Assessing the Myocardium After Attempted Reperfusion
Should We Bother?

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In patients with AMI who have undergone attempted reperfusion, two questions need to be answered. The first, and the most obvious, is whether the myocardium has been successfully reperfused. The second, and perhaps equally important, is how much of the myocardium has been salvaged, and how much can still potentially be salvaged? To answer these questions, one must have the tools to accurately assess myocardial perfusion and infarct size. The ultimate indicator of tissue perfusion is capillary flow, whereas that of myocardial infarction is myocyte necrosis. The farther we deviate from a direct assessment of these indicators, the more imprecise we become. The Figure depicts the findings generally used in the clinical setting to determine whether reperfusion has actually occurred and the extent of myocardial salvage achieved.

Although the presence of a wall motion abnormality is valuable for the diagnosis of prior infarction and resting or inducible ischemia,1 it is of limited value in patients with AMI who have recently undergone reperfusion therapy. In these patients, a wall motion abnormality is likely to be present whether or not reperfusion has been successful. Regional function will be normal only if the period of ischemia was very short (minutes), which is uncommon in the clinical setting. The degree of wall thickening also does not reflect the transmural extent of myocardial necrosis because dysfunction may be present in the noninfarcted reperfused tissue.1 For the same reason, the circumferential extent of a wall motion abnormality also does not reflect infarct size. Thus, only when the wall motion abnormality is localized to a small region of the myocardium is a sizable infarction excluded.1

The ECG is a useful clinical tool in the diagnosis of acute ischemic syndromes. Its role in determining the success of reperfusion or the extent of myocardial salvage, however, is less valuable.2,3 While resolution of ST-segment elevation can reflect the transmural extent of myocardial necrosis because dysfunction may be present in the noninfarcted reperfused tissue,1 for the same reason, the circumferential extent of a wall motion abnormality also does not reflect infarct size. Thus, only when the wall motion abnormality is localized to a small region of the myocardium is a sizable infarction excluded.1

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these exciting results create a potentially new treatment strategy for patients with AMI who have undergone reperfusion therapy.

Because of reactive hyperemia, however, caution needs to be exercised in the interpretation of MCE data immediately after attempted reperfusion. Depending on the extent of the hyperemic response (which is determined by the amount of microvascular damage and the severity of residual stenosis), the low-reflow phenomenon can be underestimated by MCE or any other method used to assess MBF. The microvasculature in normal tissue has flow reserve in excess of that in the infarcted tissue. Therefore, when a coronary vasodilator is administered, the increase in MBF caused by reactive hyperemia within the infarcted tissue is less than that caused by the vasodilator in normal tissue. The region of relative hypoperfusion in the presence of a coronary vasodilator has consequently been shown to accurately reflect infarct size after early reperfusion. Additionally, although resting MBF in the infarct bed fluctuates wildly within the first few hours after reflow, the flow reserve within the bed remains remarkably stable and could be used as an indicator of the integrity of the myocardial microvasculature. This may be another reason to use coronary vasodilators after attempted reperfusion. The safety of these agents in the early stages of AMI, however, needs to be demonstrated.

The current methods of evaluating infarct size are indirect and do not provide a complete assessment of the pathophysiology of AMI. For example, even if cardiac enzymes do provide an accurate estimate of infarct size, they do so without reference to the risk area. A transmural infarct within a small risk area has different implications than a similarly sized infarct within a large risk area. A transmural infarct will expand and can result in significant left ventricular dilation and heart failure. Being buttressed by normal tissue, a nontransmural infarct is less likely to result in these sequelae. Perhaps in the former situation, ACE inhibitors are most helpful, and they may not even be necessary in the latter situation. Cardiac enzyme determinations and the ECG cannot be used reliably to address these important pathophysiological questions.

After reperfusion, although loss and damage of capillaries within an infarct zone (no reflow) can provide an estimation of infarct size by MCE, this assessment is still indirect. A more direct delineation of infarct size could ensue from examination of myocardial tissue itself. It is in this regard that the article by Mujisilovic and colleagues in this issue of Circulation is of interest. This article is an example in which experimental data provide a biological basis for clinical findings. These authors have shown that wavelet image decomposition of ultrasound images can be used to separate necrotic from nonnecrotic tissue, although the emphasis of the article has been incorrectly placed on the detection of successful reperfusion. Because timely reperfusion is associated with less infarction, the method can by inference define patients with successful reperfusion. On the basis of the present discussion, however, MCE would be a better method to determine the success of reperfusion.

Texture analysis has been used in echocardiography for almost 2 decades and is based on alterations in myocardial tissue structure and composition caused by disease. The most obvious example in coronary artery disease is the thin, highly echogenic muscle occasionally seen in patients with old infarction. Changes that are visually less obvious can be documented by use of measurements of acoustic intensity and cyclic variation in integrated backscatter or by higher-order statistical analysis of backscatter. These procedures, however, have not entered the mainstream of echocardiography because they are not robust enough for routine clinical use. The acoustic properties of tissue on transthoracic echocardiography are affected as much by intervening tissue and lungs as by the disease process itself. The methods are also tedious and time-consuming, making them less attractive for routine clinical use.

We have observed increases in tissue echogenicity in patients with recent (weeks to months) myocardial infarction on harmonic imaging, which is not obvious on routine fundamental imaging. This increase in echogenicity can be a source of error for MCE because the entire myocardium may appear opacified after a venous injection of microbubbles, giving an impression that there is normal and homogeneous perfusion in all myocardial segments. Only on examination of the precontrast image does it become apparent that the video intensity is already increased in the infarct bed before administration of microbubbles. That the video intensity does not change in the infarct bed after microbubble injection to the same degree as within the normal bed becomes apparent on image subtraction and color coding or on quantification of myocardial video intensities. The reason for increased signals from infarcted tissue on harmonic imaging could be related to greater nonlinearity in acoustic properties of abnormal versus normal tissue and/or a higher signal-to-noise ratio. Tissue characterization with harmonic imaging therefore appears promising in determining infarct size when the injury is days to weeks old and changes in the composition and structure of the extracellular matrix have occurred. Whether similar information can be obtained immediately after reflow needs to be investigated. Furthermore, the superiority of tissue characterization for measuring infarct size over the more easily available information regarding zones with no reflow or low reflow will need to be demonstrated before it is to become accepted as a clinical tool.

Given that we may now have tools that can assess both tissue perfusion and infarct size with echocardiography, how can these be used in patients with AMI? First, it is important to define the risk area in a patient with AMI. If the risk area is small because of occlusion of a small artery or abundant collateral flow, initial treatment can be conservative. If the risk area is moderate to large, thrombolysis or mechanical reperfusion should be immediately instituted. Myocardial perfusion should be reassessed immediately thereafter. If

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Selected Abbreviations and Acronyms

AMI = acute myocardial infarction
MBF = myocardial blood flow
MCE = myocardial contrast echocardiography
TIMI = Thrombolysis in Myocardial Infarction

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after attempted thrombolysis the size of the risk area is unchanged, it denotes unsuccessful reperfusion, and a case for rescue coronary angioplasty could be made in selected patients.

Complete or nearly complete myocardial opacification of the infarct zone after attempted reperfusion would indicate either almost complete myocardial salvage or an underestimation of infarct size because of reactive hyperemia. Use of a coronary vasodilator could resolve this dilemma. If a region of reduced flow is seen within the infarct bed after reperfusion (with or without a vasodilator), pharmacological therapy aimed toward reversal of microvascular dysfunction could be initiated. MCE could then be repeated to determine if the zone of reduced perfusion has decreased in size. If infarction is transmural (based on no reflow on MCE or abnormal patterns on tissue characterization), ACE inhibitors could be initiated, regardless of global left ventricular function. If the infarction is limited to the endocardial one third of the myocardium, ACE inhibitors may not be necessary unless there is global left ventricular dysfunction from remote infarction or other pathologies.

Although all the scenarios described above represent hypotheses, each appears plausible, given our knowledge of the pathophysiology of AMI. With the methods described here, these hypotheses can be tested in small (hundreds rather than tens of thousands) numbers of patients without mortality as the end point. Because each patient with AMI is different, the newer methods described here have the potential to provide unique and valuable information regarding the reperfused myocardium on a patient-by-patient basis, which can then be used to individualize and optimize patient management. Although this editorial has focussed primarily on echocardiography, the principles discussed could be applied to other techniques that can image regional myocardial perfusion and function. The tools are becoming available. It is now time to apply them.

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