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EDITORIAL COMMENT

Microvascular reperfusion in myocardial infarction: The new concept of the open artery in the 21st century☆

Reperfusão microvascular no enfarte do miocárdio: o novo conceito da «artéria aberta» do século XXI

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There has been enormous progress in the treatment of ST-elevation myocardial infarction (STEMI) due to the use of primary percutaneous coronary intervention (P-PCI), confirming the concept of the open artery proposed by Eugene Braunwald in the 1980s.[1] Implementation of this therapy has led to a marked decrease in in-hospital mortality and dramatic improvements in the prognosis of patients suffering a first STEMI.[2] However, a puzzling morphological change frequently occurs: early P-PCI with angiographic and clinical criteria of success is followed by unexpected wall motion abnormalities and ventricular remodeling. It is estimated that adequate microvascular reperfusion is achieved in only 65% of cases, despite angiographically successful epicardial reperfusion.[3] It is the re-establishment of microvascular circulation that determines the effectiveness of reperfusion and hence cardiomyocyte recovery, enabling the recovery of adequate myocardial function.

Some of the mechanisms involved in these processes have been identified, some cellular and others vascular, that influence the results of reperfusion or modulate the manifestations of the underlying disease. The most important of these are coronary microvascular dysfunction, mechanical microvascular obstruction (MVO), endothelial dysfunction (ED), and ischemia-reperfusion injury (IRI).[4]

These pathophysiological conditions appear to interact with each other, since IRI results from cellular compromise with microstructural alterations in the cardiomyocyte that lead to apoptosis, and from vascular alterations characterized by microembolization, vasoconstriction, inflammation, edema and capillary rupture, which result in IRI and MVO.[5]

It is unclear which of these components have more important roles in the processes that lead to the functional manifestations of microvascular reperfusion and hence recovery of left ventricular wall motion, nor the part played by each in the clinical parameters that identify them as prognostic markers.[6]

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Efforts have been made to define markers of the likelihood of developing microvascular dysfunction following mechanical reperfusion in STEMI patients. One example is the ATI score,[7] which is based on age, angiographic thrombus burden in the infarct-related artery and index of microcirculatory resistance (IMR) before stent implantation. High IMR (>40) calculated immediately after P-PCI was a strong prognostic marker, associated with higher long-term mortality and hospitalization rates for heart failure.[8]

Although ischemia and IRI contribute to the pathogenesis of microvascular dysfunction and to increased infarct size, the importance of distal microembolization associated with the process of mechanical reperfusion should not be underestimated. A large thrombus burden is associated with higher per-stent implantation IMR, which may be related to greater MVO following instrumentation (balloon dilatation or mechanical thrombectomy) before implantation.[9,10]

The article by Baptista et al.[11] published in this issue of the *Journal* deals with this question, studying ED, one of the elements known to affect microvascular dysfunction in STEMI patients. The authors seek to establish a correlation between ED following STEMI and the presence of MVO and infarct extension in STEMI patients.

The authors assessed coronary ED indirectly, assessing peripheral ED by peripheral arterial tonometry within 24 hours of P-PCI, in 38 patients divided into two groups according to the presence (n=16) or absence (n=22) of ED, defined by a reactive hyperemia index (RHI) <1.67. Infarct extension was measured by maximum troponin level, and left ventricular ejection fraction (LVEF) and wall motion score index (WMSI) by echocardiography and cardiac magnetic resonance (CMR). MVO was assessed by ST-segment resolution, reperfusion-related angiographic parameters and contrast-enhanced CMR. The authors conclude that ED is associated with larger infarcts, lower LVEF, higher WMSI and higher prevalence of MVO.

Although the study's methodology is appropriate, selecting a single variable that can indirectly identify coronary ED, the sample is small (as the authors acknowledge), which weakens the significance of differences between the groups; what are presented as conclusions are in fact only tendencies that rarely reach statistical significance.

It is likely that many of these patients already had coronary microvascular dysfunction before STEMI, given the high prevalence of hypertension, diabetes and dyslipidemia in the study population. This could have biased the results, but the methodology used was unable to assess this variable.

Furthermore, the high rates of balloon predilatation (over 50%) and mechanical thrombectomy (42%) may have led to greater distal microembolization, especially considering that such interventions before stent implantation probably result in a greater thrombus burden in the infarct-related artery. This in itself could lead in a higher IMR, worse microvascular dysfunction, larger infarct area and a greater impact on left ventricular function.

There are multiple variables in the study that are only linked by the form of clinical presentation, STEMI. Analysis of the results reveals that more severe disease, as reflected by a greater number of diseased vessels and higher SYNTAX score, was more strongly associated with ED; the final result of P-PCI – with varying degrees of microvascular dysfunction – may depend not on the clinical presentation or on the type of revascularization procedure, but on previous vascular disease, which in turn is affected by the above-mentioned cardiovascular risk factors.

In view of the above and of the difficulty in identifying indisputable markers of severity, it is important to carry out further studies with larger populations, longer follow-up and clinical endpoints. There is evidence, albeit limited and controversial, that patients with ED identified within 4-6 weeks of STEMI do not suffer more major adverse cardiac events (MACE) at four years than those without ED.[12]

At the same time, there are studies that show that MVO identified by CMR predicts MACE at six years and is a more robust prognostic marker than LVEF assessed by echocardiography.[13,14] Although morphological, angiographic and laboratory parameters seem to indicate that ED can be considered a marker of severity in STEMI, for this to be accepted, clinical correlations to this effect will have to be demonstrated. If the association between MVO and ED found by Baptista et al. is confirmed in larger studies, it may come to be regarded as a marker of severity, and the methodology used in the study under analysis could be a valuable tool for its assessment.

Conflicts of interest

The author has no conflicts of interest to declare.

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