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iVIEW

EDITOR'S PAGE

Atherosclerotic Plaque Imaging: The Last Frontier for Cardiac Magnetic Resonance

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For many years, studies of atherosclerosis had been relegated to the realm of the pathologist. It has only been in the last 15 years or so that the imaging approaches have developed the ability to perform atherosclerosis imaging in vivo, enabling serial studies in animals and humans rather than post-mortem studies. The first evidence that cardiac magnetic resonance (CMR) could be used to image atherosclerosis in vivo was demonstrated in the early 1990s in a rabbit model by a group at the University of Washington (1). CMR enabled identification of the fibrous cap and lipid core as well as fissures within the plaque. This work was extended to other animal models including mice, allowing the characterization of plaques in the transgenic models. Subsequent studies extended these findings to humans, demonstrating for the first time the ability to image carotid atherosclerosis in vivo using a surface coil on the neck and black blood T1-weighted (T1-W) spin echo imaging. Validation of CMR plaque imaging of the human aorta was later performed with transesophageal echocardiography and validation of carotid plaque imaging by histopathology after carotid endarterectomy. Measurements of atherosclerotic plaque volume in the aorta and carotid vessels using these techniques have shown that statins reduce plaque volume over a 2-year time period with minimal changes in lumen dimension (2). The test-retest reproducibility of these techniques in the carotid and other vascular beds such as the superficial femoral artery allows significant reductions in sample sizes required for clinical trials of pharmacologic regression of atherosclerosis.

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The ability of CMR to differentiate plaque components in the arterial wall has advanced steadily over the past decade. Much of this work has been performed in the carotid by the group of Chun Yuan, PhD, and Thomas Hatsukami, MD, whose work is highlighted on the cover of this issue of *iJACC* (3). This group has carefully validated multispectral CMR of the carotid against histology in patients who were imaged prior to undergoing carotid endarterectomy. This multispectral imaging generally includes T1-, T2-, and proton density-weighted imaging, T1-W imaging after contrast, and a noncontrast angiographic technique that allow differentiation of the fibrous cap, lipid-rich necrotic core, calcification, intraplaque hemorrhage, and loose matrix. Prospective studies from this group have demonstrated that the presence of intraplaque hemorrhage and thin fibrous cap on CMR carotid imaging predict subsequent transient ischemic attack or stroke. These imaging findings agree closely with pathologic studies that have highlighted similar high-risk features of vulnerable plaques. Other imaging studies using a multispectral approach in patients presenting with symptoms of acute stroke show that American Heart Association type VI plaque, which includes intraplaque hemorrhage, is the most powerful prognostic predictor. Additional plaque characterization approaches are under development, including T2* imaging of changes in iron forms within atherosclerosis (4). Lower T2* values were seen in carotid atherosclerosis of patients with symptoms as compared to those without symptoms.

The addition of various contrast agents to CMR atherosclerosis imaging has further contributed to plaque characterization. Late gadolinium enhancement (LGE) helps to identify the fibrous cap in plaque within abdominal aortic aneurysms and the amount of enhancement may be a marker of the extent of acute inflammation in the cap. Other gado-

linium-based agents under development such as gadofluorine have been used to identify plaque in animal models. Gadolinium has been linked to the targeting agents directed at inflammatory markers or monocyte-macrophage receptors within the plaque to improve localization and identification of vulnerable features of atherosclerosis. In patients prior to carotid endarterectomy, the wash-in kinetics of gadolinium into the carotid atherosclerosis has been demonstrated to correlate with plaque neovascularization and other features of plaque vulnerability. Another type of contrast agent, ultra-small superparamagnetic iron oxides, is taken up by macrophages and is associated with signal loss on carotid CMR images. Signal loss is sometimes difficult to distinguish from imaging artifacts and thus pulse sequences have been developed that allow positive contrast to be generated from these iron oxide molecules. Finally, specific fibrin-targeted contrast agents can improve localization and identification of thrombus in the left atrium, pulmonary arteries, and coronary arteries in animal models. Early examples of their use in Europe have been shown in isolated cases of aortic plaque/thrombus in humans.

Imaging plaque characteristics in the coronary artery has been the holy grail of noninvasive imaging of atherosclerosis. T1-W black blood imaging approaches have been applied to the wall of the coronary artery to demonstrate increased wall thickness in patients with coronary artery disease but without obstructive stenoses. Such approaches have been used to demonstrate increased coronary wall thickness in diabetics with renal disease compared to those without nephropathy. Spatial resolution limitations of CMR do not yet allow the differentiation of plaque components in the coronary wall in humans. However, recent reports in our journal have highlighted exciting advances in this arena. One report used noncontrast T1-W imaging in patients with stable angina (5) and compared it to the computed tomographic angiography-verified plaque characteristics of instability. The plaques with higher signal on T1-W imaging correlated with high risk features identified by intravascular ultrasound including positive remodeling, ultrasound attenuation, and spotty calcification. This high T1 signal was previously associated with American Heart Association type VI plaques including intraplaque hemorrhage on carotid imaging. This suggests that techniques are evolving such that CMR would be able to identify high risk features in the coronary vessels even if specific components in the coronary plaques are not fully resolved.

LGE has also made its way to the coronary wall. Preliminary work had shown that LGE was identifiable in the coronary wall in patients with established coronary atherosclerosis, but LGE is a nonspecific finding and can be seen in states of fibrosis, edema, and inflammation. A recent report has used gadolinium and a 3-dimensional T1-W gradient echo inversion recovery pulse sequence in a group of patients after acute myocardial infarction to demonstrate that LGE of the coronary wall decreased over time after the index event (6). Although these authors suggested that this technique may be a marker of inflammation or edema within the coronary wall, the enhancement was not localized to the particular site of occlusion, and was noted diffusely in the coronary tree. More work in this area is clearly needed in larger patient cohorts with different types of coronary syndromes to further elucidate the role of LGE of the coronary wall in identifying high-risk features.

The application of CMR atherosclerotic plaque imaging is limited at present, it remains in the hands of the few research laboratories that have dedicated resources and personnel to this endeavor. A greater effort is needed to train young investigators in the methodologies and background necessary to perform studies of this kind. It will require an increase in trained investigators and dissemination of pulse sequences and specialized coils to more centers as well as studies in larger numbers of patients for these research techniques to become clinical reality. With wider recognition of the potential contribution of these imaging approaches, we certainly hope that the CMR conquers this last elusive frontier of cardiovascular imaging. *iJACC* remains committed to bringing you the latest in the field.

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