Contributions of Cardiac Magnetic Resonance to the Understanding of Myonecrosis After Percutaneous Coronary Intervention

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With >900,000 procedures performed annually in North America, percutaneous coronary intervention has dramatically altered the landscape of cardiology since its inception in 1977. Despite procedural success rates now exceeding 90%, biomarker rise indicating myonecrosis has been reported after up to 30% of otherwise successful procedures. Most agree with the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction recommendation that the same biochemical marker cutoffs be applied regardless of the clinical circumstances. However, available data suggest that mild periprocedural marker rise may not confer substantial risk in an otherwise successful procedure. Several reports have identified non-Q-wave infarctions with creatine kinase (CK)–MB elevations 3 to 5 times the upper limit of normal and Q-wave myocardial infarctions, which are largely related to procedural complications. Troponin T and I elevation occurs more frequently than CK-MB increase after percutaneous coronary intervention and does not appear to have prognostic value unless a marked increase (>5 times the upper limit of normal) occurs. A notable exception comes from saphenous vein grafts in which even mild CK-MB rise after successful intervention predicts mortality.

Mechanisms of cardiac enzyme release after percutaneous coronary intervention include procedure-related factors (side-branch occlusion, dissection, embolization, and no-reflow), lesion-related factors (thrombus burden, plaque volume, plaque composition), and patient-related factors (prothrombotic state, systemic inflammatory state). In successful intervention, the most commonly cited mechanisms remain minor side-branch occlusion and embolization of thrombus or atheroma. A study of the effects of microembolization in swine determined the importance of particle number and size (“burden”) in increasing the ischemic territory, potentially through a compensatory increase in metabolism in nonischemic areas, an increase in oxygen-derived free radicals, and a restriction of reflow. The TIMI myocardial perfusion grade (TMPG) assesses flow in small vessels at the tissue level. After coronary intervention, TMPG has been inversely correlated to CK-MB, supporting an association between microembolization and periprocedural necrosis. An intravascular ultrasound (IVUS) study determined that myonecrosis was increased in the presence of greater plaque burden; this may indicate that CK-MB rise follows embolization or side-branch occlusion from plaque shift or rather that enzyme rise simply denotes diffuse atherosclerotic disease. The importance of patient-related factors is denoted by the observation that an increased systemic inflammatory state, as indicated by increased high-sensitivity C-reactive protein, was associated with greater CK-MB rise after percutaneous intervention.

Whether this denotes the importance of atheroma biology or simply burden in determining risk of periprocedural myonecrosis remains to be elucidated.

Cardiac magnetic resonance (CMR) allows serial assessment of cardiac morphology, function, perfusion, and myocardial necrosis/viability with superior spatial resolution without ionizing radiation or nephrotoxic contrast agents. Delayed-enhancement CMR (DE-CMR) identifies necrotic myocardium 10 to 20 minutes after intravenous infusion of 0.1 to 0.2 mmol/kg gadolinium-based contrast. A T1-weighted segmented inversion-recovery pulse sequence with an inversion time adjusted to null normal myocardium allows straightforward identification of necrosis as hyperenhancement (HE). Extensive validation of DE-CMR led to the demonstration that HE occurs after irreversible myocardial injury but not after severe but reversible injury such as myocardial stunning. DE-CMR is superior to SPECT in identifying discrete areas of subendocardial necrosis. In a report from Ricciardi et al studying periprocedural infarct by DE-CMR in 14 subjects, the 9 subjects with raised CK-MB had a median mass of infarcted myocardium of 2 g. In comparison, 10 g myocardium must be injured before it will be detected by radionuclide perfusion imaging. In a report designed to clarify the significance of periprocedural troponin rise, Selvanayagam et al studied 50 subjects after intervention; 29% demonstrated HE, representing a mean loss of myocardial tissue of 6.0 g (5% of myocardial mass). A strong correlation was observed between troponin rise and mass of new HE. All patients with troponin rise after PCI presented new necrosis by DE-CMR.

Addendum: Myonecrosis After Percutaneous Coronary Intervention

Myonecrosis After Percutaneous Coronary Intervention

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The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/CIRCULATIONAHA.106.644732
In this issue of *Circulation*, Porto and colleagues\textsuperscript{15} combine DE-CMR with IVUS and coronary angiography to explore periprocedural myocardial necrosis after percutaneous coronary stenting in 64 native vessels from 52 consecutive patients. The authors selected higher-risk procedures in which necrosis was more likely: long lesions, presence of a major side branch at the site of stenting, or 2-vessel intervention. Important exclusions were prior stenting, recent severe unstable angina, and left ventricular dysfunction, presumptively to limit previous HE burden on DE-CMR. Importantly, nearly 10% of subjects were excluded because of excessive calcifications precluding IVUS interpretation, highlighting a significant limitation of IVUS for such purposes, because one would expect plaque composition (including calcification) to influence periprocedural necrosis. Roughly one quarter of study patients included a bifurcation intervention, and one quarter had chronic total occlusion. Procedural complexity was illustrated by average preintervention TIMI class of 2 and 28% incidence of decreased TMPG. All subjects benefited from aspirin and clopidogrel pretreatment and procedural intravenous heparin and abciximab, which emphasizes the use of therapies known to reduce periprocedural CK-MB rise. DE-CMR interpretation followed accepted and validated methodology. An ingenious use of DE-CMR determined the spatial relationship of new HE relative to the stent: New HE in the same short-axis slice as the stent represented “adjacent” necrosis, whereas HE at least 2 short-axis slices (ie, at least 10 mm) distal to the stent denoted “distal” necrosis. Although this methodology can be traced back to Ricciardi et al,\textsuperscript{13} Porto and colleagues are the first to systematically apply it to study mechanisms of periprocedural necrosis. Porto and colleagues should be commended for combining the use of DE-CMR for necrosis burden, angiographic analysis for myocardial tissue perfusion (by TMPG) and side-branch impairment, and IVUS for plaque burden, providing powerful synergy to explore these mechanisms.

The “distal” pattern of new HE was associated with distal embolization, whereas the “adjacent” pattern was associated with side-branch occlusion. In this series of complex procedures, nearly one quarter of vessels had new HE, which was distributed equally between side-branch impairment and distal embolization. Side-branch impairment carried an odds ratio of 16.2 and distal embolization carried an odds ratio of 8.0 for new HE. Surprisingly, no subject presented simultaneously adjacent and distal HE, a fact possibly related to mechanical phenomena or local plaque “shift” occluding the ostium of the side branch rather than drifting of material into circulation of the side branch. This concept of shifting (side-branch impairment) or drifting (distal embolization) of atheroma at the time of stenting may explain the occurrence of new necrosis despite aggressive antithrombotic therapy. Accordingly, reduced thrombus burden would be expected to limit platelet embolization but not embolization of plaque components or side-branch impairment.

In this sample, stent length and stent overlap did not independently predict new HE. Overlapping paclitaxel-eluting stents tended toward association with new “adjacent” HE, a fact that is consistent with reports of greater periprocedural enzyme rise with overlapping TAXUS.\textsuperscript{16} Too few Cypher stents were used in this study to allow comparison between the devices.

Although the report by Porto and colleagues\textsuperscript{15} provides important new information about mechanisms underlying periprocedural myonecrosis, will it change and improve current practice? A recent report by Kwong and colleagues\textsuperscript{17} established that even small areas of necrosis identified as HE on DE-CMR (1.4% of left ventricular mass) in patients without known prior myocardial infarction portended a $>7$-fold-increased risk for major adverse cardiac events. The incremental risk conferred by new HE may arise from an increased substrate for life-threatening ventricular arrhythmias and from the associated greater atherosclerosis burden demonstrated here. To better orient future efforts in the prevention of periprocedural myonecrosis, further studies should explore whether both mechanisms of new myonecrosis, distal embolization, and side-branch impairment confer the same increase in risk. Periprocedural myonecrosis may be reduced by pharmacological intervention, including aspirin, clopidogrel, glycoprotein IIb/IIIa inhibitors, statins, $\beta$-blockers, and adenosine, but the report by Porto and colleagues emphasizes that new HE occurs despite many of these therapies in close to a quarter of patients undergoing complex procedures. The greatest risks for periprocedural myonecrosis come from saphenous vein graft angioplasty and interventions in thrombus-laden vessels (ie, acute coronary syndromes), 2 situations associated with incremental risk for distal embolization. Although mechanical intervention with distal protection devices decreases myonecrosis in saphenous vein grafts,\textsuperscript{18,19} no benefit in ST resolution from distal protection was noted in ST-elevation myocardial infarction.\textsuperscript{20} Perhaps differences in the nature, particle size, and sheer volume of embolic material may explain this disparity. In the case of ST-elevation myocardial infarction, embolic burden may overload distal microcirculation before intervention occurs, defeating any beneficial effect of distal protection. Perhaps in light of the increasing use of DE-CMR illustrated here, millimeter ST-segment resolution may not be the most appropriate end point for future trials.

Several important questions remain to be addressed. Notably, we have yet to explore the nature of plaque characteris-
tics in relation to risk of periprocedural myocardial necrosis. Are atheromas carrying larger lipid and inflammatory burdens more prone to the release of material into the circulation and distal embolization? Research harnessing the ability of MRI to characterize plaque composition may provide future insights and new opportunities to improve procedural and clinical success. 20

Sources of Funding

Dr Larose receives research funding from the Canadian Stem Cell Network and the Quebec Heart Institute Foundation.

Disclosures

None.

References


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Key Words: Editorials  magnetic resonance imaging  myocardial infarction  ultrasonics
Below Radar: Contributions of Cardiac Magnetic Resonance to the Understanding of Myonecrosis After Percutaneous Coronary Intervention
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Circulation. 2006;114:620-622
doi: 10.1161/CIRCULATIONAHA.106.644732

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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