

Carotid Plaque Imaging: Strategies beyond Stenosis

Darshana Sanghvi, Manish Shrivastava

Division of Neuroradiology, Kokilaben Dhirubhai Ambani Hospital, Mumbai, Maharashtra, India

Abstract

Atherosclerosis at the carotid bifurcation in the neck is common and the result of turbulent hemodynamics in the bulb. Carotid bulb plaques cause disabling strokes. Carotid vessel wall imaging characterizes the atherosclerotic plaque, documents disease progression, and assesses lesion severity by plaque morphology in addition to the degree of stenosis. This in turn optimizes treatment selection for the individual patient. The aim of vessel wall imaging in patients of stroke is to distinguish stable plaques that may be conserved with best medical management from unstable or vulnerable plaques that require more aggressive medical treatment, carotid stenting, or carotid endarterectomy. Growing evidence suggests that depending on luminal stenosis measurements alone for management decisions will result in underestimating a number of plaques whose size may be small, but where the plaque morphology is unstable, there is a high likelihood of the patient developing a thromboembolic stroke in the near future. In today's context of aggressive management of even transient ischemic attacks and minor strokes, vessel wall imaging should be particularly performed in cryptogenic strokes without significant luminal narrowing on angiography to identify a subset of patients with nonstenotic but unstable atherosclerotic plaques that may be covert etiologies of stroke. If patients receiving the best medical management have recurrent strokes on the same side as a carotid plaque with "vulnerable" plaque features, they may deserve surgical or endovascular intervention even if they do not meet the conventional stenosis thresholds. Improved techniques for stroke imaging and consequent management have a remarkable effect in decreasing individual and public health burdens.

Keywords: Atherosclerosis, magnetic resonance imaging, plaque

INTRODUCTION

The contrast and spatial resolution of the current generation of MRI magnets and novel pulse sequences for the characterization of the morphology of the atherosclerotic plaque along the carotid vessel wall are impressive. Even in advanced atherosclerosis, the plaque is most often only a few millimeters in thickness. Assessment of histologically processed plaque specimens from endarterectomy has shown the width of individual plaque components starting from as small as 0.3 mm.^[1] The current generation of high field MRI magnets has exquisite resolution to demonstrate these small lesions. Similarly, there have been notable improvements in the use of ultrasonography (US) and computed tomography (CT) to assess the carotid plaque; albeit, with lower sensitivity and specificity as compared to MRI.^[2,3]

Atherosclerosis at the carotid bulb is common, and it is the result of turbulent hemodynamics often resulting in disabling strokes. Landmark studies such as the North American Symptomatic Carotid Endarterectomy Trial (NASCET)^[4] have historically confirmed that carotid endarterectomy (CEA) decreases the chance of stroke in significant carotid disease. Similar results have been documented for carotid stenting.^[5] However, converging evidence from more recent studies^[6,7] suggests that substantial carotid disease can exist in the absence of significant luminal stenosis, and hence biomarkers of plaque vulnerability must be included as criteria in the next generation of randomized control trials (RCT) for stroke prevention.^[8] Carotid vessel wall imaging characterizes the atherosclerotic plaque, documents disease progression, and assesses lesion

severity by plaque morphology. A recent meta-analysis^[9] reports intraplaque hemorrhage (IPH) to be a stronger predictor of stroke compared to any clinical risk factors across the spectrum of mild to significant degrees of stenosis.

State-of-the-art vessel wall imaging should be incorporated in standard clinical stroke management algorithms to optimize patient-specific risk stratification and treatment selection rather than focusing on conventional luminal stenosis measurements alone.

RATIONALE

The aim of vessel wall imaging in stroke is to distinguish stable plaques that may be conserved with best medical management from unstable or vulnerable plaques that require more aggressive treatment, such as carotid stenting or endarterectomy. Historically, the concept of plaque imaging

Address for correspondence: Dr. Darshana Sanghvi,
Kokilaben Dhirubhai Ambani Hospital, 4 Bungalows, Andheri West,
Mumbai - 400 053, India.
E-mail: darshana.sanghvi@kokilabenhospitals.com

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has been borrowed from studies of coronary circulation. Growing evidence suggests that depending on luminal stenosis measurements alone for management decisions will result in underestimating a number of plaques whose size may be small, but where the plaque morphology is unstable, there is a high likelihood of the patient developing a thromboembolic stroke in the near future. Surprisingly and perhaps counterintuitively, many high-grade stenoses are asymptomatic with low rates of symptomatic conversion.^[10] On the other hand, it is now well recognized that many symptomatic patients with <50% stenosis have significant recurring ipsilateral strokes.^[11]

The carotid bulb has an unusual shape; its diameter is wider than the distal internal carotid artery in the neck. Thus, it is possible to have a significant plaque burden in the carotid bulb without impressive luminal stenosis. Also, many atherosclerotic plaques develop in an eccentric fashion with the bulk of the plaque growing away from the lumen; again, in these cases, the luminal stenosis is unlikely to be impressive. This concept of vessel wall dilatation due to an increase in plaque volume without significant luminal narrowing is termed positive remodeling^[12] [Figure 1]. When the vessel lumen is narrowed by a plaque, it is termed negative remodeling.

Thus, the assessment of plaque morphology is as important as calculation of the degree of luminal stenosis when envisaging the probability of recurrent stroke. Biomarkers of plaque vulnerability derived from MR vessel wall imaging of the carotid bulb can improve accuracy in predicting patient-specific risk of developing thromboembolic artery to artery stroke.

TECHNICAL CONSIDERATIONS

Technically, the carotid artery lends itself to vessel wall imaging for a number of reasons; chief amongst which are its superficial location and large size. Remoteness from lung and heart motion is also an advantage.

For MR imaging of the carotid vessel wall, dedicated phased-array surface coils are commercially available. At high field strengths, multi-channel head coils provide sufficient resolution. MRI pulse sequences used to study the carotid vessel wall provide a small field of view and high-resolution axial images. A combination of “white blood”

and “black blood” pulse sequences is traditionally employed. At 3.0 Tesla field-strength, signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) for wall/lumen of the carotid bulb is superior to 1.5T.^[13-15] Contrast-enhanced ultrasound and intravascular ultrasound have added value to the sonographic assessment of the vessel wall. However, both US and CT have limitations in the assessment of the carotid vessel wall as compared to MRI.^[16]

MRI FEATURES OF UNSTABLE PLAQUES: BIOMARKERS OF STROKE RECURRENCE

Availability of plaque specimens from endarterectomy surgeries and special stains to assess the components on histology have allowed validation of the results of plaque morphology imaging. These studies have demonstrated a remarkable correlation between plaque components defined by preoperative MRI and postoperative histology using special stains. MRI findings correlated with the histologic presence of a necrotic core or recent intraplaque hemorrhage with up to 92% specificity and 85% sensitivity.^[17]

Vulnerable or unstable plaques progress rapidly and have a high association with thromboembolic events. Imaging biomarkers of the vulnerable plaque are intraplaque hemorrhage, large lipid core, thin or disrupted fibrous cap, and surface ulceration.^[18,19] Of these, the most ominous feature of the unstable plaque is the presence of hemorrhage. Intraplaque hemorrhage is considered a sensitive independent biomarker of the probability of future strokes as longitudinal studies bear witness to an exponential increase in the size of a plaque where imaging has demonstrated intraplaque hemorrhage.^[20] Hemorrhage within a plaque is readily recognized on MRI.

The other radiological feature that bears direct correlation with the likelihood of stroke recurrence is the demonstration of rupture of the fibrous cap of a lipid-rich plaque. While the stigma of prior plaque rupture has important implications, another pertinent radiological predictor of plaque vulnerability is a thin fibrous cap. The thickness (or thinness) of the fibrous cap of an atherosclerotic plaque is best determined on the post-contrast T1-weighted high resolution and small field of view axial image, in which the fibrous cap enhances,

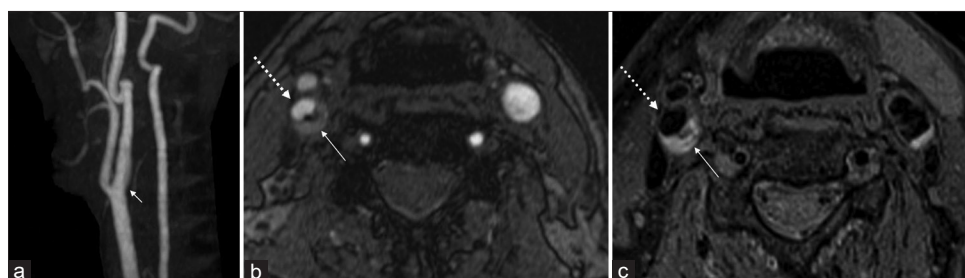


Figure 1: Middle-aged man with recurrent right MCA territory TIAs. (a) MRA shows mild stenosis at the right carotid bulb (short arrow). (b) White blood and (c) black-blood vessel wall imaging show a significant plaque burden representing a source of emboli. An ulcerated, unstable plaque (solid arrows) at the right carotid bulb has propagated away from the lumen (dotted arrows). Although the plaque burden is significant, it does not cause impressive stenosis (positive remodeling)

whereas the lipid core remains nonenhancing. Plaque burden is traditionally determined both on MRI and ultrasound by various calculations such as in the intima-media thickness. The implication of calcification in a plaque remains equivocal, with certain authors believing that calcification stabilizes a plaque and others of the opinion that calcified plaques are vulnerable and unstable.

In contradistinction, features that suggest a stable plaque size include predominant fibrous content and a thick and smooth cap.

The future of plaque imaging will feature MRI pulse sequences (plaque perfusion using dynamic contrast-enhanced MRI)^[21] and contrast agents (iron oxide)^[22] that demonstrate inflammation which is now considered to be a key player in the development of the atherosclerotic disease of the carotid vessel wall. The outcome of several recent studies have shown increased. ¹⁸F fluorodeoxyglucose (¹⁸F FDG) uptake on PET/CT represents inflammation in the plaque and is a sensitive biomarker of early recurrent stroke risk.^[23]

Finally, artificial intelligence and deep-learning technology in radiology have rapidly progressed over the past decade, with early reports^[24] of application in carotid plaque imaging, raising the exciting possibility of implementation in routine clinical practice when validated.

CHALLENGES

The central challenge in incorporating carotid plaque imaging in clinical stroke management across our country remains the lack of widespread availability of sophisticated MRI and US equipment. This includes specialized hardware -such as high-resolution linear US probes, dedicated MRI coils, and access to newer pulse sequences. MRI in particular is an expensive proposition in our resource-limited setting. Other hurdles include inadequate experience and expertise amongst radiology technologists and general radiologists in uniform acquisition and interpretation protocols. Finally, neurologists, interventionists, and neurosurgeons may benefit from more pertinent knowledge of the distinct indications of this novel technique.

CONCLUSIONS

Even in the western world, only a fraction of patients with transient ischemic attacks (TIA) and minor strokes are appropriately directed to a neurovascular clinic for detailed imaging and treatment. These patients have an exceptionally high chance of developing a subsequent major stroke in the first week after the transient ischemic event/minor stroke. Investigating and treating the patient with TIA or minor stroke early after the event can significantly decrease the recurrent stroke rate. Traditional angiograms image the arterial lumen and not the vessel wall. Relying on luminal stenosis measurements alone can underestimate the risk of stroke recurrence in the near future. Patients with atherosclerosis

may have a vulnerable plaque which is the source of emboli, in the absence of impressive luminal narrowing.

In today's context of aggressive management of the patient with TIA or minor stroke, vessel wall imaging should be performed to differentiate the stable plaque that may be conserved with best medical management from the unstable or vulnerable plaque that will benefit from more aggressive management such as carotid stenting or endarterectomy. This is particularly relevant in assumed cryptogenic strokes where luminograms such as catheter-based, CT or MRI angiograms do not show significant stenoses. Improved techniques for stroke imaging and consequent management have a remarkable effect in decreasing individual and public health burdens.

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Conflicts of interest

There are no conflicts of interest.

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