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To Determine the Implication and Patterns of Intracranial Arterial Remodelling Among Patients of Stroke

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ABSTRACT

Background: Aim: We examined the extent and ability of intracranial remodelling using high-resolution 3D black blood MRI and investigated their association with ischemic events. Place and Duration: In the Department of Neurology, Allied Hospital Faisalabad for one year duration from February 2018 to February 2019. **Methods:** 42 patients with cerebrovascular ischemic episodes were subjected to three-dimensional magnetic resonance angiography and magnetic resonance imaging tests with 1.5 T black blood contrast for intracranial atherosclerotic disease. The classification of each plaque was according to their site (e.g. Anterior Circulation) and magnetic resonance imaging (indeterminate, non-culprit or culprit) help with the possibility of causing a specific stroke. The outer area of vessel wall, lumen area and wall area were dignified at reference and damage positions. The plaque load was premeditated as the area in which the wall was divided by the area of the outer wall. **Results:** In 42 patients, 137 plaques were detected from which 50(37%), were at the posterior and at the anterior 63% (87). Compared to pre-circulation plaques, higher plaque load was observed in the posterior circulation (P = 0.008, 69.0 ± 14.0 and 77.7 ± 15.7), higher RR (P = 0.002, 0.95 ± 0.32 and 1.14 ± 0.38) and mostly positive modifications (54.0% vs. 30.0 %; P = 0.011). **Conclusion:** Remodelling of intracranial arteries in retort to formation of plaque and from the posterior circulation arteries have higher tendency for positive remodelling, as a result of which they may hamper angiographic detection.

Keywords: Atherosclerosis, intracranial arteriosclerosis, vascular remodelling.

INTRODUCTION

Intracranial atherosclerosis (DAC) is an important cause of ischemic stroke globally. Traditional diagnoses of ICAD rely on narrowing measured by angiography; however, narrowing of the lumen is a poor plaque load indicator when vessels afford formation of plaque with compensatory remodelling.[1,2] The modification may vary in direction and degree relying on the recipient [Figure 1]. Outward remodelling of coronary artery can reserve the lumen from burden of plaque as much as forty percent of the vessel, while internal carotid artery (ICA) remodelling also protects l plaque loads approaching 62%. Remodelling can also be made inward with an area of the vessel that narrows during plaque formation and accelerates narrowing.[3] Understanding remodelling of vessels can give us an idea of our ability to identify plaque by angiography and characterize better jeopardy. E.g., although external modification confines the hemodynamic effect, externally remodelling of coronary plaques may be related with high plaque susceptibility, and low results clinically after coronary intervention. However, intracranial patterns of remodelling not analysed systematically.[4] High intensity MRI of black blood (BBMRI) was used to determine extracranial vessels arterial remodelling. Newly, this method was adopted as a three-dimensional (3D) sequence that provides reliable thickness and ICAD load measurements to obtain intracranial wall images.[5,6]

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MATERIALS AND METHODS

This Prospective study was held in the Department of Department of Neurology, Allied Hospital Faisalabad for one year duration from February 2018 to February 2019. Patients were prospectively referred for the BBMRI High Resolution and MRA Neurovascular Imaging Center to assess the known ICAD.

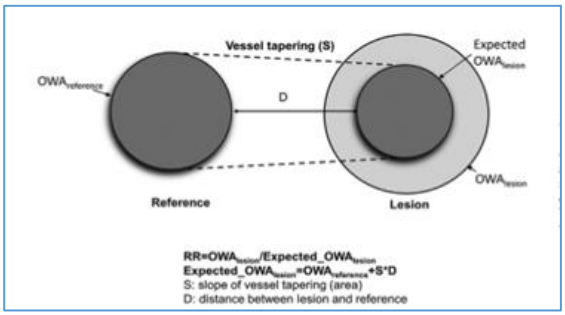
(1) There is evidence that ICAD causes 50% narrowing of the large intracranial artery based on MRA, CT or catheter angiography.
(2) Transient stroke or ischemic attack has occurred in the narrow arrangement of vessels.

Exclusion criteria

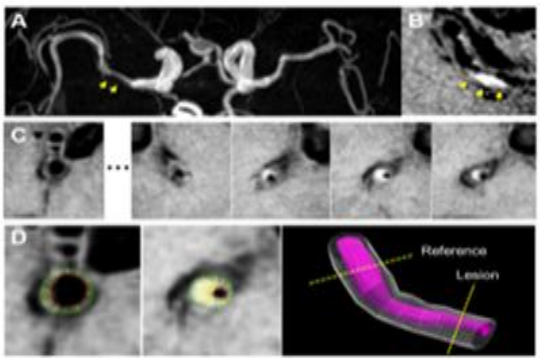
(1) Less than two cardiovascular risk factors,

(2) Non-cranial atherosclerotic pathology of blood vessels (e.g. Moy-Moy disease, vasculitis, reversible cerebral vasoconstriction syndrome, dissection),
(3) Possible sources of cardiovascular embolism
(4) Over fifty percent extracranial cervical artery stenosis near the symptomatic intracranial vessel. It is subacute when it is scanned for 4 to 12 weeks, and chronically acute when it is scanned for more than 12 weeks.

MRI was performed using an 8-channel head coil using an MRI Achieva 1.5 T scanner (The Netherlands Philips Healthcare). The high resolution intracranial wall images are based on a standard protocol that includes closed 3D light (TOF) in pre and post contrast and MRA BBMRI 3D sequences. 3D TOF MRA was obtained on transverse sections with several reasons: echo time / repetition time / angle of rotation, 3.5 ms / 23 ms / 25 °; field of view, 160 mm x 160 mm; regenerated resolution 0.55 × 0.55 × 0.55 mm 3; the resolution obtained was 0.55 x 0.55 x 1.1 mm 3; and a scanning time of six minutes. The 3D BBMRI increase perseverance method has been described above. Briefly, we used echo enhancement in the flat coronal part (40 mm thick plate) with modified volumetric isotropic turbospine (VISTA) with several limitations: echo time 38 ms / repetition time, / 2000 ms; turbo-spin-eco ratio, 6.1 ms; sensory coefficient, 56 echoes; echo range, 2; average number, 1. Resolution 0.4 x 0.4 x 0.4 mm 3 (field of view, 180 x 180 x 40 mm 3; matrix, 450 x 450 x 100) or 0.45 x 0.45 x 0, 45 mm 3 (field of view, resulting resolution) 180 × Matrix 180 × 40 mm 3, 400 × 400 × 100), with a scan time of 7.2 or 5.5 minutes, correspondingly. IV (0.1 mmol / kg) gadolinium (gadopentane dimeglumine, Schering, Magnevist) was used and BBMRI images were taken again after five minutes of contrast. Using Vessel mass software; all images of BBMRI were analysed using the previously described methods. In magnetic resonance imaging, atherosclerotic plaque was definite as an eccentric wall thickening, with or without narrowing of the lumen, as previously described in BBMRI images. MRI was measured on all plaques diagnosed in the intracranial arteries proximal parts; Degree of stenosis, including M1 and M2 sections of the MCA segment, A1 and A2 sections of the MCA segment, cavernous sections (C3) (i.e. not only patient confirmation plate) and ICA supra clinoid (C4), posterior sections of the cerebral artery P1 and P2, V4 segments basal arteries (BA) and vertebral arteries. MRI analysis was carried out by three autonomous readers using Vessel mass software. After plaque detection, the whole segment was analysed (i.e., outside the plaque edges). BBMRI 3D images were first arranged perpendicular to the axis of the container in 2.0 mm thick sections in each segment of the plaque. For each section, the thickest part of the plaque was considered to be the site of damage. The contours of the lumen and outer wall are plotted for change areas and reference areas as described above. Quantitative MRI dimensions were performed in each area using Vessel mass software, which involved the LA, OWA, plaque load ([wall surface / OWA], wall area (OWA - LA), average and maximum thickness of wall [Figure 1].



The arterial remodelling factor (RR) compares OWA with the reference region (OWA reference) in the lesion area (OWA lesion), so OWA reference should be adjusted to the expected reduction depending on the distance to the lesion (D). LA stenosis was used for OWA-based stenosis, assuming that the peripheral wall thickness was greater than the normal length of the arterial segment. To achieve this, LAVA was analysed using a deformable tubular model based on surface modelling of heterogeneous rational B scales to trace each vessel segment using TOF-MRA software [Figure 2]. This method enables semi-automatic detection of the arterial contour and accomplishes iterative regulation of LA linear regression along the segment. The gradual reduction of the vessel shown as the slope (S) of the regression line was recorded as S = area A (mm2) / distance A (mm). RR can then be determined as RR = (OWA reference/ OWA lesion + S × D) 15 (Fig. 1). As described above, 3 rearrangement categories are definite: positive if RR is above than 1.05 (wall extension); 0.95 ≤ RR ≤ 05 is indirect; and RR <0.95 is negative (vasoconstriction). The percentage of contraction of the bright area (percentage of stenosis) was calculated as the percentage of contraction = (1- [LA lesion - S × D]) / LA reference × 100. Symptomatic narrowing of the light (percentage narrowing) of symptomatic warfarin based on intracranial TOF MRA aspirin (WASID).



Each plaque is classified as indeterminate, culprit or non-culprit in terms of the likelihood of causing an MRI stroke using the criteria described above. Plaques were found culprit, unless there was another reason in the vascular area of stroke. Plaque cannot be detected if stroke was not causing the most narrowing lesion in the same vascular area. If the stroke was not in the vascular area, the injury was considered non-culprit. In TIA cases, classification of plaque was applied if the symptoms were in the arteries. Plaque calcification was defined as hypodense on pre-and post-contrast TOF and BBMRI images and, if possible, definite by CT scans of the brain. Using Stata 12.1 (College Station, Stata Inc, TX), data were analysed. Continuous comparisons of variables were achieved using Student's t-test for normal data of distribution. To compare the incidence frequency, chi-square test was used. Multilevel linear regression models of mixed effects were used to relate variations in magnetic resonance imaging measurements between anterior and posterior circulation (e.g., surface, thickness, vasodilatation, plaque load, RR, calcification). Consider random intervention conditions to measure multiple segments of patients' arteries. The classification of positive restructuring as an error (ratio of coefficients) was estimated on the basis of logistic regression of mixed effects. For participants with pre-existing anterior and posterior circulatory plaques, mean RRs between circulations were compared using a two-sided t-test. Compatibility between plaque readers was assessed using a class correlation coefficient based on repeated readings of all lesions detected by three observers. Credibility ratings less than 0.4 were defined as poor, good if 0.4 to 0.75, and greater than 0.75, considered excellent.

RESULTS

Table 1: The Plaque Characteristics of patients given

Male	29 (69.2)
Hypertension	29 (69.2)
Active smoker	08 (19.2)
DM	11 (25.93)
Hyperlipidaemia	23 (55.01)
Transient ischemic attack	5 (12.0)
Stroke	37 (87.99)
Acute	23 (55.01)
Sub-acute	07 (16.8)
Chronic	07 (16.8)
Characteristics of Plaques, N (%)*	
One	12 (28.7)
Two	7 (16.8)
Three	9 (21.5)
Four	4 (9.6)
Five or above	10 (23.9)
Number of plaques in Vessel segment and per segment (%)	
ICA	48 (35.01)
Vertebral artery	21 (15.3)
ACA	11 (8.0)
MCA	28 (20.5)
PCA	9 (6.6)
Basilar artery	20 (14.6)

45 total consecutive patients were tested. 3 volunteers were excluded due to movement. The residual forty two patients (29 men; 13 women; mean age ± SD, 56.3 ± 12.1 years), Ischemic stroke was noted in 37 (acute phase in 23, subacute and chronic in seven), and five had TIAs. The study population clinical characteristics are given in Table 1. 31 studies were performed at 0.4 mm3 at isotropic resolution and 11 at 0.45 mm3. 137 total plaques were identified in forty two patients. 87 plaques were identified in the anterior circulation (ACA 11; 48 in ICA; 28 in middle cerebral artery) and posterior circulation (20 in basilar artery; 9 in posterior cerebral artery; 21 were noted in vertebral arteries). 30 patients had compound plaques (range, 1-14 and 3.3 mean; [Table 1], and twenty four subjects had plaques in both anterior and posterior circulation.

Of the one thirty seven plaques, twenty six were culprit, non-culprit were found 77, and 34 were intermediate. There was no variation between the incidence of plaque in anterior and posterior circulation (p = 0.34). Positive remodelling concerns the classification of culprit plaque (versus non-culprit and indeterminate; confidence interval95% [CI]: 1.0-2.8, odd ratio [OR] 1.70) and marginally related (CI95%: 0.98–1.82, OR 1.34) when attuned for plaque burden. The relation was re-evaluated after removal of intermediate plaques (n = 35). Positive remodelling was related with culprit classification of plaque (non-culprit versus culprit; CI95%: 1.02–2.15, 1.49 OR) and culprit classification (1.35 OR, CI95%: 0.42–2.01) after correcting plaque load.

Table 2 showing Anterior and Posterior circulation comparison on MRI Measurements

	87 Plaques in Anterior Circulation	50 Plaques in posterior Circulation	P Value
Arterial remodelling ratio (RR)	0.95±0.32	1.15±0.38	0.002
Stenosis (diameter, WASID)	35.02±25.04	42.01±27.0	0.11
Site of Lesion			
Outer wall area, mm2	0.18±0.09	0.21±0.12	0.41
Mean wall thickness, mm	1.16±0.54	1.32±0.58	0.57
Plaque burden, %†	69.0±14.0	77.7±15.7	<0.001
Lumen area, mm2	0.07±0.10	0.05±0.05	0.20
Mean wall thickness, mm	1.16±0.54	1.32±0.58	0.57
Reference Site			
Outer wall area, mm2	0.17±0.09	0.18±0.08	0.26
Lumen area, mm2	0.10±0.10	0.08±0.05	0.15

When the analysis was done only in acute stroke patients (90 plaques in 23 patients), positive

remodelling was again related with the classification of the culprit plaque (non-culprit versus culprit; CI95%: 1, 06). -2.54, 1.64 OR). When attuned for plaque load, a fringe relation was noted (1.43 OR, CI95%: 0.90-2.27). After exclusion of 2 plaques showing artefacts in TOF MRA, calcification was found in 42 of 135 (31%) plaques (12 plaques in posterior circulation and 30 in anterior). There was no difference between anterior and posterior circulation in terms of plaque calcification frequency (35% and 24%, respectively; P = 0.17). Calcification was not related with positive remodelling. There was no significant difference between the posterior and anterior circulating plaques in terms of diameter stenosis, AL, OWA or maximum and mean and wall thickness values. However, compared to changes in the anterior circulation, the plaques in posterior circulation had a greater load (anterior and posterior: 77.7 ± 15.7 compared to 69.0 ± 13.99; P = 0.008) and higher RR (anterior and posterior): 1.15 ± 0.38 ') and 0.96 ± 0.33; P = 0.014; Table 1) and more frequent positive rebuilds (previously: 58.0%, 32.0%; P = 0.008).

Differences in RR between anterior and posterior circulation were limited to subjects with associated anterior and posterior plaques already (n = 22), but the outcomes were same to those noted in the other patients (anterior and posterior: 0.98 vs 1.15 ± 0.41) ± 0.28; P = 0.01). A linear regression fit between diameter based stenosis and plaque burden using criteria of WASID discovered that the lumen start constricted (ie, the lumen cant preserved longer by remodelling) when 55.3% plaque burden achieved.

DISCUSSION

The intracranial arteries were transformed in plaque formation response, the posterior arteries were more transformed than the anterior circulatory arteries, and stenosis occurred when plaque load reached 0.35 55.3. Our high-resolution 3D magnetic resonance imaging technique has helped to extend earlier reports defining the formation of intracranial remodelling when defining a narrowing threshold of lumen and detecting regional variations in modification.[7,8] Until now, intracranial remodelling properties have been based on 2D resonance imaging in vivo.[9,10] These 2D systems are usually restricted to lower non-isotropic resolution, which results in low observance of intracranial artery thickness measurements because of small vessels. This overestimation increases the effort of placing orthogonal 2D segments adjacent to internally curved arteries. Our 3D high resolution isotropic method minimizes errors caused by mean partial volume and allows us to set the intracranial remodelling threshold. We can examine the overall segment in details, and with our 3D processing software we determine vessel narrowing to accurate the OWA reference, which is crucial step in calculating intracranial RR.[11] Finally, 3D acquisition provided a wide range of ICAD changes that enabled full examination of intracranial circulation and facilitated the comparison of respective posterior to anterior circulatory plaques (i.e., occurring in the similar subject). As shown above, the modification of the arteries varies depending on the degree of various extravascular vessels. Astor et al. He studied 3350 common CA and 1063 internal carotid arteries and noted that common carotid arteries compensate for wall thickening than ICA. The narrowing threshold detected by ICA occurred when plaque load reached ~ 62%, as in ICA.[12] The accurate contrivance is unclear, but we suppose that sympathetic vascularization, blood flow and genetic factors have impact on remodelling response. There are area wise variations in cerebral blood flow with significantly minimum stream in the lateral circulation than in the anterior circulation (i.e. ICA). This is because of hemodynamic forces variations (e.g., endothelial shear stress) to the walls of vessel and mediates remodelling of arteries. Relatively weak posterior circulation sympathetic innervation, especially BA and VA, may be other cause for the increased positive reconstruction capacity in the positive circulation compared to the anterior circulation in the posterior circulation, because sympathetic innervation and self-diagnosis and change in brain self-regulation.[13] In addition, some genetic factors affecting atherosclerosis are site specific and related with adjustable plaque development in various arteries. The fact that intracranial arterial dolicoectase is also a pre-selection for higher circulation suggests that reconstruction may have common pathogenesis.[14] However, ICAD in ectatic intracranial arteries is rare with symptoms, so the mechanism of stroke in these patients is likely to be different from those in positive atherosclerotic lesions patients.[15] The relationship between positive remodelling and classification of offenders is confirmed by positive reports of remodelling of acute coronary events and stroke. Further research is needed to confirm these initial observations of intracranial circulation.

CONCLUSION

Remodelling of intracranial arteries in retort to formation of plaque and from the posterior circulation arteries have higher tendency for positive remodelling, as a result of which they may hamper angiographic detection.

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