EDITORIAL COMMENT
When Two Tests Are Better Than One
Adding Late Gadolinium Enhancement to First-Pass Perfusion Cardiovascular Magnetic Resonance*
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Due to the versatility of cardiovascular magnetic resonance (CMR), two distinct methods are available for stress testing in patients with suspected coronary artery disease (CAD). One method, analogous to dobutamine stress echocardiography, is dobutamine stress CMR which assesses ventricular function during incremental levels of dobutamine stress. Dobutamine stress CMR provides excellent image quality and accuracy (1), including in patients who have inadequate echocardiographic windows (2), and is useful for assessing cardiac prognosis (3). Another approach is first-pass gadolinium-enhanced myocardial perfusion imaging performed at rest and during vasodilator stress, analogous to vasodilator stress nuclear imaging. The advantage of CMR’s versatility is the potential to combine techniques in a single examination.

First-pass gadolinium-enhanced myocardial perfusion imaging by CMR is typically performed first during vasodilator stress and again at rest during the same CMR study using pulse sequences that are optimized for speed. This allows coverage of several short-axis slices within each R-R interval over a span of 40 to 50 heartbeats during the first pass of gadolinium. The optimal methodology used to perform CMR perfusion has been a subject of debate within the CMR community. Some investigators argue that qualitative analysis of stress and rest first-pass perfusion imaging will suffice, arguing that trained interpreters can recognize artifacts and that optimal sensitivity is the goal of vasodilator stress testing (4). Others suggest that quantitative analysis of the regional increase in myocardial signal intensity over time as contrast courses through the myocardium is required to deal with potential artifacts, and that specificity and overall accuracy are improved with this strategy (5–8).

The quantitative approach has been carefully validated against positron emission tomography (5), and the sensitivity, specificity, and overall accuracy in a single-center study has been reported as high as 88%, 90%, and 89% with such techniques (7). In a recent multi-center study using quantitative analysis, the specificity was not as high (75%), although stress imaging without rest imaging was used in this study (9). The drawback of quantitative analysis at present is that it is quite time-consuming with the software available and not ideal for day-to-day clinical purposes, although this is an area of rapid development.

Other strategies for identifying CAD in settings such as the emergency room (10) or in acute coronary syndromes (11) have used a more comprehensive approach, incorporating cine imaging and late gadolinium enhancement (LGE) imaging (10,11) as well as CMR coronary angiography (11). Diagnostic algorithms using the multi-modality approach afforded by CMR are becoming increasingly useful (12).

It is against this backdrop that the study of Klem et al. (13), in this issue of the Journal, comes to light. Their group studied 100 patients referred for X-ray coronary angiography, 76% of whom had had a positive exercise stress or stress nuclear or echocardiographic study. Interestingly, a sizeable proportion of these studies that prompted referral to the catheterization laboratory were false positives as only 40% of the population had CAD as defined by a stenosis ≥50% at catheterization. Klem et al. (13) performed a comprehensive CMR examination including cine imaging covering the left ventricle from apex to base and then stress and rest first-pass gadolinium-enhanced perfusion imaging. Their strategy included imaging four to five short-axis slices during first pass with a dose of 0.625 mM/kg of gadolinium using a hybrid gradient echo/echo planar sequence initially and, in the last 15% of patients, using parallel imaging to speed the image acquisition and theoretically improve image quality. Too few patients were studied with the latter technique to definitively answer the question as to whether parallel imaging improved results. Approximately 5 min after rest imaging, late gadolinium-enhanced imaging was performed with an inversion recovery sequence (14) that is excellent at identifying infarction (15) and has been shown to be superior to single-photon emission computed tomography for the identification of subendocardial myocardial infarction (16).

Several lessons can be learned from the experience of Klem et al. (13). For one, adenosine can be safely administered to patients with suspected CAD in the magnetic resonance environment. One of the 100 patients developed dyspnea requiring stoppage of the examination, one developed atrial fibrillation, and two others developed ventricular ectopy, and imaging remained analyzable, at least qualitatively, in the latter three patients. A second and more important lesson is that identification of even small infarcts improves the diagnostic accuracy of the comprehensive CMR approach. If matched stress/rest perfusion defects were seen in the absence of LGE, that defect was termed an

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artifact. This analytic strategy proved correct in 12 of 13 instances (92%). The sensitivity, specificity, and accuracy of stress/rest perfusion CMR alone were 84%, 58%, and 68%, respectively, and were improved with the additional analysis of LGE images to 89%, 87%, and 88%, respectively. Clearly the specificity is markedly improved with the addition of infarct imaging. This is a strategy that has been used for some time by the CMR community, but this is the first publication that validates this approach in a large clinical cohort. Cine imaging at rest was not additive, which is not necessarily surprising given the lack of history of CAD or infarction in this cohort. Stress functional imaging with dobutamine would likely have been additive, but rest function is insensitive.

Some questions remain from the work of Klem et al. (13). For one, what are the causes of the artifacts in the perfusion images, and can these be improved with parallel imaging or a newer pulse sequence? How would this strategy fare in a population with a higher prevalence of CAD? The 60% normal coronary artery rate in this study is high for the typical catheterization laboratory. Did any of the perfusion defects in those patients with evidence of LGE extend beyond the infarct border? If so, this would be equivalent to peri-infarct ischemia noted on single-photon emission computed tomography imaging and should be recognized as a positive result. No mention of this is made in the article. Agreement between two observers was used as the standard. It would have been more clinically relevant to have the observers interpret the data independently and assess interobserver variability. In addition, a four-point scale for qualitative analysis of the perfusion images was used, including “probably normal” and “probably abnormal.” It is not stated how often the image analysis included these categories compared with more definitive interpretation. The authors state that the final analysis included a binary analysis, normal or abnormal, but it would have helped to understand how definitive the analysis was.

The paper by Klem et al. (13) confirms the concept that infarct imaging improves the accuracy of perfusion imaging analyzed qualitatively. The parallel to the fixed defect on single-photon emission computed tomography imaging is noted, although the sensitivity of CMR for subendocardial infarct is higher (16), which adds to the clinical import of their findings. Qualitative image analysis, at least when combined with analysis of LGE images, may well be accurate enough for clinical purposes. Without the use of LGE, specificity suffers. Clearly, multi-center trials incorporating this strategy and comparing with other imaging technologies, with X-ray angiography as a reference standard, are needed in the future to allow CMR to take its proper place within the cardiac imaging community.

References