Research article

Multi-assessment of critical steno-occlusive middle cerebral arteries: transcranial Doppler combined with magnetic resonance angiography

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ABSTRACT

Background: Accurate assessment of a stenotic or occluded middle cerebral artery (MCA) is essential before making optimal therapeutic decisions. However, complete occlusion is not always easy to determine for both magnetic resonance angiography (MRA) and neurologists. We aimed to study noninvasive technology using transcranial Doppler (TCD) combined with MRA to assess severe stenosis and occlusion of the MCA.
Methods: We studied consecutive patients with severe steno-occlusive MCA by digital subtraction angiography from Oct. 2011 to Mar. 2020 in our stroke center. Hemodynamic measurements of TCD, including peak velocity (PSV), mean flow velocity (MFV) and pulse index (PI), were recorded specifically at the steno-occlusive site by MRA.
Results: A total of 152 MCAs of 148 patients were enrolled (60.0 ± 11.5 y, 107 male), including 82 severe stenotic MCAs and 70 occluded MCAs (Group S & Group O) by DSA. There were 86/152 (57%) MCAs showing discontinuity in MRA, which was significantly distributed more in Group O than in Group S (84% vs. 33%, P < 0.001). The PSV and MFV in Group S were greater (264 ± 78 cm/s vs. 33 ± 34 cm/s and 182 ± 61 cm/s vs. 21 ± 23 cm/s, respectively, P < 0.001), while the PI in Group O was greater (0.98 ± 0.49 vs. 0.72 ± 0.17, P < 0.001). PSV was positively correlated with severe MCA stenosis (β = 0.036, P < 0.001, OR = 0.965, 95% confidence interval (CI): 0.952–0.978). In severe steno-occlusive MCA, using PSV and MFV to detect MCA severe stenosis yielded areas under the curve of 0.983 (CI: 0.964–1.0) and 0.982 (CI: 0.962–1.0), respectively. The cutoff points of PSV ≥ 77 cm/s and MFV ≥ 51 cm/s both yielded an optimized sensitivity of 96.3% and specificity of 98.6%.
Conclusion: The critical velocity at the steno-occlusive site is reliable for distinguishing between severe MCA stenosis and occlusion.

1. Introduction

Stroke affects almost 14 million people worldwide each year [1]. Intracranial atherosclerotic disease (ICAD) is a major cause of ischemic stroke, and a considerable portion of ICAD is located in the middle cerebral artery (MCA) [2]. Currently, endovascular recanalization has changed the therapeutic framework of intracranial vessel occlusion. Selected cerebral ischemic individuals can benefit from endovascular therapy with good revascularization and favorable outcomes [3, 4]. In this context, accurate assessment of severe stenosis and occlusion of the

MCA is extremely essential before making optimal therapeutic decisions, including best medical treatment, balloon angioplasty, stenting and mechanical thrombectomy. However, complete occlusion is not always easy to determine for both radiologists and neurologists. Magnetic resonance angiography (MRA) and transcranial Doppler sonography (TCD) have been developed and proven to be two of the most useful techniques for the noninvasive assessment of intracranial arteries [5, 6]. In addition, they are interpreted in separate ways. What if the two conclusions are inconsistent? At present, specific criteria of TCD targeted at assessment on steno-occlusive MCA are not provided. MRA may be an

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overjudgment for severe stenosis, making it difficult to differentiate between severe stenosis and occlusion.

We aimed to explore the united assessment of TCD combined with MRA to differentiate between MCA severe stenosis and occlusion.

2. Methods

2.1. Patient population and study design

This was an observational, cross-sectional study undertaken between October 2011 and December 2020. This study was approved by the ethics committee of the Second Affiliated Hospital of Guangzhou University of Chinese Medicine, and formal consent was not needed. All clinical and imaging data were reviewed centrally by the executive committee to decide whether the patient was eligible for enrollment.

Inpatients with symptoms of cerebrovascular disease underwent TCD and cervical duplex ultrasound as part of routine workup at our Stroke Center (including five branch hospitals in Guangzhou). From October 2011 to December 2020, inpatients with steno-occlusive MCA were retrospectively and consecutively included according to the following criteria: (1) transient ischemic attack (TIA) or ischemia stroke on acute or recovery stages (in 90 days); (2) magnetic resonance angiography (MRA), TCD and digital subtraction angiography (DSA) were performed within 30 days; (3) severe stenosis ($\geq$70%) or occlusion at the M1 segment of unilateral or bilateral MCAs by DSA; and (4) sufficient temporal window to obtain high quality of flow signals by TCD. Subjects with the following situations were excluded from the study: (1) subarachnoid hemorrhage (SAH); (2) severe arrhythmia; (3) severe stenosis ($\geq$70%) or occlusion of the extracranial or intracranial carotid artery detected by carotid ultrasound and confirmed by DSA; (4) thrombolysis or endovascular treatments of the relevant MCA; and (5) obvious motion artifacts on TOF-MRA. The flow chart of inclusion and exclusion is outlined in Figure 1. The baseline characteristics, including demographics, risk factors and data of relevant etiologies, and National Institutes of Health Stroke Scale Score (NIHSS) of patients with ischemic stroke or TIA, were extracted from the big data research of the stroke unit. The TCD and MRA data were extracted from the raw images and then reassessed and recorded by trained physicians independently.

We needed to study the hemodynamics and MRA changes from severe stenosis to occlusion in detail, so the data of subgroups of <95% and $\geq$95% MCA severe stenosis were further analyzed.

2.2. TCD procedure and data management

We used 2-MHz, power motion (M-mode) Doppler (DWL, Multi Dop X, Germany) and shared a standardized insonation protocol [7]. The scanning was conducted by two qualified and sufficiently trained physicians (Z.J.X. and M.X.Y.) who specialize in vascular ultrasound (over 10 y of extensive experience with more than 3000 vascular cases per year). Patients with an adequate temporal window were examined and recorded in the supine position. MCA was routinely scanned through the range of 40–65 mm. The suspected spectra of sections were recorded in addition to the location of the probe. The optimal spectrum with adjusted distance to depth, which focused on the stenotic or signal loss core of MRA, was included and analyzed. The peak systolic velocity (PSV) and diastolic velocity (EDV) were clearly displayed, and the mean flow velocity (MFV) and pulse index (PI) were accurately measured automatically. Then, the MCA and anterior cerebral artery (ACA) data were obtained. The velocity ratios (VR) divided by contralateral MCA (PSVR & MFVR of M/Mc) and ipsilateral ACA (PSVR & MFVR of M/Ai) were calculated. All the data were recorded (H.X.M.) and reviewed (Z.T.) by team members who were blinded to the DSA results.

2.3. MRA procedure and data management

3D TOF-MRA was performed on a 3.0 T MAGNETOM Verio MR scanner (Siemens Medical, Germany) using an 8-channel head coil and a 3.0 T Siemens Prisma MRI scanner (Siemens Medical, Germany) using a 64-channel head coil. The following parameters were used for the 3D TOF-MRA: Verio scanner-TR, 21 m s; TE, 3.6 m s; flip angle, 18°; FOV, 210 mm; section thickness, 0.5 mm; matrix, 512 × 512; acquisition time, 4 min 36 s. Prisma scanner-TR, 21 m s; TE, 3.42 m s; flip angle, 18°; FOV, 200 mm × 175 mm; section thickness, 0.5 mm; matrix, 319 × 384; acquisition time, 4 min 49 s. The axial source images were postprocessed using a maximum intensity projection (MIP) algorithm to produce multiple projections rotated about the section axis.
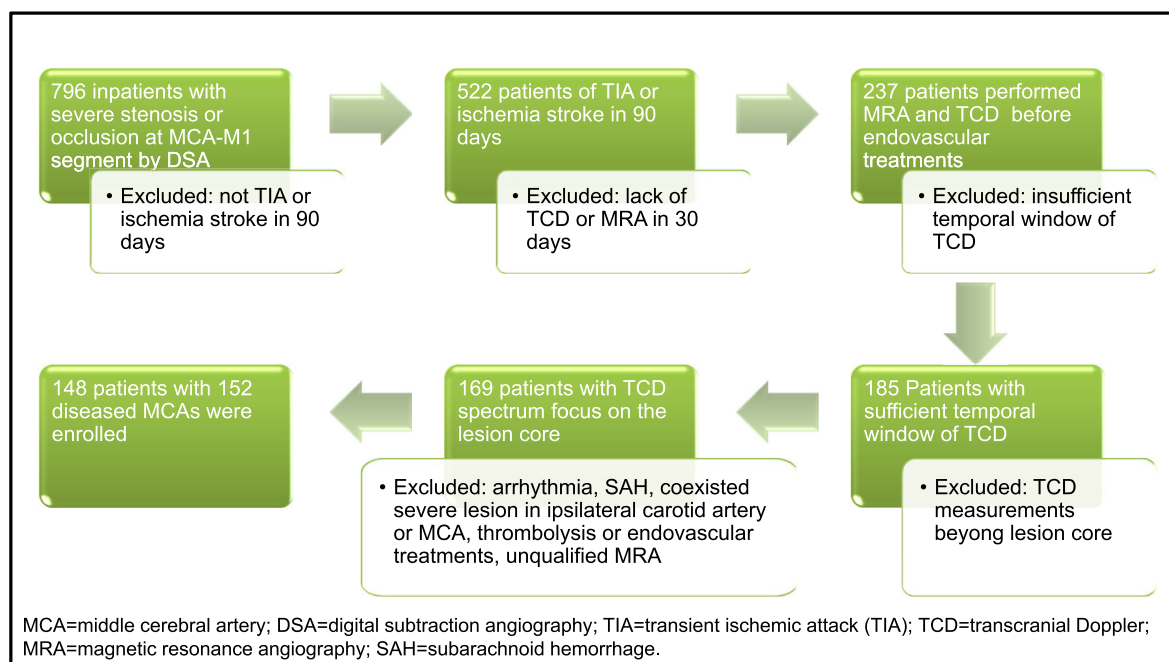

Figure 1. Flowchart of the study.

All the raw images drawn from the PACS system were reviewed and recorded independently by two different physicians (L.G.Q. and M.Z.L.) who were blinded to the DSA results. When there was a disagreement, a third physician (L.H.) reviewed the case and made the final decision through discussion. Because of a consistent overestimation of stenosis on MIP images, we combined MIP images with axial source images for image analysis. When the MR angiogram showed short segmental signal loss simulating occlusion with or without visibility of distal middle cerebral arteries and adjacent sections of the source images showed a signal, the diseased vessels were interpreted as having severe stenosis. When the MR angiogram showed segmental signal loss and adjacent sections of the source images also showed no signal, the diseased vessels were interpreted as occlusion.

2.4. DSA procedure and data management

Potential patients for further intervention procedures who had undergone DSA were included. Conventional digital subtraction angiography (DSA; Semins Arits Q, Germany) was performed and interpreted by neuroendovascular specialists who performed angiography on at least 200 cases each year. They were unaware of the TCD source data and the purposes of this study. Intravenous heparin was administered at 3000 U, followed by 1000 U/h, after placement of a 5-Fr sheath into the femoral artery. The injected volume of contrast medium was 5–8 ml Iohexol 300 (GE, USA). During DSA, the 5-Fr guiding catheter was placed into the aortic bow and then advanced into the distal cervical internal carotid artery. The anterior circulation cerebral artery system was assessed, including the MCA, with views of anteroposterior, lateral and oblique projections. If necessary, superselective angiography, rotated DSA or 3-D DSA was used to view the suspected vessels to distinguish critical stenosis, pseudoocclusion and occlusion. On DSA, the presence of intracranial stenosis was graded using WASID criteria for identification of the residual lumen [8]. The exact degree of MCA stenosis was measured by the local investigator by comparing the diameter of the vessel at the site of stenosis (D stenosis) with the normal diameter of the vessel distal to the stenosis (D distal) using the formula % stenosis = $[1 - (D\ stenosis/D\ distal)] \times 100\%$. The data of MCA severe stenosis (70–99%) and occlusion at the M1 segment were recorded. The coexistence of severe stenosis ($\geq$70%) or occlusion of the extracranial or intracranial carotid artery was confirmed by DSA and excluded.

2.5. Statistical analysis

Statistical analyses were performed with PASW statistics software (version 18.0). Continuous variables were expressed as the mean $\pm$ standard deviation and were mainly compared by the use of a t test or the Mann–Whitney U test as appropriate. The Pearson chi-square test or Fisher's exact test was performed for categorical variables. The interrater reliability was evaluated using Kappa statistics. We performed an unconditional logistic stepwise regression analysis model for variable analyses of MCA occlusion and MRA signal discontinuity. Quantitative correlational data analysis was performed using Pearson correlation and Spearman's rho as appropriate. The predictive values, including sensitivity (Se) and specificity (Sp), with corresponding 95% confidence intervals (CIs) were drawn from receiver operator characteristic curves (ROCs). Analyses of PSV, MFV, PI and VR were performed to identify cut points that yielded the greatest accuracy in discriminating between MCA severe stenosis and occlusion. Statistical significance was considered at P < 0.05.

3. Results

3.1. Baseline characteristics

Of 155 MCAs, 3 cases of both severe stenosis and occlusion at the same MCA-M1 segment were eliminated. Ultimately, a total of 152 MCAs

of 148 patients (60.0 $\pm$ 11.5 y, 107 male) suffering from ischemic stroke and TIA within 90 days were enrolled. The distribution of ischemic stroke was found in 126 (82.9%) patients, and most of them (96.0%) were first stroke. The risk factors, including hypertension (73.7%), diabetes (32.2%), hyperlipemia (38.8%), coronary artery disease (9.2%), current smoking (50.7%) and regular drinking (27.6%), were analyzed. All qualified TCD, MRA and DSA were performed within 30 days. The interval between TCD and DSA performances was 4.1 $\pm$ 3.8 days (0–25 days). Of 152 included MCAs, 82 (53.9%) MCAs with severe stenosis and 70 (46.1%) MCAs with occlusion were divided into a stenosis group (Group S) and an occlusion group (Group O) according to DSA.

The distributions of age, sex, risk factors and the presence of ischemic stroke and TIA alone in Group S and Group O showed no significant differences (P > 0.05). The baseline characteristics are listed in Table 1.

The NIHSS score on admission was significantly greater in Group O than in Group S (2.3 $\pm$ 3.2 vs. 4.3 $\pm$ 4.6, P = 0.013).

3.2. MCA signal differences of MRA

The interrater agreement of the interpreter of the MCA signal was substantial (kappa 0.734, P < 0.001). On MRA, signal discontinuity located in the M1 segment was observed in 86/152 (56.6%) cases (Table 2), and 59 (68.6%) of them matched MCA occlusion by DSA. Of MCA signal continuity in the other 66 cases, 55 (83.3%) matched MCA severe stenosis by DSA. In total, 114 (75%) MRA signals matched DSA.

Table 1. Demographics, Risk factors, Etiologies, NIHSS and Hemodynamics Comparisons Between Two Groups.

Characteristics (N = 152)	Group S (n = 82)	Group O (n = 70)	P value
Demographic			
Age (year)	59 $\pm$ 11(Y)	61 $\pm$ 12(Y)	0.187
Male sex (%)	58 (71)	53 (76)	0.183
Risk factors			
Hypertension (%)	60 (73)	52 (74)	1.0
Diabetes (%)	25 (30)	24 (34)	0.728
Hyperlipemia (%)	34 (41)	25 (36)	0.507
Coronary artery disease (%)	6 (7)	8 (11)	0.412
Current smoking (%)	38 (46)	39 (56)	0.260
Regular drinking	20 (24)	22 (31)	0.336
Etiologies			
ICAD or embolism (%)	80 (98)	65 (93)	0.249
Moyamoya disease (%)	2 (2)	5 (7)	0.322
Arterial dissection (%)	1 (1)	0 (0)	
Diagnosis			
Ischemic Stroke (%)	68 (83)	58 (83)	1.000
TIA (%)	14 (17)	12 (17)	1.000
NIHSS	2.6 $\pm$ 3.2	4.3 $\pm$ 4.6	0.013
MCA Hemodynamics			
peak systolic velocity (cm/s)	264 $\pm$ 78	33 $\pm$ 34	0.000*
mean flow velocity (cm/s)	182 $\pm$ 61	21 $\pm$ 23	0.000*
pulse index	0.72 $\pm$ 0.17	0.98 $\pm$ 0.49	0.000*
PSVR of M/Mc	2.5 $\pm$ 1.7	0.34 $\pm$ 0.39	0.000*
MFVR of M/Mc	2.9 $\pm$ 1.9	0.34 $\pm$ 0.41	0.000*
PSVR of M/Ai	2.6 $\pm$ 1.6	0.28 $\pm$ 0.29	0.000*
MFVR of M/Ai	2.9 $\pm$ 1.7	0.29 $\pm$ 0.30	0.000*

Abbreviations: NIHSS: National Institutes of Health Stroke Scale Score, ICAD: Intracranial Atherosclerotic Disease, TIA: Transient Ischemic Attack, MCA: Middle Cerebral Artery, PSVR of M/Mc: Peak Systolic Velocity Ratio (PSVR) of MCA(M) divided by contralateral MCA(Mc), MFVR of M/Mc: Mean Flow Velocity Ratio (MFVR) of MCA(M) divided by contralateral MCA(Mc), PSVR of M/Ai: Peak Systolic Velocity Ratio (PSVR) of MCA(M) divided by ipsilateral Anterior Cerebral Artery (Ai), MFVR of M/Ai: Mean Flow Velocity Ratio (MFVR) of MCA(M) divided by ipsilateral Anterior Cerebral Artery (Ai).

* P<0.001, Group S: Severe Stenosis Group, Group O: Occlusion Group.

Table 2. MCA signals in MRA.

MCA Signal (N = 152)	Group S (n = 82)	Group O (n = 70)
Continuity	55 (67.1%)	11 (15.7%)
Discontinuity	27 (32.9%)	59 (84.3%)

Group S: Severe Stenosis Group, Group O: Occlusion Group.
Abbreviations: MCA: Middle Cerebral Artery, MRA: Magnetic Resonance Angiography.

The presence of signal discontinuity was significantly more frequent in Group O than in Group S (59 vs. 27 MCAs, 84% vs. 33%, P < 0.001).

3.3. Hemodynamic differences

In hemodynamic comparisons (Table 1), PSV, MFV, PI and VRs showed significant differences between the two groups (P: 0.013–0.000). More specifically, the values of PSV, MFV and VRs in Group S were greater. In contrast, the value of PI in Group O was greater.

Taking DSA results as the dependent variable y (y = 0 indicates occlusion, y = 1 indicates stenosis) and taking PSV, MFV, PI and NIHSS as independent variables, the model difference of unconditional stepwise logistic regression analysis was statistically significant (χ = 141.451, P < 0.001), and the coincidence rate of model prediction was 95.6%. The variables entering the model included PSV, which was positively correlated with DSA (β = 0.036, P < 0.001, OR = 0.965, 95% CI: 0.952–0.978). Furthermore, Pearson correlation analysis revealed that PI was positively correlated with NIHSS (r = 0.286, P = 0.001), while PSV and MFV were negatively correlated with NIHSS (r = -0.198, P = 0.015 & r = -0.198, P = 0.014, respectively).

To differentiate MCA severe stenosis from occlusion, all the areas under the curves (AUCs) of PSV, MFV, PSVR and MFVR of M/M and PSVR and MFVR of M/A reached over 0.97, while the AUC of PI was 0.719 (Table 3 & Figure 2), according to the receiver operator characteristic curve. The cutoff points of PSV ≥ 77 cm/s and MFV ≥51 cm/s both yielded an optimized sensitivity of 96.3% and specificity of 98.6%.

3.4. MCA signals correlated with hemodynamics

Taking MRA results as the dependent variable y (y = 0 indicates signal discontinuity, y = 1 indicates signal continuity) and taking PSV, MFV, PI as independent variables, the model difference of unconditional stepwise logistic regression analysis was statistically significant (χ = 26.510, P < 0.001), and the coincidence rate of model prediction was 72.6%. The variables entering the model included PSV, which was

Table 3. ROCs of severe stenosis in steno-occlusive MCAs.

parameter	AUC	95% CI	Cutoff Points	Sensitivity	Specificity
peak systolic velocity	0.983	0.964–1.000	≥77 cm/s	96.3%	98.6%
mean flow velocity	0.982	0.962–1.000	≥51 cm/s	96.3%	98.6%
pulse index	0.719	0.632–0.807	≤0.85	52.8%	81.7%
PSVR of M/Mc	0.975	0.952–0.997	≥0.93	94.8%	93.9%
MFVR of M/Mc	0.972	0.948–0.996	≥0.94	92.2%	92.4%
PSVR of M/Ai	0.979	0.959–0.998	≥0.71	93.5%	95.5%
MFVR of M/Ai	0.978	0.958–0.998	≥0.74	93.5%	93.9%

Abbreviations: ROCs: Receiver Operator Characteristic Curves, CI: Confidence Interval. PSVR of M/Mc: Peak Systolic Velocity Ratio (PSVR) of MCA(M) divided by contralateral MCA(Mc), MFVR of M/Mc: Mean Flow Velocity Ratio (MFVR) of MCA(M) divided by contralateral MCA(Mc), PSVR of M/Ai: Peak Systolic Velocity Ratio (PSVR) of MCA(M) divided by ipsilateral Anterior Cerebral Artery (Ai), MFVR of M/Ai: Mean Flow Velocity Ratio (MFVR) of MCA(M) divided by ipsilateral Anterior Cerebral Artery (Ai).

positively correlated with MRA (β = 0.007, P < 0.001, OR = 0.993, 95% CI: 0.990–0.996).

MCA of ≥95% degree of stenosis accounted for 5.9% (9/152) of severe steno-occlusive disease. The median (P25–P75) PSV value was 254 (285) cm/s. Five of them presented with signal loss on MRA (56% vs. 33%, compared with <95% degree of stenosis). Their PSVs were 33 cm/s, 71 cm/s, 81 cm/s, 323 cm/s and 401 cm/s, respectively. The median velocity bar charts of <95%, ≥95 degree of stenosis and occlusion displayed in Figure 2 revealed that velocities of ≥95 degree of stenosis were distributed dispersedly.

One of the cases (No. 142) showing an MCA signal correlated with hemodynamics is displayed in Figure 3.

4. Discussion

The current study was the first to evaluate the hemodynamics of severe stenosis and occlusion of the MCA. The use of guided TCD parameters is reliable for distinguishing severe stenosis from occlusion and is critical for clinical prognosis and therapeutic decisions. Overestimation of MCA stenosis or underestimation of MCA occlusion may deprive the patient of the opportunity for an intervention benefit or lead to an unnecessary invasive operation.

As a widely used noninvasive technique to evaluate cerebral arteries, however, MRA alone is not sufficient for the optimal and accurate assessment of severe steno-occlusive MCA. As shown in our study, the presence of signal discontinuity was more frequent in MCA occlusion than in MCA severe stenosis (59 vs. 27 MCAs, 84% vs. 33%, P < 0.001). However, a third of MCA severe stenosis was interpreted as signal discontinuity by MRA. Including all cases, only 75% of MCAs were interpreted correctly by MRA even though the interrater agreement of the interpreter was substantial, mainly because MRA tended to overestimate the degree of stenosis and may incorrectly interpret them as occluded MCAs that were actually severely stenosed [6]. In the current study, the most common cause of overestimating severe stenosis as occlusion was misinterpreted as signal discontinuity in MRA [9]. One of the reasons is accelerated flow through the stenotic site, and blood flow turbulence may lead to dephasing and result in a loss of blood flow signal [9]. As shown in our study, a low PSV of the MCA (β = 0.007, P < 0.001) was correlated with a loss of blood flow signal in MRA. In addition, the proportion of signal loss in MCA with severe stenosis ≥95% tended to be greater than stenosis <95% (56% vs. 33%), even though it was not as statistically significant.

Unlike the morphological display on imaging, hemodynamics are more sensitive to the distinction between severe stenosis or occlusion. Blood flow velocity varies according to the changes in the cross-sectional area of the vessel. More specifically, velocities mostly increased at the stenotic site but disappeared or decreased (due to collateral compensation) at the occluded site. Therefore, hemodynamics might be helpful for accurate diagnosis when the discontinuity of the MCA signal on MRA causes neurologists to be uncertain about whether the MCA is a severe stenosis or occlusion.

All the main TCD parameters, including pulse index and velocities (PSV & MFV), were correlated with NIHSS (P < 0.05) and significantly different between severe MCA stenosis and occlusion (P < 0.01). The value of PI of MCA occlusion was greater, while the value of velocities of MCA severe stenosis was greater. This was probably because the status of lumen patency directly affected the blood flow and hemodynamic status. The occluded artery led to increased blood flow resistance and decreased blood flow velocity, which could be observed starting from the anterior section of the occluded artery. The stenotic artery matched the hemodynamics of increased blood flow velocity with relatively less blood flow resistance.

It is worth noting that not all stenotic sites lead to accelerated velocity. When severe stenosis approaches a hairline residual lumen, previously elevated flow velocities may begin to "fall off" or pseudonormalize [10, 11]. In this situation, accurate location of the TCD
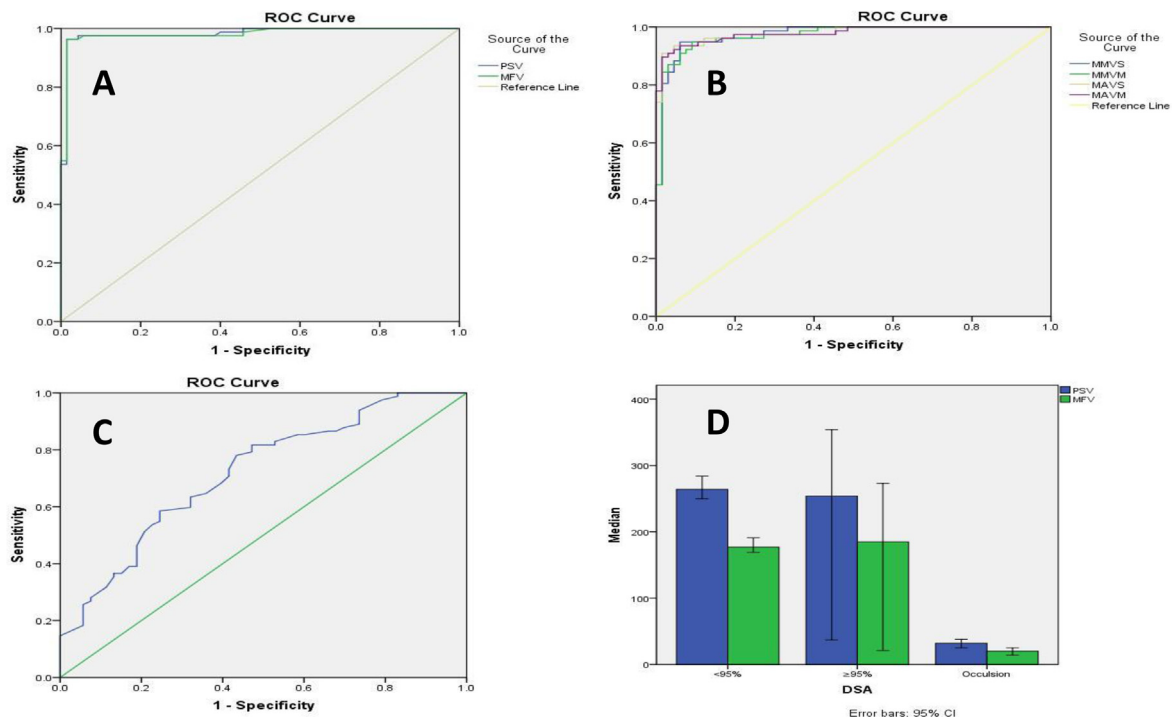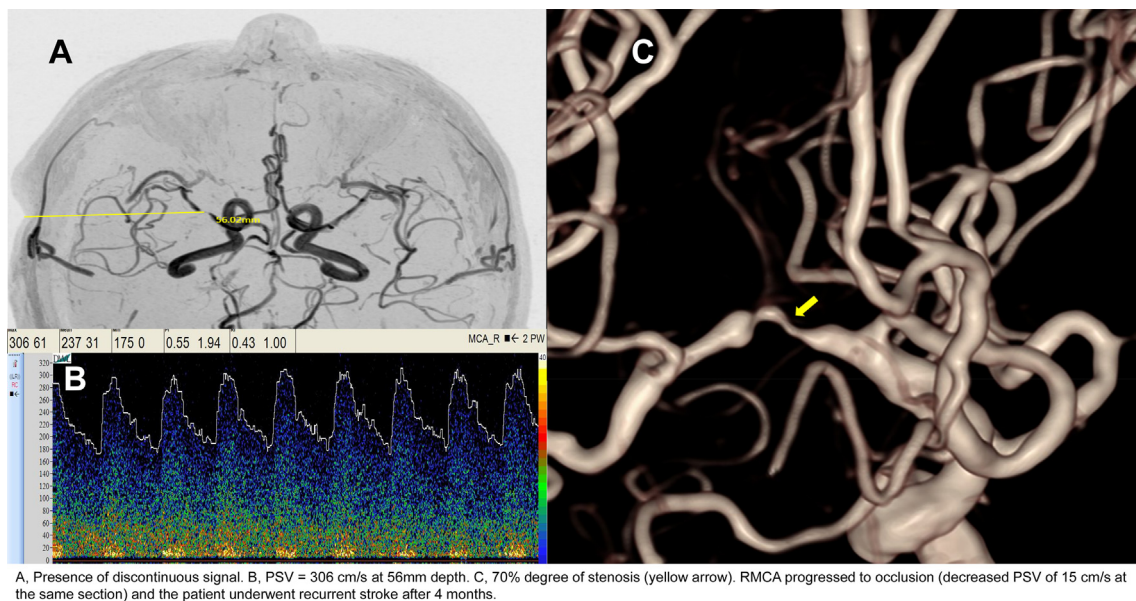
Figure 2. Receiver operator characteristic curves of velocities (A), velocity ratios(B), PI (C) and steno-occlusive median velocity bar charts (D)

A, Presence of discontinuous signal. B, PSV = 306 cm/s at 56mm depth. C, 70% degree of stenosis (yellow arrow). RMCA progressed to occlusion (decreased PSV of 15 cm/s at the same section) and the patient underwent recurrent stroke after 4 months.

Figure 3. MRA (A), TCD (B) and DSA (C) of severe stenotic RMCA at M1 section (Case NO.142 with acute ischemic stroke)

spectrum is even more crucial to assess correct velocity. The TCD spectrum obtained beyond the stenotic or occlusive core may lead to hemodynamic misinterpretation. For example, acquisition before the occlusive core could obtain a relatively high velocity, while acquisition away from the stenotic site could obtain a relatively low velocity, which may result in missed diagnosis or underestimation of the steno-occlusive MCA.

In addition, the velocity value of occlusion is not always close to zero because the TCD sampling volume is large (10–15 mm) and neighboring or recruited collateral flow may be involved. Further analysis of data of very severe MCA stenosis (≥95% degree of stenosis) may present clues of hemodynamic changes before occlusion. In our study, the velocities of ≥95% stenotic MCAs ranged dispersedly, including low velocity, normal

velocity and extremely high velocity, and a few even overlapped the velocity of occluded MCAs. Thus, hemodynamic changes within very severe stenosis (≥95%) and occlusion present a complex task of sampling, monitoring and interpretation even for experienced users. Nevertheless, it accounted for a relatively small proportion (9/152, 5.9%) of severe steno-occlusive MCAs. As shown in our study, even though we included the data of the most severe stenosis, PSV ≥ 77 cm/s and MFV ≥ 51 cm/s were reliable critical values with a high sensitivity of 96.3% and specificity of 98.6% to distinguish severe stenosis from occlusion.

MRA and TCD are widely used noninvasive techniques to evaluate cerebral arteries by hemodynamic and imaging, and they should be considered as two complementary techniques. MRA can be used to locate

the suspected lesion on clear structural visualization, and combined with the hemodynamic change by TCD, it can minimize overestimation and provide accurate distinctions in ICAD. MRA and TCD can be combined to optimize noninvasive cerebrovascular assessment to improve diagnostic accuracy.

This study encountered several limitations. First, this was a retrospective study with a relatively small sample size and inevitably encounters potential bias, and the results require validation with future larger-scale prospective studies. Second, the critical velocity was close to the value of the normal MCA; thus, it should be carefully interpreted. Specifically, it is strictly used to draw a distinction between severe stenotic and occluded MCA when imaging shows the presence of atherosclerotic disease in MRA. Hemodynamic changes in different stages of ICAD, including severe and critical stenosis, pseudo-occlusion and complete occlusion, need to be further studied.

5. Conclusions

MRA combined with TCD hemodynamics helps to determine the degree of stenosis of the MCA. The critical velocity at the steno-occlusive site may be reliable for distinguishing between severe MCA stenosis and occlusion.

Declarations

Author contribution statement

Xiuyun Mo: Conceived and designed the experiments; Wrote the paper.

Zelan Ma, Hao Lin, Guoqing Liu: Performed the experiments.

Aihua Ou, Xumin He: Analyzed and interpreted the data.

Ting Zhou: Contributed reagents, materials, analysis tools or data.

Jingxin Zhong: Conceived and designed the experiments.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

[1] L.T. Øverberg, E.F. Lugg, M. Gaarder, et al., Plasma levels of BDNF and EGF are reduced in acute stroke patients, Heliyon 8 (2022), e09661.

[2] C.P. Derdeyn, M.I. Chimowitz, M.J. Lynn, 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 383 (2014) 333–341.

[3] M. Waqas, A.D. Gong, B.R. Levy, et al., Is endovascular therapy for stroke cost-effective globally? A systematic review of the literature, J. Stroke Cerebrovasc. Dis. 30 (2021), 105557.

[4] M. Shirakawa, H. Matsukawa, N. Sakai, et al., Endovascular therapy for acute ischemic stroke in patients with large-vessel occlusion due to atherosclerotic stenosis, J. Stroke Cerebrovasc. Dis. 30 (2021), 105960.

[5] C. Gómez-Escalonilla, P. Simal, H. García-Moreno, et al., Transcranial Doppler 6h after successful reperfusion as a predictor of infarct volume, J. Stroke Cerebrovasc. Dis. 31 (2021), 106149.

[6] G.P. Anzola, R. Gasparotti, M. Magoni, et al., Transcranial Doppler sonography and magnetic resonance angiography in assessment of collateral hemispheric flow in patients with carotid artery disease, Stroke 26 (1995) 214–217.

[7] A.V. Alexandrov, M.A. Sloan, L.K. Wong, et al., Practice standards for transcranial Doppler ultrasound: Part I—test performance, J. Neuroimaging 17 (2007) 11–18.

[8] M.I. Chimowitz, M.J. Lynn, H. Howlett-Smith, et al., Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis, N. Engl. J. Med. 352 (2005) 1305–1316.

[9] X. Zhang, Y.Z. Cao, X.H. Mu, et al., Highly accelerated compressed sensing time-of-flight magnetic resonance angiography may be reliable for diagnosing head and neck arterial steno-occlusive disease: a comparative study with digital subtraction angiography, Eur. Radiol. 30 (2020) 3059–3065.

[10] The Professional Committee of Vascular Ultrasound of Stroke Prevention and Treatment Expert, Committee of the National Health Commission, The professional committee of superficial organ and peripheral vascular ultrasound of the Chinese medical ultrasound engineering, the professional committee of craniocerebral and cervical vascular ultrasound of the Chinese medical ultrasound engineering, expert consensus on some issues of cerebral and carotid vascular ultrasonography, Adv. Ultrasound Diagn. Ther. 5 (2021) 153–162.

[11] J.M. Romero, M.H. Lev, S.T. Chan, et al., US of neurovascular occlusive disease: interpretive pearls and pitfalls, Radiographics 22 (2002) 1165–1176.