HIGH-RESOLUTION 3T CAROTID MRI IDENTIFIES THE HIGH-RISK LESION IN PATIENTS WITH MODERATE (<70%) CAROTID STENOSIS

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Introduction: Large, prospective, randomized trials have identified an improvement in outcome by offering surgery to neurologically symptomatic patients with severe carotid stenosis [1]. In symptomatic patients with moderate carotid stenosis (<70%) or in asymptomatic patients with carotid disease, the optimal treatment strategy remains ambiguous. Recently, multi-contrast, *in vivo* MR vessel wall imaging has found a correspondence between carotid plaque characteristics and both previous and future ipsilateral thromboembolic events [2-4]. With the advent of 3.0 T MR imaging, high-resolution *in vivo* carotid plaque studies with improved signal-to-noise ratio [5,6] have been enabled as well as very high-resolution ($0.28\ mm^3$) contrast-enhanced carotid MR angiography (CE MRA) [7].

Purpose: We sought to identify features detected on carotid MRI and CE MRA associated with recent cerebrovascular symptoms in a population of subjects with known carotid atherosclerotic disease. Beyond evaluating the group as a whole, we utilized the CE MRA data to isolate the subgroups of individuals with <70% and 70-99% stenosis to identify differences in imaging results between symptomatic and asymptomatic groups that may discriminate between stable and unstable lesions within each particular cohort.

Methods: Ninety-seven consecutive patients with carotid artery stenosis between 50%-99% in at least one artery identified with non-invasive imaging such as duplex ultrasound or CT angiography underwent carotid MRI at 3.0 T after filling-out a healthcare questionnaire and having their height and weight measured. A standardized protocol optimized for 3.0 T imaging [5,6] was utilized to obtain 3D time-of-flight (TOF), 2D T2-weighted FSE [8], and 2D T1-weighted pre- and post-contrast quadruple inversion-recovery [9] FSE sequences. After bolus gadolinium contrast intravenous injection and prior to the post-contrast T1-weighted acquisition, a coronal elliptical-centric carotid CE MRA with $0.28\ mm^3$ resolution was performed [7]. Total scan time for all sequences was < 45 minutes. Two experienced reviewers, blinded to clinical outcome, interpreted all images by reaching a consensus opinion. Custom designed software (CASCADE [10], Seattle, WA, USA) was used to draw the lumen and outer wall boundaries of the carotid artery at each axial location. In addition, calcification, necrotic core, and type I / type II hemorrhage were identified as present or absent using previously published criteria that have been validated with histology [11]. When a component was present, the proportion of the arterial wall occupied by that component was recorded (e.g. percent calcification = calcification area / wall area). When a necrotic core was present, fibrous caps status was categorized as either "thick" versus "thin or ruptured" using previously published, histologically validated criteria [12]. In addition, the presence of smooth, irregular, or ulcerated lumen on CE MRA was determined based upon previously published standards. Finally, the NASCET percent carotid stenosis was measured from the high resolution carotid CE MRA. Univariate logistic regression analysis was used to identify associations between clinical data and metrics identified with carotid MRI/MRA and recent cerebrovascular symptoms for both the group as a whole and for the subgroup with < 70% stenosis. Meaningful multivariate analysis could not be performed because of the small number of cases with recent symptoms. Results from logistic regression analysis are presented as odds ratios (OR) with 95% confidence interval (CI).

Results: Among the 97 patients (97 arteries) evaluated, 7 (7.2%; 100% asymptomatic) arteries were excluded due to poor image quality. Of the remaining 90 subjects (male gender, 58%; mean±SD age, 71±8.7 years), 13 (14.4%) had a recent transient ischemic attack or stroke. Presence of a thin/ruptured fibrous cap (OR, 4.22; 95%CI, 1.08-16.53; p=0.037), type I hemorrhage (OR, 5.74; 95%CI, 1.60-20.59; p=0.007), and maximum % area of type I hemorrhage (OR for 10% increase, 2.78; 95%CI, 1.45-5.34; p=0.002) were identified as significant predictors of a neurological event. All the other variables, including MRA stenosis and clinical data, were not significantly associated with recent symptoms.

Of the 49 patients with < 70% carotid stenosis by MRA, 6 (12.2%) were symptomatic. Results of metrics identified with a significant association during univariate analysis are presented in Table 1. In this subgroup, we did not identify a significant association between symptom status and MRA features and/or clinical data.

Of the 41 patients with 70-99% carotid stenosis by MRA, 7 (17.1%) were symptomatic. The maximum % area of type I hemorrhage (OR for 10% increase, 3.07; 95%CI, 1.10-8.55; p=0.032) and the presence of ulcer detected by CE MRA (OR, 11.00; 95%CI, 1.18-102.38, p=0.035) were the only metrics with a significant association with symptoms.

Discussion: In our study population, there were a similar proportion of symptomatic individuals in the subgroup with <70% stenosis compared to the subgroup of 70-99% stenosis. For the population as a whole and for each subgroup, intraplaque hemorrhage, particularly Type I hemorrhage, was significantly associated with symptom status. This finding is consistent with data from previous reports [13]. In lesions with <70% stenosis by MRA, we found a strong association between fibrous cap status, intraplaque hemorrhage, and the size of the necrotic core and symptom status (Fig. 1). Arterial remodeling as proposed by Glagov [14] may enable high-risk lesions to develop before significant luminal compromise occurs.

Conclusions: In patients with moderate stenosis (<70%) by MRA, vessel wall imaging may be able to distinguish between stable and unstable lesions. Large, prospective studies are necessary to determine the ability of carotid MRI to identify high-risk plaques in this particular cohort. Identification of high-risk lesions prior to the development of neurological events would have a profound, positive impact on patient management and outcomes.

Table 1. Relationship Between MR Carotid Plaque Findings & Recent Ipsilateral Symptoms for 49 Subjects With < 70% Carotid Stenosis

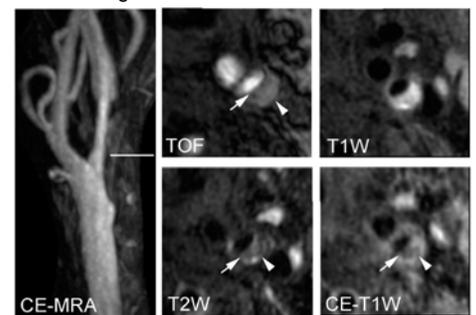| Variable	OR	95% CI	p
Presence of thin/ ruptured fibrous cap	10.8	2.0-58.7	0.002
Presence of necrotic core	9.8	1.8-53.0	0.010
Presence of type I hemorrhage	6.2	1.0-38.0	0.050
Presence of type II hemorrhage	6.6	1.1-41.5	0.044
Max % area necrotic core	1.5	1.0-2.2	0.037
Max % area type I hemorrhage	2.7	1.2-6.4	0.023

Figure 1. Images from a symptomatic patient with 55% stenosis by MRA. A thin fibrous cap (arrow) and intraplaque hemorrhage (arrowhead) are present on carotid MRI.

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