Full-Motion Pulse Inversion Power Doppler Contrast Echocardiography Differentiates Stunning From Necrosis and Predicts Recovery of Left Ventricular Function After Acute Myocardial Infarction

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OBJECTIVES
The goal of this study was to determine, in patients with a recent myocardial infarction (MI) and residual wall motion abnormalities within the distribution of the infarct-related artery, whether normal perfusion by myocardial contrast echocardiography (MCE) would accurately predict recovery of segmental left ventricular (LV) function.

BACKGROUND
Left ventricular dysfunction after acute MI may be secondary to myocardial stunning or necrosis. Recent technical innovations in contrast echocardiography, including pulse inversion imaging and power Doppler, now allow full-motion echocardiographic perfusion assessment from a venous injection of fluorocarbon-based contrast agent.

METHODS
Thirty-four patients with recent MI underwent baseline wall motion assessment and MCE two days after admission and follow-up echocardiography a mean of 55 days later.

RESULTS
Perfusion by MCE predicted recovery of segmental function with a sensitivity of 77%, specificity of 83%, positive predictive value of 90% and overall accuracy of 79%. The mean wall motion score at follow-up was significantly better in perfused, compared with nonperfused, segments (1.4 vs. 2.2, p < 0.0001). Additionally, 90% of perfused segments improved, while the majority of nonperfused segments remained unchanged.

CONCLUSIONS
Full-motion MCE utilizing an intravenous fluorocarbon-based agent and pulse inversion power Doppler techniques, identifies stunned myocardium, and accurately predicts recovery of segmental LV function in patients with recent MI. (J Am Coll Cardiol 2001; 38:1390–4) © 2001 by the American College of Cardiology

Left ventricular (LV) dysfunction after acute myocardial infarction (MI) may be secondary to myocardial stunning or necrosis. Since residual LV function is one of the primary determinants of long-term survival, differentiating between these two conditions is an important clinical goal. Unfortunately, no method for easily and accurately identifying myocardial viability at the bedside has been previously available.

Myocardial contrast echocardiography (MCE) has emerged as a promising technique for assessing microvascular perfusion in patients with coronary artery disease, including assessment of myocardial viability after MI (1). Although myocardial opacification using an intravenously injected fluorocarbon agent was first reported in an animal model in 1995 (2), attempts to apply MCE clinically have been disappointing due to technical limitations.

Recent echocardiographic innovations including pulse inversion imaging (3), power Doppler (4) and low mechanical index/high frame rate imaging (5) now allow full-motion echocardiographic perfusion assessment after intravenous injection of a fluorocarbon-based contrast agent. We hypothesized that in patients with recent MI and residual wall motion abnormalities within the distribution of the infarct-related artery (IRA), normal perfusion by full-motion MCE would accurately predict recovery of segmental LV function.

METHODS

Study design. We prospectively studied patients with recent MI. Inclusion criteria included: 1) recent confirmed MI, 2) angiographically identified IRA, and 3) wall motion abnormalities by echocardiography within the distribution of the IRA. The Institutional Review Board of St. Luke’s Hospital approved the study, and patients gave informed consent before participation.

Baseline echocardiography (BSE) and MCE were performed a mean of 2.2 days (range: 0 to 5 days) after hospital admission. All patients also underwent coronary angiography before or immediately after MCE. Patients returned 55 ± 20 days (range: 24 to 111 days) after the baseline examination for follow-up echocardiography (FUE) to assess recovery of function.

Patient population. Forty-two patients underwent baseline wall motion assessment and MCE after admission with MI. Three patients (all women with large anterior infarctions) died before follow-up, and five patients did not return. The remaining 34 patients (19 men, mean age 62 ± 12 years) comprised the study group.

The IRA was identified as the left anterior descending
coronary artery (LAD) in 20 patients, the right coronary artery (RCA) in six patients, the circumflex in three patients, saphenous vein graft (SVG)-LAD in three patients, SVG-RCA in one patient and diagonal branch in one patient. Coronary angiography identified single-vessel disease in 16 patients, two-vessel disease in 10 patients, and three-vessel disease in 8 patients. Antegrade flow was restored in the IRA by primary percutaneous coronary angioplasty in 22 patients, thrombolytic therapy in two patients and rescue angioplasty after failed thrombolysis in five patients. Of the remaining five patients, three underwent coronary artery bypass grafting to restore antegrade flow to the IRA; an occluded IRA (diagonal branch) was not intervened on in one patient, and the IRA was patent at angiography and did not require intervention in one patient.

Thrombolysis in myocardial infarction grade 3 flow was present in the IRA at angiography before or immediately after MCE in 30 patients; in the remaining four patients, the IRA was occluded or low-flow in two, and had presumably been restored in the other two by emergent coronary artery bypass grafting performed before MCE. With the exception of one patient who required repeat coronary intervention for subacute stent thrombosis, there were no significant adverse clinical events between MCE and FUE. Enzymatic evidence for recent myocardial necrosis (mean peak creatine phosphokinase = 2,307 IU/L) was present in all but one patient who was thought to have experienced a recent unrecognized MI.

**Echocardiography.** Imaging was performed using an ATL HDI 5000 echocardiography machine (ATL Ultrasound, Bothell, Washington). Baseline imaging was performed at the bedside in the left lateral decubitus position. If an intra-aortic balloon pump or arterial sheath was in place, imaging was performed with the patient supine. Standard apical views were obtained in all patients (four-chamber, two-chamber and apical long-axis), and supplemental parasternal imaging was performed if endocardial visualization was not optimal. Tissue harmonic imaging was utilized on BSE and FUE to enhance endocardial resolution. All images were stored on videotape and, in some cases, also digitally acquired and stored.

After acquisition of BSE, MCE was performed using pulse inversion imaging in power Doppler mode with a low mechanical index (Fig. 1). Specific instrumentation settings included the following: mechanical index 0.12 to 0.20 (usually 0.16), low dynamic range and maximal line density. These settings allowed a frame rate in excess of 20 Hz during perfusion imaging. Optison (Mallinkrodt, St. Louis, Missouri) was injected in slow bolus fashion (0.3 to 0.5 cc of contrast at approximately 1 cc/s) through a pre-existing intravenous catheter using a saline flush. The injection was terminated once contrast appeared in the right ventricular cavity. Separate injections were performed for each of the three apical views. A physician performed all contrast injections, with slight adjustments in contrast quantity and concentration.
bolus rate depending on the adequacy of an initial test injection in the apical four-chamber view. We attempted to inject the minimal amount of contrast necessary to achieve myocardial opacification outside the infarct zone, to avoid attenuation and blooming artifacts. Manually triggered, transient, high mechanical index imaging (“flash” imaging) was utilized at peak contrast intensity to destroy micro-bubbles within the myocardium, exclude artifact and observe myocardial replenishment (6). For frame rates greater than 20 Hz, five sequential flash frames were used.

Echocardiographic analysis. An experienced echocardiographer (A.M.) blinded to clinical and angiographic data scored all echocardiographic images. For each patient, baseline wall motion was first assessed followed by MCE scoring. Follow-up echocardiograms were evaluated at a separate sitting to avoid bias based on MCE results.

Baseline wall motion scoring was performed using the standard 16-segment American Society of Echocardiography model (7). Segments were scored as normal, hypokinetic or akinetic. Hypokinetic or akinetic segments within the distribution of the IRA were included in the subsequent analysis. Myocardial contrast echocardiography images were also scored using the standard 16-segment model with a similar semi-quantitative scoring scheme based on visual analysis as normally perfused, “patchy” perfusion or a perfusion defect (Fig. 2). On follow-up echocardiography, segments were again graded as normal, hypokinetic or akinetic. Segmental recovery of function was defined as improvement of at least one grade from the baseline to follow-up echocardiogram (akinetic to either hypokinetic or normal or hypokinetic to normal). Sensitivity, specificity, positive and negative predictive value and overall accuracy were calculated for recovery of function. Follow-up wall motion scores were analyzed using mixed effect analysis of variance, with a fixed effect of perfusion/no perfusion and random effect for subject. Segment recovery was analyzed using logistic regression. A p value <0.05 was deemed statistically significant.

RESULTS

All 16 myocardial segments were adequately visualized on baseline and follow-up wall motion assessment in all patients, and a total of 263 dysynergic segments were identified within the distribution of the IRA (7.7 ± 2.0 segments per patient). A total of 6% (n = 16) of segments were not adequately visualized during MCE. Thus, 247 dysynergic myocardial segments were available for complete analysis. At baseline, 83% (n = 204) of segments were akinetic, and 17% hypokinetic (n = 43). On follow-up imaging, 63% (n = 155) of segments were normal, 5% (n = 12) hypokinetic, and 32% (n = 80) akinetic; 32% (n = 80) were unchanged from baseline, while 22% (n = 53) improved one functional grade, and 46% (n = 114) improved from akinetic to normal.

Myocardial contrast echocardiography revealed normal perfusion in 47% (n = 116) of dysynergic segments, patchy perfusion in 11% (n = 27) and a perfusion defect in 42% (n = 104). The combined end point of either normal or patchy perfusion predicted segmental recovery of function with sensitivity 77%, specificity 83%, positive predictive value 90%, negative predictive value 63% and overall accuracy 79%.

Akinetic segments at baseline were also separately analyzed. Myocardial contrast echocardiography perfusion resulted in a significantly better mean wall motion score at follow-up (Fig. 3). Additionally, 90% of initially perfused segments improved at follow-up, while the majority of segments with a perfusion defect remained unchanged (Fig. 4).

DISCUSSION

Residual LV function after MI is a primary determinant of long-term survival. Additionally, patients with significantly
rical therapy might be particularly benefi

cation, identifying patients in whom aggressive med-

cratic myocardium early after infarction may aid in risk

arrhythmias. Thus, differentiation of stunned versus ne-

reduced ejection fraction are subject to increased complica-

ations including congestive heart failure and ventricular arrhythmias. Thus, differentiation of stunned versus ne-

crotic myocardium early after infarction may aid in risk stratification, identifying patients in whom aggressive med-

ical therapy might be particularly beneficial. In this study, we have demonstrated that “perfusion-contraction mis-

match” identified by MCE accurately detects stunned myo-

cardium and predicts spontaneous recovery of LV function in the recuperative period.

Comparison with previous studies. Ito and colleagues (8) first used MCE to define “no-reflow” after mechanical or pharmacologic revascularization in patients with acute an-

terior wall MI. Using intra-coronary injections of sonicated renografin, they identified lack of contrast effect in the infarct zone despite antegrade flow in the LAD in 23% of patients. This predicted lack of functional recovery, and patients with no-reflow were subsequently shown to have increased postinfarction complications (9). Since then, other investigators have corroborated these findings with intra-

1. JACC Vol. 38, No. 5, 2001

2. November 1, 2001:1390–4

Figure 4. Follow-up assessment of myocardial function in initially dysyn-

ergetic segments. A total of 90% of perfused segments improved, while the majority of nonperfused segments remained unchanged.

3. The use of semiquantitative visual analysis is a third limitation of our study. It is possible that quantitative techniques using videodensitometric analysis might improve overall accuracy. However, our high positive predictive value for recovery of function using visual assessment alone is a major strength.

4. Other modalities are available for assessment of myocardial viability after infarction. However, expense and need for radioactive isotopes and specialized licensure limits nuclear scintigraphy, and serial examinations are not feasible. Contr

5. actile reserve demonstrated by low-dose dobutamine echo-

6. cardiography is clinically useful (12,13,19,20), but studies cannot be performed in patients with acute infarction already requiring inotropic support. In contrast, MCE is an accurate, low-cost technique, easily performed at the bed-

7. side in critically ill patients. Despite rather adverse imaging conditions, approximately 95% of myocardial segments are assessable. Additionally, real-time, comprehensive evaluation of perfusion and function is feasible with MCE but not with any other currently available technique.

8. Conclusions. Full-motion MCE utilizing pulse inversion power Doppler techniques identifies stunned myocardium and accurately predicts recovery of segmental LV function in patients with recent MI.

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REFERENCES


3. Hope-Simpson D, Chin CT, Burns PN. Pulse inversion Doppler: a new method for detecting non-linear echoes from microbubble con-


7. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantification of the left ventricle by two-dimensional echocardiogra-


