Intracranial artery calcification to screen patients at high risk of recurrent stroke: abridged secondary publication

KS Wong *, XY Chen, TWH Leung, YW Siu, L Xiong, X Leng

KEY MESSAGES

1. Our study failed to validate the association between intracranial artery calcification (IAC) and recurrent stroke, likely owing to relatively short follow-up of 1 year. We will continue to follow up these patients to record the occurrence of ischaemic stroke and other vascular events.
2. The association between IAC and pulsitility index reflects that calcification within the arterial wall may cause arterial stiffness in cerebral arteries.

Hong Kong Med J 2020;26(Suppl 7):S42-4
HMRF project number: 11120161

[1] KS Wong, [1] XY Chen, [1] TWH Leung, [2] YW Siu, [1] L Xiong, [1] X Leng

[1] *Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong*
[2] *Department of Diagnostic and Interventional Radiology, Kwong Wah Hospital*

* Principal applicant and corresponding author: ks-wong@cuhk.edu.hk

Introduction

Intracranial atherosclerosis is a common cause of stroke, especially in Asian populations.[1-3] Arterial calcification is an active process of atherosclerosis. Computed tomography (CT) can be used to evaluate intracranial artery calcification (IAC) non-invasively. Evidence suggests associations between IAC and ischaemic stroke, vascular dementia, and other brain diseases. Our pilot study detected a high prevalence of IAC in Chinese and the association of IAC with age, history of ischaemic stroke, and white blood cell count.[4] A case-control study suggested that IAC may be a risk factor of ischaemic stroke.[5] Therefore, we aim to determine the predictive value of IAC on ischaemic stroke and its underlying mechanisms in a Chinese population using transcranial CT.

Methods

Consecutive patients were recruited from the acute stroke unit in Prince of Wales Hospital. Inclusion criteria were age of 40-85 years, Chinese ethnicity, diagnosed with ischaemic stroke according to World Health Organization stroke diagnostic criteria, presence of good temporal window, written informed consent given, and routine plain CT brain performed.

CT was performed using a 16-slice multi-detector row CT system (Light speed 16 plus, General Electric, Milwaukee [WI], USA). The unenhanced brain CT scans were acquired in axial mode with tilting along the occipito-meatal line, covering the base of the skull to vertex region and with parameters of 140 kVp, 170 mAs, and 2 s per rotation. Axial images were reconstructed at 0.625-mm intervals and stored as digital imaging and communication in medicine data for analysis.

Calcification was defined as hyperdense foci with attenuation number ≥130 HU. Both qualitative and quantitative IAC properties were measured. Intracranial arteries were assessed, including the intracranial internal carotid artery, anterior cerebral artery, middle cerebral artery, posterior cerebral artery, basilar artery, and bilateral intracranial vertebral arteries. The extent and thickness of arterial calcification were scored on a five-point scale, using the 0.625 mm unenhanced axial CT images at bone window setting (window level, 300 HU; window width, 1500 HU).

Agatston score, volume score, and mean density were assessed quantitatively using a custom-made programme to MATLAB. Calcification segmentation was the most important step. All CT images were first reconstructed to three-dimensional (3D) images, and then transferred to 3D software (Analyze 12.0), by which IAC was segmented using the 'seeding method' (Fig). The source images and segmentations were transferred to ITK-SNAP software, which automatically generated the volume and mean density data of the outlined regions. For Agatston score assessment, the 3D images with IAC segments were reconstructed into 3-mm-thick-slice images by MATLAB, and the Agatston score was generated with an algorithm, in which a weighted value was assigned to the highest artery calcium density within the slice on each 3-mm-thick CT slice, with a weighted value of 1 for 130-199 HU, 2 for 200-299 HU, 3 for 300-399 HU, and 4 for ≥400 HU. This weighted value was then multiplied by the area of calcification in the same slice.

Patients were followed up for 1 year at outpatient clinics for stroke recurrence and

treatment. All cardiovascular events (myocardial infarction, cerebrovascular events) and death secondary to vascular disease were recorded. Regular follow-up was performed to record stroke recurrence until July 2016.

Results

Of 340 patients recruited, 331 underwent transcranial CT. IAC was identified in around 88.2% of patients. Median IAC volume was 64.9 (range, 12.2-272.4) mm^3 and median total Agatston score was 24.0 (range, 2.8-118.5) [Table 1]. Recurrent stroke was recorded in 19 (5.7%) patients and myocardial infarction in 4 (1.2%) patients. The small sample size and low prevalence of recurrent stroke failed to determine any predictor.

Correlation between IAC and cerebral haemodynamic parameters in 318 (96.1%) patients was analysed. Both IAC Agatston score and IAC volume score were correlated with both high velocity (>140 cm/s) and high pulsatility index (>1.2) in the middle cerebral artery (all P<0.001) as well as in the vertebral-basilar artery (all P<0.001) [Table 2].

Discussion

Our findings failed to verify IAC as a predictor of recurrent stroke, partly owing to the low occurrence rate of recurrent stroke among our patients with mild to moderate stroke severity and the short follow-up of 1 year. Quantitative measurements of IAC (IAC Agatston score and IAC volume score) were found to be correlated with high systolic blood flow velocity and increased pulsatility index in intracranial cerebral arteries, indicating that IAC may cause generalised arterial stiffness within the cerebrovasculature.

There was selection bias in recruiting stroke patients because of poor temporal window in some female patients. This resulted in male predominance of participants. The requirements of written consent forms excluded patients with relatively severe stroke, especially those with movement disorders in upper limbs. Follow-up at 1 year was relatively short to investigate the effects of IAC on ischaemic stroke. We will continue to follow up these patients to record the occurrence of ischaemic stroke and other vascular events.

TABLE 1. Baseline characteristics of patients

Variable	Total (n=331)*
Age, y	65.3±12.0
No. of men	263 (79.5)
Hypertension	191 (57.7)
Diabetes mellitus	92 (27.8)
Chronic renal failure	12 (3.6)
Ischaemic heart disease	31 (9.4)
Ischaemic stroke history	52 (15.7)
Current smoker	79 (23.9)
Hyperlipidaemia	182 (55.0)
Presence of intracranial arterial calcification	292 (88.2)
Total intracranial arterial calcification volume, mm^3	64.9 (12.2-272.4)
Total Agatston score	24.0 (2.8-118.5)

* Data are presented as mean±standard deviation, No. (%) of cases, or median (interquartile range)

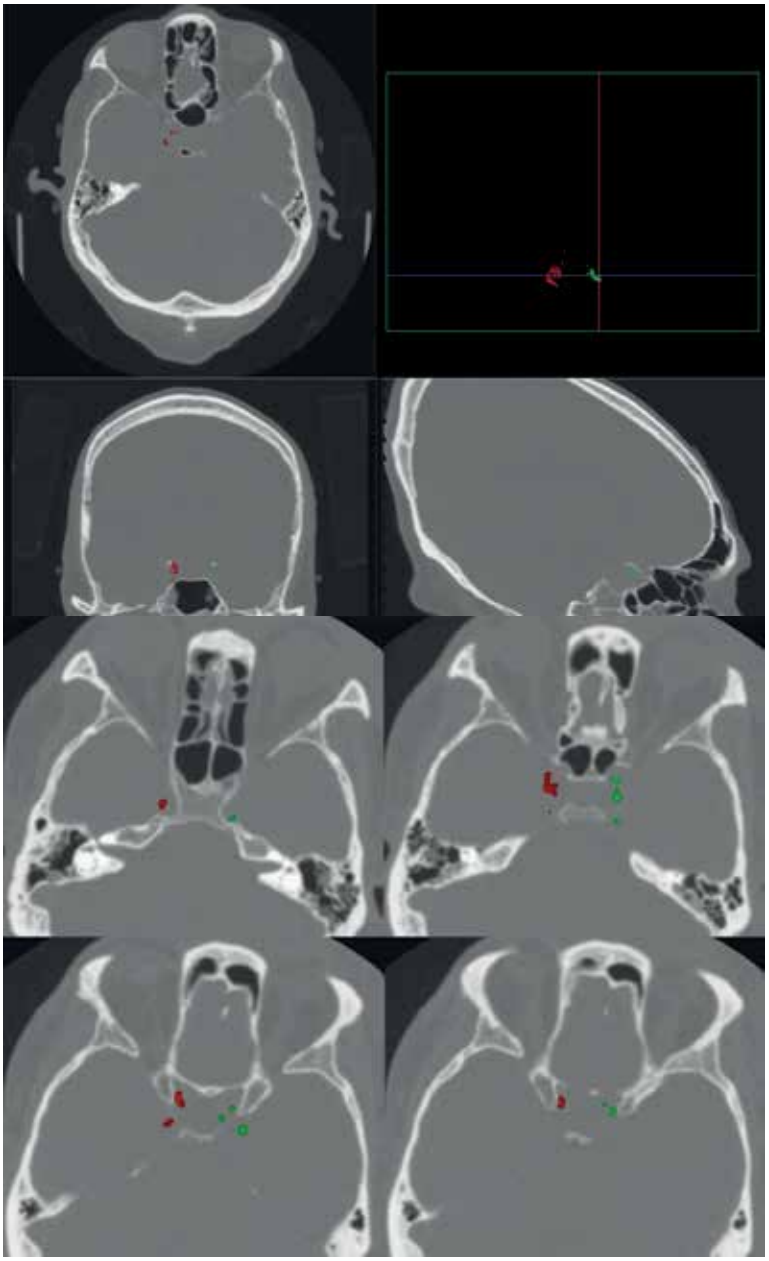

FIG. Semi-automatic segmentations of bilateral intracranial carotid artery calcification.

TABLE 2. Spearman correlation coefficients between cerebral haemodynamic parameters and intracranial arterial calcification (IAC) scores

	Overall (n=318)	IAC Agatston score		IAC volume score	
		Correlation coefficient	P value	Correlation coefficient	P value
Middle cerebral artery					
High velocity (>140 cm/s)	67 (21.1%)	0.228	<0.001	0.217	<0.001
High pulsatility index (>1.2)	121 (38.1%)	0.307	<0.001	0.318	<0.001
Vertebral-basilar artery					
High velocity (>100 cm/s)	23 (7.2%)	0.198	<0.001	0.194	<0.001
High pulsatility index (>1.2)	136 (42.8%)	0.407	<0.001	0.411	<0.001

Funding

This study was supported by the Health and Medical Research Fund, Food and Health Bureau, Hong Kong SAR Government (#11120161). The full report is available from the Health and Medical Research Fund website (https://rfs1.fhb.gov.hk/index.html).

Disclosure

The results of this research have been previously published in:

1. Wu XH, Chen XY, Wang LJ, Wong KS. Intracranial artery calcification and its clinical significance. J Clin Neurol 2016;12:253-61.
2. Wu X, Wang L, Zhong J, et al. Impact of intracranial artery calcification on cerebral hemodynamic changes. Neuroradiology 2018;60:357-63.
3. Wu XH, Chen XY, Fan YH, Leung TW, Wong KS. High extent of intracranial carotid artery calcification is associated with downstream microemboli in stroke patients. J Stroke Cerebrovasc Dis 2017;26:442-7.

References

1. Wong KS, Li H, Lam WW, Chan YL, Kay R. Progression of middle cerebral artery occlusive disease and its relationship with further vascular events after stroke. Stroke 2002;33:532-6.
2. Wong KS, Huang YN, Gao S, Lam WW, Chan YL, Kay R. Intracranial stenosis in Chinese patients with acute stroke. Neurology 1998;50:812-3.
3. Wong KS, Li H, Chan YL, et al. Use of transcranial Doppler ultrasound to predict outcome in patients with intracranial large-artery occlusive disease. Stroke 2000;31:2641-7.
4. Chen XY, Lam WW, Ng HK, Fan YH, Wong KS. The frequency and determinants of calcification in intracranial arteries in Chinese patients who underwent computed tomography examinations. Cerebrovasc Dis 2006;21:91-7.
5. Chen XY, Lam WW, Ng HK, Fan YH, Wong KS. Intracranial artery calcification: a newly identified risk factor of ischemic stroke. J Neuroimaging 2007;17:300-3.