Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

Vol. 34, No. 4, 1999
ISSN 0735-1097/99/$20.00
PII S0735-1097(99)00340-X

Low-Level Exercise Echocardiography Detects Contractile Reserve and Predicts Reversible Dysfunction After Acute Myocardial Infarction

Comparison With Low-Dose Dobutamine Echocardiography

Etienne P. Hoffer, MD, Walthère Dewé, MSc, Carmine Celentano, RN, Luc A. Piérard, MD
Liège, Belgium

OBJECTIVES The aim of this study was to evaluate low-level exercise echocardiography (LLEE) in detecting contractile reserve and predicting functional improvement of akinetic myocardium early after acute myocardial infarction (AMI).

BACKGROUND Experimental and clinical studies have shown that low-dose dobutamine enhances contractile function of dyssynergic but viable myocardium in patients with recent AMI. We hypothesized that endogenous catecholamines produced during a LLEE test could serve as a myocardial stressor to elicit contractile reserve.

METHODS Fifty-two consecutive patients with first AMI and ≥2 akinetic segments in the infarct-related territory underwent 5 ± 2 days after AMI low-dose dobutamine echocardiography (LDDE) (5, 10 and 15 μg/kg/min) and LLEE (25 W during 3 min on a supine bicycle, with continuous echocardiographic recording). Both tests were performed on the same day, in random order. Follow-up echocardiography was obtained one month later. Regional wall thickening was semi-quantitatively assessed using a 16-segment, 5-grade scale model. Contractile reserve was defined as improvement in wall thickening of ≥1 grade.

RESULTS Mean increase in heart rate during stress tests was 15 ± 7 beats/min with LLEE and 13 ± 6 beats/min with LDDE (p = NS). Contractile reserve was detected in 119 (55%) of 217 akinetic segments at LLEE and in 137 (63%) segments at LDDE. At follow-up study, functional improvement was identified in 139 (64%) segments. Sensitivity, specificity and positive and negative predictive values for predicting functional recovery were 81%, 92%, 95% and 73%, respectively, for LLEE, and 91%, 86%, 92% and 84%, respectively, for LDDE. Moreover, there was a good correlation between systolic wall thickening measured in the center of the dyssynergic area during stress tests and at follow-up study: $r = 0.77$, $p < 0.001$ with exercise testing and $r = 0.73$, $p < 0.001$ with dobutamine testing.

CONCLUSIONS Low-level exercise echocardiography provides a promising alternative to LDDE for identifying myocardial viability and predicting reversible dysfunction early after AMI. (J Am Coll Cardiol 1999;34:989–97) © 1999 by the American College of Cardiology

In patients with acute myocardial infarction (AMI), early coronary reperfusion may limit the progression of myocardial necrosis and permit functional recovery that may occur spontaneously in stunned myocardium or after revascularization in hibernating regions (1). The eventual extent of functional recovery depends on the size of salvaged tissue and the level of coronary flow reserve in the infarct-related vessel (2,3). Previous studies have demonstrated that low-dose dobutamine echocardiography (LDDE) may identify viable but noncontractile myocardium early after AMI (4–6). We hypothesized that endogenous catecholamines produced during a low-level exercise echocardiography (LLEE) test could serve as a myocardial stressor to elicit contractile reserve. A potential disadvantage of this method may be a too rapid increase in heart rate, which could induce rapid ischemia in regions supplied by critically stenotic coronary arteries. To limit this drawback, a low-level exercise protocol should be used and echocardiography should be recorded continuously. Therefore, this study was undertaken to evaluate the usefulness of LLEE for detecting contractile reserve early after AMI and predicting functional recovery by comparing the accuracy of this new method with that of LDDE.

From the Department of Cardiology, University Hospital Sart Tilman, Liège, Belgium. This work received no financial support.

Manuscript received February 11, 1999; revised manuscript received May 7, 1999, accepted June 23, 1999.

Abbreviations and Acronyms
AMI = acute myocardial infarction
LDDE = low-dose dobutamine echocardiography
LLEE = low-level exercise echocardiography
PTCA = percutaneous transluminal coronary angioplasty

METHODS

Study patients. Fifty-two consecutive patients (50 men, 2 women; mean age 57 ± 12 years; range 23 to 76 years) with a first AMI who had at least two akinetic left ventricular segments at baseline echocardiography were prospectively enrolled in this study. The diagnosis of AMI was made on the basis of the following criteria: 1) typical chest pain lasting more than 30 min; 2) acute ST-segment changes in at least two electrocardiographic leads; and 3) increase in creatine kinase and creatine kinase-MB myocardial enzymes to levels at least twice those above normal values. No contraindications to dobutamine infusion were present, namely postinfarction angina, heart failure, uncontrolled systemic hypertension or ventricular arrhythmias. No patient was excluded because of a technically inadequate echocardiogram.

Thirty-three patients (63%) were treated with thrombolytic therapy and six patients underwent primary percutaneous transluminal coronary angioplasty (PTCA) of the infarct-related vessel. All but these six patients were submitted to coronary angiography 11 ± 8 days after infarction. Elective PTCA of the infarct-related vessel was performed before stress tests in six patients and after stress tests but before follow-up examination in 18 patients. Four other patients were treated by surgical revascularization after stress tests but before follow-up. Stress echocardiographic examinations were performed 5 ± 2 days after admission on the same day, in random order. Twenty-five of the patients (48%) had dobutamine test followed by exercise stress test after a 30-min interval and the other 27 patients had exercise test first followed by dobutamine stress test after the same delay. Beta-adrenergic blocking agents, when used, were short-acting and were withdrawn at least 24 h before the tests. The study was approved by the Research Ethics Committee of our institution; informed consent was obtained for all patients before the investigations.

Exercise echocardiography. Low-level exercise echocardiography was performed in semi-supine position on a tilting exercise table, with the table tilted up to 45° in the left lateral decubitus position. A single load of 25 W was maintained during 3 min with continuous echocardiographic recording. Heart rate was also continuously monitored and blood pressure measured every minute.

Dobutamine echocardiography. Dobutamine was infused intravenously in a solution of 5% dextrose through a peripheral arm vein, at doses of 5, 10 and 15 μg/kg/min with a 3-min stage duration with the patients lying in the same left lateral decubitus position. Blood pressure was measured at the end of each dose interval. Follow-up echocardiograms were obtained in basal conditions 30 ± 3 days after AMI.

Echocardiographic imaging and analysis. Baseline, exercise and dobutamine images were digitized with the same equipment (VingMed Sonotron CFM 800 or System Five, Horten, Norway) and reviewed on a side-by-side cine-loop display. Left ventricular wall motion and thickening were evaluated with a 16-segment, 5-grade scale model, where 1 = normal wall motion and thickening or hyperdynamic; 2 = mild hypokinesis defined as reduced systolic thickening between 2.5 and 5 mm; 3 = severe hypokinesis defined as minimal thickening ≤2.5 mm; 4 = akinesis; and 5 = dyskinesis. Myocardial contractile reserve was defined as improvement in wall thickening of ≥1 grade. A dyskinetic segment (score 5) becoming akinetic (score 4) during stress was not considered viable. Contractile reserve was considered to be present in a patient when improvement in wall thickening concerned at least two contiguous infarct zone segments. For each segment, reversible dysfunction was defined as improved wall thickening of ≥1 grade at follow up. A change from dyskinesis to akinesis was not considered as improved function.

Functional recovery was considered to be present in a patient when improvement in wall thickening concerned at least two contiguous infarct zone segments. Wall thickening was measured by conventional M-mode echocardiography in the center of the dysfunctional region at baseline, at each stage of the dobutamine test, at the end of each minute during exercise test and at follow up. Measurements were acquired online on three consecutive cycles in end-diastole (beginning of QRS complex) and in end-systole (top of T-wave) and mean values were calculated. To ensure measurements of the same myocardial region during both stress tests and follow-up echocardiograms, care was taken to use as precisely as possible the same view and patient's position. All echocardiograms were analyzed and a consensus was achieved by two observers unaware of the clinical data and the results of the other stress test. Interobserver agreement regarding the presence or absence of contractile reserve in segmental analysis was 93% for LLEE ($\kappa = 0.87$) and 94% for LDDE ($\kappa = 0.88$).

Statistical analysis. Data are expressed as mean ± 1 SD. Sensitivity, specificity, positive and negative predictive values and accuracy were calculated with standard formulas and are reported with the corresponding 95% confidence interval (CI). To test differences between two groups, independent two-sample *t* tests were used. Linear regression analysis was used to correlate wall thickening measured during stress tests and at follow-up. Agreement between the two stress methods and interobserver variability of segmental wall

motion analysis was assessed as percent agreement and κ value. Statistical significance was defined as $p \leq 0.05$.

RESULTS

Patient's characteristics. Clinical, angiographic and echocardiographic characteristics of the study patients are summarized in Table 1. The site of the infarction was anterior in 21 patients and inferior or posterolateral in 31 patients. Forty-three patients (83%) had a Q-wave infarction. The mean peak creatine kinase and creatine kinase-MB were 2273 ± 1047 IU/ml and 223 ± 118 IU/ml, respectively.

Angiographic data. The infarct-related coronary artery was the left anterior descending artery in 21 patients, the right coronary artery in 19 patients and the left circumflex in the 12 remaining patients. The percentages of diameter stenosis of the infarct-related vessel are shown in Table 1. When PTCA of the infarct-related vessel was performed, values measured before and after PTCA are presented. The values at the moment of stress tests are underlined. Nine patients had no significant coronary artery stenosis (<50% luminal diameter stenosis), 24 had one-vessel disease, 12 had two-vessel disease and 7 had three-vessel disease.

Stress testing. No complications occurred as a result of dobutamine or exercise tests. Resting heart rate was 71 ± 9 beats/min before the first test and 73 ± 11 beats/min before the second test (p = NS). Mean increase in heart rate during stress tests was 15 ± 7 beats/min with LLEE and 13 ± 6 beats/min with LDDE (p = NS). There was no significant increase in systolic blood pressure during LLEE (120 ± 21 mm Hg vs. 116 ± 15 mm Hg at rest) or LDDE (112 ± 17 mm Hg vs. 115 ± 18 mm Hg at rest).

Analysis of patients. Both LLEE and LDDE identified contractile reserve in at least two contiguous segments of akinetic myocardium in 34 (65%) and 37 (71%) of the 52 patients, respectively. Follow-up echocardiography revealed functional recovery in 38 (73%) patients. Figure 1 presents end-diastolic and end-systolic stop-frame images of illustrative echocardiograms obtained at baseline, during LLEE, LDDE and at one month follow up in a patient with inferior infarction, demonstrating contractile reserve during both stress tests and follow-up functional recovery. Sensitivity, specificity, positive and negative predictive values and accuracy of LLEE and LDDE for predicting functional improvement at follow up are shown in Table 2. There were 36 patients with true positive and 13 with true negative tests with dobutamine testing, and 33 and 13, respectively, with exercise testing. One patient had a false positive test with both methods. Two patients had a false negative test—no contractile reserve, but functional recovery—with dobutamine testing and five with exercise testing. There was no significant difference in mean diameter stenosis of the infarct-related vessel at the time of stress tests between patients with (57 ± 29%) and without (57 ± 24%) contractile reserve. Complete occlusion of the infarct-related vessel was present at stress tests in six patients with contractile reserve and in two patients without contractile reserve. Contrary to the others, these two patients had a limited collateral circulation.

Analysis of segments. At baseline, 211 segments were akinetic and 6 were dyskinetic. Both LLEE and LDDE identified the presence of contractile reserve in 119 (55%) and 137 (63%) of these segments, respectively. Of the 139 (64%) segments showing functional recovery at follow up, LLEE and LDDE correctly identified 113 and 126 segments, respectively. Of the 78 segments without improvement in wall thickening at follow up, the two methods correctly identified 72 and 67 segments, respectively. Sensitivity, specificity, positive and negative predictive values and accuracy of LLEE and LDDE for predicting functional recovery of akinetic segments are shown in Table 2. One hundred and nineteen segments showed and 80 did not show contractile reserve with both methods. No segment developed contractile reserve with exercise but not with dobutamine and 18 responded to dobutamine but not to exercise (91% agreement, $\kappa = 0.82$). Figure 2 shows the evolution of akinetic and dyskinetic segments during LLEE and LDDE.

Wall thickening. Complete measurements of wall thickening could be obtained in 45 patients. Measurements could not be performed in seven of the nine patients with lateral infarction in whom the center of the dysfunctional region was located in the lateral wall. The maximal variations of wall thickening measured on-line during stress testing were limited (0.1 ± 0.1 mm at rest, 0.2 ± 0.2 mm and 0.3 ± 0.3 mm at the end of exercise and dobutamine tests, respectively). Figure 3 shows an example of conventional M-mode echocardiogram recordings in the center of the affected area obtained at baseline, during LLEE and LDDE, and at one month follow-up in a patient with inferior infarction, demonstrating improved wall thickening during both tests and at one month. In 34 of the 38 patients showing functional recovery, mean systolic wall thickening in the center of the dysfunctional region was 0.2 ± 0.3 mm at baseline and improved significantly during LLEE (2.5 ± 1.4 mm, $p < 0.001$ vs. rest), during LDDE (3.2 ± 2 mm, $p < 0.001$ vs. rest, p = NS vs. LLEE) and at follow-up study (3 ± 1.7 mm, $p < 0.001$ vs. rest, p = NS vs. LLEE and LDDE). Maximal improvement in wall thickening occurred during dobutamine infusion at 5 μg/kg/min in 5 patients, at 10 μg/kg/min in 16 and at 15 μg/kg/min in 13 patients.

During exercise, this maximal improvement in wall thickening was observed at 2.6 ± 0.2 min. No correlation was found between diameter stenosis of the infarct-related vessel at the time of stress tests and the increase in wall thickening during exercise ($r = 0.25$, $p = 0.14$) and dobutamine ($r = -0.08$, $p = 0.66$) testing. In contrast, when considering the whole study population with or without functional recovery, there was a significant correlation between systolic wall

Table 1. Clinical, Angiographic and Echocardiographic Characteristics of the Study Patients

Patient No.	Age (yr)/ Gender	Akinetic Area	Type of Infarction	Treatment	IRV	% DS of the IRV	Contractile Reserve With LLEE	Functional Recovery	Wall Motion Score Index			
									Baseline	LDDE	LLEE	FU
1	45/M	Inferior	Q	Immediate PTCA	RCA	100(C1) → 28	Yes	Yes	1.75	1.06	1.25	1.06
2	68/M	Anterior	Q	Thrombolysis	LAD	72	No	No	2.87	2.81	2.87	2.87
3	51/M	Posterolateral	Q	Thrombolysis	LCX	100(C1)	No	No	2.12	2.12	2.12	2.12
4	48/M	Posterolateral	Non-Q	Thrombolysis‡	LCX	74 → 13	Yes	Yes	1.75	1	1.25	1.25
5	67/M	Inferior	Q	Thrombolysis	RCA	75	Yes	Yes	1.75	1.12	1.25	1.5
6	57/M	Anterior	Q	Immediate PTCA	LAD	100(C0) → 38	No	No	1.81	1.81	1.81	1.81
7	74/F	Anterior	Q	*	LAD	20	Yes	Yes	1.93	1	1.31	1.18
8	56/M	Anterior	Q	Thrombolysis‡	LAD	58 → 20	Yes	Yes	1.75	1.25	1.5	1.12
9	68/M	Anterior	Q	Thrombolysis†	LAD	85 → 22	No	Yes	2.56	2.18	2.56	1.93
10	67/M	Inferior	Q	*§	RCA	100(C2)	Yes	Yes	1.37	1.25	1.25	1.18
11	76/M	Anterior	Q	Immediate PTCA	LAD	100 → 18	No	No	2.12	2.06	2.06	2.12
12	39/M	Anterior	Non-Q	*†	LAD	79 → 29	Yes	Yes	1.75	1.5	1.5	1.25
13	63/M	Inferior	Q	Thrombolysis‡	RCA	75 → 18	Yes	Yes	1.75	1.5	1.5	1.62
14	67/M	Inferior	Non-Q	*	RCA	100(C2)	Yes	Yes	1.75	1.31	1.25	1.18
15	68/M	Anterior	Q	*†	LAD	77 → 6	No	Yes	1.82	1.82	1.82	1.56
16	64/M	Anterior	Q	Thrombolysis	LAD	70	No	No	1.56	1.56	1.56	1.56
17	66/M	Inferior	Non-Q	Thrombolysis‡	RCA	80 → 23	Yes	Yes	1.37	1.12	1.25	1.18
18	50/M	Inferior	Q	Immediate PTCA	RCA	77 → 27	Yes	Yes	1.37	1.12	1.25	1.25
19	56/M	Inferior	Q	Immediate PTCA	LCX	100(C1) → 16	Yes	Yes	2.12	1.62	1.87	1.75
20	72/M	Inferior	Q	Thrombolysis	RCA	42	Yes	Yes	1.37	1.12	1.25	1.25
21	70/M	Inferior	Q	*‡	RCA	57 → 21	Yes	Yes	1.75	1.12	1.62	1.5
22	44/M	Inferior	Q	*§	RCA	100(C2)	Yes	Yes	1.68	1.25	1.25	1.43
23	50/M	Inferior	Q	Thrombolysis†	LCX	95(C1) → 33	Yes	Yes	1.75	1.06	1.5	1.37
24	50/M	Anterior	Q	Thrombolysis‡	LAD	79 → 35	Yes	Yes	1.5	1.12	1.25	1.12
25	23/M	Anterior	Q	Thrombolysis	LAD	30	Yes	Yes	1.75	1.12	1.37	1
26	56/M	Anterior	Q	Thrombolysis	LAD	42	Yes	Yes	2.12	1.5	1.75	1.87
27	61/M	Inferior	Q	Thrombolysis	RCA	77	No	No	1.37	1.37	1.37	1.37
28	65/M	Anterior	Q	*	LAD	100(C2)	Yes	Yes	2.12	1.5	1.62	1.25
29	69/M	Inferior	Q	Thrombolysis	RCA	100(C2)	Yes	Yes	1.75	1.5	1.25	1.5
30	56/M	Anterior	Q	Thrombolysis†	LAD	66 → 21	No	No	1.93	1.93	1.93	1.93
31	47/M	Inferior	Q	Thrombolysis	RCA	42	No	No	1.75	1.75	1.75	1.75
32	58/F	Anterior	Q	*‡	LAD	73 → 38	No	Yes	1.75	1.62	1.75	1.62
33	54/M	Anterior	Q	Thrombolysis	LAD	45	Yes	Yes	2.12	1.37	1.37	1.75
34	66/M	Inferior	Q	Thrombolysis‡	LCX	72 → 38	Yes	Yes	1.37	1.19	1.19	1.19
35	55/M	Posterolateral	Non-Q	Immediate PTCA	LCX	100 → 21	Yes	Yes	1.5	1.31	1.44	1.12
36	46/M	Posterolateral	Q	*‡	LCX	72 → 16	Yes	Yes	1.5	1.37	1.44	1.31
37	40/M	Inferior	Non-Q	Thrombolysis‡	RCA	69 → 24	No	No	1.56	1.5	1.5	1.5
38	47/M	Anterior	Q	Thrombolysis‡	LAD	60 → 11	Yes	Yes	2.12	1.75	1.75	1.75

Table 1. Continued

Patient No.	Age (yr)/ Gender	Akinetic Area	Type of Infarction	Treatment	IRV	% DS of the IRV	Contractile Reserve With LLEE	Functional Recovery	Wall Motion Score Index			
									Baseline	LDDE	LLEE	FU
39	41/M	Inferior	Non-Q	*‡	RCA	77 → 21	No	No	1.56	1.5	1.5	1.5
40	52/M	Inferior	Q	Thrombolysis§	RCA	100(C1)	No	No	1.75	1.75	1.75	1.69
41	33/M	Inferior	Q	Thrombolysis	RCA	40	Yes	Yes	1.37	1.12	1.25	1.25
42	53/M	Inferior	Q	*†	RCA	89 → 1	No	Yes	1.56	1.37	1.56	1.19
43	66/M	Anterior	Non-Q	*‡	LAD	72 → 27	No	No	1.75	1.75	1.75	1.75
44	40/M	Posterolateral	Q	Thrombolysis‡	LCX	78 → 16	Yes	Yes	1.75	1.37	1.37	1.37
45	72/M	Posterolateral	Non-Q	Thrombolysis§	LCX	100(C2)	Yes	Yes	1.56	1.19	1.19	1.19
46	59/M	Posterolateral	Q	Thrombolysis‡	LCX	57 → 16	Yes	Yes	1.56	1.19	1.19	1.06
47	46/M	Inferior	Q	Thrombolysis‡	RCA	71 → 11	Yes	Yes	1.56	1.31	1.19	1.19
48	72/M	Posterolateral	Q	Thrombolysis	LCX	40	No	Yes	1.75	1.75	1.75	1.56
49	64/M	Anterior	Q	Thrombolysis	LAD	52	No	No	2.12	2.12	2.12	2.12
50	52/M	Posterolateral	Q	Thrombolysis‡	LCX	55 → 7	Yes	Yes	1.56	1	1.06	1.06
51	52/M	Anterior	Q	Thrombolysis‡	LAD	72 → 13	Yes	No	2.12	2	2	2.12
52	70/M	Anterior	Q	Thrombolysis	LAD	38	Yes	Yes	2.12	1.37	1.62	1.37

*No acute reperfusion strategy. †Elective angioplasty of the infarct-related vessel before stress tests. ‡Elective angioplasty of the infarct-related vessel after stress tests but before follow-up examination. §Surgical revascularization after stress tests but before follow-up examination.

C = grade of collateral circulation in patients with complete occlusion or nearly complete occlusion of the infarct-related vessel (0 = absent; 1 = limited; 2 = important); DS = diameter stenosis (underlined values indicate the state of the vessel at the time of stress tests); F = female; FU = follow-up; IRV = infarct-related vessel; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LDDE = low-dose dobutamine echocardiography; LLEE = low-level exercise echocardiography; M = male; Non-Q = non-Q-wave infarction; PTCA = percutaneous transluminal coronary angioplasty; Q = Q-wave infarction; RCA = right coronary artery.

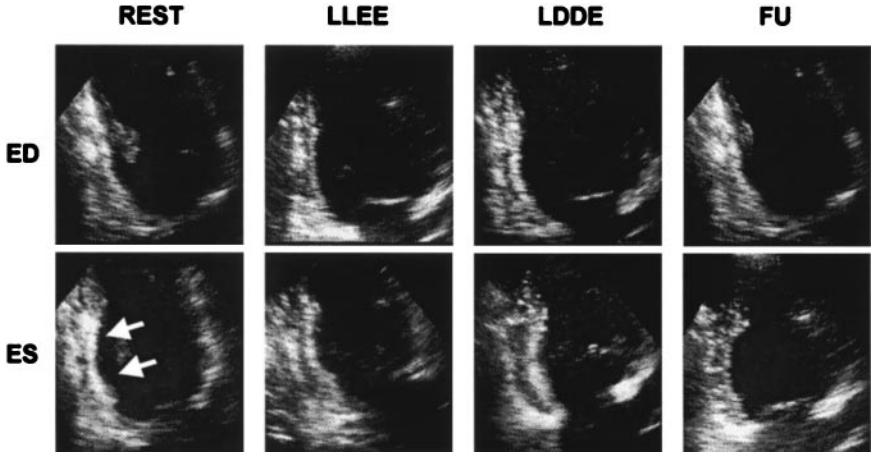

Figure 1. End-diastolic (ED) and end-systolic (ES) stop-frame images of illustrative echocardiograms (apical two-chamber views) obtained in a patient showing inferior akinesia at rest **(arrows)**, mild hypokinesis during low-level exercise echocardiography (LLEE), normal thickening during low-dose dobutamine echocardiography (LDDE) and at follow up (FU).

thickening measured during stress tests and at follow-up study, and the correlation tended to be better with exercise testing ($r = 0.77$, $p < 0.001$) than with dobutamine testing ($r = 0.73$, $p < 0.001$) (Fig. 4). No biphasic responses were observed during any stress test.

DISCUSSION

To our knowledge, this is the first study using LLEE as a stress method for identifying contractile reserve early after AMI. Because hypokinesis at baseline indicates that most of the myocardium has escaped necrosis and is therefore viable (7), only patients who had at least two akinetic segments were included in this study. The main findings can be summarized as follows: 1) contractile reserve of akinetic viable myocardium is detectable during a short, light and well-tolerated exercise early after AMI; 2) the accuracy of contractile reserve as detected by LLEE for predicting reversible dysfunction (85%) is similar to that of LDDE (89%); and 3) the magnitude of thickening elicited during the 3-min exercise test measured in the center of the ischemic area is not significantly different from the extent of contractile reserve during the 9-min dobutamine test and it correlates slightly better with systolic thickening measured at baseline on the follow-up echocardiogram.

Reversal of dysfunction by catecholamines. Several experimental studies have demonstrated that postischemic myocardial dysfunction can be reversed with beta-adrenergic stimulation. Low-level exercise echocardiography was first used in comparison with positron emission tomography for detecting viable myocardium in patients with AMI after thrombolytic therapy (4). We postulated that the increase in endogenous catecholamines resulting from dynamic exercise could also elicit contractile reserve of viable akinetic myocardium, which could be detectable echocardiographically. Our results support this hypothesis: wall thickening appeared shortly after the onset of exercise in 55% of noncontractile regions at baseline. All segments responding to dynamic exercise also showed contractile reserve LDDE. Only 18 segments in 9 patients responded

Table 2. Sensitivity, Specificity, Positive and Negative Predictive Values and Accuracy With 95% Confidence Intervals of Low-Level Exercise and Low-Dose Dobutamine Echocardiography to Predict Reversible Dysfunction

Method	Sensitivity	Specificity	PPV	NPV	Accuracy
Analysis of patients (n = 52)					
LLEE	87	93	97	72	88
95% CI	76 to 98	80 to 100	91 to 100	51 to 93	79 to 97
LDDE	95	93	97	87	94
95% CI	88 to 100	80 to 100	92 to 100	70 to 100	88 to 100
Analysis of segments (n = 217)					
LLEE	81	92	95	73	85
95% CI	74 to 88	86 to 98	91 to 99	64 to 82	80 to 90
LDDE	91	86	92	84	89
95% CI	86 to 96	78 to 94	87 to 97	76 to 92	85 to 93

CI = confidence interval; LDDE = low-dose dobutamine echocardiography; LLEE = low-level exercise echocardiography; NPV = negative predictive value; PPV = positive predictive value.

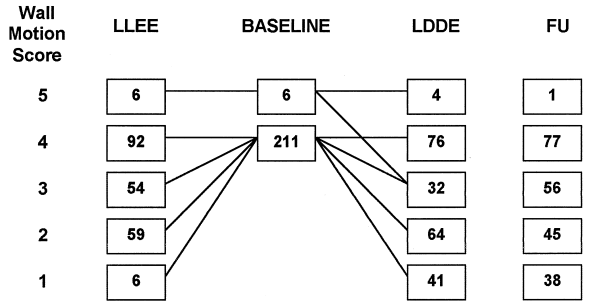

Figure 2. Evolution of the baseline dyssynergic segments with low-level exercise echocardiography (LLEE), low-dose dobutamine echocardiography (LDDE) and at follow-up study (FU).

to dobutamine but not to exercise: five of these segments presented a false positive response with dobutamine.

Contractile reserve. The two major factors that determine the absence or presence, and, if present, the extent of contractile reserve in postinfarction patients, are infarct size—the amount of viable myocardium—and vascular reserve—the maximal achievable flow in the infarct-related territory. Shortly after AMI, any retained wall thickening—hypokinesis—implies less than 20% infarct thickness (7), thus the presence of a large amount of viable myocardium. Contractile reserve has been found to be more frequent in hypokinetic than in akinetic segments (8). However, because hypokinetic territories a few days after AMI correspond to small endocardial infarcts, we focused our analysis on akinetic and dyskinetic regions.

A second determinant of contractile reserve is the presence of flow reserve within the infarct bed. Obviously, if myocardial blood flow cannot increase in response to catecholamine-induced increase in myocardial oxygen consumption, wall thickening will not develop (9). Experimental observations have indicated that, in the absence of flow-limiting stenosis, a linear relationship exists between infarct size and percent of wall thickening during dobutamine infusion (10). The dose of dobutamine determining the best relation was 15 μg/kg/min. Therefore, this dose was selected as the maximal dose in our study. In the presence of a flow-limiting residual stenosis, the increase in myocardial thickening in response to dobutamine is attenuated (11), and the respective proportion of necrotic and salvaged myocardium is no longer quantifiable.

Moreover, the improvement in wall thickening is transient, occurs at the expense of metabolic deterioration of myocardial ischemia and is followed by a reduction in thickening if dobutamine infusion is prolonged or given at higher doses (12). This biphasic response is characteristic of hibernating myocardium subtending severe coronary stenosis (13). It is therefore essential to avoid a too rapid and excessive increase in heart rate and to monitor regional wall thickening continuously during a stress test. Such a continuous observation is the rule in pharmacologic stress echocardiography but may be technically more difficult during treadmill or upright bicycle exercise. We used a special table allowing appropriate lateral tilting and head elevation with the patient in a semi-supine, comfortable position. There was no degradation of echocardiographic image quality during exercise. We selected a single low charge of 25 W in order to obtain a similar increase in heart rate as during dobutamine infusion. The short exercise duration was easily tolerated by all patients, a few days after AMI. It should be noted that 16 patients with functional recovery at follow up had a >70% stenosis of the infarct-related vessel at the time of stress testing; contractile reserve was detected in all these patients during dobutamine infusion and in 15 of them during exercise. Recruitable collateral circulation may have played a role in some of these patients. The prevalence of contractile reserve during low-dose dobutamine echocardi-

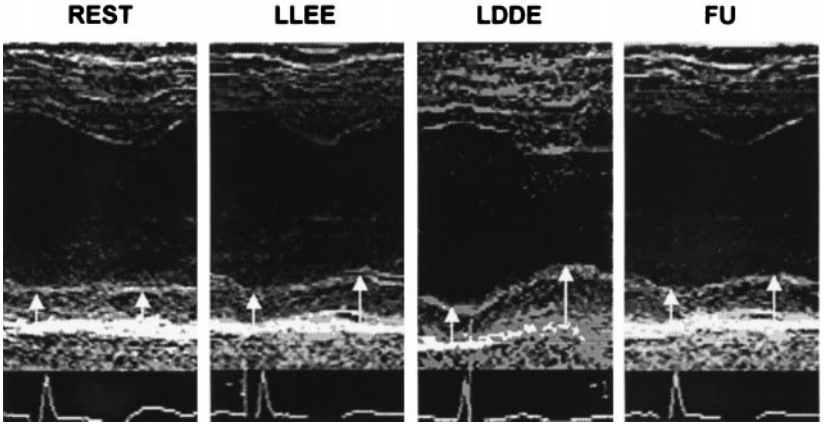

Figure 3. Conventional M-mode echocardiogram recordings obtained at rest, during low-level exercise echocardiography (LLEE), low-dose dobutamine echocardiography (LDDE) and at follow-up (FU) in a patient with inferior myocardial infarction. Images were acquired in parasternal short axis view. End-diastolic values were recorded at the beginning of QRS complex and in end-systolic values on top of T-wave. Absolute systolic thickening was 0.1 mm at baseline, 2.9 mm during LLEE 4.8 mm during LDDE, and 2.4 mm at baseline on the follow-up echocardiogram.

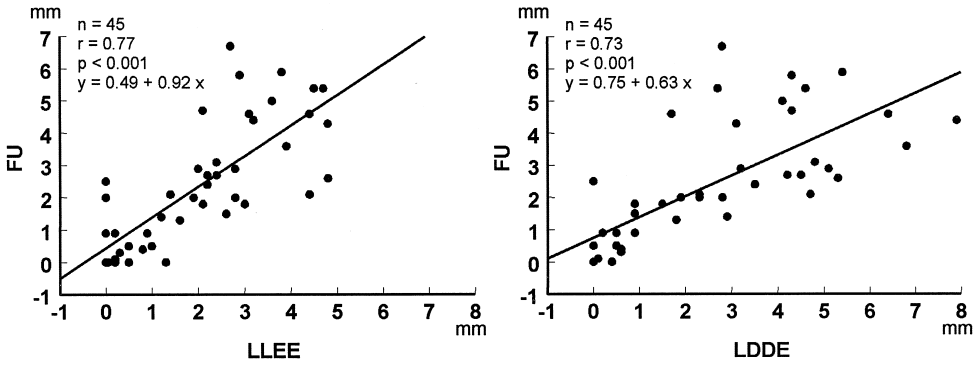

Figure 4. Relation between absolute systolic thickening in the center of the dysfunctional area measured during low-level exercise echocardiography (LLEE) and low-dose dobutamine echocardiography (LDDE), and at follow-up (FU) in the whole-study patients (n = 45).

ography has been found to be independent of the angiographic severity of coronary artery disease (14).

Functional recovery. The major determinant of functional recovery after AMI is the transmural extent of infarction. Recovery in regional function can occur spontaneously after resolution of myocardial stunning. In the presence of hibernating myocardium in the infarcted area, spontaneous recovery of function may be delayed and continue for up to seven months (15). Although difficult to evaluate, successful revascularization before hospital discharge has probably had a major effect on the presence and extent of functional recovery. Of our 52 study patients, 34 (65%) underwent revascularization before follow up; of the remaining 18 patients, 5 had a nonsignificant (<50%) diameter stenosis of the infarct-related vessel and 4 had an occluded vessel with collateral circulation. Frequent early revascularization procedures correspond to our current therapeutic strategy, which was not influenced by the study results.

Study limitations. The results of this study should be considered in light of several potential limitations. First, the therapeutic approach in the acute phase (thrombolytic therapy, primary PTCA, elective PTCA or conventional treatment) was not standardized. Patients enrolled were consecutive patients without contraindication to an early stress test, and the results of exercise and dobutamine tests were not used in the decision process.

Second, the assessment of wall thickening was obtained by measuring end-diastolic and end-systolic thickness on conventional M-mode echocardiograms. Although this approach benefits from a high temporal resolution, measurements may not have been made in strictly identical regions at different stages. The temporal heterogeneity characterizing postischemic myocardium could not be taken into account. When the center of the dysfunctional region was located in the lateral wall, satisfying measurements were impossible to obtain using the conventional M-mode echocardiogram. Quantitation of regional thickening using two-dimensional echocardiography and the entire systolic contraction sequence (16) is impractical in consecutive patients. Improvement in endocardial definition by tissue harmonic imaging and availability of anatomical M-mode echocardiography may potentially help quantitation of contractile reserve in the future.

Third, only short low-level exercise and low-dose dobutamine infusion were used in this study. The detection of jeopardized rather than simply viable myocardium is important for risk assessment and patient management. The administration of low as well as high doses of dobutamine and the observation of initial improvement of regional thickening followed by deterioration were found to be needed for optimal prediction of functional recovery after angioplasty in patients with stable coronary artery disease and ventricular dysfunction (17). Whether continuous echocardiographic monitoring of regional wall thickening during maximal exercise can accurately identify a biphasic response needs to be addressed in future clinical studies. Finally, it should be acknowledged that our observations are not necessarily applicable to other clinical settings such as chronic coronary artery disease and several global left ventricular dysfunction.

Conclusions. Our study demonstrates that LLEE performed on a tilting table allowing continuous echocardiographic observation and recording is a simple method of identifying contractile reserve and predicting the extent of functional recovery early after AMI. This technique could provide a valuable physiologic tool to detect viable myocardium.

Reprint requests and correspondence: Dr. Luc A. Piérard, Department of Cardiology, University Hospital Sart Tilman B-35, 4000 Liège, Belgium. E-mail: lpierard@chu.ulg.ac.be.

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