New Insights of Carotid High-Risk Atherosclerotic Plaques Determined by Proportion of the Arterial Wall Occupied by the Lipid-Rich Necrotic Core in Symptomatic Patients: A 3.0T MRI study

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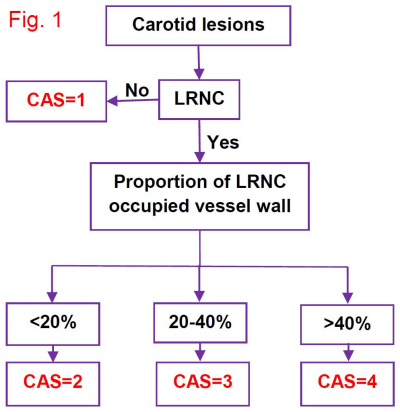
Introduction: It has been well-established that intraplaque hemorrhage (IPH) and fibrous cap rupture (FCR) are associated with cerebrovascular ischemic events [1-3]. Neurological symptoms and sequelae caused by advanced carotid lesions with above plaque features may exist as detection of these lesions. As such, investigation of carotid atherosclerotic lesions prior to occurrence of IPH or FCR might be a desirable solution for primary and secondary prevention of ischemic stroke. Recently, Underhill et al [4] proposed an algorism to calculate the carotid atherosclerosis score (CAS) that effectively stratifies plaque's risk of developing future IPH or FCR. The CAS algorism is based on the proportion of the arterial wall occupied by the lipid-rich necrotic core (LRNC) detected by MR vessel wall imaging. However, the incidence of these carotid high-risk plaques determined by CAS in symptomatic patients is unknown.

Purpose: This study sought to investigate the incidence of carotid high-risk plaque determined by CAS using MRI in patients with neurological symptoms.

Methods: One hundred fifteen patients (82 males. mean age 63.5 years) with recent TIA or stroke (≤ one week) underwent carotid black-blood MRI at a 3.0T whole body scanner (Achieva, Philips Medical System, Best, Netherlands) with an 8-channel phase-array carotid coil. ***MR imaging:*** Carotid arteries were imaged using multicontrast sequences (T1w, T2w, 3D TOF, and MP-RAGE) with the following parameters: T1w: quadruple inversion-recovery (QIR) [5], black-blood, 2D TSE, TR/TE 800/10ms; T2w: Multi-slice Double IR (MDIR), TR/TE 4800/50ms; 3D TOF: TR/TE 20/4ms, flip angle 20°; and 3D MP-RAGE: TR/TE 8.8/5.3 ms. All axial images were acquired centered to the bifurcation of index carotid artery which is responsible for the symptoms using field of view (FOV) 14cm x 14 cm^2 and acquisition matrix 256x256. The slice thickness and longitudinal coverage were 2mm and 32mm for T1w and T2w imagimging and 1mm and 40mm for TOF and MP-RAGE imaging, respectively. ***Data analysis:*** The boundaries of lumen and outer wall for each axial location were traced using custom-designed software (CASCADE [6], Seattle, WA, USA) by two experienced reviewers with consensus blinded to clinical information. The lumen area, wall area (WA), and wall thickness were measured at each axial location. The maximum wall thickness (MaxWT) was calculated for each artery. In addition, the presence or absence of plaque compositions including calcification, LRNC, and IPH/FCR was identified using previously published criteria [7]. The percentage of LRNC occupied arterial wall was also calculated for each location. According to CAS algorism, carotid plaques without IPH or FCR will be given a risk score that is based on the proportion of the arterial wall occupied by the LRNC (Fig. 1): score 1: low risk (no LRNC); score 2: medium-low risk (% LRNC ≤ 20%); score 3: medium-high risk (% LRNC = 20%-40%); score 4: high risk (% LRNC > 40%). The 3D TOF images were reconstructed using maximum intensity project approach to measure the luminal stenosis for each artery. The prevalence of carotid high-risk plaque determined by CAS algorism in carotid stenosis categories, including <70%, <50%, and <30% stenosis, was recorded.

Fig. 1



Results: Of 115 recruited patients, 105 had stroke, 11 developed TIA, and 63 (54.8%) showed MaxWT > 2mm. In this study population, 13 subjects (11.3%) had IPH/FCR, 67 (58.3%) had LRNCs, and 50 (43.5%) developed calcification in carotid arteries. IPH/FCR can be seen in 5.7% and 4.1% of carotid arteries with <70% setnosis and <50% stenosis, respectively. After calculation of the CAS for those carotid arteries with LRNC but without IPH/FCR, we found that the CAS of 6.1% of carotid arteries was equal to 4 which represents plaques at high risk of developing future IPH/FCR. In different carotid stenosis categories, we observed that 8.6%, 9.2% and 6% of arteries with <70% setnosis, <50% stenosis, and <30% stenosis exhibited CAS=3, and 5.7%, 4.1% and 2.4% of arteries with <70% setnosis, <50% stenosis, and <30% stenosis exhibited CAS=4, respectively (Table 1).

Table 1. Carotid plaque features in different stenosis categories.

	All (N=115)	Carotid stenosis categories		
		< 70% (N=105)	< 50% (N=98)	<30% (N=83)
MaxWT>2mm	63 (54.8)	54 (51.4)	48 (49.0)	33 (39.8)
Calcification	50 (43.5)	41 (39.1)	36 (36.7)	24 (28.9)
LRNC	67 (58.3)	58 (55.2)	51 (52.0)	38 (45.8)
IPH/FCR	13 (11.3)	6 (5.7)	4 (4.1)	0 (0.0)
CAS=1	48 (41.7)	47 (44.8)	47 (48)	45 (54.2)
CAS=2	37 (32.2)	37 (35.2)	34 (34.7)	31 (37.3)
CAS=3	10 (8.7)	9 (8.6)	9 (9.2)	5 (6)
CAS=4	7 (6.1)	6 (5.7)	4 (4.1)	2 (2.4)

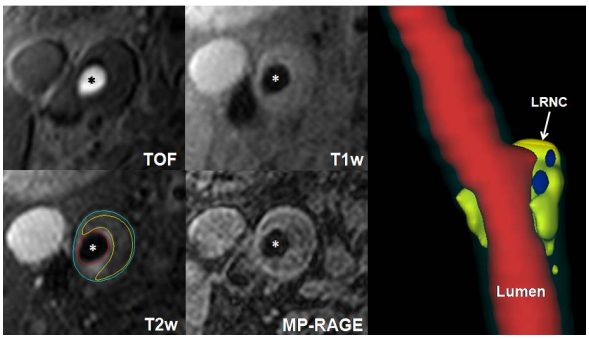


Fig. 2. An atherosclerotic lesion with large LRNC (yellow contour on T2w image, CAS=4) in right common carotid artery with low grade stenosis (33% lumen reduction).

Discussion and Conclusions: This study investigated the prevalence of carotid atherosclerotic high-risk lesions determined by CAS algorism in patients with TIA or stroke. We found that not only 11.3% of carotid arteries have advanced lesions with IPH/FCR, but also a substantial number of arteries develop large LRNCs that are at medium to high risk of developing future IPH/FCR. Recent clinical trials have shown that LRNCs in carotid atherosclerotic plaques can be regressed via administration of lipid-lowering drugs [8-10]. Therefore, to early detect and treat carotid lesions with higher CAS value may potentially block the lipid-rich lesions progressing to advanced plaques that are prone to triggering cerebrovascular events. In addition, we found that most of these lipid-rich lesions (CAS=3-4) exist in carotid arteries with low grade stenosis which cannot be captured by angiographic imaging approach (Fig. 2). These findings suggest the necessity of direct characterization of plaque compositional features, particularly the size of LRNCs, using black-blood MR imaging techniques for individuals at high risk of having cardiovascular disease.

References:

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