How should we evaluate an open artery in STEMI patients?

Stefan Agewall*

Department of Cardiology, Karolinska University Hospital, Karolinska Institute, S 141 86 Stockholm, Sweden

This editorial refers to ‘Ageing, impaired myocardial perfusion, and mortality in patients with ST-segment elevation myocardial infarction treated by primary angioplasty’ by G. De Luca et al., on page 662, and ‘Combined prognostic utility of ST-segment recovery and myocardial blush after primary percutaneous coronary intervention in acute myocardial infarction’ by P. Sorajja et al., on page 667.

Acute ST-elevation myocardial infarction (STEMI) is a major cause of mortality and morbidity. After plaque rupture and intracoronary thrombus formation, ischaemia causes damage to myocytes and coronary microcirculation soon after occlusion. In the 1980s, mortality reduction with thrombolytic therapy generated a new standard of care for medical treatment of patients with STEMI. However, fibrinolytic therapy is limited by inadequate epicardial patency, and subsequently it has been shown that mechanical revascularization of the infarct-related coronary artery offers an even greater clinical benefit to patients with STEMI. Thus, the goal of reperfusion treatment in patients with STEMI is to re-establish a patent infarct-related epicardial artery as soon as possible.

The Thrombolysis In Myocardial Infarction (TIMI) group has categorized epicardial coronary flow into four grades (0–3) to standardize the angiographic characterization of reperfusion. The restoration of TIMI flow grade 3 (normal epicardial 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’ explanation that restoration of TIMI flow grade 3 has been used as the gold standard for reperfusion success.

However, 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. When epicardial reperfusion occurs and blood flow to the infarct area is regained, reperfusion injury is caused by neutrophil infiltration, free radicals, and activation of the complement system. Especially after percutaneous coronary intervention (PCI), it is reasonable to believe that microemboli are pushed away distally, causing microvascular obstruction limiting distal tissue perfusion even after opening of the epicardial artery. Distal embolization in patients treated with primary angioplasty is visible on the coronary angiogram in ~15% of patients. Embolization is related to reduced myocardial reperfusion, more extensive myocardial damage, and a poor prognosis. Thus, it is a very significant oversimplification to only evaluate the TIMI flow of the epicardial artery in STEMI patients. The clinical importance of distal tissue perfusion has been demonstrated in several studies that have used surrogate markers such as ST-segment resolution, myocardial contrast echocardiography, and magnetic resonance imaging. After primary PCI, TIMI-3 is restored in >90% of the patients with STEMI, whereas distal microvascular flow and myocardial perfusion are normalized to a much less degree. The lack of myocardial reperfusion in spite of restored TIMI-3 flow has been called the ‘no-reflow’ phenomenon. It is therefore clearly appreciated that an open epicardial artery is a necessary but insufficient condition of a distal perfusion.

The higher mortality rate observed in older patients with STEMI has been explained by a higher frequency of comorbidities, such as previous atheroclerotic disease, higher prevalence of hypertension and diabetes mellitus, and impaired left ventricular function. In the study by De Luca et al., reperfusion was evaluated by the use of ST-segment resolution and myocardial blush in patients with STEMI, treated with primary PCI. They observed a clear and significant relationship between age and reperfusion even after adjustment for baseline confounding factors. Because myocardial perfusion is strongly associated with survival, this is an important observation. However, the CADILLAC study group did
not observe any difference between different age groups for angiographic procedural success, post-procedural TIMI-3 flow, or ST-segment resolution. Despite the different outcome of these reports, the CADILLAC group also reported an association between age and increased mortality. Furthermore, the rates of mortality and major adverse cardiovascular event were inversely related to ST-segment resolution. We still do not know why ageing is associated with such a poor outcome in patients with STEMI, but older patients more often have a complex coronary anatomy, which may be associated with a higher risk for distal embolization. It has also been shown that ageing is associated with poor endothelial and microcirculation function, which may contribute to a poor myocardial perfusion after revascularization by PCI. Thus, the report from the CADILLAC study group and the report by De Luca et al. confirm age as a risk factor for mortality and MACE and ST-segment resolution as a predictor of a better outcome in STEMI patients treated with primary PCI. We can conclude that an open epicardial artery is not good enough; also, the distal microvascular flow and myocardial perfusion must be re-established.

How should an open artery be evaluated in clinical practice?

The ST-elevation on the ECG is caused by myocytes, deprived of oxygen, and therefore, ATP-dependent transmembrane ion gradients are lost. An ST-segment recovery quantifies the reversal of this condition and has proved to be one of the most predictive measures of cellular response to reperfusion. ST-segment recovery in STEMI patients represents both reversal of ischaemia and interruption of infarction. Therefore, serial or continuous ECG assessments over time provide a non-invasive modality for tracking the status of epicardial patency. Recanalization of the epicardial artery can be recognized by >50% ST-segment recovery. The extent of ST-segment recovery in STEMI patients treated with primary PCI or thrombolysis provides prognostic information.4,6 Continuous monitoring of ST-segment resolution appears to be more advantageous than assessing ST-segment resolution at multiple time points, because it can be used to determine the exact time of reperfusion and to detect intermittent reocclusion that often occurs after fibrinolysis. The myocardial blush, an angiographic measure believed to reflect microvascular flow, relates to the contrast opacification of the myocardial bed subtended by the infarct artery. The myocardial blush scale has been found to relate to the enzymatic infarct size in patients after primary PCI for acute myocardial infarction and to have a better predictive value for long-term mortality than Killip class, TIMI grade flow, and left ventricular ejection fraction.

In contrast to many other methods of microvascular flow assessment, both restoration of myocardial blush and ST-segment recovery are readily available in clinical practice. In another report from the CADILLAC study group, clinical outcome in STEMI patients treated with primary PCI were assessed as a function of ST-segment resolution and myocardial blush.8 The authors report a strong correlation between ST-segment resolution and myocardial blush; however, the results were discordant in ~40% of the patients. Both ST-segment resolution and myocardial blush were associated with death, whereas only ST-segment resolution was an independent predictor for death. Other studies have reported that both ST-segment resolution and myocardial blush are independent predictors for death.9 A well-known knowledge is that time is muscle. All efforts should be made to shorten door-needle time as much as possible in patients with STEMI. Therefore, the observation by De Luca et al.10 that time to treatment is associated with the extent of ST-segment resolution, myocardial blush grade, and 1 year mortality is logical.

In conclusion, we know that the Open artery theory is not the only explanation in patients with STEMI. We also need to evaluate microvascular flow and myocardial perfusion. Restoration of myocardial blush and ST-segment recovery are readily available in clinical practice and both methods predict outcome. In clinics without angiographic facilities, ST-segment recovery should be assessed after treatment with thrombolysis.

In the future, efforts should be aimed at improving myocardial perfusion, beyond epicardial recanalization, to further improve the outcome of patients with STEMI. This may be achieved by a combination of a well-performed percutaneous angioplasty and adjunctive pharmacological treatment. Markers of myocardial perfusion, such as myocardial blush and ST-segment recovery, may be used as surrogate study endpoints in clinical trials. Compared with the standard clinical endpoint, mortality, the use of these surrogate endpoints in trials analysing the effect of strategies designed to improve myocardial perfusion after treatment of STEMI patients may allow a reduction of required patient numbers.

References


