

# Real Time Myocardial Contrast Echocardiography to Predict Left Ventricular Wall Motion Recovery After Reperfused Acute Myocardial Infarction

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**Introduction and objectives.** Real time myocardial contrast echocardiography (RTMCE) is a recently developed method. We sought to determine: *a*) whether RTMCE predicts recovery of left ventricular function after acute myocardial infarction (AMI), and *b*) whether data obtained with this method are comparable to those obtained with <sup>99m</sup>Tc-sestamibi single photon emission computed tomography (SPECT) and magnetic resonance.

**Patients and method.** We studied 85 patients with AMI who underwent angioplasty. RTMCE was performed 7 (4) days after AMI. Two-dimensional echocardiography was performed at the time of the RTMCE study and at follow-up (10 [4] weeks). SPECT and magnetic resonance were performed after AMI in 18 and 32 patients, respectively.

**Results.** Follow-up two-dimensional echocardiography results were available for 82 patients, who were subdivided into 2 groups: recovery (*n*=49) and no recovery (*n*=33). Regional (AMI-related) wall motion score index improved from 1.75 (0.49) to 1.32 (0.36) (*P*<.001) in the recovery group, and worsened from 1.85 (0.39) to 1.95 (0.36) in the no recovery group (*P*<.001). RTMCE perfusion score was 0.8 (0.3) in the recovery group, and 0.6 (0.4) in the no recovery group (*P*<.001). Concordance between RTMCE and SPECT in a segmental analysis was 78% (*P*<.001;  $\kappa$ =0.49), whereas concordance between RTMCE and hyperenhancement with delayed contrast magnetic resonance findings was 70% (*P*<.001;  $\kappa$ =0.35). Independent predictors of recovery were peak creatine kinase (OR=1.4 per 1000 UI; 95% CI, 1.0-1.9; *P*<.05) and RTMCE score (OR=8.8; 95% CI, 1.9-39.3; *P*<.01). A RTMCE score  $\geq$ 0.60 had a positive predictive value of 73% and a negative predictive value of 69% (*P*<.001; area under the curve 0.70).

**Conclusion.** RTMCE showed a modest predictive value for recovery of left ventricular function after reperfused AMI.

**Key words:** *Echocardiography. Perfusion. Acute myocardial infarction.*

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## Ecocardiografía de perfusión miocárdica en tiempo real para la predicción de la recuperación de la función ventricular después del infarto agudo de miocardio reperfundido

**Introducción y objetivos.** La ecocardiografía de perfusión en tiempo real (EPTR) es un método reciente. Los objetivos fueron estudiar: *a*) si la EPTR predice la recuperación después de infarto agudo de miocardio (IAM), y *b*) si los datos son comparables a los obtenidos con la tomografía computarizada por emisión de fotones simples (SPECT) marcada con <sup>99m</sup>Tc-sestamibi y la resonancia magnética (RM).

**Pacientes y método.** Hemos incluido a 85 pacientes con IAM sometidos a angioplastia coronaria transluminal percutánea (ACTP). La EPTR se realizó 7  $\pm$  4 días después del IAM. Se utilizó ecocardiografía a la vez que la perfusión y a las 10  $\pm$  4 semanas de ésta. La SPECT y la RM se realizaron después del IAM en 18 y 32 pacientes, respectivamente.

**Resultados.** Al finalizar el seguimiento dispusimos de ecocardiografía de 82 pacientes, a los que dividimos en: grupo con recuperación (GR) (*n* = 49) y grupo sin recuperación (GNR) (*n* = 33). El índice de motilidad segmentaria (IMS) regional mejoró desde 1,75  $\pm$  0,49 a 1,32  $\pm$  0,36 (*p* < 0,001) en el GR, y empeoró desde 1,85  $\pm$  0,39 a 1,95  $\pm$  0,36 en el GNR (*p* < 0,001). El índice de EPTR era de 0,8  $\pm$  0,3 en el GR y de 0,6  $\pm$  0,4 en el GNR (*p* < 0,001). La concordancia entre la EPTR y la SPECT en un análisis segmentario era del 78% (*p* < 0,001;  $\kappa$  = 0,49), y entre la EPTR y el hipercontraste tardío de la RM era del 70% (*p* < 0,001;  $\kappa$  = 0,35). Los predictores independientes de recuperación fueron el valor de la creatinina (odds ratio [OR] = 1,4 por cada 1.000 U; intervalo de confianza [IC] del 95%, 1,0-1,9; *p* < 0,05) y el índice de EPTR (OR = 8,8; IC del 95%, 1,9-39,3; *p* < 0,01). Un índice  $\geq$  0,60 tuvo un valor predictivo positivo del 73% y negativo del 69% (*p* < 0,001; ABC = 0,70).

**Conclusión.** La EPTR tiene valor moderado para predecir la recuperación funcional después del IAM reperfundido.

**Palabras clave:** *Ecocardiografía. Perfusion. Infarto de miocardio.*

## ABBREVIATIONS

AUC: area under the curve.  
 PTCA: percutaneous transluminal coronary angioplasty.  
 IRA: infarct-related artery.  
 RT-MCE: real-time myocardial contrast echocardiography.  
 AMI: acute myocardial infarction.  
 WMSI: wall motion score index.  
 MR: magnetic resonance.  
 SPECT: technetium-<sup>99m</sup>-sestamibi single photon emission computed tomography.  
 PPV: positive predictive value.  
 NPV: negative predictive value.

## INTRODUCTION

Injury to the coronary microcirculation after acute myocardial infarction (AMI) can occur despite the presence of a patent coronary artery and predicts functional recovery at follow-up.<sup>1-3</sup> Microvascular integrity has been measured through intracoronary<sup>1-5</sup> or intravenous injections of contrast agents.<sup>6-13</sup> Most studies have used a high mechanical index and harmonic gray-scale imaging<sup>6</sup> or power Doppler ultrasound.<sup>7-13</sup> Real-time myocardial contrast echocardiography (RTMCE) with accelerated intermittent harmonic imaging is a relatively recent method that avoids some of the technical limitations of image acquisition with intermittent harmonic imaging and a high mechanical index.<sup>14,15</sup> The aim of this study was to evaluate: *a*) whether perfusion evaluated with RTMCE predicts recovery of function after AMI, and *b*) whether the perfusion data are comparable to those obtained with technetium-<sup>99m</sup>-sestamibi single photon emission computed tomography (SPECT) and magnetic resonance (MR).

## PATIENTS AND METHODS

### Patients

Eighty-five consecutive patients were included with a first AMI and a moderate probability of having ventricular dyssynergy assessed via clinical and enzymatic parameters. They underwent percutaneous transluminal coronary angioplasty (PTCA) (primary in 60 patients, rescue in 25 patients, and stent implant in 79 patients) which yielded a Thrombolysis In Myocardial Infarction (TIMI)  $\geq 2$ . The selection criteria for the patients undergoing primary PTCA were characteristic precordial pain over 30 min duration and ST elevation

$>2$  mm in 2 contiguous precordial leads. In patients who underwent rescue PTCA, an increase in creatine kinase (CK) values and/or troponin I greater than twice the normal limit was required.<sup>16</sup> The culprit artery causing the AMI was the descending anterior artery in 59 patients, the right coronary artery in 21 patients and the circumflex artery in 5 patients. All the patients gave their informed consent to participate in the study.

### Study Protocol

Real-time myocardial contrast echocardiography was done  $7 \pm 4$  days after PTCA. Technetium-<sup>99m</sup>-sestamibi single photon emission computed tomography or MR with first-pass imaging and delayed hyperenhancement were done at rest in 18 and 32 patients, at an average  $30 \pm 26$  days after AMI, respectively. Echocardiography was done at the same time as myocardial perfusion and at  $10 \pm 4$  weeks later.

### Real-Time Myocardial Contrast Echocardiography

A Vivid 5 appliance (GE Medical Systems, Horten, Norway) was used to carry out the RTMCE with pulse inversion harmonic imaging and power Doppler ultrasound. Up to 3 intravenous injections of manually agitated FS-069 were administered slowly (Optison, Molecular Biosystems) and 8 ml of saline serum for 4 min each. Two-, four-, and 5-chamber apical images were acquired.

### Power Doppler Ultrasound Controls

A mechanical index of 0.1 was used throughout the study. The pulse repetition frequency was 2.5 kHz. The frequency of images per second (15.1 ips), dynamic range (6), the power of transmission ( $-20$ ), gain ( $-20\%$ ), image depth (12 cm), wall filter and color scale were kept constant. Focus was placed at the deepest level. When contrast was observed in the myocardial segments the mechanical index was increased to 1.2 ("flash") to ensure that this opacification was really true perfusion (and thus exclude artifacts). In the case of true perfusion, a progressive increase in opacification was observed in the myocardium during the following 3-15 cycles.

### Real-Time Myocardial Contrast Echocardiography Analysis

A 16-segment model was used to analyze the RTMCE. Each of the 16 segments was assigned to 1 of the 3 coronary arteries. The RTMCE was scored by 2 observers as follows: 0=absence of perfusion; 0.5=partial perfusion, and 1=complete perfusion. Grade 1 was

considered normal and degrees 0.5 and 0 abnormal. An RTMCE index was calculated for each patient according to the score obtained for each dysfunctional segment (hypokinetic, akinetic, or dyskkinetic).

### Analysis of Wall Motion

A regional (in the region of the culprit artery) and global wall motion index (WMSI) was calculated according to the 16-segment model.<sup>17</sup> Each segment was scored as: normal=1; hypokinetic=2; akinetic=3, and dyskkinetic=4. The left ventricular ejection fraction and ventricular volumes were measured using apical 2- and 4-chamber views.<sup>18</sup> A segment was considered to have improved when it changed from hypokinetic to normal or from akinetic to hypokinetic or normal from the baseline condition until follow-up. With regard to the patients, an improvement in at least 2 hypokinetic segments or 1 akinetic segment was required to be included in the functional recovery group.

### Technetium-<sup>99m</sup>-Sestamibi Single Photon Emission Computed Tomography (SPECT)

A SPECT was carried out in 18 patients at rest. The same 16-segment model was used to compare it to RTMCE. An independent observer for the RTMCE results scored each segment as normal or abnormal.

### First-Pass and Hyperenhancement With Delayed Contrast Magnetic Resonance

A first-pass and delayed hyperenhancement study was carried out in 32 patients. During the first-pass study perfusion defects can be produced by a coronary stenosis or by a reduction in microvascular flow,<sup>19-20</sup> whereas in gadolinium-delayed hyperenhancement they indicate irreversible damage.<sup>21</sup> For MR, the left ventricle was divided into 17 segments (6 basal, 6 mid-cavity, 4 mid-cavity/apical, and 1 apical segment).<sup>22</sup>

### Coronary Angiography

Angiographic data included stent implant, quantitative luminal narrowing after PTCA/stent in the culprit artery, angiographic TIMI flow,<sup>23</sup> the presence of collaterals to the culprit artery and the number of diseased vessels (luminal narrowing  $\geq 50\%$ ) after revascularization.

### Reproducibility of Real-Time Myocardial Contrast Echocardiography

Intraobserver and interobserver concordance for RTMCE was calculated for normal perfusion in the segment (versus abnormal perfusion in 20 randomized

patients). Intraobserver concordance was calculated by analyzing the images a second time after at least 60 days. Kappa coefficients are shown.

### Statistical Analysis

Standard software was used for statistical analysis (SPSS version 11.5, SPSS Inc., Chicago, Illinois). The mean  $\pm$  standard deviation (SD) is shown. Student *t* test was used to compare independent or paired data when required, and  $\chi^2$  test for comparing qualitative data. Receiver operating characteristic (ROC) curves were constructed to define the most precise perfusion values to predict functional recovery. The values of the area under the curve (AUC) are provided. Multivariable logistic regression analysis was carried out with the inclusion of those variables that were significant in the univariable analysis. *P*-values  $< .05$  were considered significant. The positive predictive value (PPV) and negative predictive value (NPV) were calculated for every cut-off value obtained with the ROC curves for the different techniques (RTMCE, delayed hyperenhanced MR, and SPECT). Positive predictive value (PPV) is defined as the quotient between the number of patients or segments with normal perfusion that recovered at follow-up and the total number of patients or segments with normal perfusion  $\times 100$ . Negative predictive value (NPV) is defined as the quotient between the number of patients or segments with abnormal perfusion that did not improve at follow-up and the total number patients or segments with abnormal perfusion  $\times 100$ . The percentage of concordance and kappa index were used to analyze concordance between the techniques used for segment evaluation. The intra-class correlation coefficient was used (Cronbach  $\alpha$ ) to determine whether the RTMCE score was similar to that of the SPECT and MR (delayed hyperenhancement).

## RESULTS

### Patient Characteristics

Follow-up data were available for 82 of the 85 patients (1 cardiac death and 2 untraceable patients). None of the 82 patients suffered events during follow-up. All of them were in a stable clinical condition and were taking platelet aggregation inhibitors, 63 (77%) were taking beta-blockers and 59 (72%), ACE inhibitors. We split the patients into 2 groups according to echocardiography at rest and at follow-up: the functional recovery group (n=49) and the group without functional recovery (n=33). Table 1 shows the clinical and angiographic characteristics, the number of non-perfused/hypoperfused segments and the perfusion index with RTMCE in both groups.

The only significant differences we found between groups were the peak CK value and the RTMCE values. Table 2 presents baseline ventricular function data and at follow-up.

### Segment Analysis Via RTMCE

In the baseline condition there were 380 dysfunctional segments (180 hypokinetic, 198 akinetic, and 2 dyskintetic) in the region of the culprit artery: 32 could not be evaluated via RTMCE (8%); 211 had normal perfusion; 36, a patchy pattern; and 101, absence of perfusion. Of the 380 dysfunctional segments, 296 corresponded to the anterior descending artery (78%), 63 to the right coronary artery (17%), and 21 to the circumflex artery (5%). At follow-up there were 252 dysfunctional segments in the region of the artery causing the heart attack (114 hypokinetic, 136 akinetic, and 2 dyskintetic). There was a

**TABLE 1. Clinical and Angiographic Data and Real-Time Myocardial Contrast Echocardiography (RTMCE) in the Recovery and Non-Recovery Groups\***

	Non-Recovery (n=33)	Recovery (n=49)	P
Age, years	61±11	59±11	NS
Male, n (%)	25 (76%)	42 (86%)	NS
Diabetes mellitus, dyslipidemia	7 (21%)	9 (19%)	NS
Number of coronary risk factors, n <sup>a</sup>	1.6±1.0	1.8±1.0	NS
Time from beginning of pain until PTCA, h	25±82	26±70	NS
Peak creatine kinase value, U/L	3.027±1.665	1.863±1.563	.002
Anterior infarct, n (%)	25 (76%)	31 (65%)	NS
Infarction with elevated ST segment, n (%)	32 (97%)	43 (88%)	NS
Fibrinolysis, n (%)	6 (18%)	13 (25%)	NS
Primary angioplasty, n (%)	26 (79%)	33 (67%)	NS
Stent use, n (%)	30 (91%)	47 (96%)	NS
Residual narrowing, %	9±16	3±15	NS
Postangioplasty TIMI flow	2.8±0.4	2.9±0.3	NS
Postangioplasty TIMI flow =2, %	5 (15%)	5 (10%)	NS
Presence of collateral circulation, n (%)	0 (0%)	0 (0%)	NS
Diseased vessels, postangioplasty, n	0.8±1.0	0.7±0.8	NS
ACE inhibitors at follow-up, %	25 (76%)	34 (69%)	NS
Beta-blockers at follow-up, %	27 (82%)	36 (75%)	NS
RTMCE score	0.59±0.39	0.85±0.26	.001
Defective segments under RTMCE, n	23±2.3	1.2±2.0	.05

\*PTCA indicates percutaneous transluminal coronary angioplasty; ACEI, angiotensin-converting enzyme inhibitors; NS, not significant.

<sup>a</sup>This included: arterial hypertension, baseline cholesterol >220 mg/100 mL, diabetes mellitus, smoking during the last 8 years and family history of ischemic heart disease.

**TABLE 2. Systolic Ventricular Function and Number of Dyssynergic Segments at Baseline and Follow-up in Both Groups\***

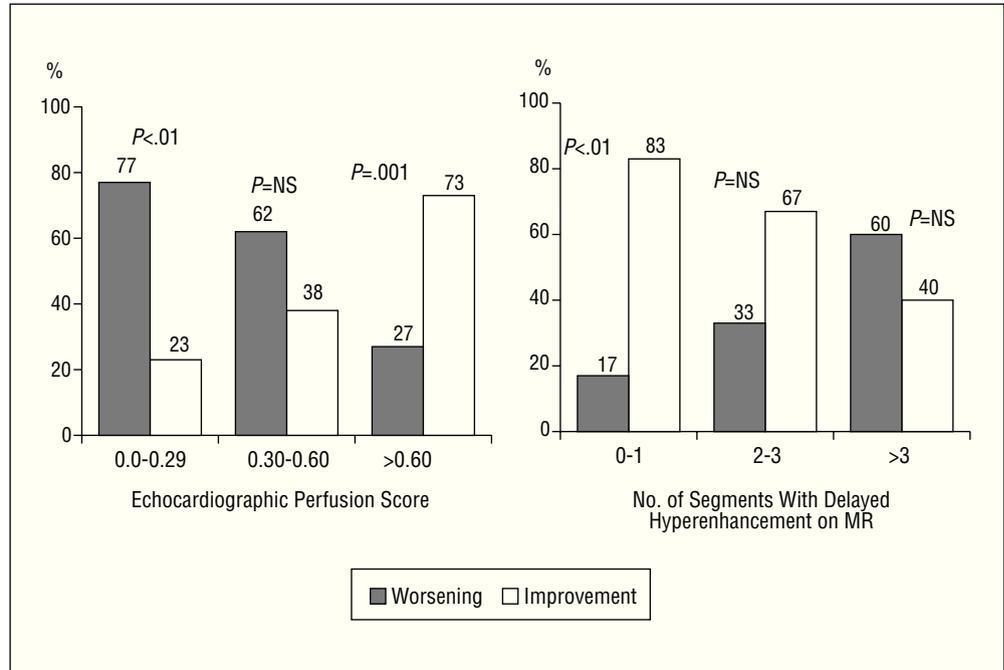
	Without Recovery (n=33)	Recovery (n=49)	P
Age, years	61±11	59±11	NS
Baseline ejection fraction	51±9	52±11	NS
Baseline LV end-diastolic volume, mL	74±24	74±14	NS
Baseline LV end-systolic volume, mL	37±20	35±12	NS
Baseline dyssynergic segments, n	4.7±1.9	4.3±2.7	NS
Baseline global WMSI	1.46±0.23	1.42±0.30	NS
Baseline regional WMSI	1.85±0.39	1.75±0.49	NS
Ejection fraction at follow-up	48±12	59±9	<.001
LV end-diastolic volume at follow-up, mL	88±29	80±15	NS
LV end-systolic volume at follow-up, mL	48±28	32±10	.004
dyssynergic segments at follow-up, n	4.8±1.7	2.0±2.2	.000
Global WMSI at follow-up	1.52±0.23	1.19±0.21	.000
Regional WMSI at follow-up	1.95±0.36	1.32±0.36	.000
Δ LV end-diastolic volume, mL	14±14	6±15	.021
Δ LV end-systolic volume, mL	10±14	-3±10	<.001
Δ ejection fraction*	-3±8	7±8	<.001

\*WMSI indicates wall motion score index; LV, left ventricle; NS, not significant.

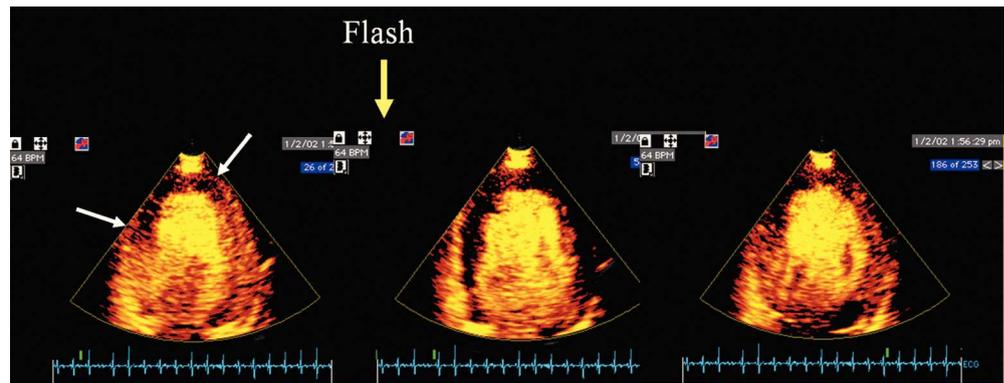
greater proportion of perfused dysfunctional segments that improved at follow-up than perfused or hypoperfused non-dysfunctional segments. Fifty-six percent of the perfused segments, 31% of the segments with patchy perfusion, and 28% of the segments without perfusion recovered ( $P<.001$  between perfused segments and hypoperfused or non-perfused segments). A similar percentage of hypokinetic and akinetic/dyskinetic segments recovered at follow-up (50% vs 39%). The sensitivity, specificity, PPV, NPV, and the diagnostic precision of RTMCE for detecting segment improvement were 74%, 51%, 56%, 71%, and 63%, respectively.

### Analysis of Real-Time Myocardial Contrast Echocardiography by Patients

An RTMCE score  $\geq 0.60$  was the most precise value to predict regional recovery, with a PPV of 73% and an NPV of 69% ( $P<.001$ ; AUC=0.70; 95% confidence interval [CI], 0.58-0.82), in the group of patients as a whole. In patients who had an anterior AMI, PPV, and NPV were 81% and 60%, respectively, ( $P<.01$ ; AUC=0.71; 95% CI, 0.57-0.85). Figure 1 shows the percentage of patients who recovered ventricular func-



**Fig. 1.** Percentage of patients who recovered and who did not recover regional ventricular function at follow-up according to the echocardiographic perfusion score (left) and the number of segments with delayed hyperenhancement under magnetic resonance (right).



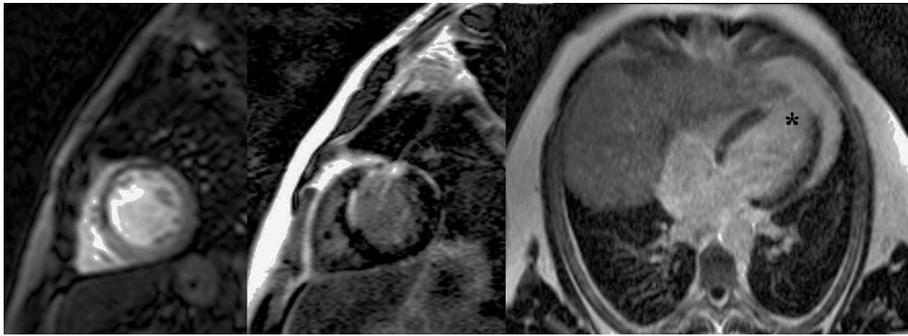
**Fig. 2.** Patient with “poor” echocardiographic perfusion score (<0.60) in the region of the descending anterior artery. Notice the wide perfusion defect (between arrows) before and after the “flash.”

tion and those who did not according to the different RTMCE scores. A logistic regression analysis was carried out introducing the 2 variables that were significant in the between-group comparison: peak CK value and the RTMCE score. Both were identified as independent predictors of functional recovery: peak CK value (odds ratio [OR] =1.4 per every 1000 U; 95% CI, 1.0-1.9;  $P < .05$ ); RTMCE score (OR=8.8; 95% CI, 1.9-39.3;  $P < .01$ ). Figures 2-7 show examples of patients with “poor” and “good” RTMCE scores, respectively.

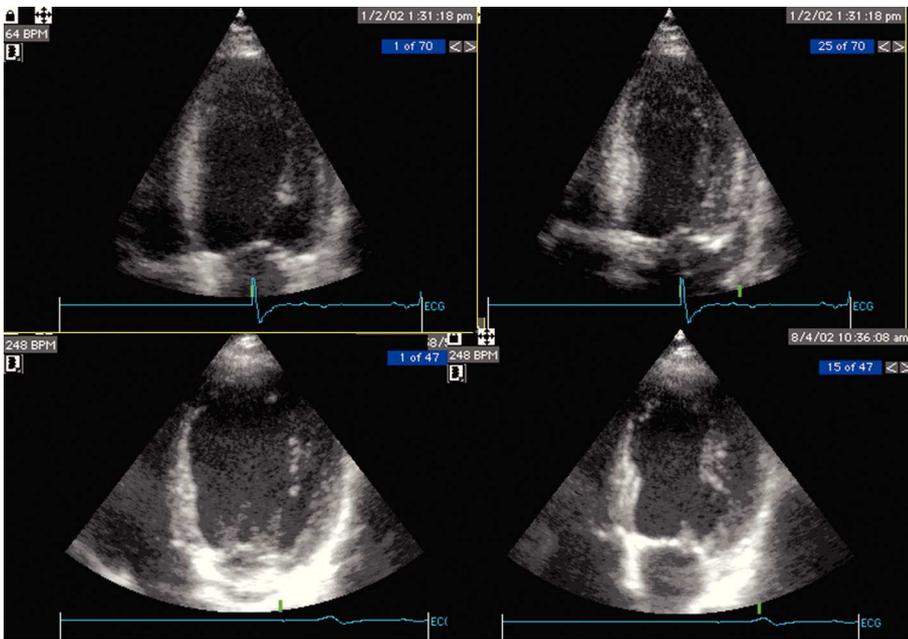
**Technetium-99m-Sestamibi Single Photon Emission Computed Tomography and MR Data**

Tables 3 and 4 show the perfusion score and the number of segments with perfusion defects with

SPECT and MR in both groups of patients. The finding of 4 or fewer perfusion defects with SPECT had a PPV of 85% and NPV of 100% for recovery of the left ventricular regional function ( $P < .01$ ; AUC=0.82; 95% CI, 0.53-1.10). Regarding MR, 47% of the patients had a segment with a first-pass perfusion defect, and 65% one with delayed hyperenhancement. Ninety-four percent of the patients with a first-pass defect also had delayed hyperenhancement in the same region, and the correlation between the number of segments with a first-pass defect and delayed hyperenhancement was significant ( $r=0.64$ ;  $P < .001$ ). However, the number of segments with a first-pass defect was of no use in differentiating the patients who recovered from those who did not. In contrast, the number of segments with delayed hyperenhancement was greater in those who did not recover re-



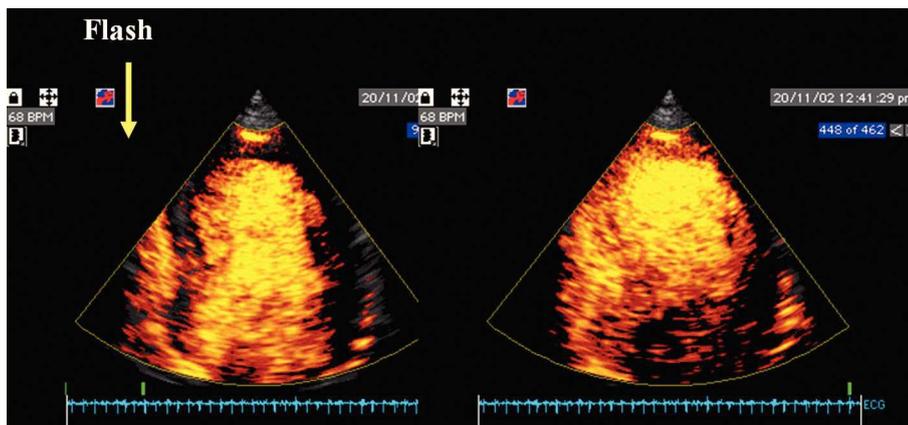
**Fig. 3.** Magnetic resonance images of the same patient as in Figure 2. A first-pass defect is evident in the intraventricular septum in the short-axis plane (arrows in left-hand image). Delayed hyperenhancement can be observed in the same area in the short-axis image (arrows in the middle image) and in the apical region in a longitudinal view (asterisk in the right-hand image).



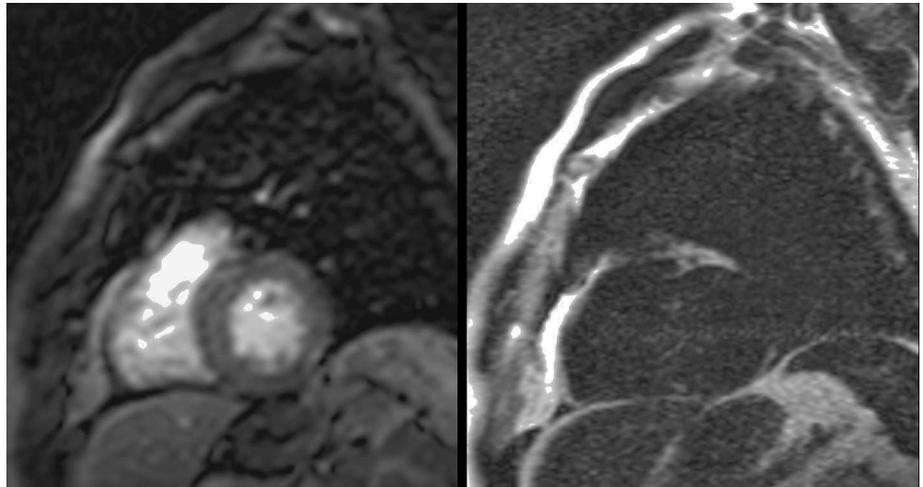
**Fig. 4.** The same patient as in Figure 2; the lack of recovery of left ventricular function is observed at follow-up. Above: baseline; below: follow-up; left: diastole; right: systole.

gional function. Findings of delayed hyperenhancement in less than 4 segments had a PPV of 80% and an NPV of 63% ( $P<.05$ ;  $AUC=0.73$ ; 95% CI, 0.54-0.91) for regional function recovery, whereas a score for the transmural extent of delayed hyperenhance-

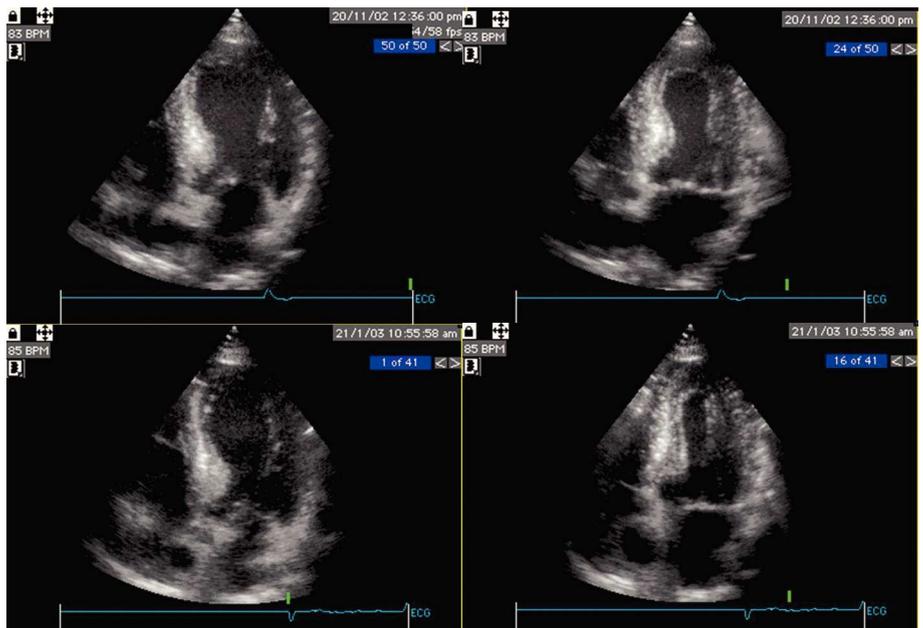
ment  $<1.6$  had a PPV of 81% and an NPV of 64% ( $P<.05$ ;  $AUC=0.71$ ; 95% CI, 0.52-0.91). Figure 1 shows the percentage of patients who recovered ventricular function and those who did not according to the number of segments observed with delayed hy-



**Fig. 5.** Patient with normal perfusion in the region of the anterior descending artery in the images after the "flash."



**Fig. 6.** Magnetic resonance images of the same patient as in Figure 5, in which no defects are observed in the first-pass study (left) or in the delayed hyperenhancement (right).



**Fig. 7.** The same patient as in Figure 5; notice the lack of recovery of left ventricular function at follow-up. Above: baseline; below: follow-up; left: diastole; right: systole.

perenhancement under MR. Figure 8 shows ROC curves for RTMCE and the MR (number of segments with delayed hyperenhancement).

**TABLE 3. SPECT in Patients With Recovery and Without Recovery of Ventricular Function at Follow-up\***

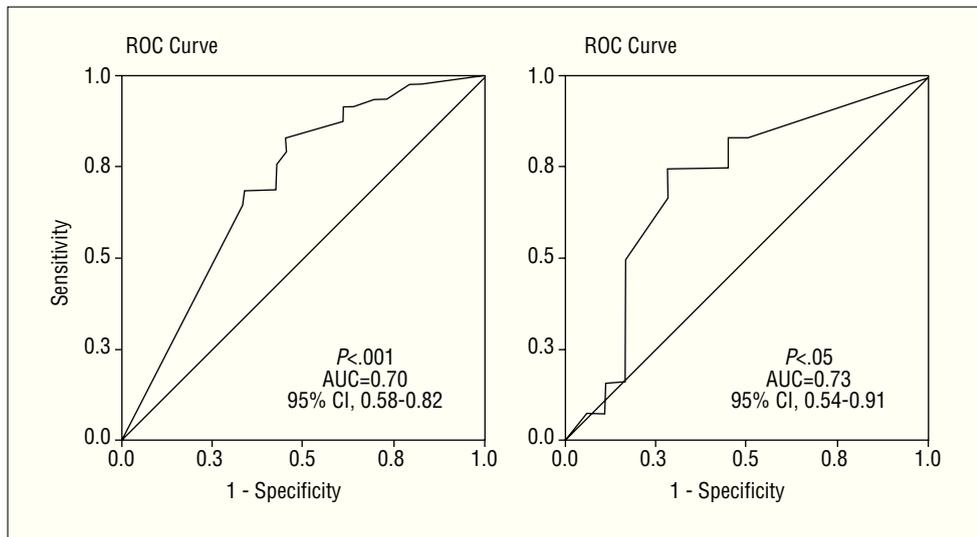
	Without Recovery (n=6)	Recovery (n=11)	P
Age, years	61±11	59±11	NS
Number of segments with perfusion defects, n	6.2±3.6	2.4±1.3	.046
Perfusion score with SPECT	0.7±0.2	0.9±0.1	.057

\*SPECT indicates technetium-99m-sestamibi single photon emission computed tomography.

**TABLE 4. Magnetic Resonance Imaging Data in the Patients Who Recovered Ventricular Function and Those Who Did Not During Follow-up\***

	Without Recovery (n=12)	Recovery (n=19)	P
Number of segments with first-pass defects, n	2.3±2.8	1.6±2.5	NS
Number of segments with delayed hyperenhancement	4.1±2.4	2.0±2.5	.037
Intramural extent of first-pass defect, %	19±22	15±18	NS
Intramural extent of delayed hyperenhancement, %	60±36	32±38	.055
Extent of delayed hyperenhancement score	3.1±2.3	1.5±2.3	.081

\*MR indicates magnetic resonance. Extent of delayed hyperenhancement score: mean intramural extension of delayed hyperenhancement multiplied by the number of affected segments/100.



**Fig. 8.** Receiver operating characteristic curves for prediction of recovery of regional function according to echocardiographic perfusion (left) and the number of segments with delayed hyperenhancement under magnetic resonance (right). CI indicates confidence interval.

### Comparison Between Real-Time Myocardial Contrast Echocardiography and Technetium-<sup>99m</sup>-Sestamibi Single Photon Emission Computed Tomography

The concordance between RTMCE and SPECT for the detection of abnormal perfusion versus normal perfusion in an analysis of the dysfunctional segments was 78% ( $P < .001$ ;  $\kappa = 0.49$ ), with a significant intraclass correlation in the perfusion scores with both techniques ( $\alpha = .79$ ;  $P < .01$ ; 95% CI, 0.45-0.92).

### Comparison Between Real-Time Myocardial Contrast Echocardiography and <sup>99m</sup>Tc-Sestamibi Single Photon Emission Computed Tomography

During an analysis of the dysfunctional segments, concordance between RTMCE and the findings of delayed hyperenhancement under MR was 70% ( $P < .001$ ;  $\kappa = 0.35$ ), although we did not find any intraclass correlation between the RTMCE score and the score for the transmural extent of delayed hyperenhancement ( $\alpha = -.2$ ;  $P = .7$ ; 95% CI, -1.6 to 0.42).

### Reproducibility of Real-Time Myocardial Contrast Echocardiography

The concordance between observers for the definition of a segment with normal or abnormal perfusion via RTMCE was 89% ( $P < .001$ ;  $\kappa = 0.70$ ), and 92% for intraobserver concordance ( $P < .001$ ;  $\kappa = 0.75$ ).

## DISCUSSION

The main points of interest in this study are: *a*) it was done with a broad series of patients with “reper-

fused” AMI (patent artery and TIMI flow  $\geq 2$ ), and *b*) it was compared with an innovative technique to study function and perfusion after AMI, such as MR. The main findings were:

1. Real-time myocardial contrast echocardiography is of moderate value to predict recovery of left ventricular function after AMI in an analysis by patient.
2. The RTMCE and the CK values have independent prognostic value for the recovery of left ventricular function.
3. The RTMCE is in moderate agreement with SPECT, but less so with the delayed hyperenhanced magnetic resonance study in AMI patients.

Most studies with perfusion echocardiography which have focused on the recovery of left ventricular function after AMI have used harmonic imaging with a high mechanical index,<sup>10-13</sup> whereas only a few have used a low mechanical index with a high frequency of images per second.<sup>24-26</sup> Intermittent harmonic imaging with a high mechanical index can be more sensitive, but is technically more difficult to carry out and normally requires higher doses of contrast agents.

### Predictive Value of Real-Time Myocardial Contrast Echocardiography

A low PPV for RTMCE has been previously described regarding functional recovery after AMI, and our study confirms this.<sup>24,25</sup> In the present article, RTMCE was carried out at least 2 days after AMI (mean,  $7 \pm 4$  days). It has been demonstrated that performing RTMCE earlier after AMI can cause underestimations of the actual area of hypoperfusion due to reactive hyperemia.<sup>27</sup> Thus, the time to carry out RTMCE appears to be correct for PPV. However, the NPV

obtained in our series was smaller than that reported in other studies. There might be different reasons for the false negative perfusion defects:

1. The time at which the RTMCE was carried out. If we had done the RTMCE later after the AMI, we would probably have achieved better results for the NPV. Some studies have reported a progressive improvement in the perfusion indexes due to recovery of microcirculation during the first months after AMI, which suggests the existence of recovery of microvasculature in some patients.<sup>28-30</sup>

2. On the other hand, the artifacts caused by attenuation and shadow due to the costal bones can explain some of the false negative defect.

3. Finally, in some cases, an insufficient quantity of the contrast agent may have been injected or it may have undergone massive destruction.

### **Technetium-<sup>99m</sup>-Sestamibi Single Photon Emission Computed Tomography and Magnetic Resonance**

Technetium-<sup>99m</sup>-sestamibi single photon emission computed tomography and MR were done on the average 4 weeks after RTMCE, which means that some perfusion defects observed in RTMCE might have recovered by the time SPECT or MR were done. Despite this, the concordance with SPECT was reasonable and suggested that RTMCE might be clinically useful to evaluate myocardial perfusion.

Previous studies have already reported a highly predictive value for SPECT for the recovery of left ventricular function after AMI,<sup>31</sup> as was found in our study. On the other hand, MR has not been widely studied. The first-pass defects that indicate coronary or microvascular obstruction have been associated with the lack of recovery of function in patients with AMI who underwent percutaneous revascularization.<sup>19</sup> In our study, first-pass defects were less frequent than delayed hyperenhancement, probably due to the elapsed time between the AMI and the MR study compared to RTMCE. The first-pass defects were not associated with the lack of functional recovery. However, the delayed hyperenhancement in the area of the infarction was usually observed in the group without functional recovery and was related to the lack of recovery, which was more probable the greater the intramural extent of the defect. A cut-off value of 37% for intramural extension had high sensitivity and specificity for the detection of viable myocardium in a previous study.<sup>32</sup> In our study, a cut-off value of 1.6 for the extension of the delayed hyperenhancement score had a PPV of 81% for the recovery. Delayed hyperenhancement indicating fibrosis has been associated with the lack of recovery in patients with chronic myocardial dysfunction who had undergone revascularization<sup>20,21,33</sup>

and in patients after AMI<sup>34</sup> It is also strongly correlated with viability determined via 18F-fluorodeoxyglucose positron emission tomography (PET).<sup>32</sup>

### **Limitations**

Segment analysis was similar with RTMCE and SPECT, but not with MR, due to the different segment configuration of the latter technique. The calculation of the baseline global and regional ventricular function and at follow-up was made through echocardiography for practical reasons. Although the reproducibility of MR is greater than that of echocardiography ( $\approx 4\%$  vs  $\approx 10\%$ ),<sup>35</sup> both the calculation of the ejection fraction and the volumes and the regional wall motion index with harmonic imaging have been satisfactorily correlated with MR and with gated-SPECT in several studies.<sup>36,37</sup>

We have already highlighted that SPECT and MR were done relatively late compared with RTMCE. Only a minority of the patients underwent SPECT and relatively few underwent MR, which means that we might have obtained extreme results.

We carried out an analysis based on the patient and an analysis based on the dyssynergic regions. From a practical standpoint, the first type of analysis seems more suited to the aim of knowing which patient has a greater probability of improving depending on the amount of non-perfused or hypoperfused myocardium. However, this aim would have had more impact if we had studied a population with more severe left ventricular dysfunction (e.g. only patients with anterior AMI and/or rescue PTCA).

Systematic coronary angiography was not done during follow-up, which means that we cannot exclude the probability of restenosis. However, the possibility of restenosis in the artery causing the heart attack at 2 months is relatively low.

Previous studies have described the drawbacks of RTMCE to suitably study the anterior and lateral wall of the left ventricle.<sup>27</sup> A poor lateral window might prevent the study of perfusion defects when the circumflex artery is causing the infarct, as occurred in three of our patients. Attenuation of the anterior wall could have impeded the study of perfusion at that level in patients with extensive infarcts due to the anterior descending artery, although the majority of anterior infarcts affected only or mainly the septoapical region.

### **CONCLUSIONS**

Real-time myocardial contrast echocardiography carried out before hospital discharge has a moderate predictive value for functional recovery after reperfused AMI. The RTMCE and SPECT findings were in agreement, but less so with those of MR. However, the delayed hyperenhancement findings had a reasonable

PPV for functional recovery. The relative value of RTMCE and MR after AMI remains to be determined, as well as the time after the acute event when such explorations should be carried out.

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