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Dobutamine-Induced Wall Motion Abnormalities: Correlations With Myocardial Fractional Flow Reserve and Quantitative Coronary Angiography

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Objectives. **This study evaluated both the relation between dobutamine-induced wall motion abnormalities and the physiologic and morphologic features of epicardial coronary artery stenoses and the impact of the extent of the area at risk on the sensitivity of dobutamine echocardiography.**

Background. **The accuracy of dobutamine echocardiography has traditionally been assessed by comparing results with stenosis geometry. Myocardial fractional flow reserve is a functional index of coronary stenosis severity that takes into account both anterograde and collateral flow and may therefore be a more appropriate standard for comparison.**

Methods. **Seventy-five patients with normal left ventricular function, good echocardiographic images and an isolated coronary stenosis underwent, within 6 h, dobutamine echocardiography, quantitative coronary angiography and intracoronary pressure measurements. Myocardial fractional flow reserve was calculated as the ratio of mean hyperemic distal coronary to aortic pressure.**

Results. **The degree of dobutamine-induced dyssynergy correlated significantly with percent diameter stenosis (r = 0.68), area stenosis (r = 0.68) and minimal lumen diameter (r = −0.60) and markedly better with myocardial fractional flow reserve (r = −0.77). However, marked dispersion of the individual data was observed. The sensitivity of dobutamine echocardiography in detecting lesions with a minimal lumen diameter ≤1 mm and diameter stenosis ≥50% was 83% and 80%, respectively. All but one patient with a myocardial fractional flow reserve >0.75 had a normal stress test result. Among patients with a myocardial fractional flow reserve ≤0.75, the sensitivity of dobutamine echocardiography was significantly lower for lesions in vessels with a reference diameter ≤2.6 mm than for lesions in larger vessels (58% vs. 90%, p = 0.008).**

Conclusions. **1) The magnitude of wall motion abnormalities induced by dobutamine infusion correlates with angiographic and, more closely, with functional indexes of stenosis severity, even though a wide scatter is observed. 2) In patients with a functionally significant stenosis, the amount of myocardium at risk is a critical determinant of the accuracy of dobutamine echocardiography.**

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Dobutamine echocardiography is an established method for the detection and risk stratification of coronary artery disease (1–6). The likelihood that a wall motion abnormality will develop during dobutamine stress testing is related to the severity of the stenosis and to the presence of collateral circulation. In many previous reports, the results of dobutamine echocardiography were compared with the results of visual interpretation of coronary angiograms, although such interpretation has high intraobserver and interobserver variability and poorly predicts the functional significance of obstructive coronary artery disease (7). In contrast, quantitative coronary angiography has been shown (8–10) to allow functional assessment of coronary stenoses. Yet even the more sophisticated quantification of lesion geometry does not account for the contribution of collateral circulation to myocardial blood flow. Recently, the concept of myocardial fractional flow reserve was introduced (11) to assess the functional significance of coronary stenoses. This index is defined as maximal myocardial blood flow expressed as a percent of its normal value. It can be calculated from coronary pressure measurements during maximal hyperemia and takes into account both anterograde and collateral contribution to maximal myocardial flow. The relation of dobutamine echocardiography to this functional index has not yet been studied.

The dual purposes of the present study were 1) to investigate the relation between dobutamine-induced wall motion abnormalities and functional and morphologic assessment of coronary artery stenoses, and 2) to study the influence of the extent of the area at risk on the sensitivity of dobutamine echocardiography in detecting significant coronary stenoses.

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Methods

Patients. Seventy-five patients with isolated single-vessel coronary artery disease, without left ventricular hypertrophy and with normal left ventricular systolic function, were selected for the present study. (The patients had a mean age ± SD of 57 ± 9 years; eight were women). The lesion was located in the left anterior descending coronary artery in 38 patients, in the right coronary artery in 32, and in the left circumflex coronary artery in 5.

Dobutamine infusion stress test. All patients underwent dobutamine stress testing within 6 h before catheterization. Administration of beta-adrenergic blocking agents and calcium channel blocking agents was stopped 36 h before the test and patients were given oral molsidomine, a direct nitrovasodilator, 4 mg three times daily. Dobutamine stress testing was performed as described by McNeill et al. (12). Briefly, after insertion of an intravenous line and acquisition of a baseline electrocardiogram (ECG), blood pressure recording and two-dimensional echocardiogram, dobutamine was infused starting at a dosage of 10 μg/kg per min and increasing by 10 μg/kg per min every 3 min up to the maximal dosage of 40 μg/kg per min. In case of inadequate increase in heart rate (failure to reach 85% of maximal age-predicted heart rate), in the absence of ischemia or other side effects, a bolus of atropine, 0.25 mg, was injected during the last minute of the test and repeated up to a maximal dose of 1 mg if necessary (12). The ECG was continuously monitored and blood pressure was measured at the end of each stage. A two-dimensional echocardiogram was monitored throughout the procedure and images were stored on videotape within the last minute of every step. The end points for dobutamine infusion were: 85% of maximal age-predicted heart rate, blood pressure >220/110 mm Hg, side effects (arrhythmias, a decrease in systolic blood pressure ≥20 mm Hg, intolerable side effects), severe chest pain. The occurrence of wall motion abnormalities was not considered a reason to stop the test.

Data analysis. Two-dimensional echocardiograms were recorded in standard views. Echocardiograms were analyzed by two experienced observers during acquisition and reviewed after the procedure from videotape. Segmental wall motion was graded as follows: 1 = normal response to dobutamine (i.e., a progressive and synchronous increase in systolic contraction; 2 = hypokinesia (i.e., a reduction of systolic wall thickening during dobutamine infusion as compared with measurements in the previous stage); 3 = akinesia (i.e., a lack of wall thickening or inward motion during dobutamine infusion); 4 = dyskinesia (i.e., an outward motion during dobutamine infusion). Delayed and asynchronous contractions or the absence of hyperdynamic response during dobutamine infusions was considered abnormal and graded as hypokinesia. Wall motion was assessed by using a 16-segment model (13,14). A wall motion score index taking into account the severity of dyssynergy and the number of abnormally contracting segments was calculated as previously described (13). These analyses were carried out without knowledge of either the fractional flow reserve or the results of quantitative coronary angiography. However, the location of the stenosis scheduled for angioplasty was known. Therefore, to study the reproducibility of both qualitative and semiquantitative segmental wall motion analysis, 25 dobutamine echocardiographic examinations were analyzed without knowledge of any patient data by two observers, one of whom was from another institution.

Quantitative coronary angiography. Coronary angiograms were obtained from the percutaneous femoral approach. Coronary stenosis was filmed in the center of the field from multiple projections, avoiding as much as possible overlap of side branches and foreshortening of the relevant segment. Quantitative analysis of the stenosis was carried out by a computer-based edge detection method (ACA system) described in detail previously (15). Briefly, a 7F or 8F guiding catheter was used as a calibration device and filmed in the center of the field. The relevant coronary stenosis was analyzed from an end-diastolic digitized image in at least two projections. Minimal lumen diameter, percent diameter and area stenosis and the interpolated reference diameter were averaged from at least two projections. The interpolated reference diameter is a computer-derived estimation of the original arterial dimension at the site of minimal lumen diameter. The calculation is based on a first-degree polynomial computed through the diameter values of the proximal and distal portions of the arterial segment. The interpolated reference diameter of the stenosed segment was considered an index of the area at risk (16,17). A reference diameter of 2.6 mm was taken as a cutoff value to separate patients into those with a small or a large myocardial area at risk (18). Qualitative assessment of stenosis morphology was performed by using the criteria of Ambrose et al. (19) and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for morphologic description of coronary stenoses (20).

Coronary pressure measurements and calculation of fractional flow reserve. Coronary pressure measurements were performed with a 0.015-in. fluid-filled pressure monitoring guide wire (21), or a 0.018-in. high-fidelity pressure monitoring wire (22). When the pressure monitoring guide wire was positioned distally to the lesion, papaverine (12 mg in the left and 8 mg in the right coronary artery) or adenosine (18 μg in the left and 12 μg in the right coronary artery) was injected through the guiding catheter to induce maximal hyperemia (23,24). Mean aortic pressure and distal coronary pressure were recorded at rest and throughout hyperemia. Figure 1 shows a typical example of pressure measurements. Myocardial fractional flow reserve (FFR_{myo}), defined as the maximal hyperemic myocardial flow expressed as a fraction of its normal maximal expected value, was calculated as follows:

$$FFR_{myo} = P_c / P_{ao},$$

where P_c is distal coronary pressure and P_{ao} is mean aortic pressure, both during peak hyperemia. The theoretic bases of the concept and the validation of the method in humans have been published recently (11,25). In light of previous results

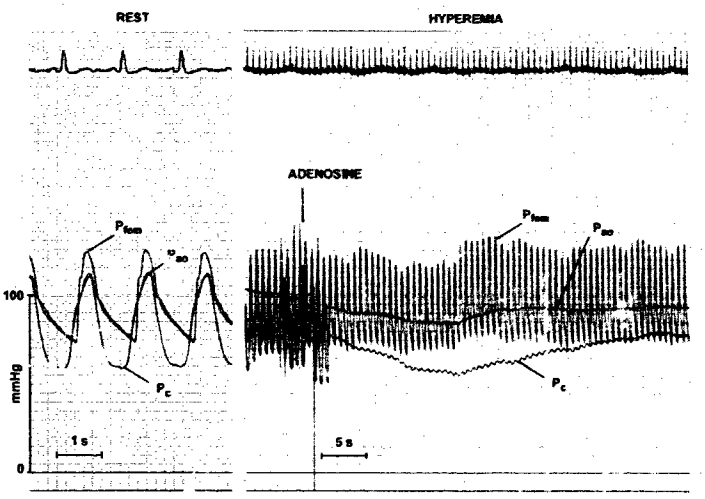

Figure 1. Example of simultaneous pressure recordings of the femoral artery pressure (P_{fem}), aortic pressure (P_{ao}) and distal coronary pressure (P_c) used to calculate myocardial fractional flow reserve. At rest, the transstenotic pressure gradient was 18 mm Hg. During maximal hyperemia, the pressure gradient reached 28 mm Hg. The myocardial fractional flow reserve ($P_c/P_{ao} \times 100$) was 66%.

from our laboratory and others (26,27), values for myocardial flow reserve ≤0.75 were considered functionally significant, that is, capable of inducing ischemia during exercise.

Statistical analysis. Data are presented as mean value ± 1 SD. Comparison between two groups of patients with positive and negative dobutamine stress test results was performed by using the Student *t* test for continuous variables and the chi-square test or Fisher exact test (depending on group size) for categoric variables. Spearman rank correlation coefficients were used to compare dobutamine echocardiographic data with morphologic and physiologic assessments of coronary stenoses. Results were not considered statistically significant when the p value was > 0.05.

Results

Clinical characteristics. The clinical, angiographic and hemodynamic characteristics of 42 patients with positive and 33 patients with negative dobutamine echocardiographic results for ischemia are shown in Table 1. Among the 42 patients with wall motion abnormalities, 12 did not receive the maximal dosage of dobutamine and 4 received atropine. Among the 33 patients without wall motion abnormalities, 2 did not receive the maximal dosage of dobutamine and 9 received atropine. During peak dobutamine infusion, heart rate and rate-pressure product were significantly lower in patients with than in patients without wall motion abnormalities (110 ± 19 vs. 131 ± 12 beats/min and 16,159 ± 4,211 vs. 19,917 ± 3,311 beats/min × mm Hg, respectively, both $p < 0.001$).

Reproducibility of echocardiographic analysis. The agreement in qualitative analysis (presence or absence of wall motion abnormalities) of dobutamine stress echocardiography was 88% between observers within a study center and 92% between observers from different centers. Concordance in grading the most severe degree of dyssynergy occurred in 80% of patients whose study was evaluated by two observers within one center and in 84% of patients whose study was evaluated by observers from two centers. Interobserver variability in semi-quantitative analysis of the wall motion score index was 5.3 ± 4.3% between observers within one study center and 4.4 ± 4.5% between observers from two centers.

Dobutamine echocardiography versus quantitative coronary angiography. Figure 2 (left panels) shows the individual angiographic data in patients with a positive and negative dobutamine stress test result. Patients with dobutamine-

Table 1. Characteristics of Patients With Abnormal and Normal Results on Dobutamine Echocardiography

	Dobutamine Stress Test		
	Abnormal (n = 42)	Normal (n = 33)	p Value
Age (yr)	58 ± 9	55 ± 7	NS
Male/Female	39/3	28/5	NS
Site of stenosis			
LAD	24 (57%)	14 (42%)	NS
RCA	16 (38%)	16 (48%)	NS
LCx	2 (5%)	3 (10%)	NS
Baseline values			
HR (beats/min)	62 ± 8	68 ± 12	0.01
BP (mm Hg)	123 ± 25	117 ± 40	NS
RPP (beats/min × mm Hg)	7,756 ± 1,995	8,486 ± 2,541	NS
Peak values			
HR (beats/min)	110 ± 19	131 ± 12	0.001
BP (mm Hg)	150 ± 21	153 ± 24	NS
RPP (beats/min × mm Hg)	16,159 ± 4,211	19,917 ± 3,311	0.001
RD (mm)	2.92 ± 0.57	2.68 ± 0.53	NS

Values are expressed as mean value ± SD or number (%) of patients. BP = blood pressure; HR = heart rate; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery; RD = reference diameter of the diseased coronary artery; RPP = rate-pressure product.

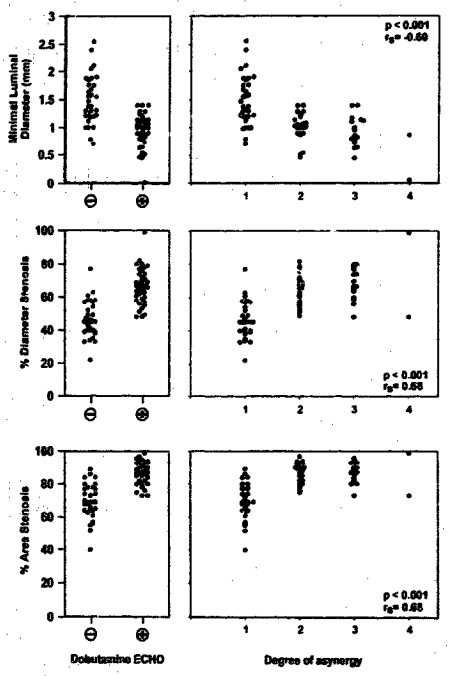

Figure 2. Relation between the percent area and diameter stenosis, minimal lumen diameter and dobutamine echocardiography (ECHO). **Left panels,** Individual angiographic values in patients with positive (+) and negative (−) dobutamine echocardiographic findings **Right panels,** Relation between the most severe dyssynergy during peak dobutamine infusion and angiographic indexes of the lesion (1 = normokinesia; 2 = hypokinesia; 3 = akinesia; 4 = dyskinesia). r_s = Spearman rank correlation coefficient.

induced wall motion abnormalities had angiographically more severe lesions than patients without such abnormalities (0.96 ± 0.3 vs. 1.5 ± 0.43 mm minimal lumen diameter, 66 ± 11% vs. 46 ± 11% diameter stenosis, 87 ± 6% vs. 69 ± 11% area stenosis, all $p < 0.001$). However, a large overlap of the angiographic data was observed between the two groups of patients. Sensitivity, specificity, positive and negative predictive values of dobutamine echocardiography for predicting coronary lesions according to their angiographic severity are summarized in Table 2. A significant relation was found between the degree of most severe dyssynergy during peak dobutamine infusion and the angiographic indexes of the lesion (Fig. 2, right panels; Table 3). A significant correlation also was found between wall motion score index during dobutamine stress testing and angiographic indexes of stenoses severity (Table 3). With qualitative assessment of stenosis morphology using the criteria of Ambrose et al. (19), 44 (58.5%) of 75 patients were classified into group I, 20 (26.5%) into group II and 11 (15%) into group III. With use of the ACC/AHA guidelines criteria, the lesion in 41 of 75 patients was classified as group A, in 25 (34%) as group B1, in 7 (9%) as group B2, and in 2 (3%) as group C. In contrast to quantitative assessment of coronary stenoses, no significant correlation was found between qualitative description of stenosis morphology and either degree of dyssynergy or wall motion score index.

Table 2. Sensitivity, Specificity and Positive and Negative Predictive Values of Dobutamine Echocardiography According to Angiographic Indexes of Stenosis Severity and Calculated Fractional Flow Reserve

	Sensitivity (%)	Specificity (%)	+PV (%)	−PV (%)
MLD ≤1 mm	83	61	58	85
MLD ≤1.5	71	100	100	46
DS ≥50%	80	88	92	63
AS ≥0.75	77	91	95	74
FFR_{myo} ≤0.75	76	97	98	61

AS = area stenosis; DS = diameter stenosis; FFR_{myo} = myocardial fractional flow reserve; MLD = minimal lumen diameter; −PV = negative predictive value; +PV = positive predictive value.

Dobutamine echocardiography versus fractional myocardial flow reserve. The individual data of myocardial fractional flow reserve of patients with and without dobutamine-induced wall motion abnormalities are shown in the left panel of Figure 3. Myocardial fractional flow reserve was significantly lower in patients with a positive than in patients with a negative dobutamine stress test result (0.47 ± 0.12 vs. 0.77 ± 0.15, $p < 0.001$), although a large overlap of the individual data was observed between the two groups. Sensitivity, specificity, positive and negative predictive values of dobutamine echocardiography for predicting a myocardial fractional flow reserve ≤0.75 were 76%, 97%, 98% and 61%, respectively (Table 2). The most severe degree of dyssynergy correlated markedly better with myocardial fractional flow reserve (Fig. 3, right panel) than with the angiographic indexes of stenosis severity (Fig. 2, right panels). Likewise, wall motion score index during dobutamine infusion correlated better with myocardial fractional flow reserve than with the angiographic indexes of stenosis severity (Table 3).

Patients with false negative results on dobutamine echocardiography (myocardial fractional flow reserve ≤0.75% and negative dobutamine echocardiographic findings) reached similar levels of heart rate, blood pressure and rate-pressure product during dobutamine infusion as those of patients with a true positive dobutamine echocardiographic results (myocardial fractional flow reserve ≤0.75% and positive dobutamine echocardiographic findings) (135 ± 9 vs. 128 ± 13 beats/min, 154 ± 16 vs. 153 ± 29 mm Hg and 20,189 ± 3,801 vs. 19,738 ± 3,153 beats/min × mm Hg, respectively, all p = NS). Furthermore, the incidence of submaximal stress test (heart rate <85% of maximal age-predicted heart rate) was similar between patients with true negative (myocardial fractional flow reserve ≥0.75% and negative dobutamine echocardiographic findings) and false negative dobutamine echocardiographic results (46% [6 of 13] vs. 45% [9 of 20], p = NS).

Influence of the area at risk. Figure 4 depicts the ability of dobutamine echocardiography to detect coronary lesions ac-

Table 3. Spearman Rank Correlation Coefficient (r_s) (with 95% confidence interval [CI])

	WMI			Dyssynergy		
	r_s	Lower CI	Upper CI	r_s	Lower CI	Upper CI
MLD	−0.60	−0.73	−0.43	−0.60	−0.73	−0.42
% DS	0.66	0.51	0.77	0.68	0.53	0.78
% AS	0.67	0.52	0.78	0.68	0.54	0.79
FFR_{myo}	−0.74	−0.83	−0.61	−0.77	−0.84	−0.65

WMI = wall motion index; other abbreviations as in Table 2.

cording to their angiographic severity and to the reference diameter of the vessel (considered as an index of perfusion area). In large vessel (reference diameter >2.6 mm), the sensitivity of dobutamine echocardiography was significantly higher than in small vessels (reference diameter ≤2.6 mm). Table 4 shows the sensitivity of dobutamine echocardiography according to vessel size and to myocardial fractional flow reserve. In patients with a functionally significant stenosis (fractional flow reserve ≤0.75), the sensitivity of the dobutamine stress test was significantly lower for lesions located in small than in large vessels. No significant difference was found in the ability of the dobutamine stress test to detect coronary lesions with myocardial fractional flow reserve ≤0.75 in the left anterior descending coronary artery as compared with the left circumflex or right coronary artery. In all patients with positive dobutamine echocardiographic results, the site of dobutamine-induced dyssynergy was in the distribution area of the lesion studied at catheterization. However, in these patients, no correlation was found between the extent score at dobutamine echocardiography and the interpolated reference vessel diameter.

Discussion

The findings of the present study may be summarized as follows: 1) The magnitude of wall motion abnormalities induced by dobutamine infusion correlates with stenosis geometry, and, more closely, with pressure-derived fractional flow reserve, a perfusion index that accounts for collateral circulation. 2) In patients with a functionally significant stenosis (myocardial fractional flow reserve ≤0.75), the extent of the area at risk greatly influences the sensitivity of dobutamine echocardiography.

Dobutamine echocardiography versus anatomic severity. The reported sensitivity of dobutamine echocardiography for the detection of significant coronary artery disease (2–6) has varied from 50% to 90%. Some of this heterogeneity might be related to the use of visual estimation of the coronary angiogram used as a reference standard. This subjective assessment of stenosis severity is hampered by large interobserver and intraobserver variability and often fails to predict the physiologic consequences of the lesion, especially those of "intermediate severity" (7). Yet, even when compared with computer-assisted quantitative coronary angiography, the reported sensitivity of dobutamine echocardiography (2,5,14,28–30) varied from 40% to 89% in detecting stenosis of >50% diameter reduction. This wide range of reported sensitivities relates to differences in patient selection and test methodology (5). Inclusion or exclusion of patients with prior myocardial infarction, cessation of antianginal therapy, a high prevalence of multivessel disease and use of high doses of dobutamine, especially with administration of atropine, all increase the sensitivity of the test. In the present study, only patients with an isolated coronary stenosis and normal left ventricular function were included. Moreover, all medications were withheld ≥36 h before the test. They were replaced by molsidomine to limit as much as possible any vasospastic components. With this study design, the sensitivity of dobutamine echocardiography was

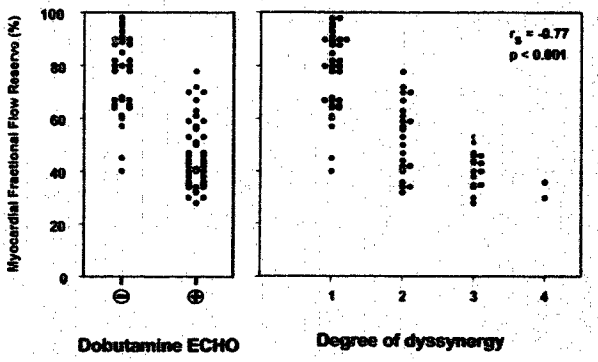

Figure 3. Relation between myocardial fractional flow reserve and dobutamine echocardiography (ECHO). **Left panel,** Individual values of the myocardial fractional flow reserve in patients with positive (+) and negative (−) dobutamine stress test results. **Right panel,** Relation between the most severe dyssynergy during peak dobutamine infusion and the value of myocardial fractional flow reserve. r_s = Spearman rank correlation coefficient.

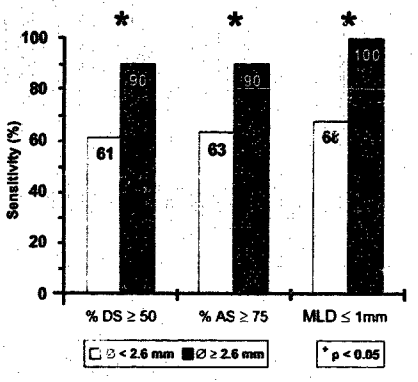

Figure 4. Incidence of abnormal dobutamine echocardiographic findings according to vessel size. AS = area stenosis; DS = diameter stenosis; MLD = minimal lumen diameter; Ø = reference diameter of the stenosed vessel.

80% to detect a lesion with a percent diameter stenosis >50% and 71% to detect a lesion with a minimal lumen diameter <1.5 mm.

In addition to this binary score system (positive or negative), this study demonstrates a significant relation between the magnitude of wall motion abnormalities and angiographic indexes of stenosis severity. However, the same degree of wall motion abnormalities occurred in the presence of a broad range of angiographic stenosis severity. Several factors may have been responsible for this wide dispersion. 1) First the classification of ischemia-induced wall motion abnormalities into hypokinesia, akinesia and dyskinesia is rather crude and depends on the operator's experience and on image quality. Closer correlations might have been observed by using M-mode analysis of the changes in left ventricular wall thickening. 2) Second other dimensional features of the lesion, including length, eccentricity, exit and entrance angles, play a role in the hemodynamic consequences of a narrowing and are not taken into account by minimal lumen diameter or percent diameter or area stenosis (31). Finally, even the most refined angiographic assessment of a coronary lesion does not take into account collateral flow, which may afford a wide range of myocardial flow reserve (32,33).

Table 4. Incidence of Abnormal Dobutamine Echocardiographic Results as a Function of Myocardial Fractional Flow Reserve and Reference Vessel Diameter

	Reference Diameter	
	≤2.6 mm	≥2.6 mm
FFR_{myo} >0.75	0/9 (0%)	1/12 (8%)
FFR_{myo} ≤0.75	14/24 (58%)	27/30 (90%)*

*p = 0.008 versus reference diameter ≤2.6 mm. FFR_{myo} = myocardial fractional flow reserve.

Dobutamine echocardiography versus lesion physiology. Myocardial flow reserve is defined as the maximal achievable flow in the presence of a coronary stenosis expressed as a fraction of maximal flow if the epicardial vessel were normal. Myocardial fractional flow reserve can be calculated from the ratio of distal coronary to aortic pressure during maximal hyperemia. Experimental demonstration and human validation of the concept have recently been reported (11,25). In previous studies (26,27), a myocardial fractional flow reserve >0.75 was uniformly associated with the absence of exercise-inducible myocardial ischemia. In the present study, all lesions, except one, with a myocardial fractional flow reserve >0.75 were associated with a negative dobutamine echocardiographic result (specificity 97%).

Dobutamine echocardiographic results correlated markedly better with myocardial fractional flow reserve than with angiographic indexes. This finding could be due, at least in part, to the fact that fractional flow reserve measurements avoid some limitations of angiography because they take into account all dimensional features of the narrowing as well as collateral contribution to myocardial perfusion (11). However, despite this improved correlation, a large overlap persisted between the flow reserve values of patients with a normal and abnormal test result, and many patients had negative dobutamine echocardiographic findings despite a markedly diminished flow reserve. Several factors may explain these false negative results. First, dobutamine does not necessarily exhaust myocardial flow reserve, in contrast to intracoronary papaverine or adenosine (administered to calculate the pressure-derived flow reserve) (23,24). In the present study, as in others (4,34,35), the rate-pressure product during the maximal dose of dobutamine was markedly lower than that usually observed during maximal exercise (a condition supposed to induce maximal arteriolar vasodilatation). Earlier experiments performed in conscious dogs (36) showed that, for an equi-inotropic effect, the increase in heart rate, blood pressure and coronary blood flow was much less with dobutamine than with exercise. These data suggest that the likelihood of inducing ischemic myocardial dysfunction is smaller with dobutamine than with exercise (37). In open chest dogs, dobutamine infusion was associated with depressed regional function only when reactive hyperemia was severely impaired (38,39). Recently, using a pig model with collateralized total occlusion, Hammond and McKirnan (40) found no regional wall motion abnormalities during high dose dobutamine infusion (50 μg/kg per min). Hence, the relative weakness of the stress induced by dobutamine may partly explain the large proportion of normal dobutamine echocardiographic findings in patients with a markedly reduced myocardial fractional flow reserve. In sharp contrast with these animal data, several studies in humans (29,34) have shown that the sensitivity of dobutamine echocardiography in detecting coronary artery disease is equal to or even higher than that of maximal exercise. This apparent paradox suggests that mechanisms other than increase in work load may play a role in dobutamine-induced wall motion abnormalities. Second, the extent of the area at risk of ischemia may also influence the

detection of dobutamine-induced wall motion abnormalities. Several investigators (2–6,14,35) observed a higher sensitivity of dobutamine echocardiography in patients with multivessel than with one-vessel disease. In patients with an isolated stenosis, the present study confirms that, even in the presence of a functionally significant lesion, dobutamine echocardiographic results were often considered normal when the reference diameter of the vessel at the level of the stenosis was small (Table 4). In contrast, the sensitivity of the test to detect a lesion was similar in all vascular territories. Subtle wall motion abnormalities in a small segment located inbetween two normally contractile territories might not be appreciated by two-dimensional echocardiography not only because of their limited size but also because of a tethering effect that might induce a passive systolic inward motion. These findings suggest that, in addition to the intensity of ischemia, the extent of ischemia in terms of area at risk plays a major role in the clinical detection of dobutamine-induced wall motion abnormalities.

Limitations of the study. Although dobutamine echocardiography is technically less demanding than exercise echocardiography, technical difficulties may obscure the interpretation of the test. In the present study, echocardiographic analysis was performed without using a side by side display of digitized images. Although there is still debate about the usefulness of *image digitization* (41), *especially for pharmacologic stress* echocardiography, side by side display may improve the detection of subtle changes such as asynchrone contraction.

Conclusions. The present study establishes a semiquantitative relation between coronary stenosis severity (both angiographically and functionally) and left ventricular systolic function during dobutamine infusion. In addition to a binary classification of the patients with suspected coronary artery disease (i.e., identification of coronary artery disease), dobutamine echocardiography provides information on the consequences of the epicardial stenosis on perfusion of the myocardium (i.e., evaluation of coronary artery disease). However, when the area at risk of stress-induced ischemia is small, dobutamine echocardiographic results are often negative even though the lesion is functionally severe.

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