Using Magnetic Resonance Imaging to Characterize Recent Myocardial Injury
Utility in Acute Coronary Syndrome and Other Clinical Scenarios

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The work of Ricardo Cury et al published this week in Circulation uses T2-weighted magnetic resonance imaging (MRI) to detect recent myocardial ischemia on the basis of subtle differences in myocardial water characteristics. They found that T2-weighted MRI improved diagnostic accuracy when characterizing patients with possible or probable acute coronary syndrome (ACS) who presented to the emergency department with chest pain.

This editorial will highlight recent developments in cardiac imaging that reliably allow differentiation of acute from chronic wall-motion abnormalities. The idea of imaging recent ischemia, either with T2-weighted MRI or with single-photon emission computed tomography (SPECT) agents such as $^{123}$I beta-methyl-p-iodophenylpentadecanoic acid (BMIPP), represents a significant step in characterizing the metabolic condition of the myocardium beyond simple indices of regional strain or contractile function. T2-weighted MRI has generated significant interest over the last few years because it offers the ability to characterize or detect a recent reversible myocardial injury.

It is important to recognize that acute and chronic myocardial infarction (MI) can be difficult to differentiate with conventional imaging. Both will typically exhibit wall-motion abnormalities on echocardiography or MRI. Chronic MI is more likely to be associated with a thin wall, but this finding is not specific for nonviable myocardium. Both acute and chronic MI cause defects on conventional SPECT scans. Acute and chronic MI both enhance with gadolinium on MRI scans. Thus, individually these imaging methods cannot reliably differentiate acute from chronic MI.

A landmark study by Abdel-Aty et al documented that T2-weighted MRI can differentiate acute from chronic myocardial infarction. In that study of 73 patients with acute or chronic myocardial infarction, T2-weighted MRI was able to differentiate acute from chronic MI with 96% specificity. They also noted that the bright zones on T2-weighted images were typically transmural abnormalities whereas the actual infarctions were frequently nontransmural, starting in the subendocardium but sparing some epicardial layers of myocardium.

On T2-weighted images of the heart, the bright myocardium most likely represents postischemic myocardial edema. Recent myocardial ischemia can alter myocardial water handling and is hypothesized to cause intracellular edema on the basis of altered transmembrane sodium gradients that are due to dysfunction of ATP-dependent sodium-potassium channels. Regional myocardial edema can also occur based on inflammatory responses to recent injury. Thus, there may be 2 distinct pathophysiological mechanisms that allow identification of acutely injured myocardium. Consistent with the hypothesis that hyperintense zones on T2-weighted images represent recent ischemic myocardium, the ischemic area at risk can be measured on such images for nonreperfused infarcts even a few hours post-MI.

The "conventional" results of Cury et al confirm prior findings from Kwong et al. A combination of cine MRI, perfusion, and delayed enhancement imaging had about 85% sensitivity and specificity for detecting ACS in both studies. Furthermore, the great majority of these patients had unstable angina because, by design, they had negative initial cardiac biomarkers and a negative ECG. Cury et al improved diagnostic accuracy by including information derived from T2-weighted images. T2-weighted images helped discriminate patients with prior MI who did not have ACS from those who did. Fundamentally, imaging that can distinguish acute from chronic wall-motion abnormalities is powerful and clinically useful.

Despite the encouraging results of Cury et al, readers should realize that T2-weighted cardiac MR images are far from perfect. For example, T2-weighted images only detected 5 of 9 patients with unstable angina. Delayed-enhancement imaging detected another 2 patients clinically described as having unstable angina and thus served an important role in detection of ACS. It is also interesting to consider why these later 2 patients were missed by biomarkers. Perhaps they had unrecognized MI >2 weeks before presenting to the emergency department with the index case of unstable angina. In our clinical experience, we commonly find MRI evidence of unrecognized MI in patients coming for stress testing, patients with unstable angina, and even in asymptomatic individuals. Kwong et al recently proved that these unrecognized MIs have prognostic significance.

Fortunately, better T2-weighted MRI methods are in development and testing. Current-generation fast spin echo or turbo...
spin echo MRI with a black blood preparation can provide high-quality cardiac images. However, with regard to detecting edema associated with recent ACS, the differences in myocardial T2 are subtle enough that any imperfections in the T2-weighted images may become significant. In particular, inhomogeneity of myocardial signal intensity caused by through-plane motion or associated with the use of surface coils can exceed the subtle differences caused by myocardial ischemia or infarction. The black blood preparation is also dependent on movement of blood through the imaging plane, a problem in patients with low ejection fraction or significant wall-motion abnormalities. In those patients, blood near the infarcted myocardium can be very bright and can be confused with myocardial edema. For these reasons, we have been studying bright blood T2-weighted methods that can minimize or eliminate problems or artifacts that reduce diagnostic confidence in the heart.10,11

The SPECT tracer BMIPP is also capable of detecting recently ischemic myocardium. BMIPP is a fatty acid. As such, uptake in recently ischemic myocardium is abnormally low, perhaps because myocardial metabolism switches from burning fatty acids to burning glucose. BMIPP is still not yet approved in the United States but has undergone some clinical testing. More experience with BMIPP exists in Japan, where it has been available clinically for a few years. In patients with intermediate diagnostic likelihood of having coronary disease, a meta-analysis of 7 studies covering 528 patients found that BMIPP has a sensitivity of about 78% and a specificity of 84% for detecting significant coronary artery disease.12 The prolonged metabolic abnormality after a bout of myocardial ischemia makes BMIPP attractive in patients with recent acute chest pain or contraindications to stress testing.13 To date, only 1 study has compared T2-weighted MRI with BMIPP.14 In that small study, T2-weighted MRI compared favorably with SPECT methods, but clearly more research is needed.

Conceptually, advanced imaging methods promise to clarify the pathophysiologic of regional wall motion abnormalities beyond that possible with simple measures of regional contractile function. These new methods appear to have significant diagnostic utility above and beyond viability assessment because knowing an event was recent has important implications for patient management. Specifically, T2-weighted images or BMIPP can determine the acuity of many patients with unstable angina, a feature that cannot be ascertained by current-generation biomarkers or MRI delayed-enhancement techniques. In addition, other disease processes might benefit from this additional level of characterization, including myocarditis,15 Tako-Tsubo cardiomyopathy,16 and transplant rejection.17 Cardiac imaging experts should understand how these methods work and recognize that characterizing the status of myocardium can clarify clinical questions that currently depend on clinical assumptions or tincture of time.

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References

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