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Steadily Straining Toward Clinical Utility:

Real-Time Quantitative CMR of Myocardial Deformation During Stress*

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Wall motion stress testing using cardiac magnetic resonance (CMR) has been performed in multiple centers around the world in thousands of patients. This method of imaging shows high utility for visualizing the left ventricular (LV) endocardial wall motion at low or high heart rates throughout a cardiovascular stress test regardless of body habitus. To date, the majority of CMR wall motion stress studies are performed using qualitative wall motion assessment. Although useful for identifying individuals with inducible myocardial ischemia or those at risk for future cardiovascular events, these testing protocols require the administration of high doses of both dobutamine and atropine to achieve 85% of the maximum predicted heart rate response for age. Although clinical studies using wall motion observation at high heart rates are performed relatively frequently, these elevated heart rates provoke some anxiety as patients lie within the bore of the magnet. In addition, the high heart rates at peak stress reduce the available time within the RR interval to image the heart. This latter issue reduces the volume of myocardium that can be assessed during testing. In general, it would be desirable to image greater amounts of the LV myocardium during each stage of stress testing.

Previous studies have shown the high accuracy of dobutamine stress using cine CMR compared with dobutamine stress echo (1) and X-ray angiography (1,2), even using older gradient echo sequences. Accuracy is similar with more up-to-date steady-state free-precession approaches with or without accelerated image acquisition (3). Quantitation of intramyocardial deformation or strain can be performed using the well-validated technique of myocardial tagging as developed by Zerhouni et al. (4) and Axel and Dougherty (5) in the late 1980s. A previous study showed an improvement in sensitivity with tagging compared

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with cine imaging during dobutamine stress for the detection of coronary artery disease (CAD) without a decrement in specificity (6). Measurement of circumferential strain as can be performed with tagging has been shown to be more accurate at detecting ischemia than that performed with radial strain, which is the principal deformation tracked by the eye during the assessment of wall thickening (7). Thus, there is evidence that quantitation of abnormalities of deformation within the wall improves overall accuracy of dobutamine stress CMR as compared with visual assessment of wall thickening. However, extensive post-processing is required for analysis of standard tagged images, limiting its clinical utility. Emerging data suggest that strain may be measurable from feature-tracking analysis of cine images (8), which would be another major advance and simplification of image acquisition, although further validation in patients with ischemic heart disease is needed before this is used in the clinical routine.

A number of approaches have been developed to get around the difficult and time-consuming problem of post-processing of tagged images. One such approach, harmonic phase (HARP), enables near–real-time analysis of circumferential strain (9). However, HARP is limited by the spatial resolution of the tags themselves and by analysis of strain in the midwall, and thus is insensitive to transmural differences in strain. A higher-spatial-resolution technique for evaluation of regional myocardial deformation called displacement-encoded stimulated echoes (DENSE) was originally developed by Aletras et al. (10) and then was enhanced by enabling a cine acquisition (cine DENSE) by Kim et al. (11). This technique allows differentiation of strain in 3 dimensions and in a transmural fashion. Although improvements in post-processing have been implemented, data analysis still must be performed offline and studies during dobutamine stress have not yet been performed.

The strain-encoded imaging (SENC) technique, developed by the investigative team at Johns Hopkins led by Dr. Nael Osman (12), is a novel and robust method for demonstrating color-coded maps of strain displayed as embedded in the myocardium. The spatial resolution of this approach is higher than that of HARP, allowing differentiation of strain across the wall of the heart. The gradations of color as demonstrated in the outstanding image examples in the report by Korosoglou et al. (13) in this issue of *iJACC* delineate variations in strain from subendocardium to subepicardium. In normal individuals and in disease states including ischemia, infarction, and cardiomyopathies, strain is higher in the subendocardium than in the subepicardium, and this is readily demonstrable with SENC.

In the present study, the SENC images were acquired not only at peak dobutamine stress, but also at lower levels of stress with low doses of dobutamine (and consequently at lower heart rates) to identify inducible ischemia. In fact, the accuracy of SENC at the lower doses of dobutamine was equivalent to that of cine CMR at higher doses of dobutamine, thus potentially allowing an abbreviated examination. In addition, these quantitative assessments were obtained in near real time and did not require excessive post-processing. This feature has the potential to provide quantitative analyses in which inducible ischemia is readily identified at low levels of stress and short total stress duration. Because heart rates are lower, more coverage of the LV can be obtained. In addition, the clinician could avoid use of higher levels of dobutamine stress, which are less comfortable for patients.

There are some limitations to the data presented by Korosoglou et al. (13). First, the normal increase in strain previously demonstrated in normal subjects with intermediate doses of dobutamine (14) was not seen. The investigators state that this may in part be due to lack of correction for through-plane motion and the limitation of the range of detectable strain in their study to 0% to 25%. Second, there is some signal dropout at the apex due to the high degree of noise inherent to the SENC technique, which may be a limitation in patients with suspected left anterior descending disease. In addition, none of the patients studied had prior infarctions; future studies will need to include such patients to be able to broaden the applicability of this technique.

These are exciting times in imaging of wall motion because the ability to quantitate and analyze data rapidly at high spatial resolution is steadily improving. We are closer to the day when images are acquired during low doses of dobutamine with color-coded displays of strain immediately available at the computer console by the side of the scanner, allowing detection of ischemia with minimal patient discomfort and post-processing time. Because wall motion analysis is typically more specific than perfusion analysis using any imaging modality, including CMR (15), these advances have significant potential to improve the accuracy and ease of noninvasive detection of CAD and to avoid unnecessary invasive diagnostics.

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