Controlled Heart Rate by Atrial Pacing in Angina Pectoris

A Determinant of Electrocardiographic S-T Depression

By SUN HING LAU, M.D., STAFFORD I. COHEN, M.D., EMMANUEL STEIN, M.D., JACOB I. HAFT, M.D., MICHAEL J. KINNEY, M.D., MELVIN W. YOUNG, M.D., RICHARD H. HELFANT, M.D., AND ANTHONY N. DAMATO, M.D.

SUMMARY

This study was undertaken with a consideration of the physiological relationship between myocardial oxygen consumption and heart rate. Atrial pacing was performed in 63 resting subjects, 36 of whom had been referred for evaluation of angina pectoris. Pacing at critical controlled heart rates evoked angina pectoris in six patients of this group with chest pain and, consistently and more frequently, produced significant S-T segmental depression in 28 patients as a manifestation of myocardial ischemia. The functional test employing controlled heart rates has several advantages over other stress tests. The use of the sole stress of controlled atrial tachycardia is a new technique which has provided relatively safe, reproducible results in the objective evaluation and investigation of myocardial ischemia.

Additional Indexing Words:
Exercise electrocardiographic test
Controlled atrial tachycardia
Myocardial ischemia
Coronary artery disease

The use of exercise in the electrocardiographic evaluation of patients with angina pectoris was introduced by Wood and associates in 1931 and was subsequently widely used as the “two-step test” by Master and Jaffe. Variations in the mode and degree of exercise in the testing have been suggested. A number of independent investigators have presented conflicting reports regarding the individual response as well as the statistical reliability of this test when applied to groups of normal persons and patients with coronary artery disease. It has, therefore, been evident that a need exists for a standardized stress test, based upon physiological considerations, which will adequately and safely test the coronary reserve of subjects suspected of having coronary artery disease.

Most investigators agree that the heart rate varies with the relative intensity of exercise according to the age and physical fitness of the subject. This response, coupled with available evidence that myocardial oxygen consumption per minute increases with heart rate and the finding that S-T segment depression may occur during induced tachycardia suggests that heart rate alone may play a significant role in uncovering inadequacies of coronary reserve.

In this study the effects of increasing heart rate alone, by means of right atrial pacing, on the electrocardiograms of normal and hypertensive subjects and of patients with angina pectoris were evaluated. This report represents an extension of our observations which we previously reported in abstract.
form. Sowton and associates used a similar technique to produce angina pectoris in 22 patients.

**Methods**

A total of 63 subjects (61 male and two female), ranging in age from 22 to 74 years (mean, 53 years) were selected for study. Seventeen subjects, age 22 to 36 years (mean, 32 years), were normal volunteers. Ten patients, age 42 to 63 years (mean, 48 years), had mild essential hypertension but no angina pectoris. The remaining 36 patients, age 28 to 74 (mean, 54 years), had typical or atypical symptoms of angina pectoris. All of the subjects were in normal sinus rhythm and were not receiving any cardiac medications except for glyceryl trinitrate taken sublingually. To compare our results with those of a generally accepted stress test, a single or double two-step test was performed by all but two subjects on the day before or after the pacing procedure.

At the onset of this investigation a protocol of study was selected which would require only a minimum of trauma or discomfort to the subject to avoid any change in the subject's state. It was decided that only the placement of an electrode catheter in the right atrium would be performed with electrocardiographic monitoring. All subjects were informed of the purpose and nature of the study and a written consent was obtained.

Patients were in the resting, postabsorptive, nonsedated state and in the supine position during the study. A number 6F or 7F bipolar electrode catheter was inserted into an antecubital vein percutaneously under local anesthesia, and positioned fluoroscopically at the junction of the superior vena cava and right atrium. Experience in our laboratory, over the past few years, with atrial pacing techniques has demonstrated that with the proper placement of the electrode catheter, the possibility of the catheter slipping into the ventricle is very remote. It has not occurred in over 200 atrial pacing studies in our series.

Care was taken to ground all electrical equipment and to avoid touching the exposed electrodes of the catheter during fluoroscopy to prevent the induction of atrial fibrillation or flutter by current leaks. No episodes of atrial fibrillation occurred in this study as a result of stimulation during the atrial vulnerable period. Electrocardiographic leads I, II, V1 or V4, and V6 were monitored and recorded simultaneously on a multichannel, oscilloscopic, photographic recorder at a paper speed of 25 mm/sec throughout the entire procedure. Heart rate was increased by single atrial pacing with a pacemaker (Medtronic pacemaker no. 5839), which delivers impulses of 2-msec duration. The milliamperage was adjusted to 2 to 5 ma to assure reliable supraventricular capture. A milliamperage greater than 5 was never used in this study. If capture was unsuccessful, the catheter was repositioned with the pacemaker off.

Table 1

<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>Mean age (yr)</th>
<th>Exercise test</th>
<th>Atrial pacing test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>17</td>
<td>32</td>
<td>17 neg</td>
<td>15 neg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 Wen</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>10</td>
<td>48</td>
<td>10 neg</td>
<td>8 neg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 Wen</td>
</tr>
<tr>
<td>Chest pain</td>
<td>36</td>
<td>54</td>
<td>25 pos</td>
<td>28 pos†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>9 neg*</td>
<td>6 neg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 Wen</td>
</tr>
<tr>
<td>Total</td>
<td>63</td>
<td>53</td>
<td>25 pos</td>
<td>28 pos†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>36 neg*</td>
<td>29 neg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6 Wen</td>
</tr>
</tbody>
</table>

Neg = negative; Pos = positive; and Wen = A-V block of the Wenckebach type.

*Does not include two patients unable to perform exercise.

†Includes four patients with negative exercise tests and one unable to exercise.

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Heart rates were increased gradually in increments of 10 to 20 beats/min up to a maximum rate of 160 beats/min. Exceeding a rate of 160/min often produced atrioventricular block of the Wenckebach type or second degree A-V block, usually with a 2:1 response. Each rate was maintained for 2 min, unless chest pain, A-V block of the Wenckebach type, or significant S-T depression occurred. An S-T segment response to atrial pacing was considered positive only when a clear, unequivocal S-T segment depression of 0.05 mv occurred in any of the recorded leads. Junctional S-T changes were not considered a positive response. In this study the judgment concerning S-T segment changes during atrial pacing was made considerably easier because of the simultaneous monitoring and recording of several electrocardiographic leads and because in the resting paced patient the reference base line (O mv) was very stable. At the appearance of chest pain, A-V block of the Wenckebach type, or significant S-T segmental depression,
Pacing was discontinued, and symptoms and electrocardiographic changes subsided rapidly in all cases. None of the study patients expressed an awareness of the alteration in heart rate, although all were informed of this possibility.

Results

The summary of the results of this study is shown in table 1.

Normal Subjects

All 17 normal subjects had negative single and double two-step exercise tests. In 15 of the 17 subjects in whom it was possible to pace the right atrium at a maximum rate of 160 beats/min with a 1:1 ventricular response, there was no alteration in the S-T segment. In two of the normal subjects A-V block of the Wenckebach type occurred at paced heart rates between 90 and 110 beats/min; a maximum heart rate stress, therefore, could not be reached. Figure 1 shows this type of A-V block during atrial pacing.

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ATRIAL PACING IN ANGINA

Figure 4

Recovery of S-T changes in leads $V_4$ and $V_6$ within 30 sec after cessation of atrial pacing. Significant S-T changes of myocardial ischemia are still present in normal sinus beats until full recovery. Same patient as in figures 2 and 3. Representative tracings of a continuous recording are shown. The minor deflection following the last paced beat, suggesting an atrial echo, is believed artifactual.
Hypertensive Subjects

All 10 subjects in this group had normal resting electrocardiograms or only voltage changes of left ventricular hypertrophy. All had negative single and double two-step exercise tests. Two developed A-V block of the Wenckebach type at paced rates of 90 to 100 beats/min, respectively, with no abnormality noted in the S-T segment. The remaining eight subjects did not manifest any significant S-T segmental depression during pacing.
Angina Patients

Of the 36 patients with angina pectoris, 25 had a positive result of the single or double two-step exercise test. Two patients were unable to perform the exercise test because of crippling arthritis. Of the 25 patients with positive exercise tests, 23 had a positive pacing test, usually at paced heart rates between 120 to 140 beats/min. In two patients A-V block of the Wenckebach type occurred at paced heart rates of approximately 100 beats/min. In six patients atrial pacing evoked chest pain similar to that previously described as angina pectoris. Figures 2 and 3 show electrocardiographic tracings from one of the patients who had both positive exercise and pacing tests. Figure 4 shows rapid recovery of the S-T segmental changes after the cessation of pacing.

Four of the remaining 11 patients in this group of 36 patients had a positive pacing test, although their double exercise test was negative. Figures 5 and 6 show a typical example of this type; figure 7 shows rapid recovery of the S-T segmental depression after cessation of atrial pacing. A positive pacing test was obtained in one of two patients who were unable to perform the exercise test.

Reproducibility

All patients had a repeat atrial pacing study approximately 15 min following the initial study. In no instance was the repeat study positive when the first pacing study was negative, and vice versa. Chest pain or S-T segment changes reappeared at the same paced heart rate as in the first study. S-T
Recovery of S-T changes in leads II and V6 within 7 sec after cessation of atrial pacing. Same patient as in figures 5 and 6. The S-T segmental changes of myocardial ischemia are still evident in the first few normal sinus beats.

Other Electrocardiographic Changes

In all cases A-V conduction time progressively increased as paced heart rate increased. This finding has previously been described. Aside from the six instances of A-V block of the Wenckebach type mentioned and the occurrence of first degree A-V block during atrial pacing at the higher heart rates, there were no other changes of A-V block, aberration, bundle-branch block, intraventricular conduction disturbances, or arrhythmias. T-wave inversions were always associated with ischemic S-T segment depression. No S-T elevation, abnormal junctional depression, or abnormal QX/QT ratios were observed with the exercise or pacing tests of this study.

Discussion

The basic physiological considerations of an investigation of myocardial ischemia and its electrocardiographic manifestations were clearly expressed in a statement by Lloyd-Thomas: “It is essential to recognize clearly that what is being tested is the adequacy of coronary blood flow in relation to the metabolic requirements of the heart muscle cells at the time of investigation, the balance between supply and demand being interpreted in terms of the electrical activity of these cells.”

Atrial pacing has provided a unique opportunity for the study of rate-dependent functions and responses of the heart in man. This technique provides the advantage of applying a single stress to the heart without changing the state of the subject tested. It requires neither the stresses and effects of exercise nor the use of drugs with their unpredictable and often persistent hemodynamic, metabolic, or neurohumoral changes.
Apprehension of the patients from the procedure was not judged to be significant in this study because (1) the resting sinus heart rate just prior to pacing the right atrium was nearly identical to the resting heart rate recorded the day prior to the study, and (2) increasing the heart rate by atrial pacing produced a progressive increase in the P-R interval. It is known that under the conditions of this study, sympathetic stimulation results in a shortening of the P-R interval at any given paced heart rate.12

A recent study by Stein and associates,6 using atrial pacing in subjects at rest and during exercise, revealed that cardiac index, left ventricular work and peripheral resistance were not significantly changed with increased heart rates, while stroke index and mean systolic ejection rate diminished linearly with heart rate. Myocardial oxygen consumption, as inferred by the tension-time index of Sarnoff and associates,14 did increase with increasing heart rate in both states. It is generally accepted that angina pectoris occurs whenever oxygen consumption exceeds oxygen supply to the myocardium.15 In the present study this supply-consumption deficit for oxygen was produced by increasing heart rate and was reflected in electrocardiographic S-T segment changes and angina pectoris.

Most graded exercise tests which are currently employed to induce ischemic S-T segment changes are based on the attainment of an exertional heart rate which exceeds 85% of the predicted maximal heart rate for a given age group.3 Doan and associates,5 studying the S-T segment response of a large group of healthy men subjected to maximal treadmill exercise, reported that the mean maximal heart rate for their subjects in the age group 40 to 54 years was 175/min and for the older group was 160/min. The mean maximal heart rate for the younger group was 200/min. In the present study, paced heart rates of 160/min were for these age groups 85% or greater of the predicted maximum rate for maximal exertion. In many patients it is possible to pace the heart at rates more than 160/min. The maximum paced heart rate for any given patient, however, depends upon the ability of the atrioventricular node to conduct the supraventricular impulses.

It is important at this point to note that in the design of this study no attempt was made to increase the heart rate of subjects to the point of producing symptoms of angina pectoris, but rather to increase the heart rate by atrial pacing up to that rate at which consistent and unequivocal S-T segment depression occurred. This probably accounts for the finding that only six patients developed chest pain. In these six patients the onset of chest pain occurred almost immediately following alterations of the S-T segment. Thus, it would appear that S-T segment changes precede the onset of chest pain in angina pectoris. Sowton and associates9 made no comment on the sequential relationship between electrocardiographic changes and clinical symptoms in their report.

Of the nine patients with angina pectoris who had a negative two-step exercise test, four had positive responses to the pacing test, which suggests that the pacing test may be more sensitive than the two-step tests in uncovering with relative safety objective evidence of inadequate coronary reserve.

The technique of atrial pacing and electrocardiographic monitoring appears to have several advantages. It is a functional test which utilizes a single standard stress of controlled heart rate only, which is performed at rest with a minimum of discomfort to the patient, and which requires no physical exertion by the patient. Multiple electrocardiographic leads are simultaneously and clearly monitored and are immediately available for interpretation. Chest pain elicited during the controlled atrial tachycardia can be immediately related to electrocardiographic changes. Both chest pain and electrocardiographic changes can be rapidly reversed by the cessation of pacing. Aside from an occasional A-V block of the Wenckebach type which precluded the maximum stress of atrial pacing, no other limitations were encountered in
our study. It is a new and relatively safe technique, providing the proper safeguards are recognized and met, with reproducible results for evaluating and investigating myocardial ischemia in any patient.

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References

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