The forgotten side: in –vivo assessment of inflammatory atheroma burden on the contralateral side to symptomatic carotid stenosis using high resolution USPIO-enhanced MR imaging

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Background

It has long been accepted that the risk of thrombo-embolic stroke in the presence of symptomatic carotid stenosis is high[1]. Indeed studies over the years have shown a definite benefit of surgery in those patients with stenosis of 70% or more of the carotid lumen. However, these studies have not addressed the risk from asymptomatic contralateral carotid stenosis. Conventional clinical measures of "plaque load" are derived from simple angiographic measures of stenosis and pay no attention to the composition of the plaque and can often underestimate the degree of stenosis due to the phenomenon of vascular remodelling. It is well known that vulnerable atheromatous plaque has a thin, fibrous cap and large lipid core with associated inflammation.[2] This inflammation can be detected on Magnetic Resonance imaging using a contrast medium, Sinerem, an Ultra Small Super-Paramagnetic Iron Oxide (USPIO).[3] Studies using USPIO to assess macrophage burden in symptomatic carotid stenosis have not yet addressed USPIO uptake in contralateral asymptomatic atheroma in this patient group.

Methods

20 patients with symptomatic carotid stenosis, all scheduled for endarterectomy were imaged at 1.5T using our carotid protocol (including T_1,T_2,T_2*, FatSat and STIR sequences) pre- and 36 hours post-Sinerem infusion. The time from USPIO infusion to endarterectomy ranged from 40 hours to 18 days (mean ± S.D, 6.9 ± 4.8 days).

Pre- and post-USPIO MR imaging was manually coregistered according to plaque morphology and distance from the carotid bifurcation.

Following this, images were manually segmented into quadrants excluding the luminal blood pool (CMR Tools, London) and signal change normalised to adjacent muscle in each quadrant was calculated following USPIO infusion. Percentage of quadrants showing a signal decrease on T_2* weighted imaging was calculated for each side and the asymptomatic and symptomatic sides were compared using a paired T-test. Regions of interest (ROIs) showing focal signal drop post USPIO were deliniated and mean number of regions of focal signal drop per slice was calculated for each side in each patient.

Results

Patient demographics were 11 males and 9 females with a median age of 72 years (range 53 – 84 years). Patients had a mean symptomatic stenosis of 77% compared with 46% on their asymptomatic side as measured by angiography.

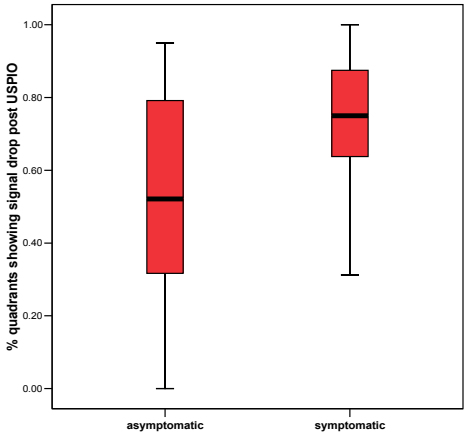

Figure 1 (left): Box plot showing median (black line) percentage of quadrants showing signal drop post-USPIO on the symptomatic and contralateral sides. Associated interquartile ranges are represented by red boxes.

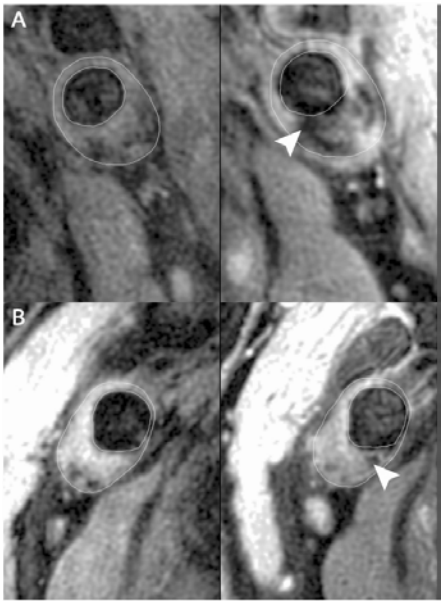

Figure 2 (right): T_1 weighted imaging of the common carotid artery of a patient pre- and post-USPIO (Sides: A contralateral , B symptomatic) Focal signal drop can clearly be seen bilaterally (white arrows)

Contralaterally there were 153 quadrants (54%+/-26%S.D.) with a signal drop post-USPIO when compared with 201 quadrants (73%+/- 19% S.D.) on the symptomatic side (**p=0.013**). Only one patient with USPIO signal drop on the symptomatic side showed no signal drop on the asymptomatic side. There was no statistical difference between the two sides in the number of regions showing focal signal drop (0.79 vs 0.81 ROIs/slice in asymptomatic side and symptomatic side respectively).

Conclusions

19 out of 20 patients (95%) showed bilateral USPIO uptake suggesting an inflammatory burden within their carotid atheroma bilaterally. This finding highlights the truly systemic nature of vulnerable atheroma and that patients showing inflammatory activity on one side may be more likely to have it contralaterally than truly asymptomatic patients. Thus patients who have a symptomatic carotid stenosis and who are found to have contralateral disease should be closely followed up with a low threshold for intervention. Luminal stesnosis alone is an inadequate predictor of risk in this patient group as illustrated by the observation that 95% of asymptomatic plaques demonstrated USPIO uptake in this symptomatic cohort despite a mean carotid stenosis contralaterally of 46%.

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References

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