Carotid atherosclerosis and cerebral small vessel disease

Canadian Atherosclerosis Imaging Network (CAIN) Project 1

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Background

Combining *in vivo* imaging of vessel wall disease with imaging of occult end-organ disease, and the acquisition of clinical-pathological end points, CAIN's central goal is to move innovations in clinical evaluation and therapeutic interventions aimed at cardiac and neurological diseases [1].

Given the increasing burden of vascular diseases world-wide with population aging, the CAIN Project 1 is a unique pan-Canadian brain and carotid imaging project focused on understanding the natural history of carotid disease and associations with cerebrovascular outcomes.

Objective

The goal of Project 1 is to recruit and serially image approx. 450 subjects with non-surgical carotid disease (stenosis between 30 and 95%).

We describe results from a preliminary analysis aimed to evaluate the role of carotid atherosclerosis in cerebral small vessel disease on a subsample (n=93) data acquired at baseline.

Discussion

These preliminary cross-sectional results suggest a potential relationship between carotid atherosclerosis and end-organ cerebral small vessel disease.

In addition to MRI-derived measures for brain volume and distribution of ischemic cerebral white matter disease, future analyses will include:

i) Progression analyses from serial assessments

ii) Predictive modelling of end-organ and clinical outcomes using 3D carotid MRI features of vessel disease and other vascular risk factors

iii) Evaluation of carotid plaque components, specifically intraplaque hemorrhage

Results

The bilateral stenosis group had significantly greater SH volumes ($p<0.05$), attributed primarily to deep white SH ($p<0.01$) rather than periventricular SH (n.s.).

No significant between group differences were demonstrated for brain tissue atrophy measures.

Demographics	Stenosis (bilateral) Yes (n=40)	No (n=53)	
Age, years	74.5 (9.0)	74.2 (9.0)	
Sex, n (%) male	24 (60.0)	30 (56.6)	
Medical History			
Hypertension, n (%)	34 (89.5)[a]	48 (92.3)[c]	
Diabetes Mellitus, n (%)	12 (30.8)[b]	12 (22.6)	
Hyperlipidemia, n (%)	37 (92.5)	47 (90.4)[c]	
Coronary Artery Disease, n (%)	14 (35.0)	13 (25.0)[c]	
Mitral Insufficiency, n (%)	2 (5.0)	-	
Peripheral Vascular Disease, n (%)	5 (12.5)	17 (32.7)[c]	
Atrial Fibrillation, n (%)	4 (10.0)	3 (5.7)[c]	
Cardiac Valve Disease, n (%)	2 (5.0)	2 (3.8)	
Hepatic, n (%)	-	2 (3.5)[c]	
Renal, n (%)	4 (10.0)	1 (1.9)	
Amaurosis Fugax, n (%)	3 (7.5)	-	
Hyperhomocysteinemia, n (%)	2 (5.0)	-	
Volumetric Analysis	**Stenosis (bilateral)**		
Whole brain	**Yes (n=40)**	**No (n=53)**	**P**
TIC	1258.7 (113.3)	1225.2 (113.6)	n.s.
BPF%	78.7 (4.7)	78.4 (3.7)	n.s.
Grey matter (GM)	557.3 (44.7)	544.0 (50.0)	n.s.
White matter (WM)	424.0 (62.3)	411.0 (55.6)	n.s.
Ventricular cerebrospinal fluid (vCSF)	37.5 (17.5)	37.2 (16.9)	n.s.
Subcortical hyperintensities (SH)	8.3 (12.4)	4.9 (8.8)	p=0.036
Deep white (dwSH)	1.3 (1.9)	0.5 (0.9)	p=0.007
Periventricular (pvSH)	7.0 (11.3)	4.4 (8.5)	p=0.083
Lacunes, mm^3	270.5 (571.3)	140.0 (299.8)	n.s.

Left hemisphere	Stenosis (left only) Yes (n=62)	No (n=31)	P
Grey matter (GM)	276.4 (21.3)	270.2 (25.5)	n.s.
White matter (WM)	211.3 (31.0)	204.7 (28.0)	n.s.
Ventricular cerebrospinal fluid (vCSF)	19.2 (9.3)	18.7 (9.0)	n.s.
Subcortical hyperintensities (SH)	4.2 (6.3)	2.4 (4.4)	p=0.066
Deep white (dwSH)	0.7 (1.0)	0.3 (0.5)	p=0.007
Periventricular (pvSH)	3.6 (5.7)	2.1 (4.3)	n.s.
Lacunes, mm^3	126.3 (273.1)	59.4 (151.7)	n.s.
	Stenosis (right only)		
Right hemisphere	**Yes (n=53)**	**No (n=40)**	**P**
Grey matter (GM)	280.9 (23.7)	273.8 (24.7)	n.s.
White matter (WM)	212.7 (31.4)	206.3 (27.8)	n.s.
Ventricular cerebrospinal fluid (vCSF)	18.3 (8.8)	18.5 (8.6)	n.s.
Subcortical hyperintensities (SH)	4.1 (6.1)	2.5 (4.5)	n.s.
Deep white (dwSH)	0.6 (0.9)	0.3 (0.4)	n.s.
Periventricular (pvSH)	3.5 (5.7)	2.2 (4.3)	n.s.
Lacunes, mm^3	144.3 (309.9)	80.6 (160.7)	n.s.

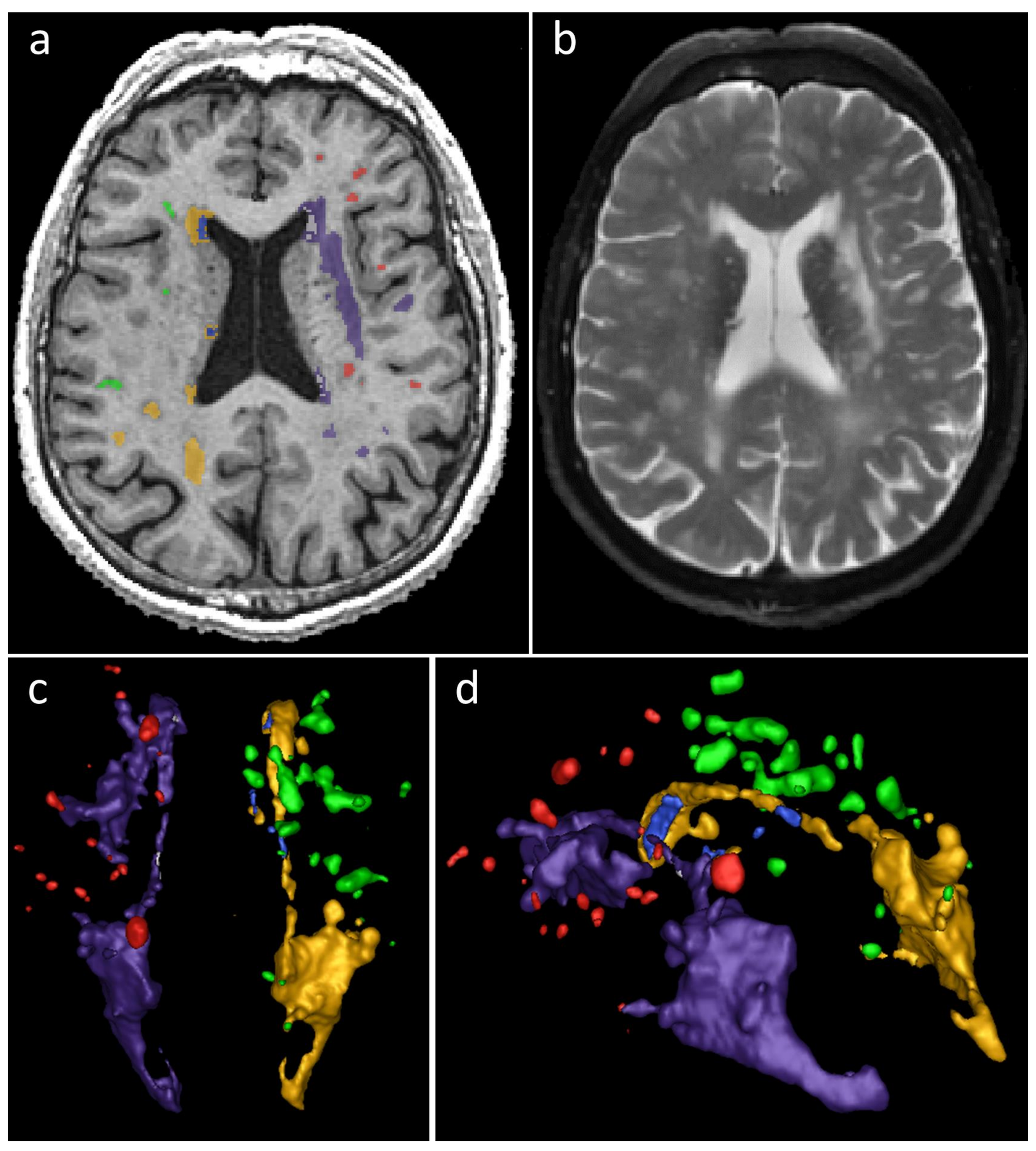
Data are presented as Mean (SD) unless otherwise stated. Raw volumes are presented for transparency, statistical analyses were performed on normalized (log transformed), head size corrected data. Volumetrics are reported in cubic centimetres (cc) unless otherwise stated.

[a] Data available for 38/40 subjects
[b] Data available for 39/40 subjects
[c] Data available for 52/53 subjects

Abbreviations: TIC=total intracranial capacity, BPF=brain parenchymal fraction

The left only stenosis group had significantly more left hemisphere deep white SH volumes than the non-left stenosis group

Methods



Lesion Explorer

Quantification of cerebral small vessel disease: periventricular (pvSH), deep white (dwSH), and lacunar infarcts [2-3].

Fig. 1 (a) SH segmentation overlayed on axial T1; (b) Axial T2-weighted; (c) 3D surface volume rendering from above and, (d) from angled side views.

Left hemisphere SH depicted in purple, lacunar infarcts depicted in red, periventricular infarcts depicted in white. Right hemisphere SH depicted in yellow, lacunar infarcts depicted in green, periventricular infarcts depicted in blue. (a&b displayed in radiological convention; c&d displayed in neurological convention).

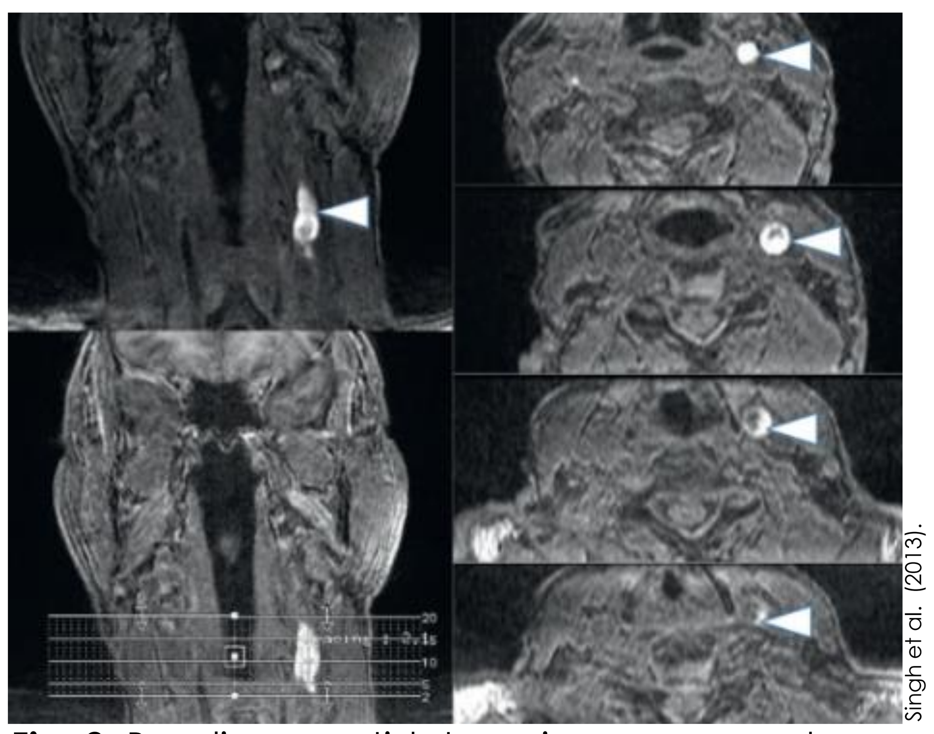


Fig. 2 Baseline carotid stenosis was assessed using routine clinical imaging and confirmed with MRI.

After head-size correction and normalization of skewed data, brain atrophy and small vessel disease burden was compared between bilateral and unilateral stenosis (>50%) groups controlling for sex and age.

References
1. Tardiff et al. (2013). *Can J Cardiol.*
2. Ramirez et al. (2011). *NeuroImage.*
3. Ramirez et al. (2014). *J Vis Exp.*
4. Singh et al. (2013). *Int J Cardiovasc Imaging.*

Main Study Reference
5. CAIN: www.canadianimagingnetwork.org/

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