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Early Changes in Myocardial Perfusion Patterns After Myocardial Infarction: Relation With Contractile Reserve and Functional Recovery

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Objectives. **The purpose of this study was to assess early temporal changes in myocardial perfusion pattern by myocardial contrast echocardiography (MCE) and their relation to myocardial viability in patients with reperfused acute myocardial infarction (AMI).**

Background. **Myocardial contrast echocardiography no-reflow is associated with poor contractile recovery after AMI. However, little is known regarding early reversibility of microvascular dysfunction and its relation to myocardial viability.**

Methods. **Intracoronary MCE was performed immediately after reflow and 9 days later in 28 patients with a first AMI and successful coronary recanalization (Thrombolysis in Myocardial Infarction trial grade 3 flow). Semiquantitative contrast score and wall motion score (WMS) were assessed in each initially asynergic segment at initial and repeat MCE study. Low dose dobutamine echocardiography (DE) was performed at day 10, and follow-up (FU) rest echocardiography was performed 6 weeks later.**

Results. **Among 200 initially asynergic segments, 49% exhibited no or heterogeneous contrast enhancement at initial MCE versus 24% at restudy ($p < 0.001$). Three groups of segments were defined according to early changes in contrast pattern: group A, "sustained no-reflow" ($n = 17$); group B, improved contrast score ($n = 68$), and group C, "sustained reflow" ($n = 112$). Group A segments showed no improvement in WMS at FU. In contrast, group B segments showed significant improvement in WMS at FU ($p < 0.0001$), and exhibited more frequently contractile reserve at DE (36% vs. 6%, $p = 0.02$) and contractile recovery at FU (34% vs. 7%, $p = 0.03$) than group A segments. Group C segments exhibited contractile reserve and contractile recovery in 47% and 51% of segments respectively.**

Conclusions. **Improvement in MCE perfusion pattern may occur after initial no-reflow in the days following reperfused AMI and is associated with preservation of contractile reserve and gradual regional functional recovery.**

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In acute myocardial infarction, successful coronary recanalization is not always associated with adequate restoration of myocardial perfusion (1). Even in patients without residual vessel obstruction, flow to the infarct myocardium may be markedly reduced, suggesting microvascular dysfunction ("no-reflow" or "low-reflow" phenomenon) (2–4). Recently, myocardial contrast echocardiography (MCE) studies have shown that the myocardial contrast pattern in the risk area immediately after recanalization of the infarct-related artery (IRA) reflects the extent of microvascular damage and is related to contractile recovery (4–6). Although not always associated with late functional improvement, microvascular integrity has been shown to be a prerequisite for myocardial viability (5,7,8). In contrast, no-reflow has been consistently associated with poor recovery of contractile function (4,5).

Although this relationship between the MCE pattern in the acute phase of AMI and myocardial viability is established, recent studies have shown that impairment of tissue perfusion may be observed early after reperfusion in viable postischemic heart muscle as well as in irreversibly damaged myocardium (9,10) and that impairment of tissue perfusion may be partially reversible in the first hours or days after coronary reflow (10–13). Late recovery of ischemic microvascular damage has also been demonstrated in patients in the convalescent stage of AMI (14). However, little is known about the early changes of segmental myocardial perfusion patterns in the days following reperfusion in humans and the relation between early improvement in microvascular perfusion and myocardial viability.

Thus, the aims of the study were to assess the temporal changes in myocardial perfusion patterns by myocardial contrast echocardiography in the early period following reperfused AMI and their relation to myocardial viability defined as late functional recovery and/or contractile reserve elicited by low dose dobutamine echocardiography.

Methods

Study population. The study population comprised 28 patients (26 men, 2 women; mean age: 50 ± 11 years) with a first

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Abbreviations and Acronyms

CK = creatine kinase
CSI = contrast score index
ECG = electrocardiographic
FU = follow-up
IRA = infarct-related artery
LDDE = low dose dobutamine echocardiography
MCE = myocardial contrast echocardiography
TIMI = Thrombolysis in Myocardial Infarction trial
WMS = wall motion score
WMSI = wall motion score index

acute transmural myocardial infarction and 1) complete angiographic patency of the IRA after primary percutaneous transluminal coronary angioplasty or thrombolysis (Thrombolysis in Myocardial Infarction trial [TIMI] grade 3 flow) obtained within 6 h of the onset of chest pain; and 2) adequate echocardiographic imaging quality. Exclusion criteria were hemodynamic instability, cardiogenic shock, previous myocardial infarction, history of coronary bypass surgery and more than 50% left main coronary artery stenosis. The diagnosis of acute myocardial infarction was based on typical chest pain of more than 30-min duration, resistant to sublingual or intravenous nitrates, associated with ST segment elevation of ≥1 mV in at least two adjacent electrocardiographic (ECG) leads. The diagnosis was eventually confirmed in all patients by elevation of creatine kinase (CK) at least twice above normal values.

Study protocol. Coronary angiography and primary angioplasty, if necessary, were performed immediately after admission or 90 min after thrombolytic therapy. Angioplasty success was defined as less than 30% residual stenosis and TIMI grade 3 flow.

Baseline left ventricular regional wall motion was assessed by two-dimensional echocardiography in the four standard parasternal and apical views immediately after completion of coronary angiography. Myocardial contrast echocardiography was performed 10 min after stable TIMI grade 3 flow in the IRA was established. Coronary angiography was repeated 9 days after infarction to assess patency of the IRA. Two-dimensional echocardiography and MCE were also repeated at this time in all the patients with the same protocol. Low dose dobutamine echocardiography (LDDE) was performed within 24 h of repeat angiography. A follow-up (FU) two-dimensional echocardiography was performed 6 weeks later to assess contractile function recovery. The protocol was approved by the institution Ethical Committee on human research, and all patients gave their informed consent to the study.

Management of acute myocardial infarction. All patients received aspirin (≥250 mg) and a bolus of intravenous heparin followed by a continuous infusion of 300 to 500 U/kg per day, titrated to maintain an activated partial thromboplastin time between 2 and 3. Patients received a second bolus of 5,000 U of heparin after the onset of coronary angioplasty. Other treatments (nitrates, beta-adrenergic blocking agents, angiotensin-converting enzyme inhibitors) were prescribed as needed; specifically all patients with anterior wall myocardial infarction or objective signs of left ventricular dysfunction received angiotensin-converting enzyme inhibitors.

Echocardiographic studies. All echocardiographic data were recorded using a commercially available phased-array system (Sonos 1500, Hewlett-Packard, 2.5-MHz transducer). Echocardiographic images were recorded on S-VHS videotapes for off-line analysis. In each patient, the same four standard parasternal and apical views were obtained for all echocardiographic studies.

Baseline two-dimensional echocardiography and MCE were performed in the catheterization laboratory with patient lying supine, a foam wedge under his right shoulder to obtain a lateral rotation of the thorax of approximately 30°.

Myocardial contrast echocardiography was performed 10 min after stable TIMI grade 3 flow in the IRA was obtained, by injecting 3 ml of sonicated Ioxaglate (Hexabrix 320, Guerbet, France) into the left main and right coronary arteries. One separate contrast injection was used for each of the four standard views to examine all myocardial segments. Echocardiographic images were recorded from 10 s before the injection until disappearance of myocardial contrast enhancement, with constant gain settings.

Low dose dobutamine echocardiography was performed 10 days after admission. After baseline echocardiography, dobutamine was infused in increments of 5, 10 and 15 $\mu g \cdot kg^{-1} \cdot min^{-1}$ IV at 5-min intervals. Echocardiographic standard-view images were recorded at baseline and during the last 2 min of each dobutamine infusion level. Echocardiographic images were continuously recorded on videotapes and digitized on-line in a quad-screen cineloop format (Freeland-Tomtec software). A 12-lead electrocardiogram and arterial blood pressure were recorded at baseline and at the end of each stage.

Echocardiographic analysis. According to the recommendations of the American Society of Echocardiography, a 16-segment left ventricular model was used for analysis of all echocardiographic data (baseline, LDDE, MCE and FU studies) (15). For the purpose of this study, myocardial risk area was defined as the area of abnormal wall motion (hypokinetic, akinetic or dyskinetic segments) in multiple tomographic planes in the acute phase of myocardial infarction.

Myocardial contrast echocardiography. Myocardial contrast echocardiography images were analyzed off-line from the videotape recording by consensus reading of two observers, blinded to wall motion scores and unaware of clinical and angiographic data. The contrast effect was graded in each initially hypo- or akinetic segment using a previously described semiquantitative contrast score (5): 0, no opacification; 0.5, heterogeneous pattern in the entire segment or opacification noted only in epicardium; 1, homogeneous opacification. In each patient, the contrast score index (CSI) for the dyssynergic area was calculated by dividing the sum of the contrast scores for individual segments within this area by the number of dyssynergic segments (5).

Myocardial segments were classified in three groups on the