured or calculated: left ventricular end-diastolic pressure (measured after the a wave
ABNORMALITIES OF VENTRICULAR MOTION

<table>
<thead>
<tr>
<th>Control</th>
<th>Left ventriculography</th>
<th>Induced asynergy</th>
<th>ECG changes (ST-T)</th>
<th>Pain</th>
<th>Myocardial lactate extraction</th>
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<tr>
<td>C hypok</td>
<td>C dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>-9.9%</td>
</tr>
<tr>
<td>Anterolat</td>
<td>Anterolat aneu</td>
<td>+</td>
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<td>0</td>
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<tr>
<td>Aneurysm</td>
<td>A&amp;C hypok</td>
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<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>D dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
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<tr>
<td>C&amp;D hypok</td>
<td>C&amp;D dysk</td>
<td>+</td>
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<td>0</td>
<td>+37.7%</td>
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<tr>
<td></td>
<td>C dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+25.5%</td>
</tr>
<tr>
<td></td>
<td>+ A dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+17.6%</td>
</tr>
<tr>
<td>C&amp;D hypok</td>
<td>C&amp;D ak</td>
<td>+</td>
<td>0</td>
<td>0</td>
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<tr>
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<td>+</td>
<td>0</td>
<td>0</td>
<td>-40.1%</td>
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<tr>
<td>C ak</td>
<td>A hypok</td>
<td>+</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td></td>
<td>C ak</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>-13.0%</td>
</tr>
<tr>
<td></td>
<td>D dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+30.3%</td>
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<tr>
<td></td>
<td>E dysk</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+43.5%</td>
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</table>

when present; mean value of five consecutive beats), cardiac index, and pressure-time per minute (PTM).

Coronary artery lesions were rated as: Total occlusion (100%) or obstruction greater than, equal to, or smaller than 75 or 50%, and the sites of the obstructive lesions were noted.

The ventriculograms of each patient were obtained at a fixed angle in the right anterior oblique position in the control and paced states. These were interpreted qualitatively for vigor and uniformity of contraction at all points along the ventricular inner surface and classified as normal; normal overall pattern but localized abnormalities of ventricular contraction were apparent in inspection of the cineventriculogram.

The measurement of ventricular volumes and the study of contraction pattern were made on normally conducted, nonpostextrasystolic beats. Some possible residual potentiation of ejection, even several beats after an ectopic contraction, cannot be excluded, however. The calibration of each ventriculogram relied on the ratio of the projected catheter diameter to known life-size catheter diameter.1

The silhouettes of the right anterior oblique view of the ventricular cavity were sequentially traced, and the areas measured by planimetry every three frames (50 msec) were plotted relative to time. End-diastolic and end-systolic areas were then traced by means of an Edwin Industries X-Y digitizing table interfaced with a Digital Equipment Corporation PDF 9 computer for calculation of end-diastolic volume (EDV) and end-systolic volume (ESV) according to the area-length method of Dodge et al.21 modified for single-plane calculation.22 Ejection fraction (EF) was derived from these values. This technic has been reported by Hugenholtz.23 Single-plane technics for calculating LV volume have proven reliable in patients with symmetrical contraction22 but there are no data concerning patients with asynergy.

In an attempt to quantify segmental abnormalities, the cardiac silhouette was divided into four quadrants: apicosuperior (A), basosuperior (B), basoinferior (C), and apicoinferior (D). These areas were planimetered and similarly plotted relative to time.
Results

The clinical information is given in table 1. The results of the coronary angiographic studies are shown in table 2. The topography and severity of lesions are also indicated in figure 1.

Acute ischemia during pacing was judged to be present when anginal pain and/or segmental ST-T changes occurred. This was supported by the subsequent demonstration of abnormal myocardial lactate metabolism (table 2).

The results of the left ventriculographic analyses are summarized in table 2, while detailed information on the individual changes in ventriculographic patterns is given in figure 1. Asynergy was present during the control state in seven patients; pacing tachycardia induced an increase in the severity of asynergy in three patients (cases 1, 5, and 7), and an increase in the topographic distribution of abnormality in three others (cases 2, 6, and 10), while one showed no change. Of three patients with normal contraction at rest, asynergy appeared de novo with pacing in two cases (3 and 9). Extensive asynergy appeared in patient 9: Segment A became akinetic, C hypokinetic and asynchronous, and D became dyskinetic in midsystole (figs. 2, 3). In patient 3, localized asynergy (segment A) was induced by pacing (fig. 4).

In five patients the mean values of cardiac output in both state were similar, averaging 2.7 and 2.7 liters/min/m², respectively.

The changes in LVEDP, LVEDV, and EF are plotted in figure 5. Ejection fraction declined in six of eight patients who developed or had augmented asynergy during

Figure 2
In contrast with the normal contraction demonstrated in the control state, extensive asynergy appeared with pacing.
ABNORMALITIES OF VENTRICULAR MOTION

EXTENSIVE ASYNERGY INDUCED BY ATRIAL PACING

Figure 3

In contrast with the harmonious decrease in area of all segments in the control state (left) asynergy appeared in three segments with atrial pacing: segment A (anteroapical) became akinetic, C (posterobasal) hypokinetic and asynchronous, and D (posteroapical) dyskinetic in midsystole (right).

![Graph showing ventricular area changes](image)

Pacing. Ejection fraction was unchanged in two patients without induced asynergy (patients 4 and 8). The values for EF are plotted against duration of symptoms in figure 6.

The relationship between abnormal lactate utilization and regionally impaired LV dysfunction during pacing was not clear in this small group. Two subjects with abnormal lactate responses (cases 4 and 8) failed to show induced asynergy, while four other subjects (5, 6, 7, and 10) without metabolic evidence of ischemia manifested an increase in severity or extent of asynergy in the paced state. The two subjects with normal ventricular motion in the control state who developed asynergy (3 and 9), both revealed metabolic evidence of ischemia.

Pressure-time per minute tended to increase with increasing heart rate (fig. 7).

Discussion

Tachycardia induced by pacing has the advantage of increasing the oxygen needs of the heart per minute on a readily reversible basis without augmentation in blood pressure or cardiac output.5, 7, 8 It has therefore been used to evoke transient myocardial ischemia in patients with coronary artery disease and limitations of coronary blood flow.4-6, 9

The physiologic consequences of induced tachycardia have been investigated in a variety of animal preparations.24-30 As heart rate is increased, ventricular filling is reduced, and both EDV and ESV fall as a consequence of the Frank-Starling mechanism.31, 32 Accordingly, stroke volume falls and cardiac output is relatively unchanged. Indeed, Bristow’s data show a parallel decrease of about 40% in both EDV and SV with 150% increase in heart rate so that ejection fraction remains essentially unchanged.28

An increase in cardiac oxygen consumption per minute generally occurs as heart rate increases. This results from a cumulative increase in stress development per minute as well as from an augmentation of contractile
While there was symmetrical decrease in total and segmental areas (left), the flattening of the curve corresponding to segment A (anteroapical) with pacing demonstrated segmental hypokinesis (right).

In the present study, it has been shown that although a synchronous contraction and normal ventricular function may be present at rest, major abnormalities of segmental motion in the wall of the ventricle may be induced by the ischemic stress of an increased heart rate. In the 10 patients studied, eight demonstrated new or increased asynergic contraction in the presence of an increased heart rate. These abnormalities of motion occurred in the distribution of known obstructive coronary lesions. Furthermore, pump function of the heart was temporarily impaired as reflected by a reduction in ejection fraction. This transitory reduction in localized myocardial function, during a period of increased oxygen requirement, may parallel events occurring during angina pectoris.

These data are in keeping with previous observations of changes in myocardial wall characteristics during experimental ischemia or ischemia induced by pacing in man. As pressure and volume were not recorded simultaneously in the present study no definite conclusion can be drawn regarding pressure-volume relationships.

The findings of the present study have theoretical and practical implications. First, they are in agreement with the model of paradoxical muscle contraction during hypoxia proposed by Tyberg et al. indicating that paradoxical motion reflects a dissociation in the time course of tension development between ischemic and nonischemic muscle. Second, they reinforce the concept that in the presence of induced ischemia, acute and reversible asynergy may play an important role in the impairment of myocardial function. The dynamic, and often reversible, aspects of asynergy with its possible role in various poorly understood clinical catastrophes, have only begun to be appreciated. This may explain “acute” left ventricular failure, pulmonary edema, or even cardiogenic shock.
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Hemodynamic changes associated with atrial pacing. The values of left ventricular end-diastolic (LVed) pressure and volume and ejection fraction are shown in the control and pacing states. The broken lines indicate the mean values. The change in mean ejection fraction was significant. The numerals correspond to the individual patients; in patient 3, LVed pressure was obtained only in the resting state (LVedp = 16 mm Hg).

A marked impairment of ejection fraction (EF) was noted in patients with 2 or more years of clinical duration of disease.

From a practical standpoint, induction of asynergy may help to localize areas of myocardial ischemia. Alternatively, these studies suggest that a reduction of oxygen requirements or the delivery of increased flow might serve to improve myocardial function when ischemia, either acute or chronic, has been present.

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potential ischemic areas of the heart during preoperative evaluation.

Acknowledgment

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Correction
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