Infarct haemorrhage detected by cardiac magnetic resonance imaging: are we seeing the latest culprit in adverse left ventricular remodelling?

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This editorial refers to ‘Impact of myocardial haemorrhage on left ventricular function and remodelling in patients with reperfused acute myocardial infarction’, by J. Ganame et al., on page 1440

The force of the heart decreases... as the greater number of its parts become tendinous instead of fleshy. De sedibus et causis morborum G. B. Morgagni, 1761

All myocardial infarctions are not equal, and those that produce more extensive left ventricular topographical alterations are much more likely to result in premature morbidity and mortality. The advent of non-invasive cardiac imaging, particularly echocardiography, provided a temporal window to evaluate the dynamics of the structural alterations produced by a myocardial infarction. In the late 1970s, infarct expansion was defined as an acute dilatation and thinning of the infarcted region leading to an elongation of that segment which was not accounted for by further necrosis.¹ This early change in ventricular contour often leading to an aneurysm identified patients at higher risk for early mortality and other infarct complications. In animal models, it became apparent that the early distortion of ventricular architecture in response to an extensive loss of myocytes was part of a more insidious progressive process of ventricular enlargement which involved the viable segment as well as the infarcted region. This architectural-modifying process termed ‘ventricular remodelling after myocardial infarction’ results in a larger ventricular chamber.² Although the early enlargement may provide some compensation by restoring stroke volume despite a reduced ejection fraction, the alterations in left ventricular architecture create a chronic imbalance in loading conditions that leads to further topographic changes which augment risks for adverse events.

Larger infarct size is the major factor promoting adverse left ventricular remodelling, and myocardial reperfusion performed during the myocyte salvage period remains the most definitive therapeutic modality to reduce adverse ventricular remodelling. Early studies also indicated that re-establishing coronary perfusion just outside of the window of salvage could still favourably attenuate some of the adverse structural changes by promoting prompt healing in the infarcted region.³ The complementary ability of angiotensin-converting enzyme (ACE) inhibitors to attenuate progressive left ventricular enlargement and improve clinical outcomes established adverse left ventricular remodelling as a therapeutic target for novel approaches for patients with high-risk myocardial infarction.⁴ By quantifying ventricular function, myocardial perfusion, and tissue viability after an acute myocardial infarction, cardiac magnetic resonance imaging (MRI) provides a direct window of the evolving infarct. While animal models of infarction have extensively validated the spatial extent of myocardial late gadolinium enhancement (LGE) by cardiac MRI to infarction in both the acute and chronic settings by histopathology,⁵ human studies have demonstrated the robustness of LGE in determining the presence, location, and extent of myocardial infarction.⁶

Although re-establishing epicardial vessel patency in ST-segment elevation myocardial infarction (STEMI) is the initial clinical aim, the real objective is the prompt restoration of tissue perfusion. Early studies using contrast echo studies as well as angiographic TIMI (thrombolysis in myocardial infarction) frame counts, and more specifically blush scores, have identified subsets of infarct patients where tissue perfusion remains compromised despite having a patent large vessel to the territory.⁷,⁸ These patients with presumed greater tissue damage impairing the integrity of the local vasculature are more likely to experience adverse ventricular remodelling and death.⁹ The extent and severity of microvascular...
obstruction (MVO) from a lack of tissue perfusion measured by contrast-enhanced cardiac MRI (Figure 1) had shown strong correlation with angiographic measurements of the no-reflow phenomenon when epicardial coronary flow in the infarct-related artery had been successfully restored. It has been proposed that reperfusion of the myocardium with MVO can result in haemorrhage within the infarct, and both entities portend to escalated risk of cardiac events.

Beyond infarct size and ventricular function, cardiac MRI-based characterization of tissue components may provide additional clinical information. Wu et al. and Hombach et al. separately demonstrated the role of quantified MVO by contrast-enhanced cardiac MRI imaging for clinical events independent of infarct size. More recently, our group found that the size of the border grey zone seen surrounding the infarct, or tissue heterogeneity, was associated with higher mortality and more malignant ventricular arrhythmias. Wu et al. have reported using cardiac MRI T2-weighted imaging in characterizing the presence and size of myocardial haemorrhage in 98 patients with a large myocardial infarction despite acute restoration of epicardial patency with percutaneous coronary revascularization. Paramagnetic properties of deoxyhaemoglobin lead to a shortening of the T2 relaxation time, considered as haemorrhage in the core of the infarcted region should appear as a darkened region, surrounded by the ‘area at risk’ seen on T2-weighted MRI. Based on this technique, the authors presented a high prevalence of myocardial haemorrhage of 25% in this patient cohort, more common amongst patients with large transmural infarction and severe left ventricular global and regional systolic dysfunction. The authors further proposed that the presence of myocardial haemorrhage is a predictor of adverse left ventricular remodelling (defined by an increase in left ventricular end-systolic volume) that occurred between 1 week and 4 months after acute infarction, independent of infarct size. The authors should be commended for their efforts in investigating the potential role of this novel yet challenging imaging technique. However, several issues remain to be addressed.

Technical differences exist between several proposed cardiac MRI techniques in imaging myocardial haemorrhage after acute injury. Lotan et al. performed ex vivo T2-weighted cardiac MRI on dogs using spin echo techniques and identified regions of myocardial haemorrhage within the zone of revascularized infarction confirmed on histological correlation. On the other hand, no macroscopic or imaging evidence of haemorrhage by T2-weighted cardiac MRI was seen in their non-revascularized experimental infarcts. The darkening T2 signal as proposed by Ganame et al. to reflect myocardial haemorrhage is determined by using two opposing imaging effects: reduced T2 signal due to methaemoglobin paramagnetism in the haemorrhage and increased T2 signal from the surrounding tissue oedema. As the authors have demonstrated, this relatively straightforward T2-weighted method can potentially capture both oedematous ischaemic at risk and haemorrhagic regions. However, their definition of 2 SDs below the periphery used to confine the size of the haemorrhage is arbitrary. Voxel sizes between the T2-weighted imaging for haemorrhage and the contrast-enhanced late enhancement imaging for MVO are also vastly different. Consistent with other reported studies using similar imaging techniques to identify myocardial haemorrhage, MVO and myocardial haemorrhage appear to be highly correlated. Both MVO and myocardial haemorrhage as described to have been identified by these separate techniques are related to larger infarction and area at risk, unsuccessful tissue perfusion, and are intricately involved in adverse ventricular remodelling. While the authors indicated that a number of variables including

Figure 1   Schematic illustration of visualization of microvascular obstruction after acute myocardial infarction. After a delay of 10–15 min, the gadolinium-enhanced region seen by a T1-weighted fast gradient inversion recovery MRI technique delineates the extent of the myocardial injury (light grey region on the corresponding sketch on the right). Within the enhanced region, there exist dark foci (black on the sketch on the right) that currently represent a microvascular obstruction secondary to the no-reflow phenomenon despite successful epicardial coronary revascularization. Whether these dark foci can also contain focal myocardial haemorrhage will need histological validation.
myocardial haemorrhage, baseline infarct size, MVO, and area at risk were all associated with adverse left ventricular remodelling, whether myocardial haemorrhage truly represents an independent marker beyond MVO or angiographic markers of tissue perfusion remains an open question. Without histological validation from an animal study, the distinction between tissue haemorrhage across a spectrum of MVO remains blurred. As stated by the authors, myocardial haemorrhage has been considered to be the result of reperfusing infarcted myocardium with severe microvascular injury and endothelial cell disruption. Restoration of epicardial coronary flow through the occluded vessel may be a prerequisite for haemorrhagic infarct. However, since all patients in the current study were revascularized, one cannot determine whether the low signal area on T2-weighted images identified as myocardial haemorrhage are specific to infarcts that have been reperfused. It is somewhat surprising, perhaps due to limitation of the current sample size, that time from infarct onset to percutaneous coronary intervention (PCI) was not different between the haemorrhagic and the non-haemorrhagic groups. Details of other potential influencing factors such as the use and dosing of antithrombin, antiplatelet therapy, and the use of a distal non-occlusive protection filter device were not provided in this report. For these reasons, the mechanism for the myocardial haemorrhage as observed by Ganame et al., and thus any inference of treatment or prevention strategy, will need to be further explored. Finally, the current study by Ganame et al. targeted a very high-risk cohort who presented with large acute myocardial infarction (cumulative of >6 mm ST-segment elevation and significant left ventricular dysfunction including a large region of wall motion abnormality as entry criteria). Average peak troponin I was 84 µg/L on average and was 149 µg/L for the patients with haemorrhagic myocardial infarction. Whether their observations using cardiac MRI play a role in the management of patients with smaller myocardial infarction will also need to be explored in future studies.

Nevertheless, Ganame et al. provide another line of evidence that contrast-enhanced cardiac MRI assessment of infarct tissue provides discrimination of high-risk patients. Having the ability to characterize the extent of restoration coronary flow and microvascular integrity, area at risk, and myocardial damage, cardiac MRI represents a unique non-invasive tool. In our view, left ventricular end-systolic volume, infarct size, and infarct location remain the most robust markers for adverse post-infarct remodelling. As shown by Ganame et al., features of tissue heterogeneity including MVO and the emerging evidence of tissue haemorrhage may provide intriguing incremental insights in post-infarct remodelling.

Conflict of interest: none declared.

References