Plaque Assessment in the Management of Patients with Asymptomatic Carotid Stenosis

J. Kevin DeMarco, MD[a,*], J. David Spence, MD, FRCPC[b]

KEYWORDS

• Carotid atherosclerosis • Plaque • MR imaging • Ultrasonography • Asymptomatic carotid stenosis

KEY POINTS

- Despite current medical therapy, some patients with asymptomatic carotid stenosis go on to stroke.
- Carotid plaque imaging may identify these high-risk asymptomatic patients who could benefit from more intensive medical therapy.
- The presence of a measurable lipid-rich necrotic core may be the phenotype of asymptomatic atherosclerotic carotid plaque disease that is more responsive to intensive medical therapy.
- Direct monitoring of the necrotic core size and/or overall plaque burden in patients with asymptomatic carotid stenosis may provide a better measure of intensive medical therapy than serum markers such as low-density lipoprotein cholesterol.
- The presence of carotid intraplaque hemorrhage and/or ulceration in patients with asymptomatic carotid stenosis may require close monitoring to identify progression despite intensive medical therapy that is better treated with surgical intervention.

INTRODUCTION

Current Medical Therapy in Patients with Asymptomatic Carotid Stenosis

The identification and treatment of cardiovascular risk factors has been the hallmark of stroke prevention, starting in the 1970s and 1980s with the medical management of hypertension associated with a sharp decline in stroke mortality.[1] With the widespread use of statin therapy to lower LDL cholesterol (LDL-C) levels there was an additional, if slower, decline in stroke mortality in the 1990s.[2]

The most recent revision of the American College of Cardiology/American Heart Association (AHA) Task Force on Practice Guidelines continued the emphasis on the use of fixed doses of cholesterol level–lowering drugs to reduce cardiovascular risk based on epidemiologically defined risk factors.[3] The members of this 2013 task force did acknowledge that other treatment approaches, including the use of carotid plaque burden features to determine individual risk and modify treatment therapy based on plaque burden, have been advocated but have not yet been evaluated in randomized

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[a] Department of Radiology, Michigan State University, Radiology Building, 846 Service Road, Room 184, East Lansing, MI 48824, USA; [b] Departments of Neurology and Clinical Pharmacology, Stroke Prevention and Atherosclerosis Research Centre, Robarts Research Institute, Western University, 1400 Western Road, London, Ontario N6G 2V4, Canada

* Corresponding author.

E-mail address: jkd@rad.msu.edu

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clinical trials. New randomized clinical trials are underway that will study carotid burden imaging in the treatment of patients with asymptomatic carotid stenosis (ACS). In addition, multiple natural history studies have confirmed the ability of carotid burden imaging to better stratify risk compared with known atherosclerotic cardiovascular disease (ASCVD) risk factors, with multiple imaging studies showing the ability to monitor therapeutic response directly.

Potential New Medical Therapy in Patients with Asymptomatic Carotid Stenosis Based on Plaque Assessment

There are 2 ongoing large randomized clinical trials evaluating medical therapy versus surgical/endovascular intervention in patients with ACS (Carotid Revascularization Endarterectomy versus Stenting Trial [CREST-2] and Asymptomatic Carotid Surgery Trial [ACST-2]). Both will include an imaging substudy to evaluate the role of vulnerable plaque imaging in asymptomatic patients with greater than 70% carotid stenosis. In addition, the Asymptomatic Carotid Stenosis and Risk of Stroke trial is a large prospective study on patients with ACS undergoing medical intervention. ACSRS showed that not all patients with ACS carry the same risk of stroke. Specifically, the severity of carotid stenosis, a history of contralateral transient ischemic attack (TIA), and several carotid plaque features on ultrasonography could stratify patients into groups of varying annual stroke risk from less than 1% to greater than 10%.[4,5] Two large prospective studies showed that microemboli on transcranial Doppler (TCD) identify high-risk patients with ACS.[6,7] More intensive medical therapy based on measurements of carotid total plaque area (TPA) calculated from high-resolution duplex ultrasonography (DUS) rather than consensus guidelines reduced the occurrence of microemboli from 12.6% to 3.7% of patients, slowed the progression of carotid TPA, and reduced the risk of stroke or myocardial infarct by more than 80%.[8] In addition, there are multiple single-center prospective trials showing the ability of multiple magnetic resonance (MR)–defined plaque characteristics to stratify risk of future juxtaluminal carotid TIA or stroke such as the size of the lipid-rich necrotic core (LRNC),[9,10] intraplaque hemorrhage (IPH),[11] and thin/ruptured fibrous cap (FC).[9]

This article reviews this growing body of literature, which suggests that carotid plaque assessment with ultrasonography and MR imaging provides superior risk stratification for individual patients compared with carotid stenosis and other epidemiologically identified cardiovascular risk factors. It also reviews current drug trials using carotid plaque imaging to assess the effectiveness of medical therapy. In addition, it reviews how certain carotid plaque features, such as a large LRNC, may represent a phenotype of ASCVD with high risk of future events that is amenable to intensive medical therapy. It also reviews other plaque features, such as IPH and ruptured FC/ulceration, that may represent vulnerable plaque that requires close monitoring to identify plaque progression or new symptoms despite intensive medical therapy and may require surgical intervention. **Tables 1** and **2** summarize these important carotid plaque features on MR imaging and ultrasonography, their associated outcomes, and potential clinical utility to optimize the clinical management of patients with ACS. The potential to individualize the patients' medical therapy for ASCVD based on carotid burden imaging is stressed. Carotid burden imaging has the potential to change the treatment paradigm of patients with ACS from treating risk factors to treating arteries.[7]

IMAGING TECHNIQUES

Overview

MR imaging depiction of plaque burden is most reliably measured as percentage wall volume (PWV), which is similar to the percentage atheroma volume measured in coronary arteries during intravascular ultrasonography. Ultrasonography depiction of plaque burden includes TPA and total plaque volume (TPV). The ultrasonography and MR imaging techniques to precisely estimate plaque burden are reviewed. The progression or regression of plaque burden can be a powerful measurement of an individual's response to medical therapy.

Histologic studies have shown that coronary artery plaques with a large LRNC and an overlying thin FC are associated with sudden cardiac death.[12] This finding and additional research have led to the concept of vulnerable plaque.[13,14] From this work emerged key plaque features of the vulnerable plaque, including a large LRNC with a thin FC, active inflammation with activated macrophages, fissured plaque, superficial calcified nodules, and IPH. The AHA has proposed a detailed classification scheme of atherosclerotic plaque[15] that has now been extended to in vivo carotid plaque MR imaging.[16] Patients with ACS with LRNC are classified with an AHA type IV to V plaque and those with IPH, ruptured FC, and/or calcified protruding nodule are showing an AHA type VI plaque, which some investigators also call a vulnerable plaque. This article reviews the histologically validated research detailing the MR imaging techniques to identify LRNC, thin/ruptured FC, protruding nodule, and IPH.