Outcome after primary percutaneous intervention in acute myocardial infarction: role of microcirculatory perfusion—a crucial piece in the puzzle

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This editorial refers to ‘Incidence, determinants, and prognostic value of reverse left ventricular remodelling after primary percutaneous coronary interventional: results of the Acute Myocardial Infarction Contrast Imaging (AMICI) multicenter study’†, by S. Funaro et al. on page 566

ST elevation myocardial infarction (STEMI) constitutes ~40% of all acute myocardial infarction (AMI), which continues to be a significant public health problem in both developed and developing counties.1,2 Primary percutaneous intervention (PCI) is now established as the reperfusion therapy of choice after STEMI. The aim of reperfusion therapy for many years has focused on achieving epicardial artery patency at the site of the occlusive thrombus. It is now possible, through advances in interventional techniques and adjunctive pharmacological treatment, to achieve TIMI (Thrombosis In Myocardial Infarction) grade 3 epicardial flow (normal) in ~95% of patients. Despite this achievement, mortality, although declining, still remains high.3 This is possibly because, despite restoration of TIMI grade 3 flow, ~40% of patients do not achieve microvascular flow, which should be the goal of reperfusion therapy.4

The no-reflow phenomenon (absence or reduced microvascular flow despite restoration of epicardial coronary artery patency) was first described by Kloner et al.5 Electron microscopy showed microvascular obstruction due to endothelial blebbing, white cell infiltration, red cell stagnation, and extracellular oedema. This process may be accelerated after reperfusion as a result of liberation of oxygen free radicals. The phenomenon of no-reflow in the clinical setting is also caused by microembolism from the occlusive thrombus and downstream plaque plugging following PCI. Microvascular spasm as a result of liberation of vasoactive amines from activated platelets is also implicated.

The consequence of no-reflow phenomenon is profound in that it results in left ventricular (LV) remodelling, LV dysfunction, heart failure, and increased mortality.2,6 Hence, the success of reperfusion therapy should be gauged not only by the rapid restoration of epicardial coronary flow but also by rapid achievement of myocardial perfusion. How can one rapidly assess myocardial perfusion? Clinical (resolution of chest pain and ST segment elevation) and coronary angiographic markers (TIMI flow, TIMI frame count, and myocardial blush grade) have been widely used. They are all indirect markers of myocardial perfusion. However, myocardial contrast echocardiography (MCE), a technique that utilizes microbubbles, which remains intravascular and accurately denotes the status of microvascular perfusion within that region. The clinical significance of no-reflow using MCE has been demonstrated previously.6 Recently, it has been shown that MCE is the best technique to assess no-reflow compared with clinical and angiographic markers.7,8

Funaro et al. have elegantly demonstrated that primary PCI improves outcome primarily by reversing LV remodelling, and this is independently predicted by the severity and extent of microvascular damage assessed by MCE.9,10 LV remodelling, after significant AMI, is an adaptive phenomenon whereby an increase in the LV size, an alteration of LV shape, and an increase in wall thickness initially reduce wall stress and maintain stroke volume despite reduced contractile function. This phenomenon after AMI is, however, associated with a poor prognosis. It has been shown in several studies that lack of microvascular perfusion despite10,11 restoration of epicardial blood flow after AMI is the prime determinant of LV remodelling. However, with the introduction of angiotensin-converting enzyme inhibitors and β-blockers, and
recently aldosterone inhibitors, cardiac remodelling is less evident and this has translated into improved outcome. Primary PCI resulted in further attenuation of cardiac remodelling. However, what is not shown so far is that LV remodelling, which occurs very early after AMI, actually regresses, i.e. reverse LV remodelling occurs after primary PCI. The study of Funaro et al. showed that reverse LV remodelling occurred in ~40% of patients. It also showed that the extent of microvascular damage assessed by MCE was a powerful predictor of reverse LV remodelling, which in turn predicted major cardiac events at a follow-up period of 2 years. Another interesting phenomenon noted in the study was ‘reversible’ no-reflow. There was a significant improvement of microvascular perfusion between 12 and 15 h after primary PCI and at 5–7 days. This has been observed previously. However, what this study further showed is that improvement in perfusion was also a strong marker of reversed LV remodelling. Reversible no-reflow may occur as a result of cellular unplugging, relief of microvascular (arteriator) spasm, or dissolution of the microembolism. However, these should occur early rather than late as prolonged reduction in microcirculatory flow will not translate into reversed LV remodelling unless myocyte ‘hibernation’ occurs which, however, is possible in the acute setting. Finally, the study also underscored the importance of assessing myocardial perfusion directly with MCE rather than relying on surrogate markers such as a myocardial blush grade.

The study of Funaro et al. indirectly also suggests that more needs to be done in AMI beyond achieving TIMI grade 3 flow. In this study almost 60% did not achieve reversed LV remodelling. This contributes significantly to the rising incidence of heart failure. Unfortunately, adjunctive measures to improve microcirculatory flow have met with little success. However, MCE is likely to provide a potent tool for the evaluation of myocardial perfusion during the development of therapy designed to improve microcirculatory flow which should undoubtedly be the next major step in the management of STEMI.

Conflict of interest: none declared.

References
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