Assessing myocardial salvage in reperfused STEMI patients by hybrid cardiac PET-MR imaging

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Abstract
To assess the efficacy of novel cardioprotective therapies for reducing myocardial infarct size, it is important to accurately measure the area at risk, as this is needed to assess myocardial salvage, a more sensitive measure of cardioprotection. Although T2-weighted cardiovascular magnetic resonance (CMR) imaging is a promising technique for quantifying the area at risk, this approach does have its limitations. With the availability of hybrid positron emission tomography–MR (PET-MR) imaging, we now have the unique opportunity to simultaneously combine tissue characterization by CMR imaging with the metabolic insights from PET. Two cases are presented to highlight the potential utility of hybrid PET-MR imaging in acute reperfused ST-segment elevation myocardial infarction in investigating the changes in cardiac metabolism in the area at risk and in the assessment of myocardial salvage. ■ Heart Metab. 2016;70:28-31

Keywords: myocardial salvage; PET-MR; ST-segment elevation myocardial infarction

Introduction
Myocardial salvage (MS) is a more sensitive measure than myocardial infarct (MI) size to assess the effectiveness of novel cardioprotective therapies; however, currently, there is no established technique to measure MS in the clinical setting. Accurate quantification of the area at risk (AAR) is a prerequisite for the calculation of MS. The AAR refers to the territory supplied by the infarct-related artery, which is at risk of being irreversibly damaged without prompt reperfusion. MS is the difference between the AAR and MI size. Single-photon emission computerized tomography (SPECT) is considered the gold standard for the assessment of MS, but it is logistically challenging to perform. The AAR can also be retrospectively assessed by cardiovascular magnetic resonance imaging with early gadolinium enhancement, endocardial surface area (ESA) calculation, T1 mapping, T2 mapping, and T2 short tau inversion recovery (STIR) imaging, with the latter two techniques showing the most promise. Certain cardioprotective therapies, such as ischemic postconditioning and remote ischemic conditioning, have recently been shown to reduce the extent of myocardial edema as delineated by T2
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mapping and T2-weighted imaging, resulting in inaccurate estimation of the AAR. Furthermore, the evolution of edema assessed by T2 mapping has recently been shown to have a bimodal pattern the first week of an MI. Interestingly, Kim et al recently showed that T2-weighted imaging did not correspond to the AAR in a canine infarct model and in a small cohort of patients. Whether hybrid positron emission tomography–magnetic resonance (PET-MR) imaging would provide a more robust method to assess the AAR has recently attracted attention. 18F-fluorodeoxyglucose (FDG) is widely used for viability assessment; its utility in the context of acute MI is not well established. This article presents two cases that highlight the potential role of hybrid PET-MR imaging in acute reperfused ST-segment elevation MI (STEMI) to assess myocardial salvage.

Case 1

A 71-year-old gentleman presented to hospital 7 hours after onset of chest pain; electrocardiogram analysis showed anterior ST-segment elevation. He did not have any past medical history of note. A diagnosis of anterior STEMI was made, and the patient underwent prompt reperfusion by primary percutaneous coronary intervention to the proximal left anterior descending artery. The thrombolysis in MI (TIMI) flow grade was 0 before the procedure and 3 after the procedure. A hybrid PET-MR scan was performed on day 5 and repeated at 1 year as part of a research protocol. In Figure 1 (top panel), the late gadolinium enhancement (LGE)-MR image from the acute scan shows a transmural anteroseptal infarct with a large burden of microvascular obstruction (red arrow). There was a corresponding large area of reduced FDG uptake (white arrow in the FDG-PET image); this is also demonstrated in the fused FDG/LGE image. The follow-up scan at 1 year showed full-thickness LGE with no salvage (Figure 1, bottom panel, red arrow) and no recovery of glucose metabolism (observable as FDG uptake) on the FDG image (white arrow).

Case 2

A 66-year-old gentleman presented to hospital within 1 hour of onset of chest pain; electrocardiogram analysis showed inferior ST-segment elevation. He was previously fit and well. A diagnosis of an inferior STEMI was made, and the patient promptly underwent primary percutaneous coronary intervention to the midright coronary artery. He had a TIMI flow grade of 1 before the procedure and 3 after the procedure. A hybrid PET-MR scan was performed on day 4 and repeated at 1 year as part of the same research protocol used for the patient above. In Figure 2 (top panel),...
the acute scan shows complete MS with no infarct (red arrow in the LGE-MR image) but reduced FDG uptake in the inferior wall (white arrow in the FDG-PET image) within the AAR. The follow-up scan at 1 year showed normalization of FDG uptake in the inferior wall (white arrow in the FDG-PET image).

Discussion

These two cases demonstrate that FDG uptake observed by an acute scan within one week of an MI is reduced not only in irreversibly injured and nonviable myocardium, but also in the salvaged myocardium, for which FDG uptake subsequently normalizes on the follow-up scan. FDG, a glucose analog with a half-life of 109.8 minutes, is widely used for viability assessment.\textsuperscript{15,16} However, FDG uptake has also been shown to be affected in the reversibly injured salvaged\textsuperscript{17} and stunned myocardium\textsuperscript{18} of animal models of ischemia-reperfusion. The mechanism for this abnormal FDG uptake in areas of salvaged myocardium is not clear, but may be due to the fact that the reversibly injured but stunned myocardium preferentially takes up more glucose than free fatty acid following a period of fasting than does normal myocardium, but has delayed glucose metabolism. Therefore, after a glucose load, the reversibly injured myocardium has a reduced FDG uptake.

Nensa et al,\textsuperscript{19} estimating the AAR based on ESA calculations, recently showed that the area of reduced FDG uptake was larger than the AAR in 18 of the patients included in the study. However, ESA is known to underestimate the AAR when compared with T2-weighted imaging.\textsuperscript{20} Our group\textsuperscript{21} recently compared FDG-PET with T2-mapping in order to delineate the AAR in 21 reperfused STEMI patients. The area of reduced FDG uptake was larger than the MI size and matched the AAR. The limits of agreement on Bland-Altman analysis were quite wide and could be due to differences in spatial resolution and acquisition of images at different phases of the cardiac cycle between the two techniques.

Conclusion and future directions

Hybrid PET-MR imaging is particularly appealing for acute STEMI patients because only one examination is required to obtain data in parallel from PET for the AAR and from cardiovascular magnetic resonance imaging for MI size; these can be used to assess MS. However, more work needs to be done to improve upon current attenuation correction techniques and to improve coregistration of regions of interest in order to minimize partial volume effects. More importantly, the dynamic changes of reduced FDG uptake within the salvaged myocardium within the first week of an MI needs to be assessed so that the optimum timing for FDG imaging to accurately delineate the AAR can be determined. There is also the opportunity to explore other ligands, not only for quantification of the AAR, but also to obtain more in-depth metabolic insight into the evolution of acute MI and the pathophysiology of adverse left ventricular remodeling.

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REFERENCES

11. White SK, Frohlich GM, Sado DM, et al. Remote ischemic con-


