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CLINICAL INVESTIGATIVE STUDY

Validation of the transcranial Doppler rescue criteria for mechanical thrombectomy

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Abstract

Background and Purpose: Transcranial Doppler (TCD) identifies acute stroke patients with arterial occlusion where treatment may not effectively open the blocked vessel. This study aimed to examine the clinical utility and prognostic value of TCD flow findings in patients enrolled in a multicenter prospective study (CLOTBUST-PRO).

Methods: Patients enrolled with intracranial occlusion on computed tomography angiography (CTA) who underwent urgent TCD evaluation before intravenous thrombolysis was included in this analysis. TCD findings were assessed using the mean flow velocity (MFV) ratio, comparing the reciprocal ratios of the middle cerebral artery (MCA) depths bilaterally (affected MCA-to-contralateral MCA MFV [aMCA/cMCA MFV ratio]).

Results: A total of 222 patients with intracranial occlusion on CTA were included in the study (mean age: 64 ± 14 years, 62% men). Eighty-eight patients had M1 MCA occlusions; baseline mean National Institutes of Health Stroke Scale (NIHSS) score was 16, and a 24-hour mean NIHSS score was 10 points. An aMCA/cMCA MFV ratio of <.6 had a sensitivity of 99%, specificity of 16%, positive predictive value (PV) of 60%, and negative PV of 94% for identifying large vessel occlusion (LVO) including M1 MCA, terminal internal carotid artery, or tandem ICA/MCA. Thrombolysis in Brain Ischemia scale, with (grade ≥1) compared to without flow (grade 0), showed a sensitivity of 17.1%, specificity of 86.9%, positive PV of 62%, and negative PV of 46% for identifying LVO.

Conclusions: TCD is a valuable modality for evaluating arterial circulation in acute ischemic stroke patients, demonstrating significant potential as a screening tool for intravenous/intra-arterial lysis protocols.

KEYWORDS
mRS, reperfusion, stroke, thrombectomy, TIBI, tPA, transcranial Doppler

INTRODUCTION

Since 1995, intravenous thrombolysis (IVT) remains the approved systemic therapy for acute ischemic stroke (AIS), with onset-to-treatment time being directly associated with improved short-term and long-term clinical outcomes.[1,2] Approximately half of IVT-treated ischemic stroke patients become disabled or die.[2] This can be explained by the modest recanalization rate of 25%-30% observed with systemic thrombolysis alone in proximal large vessel occlusion (LVO).[3,4]

Since 2015, a number of randomized control trials have demonstrated that mechanical thrombectomy (MT) is an effective treatment for proximal artery occlusions.[5–8] There has been a variable response to treatment, with some patients showing excellent recovery and others showing little improvement. MT's effectiveness is largely determined by the time of intervention, as measured by door to groin puncture, and the time and degree of meaningful recanalization (Thrombolysis in Cerebral Infarction [TICI] grade 2b, 2c, or 3 of reperfusion).[9] For that reason, early detection of a proximal arterial occlusion in the mobile stroke unit or in the ambulance is critical in transferring patients to an interventional stroke team for early intervention and better clinical results. One method of identifying appropriate patients with proximal occlusion, when IVT fails to recanalize, is to use transcranial Doppler (TCD). It can quickly determine if occlusion is present[10,11] or whether recanalization has been achieved.[12,13] It is an ideal bedside monitoring tool that can be brought to the stroke or regular ambulance and may provide noninvasive continuous monitoring of the arterial status while patient receiving intravenous tissue plasminogen activator (tPA).[10,14]

We designed the "PROspective multi-national CLOTBUST collaboration on reperfusion therapies for stroke" (CLOTBUST-PRO) that sought to determine whether early recanalization (within 1-hour from tPA-bolus), assessed with real-time TCD monitoring, is independently associated with improved 3-month outcomes in AIS patients with proximal intracranial arterial occlusions.[15] We also investigated the association between the elapsed time between symptom onset and tPA-bolus with the elapsed time between tPA-bolus and the beginning of recanalization.

We hypothesized that a baseline TCD measurement, showing a middle cerebral artery-to-contralateral middle cerebral artery (aMCA/cMCA) mean flow velocity (MFV) ratio <.6, predicts proximal arterial occlusion in the anterior circulation that requires MT.

The primary objective of this study was to evaluate whether our developed TCD criteria for MT are valid in our prospective multiple center cohort study (CLOTBUST-PRO).

METHODS

Setting and participants

We conducted a prospective, open-label, observational cohort study in 12 participating tertiary care stroke centers in North America, South America, Europe, and Asia. The rationales for the study, design details, and eligibility and exclusion criteria have been previously published.[15]

We included patients with AIS attributable to a proximal intracranial occlusion eligible for intravenous recombinant tissue plasminogen activator (rtPA), who presented within 4.5 hours to the participating sites. The study was approved by the Ethics Committees and the Institutional Review Boards of participating institutions as previously described.[15,16]

Insonation protocol and TCD criteria

Patients underwent continuous 2-MHz TCD or Transcranial color-coded Duplex assessment of recanalization up to 2 hours following tPA-bolus by experienced sonographers. The duration of continuous TCD monitoring varied between 60 and 120 minutes because if there was no ultrasonographic evidence of recanalization within 60 minutes from tPA bolus and the patient was considered by the treating physician as a candidate for additional revascularization therapies (intra-arterial thrombolysis or MT), TCD monitoring was discontinued and an additional TCD evaluation was performed at the end of endovascular reperfusion therapies. This therapeutic approach toward endovascular reperfusion therapies was based on the lack of available randomized controlled clinical trial data supporting the clinical efficacy of MT at the time of study design and patient enrollment (2008-2014).

The exact time of the beginning, duration, timing, and degree of recanalization and re-occlusion were recorded in all patients. In patients with clinical deterioration following improvement within the first 24 hours from symptom onset, an additional TCD recording was performed to assess the presence of delayed re-occlusion. Finally, late recanalization was evaluated by TCD at 24 hours from stroke onset.

Concomitant and persisting severe stenosis or occlusion of the proximal internal carotid artery (ICA) was established by carotid duplex ultrasonography or by angiography and did not preclude patient enrollment into the study. In all patients with anterior circulation occlusions, transducers were positioned over the temporal bone with a standard head frame. The depth with the worst residual flow signal was selected for display, as explained by the Thrombolysis in Brain Ischemia (TIBI) scale below. An insonation depth of 45 mm or more was used for the identification of proximal (ie, M1) MCA occlusion and depths of 30-45 mm for presumed distal occlusions (ie, M2). In the case of anterior cerebral artery occlusions, contralateral anterior cerebral artery (if available) or ipsilateral MCA was used as comparison vessels.

Early arterial recanalization was determined by unblinded onsite investigators who gave tPA and monitor the residual flow signals using the TIBI system. Complete recanalization was diagnosed if flow improved to TIBI grades 4-5 and partial recanalization was identified if flow improved by one grade or more from the baseline but not to grades 4-5 on the TIBI scale. Patients with re-occlusion within 2 hours from tPA were diagnosed if, following an improvement by at least one TIBI flow grade during TCD monitoring, the residual flow deteriorated and an arterial occlusion was diagnosed at the end of monitoring with TIBI grades 0-3.[17,18] In patients with concomitant and persisting severe stenosis or occlusion of the proximal ICA, complete recanalization of the MCA was considered if TCD showed low-resistance waveforms (TIBI 2 or greater) over both M1 and M2 segments, with an improvement in MFV to more than 20 cm/second.[18,19]

TICI was scored as follows: Grade 0, no perfusion; Grade 1, penetration with minimal perfusion—contrast passes the area of occlusion but fails to opacify the entire cerebral bed distal to the obstruction; Grade 2, partial perfusion, wherein the contrast passes the occlusion and opacifies the distal arterial bed, but the rate of entry or clearance from the bed is slower than noninvolved territories; Grade 2A, partial filling, only (<50%) of territory visualized; Grade 2B, substantial perfusion with distal branch filling of ≥50% of territory visualized; Grade 2C, near-complete perfusion except for slow flow in a few distal cortical vessels or presence of small distal cortical emboli; Grade 3, complete perfusion.[20]

TCD findings were analyzed by an MFV ratio using reciprocal MCA depths bilaterally (aMCA/cMCA MFV ratio). The highest MFV at the proximal affected MCA depth was divided into 5-mm segments (55-60, 50-55, 45-50, and 40-45 mm depth), and the corresponding contralateral MCA MFV at the same 5-mm segments was analyzed.

Outcomes measures

The main hypothesis of our analysis was to evaluate whether baseline TCD aMCA/cMCA MFV ratio <.6 predicts proximal arterial occlusion in the anterior circulation that requires MT. Our group previously derived acute TCD criteria for proximal arterial occlusion that requires MT.[21] It is a simple ratio to calculate in the acute stroke setting and requires only insonation of the proximal MCA bilaterally.

The aMCA segments were measured at depth 40-65 mm through the temporal window. The cMCA segment was chosen as the mirror segment of the aMCA. In few cases, where the cMCA segment was not insonated, we did presume the MFV is 40 cm/second as a conservative measure. Proximal occlusion on gold standard neuroimaging was defined as (M1 MCA, functional M2 occlusion, terminal internal carotid artery [TICA] criteria, tandem contralateral ICA stenosis, or occlusion with proximal M1 MCA or functional M2 occlusion). Functional M2 MCA occlusion was defined as proximal M2 MCA occlusion with a National Institutes of Health Stroke Scale (NIHSS) score >6 at baseline and on computed tomography angiography (CTA) or MR angiography (MRA) as 2 out of 3 M2 MCA branch occlusions.[22] The gold standard test was considered as baseline CTA or MRA of the extracranial and intracranial vessels.

The clinical outcome measures were the following: modified Rankin Scale (mRS) scores of 0-1 and 0-2 were evaluated at 3 months by the on-site investigators (certified in the assessment of mRS) who were unaware of TCD monitoring findings. Symptomatic intracranial hemorrhage (sICH) with clinical worsening (≥4 NIHSS points), in the opinion of the treating physician, was causatively and temporally related to neurological deterioration during the first 24 hours following tPA infusion. All radiological examinations were independently evaluated by institutional radiologists/neuroradiologists who were blinded to both TCD findings and patient clinical data.

Statistical analysis

Descriptive and inferential statistics were used to characterize the study sample and test hypotheses. Descriptive results for all continuous variables (eg, age) were presented as mean ± standard deviation, while numbers (percentage) were reported for all categorical variables (eg, gender).

Bivariate analysis (one-way analysis of variance, Pearson chi-square) was used to assess the relationship between demographic data (eg, age, gender) and clinical characteristics (eg, NIHSS, TCD MFV, mRS score) with the following groups: M1 MCA, functional M2, TICA, tandem ICA/MCA, distal M2, anterior circulation stenosis, and no occlusion.

Baseline aMCA/cMCA MFV ratios have been calculated for patients with anterior circulation stroke in the CLOTBUST PRO-trial. Then, accuracy markers were calculated using the baseline CTA or MRA as the gold standard method for proximal occlusion by 2 × 2 tables. Baseline blood flow signals were categorized using the TIBI scale into without (grade 0) and with flow (grade ≥1).

The sensitivity/specificity, positive and negative likelihood ratios (LRs), and positive and negative predictive values (PVs) were calculated for the following defined gold standards: (1) presence of proximal LVO (M1 MCA, TICA, tandem ICA/MCA, functional M2, intracranial stenosis), (2) proximal LVO (M1, TICA, tandem ICA/MCA), and (3) presence of LVO and proximal M2. A *P*-value <.05 (two-tailed) was considered statistically significant. Receiver operating characteristic curve analysis was performed for aMCA/cMCA MFV to identify patients without LVO compared to LVO.

All statistical analyses were performed using the Statistical Package for Social Sciences (Version 26, Chicago, IL, https://www.ibm.com/products/spss-statistics).

RESULTS

Study population

The predetermined sample size of 480 AIS patients (mean age: 66 ± 15 years, 60% men) with proximal intracranial occlusions, who underwent continuous 2-hour TCD monitoring following tPA bolus, were enrolled during a 7-year period (January 2008 to December 2014) from 12 participating tertiary care stroke centers from North America ($n = 2$), South America ($n = 1$), Europe ($n = 7$), and Asia ($n = 2$).

Demographic and clinical outcomes of patients

A total of 222 patients had proximal intracranial occlusions according to the gold standard (CTA) (mean age: 64 ± 14 years, 62% male). Forty-seven patients received tPA within 3 hours compared to 175 patients between 3 and 4.5 hours from symptom onset.

Patients with M1 occlusion had mean age 65 ± 15 years, and 51% were male. Patients with distal M2 occlusion had the lowest mean age of 58 ± 10 years, while patients with TICA occlusion had the highest mean age of 67 ± 12 years ($P = .014$). Patients with tandem ICA/MCA occlusion had the highest percentage of male patients at 94%, while patients with no occlusion had the lowest percentage of male patients at 26% ($P < .001$). Patients with TICA had the highest baseline and a 24-hour mean NIHSS score (19 ± 7 and 13 ± 7 points, respectively). Patients with distal M2 occlusion had the lowest baseline and a 24-hour mean NIHSS score (4 ± 6 and 1 ± 0 points, respectively). Patients with functional M2 occlusion had the highest achievement of mRS score (3 months) of 0-1, observed in 74% of the patients, and 0-2 in 80% of the patients. On the other hand, patients with TICA occlusion had the lowest achievement of mRS score of 0-1, observed in 21% of the patients, and 0-2 in 42% of the patients. sICH was observed in 9% of M1 MCA cases and 4% of anterior circulation stenosis cases that received endovascular thrombectomy (Table 1).

TIBI grading

Patients with M1 and M2 MCA had the highest TIBI flows with 23% and 50% for flow 3, respectively. Patients with TICA and tandem ICA/MCA had the lowest TIBI flows with 69% and 56% for flow 0-1, respectively (Table 1).

MFV and aMCA/cMCA ratio

For patients with M1 MCA involvement, the mean aMCA and cMCA velocities were 15 ± 10 and 54 ± 14 cm/second, respectively, with a mean aMCA/cMCA ratio of .29 ± .18. For patients with functional M2 MCA involvement, the mean aMCA and cMCA velocities were 26 ± 11 and 57 ± 11 cm/second, respectively, with a mean aMCA/cMCA ratio of .46 ± .18 (Table 1).

Recanalization

Patients with functional M2 MCA involvement demonstrated the highest proportion of 74% complete, 7% partial, and 19% persistent occlusion after recanalization. On the other hand, TICA involvement resulted in proportions of 42% complete, 11% partial, and 47% persistent occlusion after recanalization (Table 1).

TABLE 1 Demographic and clinical characteristics of the study participants.

Variables	M1 MCA (88)	Functional M2 (54)	TICA (19)	Tandem ICA/ MCA (16)	Distal M2 (3)	Anterior circulation stenosis (23)	No occlusion (19)	*P*-value
Age (mean ± SD)	65 ± 15	64 ± 14	67 ± 12	58 ± 14	58 ± 10	64 ± 15	75 ± 11	.014
Sex Male (%)	45 (51%)	37 (69%)	14 (74%)	15 (94%)	2 (67%)	19 (83%)	5 (26%)	<.001
Baseline NIHSS	16 ± 6	12 ± 5	19 ± 7	16 ± 7	4 ± 6	16 ± 6	13 ± 5	<.001
24 hours NIHSS	10 ± 7	5 ± 6	13 ± 7	9 ± 9	1 ± 0	10 ± 10	9 ± 6	<.001
Good long-term outcome								
3 months mRS 0-1	42 (48%)	40 (74%)	4 (21%)	8 (50%)	3 (100%)	14 (61%)	7 (37%)	<.001
3 months mRS 0-2	56 (64%)	43 (80%)	8 (42%)	10 (63%)	3 (100%)	14 (61%)	11 (58%)	.044
EVT	18 (21%)	0	3 (16%)	2 (13%)	0	1 (4%)	0	<.001
sICH	8 (9%)	0	0	0	0	1 (4%)	0	.03
TCD MFV (mean cm/second)								
aMCA	15 ± 10	26 ± 11	13 ± 7	12 ± 9	13 ± 16	16 ± 13	14 ± 12	<.001
cMCA	54 ± 14	57 ± 11	55 ± 16	62 ± 17	41 ± 7	55 ± 13	47 ± 16	.037
TIBI flow								.001
0	12 (14%)	2 (4%)	4 (21%)	5 (31%)	0	6 (26%)	5 (26%)	
1	39 (44%)	20 (37%)	9 (48%)	4 (25%)	1 (33%)	10 (44%)	8 (42%)	
2	17 (19%)	5 (9%)	5 (26%)	5 (31%)	0	2 (9%)	4 (21%)	
3	20 (23%)	27 (50%)	1 (5%)	2 (13%)	2 (67%)	5 (22%)	2 (11%)	
TCD								<.001
aMCA/cMCA ratio (mean ± SD)	.29 ± .18	.46 ± .18	.23 ± .13	.19 ± .15	.28 ± .31	.29 ± .23	.31 ± .27	
Ratio <.6	87 (99%)	42 (78%)	19 (100%)	16 (100%)	2 (67%)	22 (96%)	17 (89%)	<.001
Ratio ≥.6	1 (1%)	12 (22%)	0	0	1 (33%)	1 (4%)	2 (11%)	
Recanalization								
Persistent occlusion	31 (35%)	10 (19%)	9 (47%)	9 (56%)	1 (33.3%)	6 (26%)		
Partial recanalization	16 (18%)	4 (7%)	2 (11%)	0	1 (33.3%)	6 (26%)		
Complete recanalization	41 (47%)	40 (74%)	8 (42%)	7 (44%)	1 (33.3%)	11 (48%)		

Abbreviations: aMCA, affected middle cerebral artery; aMCA/cMCA, affected-MCA-to-contralateral MCA; cMCA, contralateral MCA; EVT, endovascular thrombectomy; ICA, internal carotid artery; MCA, middle cerebral artery; MFV, mean flow velocity; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; sICH, symptomatic intracranial hemorrhage; TCD, transcranial Doppler; TIBI, Thrombolysis in Brain Ischemia; TICA, terminal internal carotid artery.

TIBI criteria for predicting LVO

TIBI grade categorized into grade 0 versus grade ≥1 had a sensitivity 17.1%, specificity of 86.9%, positive PV of 62%, and negative PV of 46% for identifying LVO including M1, TICA, or tandem ICA/MCA (Table 2).

Sensitivity criteria for predicting LVO

For the identification of M1 MCA occlusion, aMCA/cMCA MFV ratio of <.6 had a sensitivity of 98.9% and a specificity of 12%. The positive LR was 1.12, the negative LR was 0.09, the positive PV was 42.4%, and the negative PV was 94%. Similarly, for TICA and tandem occlusions, the aMCA/cMCA MFV ratio of <.6 had a sensitivity of 100% for both types of occlusions. The specificity was 8.4% for TICA and 8.3% for tandem occlusions. The positive LR and the negative LR were 1.09 and 0.00, respectively, for TICA and tandem occlusions. The positive PV was 9.3% for TICA and 5% for tandem occlusions, and the negative PV was 100% for both types of occlusions (Table 3). For functional M2 MCA occlusion, aMCA/cMCA MFV ratio of <.6 had a sensitivity of 71% and a specificity of 3%. The positive LR was 0.73, the negative LR was 9.67, the positive PV was 21%, and the negative PV was 29.4%. For intracranial stenosis, aMCA/cMCA MFV ratio of <.6 had a sensitivity of 96% and a specificity of 7.2%. The positive LR was 1.03, the negative LR was 0.56, the positive PV was 11%, and the negative PV was 94%.

An aMCA/cMCA MFV ratio of <.6 had a sensitivity of 99%, specificity of 16%, positive LR of 1.18, negative LR of 0.06, positive PV of 60%, and negative PV of 94% for identifying LVO including M1, TICA, or tandem ICA/MCA.

TABLE 2 Transcranial Doppler for predicting large vessel occlusion using Thrombolysis in Brain Ischemia grade (grade 0 vs. grade ≥1).

	Sensitivity	Specificity	Positive LR	Negative LR	Positive PV	Negative PV
M1 MCA occlusion	12/88 (13.6%)	112/134 (83.6%)	0.83	1.03	12/34 (35%)	112/188 (60%)
TICA	4/19 (21.1%)	173/203 (85.2%)	1.42	0.93	4/34 (12%)	173/188 (92%)
Tandem ICA/MCA	5/16 (31.3%)	177/206 (85.9%)	2.22	0.80	5/34 (15%)	177/188 (94%)
Functional M2	2/54 (3.7%)	136/168 (81.0%)	0.19	1.19	2/34 (6%)	136/188 (72%)
Intracranial stenosis	6/23 (26.1%)	171/199 (85.9%)	1.85	0.86	6/34 (18%)	171/188 (91%)
LVO (M1,TICA, tandem ICA/MCA)	21/123 (17.1%)	86/99 (86.9%)	1.30	0.95	21/34 (62%)	86/188 (46%)
LVO and proximal M2 MCA	23/177 (13.0%)	34/45 (75.6%)	1.02	1.15	23/34 (68%)	34/188 (18%)
Proximal steno-occlusive lesion	29/200 (14.5%)	17/22 (77.3%)	0.64	1.11	29/34 (85%)	17/188 (9%)

Abbreviations: ICA, internal carotid artery; LR, likelihood ratio; LVO, large vessel occlusion; MCA, middle cerebral artery; PV, predictive value; TCD, transcranial Doppler; TICA, terminal internal carotid artery.

TABLE 3 Sensitivity of transcranial Doppler criteria for predicting large vessel occlusion using affected middle cerebral artery-to-contralateral middle cerebral artery mean flow velocity ratio 0.6.

	Sensitivity	Specificity	Positive LR	Negative LR	Positive PV	Negative PV
M1 MCA occlusion	87/88 (98.9%)	16/134 (12%)	1.12	0.09	87/205 (42.4%)	16/17 (94%)
TICA	19/19 (100%)	17/203 (8.4%)	1.09	0.00	19/205 (9.3%)	17/17 (100%)
Tandem ICA/MCA	10/16 (100%)	17/206 (8.3%)	1.09	0.00	10/205 (5%)	17/17 (100%)
Functional M2 MCA	42/54 (71%)	5/168 (3%)	0.73	9.67	42/205 (21%)	5/17 (29.4%)
Intracranial stenosis	22/23 (96%)	16/199 (7.2%)	1.03	0.56	22/205 (11%)	16/17 (94%)
LVO (M1 MCA, TICA, tandem ICA/MCA)	122/123 (99%)	16/99 (16%)	1.18	0.06	122/205 (60%)	16/17 (94%)
LVO and proximal M2 MCA	164/177 (93%)	4/45 (9%)	1.02	0.78	164/205 (80%)	4/17 (24%)
Proximal steno-occlusive lesion	186/200 (84%)	3/22 (9%)	0.92	1.78	186/205 (91%)	3/17 (18%)

Abbreviations: ICA, internal carotid artery; LR, likelihood ratio; LVO, large vessel occlusion; MCA, middle cerebral artery; PV, predictive value; TICA, terminal internal carotid artery.

Diagnostic accuracy for distinguishing patients without LVO from those with LVO

Figure 1 shows the diagnostic accuracy of the aMCA/cMCA MFV ratio for identifying patients without LVO compared to those with LVO. The aMCA/cMCA MFV ratio distinguished patients without LVO from those with LVO with a 67% area under the curve (95% confidence interval [CI]: 59%-74%). Using a cutoff of an aMCA/cMCA MFV ratio of .21, the sensitivity and specificity were 81% and 70%, respectively, according to the Youden index.

DISCUSSION

Our study showed that the derived aMCA/MCA <.6 ratio is valid with acceptable sensitivity in predicting proximal LVO that is amenable for intervention and excellent sensitivity for defining occlusion in the proximal anterior circulation. This is in agreement with our previous findings in two smaller studies.[21] Furthermore, the TIBI score improved the specificity in predicting LVO.

TCD is a noninvasive, inexpensive, repeatable bedside examination tool that can be operated by a trained paramedic.[23] It provides information about the location and degree of occlusion, collateral status, impaired hemodynamics, vascular steal phenomenon, and real-time embolization.[24] Clinically, it has shown high accuracy (93%) compared to angiography for emergent assessment not only of the anterior circulation but also of the posterior circulation stroke.[25] In addition, it contributes to the differential diagnosis of stroke mimics.[26] There are preliminary studies arguing in favor of the feasibility and high diagnostic accuracy of emergency transcranial ultrasound assessment combined with neurological examinations for major AIS detection[27,28] as magnetic resonance imaging (MRI) may be contraindicated in patients with pacemakers and CTA with renal insufficiency.

Furthermore, in a study comparing neurosonology with correlative angiography (MRA or CTA) in 58 AIS patients, MRI was inconclusive or not possible because of extensive movement artifacts or contraindications in 19% of the study patients. An additional 14% of critically ill patients could not undergo MRI due to insufficient ability to monitor vital parameters in the scanner. In contrast, ultrasound examination was possible and conclusive in 93% of the studied cases.[28]

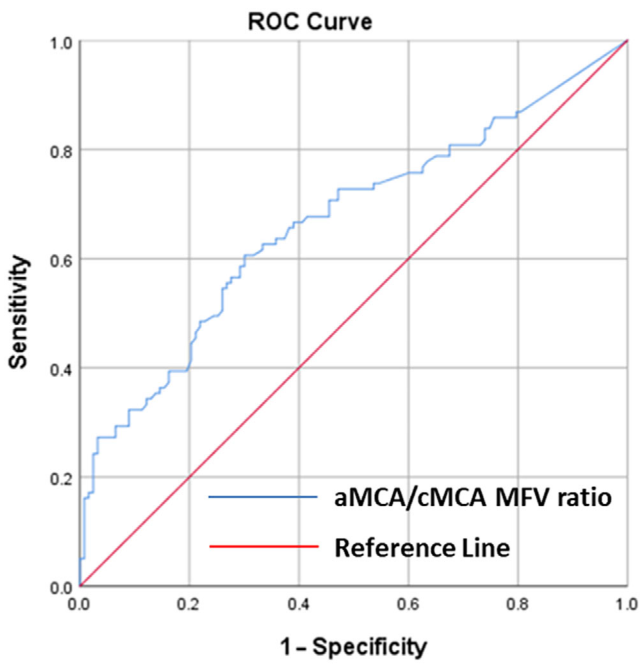

FIGURE 1 Receiver operating characteristic (ROC) analysis showing the area under the curve for affected middle cerebral artery (aMCA)/contralateral MCA (cMCA) mean flow velocity (MFV) ratio for differentiating patients without large vessel occlusion (M1 MCA, terminal internal carotid artery, tandem internal carotid artery/MCA) from those with large vessel occlusion.

Mounting evidence has shown the utility of TCD in predicting outcomes of MT.[29,30] Increased end-diastolic velocity is associated with early neurological improvement and also with the favorable functional outcomes at 3 months in LVO patients.[31] In a recent study, TCD monitoring was associated with reduced early neurological deterioration after MT (adjusted odds ratio: 0.267, 95% CI: 0.074-0.955; $P = .042$). Additionally, early neurological deterioration and 90-day mortality rates were lower in TCD-monitored blood pressure control patients compared to those without TCD-monitored blood pressure control (13.8% vs. 37.5%, $P = .036$ and 0% vs. 25.0%, $P = .012$).[32]

In our study, TCD might not be practical to apply in a busy emergency room where CTA is available and detects LVO with high accuracy, with primary focus being on reducing the door-to-groin time. However, it might be applicable in the drip-and-ship model, especially considering recent meta-analyses show limited accessibility to stroke thrombectomy care in developing countries.[33] Similarly, TCD might be used in the mobile stroke unit or by the paramedic to define LVO and better triage the patient. We believe that our developed criteria can be utilized in the future algorithm of robotic TCD[34] that is not operator dependent and can be easily used by paramedic or medical staff with no expertise in neurosonology.

Certain limitations of the current study need to be acknowledged. Although the study has the advantage of being multicenter with extensive training and credentialing of the involved sonographers, still TCD remains an operator-dependent technique. The lack of an adequate temporal bone window in some patients poses another challenge, potentially limiting the feasibility of TCD monitoring and impacting the representativeness of the sample. This limitation is more evident in the East Asian population, where 29%-34% of patients may exhibit inadequate Doppler signals due to insufficient acoustic temporal windows or window failure.[35,36] Additionally, research suggests that 28.8% of patients may lack or have inadequate temporal bone windows, with 23% experiencing complete bilateral bone window failure.[37] In contrast, the Caucasian population has demonstrated windows failure rate <10%.[38] The variation in windows failure rates might be attributed to differences in study population, methodologies, and definition of window failure. However, older age and female gender have been consistently associated with the absence or insufficiency of a temporal bone window across various factors examined.[37] The new development of robotic TCD is a promising therapeutic tool in that regard.

In conclusion, TCD is a valuable modality for evaluating arterial circulation in AIS patients, demonstrating significant potential as a screening tool for intravenous/endovascular lysis protocols. Further studies are needed to evaluate the use of TCD in prehospital settings.

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