Exercise Echocardiography for the Evaluation of Patients After Nonsurgical Coronary Artery Revascularization

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Objectives. The purpose of this study was to demonstrate the accuracy of stress echocardiography for detecting the progression of coronary artery disease after nonsurgical revascularization.

Background. The expanding role of nonsurgical coronary revascularization procedures mandates the development of sensitive noninvasive techniques for the detection of recurrent ischemia.

Methods. Bicycle stress echocardiography was performed in a series of 86 patients 6.5 ± 1.3 months after a revascularization procedure. Seven patients were excluded from analysis because of poor echocardiographic image quality.

Results. Digital analysis achieved a sensitivity of 83% for the entire group and a specificity of 85% for stress echocardiographic detection of significant coronary artery disease. Sensitivity was greater in patients with (88%) than in those without (75%) prior myocardial infarction, but this difference did not reach statistical significance. Additional analysis using an increase in end-systolic volume index or a decrease in ejection fraction during stress as an additional marker for ischemia tended to enhance sensitivity (90% for the entire group and 93% for the subgroup with prior myocardial infarction).

Conclusions. Stress echocardiography is a useful and sensitive method for the follow-up of patients undergoing nonsurgical revascularization procedures. The addition of volume determination to routine wall motion analysis may be helpful in patients with prior infarction who have scar tissue that may be difficult to distinguish from an adjacent exercise-induced wall motion abnormality.

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Since its introduction into clinical practice 14 years ago, the role of percutaneous transluminal coronary angioplasty in the management of patients with coronary artery disease has continued to expand. Recently introduced alternative or additional procedures include high frequency rotational ablation, atherectomy, laser angioplasty and coronary stenting (1–5). Despite a relatively high early success rate, restenosis remains a major limitation of these techniques (6–9). The reported restenosis rate for coronary angioplasty alone is approximately 25% to 30%. When combined with mechanical recanalization of completely occluded vessels, restenosis rates as high as 50% have been reported (10).

The detection of restenosis is a major challenge. Routine coronary angiography is not feasible in most situations. The sensitivity of stress electrocardiography is limited, especially in patients with less severe or extensive disease and those taking antianginal medication (11,12). Thallium-201 scintigraphy provides a higher sensitivity. Recent reports (13–15) based on pooled data suggest a sensitivity for the detection of coronary artery disease of 84% to 88%. However, the application of thallium-201 scintigraphy specifically to detect restenosis is less well established (16–18).

Single-photon emission computed tomography may be superior to planar thallium scintigraphy. Some investigators (19,20) have reported a sensitivity >90% for the detection of coronary artery disease. Iskandrian et al. (21) reported an overall sensitivity of 88% for detecting of coronary disease, in a larger series of patients when assessing single-vessel disease, sensitivity was significantly less (74%). However, disadvantages of thallium-201 scintigraphy include cost and radiation exposure, which limit the serial use of this technique.

Stress echocardiography is an alternative method for detecting, exercise-induced ischemia. This technique relies on the ability of two-dimensional echocardiography to record regional left ventricular wall motion and thickening before, during and after exercise. Decreased myocardial thickening or endocardial excursion, or both, during and after exercise is a relatively specific marker for induced ischemia. Stress echocardiography is superior to routine stress electrocardiography for the detection of coronary artery disease and may permit an assessment of the extent and location of coronary stenoses (22–28).

The purpose of this study was to assess the sensitivity and specificity of stress echocardiography for the detection of restenosis and the presence of additional coronary artery

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Table 1. Clinical, Angiographic and Revascularization Data for the 79 Study Patients

	No. of Patients
Male/female ratio	58/21
Extent of coronary disease	
Single-vessel	32
Two-vessel	17
Three-vessel	2
No stenosis >50%	28
Location of myocardial infarction	
Anterior	29
Inferior	17
Lateral	4
Procedure	
PTCA only	50
PTCA + Stenting	8
PTCR + PTCA	15
Rota	6

PTCA = percutaneous transluminal coronary angioplasty; PTCR = percutaneous mechanical recanalization of complete occluded vessels; Rota = high frequency rotational ablation.

lesions in patients after nonsurgical revascularization procedures.

Methods

Study patients. Eighty-six patients who underwent nonsurgical coronary revascularization at the Second Medical Clinic of Johannes Gutenberg University in 1990 and 1991 were included in the study. After coronary revascularization, all patients routinely underwent coronary angiography as a part of ongoing research protocols regardless of symptoms or the results of other diagnostic tests. A random subgroup of these patients also underwent stress echocardiography and formed the study group. Seven patients had technically inadequate echocardiograms and were eliminated from the study, leaving 79 patients (92%) available for analysis. There were 21 women and 58 men with a mean age of 56.6 ± 8.3 years. Fifty patients (63%) had a history of previous myocardial infarction. Antianginal medication included calcium channel antagonists in 48 patients, long-acting nitrates in 33 and beta-adrenergic blocking agents in 21. The interval between revascularization and stress echocardiography was 6.5 ± 1.3 months. Interventional procedures included the following: coronary angioplasty in 50, high frequency rotational ablation in 6, mechanical recanalization of a completely occluded vessel with additional angioplasty in 15 and Palmaz-Schatz stent implantation in 8. Details of the patient characteristics are given in Table 1.

All medications were continued on the day of the stress test. Patients underwent coronary angiography within 1 to 4 days of stress testing as a part of the routine postrevascularization evaluation.

Exercise echocardiography. Exercise was performed in a semisupine position with a bicycle ergometer (Ergometrics 900LR, Ergoline Vertriebsgesellschaft mbH), beginning at a work load of 50 W and increasing by 20 W each minute. Two-dimensional echocardiography was performed with commercially available phased array or mechanical sector scanners. The transducer frequency was either 2.5 or 3.75 MHz. The four- and the two-chamber views were continuously recorded from the apical window. Blood pressure and heart rate were monitored continuously and recorded every minute. The exercise test was symptom limited or discontinued at the discretion of the physician at one of the following end points: 85% of age-predicted maximal heart rate, exceeding blood pressure limits (250 mm Hg systolic, 120 mm Hg diastolic blood pressure). A 12-lead electrocardiogram (ECG) was recorded with modified placement of leads V_5 and V_6. Exercise ECGs were interpreted as positive if there was ≥1.5-mm flat or downsloping ST segment depression 60 ms after the J point in absence of baseline ST segment changes or digitalis medication, or both.

Angiographic procedure. Coronary angiography was performed with the Judkins technique. Coronary angiographic data were analyzed by experienced observers who had no knowledge of the stress echocardiographic results. Restenosis was defined as >50% decrease in lumen diameter compared with the initial postinterventional result. Other lesions were also assessed and considered to be significant if lumen narrowing was >50% compared with a normal segment of artery immediately proximal to the lesion. Patients with restenosis of the instrumented artery or significant stenoses in other vessels, or both, made up group A. Those without angiographic evidence of restenosis or other lesions were included in group B.

Echocardiographic analysis. All exercise assessments were made during peak exercise. Analysis of the echocardiographic recordings was performed after off-line digitization of images using a commercially available computer system (Hellige EchoCom). Images were digitized in a quad screen format. Rest and peak exercise four- and two-chamber views were simultaneously displayed on the screen. An ischemic response was defined as 1) development of a new wall motion abnormality during exercise in a region that was normal at baseline study, or 2) exercise-induced extension of dyssynergy to previously normal segments adjacent to a wall motion abnormality at rest. In addition, end-diastolic and end-systolic volumes were calculated by the area-length method and normalized for body surface area. Ejection fraction was defined as End-diastolic volume − End-systolic volume/End-diastolic volume × 100% (29).

The criteria for a positive test result included 1) an ischemic wall motion response, as defined previously; 2) an increase in end-systolic volume index; or 3) a decrease in ejection fraction. Semiquantitative wall motion analysis was performed in 12 segments using a wall motion scoring index, according to the guidelines proposed by the American Society of Echocardiography (30).

Table 2. Results of Bicycle Exercise Testing

Maximal work load (W)	138 ± 35
Maximal HR (beats/min)	135 ± 16
Peak HR >85% maximum	27
Peak HR <85% maximum	52
Mean SBP at peak exercise (mm Hg)	191 ± 25
Mean DBP at peak exercise (mm Hg)	101 ± 10
Angina	30

Data are expressed as mean value ± SD or number of patients. DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure.

Table 3. Follow-Up Coronary Angiographic Results in Relation to Revascularization Procedure

Procedure	Restenosis	New Stenosis	Both New and Restenosis	No Stenosis	Total
PTCA	11	16	4	19	50
PTCA + stent	0	3	0	5	8
PTCR + PTCA	5	4	1	5	15
Rota	1	2	2	1	6
Total	17	25	7	30	79

Data are expressed as number of patients. Abbreviations as in Table 1.

Statistics. For the stress echocardiographic results, sensitivity, specificity and positive predictive value were calculated. Differences in these values between subgroups were tested by the Fisher exact test. These variables were determined for the entire cohort of patients and separately for those patients with and without prior myocardial infarction. Volume and ejection fraction data are presented as mean value ± SD. To compare differences between two groups, analysis of variance was used and a value of $p < 0.05$ was considered significant.

Results

The peak exercise work load was 138 ± 35 W and the maximal heart rate 135 ± 16 beats/min (Table 2). Coronary angiography demonstrated restenosis in 24 patients (32%) (Table 3). Lesions at other locations were present in 32 (40%) of the patients. Seven patients had both restenosis and new lesions. The restenosis rate for each of the different types of revascularization and the frequency of development of new lesions are presented in Table 3. The sensitivity of the stress ECG for detection of coronary artery lesions was 42% for the entire group.

Wall motion analysis (Table 4). Overall, the sensitivity of stress echocardiography for detecting significant coronary artery disease was 83% and the specificity 85%. Of 50 patients with prior myocardial infarction, 29 developed extension of a preexisting wall motion abnormality or an induced wall motion abnormality in another region. In these patients, stress echocardiography had a sensitivity of 88% and a specificity of 81%. Fourteen patients with normal wall motion at rest exhibited stress-induced wall motion abnormalities (sensitivity 75%, specificity 91%). These differences between the groups with and without a prior infarction were not statistically significant.

Volumetric findings. Because exercise images were inadequate for volumetric analyses in 19% of patients, these analyses were performed in only 64 patients (39 in group A and 25 in group B). The end-diastolic volume index did not change significantly between rest and exercise and there was no significant difference between the exercise values for end-diastolic volume index when comparing the groups with (group A) and without (group B) angiographic evidence of restenosis or other lesions (Fig. 1). The end-systolic volume index increased from rest to exercise in group A (25.1 ± 9.9 vs. 30.1 ± 13.3 ml/m^2 body surface area, $p < 0.05$) and decreased in group B (26.2 ± 11.8 vs. 18.7 ± 10.3 ml/m^2, $p < 0.05$) (Fig. 2). Ejection fraction decreased in group A from 62 ± 11% to 56 ± 12.6% ($p < 0.05$) and increased in group B from 60.8 ± 14% to 70 ± 11.3% ($p < 0.05$) (Fig. 3).

Either a new wall motion abnormality or an increase in end-systolic volume index identified 52 patients with coronary artery stenosis (sensitivity 90%). Considering the combination of a wall motion abnormality with the change in ejection fraction also led to an enhancement in sensitivity but to a lesser extent than with end-systolic volume index (p = NS) (Table 4).

Wall motion scores increased in group A from 1.22 ± 0.3 at rest to 1.57 ± 0.5 during exercise ($p < 0.01$). There was no change in the scores from baseline to exercise in group B.

Discussion

Stress echocardiography is a feasible, cost-effective and safe diagnostic tool that is enjoying increasing utilization in several clinical situations. With the use of different forms of physical exercise, sensitivity values of 66% to 100% and specificity values of 69% to 100% have been reported (31–34). Analysis of only postexercise images lowers the sensitivity, especially in single-vessel disease, compared with imaging during peak stress (35). The value of stress echocardiography after nonsurgical revascularization procedures has not been documented in large patient groups.

In the current study, we demonstrated that stress echocardiography is a useful method for detecting restenosis or progression of known coronary disease in patients after nonsurgical revascularization procedures. The study cohort represented a randomized series and was not selected by recurrent symptoms, positive stress ECG or other diagnostic tests. Using digital imaging techniques, the success rate in obtaining images that could be evaluated was 92%, which is comparable with the findings reported by other investigators (26,32).

All patients with false negative results failed to achieve the target heart rate at peak exercise. Another factor that may have affected the sensitivity was the high frequency of single-vessel disease in our study group (Table 1). The

Table 4. Stress Echocardiographic Results

	All Patients			With Prior MI			Without Prior MI		
Criteria for a Positive Test Result	Sens (%)	Spec (%)	+PV (%)	Sens (%)	Spec (%)	+PV (%)	Sens (%)	Spec (%)	+PV (%)
WMA only	83	85	91	88	81	90	75	91	92
EF decrease only	71	80	85	77	73	83			
ESVI increase only	73	84	88	77	81	86			
WMA + EF decrease	87	71	84	90	70	83			
WMA + ESVI increase	90	75	86	93	70	84			
	Single-vessel disease								
WMA only	87	85							

EF = ejection fraction; ESVI = end-systolic volume index; MI = myocardial infarction; +PV = positive predictive value; Sens = sensitivity; Spec = specificity; WMA = new stress-induced wall motion abnormality.

sensitivity of stress echocardiography increases with the severity of coronary artery disease, perhaps because stress-induced wall motion abnormalities persist longer and are easier to detect in patients with multivessel disease (36).

As reported previously by us and others (31,37), a decrease in end-systolic volume and an increase in ejection fraction during stress occur in healthy persons. The absence of these changes is a pathologic response. In addition to qualitative wall motion analysis, we have shown a typical pattern of end-systolic volume behavior characterized by an increase in volume in the majority of patients in group A and a decrease in group B. Ejection fraction also decreased in most patients in group A and increased in group P. When using end-systolic volume in addition to the visual analysis of wall motion, sensitivity for the detection of significant coronary artery disease tended to increase from 83% to 90% in the entire group and from 88% to 93% in the subgroup with prior infarction. Because of the small number of patients with normal wall motion at rest but an abnormal exercise response of end-systolic volume and ejection fraction, these improvements in sensitivity were not significant.

There are few published data evaluating the utility of bicycle stress echocardiography after coronary angioplasty. In a few preliminary studies (38,39), the results varied considerably. A larger series addressing this question has not yet been published. Hoffmann et al. (40) used the transesophageal approach with rapid pacing over a special probe. They reported a sensitivity of 72% and specificity of 50% for detecting significant coronary artery disease, defined as >70% lumen narrowing.

The changes in end-systolic volume observed in our study are consistent with those seen with radionuclide ventriculography and constitute a standard sign of myocardial ischemia (41–44). In 41 patients, DePuey et al. (41) found a stress-induced decrease in ejection fraction when significant restenosis was present. Seventy-three percent of the patients with minimal residual coronary lesions (<20% lumen reduction) had an increase in ejection fraction during stress. O'Keefe et al. (45) performed radionuclide ventriculography 4 weeks after coronary angioplasty. Changes in end-systolic volume during exercise were highly specific but insensitive for predicting the development of restenosis. As in our study, these investigators (45) reported a significant decrease in ejection fraction in the group with restenosis.

Hecht et al. (16) studied 116 patients 6.4 ± 3.1 months after coronary angioplasty, using tomographic thallium-201

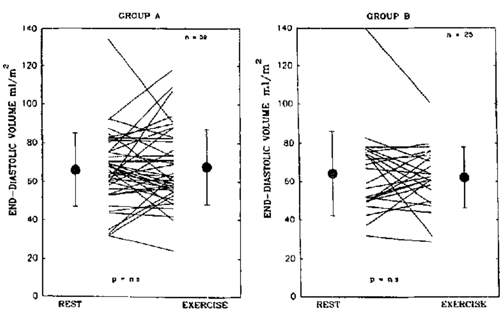

Figure 1. End-diastolic volume at rest and at peak exercise in 39 patients with (group A) and 25 patients without (group B) angiographic evidence of stenosis or other lesions.

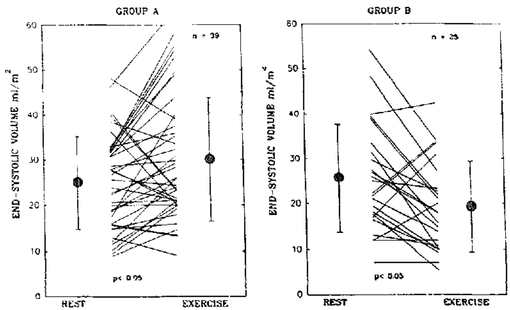

Figure 2. End-systolic volume at rest and at peak exercise in groups A and B.

scintigraphy. They reported a sensitivity of 93% and a specificity of 77%. However, 50% of their patients had multivessel disease and the patients were selected for study on the basis of recurrent angina pectoris or an abnormal stress ECG.

Breisblatt et al. (17) found a high incidence of false positive results when thallium-201 scintigraphy was performed 4 to 6 weeks after coronary angioplasty. A higher predictive value was obtained when the exercise test was performed 3 to 6 months after angioplasty.

The high frequency of single-vessel disease in our study group as well as the failure of most patients to achieve their target heart rate might account for the poor sensitivity of the stress ECG. This finding has been reported by others (11,12).

Limitations. The study did not specifically detect restenosis but rather a progression in the degree of coronary artery disease as an aid in determining the need for further diagnostic and therapeutic procedures.

Angiographic results were evaluated qualitatively. Quantitative angiography may be preferable for determining the degree of restenosis after nonsurgical revascularization procedures and may enhance the accuracy of future studies. Despite the use of digital image processing, echocardiographic assessment was not possible in some patients because of poor image quality. In our study, seven patients were excluded because of poor echocardiographic images at rest or during exercise.

The enhancement of sensitivity by calculation of end-systolic volume is limited by the fact that not every exercise cycle allows accurate tracing of endocardial contours. In this study, only 81% of the exercise images were adequate for volume determination.

Clinical implications. Stress echocardiography may be a useful tool for evaluating patients after nonoperative revascularization procedures. The sensitivity in our study was greater in patients with than in those without previous

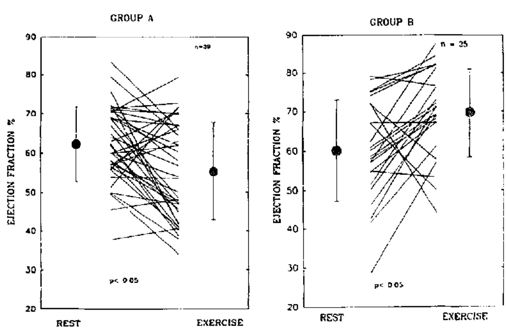

Figure 3. Ejection fraction at rest and at peak exercise.

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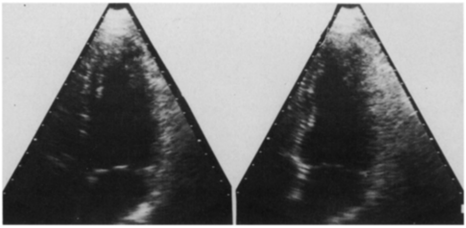

Figure 4. End-systolic contours in a patient with restenosis of the proximal left anterior descending coronary artery with normal wall motion at rest (**left**) and hypokinesia of the mid- and apical septum during exercise (**right**).

myocardial infarction, but this finding is limited by the small number of patients with significant restenosis but no prior myocardial infarction and did not reach statistical significance.

Exercise-induced wall motion abnormalities in patients with normal wall motion at rest were highly specific for significant coronary artery disease. Sensitivity seems to improve when end-systolic volume data are added to the analysis as a second criterion. Despite this, the increase was not significant because of the small number of patients with no difference in rest and stress wall motion but an increase in end-systolic volume. This additional variable might be a sign of residual ischemia in prior myocardial infarction and should be evaluated in a larger series of patients. Further diagnostic evaluation may not be necessary in asymptomatic patients with normal findings on a stress echocardiogram.

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