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iREVIEWS

STATE-OF-THE-ART PAPER

Cardiac Magnetic Resonance Features of the Disruption-Prone and the Disrupted Carotid Plaque

Baocheng Chu, MD, PhD, Marina S. Ferguson, MT, Huijun Chen, PhD, Daniel S. Hippe, BS, William S. Kerwin, PhD, Gador Canton, PhD, Chun Yuan, PhD, Thomas S. Hatsukami, MD

Seattle, Washington

Stroke is a leading cause of long-term disability and is the third most common cause of death in the U.S. and western countries. Twenty percent of strokes are thought to arise from the carotid artery. Histopathological studies have suggested that plaque disruption is a key factor in the etiology of carotid-related ischemic events. Features associated with plaque disruption include intraplaque hemorrhage, large necrotic cores with thin overlying fibrous caps, plaque neovasculature, and inflammatory cell infiltrate. In vivo high-spatial-resolution, multicontrast-weighted cardiac magnetic resonance (CMR) has been extensively evaluated using histology as the gold standard, and has documented reliability in the identification of these key carotid plaque features. This pictorial essay illustrates the capability of CMR for identifying features of disruption-prone and disrupted atherosclerotic carotid plaques. (J Am Coll Cardiol Img 2009;2:883–96)

Stroke is a leading cause of long-term disability and is the third most common cause of death in many countries (1). Twenty percent of strokes are thought to be related to extracranial carotid atherosclerosis (2). As a means to prevent such cerebrovascular events, carotid endarterectomy and carotid stenting have been advocated in patients with high-grade carotid stenosis. However, the ACAS (Asymptomatic Carotid Atherosclerosis Study) (3) showed that carotid endarterectomy reduced risk for ipsilateral stroke by only 5.9% at 5 years when compared with best medical management. Therefore, additional criteria, other than the degree of stenosis, have been sought to better identify patients most at risk of complications from carotid disease.

Based on analysis of histological findings in carotid endarterectomy specimens, plaque disruption is believed to be a major factor in the etiology of carotid-territory ischemic events. Features such as intraplaque hemorrhage, large necrotic cores with thin overlying fibrous caps, plaque neovasculature, and inflammatory cell infiltrate (4–7) may predispose the atherosclerotic lesion to disruption. Hence, these features represent targets for imaging techniques aimed at identifying high-risk, disruption-prone plaque.

Equally important is the identification of luminal surface disruption, such as fibrous

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cap rupture, ulceration, and calcified nodules. Retrospective studies have shown that these so-called culprit lesion features are associated with a prior history of recent transient ischemic attack or stroke (8). Furthermore, they may pose a persistent increased risk for secondary events, as suggested by findings from histology studies showing evidence of repeated cap ruptures (9), and by findings from the NASCET (North American Symptomatic Carotid Endarterectomy Trial). In a subgroup analysis comparing individuals with and without ulcerated carotid plaques, those with ulcers on angiography had a 1.2- to 3.4-fold increased risk for stroke (10).

As a noninvasive imaging modality with the capability to distinguish tissue characteristics, cardiac magnetic resonance (CMR) is an optimal method for characterizing the morphology and composition of atherosclerotic carotid plaques (8,11–28). Multiple centers have shown that CMR can reliably identify fibrous cap status, the lipid-rich necrotic core, intraplaque hemorrhage, and vascular wall inflammation, using histology as the gold standard (14–21,23,29–36). Additional advantages of CMR include image generation without ionizing radiation or the need for invasive procedures, which make it an ideal tool for serial, longitudinal study of plaque progression or regression.

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

K^{trans} = transfer constant

MMP = matrix metalloproteinases

MRA = magnetic resonance angiography

TOF = time-of-flight

v_p = fractional plasma volume

WSS = wall shear stress

Recently published clinical studies show the potential prognostic value of CMR in patients with moderate carotid stenosis. In a prospective study of 154 patients with 50% to 79% carotid stenosis who were asymptomatic at the time of enrollment, participants underwent baseline carotid CMR and were contacted every 3 months to identify symptoms of new-onset transient ischemic attack or stroke (25). Twelve cerebrovascular events occurred ipsilateral to the index carotid artery over a mean follow-up period of 38.2 months. Cox regression analysis showed significant associations between ischemic events and presence of a thin or ruptured fibrous cap (hazard ratio: 17.0; $p < 0.001$), intraplaque hemorrhage (hazard ratio: 5.2; $p = 0.005$), and larger mean necrotic core area (hazard ratio for 10 mm^2 increase, 1.6; $p = 0.01$) in the carotid plaque. In another prospective study of 64 recently symptomatic patients with 30% to 69% carotid stenosis, baseline carotid CMR scans were performed to identify intraplaque hemorrhage, and subjects were followed up for the development of subsequent transient ischemic attack or stroke (37). Thirty-nine (61%) of the ipsilateral arteries showed intraplaque hemorrhage on baseline CMR. Fourteen ipsilateral ischemic events were observed during follow-up. Thirteen of the 14 events occurred ipsilateral to carotid arteries with intraplaque hemorrhage (hazard ratio: 9.8, 95% confidence interval: 1.3 to 75.1, $p = 0.03$). These studies suggest that carotid CMR may provide additional diagnostic criteria to identify patients with moderate carotid stenosis who are at increased risk for subsequent stroke. Although these initial results are highly promising, larger multicenter studies are needed to confirm the role of carotid plaque imaging in routine clinical practice.

This pictorial essay illustrates the capability of CMR for the identification of the disruption-prone and disrupted carotid plaque.

Multicontrast-Weighted CMR

The greatest strength of CMR for characterizing atherosclerotic plaque is the availability of multicontrast-weighted protocols using bright- and black-blood techniques. In the past, most applications of carotid CMR have been limited to the evaluation of stenosis using bright-blood magnetic resonance angiography (MRA). These angiographic pulse sequences produce strong attenuation of signals from stationary tissues, limiting their usefulness for direct imaging of the atherosclerotic plaque. Nevertheless, bright-blood MRA using a 3-dimensional time-of-flight (TOF) technique presents specific contrast features that can be helpful in identifying certain plaque components when used in combination with black-blood imaging (16). Black-blood sequences rely on the elimination of the signal from flowing blood and represent a general approach for characterizing the vessel wall, where precise identification of the lumen–wall interface plays a critical role in assessment of morphology and tissue composition of the atherosclerotic plaque (26) (Table 1). Implementation of this multicontrast-weighted CMR protocol has been technically successful in 76% to 90% of cases. Most of the failures are attributable to poor image quality secondary to patient motion (15–18).

Numerous studies have shown that combined intensity information from different contrast weightings (Table 1) can be used to identify all major plaque components, including fibrous tissue, lipid-rich necrotic core, calcification, and intraplaque hemorrhage (8,11–28). Using established guidelines