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Additional value of intracranial vessel wall MRI as an adjunct to MRA in further differentiation of Moyamoya vasculopathy in Malaysia

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Abstract

Background & Objective: Moyamoya vasculopathy (MMV) is characterised by the progressive occlusion of the distal internal cerebral arteries (ICA) and its terminal branches, classified into Moyamoya disease (MMD) and Moyamoya syndrome (MMS). Differentiating between MMD and MMS is crucial for appropriate treatment planning. While luminal imaging aids in diagnosis, distinguishing features can sometimes be subtle. This study evaluates the additional diagnostic value of vessel wall magnetic resonance imaging (MRI) in differentiating MMD from MMS. *Methods:* Patients with clinical and imaging suspicious features of MMV underwent MRI, including additional vessel wall imaging (VWI). Two neuroradiologists initially reviewed the luminal imaging for features of MMV, and a presumed diagnosis was made in consensus. These luminal images were then correlated with clinical data to classify cases as MMD or MMS, serving as the gold standard diagnosis in this study. Subsequently, the VWI and luminal images were reviewed together, blinded to the initial luminal diagnoses and clinical data, to assess diagnostic accuracy by comparing both methods. The imaging parameters analysed included vessel wall thickening, grading, pattern of wall enhancement, and degree of collateral vessel formation. *Results:* Eighteen patients were analysed, comprising 12 with MMD and 6 with MMS. 108 vessels were evaluated, showing improved diagnostic accuracy from 55.6% to 77.8% when combining luminal and VWI. Specificity increased from 16% to 83%, with the positive predictive value rising to 90% and the negative predictive value to 62%. Our study found that MMD and MMS predominantly manifested concentric wall thickening, with no significant difference between the two groups. However, a significant difference was observed in the grading of wall enhancement, as most of the lesions in MMD showed no enhancement, whereas MMS lesions mostly exhibited moderate enhancement.
Conclusion: VWI demonstrates promise as a valuable modality for distinguishing between MMD and MMS when integrated with conventional imaging techniques.

Keywords: Moyamoya disease, Moyamoya syndrome, luminal imaging, vessel wall imaging, diagnostic accuracy.

INTRODUCTION

Moyamoya vasculopathy (MMV) is a progressive steno-occlusive disorder affecting the terminal internal carotid arteries (ICA), proximal middle cerebral arteries (MCA), and anterior cerebral arteries (ACA). This condition is characterised by compensatory collateral formation at the base of the brain, resulting in a "puff of smoke" appearance on imaging, which is reflected in the term "moyamoya", derived from Japanese. MMV is subdivided into Moyamoya disease (MMD) and Moyamoya syndrome (MMS).[1,2]

MMD is diagnosed in patients without

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identifiable associated risk factors. In contrast, MMS, also referred to as quasi-MMD, is diagnosed in patients with characteristic MMV alongside recognised associated conditions such as neurofibromatosis type 1, Down syndrome, thyroid disease, cranial irradiation, sickle cell anaemia, and others.[2,3] MMD typically presents with bilateral arteriographic features, although the severity may vary between hemispheres. Previously, patients with unilateral findings were classified as MMS regardless of the absence of other associated risk factors. However, this classification is now less favourable, as approximately 40% of patients initially diagnosed with unilateral findings develop contralateral disease over time.[4-6] Clinically, both MMD and MMS often present with ischaemic stroke and intracranial haemorrhage, with ischaemic stroke more prevalent among children and intracranial haemorrhage more common in Asian adult populations.[7]

The diagnosis of MMV typically relies on angiographic techniques such as digital subtraction angiography (DSA), magnetic resonance angiography (MRA), and computed tomography angiography (CTA). However, these approaches only identify luminal stenosis and do not reveal the underlying vessel wall pathology. MMV, atherosclerosis, and vasculitis can all lead to similar luminal stenosis.[8] In contrast to conventional MR angiographic luminal imaging, high-resolution magnetic resonance imaging (MRI) of the vessel wall (VWI) allows for direct visualisation of the diseased artery walls.

Distinguishing between MMD and MMS (vasculitis, atherosclerotic, and other aetiologies) is challenging due to significant overlaps in luminal imaging and clinical presentation. However, differentiation is crucial as treatment strategies differ significantly. Surgical revascularisation stands as the primary intervention for MMD, whereas aggressive medical management is essential for atherosclerotic (A-MMS) and vasculitic MMS (V-MMS).[6,9,10] This study evaluates the additional value of VWI in differentiating MMD and MMS, in addition to luminal imaging.

METHODS

Patient selection

This single-centre, cross-sectional study was conducted at the University Malaya Medical Centre (U.M.M.C.) with ethical approval from the Medical Research Ethics Committee (MREC ID NO: 201982-7707). Adult and paediatric patients with clinical and CT imaging features suspicious for MMV, neurovascular symptoms, and no history of cerebral revascularisation were recruited from the neurology clinic between March 2020 and January 2022. Exclusion criteria included contraindications for MRI and MRI contrast, potential sources of cardioaortic embolism, and extracranial stenosis greater than 50%.

A total of 52 patients were initially enrolled in the study, with 32 completing an MRI of the brain and an MRA of the carotid and circle of Willis vessels, including VWI. 20 patients were excluded from the analysis: five due to alternative diagnoses unrelated to MMV (i.e., ICA aneurysm, ICA dissection, and Tolosa-Hunt syndrome), five due to normal MRI findings, and 10 due to claustrophobia or reluctance to undergo MRI examination.

Image acquisition

All scans were conducted using the Siemens Magnetom Prisma A Tim+Dot 3T MRI System equipped with a 32-channel head coil. The standard sequences included T1-weighted imaging (T1W), T2-weighted imaging (T2W), turbo inversion recovery magnitude (TIRM), diffusion-weighted imaging (DWI), susceptibility-weighted imaging (SWI), arterial spin labelling (ASL), and 3D time-of-flight (TOF) magnetic resonance angiography (MRA). The VWI examinations were performed using T1W SPACE (Sampling Perfection with Application-optimised Contrast using different flip-angle Evolutions) with pre- and post-contrast sequences acquired in the sagittal plane.

Image analysis

Two neuroradiologists (N.R. and N.F.), blinded to the clinical and VWI data, reviewed the luminal imaging studies of the 32 patients. They evaluated the presence and location of the luminal disease, focusing on the terminal intracranial ICA, proximal MCA, and proximal ACA, as well as the presence of collateral vessels. Patients were classified into MMV and non-MMV based on the Tokyo Guidelines for Diagnosis and Treatment of Moyamoya Disease (2012), as shown in Figure 1.[6] The presence of beaded vessels or atherosclerotic plaques suggested a diagnosis of A-MMS. Additional long-segment extracranial circumferential narrowing indicated a diagnosis of V-MMS. The absence of these findings suggested a diagnosis of MMD. The presence of collateral

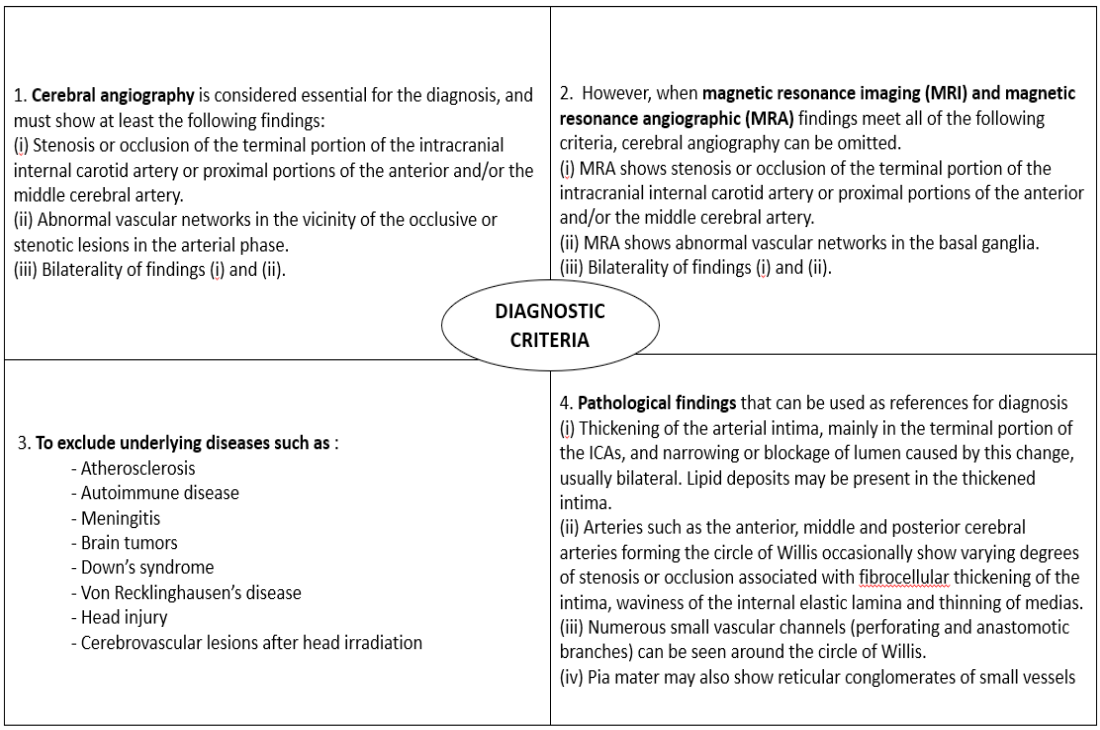

Figure 1: Diagnostic criteria for Moyamoya disease (Adapted from "Guidelines for Diagnosis and Treatment of Moyamoya Disease (Spontaneous Occlusion of the Circle of Willis)," 2012).[6]

vessels was also assessed and graded as either some or pronounced. A presumed diagnosis was then made in consensus by the neuroradiologists based solely on the luminal imaging findings.

Subsequently, patients' clinical data and blood investigations, including thyroid function tests and autoimmune evaluations, were thoroughly reviewed to establish a correlation between the presumed diagnosis based on luminal imaging and the clinical impression. This correlation further categorised patients into MMD and MMS, serving as the gold standard diagnosis in this study.

Neuroradiologists then reviewed the VWI and luminal imaging studies together while remaining blinded to the patients' gold standard diagnosis. The parameters evaluated included vessel wall thickening, vessel wall enhancement, and collateral vessel formation. The impressions from luminal imaging alone and combined with VWI were compared to the gold standard diagnosis based on the luminal imaging and clinical impressions to assess diagnostic accuracy. The flow chart of patient recruitment is presented in Figure 2.

Additionally, acute infarction in patients with MMV was evaluated using conventional MR images. Acute ischaemic infarction was determined by identifying hyperintense signals in DWI, indicating restricted diffusion.

Vessel wall thickening

Vessel wall thickening is categorised as absent, concentric, or eccentric. Concentric wall thickening is characterised by uniform and circumferential thickening, where the width of the thinnest part of the wall is at least 50% of the thickest segment. On the other hand, eccentric wall thickening is identified by thickening that occurs only on one side of the wall. Eccentric wall thickening is considered present when circumferential enhancement is observed, and the thinnest part of the wall is less than 50% of the thickness of the thickest part.[11] (Figure 3)

Wall enhancement

Vessel wall enhancement was assessed qualitatively by comparing post-contrast T1W signal intensity relative to pre-contrast T1W images. Enhancement was graded as follows: Grade 0 for no enhancement, Grade I for mild enhancement (vessel wall's signal intensity less than the pituitary infundibulum), and Grade II for pronounced enhancement (vessel wall signal intensity equal to or greater than the pituitary infundibulum).[8] (Figure 4)

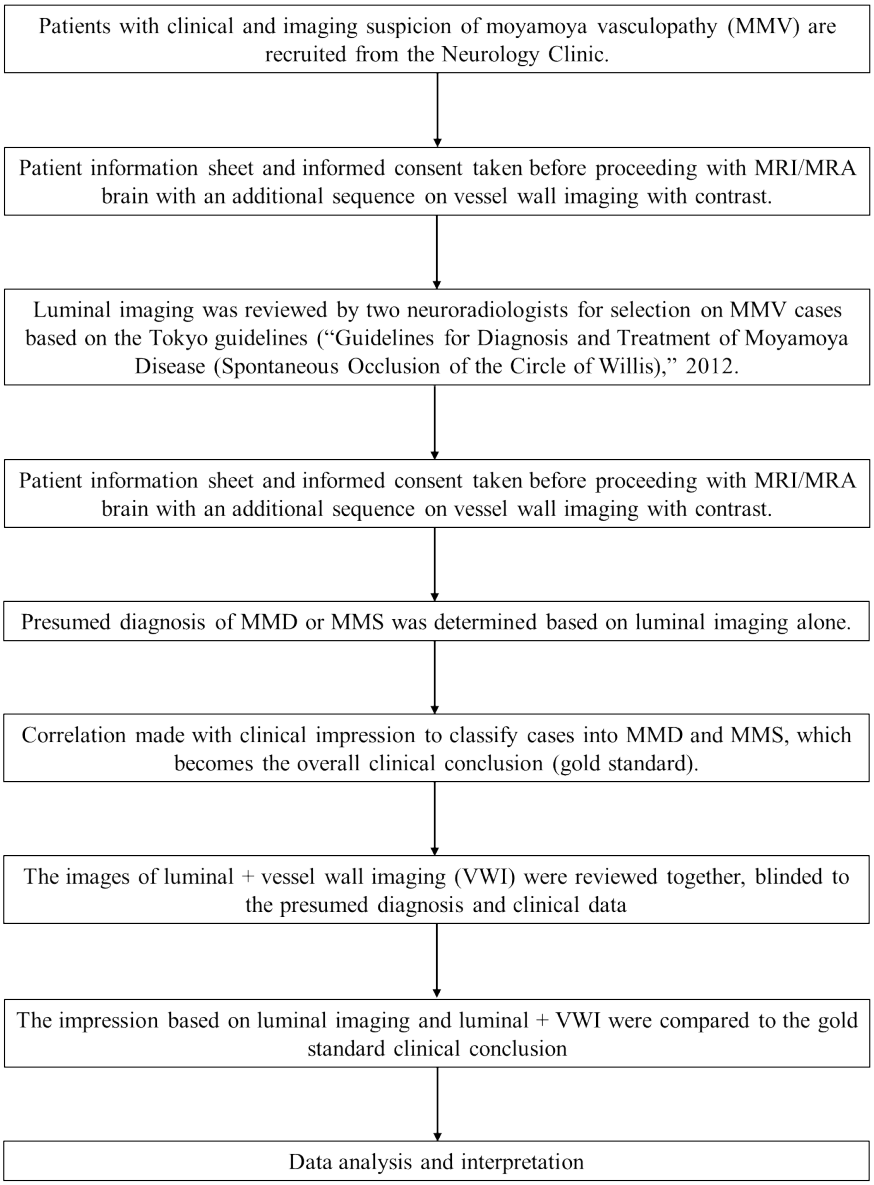

Figure 2: Flowchart for patient recruitment, image acquisition, data collection, and statistical analysis.

Pattern of enhancement

Enhancement patterns are differentiated as either homogenous or heterogeneous. Homogenous enhancement is typically characterised by smooth, concentric enhancement, whereas heterogeneous enhancement is often observed in non-concentric wall abnormalities, such as those found in atherosclerotic plaques. (Figure 5)

Collateral vessel grading

The classification and extent of collateral vessels were characterised by three levels: no collaterals, some collaterals, and more pronounced collaterals. (Figure 6)

Remodelling

Outward remodelling is considered positive if the outer wall area is qualitatively greater than that of the adjacent normal segment.

Statistical analysis

Data entry and analysis were conducted using Statistical Product and Service Solutions version 26.0. Patients' demographics were analysed and presented with descriptive statistics: mean and standard deviations for numerical data, frequencies, and percentages for categorical variables. The Shapiro-Wilk test was used to assess

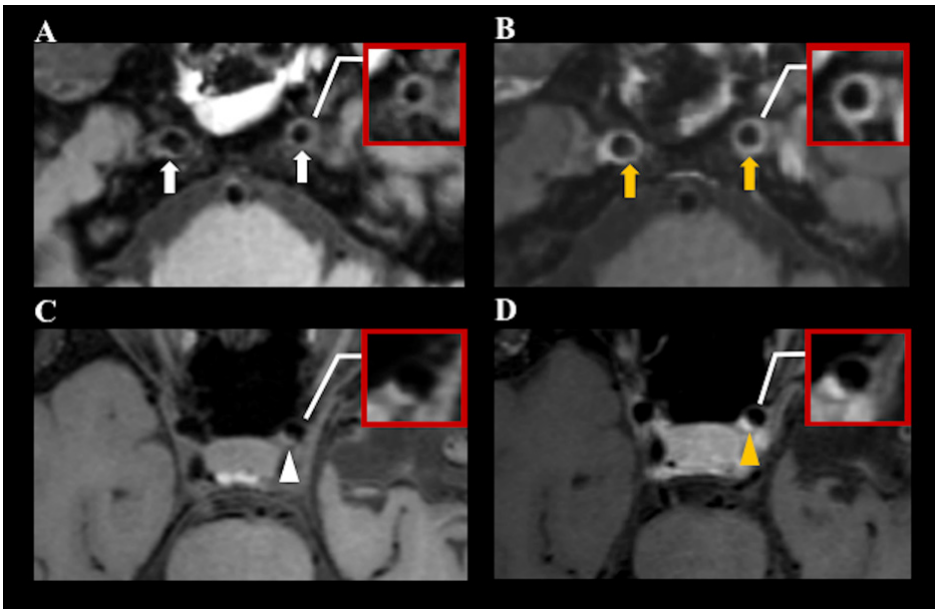

Figure 3: Wall thickening in Moyamoya vasculopathy.
(A) Pre-contrast T1W SPACE (white arrow) and (B) Post-contrast T1W SPACE images in axial projection showing concentric homogenously enhancing wall thickening (yellow arrow) in the bilateral ICA. (C) Pre-contrast T1W SPACE (white arrowhead) and (D) Post-contrast T1W SPACE images in axial projection demonstrating eccentric wall thickening (yellow arrowhead) with an adjacent atherosclerotic plaque in the distal left ICA. (Source: 3T Siemens MRI, Biomedical Imaging, UMMC)

the data normality. Patients were categorised into two groups: MMD and MMS. Due to the limited sample size, we could not subcategorise the MMS cases into A-MMS and V-MMS.

Categorical variables were analysed using the Chi-Squared or Fisher's exact test to determine significant differences in vessel involvement, wall thickening, presence or absence of enhancement, enhancement grading, enhancement pattern, and collateral grading between the two groups. A p-value of less than 0.05 was considered statistically significant. Sensitivity, specificity, accuracy, positive and negative predictive values were calculated.

RESULTS

Participants and descriptive data

A total of 18 patients participated in the study, including 3 children and 15 adults. Based on the Tokyo Guidelines for the diagnosis of MMV.[6] Twelve patients were categorised as MMD and 6 as MMS. The age of the subjects ranged from 8 to 64 years (mean = 36.1, standard deviation = 15.2). The mean age for MMD patients was 34.7 ± 18.0, while for MMS patients, it was 39.0 ± 8.0. A higher proportion of females participated in the study, with female predominance seen in both groups. There was a slightly higher number of Chinese individuals than Malay patients, with 10 (55.6%) Chinese and 8 (44.4%) Malay participants overall. However, the difference between the two groups was not statistically significant (p = 1.0).

Among the 18 patients, body weakness was the most common symptom, reported by 14 individuals (77.8%). Headache was observed in two patients (11.1%), while speech impairment and loss of vision were each indicated by one patient (5.6%). Of the 14 patients with body weakness, 9 (64.3%) were diagnosed with MMD, and the remaining 5 had MMS. Both groups had one patient reporting headaches. In the MMD group, one patient experienced speech difficulty, and another had visual field loss. None of the MMS group reported speech difficulty or vision loss. Fisher's exact test revealed no statistically significant difference between the MMD and MMS groups (p = 1.0). Patient demographic and clinical information are summarised in Table 1.

The correlation between MMD and MMS with the incidence of acute infarction was also investigated. It was found that 8 out of 18 patients (44.4%) in our study population had acute infarction. Of these, five (83.3%) patients from the MMS group developed acute infarction

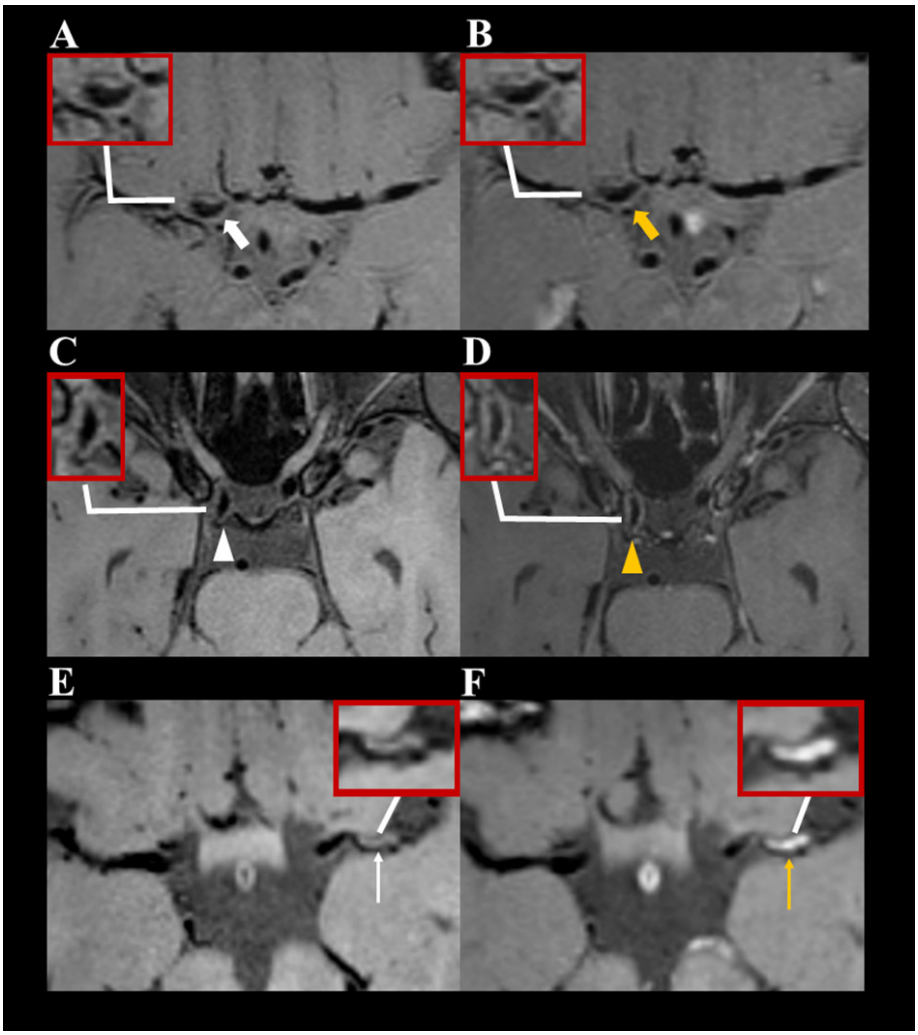

Figure 4: Vessel wall enhancement
(A, B) Pre-contrast (white arrow) and post-contrast (yellow arrow) T1W SPACE images in axial projection show no enhancement (Grade 0) in the M1 segment of the right MCA occlusion with collateral vessels.
(C, D) Pre-contrast (white arrowhead) and post-contrast (yellow arrowhead) T1W SPACE images in axial projection demonstrating mild homogenous (Grade I) concentric wall thickening in the terminal right ICA.
(E, F) Pre-contrast (white thin arrow) and post-contrast (yellow thin arrow) T1W SPACE images in axial projection depicting moderately enhancing (Grade II) eccentric wall thickening in the M1 segment of left MCA.
(Source: 3T Siemens MRI, Biomedical Imaging, UMMC).

compared to one (25.0%) in the MMD group. The initial Fisher's exact test showed a statistically significant association between the incidence of acute infarction in the MMD and MMS groups (p = 0.043). However, further a nalysis using the post hoc test for Chi-square found that the p-value (p = 0.018) was not statistically significant compared to the corrected Bonferroni threshold p-value of 0.0125.

Luminal imaging and vessel wall imaging characteristics

One hundred and eight vessel segments were evaluated across 18 patients: bilateral ICAs, proximal MCAs, and proximal ACAs. Three patients had unilateral involvement, while the remaining 15 showed bilateral involvement. Two with unilateral involvement were adults, and one was a paediatric patient. Of the 108 evaluated segments, 74 (68.5%) showed some abnormality in the vessel wall, such as remodelling, enhancement,

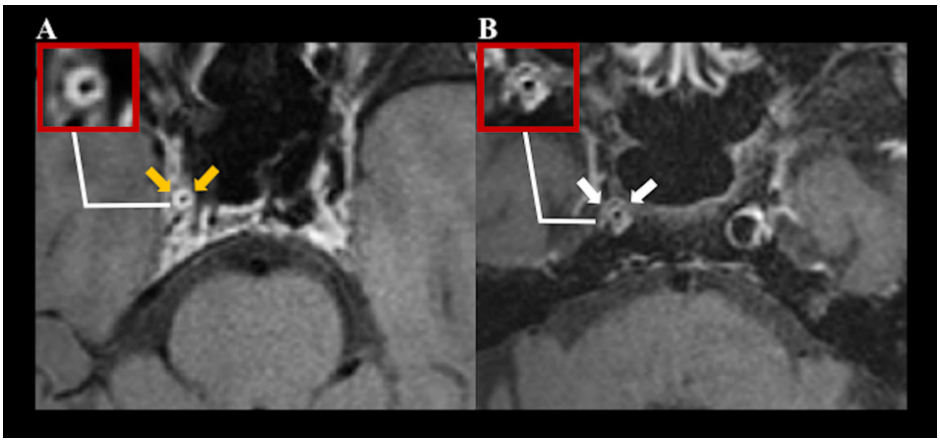

Figure 5: Pattern of intracranial vessel wall enhancement.
(A) The T1 SPACE post-contrast sequence of MRA in coronal projection shows concentric homogenous enhancement (yellow arrows) of the distal right ICA. (B) The T1 SPACE post-contrast sequence of MRA in coronal projection demonstrates heterogeneous enhancement (white arrows) of the distal right ICA. (Source: 3T Siemens MRI, Biomedical Imaging, UMMC).

or wall thickening. In the MMD group, the MCAs were the most affected vessels (29.2%, 21/72), followed by ICA (22.2%, 16/72). Conversely, in the MMS group, the ICAs were more frequently affected (33.3%, 12/36) than MCAs (30.6%, 11/36). Additionally, 14 affected ACAs (13.0%) were detected, with 10 seen (13.9%) in the MMD group and 4 (11.1%) seen in the MMS group. (Table 2)

Vessel wall thickening

Of the 108 evaluated segments, 62 (57.4%) exhibited wall thickening. In the MMD group, there were equal numbers of segments with concentric wall thickening and no wall thickening, each with 34 (47.2%) segments. In the MMS group, there were more cases with concentric wall thickening, totalling 20 (55.6%) segments. A chi-squared test indicated no statistically significant difference between concentric and eccentric wall thickening in the MMD and MMS groups ($p = 0.3$). (Table 2)

Presence of enhancement

Sixty two out of 108 evaluated vessels (57.4%) exhibited enhancement. Enhancing lesions were prevalent in MMD and MMS, with 38 lesions (52.8%) and 24 lesions (66.7%), respectively. The Chi-squared test indicated that the difference in the presence or absence of enhancement between the studied vessels in the MMD and MMS groups was not statistically significant ($p = 0.2$). (Table 2)

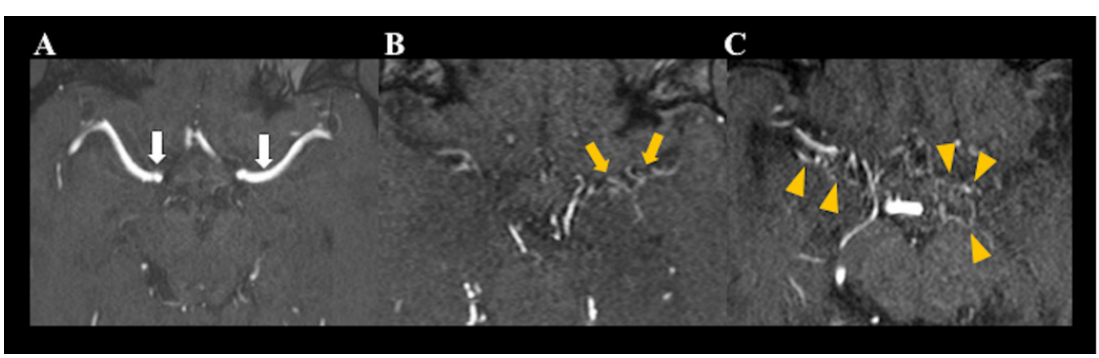

Figure 6: Degree of collateral vessel involvement.
MRA in axial projection images showing (A) bilateral MCAs with no collateral vessel formation seen (white arrows), (B) some collateral vessels at the region of M1 segment of left MCA (yellow arrows), and (C) more pronounced collateral vessel formation at the bilateral MCA (yellow arrowheads) (Source: 3T Siemens MRI, Biomedical Imaging, UMMC).

Table 1: Clinical and demographic characteristics

	Total patients (N=18)	MMD (N=12)	MMS (N=6)	*p*-value
Age	36.1 ± 15.2	34.7 ± 18.0	39.0 ± 8.0	-
Gender				
Female	13 (72.2%)	8 (66.7%)	5 (83.3%)	0.6
Male	5 (27.8%)	4 (33.3%)	1 (16.7%)	Fisher's exact test
Race				
Malay	8 (44.4%)	5 (41.7%)	3 (50%)	
Chinese	10 (55.6%)	7 (58.3%)	3 (50%)	1.0
Indian	0 (0%)	0 (0%)	0 (0%)	Fisher's exact test
Clinical symptoms				
Body weakness	14 (77.8%)	9 (75.0%)	5 (83.3%)	1.0
Headache	2 (11.1%)	1 (8.3%)	1 (16.7%)	1.0
Speech difficulty	1 (5.55%)	1 (8.3%)	0 (0.0%)	1.0
Visual field loss	1 (5.55%)	1 (8.4%)	0 (0.0%)	1.0
				Fisher's exact test
Acute infarction				
Yes	8 (44.4%)	3 (25.0%)	5 (83.3%)	0.043
No	10 (55.6%)	9 (75.0%)	1 (16.7%)	
				0.018 (post hoc test)
Vascular risk factors	**Total number of risk factors (N=17)**	**Total number of risk factors in MMD (N=8)**	**Total number of risk factors in MMS (N=9)**	
Hypertension	7 (41.2%)	4 (50.0%)	3 (33.3%)	0.6
Diabetes mellitus	5 (29.4%)	1 (12.5%)	4 (44.4%)	0.02
Dyslipidemia	5 (29.4%)	3 (37.5%)	2 (22.2%)	1.0
				Fisher's exact test

MMD: Moyamoya disease; MMS: Moyamoya syndrome.

Grading of enhancement

Most of the lesions in the MMD group showed Grade 0 and Grade I enhancement, with 34 (47.2%) showing Grade 0 and 31 (43.1%) demonstrating Grade I enhancement. On the other hand, in MMS, most lesions exhibited Grade II enhancement, with a total of 16 (44.4%) compared to 8 (22.3%) displaying Grade I and 12 (33.3%) showing no enhancement. The Chi-squared test revealed a significant association between the grading of enhancement in the two groups ($p < 0.001$). (Table 2)

Pattern of Enhancement

The MMD and MMS groups showed that most of the enhancing lesions demonstrated homogeneous enhancement, with 36 (50.0%) lesions in the MMD and 21 (58.3%) in the MMS. Heterogeneous enhancement was the least frequently observed pattern, seen only in two (2.8%) lesions in the MMD and three (8.4%) in the MMS group. Based on Fisher's exact test results ($p = 0.19$), no significant association was observed between the enhancement patterns in both groups. (Table 2)

Presence of collaterals

Collateral vessel formation was observed in all participants. Among those with MMD, seven patients (58.3%) exhibited more prominent collaterals, while five (41.7%) showed lower collateral vessel formation. In the MMS, an equal number of patients were found to have either some or pronounced collateral vessels, each accounting for 50% of the group and comprising three patients each. According to Fisher's exact test, there was no statistically significant correlation between the extent of collateral vessel formation in both MMD and MMS groups ($p = 1.0$). (Table 2)

Table 2: Luminal imaging and vessel wall imaging findings for each disease group

Luminal with vessel wall imaging findings	Total Vessels Studied (N=108)	MMD (N=72)	MMS (N=36)	p-value
Vessels involvement				
ICA	28 (25.9%)	16 (22.2%)	12 (33.3%)	
MCA	32 (29.6%)	21 (29.2%)	11 (30.6%)	0.305*
ACA	14 (13.0%)	10 (13.9%)	4 (11.1%)	
None	34 (31.5%)	25 (34.7%)	9 (25.0%)	
Wall thickening				
No wall thickening	46 (42.6%)	34 (47.2%)	12 (33.3%)	
Concentric	54 (50.0%)	34 (47.2%)	20 (55.6%)	0.3
Eccentric	8 (7.4%)	4 (5.6%)	4 (11.1%)	
Presence of enhancement				
No	46 (42.6%)	34 (47.2%)	12 (33.3%)	
Yes	62 (57.4%)	38 (52.8%)	24 (66.7%)	0.2
Enhancement grading				
No enhancement (Grade 0)	46 (42.6%)	34 (47.2%)	12 (33.3%)	
Mild (Grade I)	39 (36.1%)	31 (43.1%)	8 (22.3%)	**<0.001**
Moderate (Grade II)	23 (21.3%)	7 (9.7%)	16 (44.4%)	
Enhancement pattern				
No enhancement	46 (42.6%)	34 (47.2%)	12 (33.3%)	
Homogenous	57 (52.8%)	36 (50.0%)	21 (58.3%)	0.19
Heterogenous	5 (4.6%)	2 (2.8%)	3 (8.4%)	
Collaterals				
Some	8 (44.4%)	5 (41.7%)	3 (50%)	1.0
Pronounced	10 (55.6%)	7 (58.3%)	3 (50%)	
Remodelling				
Outward remodelling	0 (0.0%)	0 (0.0%)	0 (0.0%)	-

*Comparison between any involvement vs no involvement.
MMD: Moyamoya disease; MMS: Moyamoya syndrome; ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral artery.

Added value of vessel wall MRI

The combination of luminal imaging and VWI resulted in a notable enhancement in the overall diagnosis accuracy of diagnosing MMD and MMS cases, improving from 55.6% (10 out of 18 patients) to 72.2% (13 out of 18 patients). Following the current gold standard diagnostic criteria based on the Tokyo guidelines, 12 patients

Table 3: Diagnostic Accuracy (Percentage with Correct Diagnosis) of Luminal Imaging and Combined Luminal with Vessel Wall Imaging

Group	Number of cases based on gold standard diagnosis	Number of cases diagnosed based on LI	Number of cases diagnosed based on LI + VWI	LI		LI + VWI	
				Correctly diagnosed	Incorrectly diagnosed	Correctly diagnosed	Incorrectly diagnosed
All	18	18	18	10 (55.6%)	8 (44.4%)	13 (72.2%)	5 (27.8%)
MMD	12	14	10	9 (75.0%)	3 (25.0%)	8 (66.7%)	4 (33.3%)
MMS	6	4	8	1 (16.7%)	5 (83.3%)	5 (83.3%)	1 (16.7%)

MMD: Moyamoya disease; MMS: Moyamoya syndrome; LI: luminal imaging; VWI: vessel wall imaging.

Table 4: Comparison of sensitivity, specificity, positive predictive value, and negative predictive value between luminal imaging and luminal with a combination of vessel wall imaging for Moyamoya disease and Moyamoya syndrome

Parameters	Luminal Imaging (LI)	Luminal + Vessel wall Imaging (LI+VWI)
Sensitivity	75%	75%
Specificity	16%	83%
Positive Predictive Value	64%	90%
Negative Predictive Value	25%	62%

were diagnosed with MMD and 6 with MMS among the 18 patients studied. With luminal imaging alone, 10 patients were accurately diagnosed: 9 with MMD and one with MMS. However, when combined with VWI, 13 out of 18 patients were correctly diagnosed: 8 with MMD and 5 with MMS. (Table 3 and Figure 7)

Sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) were calculated for both luminal imaging alone and in combination with VWI. A comparable sensitivity of 75% was observed for both luminal imaging alone and when combined with VWI. However, the remaining parameters were higher for combined VWI, with 83% for specificity, 90% for PPV, and 62% for NPV. (Table 4)

DISCUSSION

The current study aimed to evaluate the utility of VWI in discriminating between MMD and MMS, focusing on various parameters, including vessel involvement, vessel wall thickening, and enhancement characteristics. Our findings demonstrated a significant improvement in diagnostic accuracy when combining luminal imaging with VWI compared to luminal imaging alone, with an increase from 55.6% to 77.8%. This result is consistent with previous studies[10,12], which also reported a significant increase in correct diagnosis rates for MMV cases when VWI was used alongside luminal imaging. While no significant improvement in diagnostic accuracy for MMD cases was observed, a substantial increase in correct diagnosis rates was noted for MMS cases, rising from 16.7% to 83.3%.

In previous years, angiographic imaging has been the gold standard for distinguishing MMV cases. However, recent studies have highlighted the superiority of VWI in evaluating specific features that conventional imaging cannot adequately visualise. Previous studies identified several differences in vessel wall findings between MMD and MMS. MMD typically shows non-eccentric lesions with robust collateral vessels, lacking remodelling and vessel wall enhancement. Rarely does it exhibit homogenous mild enhancement if enhancement occurs. In contrast, A-MMS manifests eccentric lesions with outward remodelling and mild or moderate enhancement, while V-MMS displays concentric lesions with moderate enhancement without remodelling. Some or none of the collateral vessel formation is seen in the A-MMS and V-MMS patients.[10-12]

Our study corroborated several parameters that were consistent with previous findings. However, our results did not achieve statistical significance, primarily due to our limited sample size. We observed negative remodelling in all MMD and MMS cases, consistent with previous studies.[13,14] Concentric vessel wall thickening with absence or mild homogenous enhancement was observed in most MMD cases. Pronounced collateral formation was more common in MMD cases. Similarly, MMS manifested concentric wall thickening, which, although not statistically significant, was notably characterised by the presence of homogeneous, moderately enhancing lesions. Collaterals were also noted in MMS cases, with no predominant pattern observed. The enhancement of the vessel wall in MMD remains controversial, as most studies have reported that no enhancement was seen, while some others have indicated that up to 90.6% of intracranial vessels were involved, with varying degrees of enhancement demonstrated.[15,16] This discrepancy may be attributed to ethnic and genetic heterogeneity, transient inflammatory changes, and methodological differences such as pseudoenhancement or slow flow artefacts.[16] In addition, according to Ryoo *et al*., over 80% of symptomatic MMD segments showed concentric enhancement, potentially regulated by vascular endothelial growth factor (VEGF) and its receptor, which are involved in angiogenesis and the formation of abnormal vessel networks.[16] Another study also found increased expression of intimal

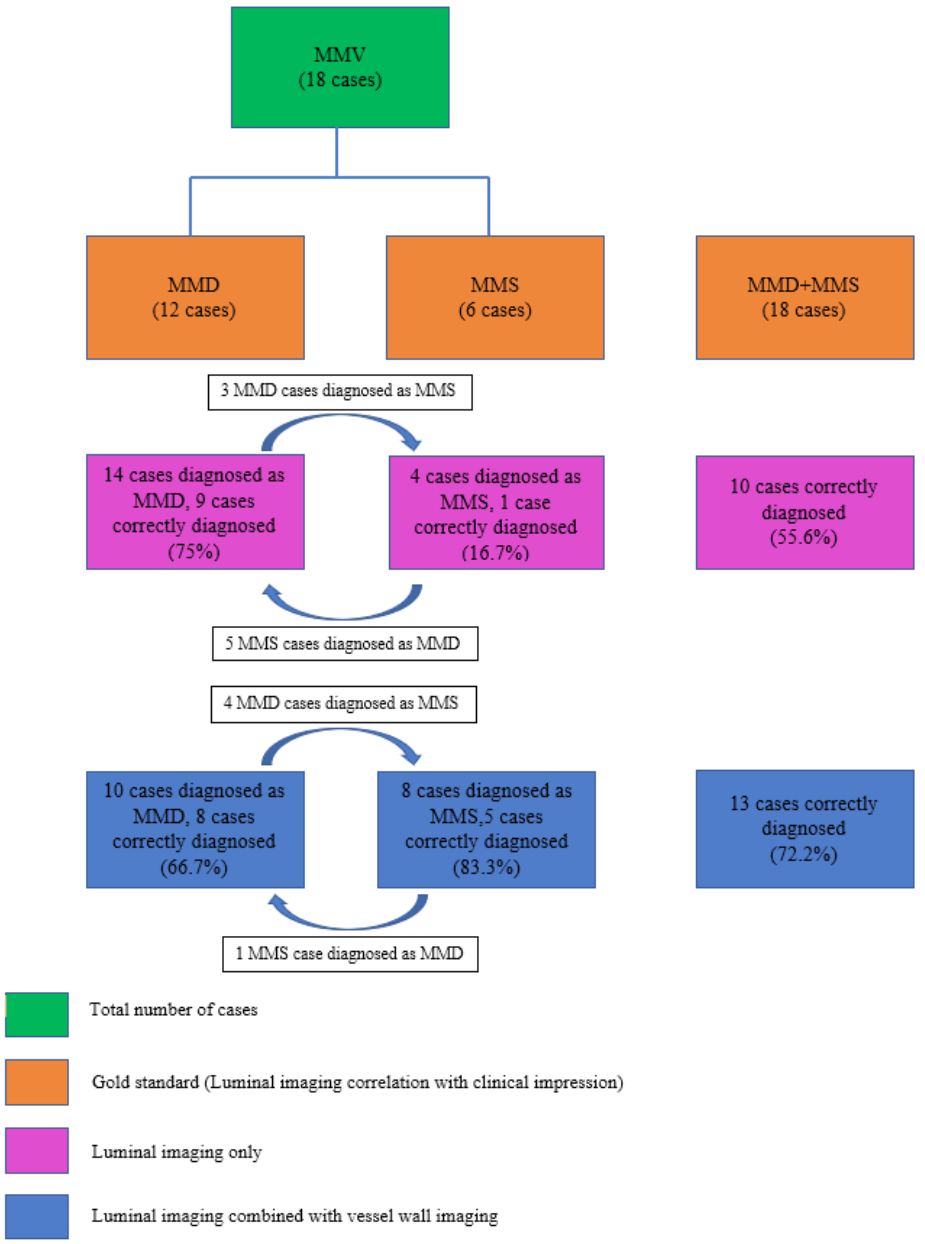

Figure 7: Graphical representation of differences in MMV diagnosis when compared to gold standard diagnosis using luminal imaging only and luminal imaging combined with VWI when compared to the gold standard diagnosis based on the Guidelines for Diagnosis and Treatment of Moyamoya Disease (Spontaneous Occlusion of the Circle of Willis).[6]

angiogenetic factors and endothelial VEGF in MMD, suggesting an active angiogenetic process in enhancing vessel walls.[17]

Moreover, we investigated the correlation between MMD and MMS and the incidence of acute ischaemic infarction. Initial analysis revealed a statistically significant association between acute infarction and the MMS group ($p = 0.043$). In our cohort, a higher incidence of acute infarction was observed in the MMS group compared to the MMD group (62.5% versus 37.5%). Most MMS cases exhibited moderately enhancing lesions, which aligns with studies reporting a significant association between moderate enhancement of intracranial vessel wall lesions and acute ischaemic infarction.[8,11] Hao *et al*. indicated that vessel wall enhancement in MMD patients had a higher incidence of ischaemia

and haemorrhage than non-enhancement.[18] In a recent study by Tagawa *et al*., there was a positive correlation between arterial wall enhancement and a history of TIA, which may predict the risk of cerebral ischaemia or disease progression. Hence, arterial wall enhancement may be a useful imaging biomarker for MMD.[13]

Our study has several limitations that warrant consideration for future outcomes. First, the small sample size due to the rarity of MMV poses a significant limitation. Second, the lack of histological confirmation of the diagnosis necessitates caution, and future studies should incorporate such confirmation where feasible. Third, diagnosing MMS can be challenging due to its association with various diseases and aetiologies. Future multicentre studies incorporating genotypic and phenotypic analyses may assist in accurately categorising MMS and differentiating MMD from other forms of MMS.

In conclusion, VWI enhances diagnostic accuracy in distinguishing between MMD and MMS, offering valuable insights beyond luminal imaging alone. It is crucial to differentiate MMD from other causes of MMS, such as A-MMS or V-MMS, as treatment options vary significantly based on the underlying cause. Therefore, accurate classification according to pathology is highly beneficial. While our study provides valuable insights, future research with larger cohort studies and histological confirmation is essential to refine diagnostic criteria and reduce the reliance on invasive procedures in MMV assessment.

REFERENCES

1. Suzuki J, Takaku A. Cerebrovascular moyamoya disease: disease showing abnormal net-like vessels in base of brain. *Arch Neurol* 1969;20(3):288-99.
2. Scott RM, Smith ER. Moyamoya disease and Moyamoya syndrome. *N Engl J Med* 2009;360(12):1226-37. doi: 10.1056/nejmra0804622.
3. Phi JH, Wang KC, Lee JY, Kim SK. Moyamoya syndrome: A window of moyamoya disease. *J Korean Neurosurg Soc* 2015;57(6):408-14. doi: 10.3340/jkns.2015.57.6.408.
4. Fujimura M, Bang OY, Kim JS. Moyamoya disease. *Front Neurol Neurosci* 2016;40:204-20. doi: 10.1159/000448314.
5. Kelly ME, Bell-Stephens TE, Marks MP, Do HM, Steinberg GK. Progression of unilateral moyamoya disease: a clinical series. *Cerebrovasc Dis* 2006;22(2-3):109-15.
6. Guidelines for diagnosis and treatment of Moyamoya disease (Spontaneous occlusion of the circle of Willis). *Neurol Med Chir* (Tokyo) 2012;52(5):245-66. doi: 10.2176/nmc.52.245.
7. Liu XJ, Zhang D, Wang S, *et al*. Clinical features and long-term outcomes of moyamoya disease: a single-center experience with 528 cases in China. *J Neurosurg* 2015;122(2):392-9.
8. Wang M, Yang Y, Zhou F, *et al*. The contrast enhancement of intracranial arterial wall on high-resolution MRI and its clinical relevance in patients with Moyamoya vasculopathy. *Sci Rep* 2017;7(July 2016):1-7. doi: 10.1038/srep44264.
9. Derdeyn CP, Chimowitz MI, Lynn MJ, *et al*. Aggressive medical treatment with or without stenting in high-risk patients with intracranial artery stenosis (SAMMPRIS): the final results of a randomised trial. *Lancet* 2014;383(9914):333-41. Epub 2013/10/31. doi: 10.1016/s0140-6736(13)62038-3.
10. Yang S, Wang X, Liao W, *et al*. High-resolution MRI of the vessel wall helps to distinguish moyamoya disease from atherosclerotic moyamoya syndrome. *Clin Radiol* 2021;76(5):392.e11-.e19. doi: 10.1016/j.crad.2020.12.023.
11. Kathuveetil A, Sylaja PN, Senthilvelan S, Chandrasekharan K, Banerjee M, Jayanand Sudhir B. Vessel wall thickening and enhancement in high-resolution intracranial vessel wall imaging: A predictor of future ischemic events in moyamoya disease. *Am J Neuroradiol* 2020;41(1):100-5. doi: 10.3174/ajnr.A6360.
12. Mossa-Basha M, De Havenon A, Becker KJ, *et al*. Added value of vessel wall magnetic resonance imaging in the differentiation of moyamoya vasculopathies in a non-asian cohort. *Stroke* 2016;47(7):1782-8. doi: 10.1161/STROKEAHA.116.013320.
13. Tagawa H, Fushimi Y, Funaki T, *et al.* Vessel wall MRI in moyamoya disease: arterial wall enhancement varies depending on age, arteries, and disease progression. *Eur Radiol* 2024;34(4):2183-94. doi: 10.1007/s00330-023-10251-9.
14. Larson AS, Klaas JP, Johnson MP, *et al*. Vessel wall imaging features of Moyamoya disease in a North American population: patterns of negative remodelling, contrast enhancement, wall thickening, and stenosis. *BMC Med Imaging* 2022;22(1):198. doi: 10.1186/s12880-022-00930-2.
15. Kim YJ, Lee DH, Kwon JY, *et al.* High resolution MRI difference between moyamoya disease and intracranial atherosclerosis. *Eur J Neurol* 2013;20(9):1311-8. doi: 10.1111/ene.12202.
16. Ryoo S, Cha J, Kim SJ, *et al*. High-resolution magnetic resonance wall imaging findings of moyamoya disease. *Stroke* 2014;45(8):2457-60. doi: 10.1161/STROKEAHA.114.004761.
17. Chmelova J, Kolar Z, Prochazka V, *et al.* Moyamoya disease is associated with endothelial activity detected by anti-nestin antibody. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2010;154(2):159-62.
18. Hao F, Han C, Lu M, *et al.* High-resolution MRI vessel wall enhancement in moyamoya disease: risk factors and clinical outcomes. *Eur Radiol* 2024:34(8):5179-89. doi: 10.1007/s00330-023-10535-0.