Editorial Comment

Transesophageal Atrial Pacing or Pharmacologic Stress Testing in Detection of Coronary Artery Disease in Patients Who Are Unable to Undergo Exercise Stress Testing*

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Dynamic exercise is the stress test of choice in assessing symptoms and functional capacity in patients with suspected or proved coronary heart disease. Exercise electrocardiography, radionuclide angiography, thallium-201 scintigraphy and two-dimensional echocardiography provide diagnostic information, as well as prognostic risk assessment. In patients unable to exercise adequately because of severe peripheral vascular disease, arthritis, fracture, neuromuscular weakness, obesity, chronic obstructive pulmonary disease, advanced age or generalized weakness, as well as those recovering from surgery, alternative forms of testing are required for the evaluation of the physiologic extent of coronary artery disease (1). In addition, in patients who are unable to cooperate during exercise stress testing or in unmotivated patients, detection of coronary artery disease must be assessed by other means. Although environmental stress tests including the cold pressor test, isometric handgrip exercise and arm ergometry have been proposed (1), the two most frequently used tests are atrial pacing and pharmacologic stress testing utilizing dipyridamole, dobutamine or adenosine.

Atrial pacing. In 1967 Sowton et al. (2) introduced right atrial pacing as a stress test for assessing the presence and severity of coronary artery disease. Since then, several investigators (3,4) have utilized the ability to control increases in heart rate by pacing techniques to precipitate coronary insufficiency.

Atrial pacing produces minimal or no change in systolic or diastolic blood pressure; thus, the rate-pressure product is less with atrial pacing than that obtained during exercise testing (5). Despite this limitation, several investigators (6-11) have demonstrated similar sensitivity and specificity for atrial pacing and exercise testing in the detection of coronary artery disease. Atrial pacing produces a decrease in left ventricular end-diastolic pressure during maximal pacing tachycardia and in the immediate period after pacing in normal subjects. In contrast, in patients with coronary disease there is no change or a slight increase in left ventricular end-diastolic pressure during maximal pacing tachycardia and a marked increase immediately after pacing (4). Some investigators (4) have also demonstrated that cardiac output may decrease and systemic vascular resistance may increase.

Transesophageal pacing of the left atrium has also been described with use of a standard transvenous catheter or bipolar catheter that is passed into the esophagus in a manner similar to nasogastric tube insertion (9,10) or in a special gelatin capsule that encases a bipolar electrode that is swallowed (11). Pacing is usually started at 80 to 100 beats/min and increased by 10 to 20 beats/min every 1 to 3 min. End points for the test include achievement of a target rate (140 to 150 beats/min) or 80% to 100% of the age-predicted maximal heart rate, chest pain or marked (≥2 mm) ST depression (1). However, the development of horizontal or downsloping ST depression ≥1 mm at 0.08 after the J point defines an ischemic response (1). In some patients who develop atrioventricular (AV) Wenckebach block, administration of intravenous atropine (0.5 to 1.0 mg) may improve AV node conduction and achievement of a increased heart rate. Hypokalemia, digitalis, left bundle branch block and left ventricular hypertrophy may produce a false positive electrocardiographic (ECG) response (1). In addition, false positive ST depression may occur in patients with normal coronary arteries at very high pacing rates, generally ≥180 beats/min (1).

Electrocardiographic responses, derangements of myocardial lactate metabolism and regional wall motion abnormalities have all been considered end points (1). Increased sensitivity of the ECG alone has been reported (6) with use of a 12 lead ECG recorder and attention paid to the duration of the pacing test. An increase in the sensitivity and specificity of atrial pacing in detecting significant coronary artery disease has been obtained when cardiac imaging techniques are also employed (9,10). Advantages of atrial pacing techniques include the ability to abruptly stop the test when end points are achieved, which is especially important in patients.
who develop ischemia. Disadvantages include the development of AV node block in some patients and chest or esophageal pain as a result of esophageal pacing.

The present study. In this issue of the Journal, Lambertz et al. (12) describe a technique utilizing simultaneous transesophageal atrial pacing and transesophageal two-dimensional echocardiography in evaluating patients with coronary artery disease. The advantage of their new instrument is the ability to perform transesophageal echocardiography with simultaneous transesophageal atrial pacing by means of the same probe and requiring only one insertion of the probe into the esophagus and stomach. High resolution two-dimensional echocardiographic images were obtained in 100% of patients and baseline studies were compared with images obtained during maximal atrial pacing utilizing a cine loop format. The disadvantages include the passage of a large probe into the esophagus with all the precautions and complications inherent in transesophageal echocardiography. In addition, chest pain or discomfort due to esophageal pacing occurred in five patients. However, the main disadvantage appears to be the limited short-axis views of the left ventricle obtained at the midpapillary muscle level. In patients with mid or distal vessel disease, wall motion abnormalities may not be detected by the single, limited short-axis view of the left ventricle. In addition, for an individual patient, coronary anatomy may overlap territorial supply and precise identification of the culprit obstructed coronary vessel may not be possible. Despite these limitations, the ability to utilize different views and image planes, as well as the use of biplane and multiplane transesophageal echocardiography, will enhance the visualization of all wall segments. The results of the study by Lambertz et al. (12) utilizing this technique is compared with some recent studies with atrial pacing (Table 1).

**Table 1. Atrial Pacing in Detection of Obstructive Coronary Artery Disease (CAD)**

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Total No. of Patients</th>
<th>No. With CAD</th>
<th>Type of Pacing</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heller et al. (6)</td>
<td>22</td>
<td>16</td>
<td>Right atrial bipolar pacing catheter</td>
<td>94</td>
<td>83</td>
</tr>
<tr>
<td>Chapman et al. (7)</td>
<td>24</td>
<td>19</td>
<td>Transesophageal rubber endocardial pacing lead</td>
<td>87</td>
<td>100</td>
</tr>
<tr>
<td>McKay et al. (8)</td>
<td>25</td>
<td>20</td>
<td>Right atrial bipolar pacing catheter</td>
<td>85</td>
<td>75</td>
</tr>
<tr>
<td>Liceto et al. (9)</td>
<td>81</td>
<td>56</td>
<td>Transesophageal bipolar permanent transvenous catheter</td>
<td>91</td>
<td>88</td>
</tr>
<tr>
<td>Liceto et al. (10)</td>
<td>176</td>
<td>126</td>
<td>Transesophageal bipolar permanent transvenous catheter</td>
<td>89</td>
<td>84</td>
</tr>
<tr>
<td>Matthews et al. (11)</td>
<td>22</td>
<td>14</td>
<td>Esophageal capsule electrode pacing decrease in EF Failure to increase P/V P/V &lt; 6.0</td>
<td>71</td>
<td>75</td>
</tr>
<tr>
<td>Lambertz et al. (12)</td>
<td>50</td>
<td>41</td>
<td>Simultaneous transesophageal and two-dimensional echocardiography</td>
<td>93</td>
<td>100</td>
</tr>
</tbody>
</table>

EGC = electrocardiographic; EF = ejection fraction; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; P/V = pressure/volume.

Comparison of Atrial Pacing With Pharmacologic Stress Testing

Dipyridamole (Persantine) thallium-201 scintigraphy and two-dimensional echocardiography. Dipyridamole is used frequently for assessing the presence and extent of coronary artery obstruction (13-23). With dipyridamole and both imaging techniques the reported sensitivity and specificity have been reported to range between 80% and 90% (24). In addition, dipyridamole thallium-201 scintigraphy or two-dimensional echocardiography has provided useful prognostic information in postmyocardial infarction patients, (23) as well as in patients with coronary artery disease undergoing...
risk assessment before peripheral vascular or aortic surgery (25-28). Dipyridamole increases peak coronary blood flow fivefold in normal arteries, as well as in arteries with mild or moderate stenosis (23). The increase in blood flow proximal to a coronary lesion is associated with an increase in pressure gradient across the stenosis and a drop in pressure distally (23). Subendocardial flow is relatively less than epicardial flow, resulting in relative hypoperfusion of areas of myocardium supplied by a stenotic artery compared with those segments supplied by a normal or less stenotic vessel.

The inhomogeneity of flow is detected by abnormal thallium uptake when tracer thallium-201 is injected during the peak vasodilative effect of the drug. In contrast, regional wall motion abnormalities detected by two-dimensional echocardiography occur as a result of ischemic changes in wall motion due to its unique pharmacologic action. The coronary vasodilating action occurs as a result of inhibition of myocardial adenosine and capillary endothelial transport of endogenously produced adenosine (23). The usual dose of dipyridamole is 0.56 mg/kg body weight infused intravenously over 4 min or 300 to 400 mg given orally (23,24). Both methods of delivery yield comparable scintigraphic results but headache and nausea with oral dipyridamole occur more frequently (30). More recently the dose of dipyridamole has been increased to 0.84 mg/kg over 10 min with improved sensitivity and no change in specificity (23). Side effects with dipyridamole occur in many patients. In a recent study (30) of 3,911 patients, major adverse reactions were rare and occurred in 10 patients (0.26%). Fatal and nonfatal myocardial infarction and asthmatic attacks were considered serious; the acute bronchospasm was reversed in all instances by intravenous theophylline (30,31). Minor side effects included chest pain (29.7%), headache (12.2%), dizziness (11.8%), ECG ST segment changes (7.5%), nausea (4.6%) and hypotension (4.6%) (31,32). Ninety-seven percent of patients receiving theophylline had prompt relief of these side effects. Despite widespread use of dipyridamole stress testing, the Food and Drug Administration has not approved it for clinical use.

Adenosine. More recently, adenosine and thallium-201 scintigraphy have been advocated for patients unable to exercise (32). Dosages of 50 μg/kg per/min increasing up to 140 μg/kg per/min were infused. Side effects occurred in 83% of patients and included chest, throat and jaw pain, headache, flush, ischemic ECG changes and transient AV block. All side effects resolved within 1 to 2 min and no patient required theophylline. Sensitivity was 83% and specificity was 94% for detection of coronary artery disease.

Dobutamine stress testing. Dobutamine is a potent stimulator of β1-, β2- and α1-adrenoceptors with predominant inotropic and some chronotropic activity (33-35). It is now regarded as a form of a pharmacologic exercise test because it increases contractility, systolic blood pressure and heart rate at higher doses, thereby provoking myocardial ischemia (36,37). Although dobutamine produces similar inhomogeneity of coronary blood flow in patients with coronary stenotic lesions as compared with dipyridamole infused intravenously, it also increases the rate-pressure product and myocardial oxygen demand as compared with dipyridamole administered intravenously (35). The sensitivity and specificity of dobutamine stress testing have been reported to range between 90% and 80%, respectively (37,38).

The advantages of dobutamine include easy administration and rapid onset and cessation of action. Results of its use are not influenced by patient motivation or ability to exercise and the hemodynamic response can be controlled (35). The study can be immediately terminated when ischemic regional wall motion abnormalities are recognized by two-dimensional echocardiography, thus avoiding serious side effects. Disadvantages include ventricular arrhythmias, significant sinus tachycardia, nausea and tremor and marked ST depression in some patients (37). Minor symptoms, such as palpitation, headache, paresthesia and a cold or hot feeling, have been reported that generally disappear promptly when the medication is stopped. The starting dose of dobutamine given intravenously is 5 μg/kg per min, which can then be increased to 10, 15 and 20 μg/kg per min every 3 to 5 min; rarely, 40 μg/kg per min had to be used to increase heart rate at rest by at least 20 beats/min or achievement of 85% of maximal predicted heart rate (37). Intravenous administration of atropine has been recommended if heart rate response is inadequate; if severe ischemia occurs, it can be rapidly reversed with intravenous infusion of esmolol.

Conclusions. A variety of stress tests are available for the detection of coronary artery disease in patients who are unable to undergo dynamic exercise testing. Esophageal atrial pacing with simultaneous transesophageal detection of wall motion abnormalities has a high sensitivity and specificity in detecting coronary artery disease. Because adequate images are obtained in 100% of patients using transesophageal two-dimensional echocardiography, the technique should be employed in patients with unsatisfactory images obtained during transthoracic echocardiographic stress tests. Further studies are needed with larger numbers of patients to compare esophageal pacing echocardiography with pharmacologic stress testing in the detection of coronary artery disease in patients unable to undergo exercise stress testing.

References