Advantages and Disadvantages of Dobutamine Stress Echocardiography Compared With Treadmill Exercise Electrocardiography in Detecting Ischemia

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We compared the effectiveness and practicability of dobutamine stress echocardiography (DSE) and treadmill exercise electrocardiographic testing (TMT) for detecting coronary artery disease. Ninety-six patients (mean age 58.8±9.0 years) who presented for coronary angiography underwent both DSE and symptom-limited TMT. Two-dimensional echocardiography was performed to detect ischemia-induced wall motion abnormalities during incremental dobutamine infusion (5−40 μg/kg per min administered in 5 min steps). The sensitivity of detecting ischemia was 63% for TMT and 79% for DSE (p<0.05); the specificity was 61% for TMT and 88% for DSE (p<0.05). The accuracy of TMT was 63% and of DSE 82% (p<0.01). In patients in whom both tests gave true-positive results, the maximum ST depression was evaluated during DSE and TMT (n=31). The ST segment depressions detected by DSE were significantly smaller than those detected by TMT (0.04±0.04 mV vs 0.17±0.07 mV, p<0.01), and 10 patients had no evidence of ST segment depression despite the presence of new wall motion abnormalities. DSE took significantly longer to perform than TMT (26.0±5.0 min vs 5.5±2.0 min, p<0.01). Thus, DSE is more sensitive, specific and accurate than TMT in detecting coronary artery disease and can detect ischemia at an earlier stage. However, it takes longer to perform than TMT and thus may be less suitable for routine clinical use.

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STRESS testing is essential to the management of patients with known or suspected coronary artery disease. Treadmill exercise ECG testing (TMT) has been the preferred method of evaluating patients with suspected coronary artery disease for decades, although its sensitivity and specificity may be unsatisfactory. Currently, the most widely used noninvasive technique for evaluating the severity of coronary artery disease is exercise thallium-201, single-photon emission computed tomography. Exercise echocardiography is also used, as it is well known that mechanical and perfusional changes occur earlier than electrical changes during an ischemic attack. The relatively poor quality of the echo images during and immediately after exercise limits the clinical use of exercise echocardiography. To achieve the best body position to obtain high-quality echocardiographic images during stress, dipyridamole and dobutamine stress echocardiogra-
DSE Versus TMT in Ischemia Detection

Dobutamine (DSE) were introduced, and are now widely used. It has been assumed that dobutamine induces ischemia by increasing myocardial oxygen demand, which is thought to be compatible with exercise. In addition, dobutamine is more effective than dipyridamole or adenosine in inducing ischemic wall motion abnormalities. Thus, dobutamine stress would be most suitable for detecting ischemia using echocardiography.

We designed this study to compare the efficacy and clinical practicability of DSE and TMT for detecting coronary artery disease. Routine physiologic parameters, the degree of ischemic ECG change and stress duration were also compared at the ischemic threshold to evaluate the clinical problems and to compare the effectiveness of DSE and TMT for the detection of coronary artery disease.

PATIENTS AND METHODS

Between June 1992 and May 1994 we screened 98 patients referred for coronary angiography for suspected coronary artery disease who satisfied the study criteria. Those with cardiac failure, unstable angina, congenital or valvular heart disease, cardiomyopathy, uncontrolled systemic hypertension or myocardial infarction during the preceding month were excluded from study, as were those with bundle branch block, >1 mm ST segment deviation from the isoelectric line on the baseline ECG or a history of significant arrhythmias. We did not perform DSE on 2 patients who had poor endocardial definition on transthoracic imaging at baseline. The remaining 96 patients (67 men and 15 women; mean age 58.8±9.0 years, range 39—82 years) underwent DSE, TMT, and coronary angiography in random order within a 2-week period. No significant cardiac events occurred during this time. All patients were in normal sinus rhythm. Coronary angiography revealed normal coronary arteries in 33 patients, single-vessel disease in 35 patients, and multivessel disease in 28 patients. Twenty-nine patients had a history of previous myocardial infarction (post-infarction time >1 year in 17 patients and 3—12 months in 12 patients). Eighteen patients had undergone successful percutaneous transluminal coronary angio-

plasty (PTCA) with no evidence of significant residual stenosis.

Beta-blocker therapy was withheld the day before testing, but cardiac medication such as angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, and nitrates was continued. All patients gave their informed consent to participate in the study.

Dobutamine Stress Echocardiography

Using a commercially available 2-dimensional echocardiography system (Toshiba SSH-160A or Hewlett-Packard SONOS-1000, both with a 2.5 MHz transducer), we imaged the motion of the entire left ventricular wall using the parasternal long-axis, short-axis and apical 4- and 2-chamber views, and recorded them on 12 mm S-VHS videotape. Dobutamine was administered intravenously at an initial dose of 5 μg/kg per min for 5 min. The dose was increased by 5 μg/kg per min at 5 min intervals up to a maximum dose of 40 μg/kg per min. A 9-lead ECG that resembled a conventional 12-lead ECG system but excluding leads V2, V3, and V4 was used. This lead system allowed easy access to echocardiographic windows during continuous monitoring of each stage of dobutamine infusion, and for 10 min after terminating the infusion. Blood pressure was measured during the last 2 min of each stage of dobutamine infusion. Testing was terminated if any of the following end points was detected: development of new regional wall motion abnormalities, ST segment depression of 2 mm or more, angina, significant symptoms, or arrhythmias. A systolic blood pressure of 220 mmHg or a decrease >30 mmHg, or to a value <100 mmHg, was also an indication for test termination.

Echocardiographic Image Analysis

Blind evaluation of 2-dimensional echocardiographic images from videotape playback was conducted by 2 independent experienced observers who adopted the same assessment criteria. A normal study was defined as normal wall motion at rest and hyperdynamic wall motion after dobutamine infusion in all regions of the myocardium.

An ischemic stress response was defined as transient asynery of contraction that was either absent or occurred to a lesser degree in the basal condition as detected by 2-
dimensional echocardiography. Akinesia or dyskinesia in the basal condition that did not worsen after dobutamine infusion was not defined as an ischemic stress response.

**Treadmill Exercise Test**

All treadmill exercise tests were performed according to a modified Bruce protocol for Japanese patients using a computerized ST segment analysis system (ML-8000, Fukuda Densi). Treadmill exercise end points included limiting symptoms (severe chest pain, dyspnea or leg fatigue), a heart rate ≥85% of the age-predicted maximum, markedly elevated systolic blood pressure or a decrease >10 mmHg and significant ST segment shift or serious ventricular arrhythmias. An ischemic ECG response was defined as new-onset ST segment elevation >1 mm or planar or downsloping ST segment depressions 80 ms after the J point in any lead during or after exercise. The degree of ST depression was measured 80 ms after the J point just after exercise, with the subject in the supine position, and compared with the level of ST depression during peak infusion of dobutamine. An observer unaware of the other investigative findings interpreted the ECG results.

**Coronary Angiography**

Coronary angiography was performed using the Judkins or Sones technique and 2–6 projections for each coronary artery. Coronary angiograms were visually analyzed for the degree of stenosis in major epicardial coronary arteries or their major branches. A coronary artery stenosis was considered significant if the vessel diameter was reduced by ≥70% in each of 2 orthogonal projections, as determined by an observer who was unaware of the other results.

**Statistical Analysis**

Data are reported as means±SD. Statistical analysis of paired data was performed using Student’s t-test. Sensitivity, specificity, and predictive accuracy were calculated using standard methods. Frequency data were compared by chi-square analysis. A value of p<0.05 was considered statistically significant.

**RESULTS**

There were no complications during either pharmacological or exercise stress testing. Fig 1 shows dyskinesia of the distal septum and apex in a 43-year-old man with a 90% proximal left anterior descending stenosis. Fig 2 shows the difference between the maximum ST segment depression in lead V5 just after TMT and during peak infusion of DSE in the same patient. As shown in Table I, the sensitivity of DSE was 16% higher than that of TMT for the detection of significant coronary artery disease [79% (50/63) vs 63% (40/63), p<0.05], and specificity was 27% higher [88% (29/33) vs 61% (20/33), p<0.05]. DSE was 19% more accurate than TMT [82% (79/96) vs 63% (60/96), p<0.01]. The peak heart rate and systolic blood pressure were significantly lower during DSE than during TMT (101±20 beats/min vs 123±23 beats/min, p<0.001; and 155±26 mmHg vs 177±32 mmHg, p<0.01). However, the duration of stress testing was significantly longer for DSE than for TMT (26.0±5.0 min vs 5.5±2.0 min, p<0.01). The degree of ST segment depression measured by DSE and TMT was compared only in patients in whom both tests gave true-positive results (n=31). The ST segment depressions of the ischemic ECG threshold induced by DSE were significantly smaller than those induced by TMT (0.04±0.04 mV vs 0.17±0.07 mV, p<0.01, Fig 3), and 10 patients showed no ST segment depressions despite the development of new wall motion abnormalities during DSE. Angina developed in 6 patients (10%) during dobutamine infusion, but this was not severe, and therapy with sublingual nitroglycerin was required in only 2 cases. The incidence of induced angina during TMT was 22% (14/63), and sublingual nitroglycerin therapy was administered in 8 patients.

**Side-Effects of Dobutamine Infusion and TMT**

All adverse reactions to dobutamine infusion were mild, and only in 2 cases was it necessary to terminate the test, in 1 case because of accelerated idioventricular rhythm and in 1 case because of ventricular bigeminy. Thirteen patients experienced palpitations (14%), 5 chills (5%), 2 flushing
Fig 1. Two-dimensional echocardiograms, apical 4-chamber view. Top, end-systole; bottom, end-diastole. Left: A normally contracting septum, apex and posterior wall during control conditions. Right: Two minutes after infusion of 20 \( \mu \)g/kg per min dobutamine, apical dyskinesia is observed during end-systole (arrow). Coronary angiography demonstrated 2-vessel disease with 90% proximal stenosis of the left anterior descending artery.

Fig 2. Electrocardiograms, using lead V5, from the same patient as in Fig 1 in the supine position. Left: During control conditions no ST segment depression is noted. Middle: Just after termination of treadmill exercise, horizontal ST segment depressions are observed. Right: In contrast, only mild upsloping ST depressions are seen during peak infusion of dobutamine stress echocardiography.

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TABLE I

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Fig.3. The degree of ST segment depression induced by dobutamine stress echocardiography and treadmill exercise ECG tests in patients in whom both tests gave true-positive results.

(2%), 1 dizziness (1%) and 1 developed a headache (1%). In contrast, no adverse reactions were noted with TMT other than the more frequent incidence of induced anginal pain.

DISCUSSION

DSE has recently been proposed as a clinically useful noninvasive test for the detection of coronary artery disease. Recent reports have demonstrated a high sensitivity and specificity for detecting coronary artery disease using this technique. Our findings confirm the comparatively high sensitivity, specificity and accuracy of this technique. In addition, our study compared the clinical utility and problems of DSE with those of TMT for the detection of coronary artery disease. Previous studies compared the 2 methods but did not compare the severity of the inducible ischemic threshold.

The following regular sequence of abnormalities has been observed during the onset of myocardial ischemia in experimental and clinical studies: relaxation abnormalities, contraction abnormalities, increased filling pressures, electrocardiographic changes, and, finally, angina. Regional contractile abnormalities would thus be more sensitive than ST segment changes in the early detection of myocardial ischemia, and dobutamine stress testing could be discontinued at a lower ischemic threshold.

In our study, the degree of dobutamine-induced ST segment depression was significantly lower than symptom-limited ST segment depression in patients with inducible ischemia. This finding suggests that wall motion abnormalities would precede electrocardiographic changes during ischemia. During TMT, the detection of ischemia depends on the development of unreliable markers such as anginal pain and/or ECG changes, which may occur late in the course of ischemic events.

Although the safety of maximal exercise testing has been confirmed complications can occur (0.8 complications per 10,000 tests). The fact that DSE is capable of detecting ischemia earlier than symptom-limited TMT may increase the margin of safety. Indeed, Marcovitz and Armstrong reported that, in contrast to wall motion analysis, 12-lead ECG during dobutamine infusion revealed ischemic changes in only 17% of patients with coronary artery disease. However, in patients with poor ultrasound images, wall motion abnormalities and electrocardiographic changes can be detected simultaneously. Similar findings were reported during coronary angioplasty.

The problem of poor image resolution is inherent to echocardiography, particularly in patients with obesity or pulmonary emphysema. Transesophageal dipyridamole or dobutamine stress echocardiography has also been proposed for diagnosing coronary artery disease, but its clinical applicability may be rather limited. In contrast, the presence of ischemic ST segment depression in the absence of wall motion abnormality is highly predictive of angiographically normal coronary arteries.
Disadvantages of DSE

DSE is a time-consuming and relatively labor-intensive process. In our study, the entire procedure took approximately 60 min whereas the total time required for TMT was approximately 30 min. It takes at least 3 min for dobutamine to achieve a pharmacological steady state, and shorter periods may result in incomplete stress. Shorter stress times have been reported with other pharmacologic stress agents, such as dipyridamole or adenosine (17 min vs 27 min) but these agents are reported to be less sensitive in detecting ischemia using echocardiography. They are also contraindicated in patients with asthma because of the risk of bronchospasms. The use of dobutamine stress in asthmatic patients is reportedly safe. Another disadvantage of DSE is its known arrhythmogenic potential. Recently, Picano et al in a multicenter study, reported that complex ventricular tachyarrhythmias occurred relatively frequently (38% of all submaximal tests), although rather high doses of atropine (0.25 mg up to a maximum of 1.00 mg) were administered in this case. In our study, the test was terminated in 2 patients because of the development of complex ventricular tachyarrhythmias, but these arrhythmias subsided within 30 s after dobutamine withdrawal. Despite its arrhythmogenic potential, DSE appears to be a safe and inexpensive modality that is suitable for clinical use, although the test takes longer to perform than other methods.

CONCLUSION

DSE was more specific and accurate than TMT in the detection of coronary artery disease. In addition, because DSE detected ischemia at an earlier stage than TMT, it may have a higher margin of safety, although dobutamine has arrhythmogenic potential. However, as DSE takes longer to perform than TMT, its routine clinical use may be limited.

REFERENCES

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