

Dobutamine Stress Echocardiography in Patients With Stable Chronic Angina and a Low- or Medium-Risk on Exercise Testing: Usefulness for Assessing Long-Term Prognosis

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Introduction and objectives. The ability of stress echocardiography to provide prognostic information that supplements that obtainable from clinical data and exercise electrocardiography is still controversial. Our aim was to determine whether dobutamine stress echocardiography provides additional information on long-term prognosis after conventional exercise testing has indicated that a patient with chronic stable angina has a low or intermediate risk of a cardiac event.

Patients and method. The study included consecutive patients with stable angina who were not found to be at high risk on a previous exercise test. All patients underwent dobutamine stress echocardiography. The mean follow-up period was 4.5 ± 1.76 years. The single combined end-point was defined as death due to cardiac disease, nonfatal myocardial infarction, or hospitalization for unstable angina. Multivariate analysis was used to identify independent predictors of cardiac events.

Results. There were 24 (19%) cardiac events in the 124 participants: four deaths due to cardiac disease, 10 nonfatal myocardial infarctions, and 10 hospitalizations for unstable angina. Associations were found between a higher event rate during follow-up and previous myocardial infarction, Duke treadmill score, and the detection of regional wall motion abnormalities indicative of multivessel disease by stress echocardiography.

Conclusions. In patients with stable angina who have undergone an exercise test that indicates that they have a low or intermediate risk of cardiac events, dobutamine stress echocardiography provides additional prognostic information to that obtainable from clinical data and exercise testing.

Key words: *Stable angina. Prognosis. Exercise test. Stress echocardiography.*

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Ecocardiografía con dobutamina en pacientes con angina crónica estable y ergometría de riesgo bajo o intermedio: utilidad en la valoración del pronóstico a largo plazo*

Introducción y objetivos. La capacidad de la ecocardiografía de estrés para añadir información pronóstica a los datos clínicos y la prueba de esfuerzo convencional cuando ésta es valorable es motivo de debate. Nuestro objetivo fue evaluar si la ecocardiografía con dobutamina aporta información, tras la realización de una prueba de esfuerzo de riesgo bajo o intermedio, en la valoración del pronóstico a largo plazo de la angina estable.

Pacientes y método. Se realizó un ecocardiograma con dobutamina en una serie consecutiva de pacientes con angina estable en los que previamente se había efectuado una ergometría que no había mostrado criterios de alto riesgo. El tiempo de seguimiento medio fue de $4,5 \pm 1,76$ años. Se definió un único criterio de valoración compuesto por la incidencia de muerte cardíaca, infarto de miocardio no mortal u hospitalización por angina inestable. Se realizó un análisis multivariable para determinar los predictores independientes de sucesos.

Resultados. De los 124 pacientes incluidos, 24 (19%) presentaron algún suceso (4, muerte cardíaca; 10, infarto de miocardio no mortal, y 10, ingreso hospitalario por angina inestable). El antecedente de infarto de miocardio, la puntuación de Duke de la ergometría y la detección de anomalías de la contractilidad regional correspondientes a enfermedad multivascular mediante el ecocardiograma de estrés se asociaron con una mayor incidencia de acontecimientos en el seguimiento.

Conclusiones. En pacientes con angina estable clásica que realizan una prueba de esfuerzo de riesgo bajo o intermedio, la ecocardiografía con dobutamina ofrece información pronóstica adicional a la proporcionada por los datos clínicos y la prueba de esfuerzo.

Palabras clave: *Angina estable. Pronóstico. Prueba de esfuerzo. Ecocardiografía de estrés.*

ABBREVIATIONS

DSE: dobutamine stress echocardiography.
LVEF: left ventricular ejection fraction.
RWMS: regional wall motion score.
SBP: systolic blood pressure.

INTRODUCTION

Exercise testing is the most widely used technique for assessing prognosis of ischemic heart disease in patients who are able to withstand exercise and who have no substantial abnormalities in the resting electrocardiogram (ECG).^{1,2} It is assumed that the general population of patients with suspicion of ischemic heart disease and a low-risk exercise test result have a favorable prognosis.³⁻⁵ However, patients with classic chronic stable angina are at a high risk of coronary artery disease and, therefore, have a higher risk of adverse events than those with a lower pretest probability of coronary artery disease. Adverse events occur in the clinical course of certain patient populations with ischemic heart disease and at high clinical risk despite a low-risk exercise test result.⁶⁻⁸

Stress echocardiography is a useful tool for stratifying risk in coronary artery disease,⁹⁻¹² and is used without hesitation when exercise testing cannot be done or when the findings cannot be interpreted.^{1,2} However, it is still debated whether stress echocardiography can add prognostic information to that provided by an interpretable exercise test because very few prospective studies have been done that specifically address this question.^{1,13} Some experts have suggested that, in view of the prognostic value of myocardial perfusion studies,¹⁴ systematic use of imaging techniques for prognostic assessment of patients with an interpretable exercise test could be sufficient.¹ The prognostic value of different imaging techniques has been evaluated mainly in patients at an indeterminate risk of coronary artery disease and the imaging tests in such cases were done mainly for diagnostic reasons.

The objective of our study was to assess whether dobutamine stress echocardiography (DSE) could add information to that obtained after an exercise test result not indicative of high risk in a specific patient population with chronic stable angina and a high risk of coronary artery disease.

PATIENTS AND METHODS

Patient Selection

Patients who were diagnosed with chronic stable angina and who underwent exercise testing between

1998 and 1999 in our hospital were selected for assessment of prognosis. The study population comprised patients who did not meet the criteria for high risk in the exercise test and who underwent DSE according to a prospective study protocol.

All patients with chronic stable angina presented signs and symptoms of angina pectoris.¹ These signs and symptoms had not changed over the preceding 2 months. To ensure a high pretest probability of coronary artery disease, only women aged 60 years or over and men aged 40 years or over were included.¹ Patients with resting ECG abnormalities (left-bundle branch block, pacemaker, preexcitation, more than 1 mm baseline ST segment depression, or less than 1 mm baseline ST segment depression with digoxin treatment, or other indicators of left ventricular hypertrophy) that confound ECG interpretation for ischemia in the exercise test,⁵ patients with left ventricular systolic dysfunction (left ventricular ejection fraction [LVEF] <40%), and patients who had undergone prior revascularization were not included. Patients with findings indicative of high risk in exercise testing and identified as a group with poor prognosis as well as patients with atrial fibrillation were excluded from the study in order not to expose them to potential complications of DSE.

During the study period, exercise testing was done in 1754 patients in our hospital. Of these, 235 had been diagnosed with chronic stable angina with a high risk of coronary artery disease and were referred for prognostic assessment. Eighty-nine (38%) of the 235 patients had high-risk exercise test results. The remaining 146 patients with exercise-test findings indicative of low risk were considered for inclusion in the study. Eight patients refused to participate. A further 5 patients were excluded because they were poor candidates for echocardiography, 3 because of atrial fibrillation, and 2 because of left ventricular systolic dysfunction (LVEF<40%) in the resting echocardiogram. Finally, 4 patients were lost to follow-up. Therefore, the study population comprised of 124 patients (Figure 1).

In our patient population, DSE was done at a median of 4 days after exercise testing, with the same pharmacological treatment. All patients signed informed consent before inclusion in the study.

Exercise Testing

Symptoms-limited exercise testing was done on a treadmill according to the standard or modified Bruce protocol. The test was ended in the following cases: *a*) exhaustion or if the heart rate reached the maximum age-predicted heart rate (220 beats/min –age); *b*) clear decrease in systolic blood pressure (SBP) with progressive exercise, particularly in presence of other signs of ischemia, or a hypertensive response

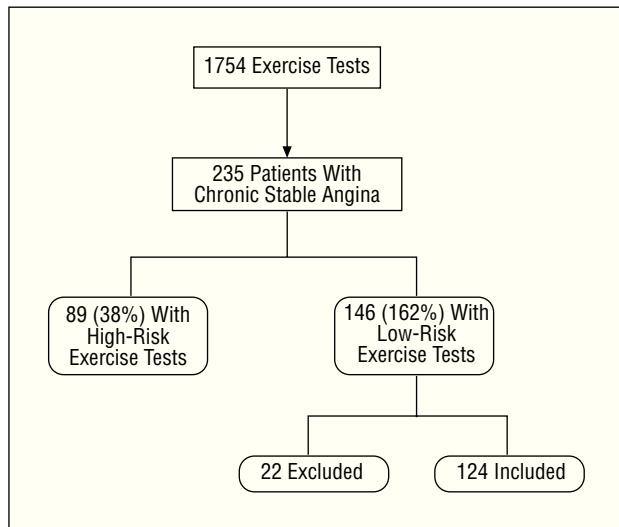


Figure 1. Selection of the 124 patients of the study population from patients who underwent exercise testing during the inclusion period.

(SPB>230 mm Hg or diastolic blood pressure >130 mm Hg); *c*) dizziness, intense dyspnea, severe claudication, or evidence of peripheral hypoperfusion; *d*) ventricular arrhythmias (frequent ventricular extrasystoles, multiform complexes, or bursts of 3 or more beats); *e*) technical problems with monitoring the ECG or blood pressure; *f*) severe angina pectoris; *g*) ST-segment depression of 3 or more mm; and *h*) at the request of the patient.

Positive findings in the exercise test were considered as an ST-segment depression of 1 mm or more or an ST-segment elevation of 1 mm or more at leads with no pathological Q wave (other than at the aVR lead), measured 80 ms from the J point. Reading of the deviation of the ST segment by the computerized unit of the exercise electrocardiogram was permitted. Readings were confirmed by an expert cardiologist.

The following were considered as high-risk exercise test results: *a*) positive response during the first 2 stages of the Bruce protocol; *b*) ST-segment depression of 1 mm or more at 5 or more leads or depression that persisted for 6 minutes or more in the recovery phase; *c*) ST-segment depression of 2 mm or more at any stage of exercise; *d*) ST-segment elevation at leads with no pathological Q waves (except at the aVR lead); *e*) sustained decrease in SBP during progressive exercise; *f*) ventricular tachycardia; *g*) Duke score below -10 , where the Duke score is calculated according to the following formula⁴:

Metabolic equivalents (MET) $-(5 \times \text{maximum net ST-segment deviation during or after exercise, in millimeters}) - (4 \times \text{angina index})$

The angina index was set to 0 if the patient had no angina during the test; 1 if the patient had angina that did not limit exercise; and 2 if the angina was the reason for stopping the test.

Dobutamine Stress Echocardiography

Dobutamine was administered initially at a dose of $10 \mu\text{g}/\text{kg}/\text{min}$ then increased by $10 \mu\text{g}/\text{kg}/\text{min}$ every 3 minutes until a dose of $40 \mu\text{g}/\text{kg}/\text{min}$ was reached. If the patient did not reach 85% of the age-predicted heart rate after dobutamine infusion, atropin was administered (up to a maximum of 1 mg) while dobutamine infusion continued at a dose of $40 \mu\text{g}/\text{kg}/\text{min}$. Digital images were acquired in the long parasternal-long and apical-short 4- and 2-chamber views. Regional wall motion was analyzed by determining the regional wall motion score (RWMS) with a model that divides the left ventricular myocardium into 16 segments and assigns a wall motion score of 1 to 4 to each segment (1 = normal or hyperkinetic; 4 = dyskinetic) in accordance with the recommendations of the American Society for Echocardiography.¹⁵ The RWMS was calculated by dividing the sum of scores for each segment by the number of segments analyzed.¹⁵ We considered that abnormal wall motion of the anterior septal, medial septal, apical, and anterior segments indicated disease of the left anterior descending coronary artery, whereas abnormal motion of the lateral and posterior segments indicated diseased circumflex artery, and abnormal motion of the inferior and basal septal segments indicated right coronary artery lesions.

The test was ended before completing the infusion regimen in the following cases: *a*) presence of clear regional wall motion abnormalities; *b*) decrease in absolute or relative SBP by more than 30 mm Hg; and *c*) any of the circumstances listed as criteria for ending the exercise test. The findings of the DSE were considered positive when regional wall motion of a normal or hyperkinetic segment deteriorated. Findings were not considered positive when an akinetic segment became dyskinetic unless wall motion had previously improved.¹⁶ The interpretation of the test was done by an expert echocardiographer who was blinded to the findings of exercise testing.

Patient Follow-up

The corresponding clinical cardiologist assessed the patients in outpatient clinics. Not more than 1 year was allowed between visits. If patients did not keep their appointment, follow-up was done by a telephone interview carried out by medical personnel. Mean follow-up time was 4.55 (1.76) years (lower quartile, 3.32 years; upper quartile, 5.9 years). A single endpoint was defined as time to any of the follow events:

cardiac death or admission to hospital for nonfatal myocardial infarction or unstable angina. If any of these events occurred, confirmation was obtained from the corresponding medical reports issued by the hospital or from review of the medical histories. Myocardial infarction during follow-up was defined as a typical elevation of biochemical markers of myocardial necrosis (creatinine kinase MB isoenzyme [CK-MB] and/or troponin) and at least one of the following conditions: symptoms of acute myocardial infarction, development of pathological Q waves in the ECG and/or ischemic changes of the ST segment or the T wave after a myocardial revascularization procedure. For a patient to be considered as having unstable angina during follow-up, clinical signs and symptoms compatible with at least one of the following conditions had to be present: ischemic changes in the ECG, known coronary artery disease, or a positive noninvasive finding. In patients with more than one event, only the most serious event was counted for the purposes of the analysis.

Statistical Analysis

Quantitative variables were expressed as mean (SD). Univariate comparisons between groups of continuous variables were done with the Student *t* test for unrelated samples or with the Mann-Whitney U test if the data were not normally distributed. Qualitative variables were presented as percentages and univariate comparison was done with the χ^2 test, applying the Fisher exact test when necessary. Kaplan-Meier curves were calculated to display the time to event. These curves were compared by a log-rank test. Multivariate analysis of event-free survival was done by Cox regression. Variables associated with events in the univariate analysis ($P < .05$) were included. The following variables were prospectively recorded: *a*) clinical: age, sex, smoking habit, hypertension, hypercholesterolemia, diabetes mellitus, and previous myocardial infarction; *b*) exercise test results: Duke score; and *c*) echocardiographic: DSE findings, RWMS at maximum dobutamine dose (peak RWMS), regional wall motion abnormalities corresponding to more than one vascular territory after dobutamine infusion. Previous myocardial infarction was defined as documented infarction of more than 3 months duration. Hypertension was recorded if diagnosed previously and treated pharmacologically. Hypercholesterolemia was taken to be total cholesterol level greater than 200 mg/dL or low-density lipoprotein cholesterol (LDL-C) greater than 130 mg/dL (or >100 mg/dL in patients with a history of myocardial infarction or coronary artery disease diagnosed in a previous angiographic examination). The inter-observer variability of the DSE findings was determined for a random sample of 30 patients and the presence of regional wall motion abnormalities sug-

gestive of multivessel disease was determined by calculating the kappa coefficient. Kappa values greater than 0.70 represented a good degree of agreement. Comparisons were considered significant if *P* values were less than .05.

RESULTS

Clinical Characteristics

The study population comprised 124 patients. Patients with low-risk exercise test results who were finally included had similar clinical characteristics and findings in the exercise test to the remaining 22 patients (Table 1).

Treatment for angina (either single or combined therapy) was not withdrawn from patients for the tests. At the time of exercise testing and DSE, 33 patients (27%) were taking nitrate treatment, 48 (39%) beta-blockers, and 33 (27%) calcium antagonists.

Exercise Test Results

The following mean values were reported from the exercise testing: *a*) peak exercise capacity, 8.6 ± 2.2 MET; *b*) maximum heart rate, 128 ± 23 beats/min; *c*) peak SBP, 169 ± 24 mm Hg; *d*) double product (heart rate \times SBP) $21\,855 \pm 5598$; and *e*) Duke score 4.17 ± 5 . Positive exercise tests were reported in 66 patients (53%). Twenty patients (16%) developed angina during exercise testing. In 11 (9%), both clinical and electrocardiographic findings were positive. The mean ST-segment depression was 0.79 ± 0.84 mm in the whole population and 1.523 ± 0.5 mm in patients with a positive exercise test. The Duke score was ≥ 5 in 66 (53%) and between 4 and -10 in 58 (47%) of the patients. A total of 55 (44%) patients exceeded 85% of the age-predicted maximum heart rate.

TABLE 1. Clinical Characteristics and Exercise Test Findings for 146 Patients With Low-Risk Exercise Test*

Patients Included (n=124)	Patients Excluded (n=22)	<i>P</i>	
Age, years†	1±9	62±10	NS
Men	99 (80%)	16 (73%)	NS
Smokers	31 (25%)	6 (27%)	NS
Hypertension	58 (47%)	11 (50%)	NS
Hypercholesterolemia	67 (54%)	12 (55%)	NS
Diabetes	20 (16%)	5 (23%)	NS
Previous infarction	23 (19%)	4 (18%)	NS
Positive exercise test	66 (53%)	13 (59%)	NS
Duke score†	4.17 (5)	4.3 (4)	NS

*NS indicates non significant.

†Mean±SD.

Findings of Dobutamine Stress Echocardiography

Atropin was given to 74 patients (60%) during DSE. The following mean values were reported: *a*) maximum heart rate, 126±23 beats/min; *b*) maximum SBP, 148±24 mm Hg; and *c*) maximum double-product (heart rate ×SBP) 18 915±4942. Resting echocardiographic RWMS was 1.08±0.15 and increased to 1.19±0.2 at peak stress. The findings of DSE were positive in 59 patients (46%). In 22 patients (18%), abnormalities in segment wall motion corresponding to more than 1 vascular territory were reported. No complications occurred during DSE.

Inter-observer agreement was good both for DSE findings (agreement of 94%; kappa =0.78) and for identification of regional wall motion abnormalities suggestive of multivessel disease (agreement of 88%; kappa =0.72).

In most patients (77%), exercise-test and DSE findings coincided (both tests were positive in 48 patients and both negative in 47). In 11 patients, the exercise test was negative but DSE findings were positive, whereas in 18 patients, the exercise test was positive but the DSE findings were negative.

Patient Follow-up

At least 1 adverse event was reported in 24 patients (19%). Four cardiac deaths (sudden death in 2 patients, fatal acute myocardial infarction in 1 patient, and early infarction after myocardial revascularization surgery in 1), 10 nonfatal myocardial infarctions, and 10 admissions to hospital for unstable angina were reported. The positive predictive values for exercise testing and DSE were 27% (18/66) and 35% (21/59), respectively. Negative predictive values for exercise testing and DSE were 89% (52/58) and 95% (62/65), respectively. The positive predictive value of exercise testing was 11% in patients with negative DSE findings (2/18), and 33% in those who also had positive DSE findings (16/48). The positive predictive value of DSE remained relatively high, even in patients with a negative exercise test (45% [5/11]). Table 2 shows the relationships between the different characteristics analyzed and the combined endpoint in the univariate analysis. In the multivariate analysis (Table 3), history of myocardial infarction, Duke score in the exercise test, and positive DSE with wall motion abnormalities suggestive of multivessel disease were independent predictors of adverse events.

DISCUSSION

Most information on the usefulness of exercise testing to assess patients with coronary artery disease comes from studies that included broad populations

TABLE 2. Univariate Association Between Adverse Events and Clinical Characteristics, Exercise Test Results, and Dobutamine Stress Echocardiography Findings*

	With Event (n=24)	Without Event (n=100)	P
Age, years†	65±6	61±10	NS
Men	19 (79%)	80 (80%)	NS
Smokers	8 (33%)	23 (23%)	NS
Hypertension	14 (58%)	44 (44%)	NS
Hypercholesterolemia	15 (62%)	52 (52%)	NS
Diabetes	8 (33%)	12 (12%)	.01
Previous infarction	9 (37%)	14 (14%)	.007
Positive exercise test	18 (75%)	48 (48%)	.017
Duke score‡	-0.29±5	5.25±4	.0001
Positive DSE	21 (87%)	38 (38%)	<.0001
Maximum RWMS†	1.43±0.23	1.13±0.17	.0008
DSE positive for multivessel disease	14 (58%)	8 (8%)	<.0001

*DSE indicates dobutamine stress echocardiography; RWMS, regional wall motion score; NS, not significant.

†Mean±SD.

TABLE 3. Independent Predictors of Events During Follow-up (Cox Analysis)*

	HR (95% CI)	P
Previous Infarction	2.71 (1.01-7.26)	.04
Duke Score	0.83 (0.75-0.91)	.0002
DSE positive for multivessel disease	3.63 (1.27-10.41)	.016

*DSE indicates dobutamine stress echocardiography; HR, hazard ratio; CI, confidence interval.

covering the entire range of ischemic heart disease.¹⁻⁴ In these studies, the variables measured during the exercise test showed predictive value regardless of the clinical findings. A favorable course is generally anticipated for patients who have low-risk findings in the exercise test. However, prognosis for patients with coronary artery disease is varied, and low-risk exercise test results may not necessarily imply favorable prognosis in certain groups of patient with coronary artery disease.⁶⁻⁸ Patients with chronic stable angina have a high risk of coronary artery disease and suffer a significant number of adverse events over extended follow-up.

Our patient population represents a selected subgroup, with no significant abnormalities in the resting ECG and no history of revascularization, a low incidence of prior myocardial infarction, and no substantial ventricular dysfunction. The aim of this selection was to obtain a population representative of patients with chronic stable angina for whom the benefit of exercise testing as an initial test for assessing prognosis was beyond question. The incidence of events in our population did not differ from that published in a

recent clinical study done in patients with chronic stable angina over a similar follow-up period.¹⁷

Our study further validated the Duke score^{3,4} as a means of stratifying prognosis in a population of patients with chronic ischemic heart disease. The incidence of serious events (death or nonfatal myocardial infarction) in our patients was as anticipated in a population of patients with coronary artery disease and low-intermediate risk in exercise testing.^{3,4}

Additional Prognostic Value of Dobutamine Stress Echocardiography

The most important finding of our study was the demonstration that DSE is useful for adding long-term prognostic information to that obtained from clinical variables and exercise testing in patients with stable angina. Particularly relevant for the clinical cardiologist is whether stress echocardiography adds to prognostic information from the clinical assessment and exercise testing—another widely used noninvasive test of proven value when interpretable. Few studies have specifically addressed this question. In particular, prospective studies of patients outside the acute phase of myocardial infarction are lacking. The prognostic value of the findings of DSE seems to be independent of exercise testing in patients with acute myocardial infarction, given that DSE has a similar negative predictive value and a greater positive predictive value than exercise testing.¹⁸

Some studies have compared the value of exercise testing with different forms of stress echocardiography, such as exercise echocardiography,¹² DSE,¹⁹ or dipyridamole echocardiography,²⁰ for stratifying risk in patients with known or suspected coronary artery disease after the acute phase of infarction. These studies included mainly patients at intermediate risk of coronary artery disease and most of them did not cal-

culate the Duke score from exercise testing. Use of risk stratification models based on different variables allows all the information provided by a given test to be integrated, thus improving the predictive value. In our study, the Duke score in exercise testing was an independent predictor of events, whereas a positive exercise-test result as an individual variable was not. If these types of validated model are not used in studies that compare the prognostic value of exercise testing with other techniques, the predictive value of exercise testing could be underestimated. In any case, the available data suggest the additional usefulness of different types of stress echocardiography. This may be because they can more accurately detect ischemia²¹ or, as indicated in our study, because stress echocardiography can provide information that cannot be obtained from exercise testing, such as the extent of ischemia (Figure 2). However, we should emphasize that the design of the present study, in which the population was selected according to the results of the exercise testing, does not allow direct comparison between the 2 techniques. In contrast, the study was designed to assess the additional information that can be obtained from DSE rather than investigate whether this technique was better than conventional exercise testing. We found that, although exercise testing and DSE had a similar predictive value, the positive predictive value of exercise testing decreased when DSE findings were negative, and the positive predictive value of DSE remained relatively high, even when the exercise test was negative.

We have been unable to find any studies like ours that have prospectively assessed the additional information provided by DSE for assessing long-term prognosis in patients with chronic stable angina and interpretable conventional exercise testing. Nevertheless, our findings agree with 2 recent studies that show that exercise echocardiography offers additional prognostic information to that obtained from conventional exer-

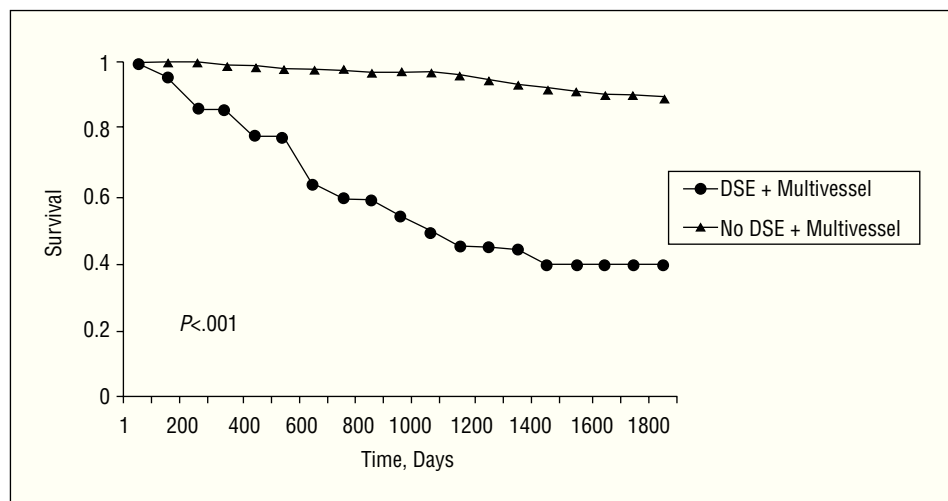


Figure 2. Kaplan-Meier event-free survival curves for patients with or without positive findings in dobutamine stress echocardiography suggestive of multivessel disease (DSE + multivessel).

cise testing when risk is stratified according to the Duke score in patients with chronic stable ischemic heart disease,¹³ or in patients with classic angina pectoris.²² Marwick et al,¹³ in a study of a heterogeneous population of patients with documented or suspected coronary artery disease, showed that the findings of exercise echocardiography offer additional prognostic information to clinical findings, the Duke score, or ventricular function at rest. The authors found that exercise echocardiography could be particularly useful in patients with a Duke score indicative of intermediate risk. More recently, a study has been published on the prognostic value of exercise echocardiography in a population of patients similar to ours with classic angina pectoris.²² The authors used a multivariate analysis showing the independent predictive value of regional wall motion abnormalities suggestive of multivessel disease to demonstrate the usefulness of exercise echocardiography. We used dobutamine because our echocardiography laboratory was most familiar with this stress technique, and it was the most widely used stress technique in many other laboratories,²³ at the time when study was initiated. Hospitals with capacity and experience in exercise echocardiography may find that this technique is the most appropriate form of stress echocardiography in patients able to withstand the required physical exertion.

Clinical Implications

Our findings do not question the use of conventional exercise testing as an initial noninvasive test to assess prognosis in selected patients with chronic stable angina who can withstand exercise. It is advisable to carry out a coronary angiogram in patients with a high-risk exercise test. If the findings of the exercise test are not high risk, DSE adds prognostic information that complements the findings of the clinical examination and exercise testing. This information may contribute to clinical decisions. Therefore, we propose that DSE be done in selected patients with chronic stable angina and at a high risk of coronary artery disease with low-risk or intermediate-risk exercise test results. If DSE findings are negative, prognosis will generally be favorable, and systematic coronary angiography may not be justified. In contrast, if DSE is positive, in particular with wall motion abnormalities suggestive of multivessel disease, coronary angiography should be considered and revascularization should be done if necessary.

CONCLUSIONS

A history of myocardial infarction, Duke score from the exercise test, and regional wall motion abnormalities indicative of multivessel disease during DSE are independently predictive of adverse events in the long-

term in selected patients with chronic stable angina and low or intermediate risk in the exercise test. Therefore, DSE adds prognostic information to that provided by clinical findings and exercise testing in this group of patients.

REFERENCES

- Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS, et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to update the 1999 Guidelines for the Management of Patients With Chronic Stable Angina). 2002. Available from: www.acc.org/clinical/guidelines/stable/stable.pdf
- Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina). 2002. Available from: www.acc.org/clinical/guidelines/unstable/unstable.pdf
- Mark DB, Hlatky MA, Harrell FE Jr, Lee KL, Califf RM, Pryor DB. Exercise treadmill score for predicting prognosis in coronary artery disease. *Ann Intern Med.* 1987;106:793-800.
- Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR, et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. *N Engl J Med.* 1991;325:849-53.
- Gibbons RJ, Baladi GJ, Bricker JT, Chaitman BR, Fletcher GF. ACC/AHA Guideline Update for Exercise Testing. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on exercise testing). 2002. American College of Cardiology Web site. Available from: www.acc.org/clinical/guidelines/exercise/dirIndexx.htm
- Moreno R, López de Sá E, López Sendón JL, Ortega A, Fernández MJ, Fernández-Bobadilla J, et al. Prognosis of medically stabilized unstable angina pectoris with a negative exercise test. *Am J Cardiol.* 1998;82:662-5.
- Castillo, JA, Florenciano R, Molina E, Jiménez M, García P, Egea S, et al. Prueba de esfuerzo de bajo riesgo en pacientes con angina inestable: ¿implica un pronóstico favorable? *Rev Esp Cardiol.* 2000;53:783-90.
- Säfstrom K, Lindahl B, Swahn E, and the FRISC-Study group. Risk stratification in unstable coronary artery disease. Exercise test and troponin T from a gender perspective. *J Am Coll Cardiol.* 2000;35:1791-800.
- Chuah S, Pelliikka PA, Roger VL, McCully RB, Seward JB. Role of dobutamine stress echocardiography in predicting outcome in 860 patients with known or suspected coronary artery disease. *Circulation.* 1998;97:1474-80.
- Krivokapich J, Child JS, Walter DO, Garfinkel A. Prognostic value of dobutamine stress echocardiography in predicting cardiac events in patients with known or suspected coronary artery disease. *J Am Coll Cardiol.* 1999;33:708-16.
- Pingitore A, Picano E, Varga A, Gigli G, Cortigiani L, Previtali M, et al. Prognostic value of pharmacological stress echocardiography in patients with known or suspected coronary artery disease. *J Am Coll Cardiol.* 1999;34:1769-77.
- Marwick TH, Mehta R, Arheart K, Lauer MS. Use of exercise echocardiography for prognostic evaluation of patients with known or suspected coronary artery disease. *J Am Coll Cardiol.* 1997;30:83-90.

13. Marwick TH, Case C, Vasey C, Allen S, Short L, Thomas JD. Prediction of mortality by exercise echocardiography. A strategy for combination with the Duke treadmill score. *Circulation*. 2001; 103:2566-71.
14. Hachamovitch R, Berman DS, Kiat H, Cohen I, Cabico JA, Friedman J, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. *Circulation*. 1996;93: 905-14.
15. Schiller NB, Shah PM, Crawford M, DeMaría A, Devereux R, Feigenbaum H, et al. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr*. 1989;2:358-67.
16. Arnese M, Fioretti PM, Cornel JH, Postma-Tjoa J, Reijts AE, Rolandt JR. Akinesis becoming diskinesis during high-dose dobutamine stress echocardiography: a marker of myocardial ischemia or a mechanical phenomenon? *Am J Cardiol*. 1994;73:896-9.
17. Poole-Wilson PA, Lubsen J, Kirwan BA, Van Dalen FJ, Wagener G, Danchin N, et al. Effect of long-acting nifedipine on mortality and cardiovascular morbidity in patients with stable angina requiring treatment (ACTION trial): randomised controlled trial. *Lancet*. 2004;364:849-57.
18. Greco CA, Salustri A, Secaareccia F, Ciavatti M, Biferali F, Val-torta C, et al. Prognostic value of dobutamine echocardiography early after uncomplicated acute myocardial infarction: a comparison with exercise electrocardiography. *J Am Coll Cardiol*. 1997;29:261-7.
19. Sitges M, Azqueta M, Paré C, Magriñá J, Miranda-Guardiola F, Velamazán M, et al. Dobutamine stress echocardiography and exercise electrocardiography for risk stratification in medically treated unstable angina. *J Am Soc Echocardiogr*. 2000;13:1084-90.
20. Severi S, Picano E, Michelassi C, Lattanzi F, Landi P, Distanto A, et al. Diagnostic and prognostic value of dipyridamole echocardiography in patients with suspected coronary artery disease: comparison with exercise electrocardiography. *Circulation*. 1994;89:1160-73.
21. San Román JA, Vilacosta I, Castillo JA, Rollán MJ, Hernández M, Peral V, et al. Dipyridamole and dobutamine-atropine stress echocardiography in the diagnosis of coronary artery disease. Comparison with exercise stress test, analysis of agreement and impact of antianginal treatment. *Chest*. 1996;110:1248-54.
22. Elhendy A, Mahoney DW, Burger KN, MCCully RB, Pellikka PA. Prognostic value of exercise echocardiography in patients with classic angina pectoris. *Am J Cardiol*. 2004;94:559-63.
23. Acquatella H. Ecocardiografía de estrés en Latinoamérica. Revisión de cinco años (1997-2002). *Rev Esp Cardiol*. 2003;56 Supl 1:21-8.