Myocardial contrast echocardiography in the assessment of pharmacologic intervention of the reperfusion injury

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Treatment of patients with an acute myocardial infarction (AMI) aims at timely restoration of adequate flow in the infarct related coronary artery. Percutaneous coronary intervention (PCI) has been shown to be superior compared to thrombolysis in terms of achieving immediate and long term patency of the epicardial artery. The adequacy of myocardial perfusion in acute infarction, however, also depends on the integrity of the distal circulation. In recent years, it has become clear that in a substantial percentage of patients, even in the presence of adequate epicardial coronary flow, lack of microvascular reperfusion may be observed. This event has been described as the no-reflow phenomenon. In this situation distal embolization of platelet aggregates, release of vasoconstrictive platelet mediators and/or microvascular reperfusion injury due to cardiac inflammatory responses, compromise the perfusion at the microcirculatory level.

In this issue, Petronio et al. describe the effect of abciximab on microvascular perfusion and recovery of left ventricular function in 31 patients who underwent PCI in the setting of an acute myocardial infarction. Patients were randomized to abciximab or placebo before reperfusion and a coronary stent was always implanted. To evaluate microvascular integrity, intracoronary (IC) myocardial contrast echocardiography (MCE) was performed immediately after PCI, and intravenous MCE at 48 h and at 1 month. In patients treated with abciximab, the authors more often found homogeneous myocardial contrast enhancement than in those treated with placebo. This improved microvascular integrity was observed immediately after PCI and remained consistent at the follow-up studies. At 1 month follow-up, more complete recovery of regional and global left ventricular function was found in the abciximab group compared to the placebo group.

This small study is interesting since it uses the technique of MCE in the assessment of a treatment strategy to reduce no-reflow. Myocardial contrast echocardiography has extended our knowledge of microvascular perfusion and has provided useful information for predicting the success of reperfusion therapy at the microcirculatory level. Ito et al. were one of the first to demonstrate that an apparent discrepancy may exist between perfusion at the myocardial level and the epicardial coronary flow. The extent of the contrast defect, as measured by endocardial length of residual defect, has been shown to be a prognostic index to determine the extent of myocardial salvage and recovery of left ventricular function after reperfusion therapy in patients with AMI. Myocardial perfusion evaluated by intravenous MCE corresponds to results on microcirculatory function, as assessed by coronary flow reserve measurements with an IC Doppler wire. The potential role of MCE to predict viability of myocardium has been evaluated. Intense homogeneous contrast enhancement after IC administration of a contrast agent predicts myocardial viability with a high sensitivity and specificity. The optimal time to estimate microvascular integrity for predicting myocardial viability is probably one day after recanalization; measurements shortly after recanalization or during the convalescent...
stage were found less predictive due to hyperemia.8

Contrast echocardiography has made significant advances in the past decade, due to developments of contrast agents and ultrasonic modalities such as intermittent harmonic imaging, resulting in improved contrast detection after intravenous administration. Before this technique is ready for widespread application in the assessment of the no-reflow in clinical practice, a number of hurdles have to be overcome, viz. optimal echocardiographic machine settings, which probably are dependent on the applied contrast agent. Little is known whether the images obtained after IC injection and after IV injection are fully comparable. The reproducibility of MCE needs to be established in larger studies. Currently, only a semiquantitative analysis of contrast images is possible in clinical practice. The inferior wall regularly yields suboptimal opacification. A better estimate of ultimate infarct size might be possible when pharmacological vasodilation is used as an adjunct to the application of contrast material following reperfusion.9

It has consistently become clear that perfusion patterns are closely linked to the recovery of contraction in the infarct region. An important challenge for the coming years will be the development of agents that can reduce no-reflow. A number of agents have been tested in animal models, including drugs with vasodilating effects, such as adenosine, papaverine or calcium antagonists; in the clinical situation some of these agents also had a beneficial effect. Recently a number of clinical studies have shown that glycoprotein IIb/IIIa receptor blockade in conjunction with thrombolytics or PCI may not only maintain patency of the recanalized vessel but also improve microvascular function.10,11 Many other pharmacologic treatments, including strategies applied prior to reperfusion are currently under investigation. At this time, intracoronary devices for prevention of microembolization are also being investigated in the setting of AMI.

MCE is a low cost tool, which can easily be performed by peripheral venous injection at the bedside, even in critically ill patients. Thus, as a widely used research tool, for studying the effect of current and future treatment strategies on microcirculatory reperfusion, its future is bright.

References