To See or Not to See: Beyond the Open Artery in Myocardial Reperfusion

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Acute ST-elevation myocardial infarction (STEMI) is the major cause of mortality and morbidity in industrialised countries. The pathogenesis of STEMI is well know in the present; after plaque rupture and intracoronary thrombus formation, ischemia causes damage to myocytes and coronary microcirculation, soon after occlusion. Thus, the goal of therapy in patients with STEMI is to re-establish a patent infarct-related epicardial artery as soon as possible.

Primary percutaneous coronary intervention (PCI) has now emerged as the optimal mode of reperfusion therapy, if performed by an experienced team within 90 minutes after the onset of symptoms [1]. The Thrombolysis In Myocardial Infarction (TIMI) group has categorized epicardial coronary flow into four grades (0–3) to standardize the angiographic characterization of reperfusion. [Primary PCI results in patency of the occluded artery in almost all patients and in restoration of TIMI flow grade 3 (normal epicardial flow) in more than 90% of patients [2].]

The restoration of TIMI-3 coronary flow in patients with STEMI is associated with improved survival and enhanced recovery of left ventricular function. This observation has led to the ‘Open artery theory’ explaining that restoration of TIMI-3 flow has been used as the gold standard for reperfusion success [3].

However, it is a oversimplification to appreciate the results of PCI in STEMI patients only by evaluation the TIMI flow of the epicardial artery. The angiographic picture only gives an acute image of the flow in the epicardial artery and, therefore, a normal TIMI flow grade does not necessarily mean that microvascular flow and myocardial perfusion have been normalized. It is now clear that an open epicardial artery is a necessary but insufficient condition of a distal perfusion.

Inadequate myocardial perfusion in the absence of angiographic evidence of mechanical vessel obstruction has been called the “no-reflow” phenomenon. This inadequate myocardial perfusion despite the success of primary PCI is present in approximately 15% of patients and is clinically relevant, since it is associated with larger myocardial infarcts, greater impairment of left ventricular function and a worse clinical outcome than in patients with adequate perfusion [4].

Many mechanisms are involved in “no-reflow” phenomenon: microvascular damage and endothelial dysfunction after myocardial ischemia, cell necrosis and regional inflammatory responses induced by reperfusion. In addition, microvascular obstruction may be caused by the embolization of atheromatous and thrombotic debris, either spontaneously or after mechanical dilation of the culprit lesion. The incidence and clinical importance of these various mechanisms are unknown [5].

In this context, the study by Baba C. et al. in this issue of the Acta Medica Marisiensis is of particular interest. The investigators evaluated 162 patients with acute myocardial infarction, treated with primary angioplasty. Distal embolization, defined as a distal filling defect with an abrupt “cut-off” in the peripheral coronary artery branches, was present in 11.11% of patients. In patients with distal embolization myocardial blush and ST-T segment elevation resolution after angioplasty were reduced and the low left ventricular ejection fraction at discharge has been more frequently [6].

The findings of the study are important in the context of the increasing the accessibility to STEMI reperfusion by primary PCI and therefore, the strategy for treatment of STEMI should include attempts to correct microvascular perfusion as well as large-vessel perfusion [7].

Mechanical thrombectomy and embolic protection devices are logical therapeutic approaches to treat or prevent microembolization. On the basis to the fact that distal embolization of plaque and thrombus material is considered to be a major cause for insufficient reperfusion, despite a fully patent infarct-related artery, it was hypothesized that distal protection devices that prevent embolization during primary PCI may improve distal perfusion. This concept, however, could not be proved in randomized studies. The consistent results of EMERALD (Enhanced Myocardial Efficacy and Recovery by Aspiration of Liberalized Debris) and PROMISE (Protection Devices in PCI Treatment of Myocardial Infarction for Salvage of Endangered Myocardium) studies clearly suggest that irrespective of the technology, distal protection does not improve reperfusion after primary PCI in myocardial infarction to a clinically detectable degree [8].

Some small studies investigating the usefulness of thrombectomy systems in STEMI showed encouraging results with preventing slow-flow, no-reflow and distal embolization, as measured by improved myocardial perfusion, by angiography and improved elevated ST segment resolution after PCI. Large, multi-center studies did not confirm clinical benefit. However, thrombectomy may be very effective in the situation of large thrombus bulk present after first balloon catheter inflation [9]. In the European Society of Cardiology STEMI guidelines thrombus aspiration is a class IIb level of evidence B indication [1].
Various pharmacological approaches to improve reperfusion have been tested. These included antioxidants to mitigate reperfusion-associated oxidative stress, rheological agents to improve blood viscosity and anti-inflammatory agents. However, none of the clinical trials yielded convincing results [11]. Among the pharmacological approaches, high-dose adenosine infusion holds promise but has to be proved by further clinical studies [12].

Glycoprotein IIb/IIIa receptor blockade with abciximab has a documented efficacy in improving microvascular flow, contractile recovery, and patient survival after primary PCI in AMI [13]. In addition to the inhibition of platelet aggregation, prevention of pro-inflammatory heterotypic platelet interactions may contribute to the beneficial effect of this drug. Five larger randomized clinical studies addressed the clinical relevance of this effect. These studies included RAPPORT (ReoPro and Primary Percutaneous Transluminal Coronary Angioplasty Organization and Randomized Trial), ISAR-2 trial, ADMIRAL (Abciximab before Direct Angioplasty and Stenting in Myocardial Infarction Regarding Acute and Long-Term Follow-Up), CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) and ACE (Abciximab Carbostent Evaluation). With respect to combined endpoint of death, recurrent myocardial infarction, and target vessel revascularization at 30 days, each of these trials showed a significant benefit of abciximab over control [11].

A meta-analysis on abciximab in primary PCI, which also included smaller studies, revealed a significant reduction by abciximab in the 30-day incidence of reinfarction when compared with control group. Most importantly, abciximab was associated with a significant reduction in 30-day and long-term (6–12 months) mortality. Thus, peri-interventional administration of abciximab for primary PCI affords a sustained clinical benefit with improved survival [14].

Therefore it is clear that to optimize microvascular reperfusion and clinical outcomes during PCI for STEMI, additional measures are needed. Even from clinician point of view, it is important a physiological concept: open artery is a surrogate outcome and the most important target is myocardial preservation.

References