Coronary Microvascular Obstruction
Key Factor in the Prognosis of ST-Segment–Elevation Myocardial Infarction

Thomas Stiermaier, MD; Holger Thiele, MD; Ingo Eitel, MD

During the past decades, advances in percutaneous coronary intervention and antithrombotic therapy have improved the prognosis of patients with ST-segment–elevation myocardial infarction (STEMI).1 However, in a substantial number of STEMI patients, myocardial perfusion remains impaired despite successful recanalization of the infarct-related epicardial coronary artery, and this scenario has been shown to increase the risk of future cardiovascular events.2 Therefore, coronary microcirculation has been identified as an important determinant of outcome after STEMI.3 The potential causes and mechanisms of coronary microvascular dysfunction include pre-existing transient or permanent alterations, individual susceptibility, ischemic injury, reperfusion injury, and distal embolization of thrombotic material.4,5 The no-reflow phenomenon after percutaneous coronary intervention is the angiographic correlate for microvascular dysfunction and relies on reduced antegrade blood flow (thrombolysis in myocardial infarction flow grade and thrombolysis in myocardial infarction frame count) and impaired penetration of dye into the myocardium (myocardial blush grade and thrombolysis in myocardial infarction myocardial perfusion grade). Cardiac magnetic resonance (CMR) imaging enables the direct visualization and quantification of microvascular obstruction (MVO), which reflects myocardial damage resulting from microvascular dysfunction.

See Article by Durante et al

In this issue of Circulation: Cardiovascular Imaging, Durante et al4 report results from a prospective single-center study on the diagnostic and prognostic utility of angiographic and CMR parameters of microvascular dysfunction in STEMI. The authors directly compared angiographic no-reflow (defined as thrombolysis in myocardial infarction flow grade ≤2 and myocardial blush grade <2) with the assessment of structural myocardial changes in terms of MVO on CMR imaging in 88 STEMI patients. The occurrence of major adverse cardiovascular events consisting of death, non-fatal re-infarction, unplanned revascularization, admission for heart failure, and cardioverter-defibrillator implantation was evaluated at a median of 464 days after infarction. Although the study is obviously limited by its small sample size and the high exclusion rate (only 35% of the screened STEMI patients were enrolled), the authors report some interesting observations that are both reassuring and expand our current knowledge.

First, the incidence of MVO on CMR imaging (67%) was higher than that of angiographic no-reflow (36%).4 Variable incidences of microvascular dysfunction with different diagnostic tools have been reported and range from 10% using angiographic methods to 60% using imaging modalities (CMR and contrast echocardiography).2 This discrepancy might, in part, be explained by the fundamentally different concepts of assessing functional alterations of coronary blood flow and structural changes at the tissue level. Furthermore, microvascular dysfunction is thought to be a dynamic process involving multiple mechanisms, which can cause reversible or irreversible damage.3 Therefore, the timing of assessment (early after revascularization in angiography versus usually several days thereafter using CMR imaging) might also impact the frequency of detecting microcirculatory alterations.

The second major finding of the study is that MVO provides better risk stratification of STEMI patients compared with angiographic no-reflow.4 Surprisingly, the analysis did not reveal differences regarding major adverse cardiovascular events rates in patients with and without angiographic no-reflow, which contradicts previous studies. Sound evidence supports the prognostic use of angiographic indexes, although using dedicated intracoronary wires to measure coronary flow reserve or the index of microvascular resistance is the invasive reference method to assess microcirculatory function.6,7 Therefore, the observations in the current investigation are most likely attributable to the small sample size resulting in low statistical power. However, the study by Durante et al confirms the excellent prognostic value of CMR-derived MVO, the noninvasive reference method to determine microvascular injury. Several previously published trials consistently showed that MVO has the best predictive value of all CMR parameters over and above clinical scores, left ventricular ejection fraction, and infarct size.8–10 Furthermore, quantifying the extent of MVO enables an even better risk stratification compared with sole assessment of its presence.8,9 These data prove that direct visualization of the irreversible myocardial damage resulting from microcirculatory disturbances provides the most relevant prognostic information and underscores the value of CMR imaging in postmyocardial infarction patients.
The third and probably most interesting finding of the current study is the association between MVO and clinically driven target lesion revascularization. Although target lesion failure was not observed in patients without MVO, 12 patients in the MVO group required target lesion revascularization (23%; 1 patient with stent thrombosis). In view of the statistical limitations of the current analysis, these results have to be considered as preliminary and require validation in future trials. Moreover, 23% restenosis rate seems rather high compared with usually reported rates in new-generation drug-eluting stents.11,12 Identifying patients at increased risk of in-stent restenosis or stent thrombosis is particularly important to guide management of STEMI patients. Established predictors include patient characteristics, lesion complexity, and mechanical factors (e.g., stent length or underexpansion).14 The results reported in this issue of the journal indicate that microcirculatory dysfunction might provide additional predictive information and improve risk assessment. The authors suggest that changes in coronary hemodynamics because of microvascular dysfunction could promote in-stent restenosis.4 Inflammatory mediators predisposing to aggravation of microvascular injury and neointimal thickening and restenosis could provide another potential explanation for the observed association.2,4

The overwhelming evidence on the prognostic implications of microvascular dysfunction emphasizes the need for sufficient strategies to protect or restore coronary microcirculation. Several approaches addressing different aspects of the presumed pathophysiological mechanisms were evaluated in clinical trials. These included reduction of thrombus burden, conditioning strategies, and administration of drugs with cardioprotective or vasodilatory effects.2 However, published studies to date either failed to show convincing benefits in unselected STEMI patients or require further validation with regard to hard clinical end points.13 Therefore, evidence-based strategies to avoid or reduce microvascular dysfunction are lacking. Because the extent of MVO evolves over time,16 the established principle to immediately restore coronary blood flow without time delays is the most effective strategy to limit microvascular injury in STEMI patients.

In conclusion, microvascular dysfunction is a key factor in the prognosis of STEMI and the most appealing target to further improve outcome. The study by Durante et al confirms and expands the currently available evidence on the prognostic implications of MVO assessed by CMR imaging. Moreover, MVO was identified as a potential predictor of target lesion failure in STEMI patients. These results and novel strategies to maintain or restore microvascular perfusion require further investigation in future large-scale trials with clinical end points.

Disclosures

None.

References


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