When anterograde flow is restored to an occluded coronary artery in patients with acute myocardial infarction (AMI), it is generally presumed that flow is also restored to the myocardium. The article by Ito et al in this issue of Circulation reports that myocardial perfusion is absent in about one fourth of their population of patients with AMI despite reflow being achieved in the occluded vessel within 6 hours of onset of symptoms. In this study, myocardial contrast echocardiography (MCE) was used at the time of emergent cardiac catheterization to assess myocardial perfusion before and 15 minutes after successful reflow to the occluded coronary artery. This is the first published study demonstrating the no reflow phenomenon in patients with AMI using MCE.

Another study by Kloner and colleagues also suggests that myocellular necrosis may precede microvascular damage, and that the latter may be a predictor of infarct size. It is, therefore, probable that the presence of no reflow in the study by Ito and colleagues identified patients with larger infarcts and hence, those least likely to demonstrate myocardial salvage. In a study from our laboratory in which flow was established within an occluded vessel several days after an AMI, patients with no reflow on MCE had the largest infarcts by cardiac enzymes.

In a study using a canine model of coronary occlusion followed by reperfusion, Kemper and colleagues first suggested the possibility of using MCE to define the success of reperfusion. These authors demonstrated that when contrast was injected into the aortic root during coronary occlusion, the MCE-defined risk area correlated well with that defined on postmortem technetium autoradiography. After the occlusion was reversed and contrast was reinjected into the aortic root, the myocardial contrast defect correlated well with infarct size. In preliminary studies, similar results have been observed in our laboratory from both left and right atrial injection of contrast. MCE, therefore, offers the unique opportunity of defining in vivo the risk area during acute coronary occlusion and infarct size after reperfusion.

A limitation of the study by Ito and colleagues is that they defined risk area in the apical two-chamber view using only left main coronary artery injection of contrast. As such, right-to-left collaterals were not demonstrated during MCE by using their method, and hence, the functional risk area was likely overestimated. We have shown that most MCE-defined collateral flow to the occluded left anterior descending coronary artery bed in patients with coronary artery disease comes from the right coronary artery and that MCE is superior to coronary angiography in defining collateral flow. Because some degree of perfusion is maintained during coronary occlusion to regions supplied by collateral flow, these regions escape the extreme ravages of ischemia and hence do not demonstrate the no reflow phenomenon after successful reperfusion. Similar results have been reported in canine studies using other techniques. Demonstration of collateral flow before reperfusion might, therefore, predict the absence of no

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From the Division of Cardiology, Department of Medicine, University of Virginia, Charlottesville.

Address for reprints: Sanjiv Kaul, MD, Division of Cardiology, Box 158, University of Virginia, Charlottesville, VA 22908.
reeflow phenomenon and hence, the likelihood of myocardial salvage after reperfusion.

In the report by Ito and colleagues, the region most likely to demonstrate the no reflow phenomenon was the left ventricular apex. The myocardium in this region is the thinnest and is poorly supplied by blood vessels; therefore, it is not surprising that it is most likely to undergo myocardial necrosis. We have previously demonstrated that even after successful early reperfusion, recovery of function is least likely to occur in the apex. Apical no reflow is, therefore, very likely to occur in all left anterior descending coronary artery infarcts. Of clinical relevance would be the demonstration of this phenomenon in other regions of the left ventricular myocardium.

An issue not addressed by Ito and colleagues is the proper timing of MCE after attempted reperfusion. The patients in their study who showed myocardial perfusion after reflow also had myocardial necrosis. The injection of contrast 15 minutes after reflow may have underestimated infarct size in these patients. It has been demonstrated in the canine model that hyperemia is present initially after reflow in regions that several hours later demonstrate the no reflow phenomenon. This hyperemia may, therefore, mask the degree of underlying myocardial necrosis when a marker of flow is used to assess myocardial salvage immediately after reperfusion. It may take several hours before a flow marker can accurately define the region with no reflow. On the other hand, imaging the heart days after reperfusion may not be very useful, because flow ultimately improves within regions initially showing no reflow. It is likely that after reperfusion, microvascular plugging increases over several hours, resulting in progressive decrease in flow to the infarct zone. With time, either the microvascular injury partially reverses, or new vessels are formed to increase flow to the infarct zone.

The best time to image after reperfusion with a flow marker to determine infarct size is, therefore, not known. One way to determine infarct size and hence the degree of myocardial salvage without having to worry about the timing of imaging may be to inject contrast just after reperfusion in the presence of intravenously administered diprydamole. In this situation, despite the presence of hyperemia in the infarcted bed, the noninfarcted beds will demonstrate more flow, resulting in relatively lower flow within the infarcted bed. Because regions that ultimately develop the no reflow phenomenon have impaired coronary blood flow reserve soon after reperfusion compared with regions that have been salvaged, such an approach seems logical. In fact, we have used it successfully for predicting actual infarct size in the canine model even after 15 minutes of reflow.

The report by Ito and colleagues in this issue of *Circulation* indicates that the determination of myocardial perfusion is necessary to indicate the degree of success achieved by reperfusion. Observing restoration of anterograde flow to an infarct-related artery alone is not sufficient to determine how well the myocardium has been reperfused. The results of this study are in close agreement with previous animal studies using MCE and other techniques for estimating blood flow during coronary occlusion and reperfusion. Because MCE can be used as an adjunct to cardiac catheterization, it could be used in patients undergoing reperfusion in the cardiac catheterization laboratory. Most patients, however, undergo reperfusion either in the emergency room or the coronary care unit. Because it requires an intra-arterial injection of contrast, MCE cannot be used in such patients at the present time. However, with the possibility of achieving myocardial opacification from a venous injection of contrast, MCE may find increasing use in determining the success of reperfusion therapy in patients with AMI. In the meantime, one should not forget that an open infarct-related artery does not necessarily imply the presence of myocardial perfusion.

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Is the determination of myocardial perfusion necessary to evaluate the success of reperfusion when the infarct-related artery is open?

S Kaul and F S Villanueva

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