Atherosclerosis 207 (2009) 434–439

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Utility of high resolution MR imaging to assess carotid plaque morphology: A comparison of acute symptomatic, recently symptomatic and asymptomatic patients with carotid artery disease

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ARTICLE INFO

Article history:
Received 4 February 2009
Received in revised form 21 March 2009
Accepted 4 May 2009
Available online 13 May 2009

Keywords:
MRI
Carotid artery
Atheroma
TIA

ABSTRACT

Objectives: Compare carotid plaque morphology of acute symptomatic, recently symptomatic and asymptomatic patients (groups 1, 2 and 3 respectively) with carotid artery disease using high resolution magnetic resonance imaging (MRI), to identify high-risk plaque characteristics best associated with risk of recurrent thrombo-embolic events.
Methods: 60 patients underwent multi-contrast imaging of their internal carotid arteries. Different plaque components were manually delineated on acquired axial images to assess the difference in prevalence of plaque hemorrhage, fibrous cap (FC) rupture and FC thickness among the three groups.
Results: 55% acute symptomatic patients had plaque hemorrhage vs. 35% for recently symptomatic group and 5% for asymptomatic group (p-value: group 1 vs. 3: 0.001, group 2 vs. 3: 0.04). Type 1 hemorrhage was more common in acute symptomatic patients than recently symptomatic patients (40% vs. 5%, $p = 0.01$). Type 2 hemorrhage was more common in recently symptomatic vs. acute symptomatic patients (15% vs. 30%). FC rupture was observed in 50% of patients in group 1 vs. 35% of group 2 patients ($p = 0.02$) but none in group 3. The mean minimum FC thickness was same in acute and recently symptomatic groups (600 ± 200 μm), compared to 800 ± 200 μm for asymptomatic patients (p-value: 0.03 and 0.007 respectively). Good correlation was present among the three MR readers (intra-class correlation coefficient = 0.71).
Conclusion: High resolution MRI can differentiate plaque components associated with increased risk of thrombo-embolic events.

1. Introduction

It is well recognized that the risk of thrombo-embolic stroke in the presence of symptomatic carotid artery stenosis is high. Large randomized controlled trials have shown significant benefit from carotid endarterectomy (CEA) for patients with a severe carotid stenosis (≥70%) and moderate benefit for those with moderate stenosis (50–69%) [1]. Over 150,000 people per year have a suspected minor stroke or transient ischemic attack (TIA) in the United Kingdom, but only 35% are seen and investigated within 7 days in a neurovascular clinic [2]. For these patients there is a 6.7% risk of having a stroke in the first 2 days post-event and 13.4% risk in the first 4 weeks after a TIA [3]. Investigating and treating high-risk patients with TIA within 24 h can produce an 80% reduction in the number of people who go on to have a full stroke [4].

Though there may be higher risk of 30 day death and stroke following CEA if done within 48 h (approximately 7%) [5], performing CEA with a 10% risk within 14 days will prevent approximately 150 strokes at 6 yrs per 1000 CEAs. By contrast, if one were to defer CEA until >4 weeks had elapsed and then undertake the intervention with 3% risk, only 100 strokes would be prevented [3,6]. From the report of the carotid endarterectomy trialists collaboration (CETC), it can be appreciated that though annual risk reduction (ARR) is quite high (23.0%) in 70–99% stenosis group, there is a high ARR for 50–69% stenosis group as well (14.8%), if CEA was done within 2 weeks of ipsilateral carotid artery ischemic stroke. The benefit then declines up to 12 weeks for moderate stenosis group after which

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doi:10.1016/j.atherosclerosis.2009.05.002

CEA confers no benefit. However, high stenosis group continue to have some benefit even later on [5].

This has led to drastic changes in the national stroke strategy in UK, calling for emergency initial assessment of carotid arteries within 24 h and emergency carotid intervention for patients who are neurologically stable ideally within 48 h of a TIA or minor stroke, in high-risk patients (Department of Health, UK, 2007).

Though digital subtraction angiography (DSA), magnetic resonance angiography (MRA), and computerized angiography (CTA) and duplex imaging can provide information about luminal stenosis, they are unreliable in the presence of positive arterial remodeling [7] and may give normal luminal measurements despite large atheroma burden. Moreover, it has been shown that plaque rupture can occur in the presence of a low degree of luminal stenosis and the degree of narrowing predicts events poorly [8]. The concept of plaque vulnerability initially derived from studies of the coronary circulation is now also widely accepted in carotid circulation as well. High resolution magnetic resonance imaging (MRI) can accurately differentiate a stable plaque from an unstable plaque [9–11]

In today's context of aggressive management for symptomatic patients [6], we hypothesize that carotid MRI can be used to identify plaques when they are most unstable and present the highest risk of a recurrent thrombo-embolic event, e.g. immediately following a transient ischemic attack or stroke. This can help us identify high-risk patients with vulnerable plaques, who can benefit from aggressive management, thereby reducing risk of future thrombo-embolic events.

2. Methods

2.1. Patients

Sixty patients with carotid artery disease were recruited for this study. Three groups of patients were established, with twenty patients in each group. Patients in group 1 (acutely symptomatic) had suffered either a TIA or minor stroke and underwent carotid MRI within 72 h of the onset of their symptoms. A retinal TIA was defined as a partial or complete visual field loss in one eye of ischemic origin lasting less than 24 h [12] with a hemispheric TIA being defined as a focal cerebral dysfunction of ischemic origin lasting less than 24 h [12]. A minor stroke was defined as a neurological dysfunction of ischemic origin with deficits persisting longer than 24 h, but with a Rankin score $\leq$3.

Group 2 (recently symptomatic) comprised of patients who underwent imaging in the period 2 weeks to 6 weeks following either a retinal TIA, hemispheric TIA or a completed hemispheric stroke in the carotid artery territory of interest.

Patients in group 3 (asymptomatic) were either true asymptomatic (i.e. their stenosis was picked up coincidentally, e.g. cervical bruits picked up by physical examination) or had been asymptomatic for >6 months [13].

The study procedure was reviewed and approved by the regional research ethics committee. All patients gave written, informed consent.

The inclusion criteria for inclusion in the study were:

- ICA stenosis of $\geq$30–99% on duplex imaging during screening assessment.
- Sufficient MR image quality to identify the lumen wall and outer boundary of the arterial wall. [The image quality (IQ) was rated before review by using a previously published five-point scale [9,14]. Images with IQ >3 were included for morphological analysis, while images with IQ >4 were included for quantitative analysis].

Exclusion criteria included:

- Previous CEA.
- Cardiac arrhythmias.
- Known coagulation/clotting disorder responsible for patient's symptoms.
- Patients undergoing thrombolysis following the acute cerebrovascular event.
- Clinical contraindications to MRI, e.g. inner ear implants, pacemaker, etc.

2.2. High resolution multi-sequence MR imaging

Multi-contrast imaging of both ICAs was acquired using a 1.5 T MRI system (Signa HDx GE Healthcare, Waukesha, WI) and a 4-channel phased array neck coil (PACC, Machnet BV, Elde, The

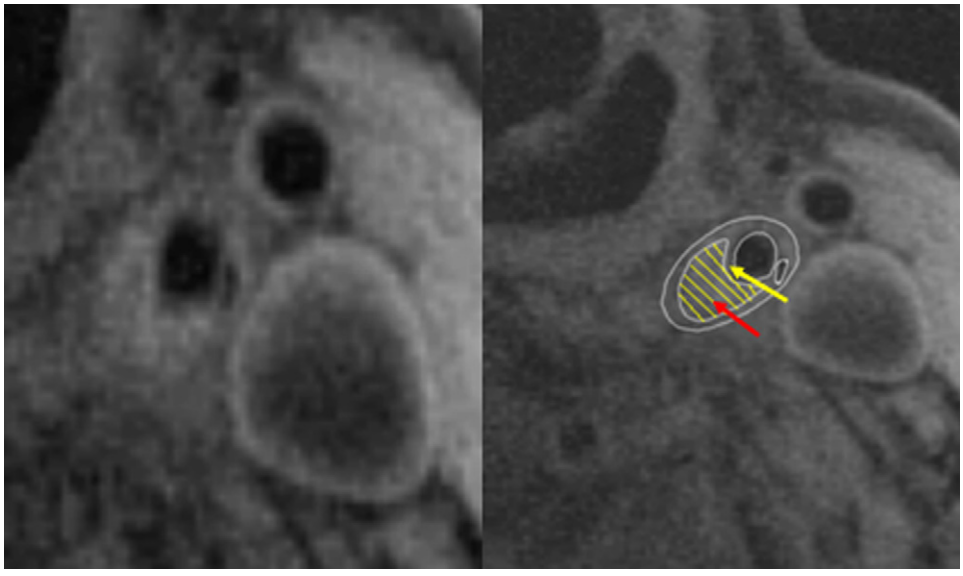

Fig. 1. T_1-weighted image of left ICA showing plaque with LR/NC area (red arrow) and FC (yellow arrow), demarcated using CMR Tools. Upper panel shows same image before regions of interest were drawn (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article).