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Stress Echocardiography in Elderly Patients With Coronary Artery Disease

Applicability, Safety and Prognostic Value of Dobutamine and Adenosine Echocardiography in Elderly Patients

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Objectives. **Our aim was to determine the applicability, safety and prognostic value of adenosine and dobutamine stress echocardiography in patients ≥70 years old.**

Background. **These tests are sometimes mandatory because of difficulties and inaccuracies in interpreting traditional electrocardiographic stress tests. Furthermore, if these tests could be used to avoid coronary arteriography and cardiac catheterization, they would become essential in the care of the elderly, whose numbers are increasing.**

Methods. **We performed coronary arteriography and dobutamine and adenosine stress echocardiographic tests in 120 patients (72 men) ≥70 years old who entered the hospital because of chest pain and had known or suspected coronary artery disease. The stress tests were performed on separate days, within 2 weeks of coronary arteriography. Both the arteriograms and the echocardiograms were analyzed by two experts who had no knowledge of the patients' other data or the other interpreter's report. Tests were judged to have positive or negative results, and the patients were followed up for the development of cardiac events. Univariate and multivariate analyses and other statistical modalities were applied for comparisons.**

Results. **Documented coronary artery disease was found in 89 patients. During the 14 ± 7 months of follow-up, cardiac events developed in 50 patients, including 3 (7.9%) of 38 patients with negative dobutamine and 12 (20.7%) of 58 patients with negative adenosine test results. Demonstration of any abnormality on stress echocardiography was an independent factor for cardiac events, both for dobutamine (relative risk 7.3) and for adenosine (relative risk 3.0). Both cessation of dobutamine or adenosine tests and diagnosis of disease in two or more coronary vessels were also independent predictors. ST segment depression ≥1 mm was related to future events only with the dobutamine test.**

Conclusions. **These echocardiographic stress tests proved safe and well tolerated. They successfully stratified this cohort of elderly patients with coronary artery disease to low or high risk subgroups for subsequent cardiac events.**

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The mean life expectancy in the United States has been prolonged from 45 to nearly 75 years (1). Consequently, increasing numbers of elderly people enter the hospital for assessment of chest pain. In these patients, coronary artery disease is highly prevalent (2–6) and is the leading cause of morbidity and mortality. Furthermore, the use of more aggressive diagnostic and therapeutic strategies in these patients has improved the quality of life and decreased cardiac morbidity and mortality (7–9). However, clinical assessment of these patients with conventional stress tests is inadequate because of their limited capacity to perform or complete these tests (10,11). Dipyridamole, adenosine and dobutamine stress echocardiography have been previously used as alternatives to exercise testing for detecting coronary artery disease (12–15). The combination of clinical findings and echocardiographic test results could help to stratify these patients into low and high risk subgroups (16,17). The aim of this work was to investigate the safety and applicability of dobutamine and adenosine stress echocardiography and to compare their prognostic value in the elderly. We anticipated that some guidelines for the use of these tests in the clinical management of elderly patients with coronary artery disease could be established.

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Methods

Study group. One hundred twenty consecutive patients ≥70 years of age with suspected or known coronary artery disease underwent dobutamine and adenosine stress echocardiography on different days and in random sequence. The patients were included in the study because they reported typical or atypical chest pain and also showed a compromised ejection fraction ≥30%. The presence and degree of heart failure or arrhythmias were not classified. All patients underwent coronary arteriography within 2 weeks of dobutamine and adenosine stress echocardiography. We excluded 22 patients: 4 with heart failure (ejection fraction <30%), 3 with valvular heart disease, 2 with ventricular arrhythmias, 2 with left bundle branch block, 6 with a recent history of asthma or severe chronic obstructive pulmonary disease and 5 with unstable angina. All patients had sinus rhythm. None was receiving atropine. Thirty patients were capable of completing a stress electrocardiogram (ECG); the results were positive in 16, negative in 10 and nondiagnostic in 4. Thus, in this subgroup of the study patients, the ECG stress test showed a sensitivity of 86.7%, a specificity of 72.7% and a relative predictive value of 81.3%. The study protocol was approved by the Ethics Committee of the hospital. All patients signed an informed consent form to enter the study.

Cardiac catheterization. Coronary arteriograms (Judkins or Sones technique) were obtained by using multiple views and were recorded on 35-mm cine film. Coronary stenoses were evaluated visually by two experienced angiographers unaware of the other data of each patient. Significant coronary artery disease was diagnosed when at least one ≥50% diameter stenosis in a major epicardial artery was observed.

Dobutamine stress. After routine preparation for stress testing, a rest ECG and a two-dimensional echocardiogram were obtained. Dobutamine was administered intravenously with a pump, starting at a dose of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and then increasing in increments of 5 $\mu g \cdot kg^{-1}$ every 3 min, up to the maximal dose of 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$. An ECG was continuously monitored. Before the test, at the end of each stage and up to 10 min after the end of the infusion, clinical signs, blood pressure, 12-lead ECG and two-dimensional echocardiographic images were recorded. End points of the test were either the achievement of the peak dose administration, or the development of: severe ischemia or extensive wall motion abnormality (in >10 of the 16 segments), severe hypertension (systolic arterial pressure >230 mm Hg), or hypotension (decrease of systolic arterial pressure >20 mm Hg from baseline value or an absolute value ≤90 mm Hg), ventricular tachycardia or complex ventricular extrasystoles and ST segment elevation or depression ≥1 mm.

Adenosine stress. Adenosine was infused intravenously at a dose of 140 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 6 min under ECG monitoring. Before the test, at the end of each minute and up to 2 min after the end of the infusion, clinical signs, 12-lead ECG, blood pressure and two-dimensional echocardiographic results were recorded. All patients were advised to avoid consuming coffee, tea or caffeine-containing food or beverages for the preceding 12 h. End points equivalent to those used with the dobutamine stress echocardiographic test were used, but with this protocol, severe side effects leading to termination of the test at a submaximal dose included development of sinoatrial or third-degree atrioventricular (AV) block and other symptoms, such as severe dyspnea or flushing (which rarely occurred with the dobutamine infusion).

Echocardiographic studies. Two-dimensional echocardiography at standard projections (parasternal long- and short-axis and apical four- and two-chamber views) were recorded on videotape at baseline and during the tests (at the end of each stage for the dobutamine test, continuously during the adenosine test and up to 10 and 2 min during the recovery phase, respectively). The echocardiographic images were assessed by two experienced observers working separately, without knowledge of the patients' clinical or angiographic data or the results of the echocardiographic stress test assessed by their counterpart.

For the purpose of analysis, a 16-segment model of the left ventricular wall was used (18). Both systolic wall thickening and inward motion were evaluated and, according to a generally accepted qualitative analysis (19), wall motion was graded as 1 (normal), 2 (hypokinetic), 3 (akinetic) or 4 (dyskinetic). An ischemic response was defined by echocardiography as the development or worsening of a wall motion abnormality compared with baseline. On this basis, a wall motion abnormality already present in basal conditions was not considered a positive result test. Segments that were hypokinetic at baseline and became akinetic on testing were considered positive for ischemia. However, segments that were akinetic at baseline and became dyskinetic on testing were not considered ischemic (20) unless a new or worsening wall motion abnormality also developed in two or more adjacent segments.

Follow-up data were obtained through a telephone interview, a medical clinic visit or by contacting the referring physician. Events included cardiac deaths, nonfatal myocardial infarction (hard events), unstable angina necessitating hospital admission, coronary bypass surgery or angioplasty. For survival analysis, only one event was considered in each patient; therefore, any subsequent event was not considered.

Statistical analysis. Multivariate stepwise regression analysis was performed to detect independent predictors of cardiac events. A log-linear model was used to treat the dependent (event) and independent variables measured on a nominal scale. Those independent variables traditionally considered to be related to the evolution of the coronary artery disease were included in the analysis. These were gender, history of hypertension, smoking, hypercholesterolemia, diabetes mellitus, typical angina, myocardial infarction and dyspnea, Q wave (rest ECG), dyskinesia (rest echocardiogram), disease of two or more vessels (angiogram), ST depression ≥1 mm, cessation of the dobutamine or adenosine stress test, positive test results and worsening of wall motion.

A step by step examination of combinations of variables was performed and the results were compared among these com-

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Table 1. Clinical Characteristics and Investigative Variables of the 120 Study Patients Stratified by Presence or Absence of Cardiac Events

	Cardiac Events (n = 50)	No Cardiac Events (n = 70)	p Value
Mean age (yr)	75.7 ± 3.3	74.9 ± 2.6	0.182
Men	35 (70%)	37 (52.8%)	0.056
Asymptomatic	17 (34%)	31 (44.3%)	0.079
Atypical chest pain	5 (10%)	15 (21.4%)	0.052
Typical angina	28 (56%)	24 (34.3%)	<0.05
Previous MI	29 (58%)	19 (27.1%)	<0.01
Smoking history	23 (46%)	25 (35.7%)	0.079
Hypertension	34 (68%)	44 (62.8%)	0.131
Hypercholesterolemia	33 (66%)	46 (65.7%)	0.155
Diabetes mellitus	15 (30%)	13 (18.6%)	0.061
Smoking and hypertension	19 (38%)	13 (18.6%)	<0.05
Beta-blocker therapy	26 (52%)	29 (41.4%)	0.078
Calcium antagonist therapy	33 (66%)	34 (48.6%)	0.054
Nitrate therapy	47 (94%)	50 (71.4%)	<0.01
Digitalis therapy	9 (18%)	14 (20%)	0.180
Baseline ejection fraction (%)*	48.9 ± 10.7	50.85 ± 10.6	0.328
WMA at rest*	41 (82%)	39 (55.7%)	<0.01
2- or 3-vessel disease†	43 (86%)	27 (38.6%)	<0.01

*Assessed by two-dimensional echocardiography. †Assessed by coronary arteriography. Data presented are mean value ± SD or number (%) of patients. MI = myocardial infarction; WMA = wall motion abnormalities.

Table 2. Dobutamine and Adenosine Echocardiographic Findings in the 120 Study Patients

	Cardiac Events (n = 50)	No Cardiac Events (n = 70)	p Value
Dobutamine stress test			
Positive result	47 (94%)	35 (50%)	< 0.001
Angina	24 (48%)	10 (14.3%)	< 0.001
ST depression ≥1 mm	27 (54%)	10 (14.3%)	< 0.001
Infusion duration (min)	17.5 ± 5.3	21.8 ± 4.5	< 0.001
Discontinuation of the test*	34 (68%)	15 (21.4%)	< 0.001
SBP reduction ≥20 mm Hg	5 (10%)	3 (4.3%)	0.138
Adenosine stress test			
Positive	38 (76%)	24 (34.3%)	< 0.001
Angina	24 (48%)	19 (27.1%)	< 0.05
ST depression ≥1 mm	9 (18%)	3 (4.3%)	< 0.05
Infusion duration (min)	5.1 ± 1.3	5.7 ± 0.7	< 0.01
Discontinuation of the test*	19 (38%)	8 (11.4%)	< 0.01

*Because of chest pain, ST segment depression ≥1 mm or extensive wall motion abnormality. Data presented are mean value ± SD or number (%) of patients. SBP = systolic blood pressure.

binations step by step until the procedure reached a maximal p value for these variables. At each step, after the addition of a new variable, the resulting p value was checked to make sure that the log-linear model was improving. Variables producing a smaller p value were excluded from the next step. Care was taken so that the patient's condition was best represented with the independent variables in use. Relative risk ratios were calculated for those variables, found to be statistically significant in the multivariate analysis. Actuarial event-free rates were analyzed by using survival curves. Data were expressed as mean value ± SD. Where appropriate, 95% confidence intervals (CI) are given. The calculation of sensitivity, specificity and accuracy relied on standard definitions. Univariate analysis was performed by using the Student *t* test for interval data and chi-square test for categoric data. A p value <0.05 was considered statistically significant.

Results

Follow-up data. The 120 patients had an overall total of 50 (42%) cardiac events during the 14 ± 7 month follow-up period: 9 cardiac deaths, 4 nonfatal myocardial infarctions, 14 episodes of unstable angina, 19 coronary bypass grafting procedures and 4 coronary angioplasty procedures. As a rule, revascularization was undertaken for persistent or worsening symptoms despite medical treatment, taking also into consideration the echocardiographic findings. In only two patients the decision for revascularization was also based on the coronary anatomy. The patients' characteristics are presented in Table 1. The mean age of the patients was 75.3 ± 3 years; 72 (60%) of the 120 patients were men. Forty-eight patients (40%) had a history of previous myocardial infarction and three had undergone previous aortocoronary bypass surgery.

All the patients are being followed up. The average follow-up time is 14 ± 7 months. Of the 42 patients who have been followed up for <14 months, 9 had had normal arteriographic findings; among the 33 with abnormal findings, events developed in 17 during this follow-up period. The 14-month cardiac event rate was higher in patients with than in those without a prior myocardial infarction (58% vs. 27%, $p < 0.01$) and in patients with typical angina (56% vs. 34%, $p < 0.05$). The combination of hypertension and smoking (38% vs. 19%, $p < 0.05$) and wall motion abnormalities at rest (82% vs. 56%, $p < 0.01$) were also univariate predictors of cardiac events. Coronary arteriography demonstrated one-, two- or three-vessel disease in 19, 25 and 45 patients, respectively. The incidence of all (n = 50) and hard (n = 13) cardiac events was greater in patients with multivessel disease (43 of 50 vs. 27 of 70, $p < 0.001$ for all cardiac events, 12 of 50 vs. 1 of 70, $p < 0.001$ for hard events).

Dobutamine echocardiography (Table 2). The dobutamine infusion was well tolerated without serious complications in most patients. In 12 patients infusion was discontinued because of adverse effects: hypotension in 8, hypertension (systolic arterial pressure ≥230 mm Hg) in 2 and paroxysmal atrial fibrillation in 2. Paroxysmal atrial fibrillation developed in one additional patient just after the end of the test. In all patients, blood pressure returned to the baseline value after discontinuation of the dobutamine infusion without additional treatment. Both patients who had systolic arterial pressure ≥230 mm Hg during the test gave a history of hypertension. Two of the patients who experienced atrial fibrillation had a previous history of intermittent atrial fibrillation. The atrial

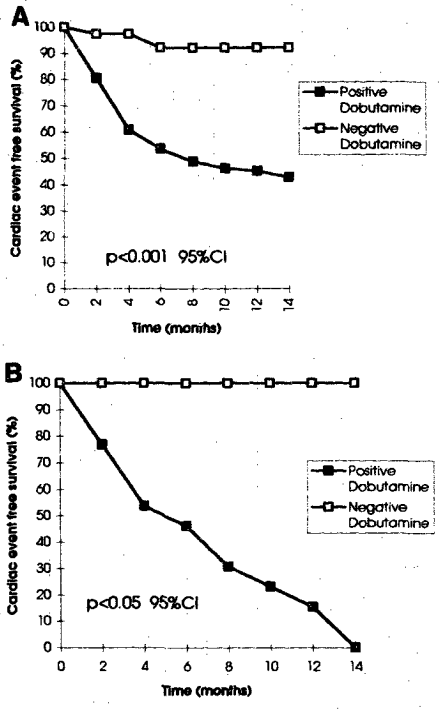


Figure 1. Survival curves for all (**A**) and hard (**B**) cardiac events during a 14-month follow-up period, according to the results of dobutamine stress echocardiography. CI = confidence interval.

fibrillation reverted to sinus rhythm either after administration of metoprolol or, spontaneously, within 8 h after cessation of the test. Other patients experienced minor adverse effects (headache or premature atrial or ventricular contractions) that did not prevent completion of the test.

Both, all (n = 50) and hard (n = 13, 13 of 13 vs. 69 of 107, $p < 0.05$) cardiac events (Fig. 1, A and B) occurred more often in patients with positive dobutamine stress test results. One hundred forty-three new and 127 worsening wall motion abnormalities were recorded during the test in 82 patients, and transient dyskinesia was recorded in 30 (Table 3). ST segment depression ≥1 mm (Fig. 2) and chest pain after dobutamine infusion occurred in 37 (31%) and 34 (28%) patients, respectively, and were related to cardiac events. Furthermore, the duration of the dobutamine infusion was significantly less in patients with cardiac events. Discontinuation of the test was also related to adverse outcome.

The sensitivity, specificity and accuracy of dobutamine echocardiography are shown in Table 4. The overall sensitivity of the dobutamine test for the patients who received or did not receive beta-adrenergic blocking agents was similar (86% and 87%, respectively).

Adenosine echocardiography (Table 2). The only serious adverse effect noted during adenosine infusion was AV block. Transient AV block developed in seven patients, including

Table 3. Recorded New or Worsening (or both) Wall Motion Abnormalities and Transient Dyskinesia During Stress Tests in the 120 Study Patients

	Cardiac Events (n = 50)	No Cardiac Events (n = 70)	p Value
Dobutamine stress test			
Only new WMA	15 (30%)	17 (24.3%)	0.129
Only worsening WMA	12 (24%)	11 (15.7%)	0.097
Both new and worsening WMA	20 (40%)	7 (10%)	< 0.001
Transient dyskinesia	23 (46%)	7 (10%)	< 0.01
Adenosine stress test			
Only new WMA	18 (36%)	10 (14.3%)	< 0.05
Only worsening WMA	17 (34%)	9 (12.8%)	< 0.05
Both new and worsening WMA	3 (6%)	5 (7.1%)	0.282
Transient dyskinesia	8 (16%)	3 (4.3%)	0.052

Data presented are number (%) of patients. WMA = wall motion abnormalities.

three patients with first-degree block, two with Wenckebach block and two with Mobitz type II second-degree AV block. None of the patients experienced symptoms, and the AV block was transient and self-limited. Other patients exhibited minor adverse effects (dyspnea, flushing, headache, nausea). No patient required treatment with aminophylline and in only one patient was adenosine infusion terminated before the end of the test, because of flushing and headache. All cardiac events (Fig. 3), but not the hard events (9 of 13 vs. 53 of 107, $p = 0.098$), were encountered significantly more often in patients with a positive adenosine test result. Seventy-eight new and 83 worsening wall motion abnormalities were recorded during the test in 62 patients, and transient dyskinesia was recorded in 11 (Table 3).

Results of both dobutamine and adenosine tests were positive in 59 patients and negative in 35. ST segment depression ≥1 mm after dobutamine and adenosine infusion occurred in 37 (31%) and 12 (10%) patients, respectively ($p <$

Figure 2. Actuarial event-free survival rate for patients with (n = 37) and without (n = 83) electrocardiographic ST segment depression ≥1 mm. The rate was significantly better for the patients without such ST depression. CI = confidence interval.

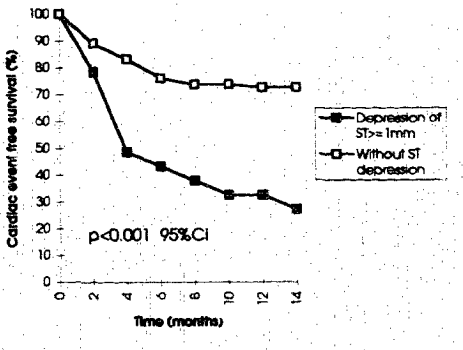


Table 4. Sensitivity, Specificity and Accuracy of Dobutamine and Adenosine Stress Echocardiography in the Detection of Coronary Artery Disease

	Sensitivity					
	Overall	1-VD	2-VD	3-VD	Specificity	Accuracy
Dobutamine	86.5% (77/89)	74% (14/19)	88% (22/25)	91% (41/45)	84% (26/31)	86% (103/120)
Adenosine	66.3% (59/89)	42% (8/19)	76% (19/25)	71% (32/45)	90% (28/31)	72.5% (87/120)
p value	< 0.001	0.227	0.124	< 0.01	< 0.001	< 0.001

Data in parentheses indicate number of patients. 1-VD, 2-VD, 3-VD = one-, two- and three-vessel disease, respectively.

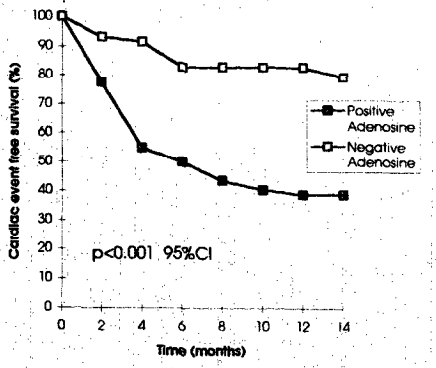
0.01). In nine patients ST segment depression ≥1 mm was detected in both tests; all nine patients had coronary artery disease on coronary arteriography. ST segment depression ≥1 mm was related both to cardiac events ($p < 0.05$) and to multivessel disease (11 of 70 vs. 1 of 50, $p < 0.05$). The development of chest pain (48% vs. 27%, $p < 0.05$) and discontinuation of the test (38% vs. 11%, $p < 0.01$) were more common in patients with cardiac events. The duration of adenosine infusion was also significantly less in patients with cardiac events.

The sensitivity, specificity and accuracy of the adenosine test are shown in Table 4. The sensitivity and accuracy of this test were statistically lower than those of the dobutamine test. The adenosine test presented the lowest sensitivity in patients with one-vessel disease.

Statistical analysis. Univariate analysis was applied to determine significant predictors of cardiac events from the outcome of dobutamine and adenosine testing. As shown in Table 1, clinical and investigative predictors were prior myocardial infarction, typical angina, the combination of smoking and hypertension, wall motion abnormalities at rest, and presence of multivessel disease on coronary arteriography. The univariate predictors of the dobutamine test (Table 2) were a positive test result, presence of chest pain, ST depression ≥1 mm, discontinuation of the test, presence of dyskinesia at least once during the test and presence of both new and worsening wall motion abnormalities during the test. The predictive variables of the adenosine test (Table 2) were a positive test result, presence of chest pain, ST depression ≥1 mm, discontinuation of the test and presence of worsening wall motion abnormalities at least once during performance of the test.

These univariate predictors were entered into multivariate stepwise analysis to detect independent predictors of cardiac events. These were for both tests: a positive test result (relative risk 7.3 for dobutamine and 3.0 for adenosine), presence of two- or three-vessel disease (relative risk 4.4) and discontinuation of the test (relative risk 3.1 for dobutamine and 2.1 for adenosine). In addition, ST depression ≥1 mm was an independent factor for dobutamine stress echocardiography only (relative risk 2.63). The best independent predictor was a positive dobutamine stress test result; patients with this finding were 7.3 times more likely to have a cardiac event than were patients with normal test findings.

Figure 3. Actuarial event-free survival rate for patients with positive (n = 62) and negative (n = 58) results of adenosine stress echocardiography. The rate was significantly better for the patients with negative echocardiographic findings. CI = confidence interval.



Discussion

Elderly people presenting with chest pain constitute a large group of hospital patients who need careful clinical assessment. Because many exhibit silent ischemia (21) and are unable to perform exercise tests (22), their investigation with pharmacologic tests is sometimes mandatory. In this study we used dobutamine and adenosine stress echocardiography to evaluate 120 consecutive patients ≥70 years old with suspected or known coronary artery disease.

Pharmacology of the agents used. Dobutamine is a predominantly beta-receptor agonist and induces myocardial ischemia in patients with coronary artery disease by increasing myocardial oxygen demand beyond that which can be met by the available coronary vasculature (15,23). Adenosine is a vasodilator stressor and was chosen for this study instead of dipyridamole because of its shorter half-life and more rapid action (24). Furthermore, no previous study had investigated the prognostic value of adenosine stress echocardiography in elderly patients.

Studies using adenosine (13,25,26) and dobutamine (12,27,28) echocardiography have suggested a high sensitivity and specificity for the detection of coronary artery disease. The prognostic value of dobutamine stress echocardiography (16,29–31) also has been investigated in many studies. However, these studies have not focused on the prognostic value of

these tests in the elderly, exception for the study of Poldermans et al. (15), which used the combination of dobutamine and atropine. In their study both sensitivity and specificity, as well as the predictive value of the tests, were proved satisfactory.

Comparison of the two tests: predictive value. Our observations in this cohort of patients indicate that dobutamine and adenosine echocardiographic stress tests are capable of identifying elderly patients with extensive (two or more vessels) coronary artery disease. In addition, the need to interrupt either test predicts the presence of severe coronary artery disease. Adenosine stress echocardiography demonstrated its lowest sensitivity in the presence of one-vessel disease. It was less sensitive but more specific than dobutamine stress echocardiography in detecting coronary stenoses. These results are similar to those reported previously (25,26) and indicate that both tests can detect the presence of coronary artery disease. Although adenosine—a vasodilator substance—would not be expected to increase cardiac work and, hence, the oxygen demands of the myocardium, the rate-pressure product increased significantly in our study patients during this test. Of course, dobutamine stress echocardiography proved more sensitive in detecting milder forms of coronary artery disease. Nevertheless, adenosine echocardiography should not be excluded from clinical applications, particularly in elderly patients, whenever the clinician does not have enough experience with, or does not wish to use, dobutamine stress echocardiography.

The positive and negative predictive value for foreseeing cardiac events was, respectively, 57% and 92% for dobutamine stress echocardiography and 61% and 79% for adenosine stress echocardiography. The predictive value of adenosine stress echocardiography has not been reported, but the positive predictive value of dobutamine stress echocardiography in the present study is similar to that previously described (15,16) for dobutamine echocardiography. Mazeika et al. (16) found a positive predictive value of 68%. In the same study, the negative predictive value was 77%, less than that in our series; however, Lalka et al. (31) and Poldermans et al. (29) reported, respectively, a negative predictive value of dobutamine stress echocardiography for perioperative events of 95% and 99%. The positive predictive value of positive findings on dobutamine or adenosine stress echocardiography is at least comparable to that of dipyridamole thallium scintigraphy (positive predictive value 27% to 58%, negative predictive value 82% to 100%) (32) for subsequent events and to that of adenosine thallium-201 single-photon emission computed tomography (positive predictive value 43%, negative predictive value 91%) (33) for postinfarction events. These results suggest that in many hospitals both dobutamine and adenosine stress echocardiography could be used as alternative tests for predicting cardiac events in unclear cases at a rather low cost. The dobutamine test was superior to that of adenosine.

Numerous studies have used a pharmacologic stress combined with echocardiography or thallium scintigraphy (34–36) to elicit myocardial ischemia and thus determine variables associated with an adverse outcome. Age has been reported (36) to be a significant predictor for cardiac events. By multivariate regression analysis of clinical and intravenous dobutamine stress echocardiographic data in patients undergoing major vascular surgery, age >70 years was a significant predictor of perioperative events. In the postoperative series of Poldermans et al. (29), nearly 60% of the patients having a postoperative cardiac complication, were >70 years of age. Similar results were reported by Eagle et al. (37). In another study (38), patients who had a cardiac event were significantly older (67 ± 10 years) than those who did not (64 ± 11 years) during a mean follow-up period of 21 months.

Baudhuin et al. (39) found that dobutamine stress echocardiography was safe in their elderly patients (mean 66 ± 5 years, range 60 to 78) with a sensitivity and specificity similar to those in their young patients (mean 40 ± 7 years, range 50 to 59).

Dobutamine stress echocardiography caused fewer minor adverse effects (headache, tremor, flushing, etc.) than did adenosine stress echocardiography, but the procedure lasted longer (24 vs. 6 min). However, the two tests were equally well tolerated. We found, as have others (40) that the development of hypotension with dobutamine infusion was not associated with an ischemic response. The percent of AV block recorded during adenosine infusion in the elderly was also similar to that reported by others (41). In our series, although subjective untoward effects were more frequent with adenosine infusion, more serious (and "objective") untoward effects (ECG irregularities and arrhythmias) were recorded with dobutamine stress echocardiography. These data indicate that these tests can be used as screening tests (dobutamine more so than adenosine) to help determine which of these elderly patients will need more detailed hemodynamic-angiographic investigations.

Predictive factors and patient classification. The presence of any dobutamine echocardiographic abnormality was the most powerful independent predictor of future cardiac events. Ninety-four percent of such events occurred in patients with a positive dobutamine stress test result in contrast to 86% in patients with two- or three-vessel disease and 76% in patients with a positive adenosine stress test result. Only 3 patients with a negative dobutamine stress test result, but 12 with a negative adenosine stress test result, had a cardiac event during the follow-up period. Mazeika et al. (16) reported a similarly low incidence of cardiac events in patients with negative dobutamine echocardiographic findings. Krivokapich et al. (17) reported that rest wall motion abnormalities were predictive of ischemic events, but Eichelberger et al. (30) found the opposite. Wall motion abnormalities at rest were present in 80 (67%) of our patients (41 with and 39 without cardiac events) and constituted a significant predictor only in patients with a history of myocardial infarction (26 of 50 vs. 18 of 70, $p < 0.01$). In the remaining patients (15 of 50 vs. 21 of 70, $p = 0.159$), because rest wall motion abnormalities do not necessarily reflect ischemia, it is reasonable to assume that their presence is not necessarily related to ischemic events.

The discontinuation of dobutamine or adenosine stress echocardiography (because of chest pain, ST depression

>1 mm or extensive wall motion abnormalities) was predictive of a 3.1 and 2.1 times greater risk for cardiac events, respectively. The only clinical univariate predictors were a history of myocardial infarction and presence of typical angina. Even though risk factors such as smoking, hypercholesterolemia, hypertension or diabetes mellitus did not predict cardiac events, the combination of smoking and hypertension was a significant predictive factor. The patients who had a cardiac event, even if results of dobutamine or adenosine stress echocardiography, or both, were negative, could be identified as a higher risk subset by using these clinical predictors. In our study, all patients could be classified in an intermediate risk group, because they had at least one clinical risk factor: age ≥70 years. The existence of other clinical entities (overt or hidden) could possibly classify the elderly in a significantly higher risk class and the presence of positive findings on dobutamine or adenosine stress echocardiography at the greatest risk subset. Furthermore, as a rule, revascularization was undertaken for persistent or worsening symptoms despite medical treatment.

Limitations of the study and clinical implications. One limitation of the present study, as of other similar studies, is the subjective, nonquantitative interpretation of echocardiographic images (16). However, the echocardiograms were always assessed by two investigators who had no knowledge of the clinical and angiographic data.

Our study demonstrates that dobutamine and adenosine stress echocardiography are safe and sensitive for diagnosing and stratifying elderly persons with suspected or known coronary artery disease. These persons already have an increased risk for cardiac events, even in the absence of prior myocardial infarction or typical angina. Their prognosis can be defined further with dobutamine or adenosine stress echocardiography. Abnormal findings on dobutamine stress echocardiography (relative risk 7.3) or adenosine stress echocardiography (relative risk 3.0) is an independent predictive factor for cardiac events and can identify those patients who are at greatest risk for adverse outcome. It is important for the clinical cardiologist to be able to classify elderly patients in risk level subgroups and to assess their further treatment with the use of a simple, safe, nonexpensive, noninvasive test.

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