Trans-cranial Doppler predicts early neurologic deterioration in anterior circulation ischemic stroke after successful endovascular treatment

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Abstract

Background: Early neurologic deterioration (END) may occur in patients with anterior circulation ischemic stroke (ACIS) after receiving endovascular treatment (EVT). Hemodynamic insufficiency, re-occlusion, and post-re-canalization hyper-perfusion are likely to play a critical role in END. We hypothesized that hemodynamic changes can predict END in patients with ACIS post-successful EVT using trans-cranial Doppler (TCD).

Methods: We utilized a prospectively maintained database of ACIS patients treated with EVT between September 2016 and June 2018 in the Xuanwu Hospital, Capital Medical University. TCD parameters including peak systolic velocity (PSV), bilateral mean flow velocity (MFV), and pulse index (PI) were determined via the middle cerebral arteries within 72 h post-EVT. A logistic regression model was applied to detect independent predictors for END.

Results: Totally, 112 EVT patients were included in this study and 80/112 patients experienced successful re-canalization with <50% residual stenosis, while 17/80 (21.3%) patients suffered END, for which vasogenic cerebral edema (11/17) was considered as a leading role and followed by symptomatic intra-cranial hemorrhage (sICH), and ischemia progression (2/17). For the 80 patients, the PSV (median: 127 cm/s vs. 116 cm/s, \( P = 0.039 \)) and the ratio of ipsilateral-MFV/contra-lateral-MFV (iMFV/cMFV) (median: 1.29 vs. 1.02, \( P = 0.036 \)) were independent predictors of END (odds ratio: 9.20, 95% confidence interval: 2.07–40.84, \( P = 0.004 \)) were independent predictors of END in a multivariate logistic regression model, with a sensitivity of 82.4% and 76.5% and a specificity of 38.2%, respectively, and had the positive predictive values of 29.0% and 38.2%, and negative predictive values of 90.0% and 91.3%, with an area under the receiver-operating characteristic curve of 0.57 and 0.71, respectively.

Conclusion: TCD examination of EVT patients may be used as a real-time tool to detect END predictors, such as the higher PI and iMFV/MBP, allowing for better post-thrombectomy management in ACIS patients.

Keywords: Cerebrovascular disease/acute ischemic stroke; Endovascular treatment; Thrombectomy; Diagnostic methods; Trans-cranial Doppler

Introduction

Endovascular treatment (EVT) is an effective method of treatment for patients with acute ischemic stroke caused by the proximal occlusion of a large vessel in the anterior circulation.[1] An emerging phenomenon, known as early neurologic deterioration (END), has been observed to develop within 72 h of receiving EVT.[2,3] This phenomenon has been reported to develop in 40.2% to 42.9% of patients[2,3] and has been associated with worse patient outcomes and a higher mortality at discharge.[2,3] It has been reported that the main clinical types of END are as follows: ischemia progression (IS), symptomatic intra-cranial hemorrhage (sICH), and vasogenic cerebral edema (VCE).[2,3] Perfusion abnormalities, hemodynamic insufficiency, re-occlusion, and post-re-canalization hyper-perfusion are likely to play critical roles in END.[4,5]
Transcranial Doppler (TCD) has been used to assess the state of hyper-perfusion after successful re-canalization and END, through hemodynamic changes in intravenous thrombolysis.\textsuperscript{[6-9]} A retrospective study on post-EVT TCD found that the increase in the mean flow velocity (MFV) index of the middle cerebral artery (MCA) after complete re-canalization was associated with an increased risk of intracranial hemorrhage within 24 h of therapy.\textsuperscript{[10]} However, the significance of this tool in predicting the risk of END after EVT has not been further elucidated. Therefore, we hypothesized that TCD examination would be a useful method of detecting vascular re-canalization and blood flow status, to predict END parameters in real-time, as well as post-EVT prognosis, thereby providing an indication of the need for early interventional strategies.

Methods

Ethical approval

The study was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University. Informed (No. [2017]057) consent was given by family members or patients who participated in this study.

Patient selection

This study prospectively included patients with large vessel occlusion (LVO) (terminal internal carotid artery, MCA M1 segment or M2 segment occlusion, or both) in anterior circulation (ACIS) who received EVT between September 2016 and June 2018. All patients received a computed tomography (CT) and/or CT perfusion (CTP) or a magnetic resonance imaging (MRI) examination prior to treatment to confirm the diagnosis. Exclusion criteria: bilateral temporal TCD windows not available; TCD evaluation was not performed before the onset of END; presence of severe systemic diseases such as heart failure and acute respiratory distress syndrome.

Clinical assessment

Clinical data including gender; age; medical history; vessels of occlusion and National Institute of Health stroke scale (NIHSS) scores at the following time points: immediately after EVT, within 24, 48, and 72 h post-EVT once sedation was withheld; fasting blood glucose at admission; admission and preoperative heart rate; systolic blood pressure/diastolic blood pressure/mean arterial blood pressure (MBP) at admission and at the time of TCD examination; time from onset to EVT; and time from onset to re-canalization were extracted from the medical records.

EVT included mechanical thrombectomy using stent retrievers or clot aspiration systems, stent implantation, balloon dilation, or intravenous thrombolysis combined with mechanical thrombectomy (bridging thrombolysis). All procedures were conducted using standard protocols.\textsuperscript{[11]} All procedures were conducted using standard protocols.\textsuperscript{[11]} TICI level 0-1 indicated no re-canalization; TICI level 2a indicated partial re-canalization; while TICI level 2b-3 indicated successful re-canalization. Operators of all EVT procedures had worked in neurologic intervention for a minimum of 10 years and had conducted more than 50 operations each year.

TCD sonography

The German DWL model DB-1395 portable bedside TCD-Box probe with a 2-MHz pulse was used (Compumedics Germany GmbH, Singen, Germany). Parameter settings were set as follows: sampling volume 12 to 15 mm and monitoring at a depth of 40 to 65 mm. TCD was performed at 24, 24 to 48, and 48 to 72 h after EVT. The main outcomes measured were thrombolysis in brain ischemia (TIBI) scores, peak systolic velocity (PSV), end-diastolic velocity (EDV), MFV of ipsilateral and contra-lateral MCA (MFV = [PSV + 2EDV]/3), ipsilateral pulse index ($iPI = iPSV - iEDV$/iMFV), MFV index of MCA (MFV of ipsilateral re-canalized MCA/iMFV of contra-lateral MCA, iMFV/cMFV), and the iMFV/MBP (TCD examination) index.

TIBI grading criteria used are mentioned in Burgin et al\textsuperscript{[12]} study: TIBI 0-5 grading. TCD re-canalization criteria: TIBI level 0-1 indicated complete occlusion, TIBI level 2-3 indicated partial re-canalization and TIBI level 4-5 indicated complete re-canalization, corresponding with TICI grade TICI 0-1, TICI 2a, and TICI 2b-3, respectively. The maximum PSV, EDV, MFV, PI, and TIBI of the ipsilateral and contra-lateral vessels were obtained through TCD monitoring before END and these values were included in the analysis. If END did not occur, the first TCD outcomes were used in the analysis.

Diagnosis and definition of END

Dual-energy CT scan was performed on all the patients within 24 h and if necessary, CT/MRI-diffusion weighted imaging (MRI-DWI)/MRI-apparent diffusion coefficient (MRI-ADC)/CTP was conducted within 72 h after EVT. END was defined as an NIHSS score increase of $\geq 1$ point in category 1a or $\geq 4$ points in total within 72 h in an unsedated patient.\textsuperscript{[13,14]} END classification criteria: (1) IS: MRI indicating enlargement of the original infarction area, or new infarction in other arterial regions (MRI-DWI) with a high signal and MRI-ADC showing a low signal, or continuous CT scan showing enlargement of the infarction area\textsuperscript{[15,16]}; (2) sICH: CT confirming intra-cerebral hemotoma or subarachnoid hemorrhage or lateral ventricular hemorrhage\textsuperscript{[17]}; and (3) VCE: MRI showing a high signal in the infarcted area both in the MRI-DWI and ADC.\textsuperscript{[6,16,18,19]}

Prognosis assessment

Follow-up was conducted 3 months after the procedure was performed through a telephone call with the patient or the patient’s relatives. The modified Rankin scale (mRS) score was used to indicate patient outcomes. An mRS score of 0 to 2 indicated a good outcome, while an mRS score of 3 to 6 indicated a poor outcome. The TCD operator, clinical therapist, and follow-up physician of each patient were three separate individuals.
Statistical analysis

Statistical analyses were performed using the Statistical Package of Social Sciences (SPSS version 19; International Business Machines Corporation, Armonk, NY, USA) program. The Chi-squared test or exact Fisher test was used to analyze differences among categorical variables between END and non-END patients. The normal distribution data between groups were analyzed using Student t test, with the results expressed as mean ± standard deviation. Non-normal distribution data were analyzed using the Mann-Whitney U test in terms of median values (range). Several continuous variables were applied to the receiver-operating characteristic (ROC) curve to obtain a cut-off value for END and the area under ROC curve (AUC) of each predictor through the MedCalc application. A P value of <0.05 was considered as statistically significant. Single factor variables with a P value of <0.1 were included in the multivariate logistic regression equation. Multivariate logistic regression and Hosmer-Lemeshow good-of-fit test were used to construct a predicted model.

Results

Patient characteristics and END

A total of 112 ACIS patients received EVT and TCD examination, of whom END occurred in 33 patients (29.5%). Thirty-two of 112 patients were not included in our final analysis due to incomplete re-canalization or re-occlusion (six patients) of the ipsilateral vessel (TICI 0–2a/TIBI 0–3, 20 patients, 17.9%), or an additional ≥50% vessel stenosis at the end of the procedure (TICI2b-3/ TIBI4, 12 patients, 10.7%) [Figure 1]. Among 80 patients who successfully underwent re-canalization with <50% residual stenosis, 17 patients (21.3%) experienced END. The distribution of clinical END subtypes was as follows: VCE, 11 patients (64.7%); sICH; four patients (23.5%); and IS, two patients (11.8%). Eleven of 17 occurrences of END presented within 24 h after EVT (VCE, eight patients, sICH, two patients, and IS, one patient), the other six occurrences (VCE, three patients, sICH, two patients, and IS, one patient) presented within 24 to 48 h after EVT. The baseline NIHSS scores in the END group (median: 14 [8–33]) had no difference from that in the non-END group (median: 14 [4–39]; Z = −0.821, P = 0.412), and there was a lower proportion of hyper-tension history in the END group compared with that in the non-END group (47.1% vs. 76.2%, χ² = 5.410, P = 0.020). Other clinical characteristics are listed in Table 1.

TCD parameters and END

We focused on the 80 patients who had experienced successful re-canalization with <50% residual stenosis to explore the ability of TCD evaluation to predict the

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**Figure 1**: Composition of all anterior circulation ischemic stroke patients received endovascular treatment. ACIS: Anterior circulation ischemic stroke; TCD: Trans-cranial Doppler; EVT: Endovascular treatment; END: Early neurologic deterioration; TICI: Thrombolysis in cerebral infarction; TIBI: Thrombolysis in brain ischemia.
occurrence of END. The median time of first TCD monitoring was 8.5 h (2.0–29.0 h) for the END group and 9.0 h (1.0–32.0 h) for the non-END group. We found that iPSV (median: 127 cm/s [100–262 cm/s] vs. 116 cm/s [70–250 cm/s], Z = −2.065, P = 0.039), the ratio of iMFV/cMFV (median: 1.29 [0.81–3.41] vs. 1.02 [0.40–3.53], Z = −2.094, P = 0.036), and iMFV/MBP (median: 0.97 [0.61–2.19] vs. 0.79 [0.41–1.96], Z = −2.659, P = 0.008) were higher in the END group than those of the non-END group [Table 2].

ROC analyses for critical iPSV, iMFV, iPI, ratio of iMFV/cMFV and iMFV/MBP values [Table 2], after adjusting for conventional END predictors such as hyper-tension history listed in Table 1, TCD parameters iPI ≥0.85 (odds ratio [OR]: 11.03, 95% confidence interval [CI]: 1.92–63.46, P = 0.007) and iMFV/MBP ≥0.84 (OR: 9.20, 95% CI: 2.07–40.84, P = 0.004) were found to be independent risk factors for END through the multivariate logistic regression model, with a sensitivity of 82.4% and 76.5% and a specificity of 42.9% and 66.7%, respectively, and the positive predictive value of 29.0% and 38.2%, and negative predictive value of 90.0% and 91.3% [Table 2], with an AUC of 0.57 and 0.71, respectively. And iMFV/cMFV ≥ 1.12 demonstrated a trend for independently predicting END (OR: 3.90, 95% CI: 0.91–16.73, P = 0.067). And the ROC of the predicted probability model had an AUC of 0.83 (95%CI: 0.73–0.94); and Hosmer-Lemeshow goodness-of-fit test, χ² = 1.52, P = 0.98), which demonstrated that the predicted regression model had good discrimination and calibration of END.

In the subgroup analysis, END_VCE (11 cases) and END_MCH (four cases) accounted for the majority of END patients (13/17). And the results are listed in Table 3. Compared with that of the non-END group, there were a higher iPSV (median: 131 [100–262] vs. 116 [70–250], Z = −2.283, P = 0.022), iMFV (median: 81 [55–174] vs. 74 [40–163], Z = −1.719, P = 0.086), ratio of iMFV/cMFV (median: 1.36 [0.81–3.41] vs. 1.02 [0.40–3.53], Z = −2.371, P = 0.018) and iMFV/MBP (median: 0.98 [0.61–2.19] vs. 0.79 [0.41–1.96], Z = −2.762, P = 0.003) in END_VCE and END_MCH group. And ROC analyses for critical iPSV, iMFV, ratio of iMFV/cMFV and iMFV/MBP values for END_VCE and END_MCH and after adjusting for hyper-tension history, iPSV ≥118 cm/s and iMFV ≥66 cm/s in logistic regression analysis, iMFV/MBP ≥0.85 (OR: 6.47, 95% CI: 1.43–29.31, P = 0.015) were found to be an independent risk factor for the END_VCE and END_MCH with a sensitivity and specificity of 80.0% and 67.7%, respectively, and had a positive predictive value 36.4% and negative predictive value 93.3%, respectively, with an AUC of 0.75. And iMFV/cMFV ≥ 1.12 showed a trend for independently predicting END_VCE (OR: 4.09, 95% CI: 0.89–18.94, P = 0.071).

Table 1: Demographics, medical history and clinical features in 80 patients received successful re-canalization with <50% stenosis.

| Items                                      | Total (n = 80) | END (n = 17) | Non-END (n = 63) | Statistical values | P      |
|--------------------------------------------|----------------|--------------|------------------|------------------|--------|
| Age (years)                                | 63.0 ± 12.0    | 63.5 ± 11.6  | 61.6 ± 12.3      | −0.572*          | 0.569  |
| Male                                       | 69 (86.3)      | 13 (76.5)    | 56 (88.9)        | –                | 0.234  |
| Hyper-tension                              | 56 (70.0)      | 8 (47.1)     | 48 (76.2)        | 5.410            | 0.020  |
| Diabetes mellitus                          | 16 (20.0)      | 3 (17.6)     | 13 (20.6)        | –                | 1.000  |
| Atrial fibrillation                        | 20 (29.4)      | 5 (29.4)     | 15 (23.8)        | –                | 0.753  |
| Dyslipidemia                               | 10 (12.5)      | 2 (11.8)     | 8 (12.7)         | –                | 1.000  |
| Previous cerebral vascular disease         | 19 (23.8)      | 4 (23.5)     | 15 (23.8)        | –                | 1.000  |
| Previous anti-platelet therapy             | 12 (15.0)      | 3 (17.6)     | 9 (14.3)         | –                | 0.711  |
| Time from onset to EVT (h)                 | 4.9 ± 1.8      | 5.1 ± 1.5    | 4.9 ± 1.9        | −0.567*          | 0.572  |
| Time from onset to re-canalization (h)     | 6.7 ± 2.0      | 6.8 ± 1.7    | 6.7 ± 2.0        | −0.124*          | 0.902  |
| Baseline NIHSS                             | 14 (4–39)      | 15 (8–33)    | 14 (4–39)        | −0.821*          | 0.412  |
| FBG (mmol/L)                               | 6.8 (3.2–17.7) | 7.6 (4.4–17) | 6.5 (3.2–17.7)   | −1.406*          | 0.160  |
| Blood pressure post-EVT (mmHg)             |                |              |                  |                  |        |
| SBP                                        | 133 ± 21       | 133 ± 22     | 133 ± 21         | −0.013*          | 0.989  |
| DBP                                        | 78 ± 15        | 78 ± 15      | 80 ± 15          | 0.495*           | 0.622  |
| MBP                                        | 98 ± 16        | 97 ± 17      | 98 ± 16          | 0.324*           | 0.746  |
| MDP (mmHg) during the TCD examination      | 91 ± 16        | 87 ± 14      | 92 ± 16          | 1.161*           | 0.249  |
| Bridging thrombolysis                      | 36 (44.4)      | 8 (47.1)     | 28 (44.4)        | 0.037            | 0.848  |
| General anesthesia                         | 19 (24.7)      | 5 (29.3)     | 14 (22.2)        | –                | 0.534  |
| Time from post-EVT to first TCD (h)        | 9.0 (1.0–32.0) | 8.5 (2.0–29.0)| 9.0 (1.0–32.0)  | 0.407            | 0.684  |
| Death in hospital                          | 2 (2.5)        | 2 (11.8)     | 0               | –                | 0.043  |
| mRS 3–6 at discharge                       | 40 (50.0)      | 17 (100.0)   | 23 (36.5)        | 21.587           | <0.001 |
| Death at 3 months                          | 3 (4.9)        | 3 (17.6)     | 0               | –                | 0.008  |
| Death at 3 months                          | 35 (43.8)      | 16 (94.1)    | 19 (30.2)        | 22.254           | <0.001 |

Data are shown as mean ± standard deviation, n (%), or median (range). Student t tests, Mann-Whitney U test; otherwise Pearson Chi-squared test or Fisher exact test. END: Early neurologic deterioration; SD: Standard deviation; EVT: Endovascular therapy; NIHSS: National Institutes of Health Stroke Scale; TCD: Trans-cranial Doppler; FBG: Fasting blood glucose; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure; mRS: Modified Rankin scale score; *: Not applicable.

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Table 2: Post-interventional trans-cranial Doppler findings in early neurologic deterioration and non-early neurologic deterioration patients and the cut-off values for predicting the early neurologic deterioration.

| TCD parameters | Total (n = 80) | END (n = 17) | Non-END (n = 63) | Statistical values | P | Cut-off value | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Statistical values |
|----------------|---------------|-------------|-----------------|-------------------|---|---------------|----------------|----------------|---------|---------|-------------------|
| iPSV (cm/s)    | 124 (70–226)  | 127 (100–262) | 116 (70–250)   | −2.063            | 0.039 | ≥118          | 88.2           | 52.4           | 33.3    | 94.3    | 6.526             | 0.011 |
| iEDV (cm/s)    | 52 (7–145)    | 53 (33–145)  | 49 (23–119)    | −1.083            | 0.280 | ≥44           | 76.5           | 41.3           | 26.0    | 86.7    | 1.798             | 0.180 |
| iMFV (cm/s)    | 75 (29–174)   | 79 (55–174)  | 74 (40–163)    | −1.488            | 0.140 | ≥66           | 88.2           | 41.3           | 28.8    | 91.3    | 5.123             | 0.024 |
| iPI            | 0.92          | 0.95         | 0.89           | −0.818            | 0.410 | ≥0.83         | 82.4           | 42.9           | 28.0    | 90.0    | 3.630             | 0.057 |
| iMFV/cMFV      | 1.10          | 1.29         | 1.02           | −2.094            | 0.036 | ≥1.12        | 70.6           | 58.7           | 31.6    | 88.1    | 2.958             | 0.085 |
| iPSV/iEDV/iMFV | 0.99          | 0.97         | 0.79           | −2.659            | 0.008 | ≥0.84        | 76.5           | 66.7           | 38.2    | 93.1    | 7.667             | 0.006 |

Data are shown as median (range) or otherwise noted. Mann-Whitney U test. ∗Obtained through the receiver-operating characteristic curve. †Pearson Chi-squared test. ‡Indicate independent predictors and a predicted trend for END, respectively, in logistic regression model. TCD: Trans-cranial Doppler; END: Early neurologic deterioration; PPV: Positive predictive value; NPV: Negative predictive value; iPSV/iEDV/iMFV: Peak systolic velocity/end diastolic velocity/mean flow velocity of ipsilateral middle cerebral artery; iPI: Pulse index of ipsilateral middle cerebral artery; cMFV: Flow velocity of contra-lateral middle cerebral artery; MBP: Mean blood pressure when TCD examination.

Mortality and poor outcome of END

The mortality among the 80 patients who had undergone complete re-canalization with less than 50% residual stenosis, was found to be higher in the END group (3/17) at 3 months after onset, compared with that of non-END patients (0/63, Fisher exact test, \( P = 0.008 \)). A significantly higher proportion of END patients were found to have a worse prognosis (mRS 3–6) (16/17) in contrast with non-END patients (19/63, \( \chi^2 = 22.23, P < 0.001 \)).

Discussion

This study utilized TCD to predict the END development in ACIS patients after successful EVT, and results demonstrated that ACIS patients may also endure END, even after successful EVT, and that ENDVCEandiCH were the most common clinical subtypes. Two TCD parameters, iPI ≥0.85 and iMFV/MBP ≥0.84, were found to be independent predictors of END, while iMFV/MBP ≥0.85 was probably identified as an independent predictor for ENDVCEandiCH.

EVT is known as one of the most effective methods of treatment for ACIS patients with LVO to date. Previous studies have documented sonographic abnormalities in TICI 2b-3 after successfully successful angiographical re-canalization of vessels in 36% of patients within 72 h of mechanical thrombectomy. [20] This was found to be an independent predictor of a poor outcome. [20] Our study, much like previous studies, [2,3,10] found that a significant proportion of EVT patients may develop END, despite complete vascularization with <50% residual stenosis. This phenomenon is thought to be linked to the expansion of the ischemic penumbra, irreversible ischemic injury as well as regional reperfusion injury. [31]

Our results revealed that a PI ≥0.85 and iMFV/MBP ≥0.84 are independent predictors of END. PI is indirectly correlated with intra-cranial pressure, [21,22] with a higher
PI indicating increased intra-cranial pressure. Reperfusion injury is thought to aggravate ischemia of the ischemic penumbra, trigger vasodilatation and promote hemorrhage, all of which may lead to the progression of the infarction. The development of VCE and sICH, culminating in raised intra-cranial pressures are hallmarks of END. While PI may indicate an increase in intra-cranial pressure, this index cannot be used to determine the subtype of END. The iMFV/MBP ratio may be a better reflection of cerebral perfusion, especially in the presence of an impaired cerebrovascular auto-regulatory system. We speculated that the iMFV/MBP ratio may reflect several aspects of cerebral perfusion. Dysfunction in cerebral blood flow auto-regulation is indicated by an unchanged MBP value, accompanied by an increased MFV value, or by an increase in both MFV and MBP values, with the increase in MFV being drastically greater than that of MBP. The END results in an increase in the amount of oxygen-derived free radicals produced within ischemic brain tissue, leading to micro-vascular and endothelial dysfunction during the restoration of perfusion pressure. This can further worsen blood-brain barrier integrity.[12,23] END risk increases in states of hyper-perfusion where cerebral blood flow exceeds the metabolic requirements of the brain tissue, thereby enhancing edema surrounding the ischemic tissues.[24] The use of this novel TCD parameter may decrease the impact of blood pressure changes on cerebral blood flow velocity detection, thereby improving the accuracy of END prediction. Further studies are necessary to further explore the clinical significance of TCD after EVT.

We found that a majority (15/17) of patients with successful re-canalization experienced END [VCE and/or sICH], both of which may indicate cerebral hyper-perfusion syndrome. TCD is commonly used to detect cerebral hyper-perfusion syndrome post-carotid artery revascularization. Nevertheless, reports of usage of TCD to monitor cerebral hyper-perfusion in ACIS patients who have undergone successful re-canalization are scarce.[24,26] Reactive hyperemia and hyper-perfusion of the brain tissue can appear rapidly after revascularization of an arterial occlusion.[10] There is a higher risk of hyper-perfusion under higher peak flow velocity states, especially in cases with no residual vessel stenosis post-EVT as observed through by TCD monitoring.[10,24] Cerebral hyper-perfusion may also be caused by even an about 25% to 30% increase in the PSV or MFV of the ipsilateral arteries.[10,11,24,25] ICH risk increased along with an increase in the iMFV/cMFV index (≥1.25).[11] Our studies validate these findings as we have demonstrated that both a PSV ≥118 cm/s and iMFV/cMFV ≥1.12 increased the risk of END [VCE and/or sICH]. The increase in cerebral blood flow velocity as detected through TCD is an indication of raised cerebral blood flow under no vessel stenosis states. Our findings suggest that if the MFV of the affected side is higher than that of the contra-lateral side and the increase in MFV is drastically greater than that of MBP (iMFV/MBP ≥0.84) after successful EVT, the risk of reperfusion injury may increase. This further confirms the value of TCD examination for END prediction. Other strengths of TCD while not assessed in our study, include microscopic embolic signals count (MES) with continuous recording post-EVT. Farina et al[26] assessed MES over 60 min immediately and 15 days later, and observed MES hits in 60% of post-EVT patients. Furthermore, inadequate collaterals, >50% ipsilateral carotid stenosis and incomplete re-canalization were all found to be associated with more MES using TCD after EVT, which was found to be associated with worse prognosis, mortality, and higher distal embolic load. Our results indicated that END increased the risk of poor outcome in ACIS patients after EVT at 3 months, which coincided with the previous studies.[2,3,13]

This study possesses several limitations. TCD is operator dependent and the lack of trained operators may result in delayed evaluation. It is for this reason that several patients were excluded from our study. Moreover, we found that the relationship detected between TCD parameters and END supports the hypothesis that hemodynamics/auto-regulation may contribute to the presumed pathologic mechanism of END. However, we are unable to speculate the exact time preceding END at which the parameter (such as PI) increased. Furthermore, our research findings are only representative of data obtained from a single center and may not be representative of the population. Therefore, large multicenter studies are required to verify our results.

TCD evaluation in patients with ACIS after EVT can be performed easily, is reproducible, and is readily available for investigation to be carried out within 72 h. Novel TCD parameters (PSV, PI, and iMFV/cMFV) may be combined with conventional parameters to produce better and more accurate indices (iMFV/MBP). In conclusion, this method is useful in providing for the quick, sensitive, and specific prediction of END in patients with different cerebral vessel re-canalization statuses, which may, in turn, reduce the overall incidence of this debilitating phenomenon.

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Conflicts of interest
None.

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