JACC: CARDIOVASCULAR IMAGING
VOL. 7, NO. 4, 2014

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2013.09.022

Prediction of High-Risk Plaque Development and Plaque Progression With the Carotid Atherosclerosis Score

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OBJECTIVES The goal of this prospective study was to evaluate the carotid atherosclerosis score (CAS) for predicting the development of high-risk plaque features and plaque burden progression.

BACKGROUND Previous studies have shown that carotid intraplaque hemorrhage (IPH) and a disrupted luminal surface (DLS), as identified by using magnetic resonance imaging, are associated with greater risk for cerebrovascular events. On the basis of data from a large cross-sectional study, a scoring system was developed to determine which plaque features are associated with the presence of IPH and DLS. However, the predictive value of CAS has not been previously tested in a prospective, longitudinal study.

METHODS A total of 120 asymptomatic subjects with 50% to 79% carotid stenosis underwent carotid magnetic resonance imaging scans at baseline and 3 years thereafter. Presence of IPH and DLS, wall volume, maximum wall thickness, and maximum percent lipid-rich necrotic core area were measured at both time-points. Baseline CAS values were calculated on the basis of previously published criteria.

RESULTS Of the 73 subjects without IPH or DLS at baseline, 9 (12%) developed 1 or both of these features during follow-up. There was a significant increasing trend between CAS and the development of new DLS ($p < 0.001$) and with plaque burden progression ($p = 0.03$) but not with the development of new IPH ($p = 0.3$). Percent carotid stenosis was not significantly associated with new DLS ($p = 0.2$), new IPH ($p = 0.1$), or plaque progression ($p = 0.6$).

CONCLUSIONS CAS was found to have a significant increasing relationship with incident DLS and plaque progression in this prospective study. CAS can potentially provide improved risk stratification beyond luminal stenosis. (J Am Coll Cardiol Img 2014;7:366–73) © 2014 by the American College of Cardiology Foundation

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Stroke is one of the leading causes of mortality and morbidity worldwide, and carotid atherosclerotic disease is a primary etiologic factor (1,2). Currently, the risk of stroke associated with carotid atherosclerosis is stratified according to the severity of luminal stenosis (3). Several large prospective clinical trials (4–6) have supported intervention with carotid endarterectomy (CEA) or stenting for symptomatic patients with >70% stenosis to reduce stroke risk. However, for symptomatic patients with <70% stenosis and for asymptomatic patients, stenosis alone may not be a reliable measure of stroke risk. A growing body of evidence suggests that plaque composition, as detected using magnetic resonance imaging (MRI) rather than luminal narrowing, is the critical factor governing risk of ischemic cerebrovascular events originating from the carotid artery (7–12). Specifically, the presence of a disrupted luminal surface (DLS) (e.g., fibrous cap rupture [FCR], ulceration) and/or intraplaque hemorrhage (IPH) is indicative of a high-risk lesion for ischemic events (13–16).

Although results from studies to better characterize carotid atherosclerosis using MRI hold great promise, progress toward its translation into clinical practice has been hindered by the complex nature of analysis of the multicontrast-weighted images. A simple-to-use method to classify plaque that has predictive value for carotid lesion progression and future ischemic events is essential to move the field forward.

In a cross-sectional study of 435 subjects from 4 imaging sites in the United States and China, Underhill et al. (17) proposed a rapid risk stratification strategy, known as the carotid atherosclerosis score (CAS), based on maximum wall thickness (WT) and the maximum lipid-rich necrotic core percentage (%LRNC). Statistical analysis found that CAS was an accurate predictor for the presence of IPH and FCR in the test subgroup of this single time-point study. Furthermore, when compared with stenosis measured using magnetic resonance angiography, CAS was a stronger classifier of high-risk features.

Although CAS was successfully designed and tested in a cross-sectional study (17), it is unclear if it can predict the development of high-risk plaque features and plaque burden progression in a prospective, longitudinal study. The goals of the present study were to: 1) investigate the associations between the CAS, incident IPH, or DLS and plaque burden progression during follow-up; and 2) to compare CAS and stenosis in risk prediction among asymptomatic individuals with 50% to 79% carotid stenosis.

METHODS

Study subjects. Subjects with 50% to 79% carotid stenosis on at least 1 side consented to be recruited into this study at the University of Washington Medical Center and the Veterans Affairs Puget Sound Health Care Systems. Carotid stenosis was determined with duplex sonography using the Strandness criteria (18). The side with greater stenosis was defined as the index artery. All subjects were asymptomatic with regard to their carotid disease for the 6 months before recruitment. One hundred twenty subjects underwent a baseline carotid MRI and follow-up scan 3 years thereafter.

Subjects with any of the following conditions were excluded: 1) CEA before or during the study on the index carotid artery; 2) previous radiation therapy to the neck; and 3) contraindication to MRI.

MRI. All subjects underwent MRIs at baseline and at the 3-year follow-up on a 1.5-T scanner (Signa Version 5.8, GE Healthcare, Milwaukee, Wisconsin) with a bilateral, 4-element, phased array surface coil (Pathway MRI, Seattle, Washington). A multicontrast protocol for carotid MRI (19) was used to acquire axial images with the parameters listed in Table 1.

Image analysis. The index arteries of all subjects were interpreted via consensus opinion by 2 experienced reviewers who received certified training at the Vascular Imaging Laboratory, University of Washington, Seattle, Washington. Both reviewers were blinded to the time-point and clinical information during image analysis. For each scan, multicontrast magnetic resonance images were aligned using the carotid bifurcation as a landmark. At each registered axial slice, images were graded for image quality on a 4-point scale in which 1 = poor and 4 = excellent. Slices with image quality ≥2 at both time-points were interpreted using

ABBREVIATIONS AND ACRONYMS

AUC = area under the curve
CAS = carotid atherosclerosis score
CEA = carotid endarterectomy
CI = confidence interval
DLS = disrupted luminal surface
FCR = fibrous cap rupture
IPH = intraplaque hemorrhage
LRNC = lipid-rich necrotic core
MRI = magnetic resonance imaging
NWI = normalized wall index
WT = wall thickness

consultant for Bristol-Myers Squibb, Imagepace, Merck, Boehringer Ingelheim, and Pfizer. Dr. Hatsukami has received research grant support from the National Institutes of Health and Philips Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received May 24, 2013; revised manuscript received September 13, 2013, accepted September 19, 2013.