OBJECTIVES
To compare transesophageal atrial pacing stress echocardiography with dobutamine stress echocardiography for feasibility, safety, duration, patient acceptance and concordance in inducing wall motion abnormalities.

BACKGROUND
Transesophageal atrial pacing is an effective method of increasing heart rate and has been used in the assessment of coronary artery disease.

METHODS
Both tests were performed in sequence on the same patients in random order. Transesophageal atrial pacing stress echocardiography began at a heart rate of 10 beats/min above the baseline value and was increased by 20 beats/min every two min until 85% of the age-predicted maximum heart rate or another end point was reached. Dobutamine echocardiography was performed using three-min stages and a maximum dose of 40 μg/kg per min. Atropine (total dose ≥2 mg) was administered at the start of the 40 μg/kg per min stage if needed to augment heart rate or during pacing if Wenckebach heart block occurred.

RESULTS
Transesophageal atrial pacing stress echocardiography was feasible in 100 of 104 patients (96%); the duration (8.6 ± 3.6 min) was significantly shorter than that of dobutamine stress echocardiography (15.1 ± 3.9 min) (p = 0.0001). With transesophageal atrial pacing stress echocardiography, the recovery period was shorter, symptoms and dysrhythmias were fewer, hypertension and hypotension were less common and target heart rate was more frequently achieved. No complications occurred with either test. Patient acceptance was satisfactory. Agreement between results of both tests was good for segmental wall motion scoring with a 16-segment model, scores 1 to 5 (kappa: rest, 0.79; peak, 0.57) and test interpretation (normal, ischemia, infarction or resting wall motion abnormality with ischemia) (kappa: 0.77).

CONCLUSIONS
Transesophageal atrial pacing stress echocardiography is a feasible, well-tolerated alternative to dobutamine stress echocardiography. It can be performed rapidly and shows good agreement with dobutamine stress echocardiography in the induction of myocardial ischemia.

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Dobutamine stress echocardiography is a safe and accurate technique for the detection of significant coronary artery disease (1–5). The hemodynamic response to dobutamine is variable; the test may be terminated in some patients because of hypertension or hypotension (4,5). Adverse effects may include nausea, headaches, tremors, dysrhythmias and symptoms attributable to intracavitary or left ventricular outflow tract obstruction that may occur when the left ventricle is hyperdynamic (6). Additionally, dobutamine stress echocardiography is labor intensive, requiring supervision by trained personnel throughout the period of drug infusion and recovery. Test duration usually exceeds that of exercise stress testing.

Transesophageal atrial pacing has been proposed as an efficient alternative method to increase heart rate and induce myocardial ischemia (7–14). Early experience with transesophageal pacing has been limited by patient intolerance. With newer pacing technology, however, experience has improved (14).

A head-to-head comparison study of dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography has not been done in a large group of patients. The purpose of the present study was to prospectively compare the safety, feasibility, patient tolerance and time requirements of both types of stress transthoracic echocardiography and to determine the concordance of the
two methods for induction of regional wall motion abnormalities.

**METHODS**

**Study patients.** The study was approved by the Institutional Review Board of the Mayo Clinic. Outpatients scheduled for clinically indicated dobutamine stress echocardiography were eligible for the study. Exclusion criteria were recent myocardial infarction (within two weeks), unstable angina, complex ventricular dysrhythmias, uncontrolled systemic hypertension, untreated glaucoma, atrial fibrillation or flutter, permanent pacemaker or defibrillator, significant valvular disease, complete atrioventricular block, untreated esophageal stricture, gastroesophageal varices and recent upper gastrointestinal bleeding. One hundred four patients gave informed consent for participation in the study. Antianginal medications were not changed. After fasting for at least 3 h, each patient underwent transesophageal atrial pacing stress echocardiography and dobutamine stress echocardiography in a sequence determined randomly. The second test was started after a 20-min rest period, which began after a recovery period that ended with the resolution of any stress-induced evidence of myocardial ischemia and after heart rate had returned to within 10 beats of the baseline heart rate.

During both protocols, symptoms, heart rate, blood pressure, arrhythmias and adverse effects were recorded. At any stage, one or two mg of midazolam was given intravenously if necessary to alleviate patient anxiety, discomfort or gagging. The duration of each protocol from start of dobutamine infusion or start of placement of the transesophageal atrial pacing catheter to completion of the acquisition of peak stress images was recorded. The duration of the recovery period was also recorded. After both tests had been performed, patients completed a questionnaire, scoring the tests for comfort and acceptance on a scale of 1 (intolerable) to 5 (very satisfactory).

**Instrumentation.** Transthoracic two-dimensional echocardiography was performed with either a Hewlett-Packard Sonos 2500 (Andover, Massachusetts) or an Acuson XP 128 (Mountain View, California). The complete studies were recorded on 3/4-in. videotape. Images of baseline and stress cardiac cycles were digitally stored on a Nova Microsonics system (Allendale, New Jersey). During transesophageal atrial pacing stress echocardiography, the start-delay time interval to digital image acquisition was increased in accordance with the duration between the pacing spike and R wave because the high-amplitude pacing spike triggered digital image acquisition. Atrial pacing was performed with a bipolar esophageal cardiac pacing and recording catheter (Pacescope; Cardiocommand, Inc., Tampa, Florida) housed in a flexible 18-French USC class IV polyvinyl chloride sheath. The catheter was connected to a Model 7A stimulator and Model 3 preamplifier (Tapstress System; Cardiocommand, Inc.) and Hewlett-Packard echocardiograph for display of atrial signals from the esophageal electrode.

**Protocol for transesophageal atrial pacing stress echocardiography.** The oropharynx was anesthetized with 10% lidocaine aerosol, and the pacing catheter was introduced orally by instructing the patient to swallow. Catheter position was optimized by maximizing the size of the esophageal P wave on the electrocardiogram. Pacing was initiated at 10 beats/min above the patient’s baseline heart rate and at 3 to 5 mA above the threshold for stable atrial capture. A pulse width of 10 ms was used. The pacing protocol consisted of 2-min stages with the paced heart rates increasing by 20 beats/min at every stage until the target heart rate (85% of age-predicted maximum) or another end point was reached. Blood pressure was measured at each stage. If Wenckebach second-degree heart block occurred, atropine was administered intravenously in 0.5-mg increments, to a maximum dose of 2 mg. End points were target heart rate, new or worsening wall motion abnormalities of at least moderate severity, ventricular or supraventricular tachycardia, electrocardiographic evidence of severe ischemia (2-mm horizontal or downsloping ST depression at 80 ms after J point), severe angina, intolerable symptoms, systolic blood pressure ≥240 mm Hg, diastolic blood pressure ≥120 mm Hg and systolic blood pressure <90 mm Hg.

**Protocol for dobutamine stress echocardiography.** Dobutamine was infused incrementally by a standard protocol with 3-min stages (5) and a maximum dose of 40 μg/kg per min. Atropine was administered intravenously to augment the heart rate if the target rate or another end point had not been achieved, starting with 0.25 mg and increasing the amount to a maximum total dose of 2 mg. In addition, if at the end of the 30 μg/kg per minute stage the heart rate was <75% of the age-predicted maximum, atropine was administered concurrently with an increase of dobutamine to 40 μg/kg per minute. End points were the administration of maximum doses of dobutamine and atropine in addition to the end points used for the pacing protocol.

**Image analysis and interpretation.** Dobutamine and pacing stress echocardiography tests were interpreted by experienced echocardiologists who were unaware of the results of the other test. Regional wall motion was evaluated at rest and at peak stress in each of 16 left ventricular segments by use of the 1 through 5 scoring system of the American Society of Echocardiography (15), and the regional wall motion score index was calculated. A normal response to stress was characterized by normal or hyperdynamic systolic function of all left ventricular segments. Infarction was characterized by resting wall motion abnormalities that did not change with stress. An akinetic segment that did not improve but became dyskinetic was considered to represent infarction (16). The development of new wall motion abnormalities was considered indicative of myocardial ischemia. Worsening of resting wall motion abnormalities,
including deterioration after initial improvement, was classified as resting wall motion abnormality with ischemia. The heart rate at which a new or worsening wall motion abnormality was first noticed (ischemic threshold) was recorded. On the basis of wall motion changes induced, myocardial segments were grouped by coronary artery distribution (17) and classified as normal, ischemic, infarcted or resting wall motion abnormality with ischemia. Ejection fractions at baseline and peak stress were determined by visual estimation.

Coronary angiography. Fourteen patients underwent clinically indicated coronary angiography within 6 months of the stress echocardiography protocols. Coronary vessels were visually assessed, and ≥50% narrowing of the lumen diameter of one or more major epicardial vessels was considered significant.

Statistical analysis and estimation of agreement of results. Paired Student’s t-test and McNemar’s test were used for paired continuous data and paired proportions, respectively. A p value of <0.05 was considered significant. The degree of agreement between results of dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography was estimated by the kappa coefficient: kappa of 1 denoted perfect agreement; kappa >0.5, good agreement; and kappa >0.8, excellent agreement (18). The agreement between the two tests for producing resting wall motion abnormalities was evaluated in two ways: 1) comparison of wall motion scores 1 through 5 for individual myocardial segments; and 2) comparison of classification of each coronary artery territory as normal, ischemic, infarcted or having resting wall motion abnormalities with ischemia.

RESULTS

Patient characteristics. Dobutamine stress echocardiography was performed in all 104 recruited patients. Transesophageal atrial pacing stress echocardiography was not feasible in four patients (4%) (three had inconsistent atrial capture; one patient did not tolerate esophageal intubation). One hundred patients were successfully paced and formed the study group. There were 53 men and 47 women; the mean age was 69 ± 10 years (range, 39 to 86 years). The causes of inability to exercise were orthopedic limitation in 40 patients, peripheral vascular disease in 29 and other physical limitations in 31. Indications for stress testing were evaluation of chest pain or dyspnea in 64 patients and evaluation of known coronary artery disease in 36 patients. Seventeen patients had a previous myocardial infarction. Twenty had a history of coronary revascularization, including percutaneous angioplasty in 12, bypass grafting in eight, and both in one. Hypertension, hyperlipidemia and diabetes mellitus were present in 63, 56 and 17 patients, respectively; 57 were smokers. Three or more coronary risk factors for atherosclerosis were present in 31 patients. Thirty patients were taking beta-blocker medications.

Table 1. Comparison of Hemodynamic Variables Between Dobutamine Stress Echocardiography and Transesophageal Atrial Pacing Stress Echocardiography

<table>
<thead>
<tr>
<th>Measurement</th>
<th>DSE</th>
<th>TAP</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>69 ± 12</td>
<td>72 ± 11</td>
<td>0.003*</td>
</tr>
<tr>
<td>Peak</td>
<td>133 ± 11</td>
<td>132 ± 9</td>
<td>0.559</td>
</tr>
<tr>
<td>Change in</td>
<td>63 ± 14</td>
<td>57 ± 13</td>
<td>0.018</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>143 ± 21</td>
<td>144 ± 19</td>
<td>0.482</td>
</tr>
<tr>
<td>Peak</td>
<td>142 ± 29</td>
<td>151 ± 20</td>
<td>0.0001</td>
</tr>
<tr>
<td>Change in</td>
<td>−1 ± 25</td>
<td>8 ± 15</td>
<td>0.0001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>80 ± 9</td>
<td>78 ± 8</td>
<td>0.451</td>
</tr>
<tr>
<td>Peak</td>
<td>74 ± 11</td>
<td>83 ± 12</td>
<td>0.0001</td>
</tr>
<tr>
<td>Change in</td>
<td>−6 ± 12</td>
<td>5 ± 12</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*From paired t-test.

DSE = dobutamine stress echocardiography; TAP = transesophageal atrial pacing stress echocardiography.

Hemodynamic end points and symptoms during stress echocardiography. During dobutamine stress echocardiography, the mean dobutamine dose was 35 ± 9 μg/kg per min (range, 20 to 40 μg/kg per min). Atropine (mean dose, 0.99 ± 0.62 mg; range, 0.25 to 2.0 mg) was administered to 44 patients. In the transesophageal atrial pacing stress echocardiography protocol, the mean pacing threshold was 15.2 ± 4.8 mA (range, 10 to 35 mA). Atropine was administered in 13 transesophageal atrial pacing stress echocardiography studies (mean dose, 0.58 ± 0.26 mg; range, 0.50 to 1.50 mg) because of Wenkebach second-degree heart block.

The baseline and peak stress heart rates and blood pressures are shown in Table 1. Target heart rate was achieved more often with transesophageal atrial pacing stress echocardiography (98%) than with dobutamine (89%) (p = 0.001). With pacing, there was a mild increase in systemic blood pressure. Dobutamine stress echocardiography was associated with greater variability in systolic blood pressure response. Development of regional wall motion abnormalities was the end point for dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography in five patients and one patient, respectively (p = 0.219). Intolerable symptoms were the end point for four patients with transesophageal atrial pacing and one patient with dobutamine stress echocardiography (p = 0.31). Angina was the end point for one patient for both tests. Nonsustained ventricular tachycardia (two patients) and hypotension (one patient) were additional end points during dobutamine stress echocardiography.

Symptoms during transesophageal atrial pacing stress echocardiography and dobutamine stress echocardiography are compared in Table 2. Symptoms were more frequent.
duration of transesophageal atrial pacing stress echocardiography (51 patients) than during the transesophageal procedure (32 patients) \( (p = 0.008) \). Common symptoms during transesophageal atrial pacing stress echocardiography were gagging during insertion of the catheter and mild retrosternal discomfort, which resolved with termination of pacing. Retrosternal discomfort occurred in 20 patients but was an end point in only four transesophageal atrial pacing stress echocardiography studies. Pacing of the diaphragm was not observed. Small intravenous doses of midazolam were administered in 23 of the transesophageal atrial pacing stress echocardiography studies at a mean dose of 2.1 ± 1 mg (range, 1 to 4 mg). Dysrhythmias occurred more frequently during dobutamine stress echocardiography.

The mean patient acceptance scores for dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography were 4.2 ± 0.9 and 4.0 ± 0.9, respectively \( (p = 0.11) \). Forty-four patients preferred dobutamine stress echocardiography, 29 preferred the transesophageal procedure and 27 had no preference.

**Duration of tests.** The mean duration of transesophageal stress echocardiography was 8.6 ± 3.6 min (5.0 to 21.0 min). This was significantly shorter \( (p = 0.0001) \) than the dobutamine studies \( (15.1 ± 3.9 \text{ min; } 7.3 \text{ to } 25.1 \text{ min}) \). The recovery period after termination of pacing was significantly shorter with transesophageal stress \( (1.0 ± 2.8 \text{ min}) \) than with dobutamine stress \( (13.9 ± 7.5 \text{ min}) \) \( (p = 0.0001) \).

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**Table 2. Comparison of Symptoms and Dysrhythmias Between Dobutamine Stress Echocardiography and Transesophageal Atrial Pacing Stress Echocardiography**

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>DSE</th>
<th>TAP</th>
<th>McNemar’s p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>27</td>
<td>20</td>
<td>0.178</td>
</tr>
<tr>
<td>Other symptoms*</td>
<td>25</td>
<td>16</td>
<td>0.117</td>
</tr>
<tr>
<td>Complex VE/NSVT</td>
<td>8</td>
<td>1</td>
<td>0.016</td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>5</td>
<td>0</td>
<td>0.063</td>
</tr>
</tbody>
</table>

*Includes 16 patients with gagging during TAP and 12 patients with tremors, 8 with nausea, 5 with headache and 4 with lightheadedness during DSE.

**Table 3. Comparison of Stress Echocardiography Interpretations Between Dobutamine Stress Echocardiography and Transesophageal Atrial Pacing Stress Echocardiography**

<table>
<thead>
<tr>
<th>Dobutamine Stress Echocardiography</th>
<th>Transesophageal Atrial Pacing Stress Echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Infarction and Ischemia</td>
</tr>
<tr>
<td>Ischemia</td>
<td>3</td>
</tr>
<tr>
<td>Infarction and ischemia</td>
<td>0</td>
</tr>
<tr>
<td>Infarction</td>
<td>0</td>
</tr>
</tbody>
</table>

**Agreement between dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography.** Among 1,599 segments evaluable by both techniques at rest, agreement was complete (with 1 to 5 scoring) in 1,478 segments \( (92\%) \). Among 1,579 segments evaluable during stress, there was agreement \( (\text{normal or abnormal}) \) in 1,436 segments \( (91\%) \). There was exact agreement \( (\text{with } 1 \text{ to } 5 \text{ scoring}) \) in 1,352 segments \( (86\%) \). The coefficient of agreement \( (\text{kappa}) \) for exact interpretation of individual segments at baseline ranged from 0.57 \( (\text{for mid inferoseptum}) \) to 1.0 \( (\text{for basal and mid anteroseptum and mid anterolateral segments}) \). The mean coefficient of agreement at baseline was 0.79 ± 0.04. With stress, the coefficient of agreement ranged from 0.53 \( (\text{for mid inferoseptum}) \) to 0.88 \( (\text{for basal inferior segments}) \). The mean coefficient of agreement with stress was 0.57 ± 0.04.

Interpretations of the two stress echocardiographic methods are compared in Table 3. For classification of studies as normal, ischemia, infarction or resting wall motion abnormalities with ischemia, there was agreement between dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography in 84 of 100 studies \( (84\%) \), kappa 0.77. In six of the 16 discordant studies, transesophageal atrial pacing identified a single segment in the septum or the inferobasal segment as abnormal. These segments were considered normal during dobutamine stress echocardiography. In two studies, transesophageal atrial pacing stress echocardiography caused worsening of wall motion abnormality in segments with resting wall motion abnormality; this worsening was not seen during dobutamine stress echocardiography.

When wall motion abnormalities were summarized by coronary artery territory as normal, ischemia, infarction or resting wall motion abnormalities with ischemia, the average agreement for the coronary artery territories was 0.70 ± 0.05. Kappa values were 0.72 for left anterior descending artery territory, 0.74 for right coronary and 0.65 for the left circumflex artery.

In Table 4, stress electrocardiography and wall motion score index and ejection fraction at rest and at peak are compared for the two stress modalities. Ejection fraction at peak stress was higher with dobutamine \( (69\% ± 11\%) \) vs. \( 61\% ± 11\% \) \( (p = 0.0001) \). The ischemic threshold was lower for dobutamine stress echocardiography \( (110 ± 20 \% \text{ systolic}) \).
beats/min) than for transesophageal atrial pacing stress echocardiography (121 ± 13 beats/min) (p = 0.0001). The order of testing did not have a significant effect on the duration, baseline or stress wall motion score index, or ischemic threshold of either test.

Accuracy of dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography.

Fourteen patients with positive results of both dobutamine stress echocardiography and transesophageal atrial pacing stress echocardiography underwent coronary angiography. Thirteen had significant coronary artery disease. The other patient had previously had an inferior myocardial infarction; rest inferior and inferoseptal hypokinesis worsened with both modalities of stress echocardiography. Mild coronary artery disease (20% to 30% stenoses) was found on angiography.

**DISCUSSION**

The results of this study show that transesophageal atrial pacing stress echocardiography is a safe, feasible and efficient method for assessment in patients with suspected or known coronary artery disease. The protocol for transesophageal atrial pacing stress echocardiography was significantly shorter than that for dobutamine stress echocardiography. Recovery times were also shorter, with rapid return to baseline heart rate and wall motion when pacing was terminated. Recent improvements in the design of catheters for transesophageal atrial pacing permit pacing with lower energy levels, so that this procedure is well tolerated. Transesophageal atrial pacing stress echocardiography was satisfactory in patient acceptance, although 23 patients received midazolam intravenously, and none required this drug with dobutamine stress echocardiography.

There was good agreement of the two stress echocardiographic methods in assessment of wall motion abnormalities. This was true when the two techniques were compared for their ability to induce ischemia and when wall motion scores were compared on a segment-by-segment basis. Although coronary angiography findings were available in only a small subset of patients, the good agreement of the two techniques suggests that transesophageal atrial pacing stress echocardiography has a diagnostic accuracy similar to that of dobutamine stress echocardiography, a well-validated stress testing modality for the detection of coronary artery disease (1–4).

Transesophageal atrial pacing has been used simultaneously with transesophageal echocardiography (8,11,12) and also with transthoracic echocardiography (9,10,13,14) for the detection of ischemic heart disease. These studies showed variable feasibility (77% to 100%), sensitivity (83% to 93%) and specificity (76% to 100%) for the detection of angiographic coronary artery disease.

The hemodynamic effects of transesophageal atrial pacing (19–21) and dobutamine stress echocardiography (22) have been studied but have not previously been compared. Hemodynamic studies during atrial pacing have demonstrated that the oxygen demands of the heart are increased and myocardial lactate production is increased in patients with angina (23). During atrial pacing, heart rate is increased without an augmentation of cardiac output (20). In contrast, both heart rate and cardiac output increase during dobutamine stress testing (22). In the present study, peak heart rates were similar with both stress modalities, but systolic and diastolic blood pressures were modestly higher with transesophageal atrial pacing. The ejection fraction at peak stress was higher with dobutamine stress. The ischemic threshold was approximately 10 beats/min higher with transesophageal atrial pacing than that observed with dobutamine stress echocardiography. This was not unexpected, because of the inotropic effects of dobutamine.

**Limitations.** Coronary angiographic data were insufficient for an estimation of the relative diagnostic accuracy of transesophageal atrial pacing stress echocardiography and dobutamine stress echocardiography. However, the agreement of the test results was good. In the transesophageal atrial pacing stress echocardiography studies preceded by dobutamine stress echocardiography, the resting heart rate was higher (by 5 ± 11 beats/min). Although a 20-min period separated the two tests, a residual dobutamine effect may have potentiated ischemia induced by transesophageal atrial pacing stress echocardiography. Order of testing did not affect test agreement, however.

Limitations of transesophageal atrial pacing stress echocardiography include the requirement for intact atrioventricular conduction and absence of significant esophageal disease. Additionally, some patients required an anxiolytic agent.

**Implications.** Our findings may have important implications for the clinical assessment and investigation of coro-
nary disease. Dobutamine-atropine stress protocols are more labor intensive than transesophageal atrial pacing stress echocardiography or exercise echocardiography. Adverse drug effects and the prolonged recovery period are limitations of dobutamine stress. Although the use of an esophageal catheter might be expected to be less appealing to the patient, because of mild oral analgesia and midazolam administration in 23%, this was not found to be the case.

Intermediate stages of transesophageal atrial pacing stress echocardiography were utilized to allow for detection of new or worsened wall motion abnormalities at heart rates lower than the target heart rate. However, an even more rapid protocol would be feasible. Thus, transesophageal atrial pacing stress echocardiography can find application in a clinical context in which a rapid test with no adverse drug effects and a rapid return to baseline are desired. Transesophageal atrial pacing stress echocardiography may also find a niche in the evaluation of patients who are intolerant of pharmacologic stress echocardiography, who have chro-notropic incompetence (including those receiving beta-blockers) or who require rapid evaluation of chest pain.

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**REFERENCES**