Reproducibility of Clinical and Hemodynamic Parameters During Pacing Stress Testing in Patients with Angina Pectoris

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SUMMARY The reproducibility of clinical and hemodynamic events during two successive pacing periods separated by a 20-minute interval was evaluated in 33 patients with stable angina pectoris. Continuous pacing with stepwise increase in pacing rate was assessed in 19 patients and discontinuous pacing in which pacing was temporarily interrupted at each rate was evaluated in the other 14 patients.

During continuous pacing, the group values for pacing rates that induced angina, the pacing time to angina, ST-segment depression, rate-pressure product, cardiac output and left ventricular end-diastolic pressure (LVEDP) were similar during the two pacing periods, but postpacing LVEDP was lower after the second pacing period (p < 0.05). During the second pacing period, angina could not be reproduced at the same pacing rates in four patients and postpacing LVEDP varied by 5 mm Hg or more in 10 of the 19 patients.

During discontinuous pacing, the group mean values for pacing rates that induced angina and the pacing time to angina were higher (p < 0.05), and cardiac output lower (p < 0.05) during the second pacing period, while rate-pressure product, ST-segment depression, and LVEDP were similar during the two pacing periods. During the second pacing study, angina could not be induced at the same pacing rates in six patients and the postpacing LVEDP varied by 5 mm Hg or more in three of the 14 patients.

The results show that continuous pacing is preferable to discontinuous pacing. With continuous pacing, the group values for the clinical and many of the hemodynamic parameters were reproducible. We recommend the demonstration of the reproducibility of events during pacing in studies in which the effects of therapeutic interventions are being assessed, especially in a small number of patients.

ATRIAL PACING was first described by Sowton and colleagues in 1967. These workers found that the value for tension-time index at the onset of angina pectoris was reproducible in the majority of patients. Since then, atrial and coronary sinus pacing have been widely used to study the hemodynamic and metabolic patterns during myocardial ischemia and to assess the efficacy of therapeutic interventions in patients with angina pectoris. Investigators have generally assumed that the clinical and hemodynamic changes induced by pacing are reproducible, and have made conclusions regarding the effects of therapeutic interventions on the basis of comparison with a single control pacing study. However, little is known about the reproducibility of the anginal threshold and hemodynamic response to pacing. Since such information is important in determining the efficacy of therapeutic interventions, we studied the reproducibility of the clinical and hemodynamic profiles during pacing-induced angina in patients with coronary artery disease.

Methods

Patients

Hemodynamic investigations with subsequent selective coronary cineangiography and left ventriculography were performed in 33 patients aged 40–66 years (average 57 years). All patients were in sinus rhythm and had stable exertional angina pectoris that could be reproduced during treadmill exercise. Ten of the 33 patients had sustained a previous myocardial infarction at least 6 months before the study. Twenty-three of the 33 were normotensive. Ten had systolic blood pressure (SBP) above 150 mm Hg, but only five had diastolic blood pressure (DBP) exceeding 95 mm Hg (range 95–105 mm Hg). None was receiving antihypertensive therapy or digoxin. Some patients had been treated with propranolol and long-acting nitrates, but they had not taken these drugs for at least 7 days before the investigation. Sublingual nitroglycerin was the only medication taken during the 7 days before the study, and it was discontinued on the morning of the study. The study was explained to each patient and informed written consent obtained.

Description of Pacing Techniques

The reproducibility of the clinical and hemodynamic profiles during different pacing protocols was
evaluated prospectively. The first protocol, referred to as discontinuous pacing, was used in the first 14 patients during 1976 and 1977, and the second protocol, first described by Sowton and colleagues,1 is referred to as continuous pacing, and was evaluated in the remaining 19 patients during 1977–1978.

**Discontinuous Pacing Protocol**

The pacing rate was started at 10 beats/min above the sinus rate and increased by 10 beats/min every 180 seconds until the onset of angina, the occurrence of noncapture, or until a rate of 160 beats/min was reached. At each pacing rate, pacing was temporarily discontinued during the final 15 seconds so that left ventricular end-diastolic pressures (LVEDP) during sinus rhythm could be recorded after each pacing rate. Once the patient experienced anginal pain during pacing, the pacing was continued at that rate for an average of 2–3 minutes to allow hemodynamic and cardiac output (CO) measurements. Thereafter, pacing was discontinued and pressures measured in the immediate postpacing period and after 3 and 5 minutes.

**Continuous Pacing Protocol**

The pacing rate was started at 10 beats/min above the sinus rate and increased by 10 beats/min every 90 seconds until the onset of angina, the occurrence of noncapture, or a rate of 160 beats/min was achieved. When the patient experienced anginal pain during pacing, the pacing was continued at that rate for an average of 2–3 minutes to allow hemodynamic and CO measurements. Thereafter, pacing was discontinued and pressure recorded in the immediate postpacing period and at 3 and 5 minutes.

**Study Protocol**

Patients were studied in a fasting state without premedication. Under local anesthesia, the brachial artery and two veins were isolated in the right antecubital fossa. A #8 Courand catheter was passed into the right side of the heart and advanced to the main pulmonary artery. A #8 Sones catheter was inserted into the left ventricle from the right brachial artery, and the left brachial artery was cannulated with a Teflon needle using the Seldinger technique. A #7 or #8 Gorlin pacing catheter was advanced to the midportion of the coronary sinus.

The patients rested for 15 minutes after instrumentation. Modified lead V₆ of the ECG and intracardiac and intravascular pressures were recorded at 5-minute intervals during a 10-minute control period (C₁). During the final 2 minutes of the control period, CO was measured in duplicate by the dye-dilution technique using indocyanine green. Pacing (PC₁) was then started as described above. During pacing, the ECG and pressures were monitored continuously and recorded at 1-minute intervals. Further records of the ECG and pressures were made at the onset of angina, but pacing was continued to permit the duplicate determination of CO. Thereafter, final pressures were recorded and pacing was discontinued. Left ventricular and brachial arterial pressures and the ECG were recorded immediately before and for 30 seconds after pacing, and after 3 and 5 minutes. After a 10-minute recovery period, the protocol was repeated and observations were made during sinus rhythm (C₂), pacing (PC₂), and after termination of pacing.

Pressures were recorded with P23Db Statham strain gauges from a zero reference level 5 cm below the level of the angle of Louis. Recordings were made 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. The recording speed was normally 25 mm/sec, but for the LVEDP, a speed of 100 mm/sec at high sensitivity was used. The diagnostic criteria of ischemic response was a flat or downward-sloping depression of the ST segment of at least 1.0 mm (0.10 mV) persisting for 0.08 second or longer during sinus rhythm in the postpacing period. ST-segment measurements were averaged over 10 beats.

Left ventricular stroke work index (LVSWI) in g·m/m² was calculated using the formula

\[
LVSWI = SI \times (\text{BA} - \text{LVEDP}) \times 13.6
\frac{1000}{LVEDP}
\]

where SI = stroke index, \text{BA} = brachial artery mean pressure, and \text{LVEDP} = left ventricular end-diastolic pressure. The rate-pressure product (RPP) was calculated as the product of systolic arterial pressure and heart rate (HR) \times 10⁻².

After these hemodynamic studies, selective cinecoronary angiography and left ventriculography were carried out in all patients. The paired t test was used for statistical analysis.

**Results**

The hemodynamic and angiographic studies were completed without untoward events. All patients had angiographic evidence of luminal narrowing of 75% or more of one or more coronary arteries. Of the 14 patients in whom the discontinuous pacing protocol was evaluated, eight had triple-vessel disease, five double-vessel disease and one single-vessel disease; the resting left ventriculogram showed normal contractility in nine, localized hypokinesis in two, and generalized hypokinesis in three. In the 19 patients in whom the continuous pacing protocol was evaluated, 12 had triple-vessel disease and seven patients had double-vessel disease; the resting left ventriculogram showed normal contractility in 12, evidence of localized hypokinesis in three, and generalized hypokinesis in the remaining four patients.

**Discontinuous Pacing Protocol (tables 1 and 2, figs. 1–6)**

Table 1 shows the group mean data for the various hemodynamic parameters and ST-segment depression
Table 1. Summary of Hemodynamic Data During Control Period and Pacing-Induced Angina

<table>
<thead>
<tr>
<th></th>
<th>Continuous pacing protocol</th>
<th></th>
<th></th>
<th>Discontinuous pacing protocol</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C1</td>
<td>C2</td>
<td>PC1</td>
<td>PC2</td>
<td>C1</td>
<td>C2</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>76 ± 11</td>
<td>76 ± 10</td>
<td>128 ± 17</td>
<td>128 ± 18</td>
<td>72 ± 15</td>
<td>72 ± 15</td>
</tr>
<tr>
<td>SEB (sec)</td>
<td>0.31 ± 0.03</td>
<td>0.34 ± 0.02</td>
<td>0.24 ± 0.03</td>
<td>0.24 ± 0.03</td>
<td>0.32 ± 0.03</td>
<td>0.32 ± 0.01</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>154 ± 28</td>
<td>156 ± 27</td>
<td>163 ± 31</td>
<td>158 ± 27</td>
<td>143 ± 15</td>
<td>146 ± 18</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>85 ± 13</td>
<td>87 ± 13</td>
<td>103 ± 21</td>
<td>101 ± 17</td>
<td>80 ± 9</td>
<td>83 ± 13</td>
</tr>
<tr>
<td>RPP (mm Hg × 10⁻⁴)</td>
<td>115 ± 23</td>
<td>119 ± 22</td>
<td>208 ± 44</td>
<td>202 ± 38</td>
<td>106 ± 27</td>
<td>109 ± 26</td>
</tr>
<tr>
<td>FA (mm Hg)</td>
<td>16 ± 3</td>
<td>15 ± 3</td>
<td>19 ± 6</td>
<td>16 ± 5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>11 ± 4</td>
<td>12 ± 5</td>
<td>11 ± 5</td>
<td>9 ± 4</td>
<td>14 ± 8</td>
<td>13 ± 7</td>
</tr>
<tr>
<td>ST (mm)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1.0 ± 0.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>6.4 ± 1.7</td>
<td>6.1 ± 1.5</td>
<td>6.9 ± 1.7</td>
<td>6.6 ± 1.5</td>
<td>5.9 ± 1.6</td>
<td>5.3 ± 1.2</td>
</tr>
<tr>
<td>SV (ml/beat)</td>
<td>86 ± 23</td>
<td>80 ± 18</td>
<td>55 ± 18</td>
<td>53 ± 16</td>
<td>85 ± 20</td>
<td>74 ± 13</td>
</tr>
<tr>
<td>LVSWI (g-m/beat/m²)</td>
<td>63 ± 18</td>
<td>59 ± 13</td>
<td>46 ± 15</td>
<td>44 ± 13</td>
<td>60 ± 19</td>
<td>52 ± 10</td>
</tr>
</tbody>
</table>

Values are mean ± sd. *Postpacing LVEDP values.

Abbreviations: C1 = first control study; C2 = second control study; PC1 = first pacing study; PC2 = second pacing study; HR = heart rate; SEB = systolic ejection period; SBP = systolic blood pressure; DBP = diastolic blood pressure; RPP = rate-pressure product; FA = pulmonary arterial mean pressure; LVEDP = left ventricular end-diastolic pressure; ST = ST-segment depression in the immediate postpacing period; CO = cardiac output; SV = stroke volume; LVSWI = left ventricular stroke work index.

during the first and second control studies and during the two pacing studies. Table 2 shows the average differences and the range of differences in hemodynamics between the first and second control and between the first and second pacing periods. The group mean values for HR, SBP, DBP, RPP, systolic ejection period (SEP), LVEDP, and LVSWI were similar during C1 and C2, while CO and stroke volume (SV) were lower (p < 0.05) during C2. During C1 and C2 we saw variations in HR by 10 beats/min or more in one patient (fig. 1), SBP by 10 mm Hg or more in three patients (fig. 2), RPP by 200 mm Hg/min or more in seven patients (fig. 3), LVEDP by 5 mm Hg or more in one patient (fig. 4A), CO by 10% or more in four patients (fig. 5), and SV by 10 ml or more in four patients.

Figure 1. Individual and group values (mean ± sd) for heart rate during the first (○) control (C1) and the second (●) control (C2) studies, and at the onset of angina during the first (○) pacing (PC1) and the second (●) pacing (PC2) studies. The group mean values for pacing rates required to induce angina were similar during PC1 and PC2 of continuous pacing protocol, but were significantly higher during PC2 than PC1 (p < 0.025) of the discontinuous pacing protocol.
Two tricular end-diastolic pressure (mm Hg) during the cardiac output (CO) (l/min) first pacing study was significantly higher during pacing than the first pacing study (p < 0.025) (fig. 1). Figure 6 shows the individual and group mean values for the time (in seconds) required to induce angina during PC1 and PC2. Because of the variation in the sinus rate during the preparcing control periods, the time to angina was defined as the total pacing time at the highest pacing rate in a given patient during the first pacing study. This was used as a reference for the second pacing study. Thus, if a patient experienced angina after 60 seconds at a pacing rate of 120 beats/min during the pacing study, the time to angina was 60 seconds.

However, if during the second pacing study angina occurred after 60 seconds of pacing at a rate of 130 beats/min, the time to angina would be 240 seconds (180 seconds at pacing rate of 120 beats/min + 60 seconds at pacing rate of 130 beats/min). However, if angina during the second pacing study occurred earlier, for example, after 60 seconds at a pacing rate of 110 beats/min, the time to angina would be -180 seconds. This calculation was derived from the fact that the patient was not paced at 120 beats/min (-60 seconds) and was paced for 120 seconds less at 110 beats/min (-120 seconds) during the second pacing study. The group mean values for pacing time to angina were significantly higher during PC2 than PC1 (p < 0.05) (fig. 6). Individual data during PC1 and PC2 showed variation in pacing time to angina by 60 seconds or more in six patients (fig. 6).

The group mean values for SBP (fig. 2), DBP, RPP

### Table 2. Comparison of Results During Two Control and Pacing Periods

<table>
<thead>
<tr>
<th></th>
<th>Continuous pacing protocol</th>
<th>Discontinuous pacing protocol</th>
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<tbody>
<tr>
<td></td>
<td>C</td>
<td>PC</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>-0.84 (-12 + 12)</td>
<td>-0.74 (-30 +18)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.70 &gt;0.90</td>
<td></td>
</tr>
<tr>
<td>SEP (sec)</td>
<td>0.015 (-0.02 +0.04)</td>
<td>0.003 (-0.03 +0.04)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.30 &gt;0.50</td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>-1.95 (-11 +10)</td>
<td>-1.83 (-18+25)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.50 &gt;0.10</td>
<td></td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>-1.95 -2.47 (-14 +10)</td>
<td>-1.95 (-5 +15)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.20 &gt;0.20</td>
<td></td>
</tr>
<tr>
<td>RPP (mm Hg/min)</td>
<td>-301.37 (-3672 +500)</td>
<td>297.60 (-6720 +2940)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.25 &gt;0.70</td>
<td></td>
</tr>
<tr>
<td>FA (mm Hg)</td>
<td>0.24 (-5 +4)</td>
<td>3.53 (-2 +16)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.80 &gt;0.02</td>
<td></td>
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<tr>
<td>LVEDP (mm Hg)</td>
<td>-0.37 (-4 +5)</td>
<td>1.68 (-3 +10)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.60 &gt;0.10</td>
<td></td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>0.34 (-0.43 +2.8)</td>
<td>0.16 (-1.1 +1.3)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.10 &gt;0.50</td>
<td></td>
</tr>
<tr>
<td>SV (ml/beat)</td>
<td>5.87 (-18 +45)</td>
<td>2.20 (-9 +46)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.10 &gt;0.30</td>
<td></td>
</tr>
<tr>
<td>LVSWI (g/m/beat/m²)</td>
<td>3.48 (-14.1 +36)</td>
<td>1.50 (-0.7 +10)</td>
</tr>
<tr>
<td></td>
<td>p &lt;0.20 &gt;0.30</td>
<td></td>
</tr>
<tr>
<td>ST (mm)</td>
<td>0.0 (-0.5 +0.5)</td>
<td>0.0 (-1.0 +1.0)</td>
</tr>
<tr>
<td></td>
<td>p &gt;0.60 &gt;0.90</td>
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</table>

Data represent mean differences between first and second run. Figures in parentheses represent range of difference between the two runs.

*Postpacing LVEDP.

Abbreviations: C = control; PC = pacing; HR = heart rate; SEP = systolic ejection period; SBP = systolic blood pressure; DBP = diastolic blood pressure; RPP = rate pressure product; FA = pulmonary arterial mean pressure; LVEDP = left ventricular end-diastolic pressure; CO = cardiac output; SV = stroke volume; LVSWI = left ventricular stroke work index; ST = ST-segment depression in the immediate post-pacing period.

**Data During Pacing**

All 14 patients developed angina pectoris during the first pacing study and by 12 of the 14 experienced it during the second pacing study. The group values for pacing rates required to induce angina were significantly higher during the second pacing than the first pacing study (p < 0.025) (fig. 1). Figure 6 shows the individual and group mean values for the time (in seconds) required to induce angina during PC1 and PC2. Because of the variation in the sinus rate during the preparcing control periods, the time to angina was defined as the total pacing time at the highest pacing rate in a given patient during the first pacing study. This was used as a reference for the second pacing study. Thus, if a patient experienced angina after 60 seconds at a pacing rate of 120 beats/min during the pacing study, the time to angina was 60 seconds.
Data in the Postpacing Periods

The group mean for postpacing LVEDP was similar after PC₁ and PC₂ (fig. 4B). Individual data after PC₁ and PC₂ showed variation in postpacing LVEDP of 5 mm or more in three patients between the two studies. In the postpacing period, ST-segment depression of 1 mm or more was observed in 11 of the 14 patients during both pacing studies, and the group mean values were similar (table 1).

Continuous Pacing Protocol (tables 1 and 2, figs. 1–6)

Table 1 shows the group mean values for the hemodynamic parameters and ST-segment depression during the two control and during the two pacing studies, and table 2 shows the average difference and the range of differences in hemodynamics between the C₁ and C₂ and between the PC₁ and PC₂.

Hemodynamic Data at Rest

The group mean values for HR, SBP, DBP, RPP, SEP, pulmonary arterial mean pressure (PA), LVEDP, CO and SV were similar during C₁ and C₂. During C₁ and C₂ HR varied by 10 beats or more in three patients (fig. 1), SBP by 10 mm Hg or more in six patients (fig. 2), RPP by 200 mm Hg/min or more in six patients (fig. 3), LVEDP by 5 mm Hg or more in three patients (fig. 4A), and CO by 10% or more in two patients (fig. 5), but the changes in SV were less than 10 ml in all patients.

Data During Pacing

All patients developed angina pectoris during both pacing studies. The group values for pacing rates required to induce angina during the first and second pacing studies were similar (fig. 1). Figure 6 shows the time required to induce angina during the pacing studies. The time to angina was defined as the total time of pacing at the highest rate in a given patient during the first pacing study. This was used as described in the discontinuous pacing protocol, but the pacing intervals were only 90 seconds. The group mean values for pacing time to angina were similar during PC₁ and PC₂ (fig. 6). Individual data during PC₁ and PC₂ showed variation in pacing time to angina by 60 seconds or more in four patients.

The group mean values for HR, SBP, DBP, LVEDP, CO and SV were similar during the two pac-
ing studies, but the PA pressure was lower during PC2 ($p < 0.02$) (table 1 and 2). At the onset of angina during PC1 and PC2, HR varied by 10 beats or more in four patients (fig. 1), SBP by 10 mm Hg or more in 10 patients (fig. 2), RPP by 200 mm Hg/min or more in eight patients (fig. 3), LVEDP by 5 mm Hg or more in four patients (fig. 4A), CO by 10% or more in five patients (fig. 5), and SV by 10 ml or more in two patients.

Data in the Postpacing periods

The group mean value of postpacing LVEDP was lower after PC2 than after PC1 ($p < 0.05$) (fig. 4B). LVEDP varied 5 mm Hg or more in 10 patients between the two studies (fig. 4B).

In the postpacing period, 12 of the 19 patients had ST-segment depression of 1 mm or more during both pacing studies, and the group mean values were similar (table 1).

Discussion

Our results show that many of the hemodynamic and clinical parameters during two successive pacing periods are reproducible. Continuous pacing with stepwise increases in pacing rate produced more reproducible results than discontinuous pacing.

In 1967 Sowton and co-workers studied the reproducibility of the anginal threshold during atrial pacing in 13 patients. They used a pacing protocol with stepwise increases as in our continuous pacing protocol and repeated the second pacing study within 10 minutes. Angina induced by atrial pacing occurred at a reproducible HR and tension time index in 10 of the 13 patients. Using an identical pacing protocol, O'Brien and co-workers in seven patients, and Lau et al. in six patients, induced angina when pacing was repeated at identical HRs. In the present study, the second pacing study was repeated within 20 minutes, and group mean values for pacing rate and pacing time to angina during the first and second pacing studies were similar when the continuous pacing protocol was used, but these values were significantly higher during the second pacing study when the discontinuous pacing protocol was used. These findings indicate that continuous pacing was better than discontinuous pacing. However, the pacing rates required to induce angina varied by 10 beats or more and the pacing time to angina varied by 60 seconds or more in four of the 19 patients during continuous pacing and in six of the 14 patients during discontinuous pacing. The inability to reproduce angina in 20–43% of the patients with either protocol is in agreement with a previous report. In the present study the better reproducibility
FIGURE 4. A) Individual and group values (mean ± SD) for left ventricular end-diastolic pressure during the first (○) control (C₁) and the second (●) control (C₂) studies, and at the onset of angina during the first (○) pacing (PC₁) and the second (●) pacing (PC₂) studies. The group values were reproducible both during control and pacing studies with either protocol. B) Individual and group values (mean ± SD) for left ventricular end-diastolic pressure in the immediate post-pacing period after first (○) pacing study (PC₁) and after the second (●) pacing study (PC₂). The group values after PC₁ and PC₂ were similar with the discontinuous pacing protocol, but were significantly lower after PC₂ than PC₁ (p < 0.05) of the continuous pacing protocol.
of pacing threshold and the duration of pacing to angina during continuous than during discontinuous pacing could not be explained by different patient populations in the two groups. The extent of coronary artery disease and resting left ventriculographic appearances were similar in the two groups. Also, the group values for HR (fig. 1), SBP (fig. 2), RPP (fig. 3) and LVEDP (fig. 4A) during the control periods were similar in the two groups. Jackson and co-workers have suggested that a 10-minute recovery period between two pacing periods is inadequate and the pacing time to angina is reproducible when the pacing protocol is repeated after 30 minutes. However, in the present study the recovery period between the two pacing periods was 20 minutes, and the pacing rates and the pacing time to angina was highly reproducible in 15 of the 19 patients during continuous pacing. Had Jackson and co-workers studied a larger group of patients they might have found variations in reproducibility between the two pacing studies, as we observed.

Little is known about the reproducibility of hemodynamic parameters during two successive pacing periods and how angina pectoris induced by pacing modifies hemodynamics during a subsequent period of sinus rhythm. In the present study, the group mean values for various control hemodynamic parameters were similar 10 minutes after pacing-induced angina using the continuous pacing protocol. However, after discontinuous pacing, CO was significantly lower 10 minutes after pacing than during the initial control period.

During pacing-induced angina with both the continuous and discontinuous protocols, the group values for most of the hemodynamics measured were reproducible. However, PA pressure was significantly lower during the second pacing study of the continuous pacing protocol and CO and SV were significantly lower during the second pacing study of the discontinuous pacing protocol. However, during the two successive pacing studies, we observed that during continuous pacing, SBP varied by 10 mm Hg or more in 10 (53%), RPP by 200 or more in eight (47%), CO by 10% or more in five (27%), SV by 10 ml or more in two (11%), and LVEDP by 5 mm Hg or more in four (21%) patients. Similarly, during discontinuous pacing, three patients (21%) had variation in SBP of 10 mm Hg, RPP of 200 or more in four (29%), CO of 10% or more in two (14%), and LVEDP of 5 mm Hg or more in three (21%) patients.

In the postpacing period, group values for LVEDP were reproducible during the discontinuous pacing study but were significantly lower in the second postpacing period after continuous pacing. In individual patients, postpacing LVEDP varied by 5 mm Hg or more in 10 (53%), and in three (21%) of the patients after continuous and discontinuous pacing protocols. These results were in contrast to ST-segment depression, which was more often reproducible in the postpacing period after either pacing protocol. The reproducibility of ST-segment depression during pacing has also been reported by Lau and co-workers.

The explanation for the lack of reproducibility of the clinical and hemodynamic events in some of the patients is not clear from the results of the present study. It is possible that after a period of pacing-induced angina, a steady state is not achieved within 20 minutes. However, our results suggest that this explanation was unlikely, because the hemodynamic

**Figure 5.** Individual and group values (mean ± SD) for cardiac output during the first (○) control (C₁) and the second (●) control (C₂) studies and during angina pectoris induced by the first (○) pacing (PC₁) and the second (●) pacing (PC₂) studies. Cardiac output during C₂ of discontinuous pacing protocol was significantly lower than C₁ (p < 0.05).
parameters during the second control period after a period of pacing-induced angina were similar to the prepacing control values. It is also conceivable that patients in whom angina could not be reproduced during the second study had increased coronary blood flow due to opening of collaterals after a period of pacing-induced angina. We have no information to assess this possibility.

The results of the present study indicate that the continuous pacing protocol is preferable to the discontinuous pacing protocol, because only with the former technique are the group values for pacing rates required to induce angina and the duration of pacing time to angina reproducible. Since the completion of this study, we have used the continuous pacing protocol exclusively. However, even with this technique, in four of the 19 patients angina could not be reproduced at the same pacing rates and the group values for postpacing LVEDP were significantly lower during the second pacing study. These findings have important implications. In studies in which an atrial pacing stress test is used to assess the efficacy of therapeutic interventions, we recommend that the reproducibility of clinical and hemodynamic parameters be demonstrated in a given patient, especially when only a small number of patients are being studied. Without the demonstration of reproducibility, we feel that it is not valid to subdivide patients into smaller subgroups of responders and nonresponders to therapy on the basis of changes in clinical and hemodynamic parameters. These objections may be surmounted by studying groups of adequate numbers of patients. Alternatively, the effects of therapy should be compared with placebo therapy in a double-blind fashion, as is used in noninvasive studies.

References


FIGURE 6. Individual and group values (mean ± sd) for pacing (stress) time to angina during the first (O) pacing (PC1) and the second (●) pacing (PC2) studies. The group values were significantly higher during PC2 than PC1 of the discontinuous pacing protocol (p < 0.05), but were similar during PC1 and PC2 of the continuous pacing protocol.
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U Thadani, J R Lewis, T M Mathew, R O West and J O Parker

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