Beyond TIMI III Flow

Terry R. Bowers, MD; William W. O’Neill, MD

With the widespread use of catheter-based reperfusion therapies, an ideal opportunity exists to use more sophisticated invasive modalities to overcome the imprecision of angiographic flow and to characterize myocardial perfusion more accurately. These findings will hopefully allow more precise prediction of the potential for myocardial salvage in individual patients. These modalities can be divided into methods that characterize impaired perfusion due to persistent epicardial obstruction using either coronary vasodilatory reserve (CFR) or translesional-pressure derived fractional flow reserve (FFR) and into methods that characterize microcirculatory perfusion using Doppler flow patterns and myocardial contrast echocardiography (MCE).

Doppler-tipped angioplasty guidewires measure coronary blood flow velocity, and they provide a means to quantitatively measure infarct artery velocity and CFR. CFR is a well-established measure of the physiological significance of an epicardial stenosis, both before and after elective coronary intervention. The application of this technique to patients with acute MI has been limited because CFR measures the summed functional status of the coronary conduit and the distal microvascular bed. Unfortunately, microvascular abnormalities are often present in myocardium exposed to prolonged ischemia due to a multitude of processes that result in resistance vessel dysfunction; these include tissue edema, platelet plugging, neutrophil adhesion, and myonecrosis. This makes intermediate lesion assessment during or after MI complex because of our inability to decipher the contributions of the microcirculatory abnormalities and the hemodynamic contributions of the stenosis when the CFR is abnormal.

Relative CFR, the ratio of the CFR in the target vessel to the CFR in a “normal” reference artery, has been proposed as a way to identify coexistent microvascular disease. An evaluation of the flow reserve in the reference artery will help identify preexistent microcirculatory abnormalities, yet prolonged ischemia will create new influences on the microcirculation in the target vessel, which will continue to confound interpretation. In addition, compensatory hyperkinesis of the noninfarct zone places demands on the reference artery that can confound interpretation of velocity measures in this vessel. Thus, relative CFR has broadened the application of this measurement to include diabetics and hypertensives, yet it remains clinically useful in MI patients only when it is normal.

Akasaka et al have identified phasic flow patterns that seem to differentiate patients with residual flow-limiting obstructions from those with severe microvascular injury leading to persistent slow reflow. These novel flow patterns, which focus on the diastolic predominance of flow and the presence of systolic flow reversal, will need to be applied to a broader range of patients and correlated with functional...
recovery to determine the true predictive value of these findings.

An additional promising catheter-based method to evaluate the hemodynamic significance of a stenosis in the face of a MI is the assessment of the FFR of the myocardium. FFR represents the maximal flow across the stenosis compared with the theoretical maximal flow in the vessel without a stenosis, and it is calculated as the distal mean coronary pressure (measured with an 0.014-inch pressure wire during maximal hyperemia) divided by the simultaneous mean aortic pressure. FFR, unlike CFR, is independent of changes in heart rate, blood pressure, contractility, and microvascular influences. For this reason, this technique will likely emerge as a reliable and easy method to assess the functional significance of intermediate lesions in the peri-MI period. Further study is necessary to ensure that the FFR can be used for clinical decision-making in individual patients with acute MI.

The application of Doppler-derived CFR after infarct angioplasty to assess myocardial viability and predict myocardial functional recovery has evolved, despite initial observations that the vasodilator reserve is severely impaired immediately after reperfusion, even with a widely patent infarct artery and TIMI 3 flow. The time course of this abnormal vasodilatory reserve varies in each patient, and it remains impaired for up to 6 months. Interestingly, impaired CFR after infarct angioplasty did not correlate with impaired regional wall motion at the time of assessment. However, the CFR measured after revascularization was significantly related to the recovery of regional myocardial contractility. CFR measurements after MI seem to be more linked to viability than contractility.

In clinical practice, a reference threshold for CFR to sharply define myocardial viability has not been developed because of the wide range of values in patients with angiographic TIMI 3 flow. Stenting eliminates the flow-limiting obstruction of the infarct artery, and in one small series, it led to consistent early and sustained near-normalization of CFR and myocardial functional recovery. However, Akasaka et al identified a flow pattern, systolic flow reversal, that was associated with impaired coronary flow reserve and poor wall motion recovery at 1 month, even after stent implantation. This finding cautions against primary stenting without an understanding of the effect of the microvascular injury in the individual patient. Irreversible microvascular injury without the potential for functional recovery seems to be present when the hyperemic response in the infarct artery is absent, leading to a CFR ≤ 1, or when systolic flow reversal is present with a negative diastolic/systolic average peak velocity ratio, even when the infarct artery is widely patent.

To further characterize microvascular perfusion, MCE, a relatively new technique using the intracoronary injection of sonicated contrast medium to visualize the pattern of intramyocardial perfusion, was developed. The echocardiographic visualization of the contrast, which is a microvascular tracer, is a reliable indicator of myocardium at risk of necrosis and gives information about the anatomical integrity of the microvasculature with the presence of intramyocardial reflow. This technique has the unique ability to identify the reflow effect after infarct artery angioplasty on the restoration of flow at the level of the microvasculature. Ito et al demonstrated that angiographically successful reflow cannot predict microcirculatory reflow after acute MI. In fact, many patients with angiographic TIMI III flow had persistent, severe abnormalities of tissue perfusion. The microvascular perfusion pattern determined using the MCE of the infarct zone after successful reperfusion correlates with functional recovery. Homogeneous or complete tissue perfusion leads to functional recovery, yet one must be cautious because preserved microvascular integrity by MCE does not translate into viability, as is evident by sestamibi single photon emission computed tomography, or late functional recovery in up to 50% of patients. More impressive is the negative predictive value of the lack of perfusion (89%) in predicting the absence of functional recovery.

Akasaka et al have contributed to the recent body of knowledge that has propelled us forward and beyond arterial patency alone as a measure of reperfusion in patients with MI by providing insight into the identification and mechanism of flow disturbances after mechanical reperfusion. They have recognized new aspects of the phasic Doppler waveform, namely prolonged diastolic deceleration with a positive diastolic/systolic average peak velocity ratio, which translates into functional myocardial recovery after stenting despite the presence of an abnormal CFR. In addition, in each patient in whom a rapid diastolic deceleration occurred with a significant systolic flow reversal pattern before or after stenting, the microcirculatory abnormalities must have been extensive and prohibitive regarding functional recovery. We must now look beyond arterial patency, crude angiographic flow grades, and simple coronary flow reserve and pay close attention to the microcirculation evident in phasic flow velocity patterns or MCE to corroborate the observations discussed and to identify high-risk patients who may require further, presently undefined intervention. These novel therapies must have microvascular perfusion as their target.

Catheter-based observations ushered in the modern era of reperfusion therapy. Now, catheter-based measurements of microvascular function promise to further improve outcome for MI patients by propelling us past angiographic flow to microvascular preservation as the gold standard for reperfusion therapy.

References


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