Stress Testing

Pacing Stress Echocardiography: An Alternative to Pharmacologic Stress Testing

Shaul Atar, MD, Tomoo Nagai, MD, Bojan Cercek, MD, PhD, FACC, Tasneem Z. Naqvi, MD, MRCP, FACC, Huai Luo, MD, Robert J. Siegel, MD, FACC

Los Angeles, California

OBJECTIVES

We sought to evaluate the diagnostic accuracy and feasibility of bedside pacing stress echocardiography (PASE) as a potential substitute for pharmacologic stress echocardiography in patients admitted to the hospital with new-onset chest pain or worsening angina pectoris.

BACKGROUND

Accurate and rapid noninvasive identification and evaluation of the extent of coronary artery disease (CAD) is essential for optimal management of these patients.

METHODS

Bedside transthoracic stress echocardiography was performed in 54 consecutive patients admitted to a community hospital with new-onset chest pain, after acute myocardial infarction had been excluded. We used 10F transesophageal pacing catheters and a rapid and modified pacing protocol. The PASE results were validated in all patients by coronary angiography performed within 24 h of the test. Significant CAD was defined as $\geq 75\%$ stenosis in at least one major epicardial coronary artery.

RESULTS

The sensitivity of PASE for identifying patients with significant CAD was 95%, specificity was 87% and accuracy was 92%. The extent of significant CAD (single- or multivessel disease) was highly concordant with coronary angiography ($kappa = 0.73, p < 0.001$). Pacing stress echocardiography was well tolerated, and only 4% of the patients had minor adverse events. The mean rate–pressure product at peak pacing was $22,313 \pm 5,357$ beats/min per mm Hg, and heart rate $>85\%$ of the age-predicted target was achieved in 94% of patients. The average duration of the bedside PASE test, including image interpretation, was $38 \pm 6$ min.

CONCLUSIONS

Bedside PASE is rapid, tolerable and accurate for identification of significant CAD in patients admitted to the hospital with new-onset chest pain or worsening angina pectoris.

Pharmacologic stress echocardiography, mainly using dobutamine, is frequently used for the detection, localization and estimation of the severity of myocardial ischemia (1–4). Optimally, noninvasive cardiac imaging tests should be rapid, safe, feasible, highly accurate and cost-effective (1,2). However, dobutamine stress echocardiography (DSE) is time-consuming and may be associated with a high frequency of side effects, such as hypotension, atrial and ventricular arrhythmia, tremor and nausea (4–6). In addition, pharmacologic stress testing may not be feasible for all patients owing to contraindications to its use (5,6).

Relatively little data are available on the use of transesophageal atrial pacing in combination with transthoracic echocardiography, as compared with standard methods of cardiac stress testing. Previously published studies suggest that pacing stress echocardiography (PASE) is a safe and accurate method for the detection of coronary artery disease (CAD) in outpatients and for the evaluation of patients early after myocardial infarction (7–15). More recently, it has been shown that the diagnostic accuracy of PASE in outpatients compares favorably with DSE, and that PASE is as tolerable as DSE (16). We therefore examined the utility of bedside PASE and a rapid and modified pacing protocol as a potential substitute for pharmacologic stress echocardiography in patients admitted to the hospital with new-onset chest pain or worsening angina pectoris.

METHODS

Study patients. The hospital’s Institutional Review Board approved the study, and all patients gave informed consent. Fifty-four consecutive patients admitted to the Cardiac Intensive Care Unit or Cardiac Observation Unit who agreed to undergo PASE as well as coronary angiography within 24 h were included in the study. Inclusion criteria were 1) new-onset chest pain, clinically suspected to be ischemic in origin; and 2) no enzymatic (troponin I or creatine kinase and creatine kinase, MB fraction) or electrocardiographic (ECG) evidence of a new myocardial infarction. Exclusion criteria were 1) known esophageal disease; 2) atrial fibrillation or advanced heart block; 3) moderate or severe valvular aortic stenosis; and 4) an International Normalized Ratio of $>2.5$. We did not exclude patients from evaluation if they had a previous myocardial infarction, cardiomyopathy, complete bundle
branch block on the baseline ECG or baseline echocardiographic wall motion abnormalities. To assess the practical utility of PASE, we included patients even if they had suboptimal two-dimensional echocardiographic image quality. The patients were all tested after fasting for at least 4 h.

**Feasibility of PASE.** The feasibility of PASE was evaluated by the following variables: rapidity, safety and tolerability. The time elapsed from the beginning of technical preparations to the end of the study (including study image interpretation) was recorded. Adverse events were categorized as minor (transient atrial arrhythmia, vomiting) or major (ventricular tachycardia, ECG changes compatible with evolution of acute myocardial infarction, worsening of heart failure or esophageal perforation).

Immediately after termination of pacing, the patients were asked to grade their level of discomfort and the tolerability of the test on a scale of 1 to 10 (1 = intolerable; 10 = not causing any discomfort).

**Transesophageal atrial pacing protocol.** The studies were performed at the patient’s bedside. Noninvasive blood pressure was measured by an automatic device and recorded every 2 min. Heart rate was continuously monitored throughout the study. A twelve-lead ECG was performed at baseline, at peak heart rate and immediately after pacing. An ischemic response on the ECG was defined as ≥0.1 mV horizontal or downsloping ST segment depression at 80 ms after the J point in at least two contiguous leads at peak pacing heart rate. Chest pain, any associated symptoms and side effects were recorded during the test.

Transesophageal atrial pacing was performed with the Tapstress pacing system and Tapscope 10F transesophageal bipolar pacing catheters (model 7A of the transesophageal cardiac stimulator and model 3 of the recording preamplifier, Cardiocommand, Tampa, Florida). Before insertion of the pacing catheter, the patients were given a local anesthetic spray (20% benzocaine, Hurricane, Beutlich, Waukegan, Illinois). The pacing catheter tip was covered with lubricating jelly (K-Y, Johnson & Johnson, Arlington, Texas). Intravenous sedation (midazolam, 1 mg) was offered to patients who were anxious before the procedure. The patients were asked to lie in the left lateral recumbent position. The pacing catheter was inserted through the oropharynx to the esophagus to the 40-cm mark by instructing the patient to swallow, and then it was withdrawn until a 1:1 capture of atrial/ventricular activity was achieved. Pacing was then started at a rate of 120 beats/min (pulse width 10 ms, output current 20 mA), and the pacing rate was increased within 30 s to a target heart rate calculated as equal to 220 - age. Echocardiographic imaging was started after constant pacing at peak heart rate was achieved. Pacing and echocardiographic imaging were discontinued immediately after all myocardial segments were imaged in the five conventional transthoracic echocardiographic views (parasternal long- and short-axis, as well as apical four-, two- and three-chamber views). Other end points to the PASE test were severe angina, systolic blood pressure >240 mm Hg or <90 mm Hg, diastolic blood pressure >120 mm Hg or intolerable symptoms. The pacing output current was adjusted during the test to decrease the patient’s discomfort to a minimum, while allowing for continuous and stable pacing. Patients sustaining second-degree Wenckebach atrioventricular block during pacing were given intravenous atropine, 0.4 to 2 mg, as necessary, in 0.4-mg increments every 30 s until a 1:1 capture was achieved.

**Echocardiographic imaging.** Transthoracic echocardiography was performed with tissue harmonic imaging (P4-2 transducer, HDI 5000, ATL, Bothell, Washington; and 3.5-MHz transducer, Sequoia, Acuson, Mountain View, California). We compared baseline images (before pacing) with peak pacing images and postpacing images acquired 5 min after termination of pacing. The studies were interpreted by a consensus of three experienced readers who had no knowledge of the patients’ clinical profile or ECG tracings during or after the test. For interpretation of the studies, we used the 16-segment model as adopted by the American Society of Echocardiography (17). Wall motion was graded as 1 = normal; 2 = hypokinetic; 3 = akinetic; and 4 = dyskinetic. Segments were considered ischemic if a new wall motion abnormality or worsening of preexisting abnormalities of at least one grade was detected at the peak pacing heart rate and returned to baseline wall motion in the postpacing images. Segments with baseline abnormalities that did not change in severity during pacing were evaluated as nonischemic. The 16 echocardiographic myocardial segments were assigned to coronary vascular territories, as suggested by Segar et al. (18).

**Level of confidence.** Each myocardial segment was interpreted by the readers according to a level of confidence ranging from 100% to 0% (100% = very confident; 0% = unable to interpret), by assessing wall motion and wall thickening. The level of confidence was divided to three categories: high level of confidence (≥90%); intermediate (50% to 89%) and low (<50%). A PASE test had a high level of confidence only if all three coronary vascular territories were interpreted with a high level of confidence.

**Angiographic imaging.** Coronary angiography was performed with biplane acquisition (Advantex, GE Medical System, Wakeshaw, Wisconsin). The angiograms were interpreted by a consensus of three experienced readers using a semiquantitative grading system (0%, 25%, 50%, 75%, 99% or 100% diameter stenosis), as recommended by the American Heart Association (19). The readers had no knowledge of the results of the PASE test. Significant CAD...
was defined as lumen diameter stenosis $\geq 75\%$. As in other studies assessing the utility of stress echocardiography for the detection of CAD (14,16,20,21), we also have analyzed our data using $\geq 50\%$ lumen diameter stenosis for defining significant CAD. The results of this analysis are presented in the Results section.

Validation of study results by myocardial single-photon emission computed tomography (SPECT). The patients underwent myocardial SPECT within 24 h (usually within 3 h) after performing PASE. The protocol used for myocardial SPECT was previously described by Berman et al. (22). A semiquantitative visual interpretation was performed utilizing short-axis and vertical long-axis myocardial tomograms and a 20-segment model, as previously described (22). The method of assignment of tomographic myocardial segments to vascular territories was performed as previously described (23). The abnormal vascular territories, as identified by PASE, were then compared with the assignment of segments to vascular territories by SPECT.

Statistical analysis. We correlated PASE and coronary angiography for 1) the presence or absence of significant CAD; and 2) the extent and location of myocardial ischemia by coronary vascular territories. The results are presented using the definition of lesion diameter stenosis $\geq 75\%$ to represent significant CAD, unless stated otherwise. The kappa coefficient was used for agreement and concordance analysis. Continuous measures are expressed as the mean value $\pm$ SD. Mean differences for continuous variables were compared using the paired Student $t$ test. A $p$ value $<0.05$ was considered significant.

RESULTS

Fifty-four consecutive patients (21 women, 33 men; age 66 $\pm$ 10 years [range 40 to 85]) were studied. The patients' characteristics are presented in Table 1. We were unable to perform pacing in one patient. In the other 53 patients, the mean total duration of the test, including technical preparations and interpretation of the echocardiographic images, was 38 $\pm$ 6 min, with a median time of 35 min (range 30 to 60). The mean duration of pacing was 6.6 $\pm$ 2.6 min, with a median time of 6 min. Midazolam was administered to 8 patients (15%). Intravenous atropine, 0.4 to 2 mg, was administered to 21 patients (40%, average dose 0.8 mg) sustaining second-degree Wenckebach atrioventricular block during pacing.

Feasibility of bedside PASE. Pacing stress echocardiography was completed in all patients enrolled except for one. In this patient, we were unable to get any atrial capture. One patient who received 0.8 mg of atropine developed supraventricular tachycardia during pacing and was subsequently treated successfully with intravenous adenosine. Another patient vomited at the end of the test. No other adverse events were noted. The mean tolerability score, as graded by the patients immediately after the end of the PASE test, was 8.3 $\pm$ 1.1 (on a scale of 1 to 10), with a median score of 9.

**Table 1. Patients Characteristics (n = 54)**

<table>
<thead>
<tr>
<th>n (%)</th>
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<tbody>
<tr>
<td>Age (years) 64 $\pm$ 10</td>
</tr>
<tr>
<td>Gender (F/M) 21/33 (39%/61%)</td>
</tr>
<tr>
<td>Diabetes mellitus 19 (35%)</td>
</tr>
<tr>
<td>Systemic hypertension 34 (63%)</td>
</tr>
<tr>
<td>Hyperlipidemia 34 (63%)</td>
</tr>
<tr>
<td>Smoking 19 (35%)</td>
</tr>
<tr>
<td>Family history of CAD 6 (11%)</td>
</tr>
<tr>
<td>Obesity 7 (13%)</td>
</tr>
<tr>
<td>$\geq 3$ Risk factors for CAD 17 (31%)</td>
</tr>
<tr>
<td>Previous MI 16 (30%)</td>
</tr>
<tr>
<td>PTCA 16 (30%)</td>
</tr>
<tr>
<td>CABG 13 (24%)</td>
</tr>
<tr>
<td>PVD 4 (7%)</td>
</tr>
<tr>
<td>CVA 4 (7%)</td>
</tr>
<tr>
<td>Beta-blocker/calcium antagonist treatment 28 (52%)</td>
</tr>
</tbody>
</table>

Data are presented as the mean value $\pm$ SD or number (%) of patients.

CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; CVA = cerebrovascular accident; F = female; M = male; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; PVD = peripheral vascular disease.

**Hemodynamic data.** Of 53 patients, 50 (94%) achieved $\geq 85\%$ of their predicted target heart rate (220 $-$ age), and 34 patients (64%) were paced to $>$95% of their target heart rate. The mean baseline heart rate was 70 $\pm$ 13 beats/min, and the peak heart rate achieved was 149 $\pm$ 12 beats/min ($p < 0.0001$). The mean baseline systolic blood pressure was 142 $\pm$ 23 mm Hg, and the mean peak systolic blood pressure achieved was 149 $\pm$ 29 mm Hg ($p = 0.0003$). In 34 patients (64%), there was a mean increase of 19 $\pm$ 13 mm Hg in systolic blood pressure. In one patient (2%), there was no change in systolic blood pressure, and in 18 patients (34%), there was a mean drop in blood pressure of 15 $\pm$ 15 mm Hg. For the entire cohort ($n = 53$), the mean rate–pressure product achieved at peak pacing heart rate was $22,313 \pm 5,357$ beats/min per mm Hg.

**Diagnostic accuracy of PASE.** In 49 of 53 patients, the PASE findings were concordant with the findings of coronary angiography (92% accuracy). There were 36 patients with true positive and 13 patients with true negative results. Two patients had false positive PASE, and two had a false negative test. Table 2 presents PASE results for identifying patients with significant CAD, as well as the results for specific vascular territories. The sensitivity of PASE for identifying patients with significant CAD was 95%, and the specificity was 87%. The negative predictive value of the test was 87%, and the positive predictive value was 95%. Table 3 summarizes the concordance of PASE test and coronary angiography by the extent of CAD. In 44 (83%) of 53 patients, there was full concordance of the PASE test and coronary angiography with regard to the extent of significant CAD (kappa = 0.73, $p < 0.001$). Overall, the PASE test overestimated the extent of significant CAD in five patients (9%) and underestimated the extent of significant CAD in four patients (7%).

**Analysis by level of confidence.** In 46 (87%) of 53 patients, our level of confidence in interpreting all three
coronary vascular territories for identifying inducible segmental myocardial ischemia by PASE was graded as high (>90%). In these 46 patients, the accuracy, sensitivity and specificity of PASE were all 97%. In seven patients, the level of confidence in interpreting any coronary vascular territory was intermediate (50% to 89%). For the entire study group, 25 (3%) of 848 echocardiographic myocardial segments were interpreted with an intermediate or low level of confidence. The specific segments were as follow: basal inferior wall (n = 6), mid and apical inferior wall (n = 6), posterobasal interventricular septum (n = 3), mid and distal interventricular septum (n = 2), basal and mid posterior wall (n = 2) and basal, mid and apical anterior wall (n = 6).

Analysis of PASE results according to baseline wall motion abnormalities. Thirty-one patients had normal wall motion on baseline rest two-dimensional echocardiography. Twenty-seven patients (87%) were correctly identified by PASE (16 as true positive, 11 as true negative). One patient was falsely identified as positive, and two were falsely identified as negative. As shown in Table 2, the sensitivity of PASE in this group was 89%, specificity was 92% and accuracy was 90%. The positive and negative predictive values of PASE in patients with normal baseline echocardiograms were 94% and 85%, respectively. In the 22 patients with abnormal rest wall motion (Table 2), the sensitivity of PASE was 100%, yet the specificity was 67% and the accuracy 95%.

Analysis of PASE for ≥50% lumen diameter stenosis. We have also analyzed PASE accuracy for the detection of CAD by defining significant CAD as ≥50% lumen diameter stenosis. In the entire cohort, there were 14 coronary arteries in 13 patients with ≥50% and <75% lumen diameter stenoses. When we considered these lesions to represent significant CAD, 37 patients were now identified by PASE as having true positive and 10 as having true negative results (accuracy 89%, sensitivity 88% and specificity 91%). The results of PASE using a definition of significant CAD as either ≥50% or ≥75% diameter stenosis are compared in Table 4.

Correlation with myocardial SPECT. Of the 54 patients who underwent both PASE and coronary angiography, 16 also underwent myocardial SPECT within 24 h. The PASE and myocardial SPECT results correlated in 15 of the 16 patients. The PASE and coronary angiographic results correlated in 15 of these 16 patients. Fourteen patients had complete concordance between angiography and positive myocardial SPECT and PASE results. One patient had a positive PASE and myocardial SPECT test but no significant lesions detected on angiography, whereas another patient had a positive myocardial SPECT test but no significant coronary angiographic lesions, which was concordant with the normal PASE study. Using coronary angiography as a gold standard, the sensitivity of PASE in this subgroup was 93% and the specificity was 100%.

Electrocardiographic data. The baseline ECG was normal in 31 patients (58%). Two patients (4%) had complete right bundle branch block, two (4%) had complete left bundle branch block, three (6%) had first-degree atrioventricular block and four (7%) had evidence of left ventricular hypertrophy with a strain pattern. Electrocardiographic evidence of a previous myocardial infarction was noted in 11 patients (21%). New ischemic changes on the ECG (≥1 mm ST segment depression) during pacing were recorded in 16 patients (30%). One patient had ischemic ECG changes and a normal coronary angiogram. The sensitivity of electrocardiography at peak stress was 38%, the specificity was 89% and the accuracy was 43%.

Table 3. Coronary Angiography

<table>
<thead>
<tr>
<th>PASE Test</th>
<th>NS</th>
<th>SVD</th>
<th>MVD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS</td>
<td>15</td>
<td>2</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>SVD</td>
<td>0</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>MVD</td>
<td>2</td>
<td>3</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>13</td>
<td>25</td>
<td>53</td>
</tr>
</tbody>
</table>

Concordance of PASE and coronary angiography for the extent of significant CAD (kappa = 0.73). As indicated by the boldface numbers, 44 (83%) of 53 patients were correctly identified for the extent of significant CAD (13 without significant coronary stenoses, 8 with single-vessel disease and 23 with multivessel disease). Pacing stress echocardiography underestimated the extent of significant CAD in four patients (7%) and overestimated it in five (9%). Data are presented as number of patients.

MVD = multivessel disease; NS = nonsignificant coronary stenoses; PASE = pacing stress echocardiography; SVD = single-vessel disease.

Table 4. Pacing Stress Echocardiographic Results According to Lesion Severity

<table>
<thead>
<tr>
<th>Diameter Stenosis</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥50%</td>
<td>88</td>
<td>91</td>
<td>98</td>
<td>89</td>
<td>61</td>
</tr>
<tr>
<td>≥75%</td>
<td>95</td>
<td>87</td>
<td>92</td>
<td>89</td>
<td>87</td>
</tr>
</tbody>
</table>

Accuracy, Sensitivity and Specificity of Pacing Stress Echocardiography

Table 2. Accuracy, Sensitivity and Specificity of Pacing Stress Echocardiography

<table>
<thead>
<tr>
<th>Patients</th>
<th>LAD</th>
<th>LCx</th>
<th>RCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Sens</td>
<td>Spec</td>
<td>Acc</td>
</tr>
<tr>
<td>Cohort</td>
<td>53</td>
<td>95</td>
<td>87</td>
</tr>
<tr>
<td>Abnormal B/L</td>
<td>22</td>
<td>100</td>
<td>67</td>
</tr>
<tr>
<td>Normal B/L</td>
<td>31</td>
<td>89</td>
<td>92</td>
</tr>
</tbody>
</table>

*Accuracy, sensitivity and specificity are presented as percentages.

Acc. = accuracy; B/L = baseline two-dimensional echocardiography; cohort = entire group of patients; LCx = left circumflex coronary artery; LAD = left anterior descending coronary artery; RCA = right coronary artery; Sens. = sensitivity; Spec. = specificity.
DIscussion

Lee et al. (16) from the Mayo Clinic were the first to compare PASE and dobutamine pharmacologic stress echocardiography for the detection of inducible myocardial ischemia in outpatients with chronic stable angina. To our knowledge, our study is the first to examine PASE as an alternative to pharmacologic stress echocardiography for rapid bedside identification of CAD in intermediate to high risk patients admitted to the hospital with new-onset chest pain or worsening angina pectoris.

Feasibility of PASE. In an intermediate to high risk group of patients, we found PASE to be feasible and tolerable. Only two patients (4%) had minor adverse events that resolved shortly after termination of pacing, without further medical consequences. This high degree of safety of transesophageal atrial pacing is probably due to the ability to terminate pacing immediately if any adverse events occur, thus allowing the heart rate and myocardial oxygen consumption to return immediately to the baseline level (6,12).

Despite its reported high accuracy, sensitivity and specificity, transesophageal atrial pacing has not been adopted as a common method for cardiac stress induction. Previously, transesophageal atrial pacing methods were poorly tolerated owing to the nasal route of insertion of the pacing catheter, as well as to the pacing stimulus itself (13,14). We believe the improved tolerability in our study is related to 1) the use of smaller, specially designed pacing catheters (10F instead of 18F or transvenous pacing electrodes); 2) a modified and rapid pacing protocol; and 3) the oral route of pacing catheter insertion. Our “tolerability score” correlates with the “acceptance score” recently published by Lee et al. (16)(8 on a scale of 10 and 4 on a scale of 5, respectively).

The mean duration of the bedside PASE test, including technical preparations and image interpretation, was 38 min. This is significantly shorter than the durations in other widely used noninvasive cardiac imaging modalities (4,16). Although we did not exclude patients with suboptimal echocardiographic images, PASE was feasible in nearly all the patients enrolled, probably because of the use of harmonic imaging, as well as the lack of an increase in the respiratory rate or change in the magnitude of respiration during PASE. Thus, bedside PASE has a high utility for safe and rapid identification of significant coronary artery stenoses in patients admitted to the hospital with new-onset chest pain or worsening angina pectoris.

Diagnostic accuracy of PASE. We found PASE to have an accuracy, sensitivity and specificity of 92%, 95% and 87%, respectively, for detecting patients with significant CAD, as well as for detecting ischemic vascular territories. Our findings indicate that PASE is also accurate in patients with normal wall motion on rest echocardiography. These patients have been previously noted to have a relatively low sensitivity for the detection of CAD by stress echocardiography (1). The possible etiologies for the false positive results were not different from those encountered by other echocardiographic stress tests (1). The accuracy, sensitivity and specificity of PASE are similar or superior to those in other validation studies of pharmacologic or exercise stress echocardiography (2–4,24). Moreover, in a subgroup of patients who underwent myocardial SPECT within 24 h of the PASE test, in addition to coronary angiography, the three methods correlated well. Thus, a “perfusion” gold standard, as well as an anatomic gold standard, validated the accuracy of PASE in our study.

It is well recognized that stenosis severity may affect the sensitivity of stress echocardiography (21,25). Frequently, a 50% reduction in coronary artery diameter is used to define significant CAD (1,14,16,21,25). Although coronary angiography is often used as a gold standard for identifying the presence of significant CAD, there is some controversy and inconsistency as to what constitutes a significant coronary angiographic diameter stenosis—50%, 70%, or 75%? We therefore wanted our data to be comparable to those of other studies, whether they considered a 50% or 75% diameter of coronary stenosis as significant. In the entire cohort, there were 14 coronary arteries in 13 patients with ≥50% and <75% lumen diameter stenosis. Because of the documented limitation in the precision of coronary angiographic assessment of coronary obstruction of intermediate severity (26–28), we separately analyzed lesions with ≥50% and <75% and those with ≥75% diameter stenosis. We analyzed our data using either ≥50% or ≥75% diameter stenosis to define significant CAD, and as presented in Table 4, we found PASE to be highly sensitive and specific for the detection of significant CAD by either criteria (88% and 95%, respectively).

Level of confidence. We have previously validated the reproducibility of the echocardiographic (29,30), coronary angiographic (31) and cardiac scintigraphic (22) methods used in this study at our institution. The level of confidence for the interpretation of 87% (46 of 53) of the PASE studies was high. Seven studies (13%) were interpreted with an intermediate level of confidence, and no study was interpreted with a low level of confidence. This proportion is similar to that ascribed to other imaging tests (5,32). In the group of patients interpreted with a high level of confidence for all three coronary vascular territories, the accuracy, sensitivity and specificity rose to 97% for all.

Effect of pacing protocol. We used a modified and rapid pacing protocol not only to shorten the duration of the test and to improve tolerability, but also to induce an abrupt increase in myocardial oxygen consumption. The increase in myocardial oxygen consumption is due not only to the increase in heart rate, but also to the increase in myocardial contractility, which occurs as a consequence of the increased heart rate (Bowditch-Treppe effect) (32–34). Using this modified protocol, we were able to achieve >85% of the age-predicted target heart rate in 94% of the patients, even though a substantial number of patients (52%) were treated with beta-receptor or calcium channel antagonists at the time of PASE testing.
The significant increase in heart rate, together with a mild increase in systolic blood pressure in the majority of our patients, resulted in a mean rate-pressure product that is either equal to or higher than that induced by dobutamine/atropine or exercise stress in previously published studies (4,5,16,35,36). The rate-pressure product is known to be an indirect index of the stress imposed on the heart. Thus, PASE results in sufficient stress to accurately evaluate inducible myocardial ischemia.

**Study limitations.** The patients in our study may have had a high pretest likelihood of having CAD. However, 25% of the patients had normal arteries or stenoses <50% diameter stenosis and 15% had single- vessel coronary disease. This distribution is similar to that of previous reports (20) and is representative of patients with new-onset chest pain, as we did not exclude patients with baseline wall motion abnormalities or suboptimal echocardiographic images. No direct comparison of PASE and DSE, or other methods of pharmacologic stress echocardiography, was performed. Conventional coronary angiographic interpretation was used to identify the severity of CAD. The limitations of this technique are well recognized (37–40). However, it is the most commonly used method to interpret coronary angiography (20). Consequently, assessment of the echocardiographic results by this method is important for the generalization of our findings to clinical practice. In addition, it is important to note that, like any method of stress echocardiography, for accurate results, the cardiologist must be meticulous to ensure that the sonographer performing the studies obtains images so that at least 90% of the myocardial segments can be interpreted with a high level of confidence.

**Conclusions.** Pacing stress echocardiography is accurate for the detection of significant CAD in patients admitted to the hospital with new-onset chest pain. Furthermore, the test is well tolerated and feasible at the bedside. We believe the safety of PASE is partly related to the ability to immediately terminate pacing and stress-induced ischemia. Thus, PASE may be used as a substitute for pharmacologic DSE for rapid evaluation of inducible myocardial ischemia, especially in patients who may be more unstable and who could benefit from a method of stress that can be abruptly terminated.

**REFERENCES**


