BACKGROUND: Intracranial hemorrhage (ICH) is the most feared complication of endovascular treatment (EVT) for acute ischemic stroke because of anterior circulation large vessel occlusion (LVO). The purpose of this study was to identify cerebral hemodynamic predictors of ICH and poor outcome in patients with successful recanalization.

METHODS: Serial transcranial color-coded sonography (TCCS) examinations assessed vessel status and cerebral hemodynamics of 226 (mean age, 69.8 ± 12.5 years; 130 men [57.5%]) consecutive patients with acute anterior circulation LVO at 48 hours and 1 week after EVT. Middle cerebral artery peak systolic velocity (PSV\textsubscript{MCA}) and PSV\textsubscript{MCA} ratio (recanalized PSV\textsubscript{MCA}/contralateral PSV\textsubscript{MCA}) were recorded.

RESULTS: Out of 180 successfully recanalized patients (79.6%), 28 patients (15.5%) had ICH. They more often had arterial hypertension (25/28 [89.3%] vs. 106/152 [69.7%], \(P = 0.04\)), a more severe stroke syndrome (18 [range, 10–23] vs. 16 [range, 5–26], \(P = 0.01\)), a worse clinical outcome (90-day modified Rankin Scale [mRS] score 3–5: 16/28 [57.1%] vs. 42/152 [27.6%], \(P = 0.004\)), and soon after EVT showed a significantly higher mean PSV\textsubscript{MCA} ratio (3.4 ± 0.1 vs. 2.4 ± 0.1, \(P < 0.0001\)) than patients without ICH, respectively. In multivariate analysis, early PSV\textsubscript{MCA} ratio was independently associated with postinterventional ICH (odds ratio, 13.379; 95% confidence interval, 2.466–50.372; \(P < 0.01\)). The patients with ICH (19/28 [67.9%]) who resumed normal PSV\textsubscript{MCA} values at 1 week after EVT had a better outcome (90-day mRS score 0–2: 8/19 [42.1%] vs. 0/9 [0%], respectively).

CONCLUSIONS: Early TCCS detection of a high PSV\textsubscript{MCA} ratio in successfully recanalized stroke patients indicates an increased risk of ICH, whereas cerebral hemodynamics normalization at 1 week in patients with postinterventional ICH predicts a relatively better 3-month outcome.

INTRODUCTION

despite the proven benefit of endovascular treatment (EVT) for patients with acute ischemic stroke with large vessel occlusion (LVO) of the anterior circulation,\(^1^\) intracranial hemorrhage (ICH) represents the most feared procedural complication because it is associated with poor clinical outcome.\(^2\) In fact, ICH can nullify the benefit of stroke treatments or even invert the benefit-risk ratio.\(^5\)

With the recent recommendations of EVT for acute ischemic stroke,\(^6,7\) the number of patients treated with this new strategy will increase significantly. Therefore, it is important to understand the mechanisms responsible for ICH occurrence and to ascertain possible predictors of cerebral bleeding. Prestroke anticoagulants, uncontrolled arterial hypertension, hyperglycemia, atrial fibrillation, severe stroke syndrome, poor collateral circulation, prolonged onset-to-recanalization time, and systemic thrombolysis

Key words
- Endovascular treatment
- Intracranial hemorrhage
- Transcranial ultrasound

Abbreviations and Acronyms
BBB: Blood–brain barrier
CT: Computed tomography
CTA: Computed tomography angiography
DSA: Digital subtraction angiography
EVT: Endovascular treatment
ICA: Internal carotid artery
ICH: Intracranial hemorrhage
LVO: Large vessel occlusion
MCA: Middle cerebral artery
MRI: Magnetic resonance imaging
mRS: Modified Rankin Scale
mTICI: Modified treatment in cerebral infarction
NIHSS: National Institutes of Health Stroke Scale
PSV: Peak systolic velocity
PSV\textsubscript{MCA}: Middle cerebral artery peak systolic velocity
TCCS: Transcranial color-coded sonography

From the \(^2\)Stroke Unit and Neuroradiology Laboratory, Department of Neuroscience and \(^2\)Neuroradiology Unit, University of Padua School of Medicine, Padua, Italy

To whom correspondence should be addressed: Claudio Baracchini, M.D.
[E-mail: claudiobaracchini@gmail.com]

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have been shown to be associated with ICH.\textsuperscript{8–10} However, their predictive power is still inadequate when routinely dealing with patients affected by acute ischemic stroke, suggesting that other factors might play a role in ICH occurrence.

Regarding mechanisms, mechanical lesion of the vessel wall,\textsuperscript{3} blood–brain barrier (BBB) disruption,\textsuperscript{11,12} or hemodynamic damage because of cerebral hyperperfusion\textsuperscript{12} have been all considered as causes of ICH, but evidence is still limited mostly because of the lack of dedicated studies. Among the diagnostic tools that can investigate postinterventional cerebral hemodynamic changes, transcranial color-coded sonography (TCCS) is a noninvasive technique that can be repeated bedside during the disease course. TCCS provides complementary information to periprocedural radiologic data and might help to gain more insight into the complex changes occurring not only after artery occlusion but also after its successful recanalization.

The purpose of this study was to identify hemodynamic predictors of ICH and hemodynamic clues of ICH pathogenesis with serial TCCS examinations in patients with successful recanalization after EVT.

MATERIALS AND METHODS

General Study Protocol

Patients consecutively admitted to the stroke unit of the University Hospital of Padua (Italy) between January 1, 2015, and June 30, 2018, for their first-ever acute ischemic stroke caused by anterior circulation LVO (defined as occlusion of the intracranial internal carotid artery [ICA] and/or middle cerebral artery [MCA] [M1 segment and/or proximal M2 segment]) were prospectively evaluated and treated according to standardized diagnostic and therapeutic procedures as recommended by the European Stroke Organisation.\textsuperscript{11} All patients undergoing EVT, with or without previous intravenous recombinant tissue plasminogen activator, were recruited.

Patients details were entered in a computerized database, including demographic characteristics, routine blood tests, and vascular risk factors such as arterial hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or current/past use of antihypertensive medication), diabetes mellitus (fasting serum glucose level >7.0 mmol/L [>126 mg/dL], nonfasting serum glucose level >11.1 mmol/L [>200 mg/dL], glycated hemoglobin level >48 mmol/mol, or the use of glucose-lowering drugs), hypercholesterolemia (total cholesterol level >6.2 mmol/ L [>240 mg/dL] or the use of lipid-lowering drugs), smoking (current or stopped within 5 years), cardiac disease (history of angina pectoris, myocardial infarction, coronary treatment [angioplasty/stenting or bypass surgery], any cardiac arrhythmia such as atrial fibrillation), peripheral arterial disease, or previous transient ischemic attack. Clinical and functional status were assessed with the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS), respectively, both on admission and at discharge. Territorial distribution was evaluated in all patients with magnetic resonance imaging (MRI) or repeat computed tomography (CT) scan and with the Oxfordshire Community Stroke Project classification system.\textsuperscript{14} In all patients, the extracranial and intracranial vessel status was assessed by TCCS,\textsuperscript{15} computed tomography angiography (CTA), magnetic resonance angiography, or digital subtraction angiography (DSA). Further diagnostic workup included standard blood tests, routine electrocardiography, transthoracic echocardiography, and 24-hour electrocardiography monitoring, plus coagulation studies and transesophageal echocardiography, if appropriate.

During hospitalization, the vital parameters of all enrolled patients were continuously monitored for the first 72 hours to detect and treat any alteration in heart rate, heart rhythm, respiratory dynamics, oxyhemoglobin saturation, arterial blood pressure, and body temperature. Specifically, arterial blood pressure was measured invasively by an arterial catheter or by a sphygmomanometer, and treatment was indicated according to current guidelines whenever the values were >180/105 mm Hg.\textsuperscript{13}

Finally, depending on stroke etiology, an antithrombotic (anti-platelet or anticoagulant) drug was administered to all patients, and modifiable risk factors (e.g., hypertension, hypercholesterolemia, hyperglycemia) were corrected according to current guidelines.\textsuperscript{16}

Endovascular Intervention Protocol

EVT was decided based on a direct cerebral CT scan (Alberta Stroke Program Early CT score >5), CTA (anterior circulation LVO), and clinical characteristics (NIHSS score >6 or evolution of stroke symptoms) and was performed within 6 hours of symptom onset, under conscious sedation or general anesthesia depending on clinical neurologic conditions by 3 experienced neuroradiologists (F. C., G. C., and J.-D. G.), who shared the same interventional protocol. The occluded target vessel was the first vessel to be studied with DSA when perfusion CT scan and CTA guaranteed adequate information on the collateral circulation; otherwise, contralateral carotid and vertebral arteries were studied before reaching the occluded site. Collaterals were graded according to the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology system,\textsuperscript{17} and patients were categorized accordingly into 3 groups: absent collateralization (grade 0), poor collateralization (grades 1 and 2), and good collateralization (grades 3 and 4).

An 8-F guiding catheter (Destination 6F [Terumo, Elkton, Maryland, USA] or Neuron Max 2.24 mm [Penumbra Inc., Alameda, California, USA]) was positioned in the cervical ICA and a distal aspiration catheter (5Max [Penumbra Inc.], Catalyst 6F [Stryker Corp., Freemont, California, USA], or SOFIA Plus 2.1 mm [MicroVention Inc., Tustin, California, USA]) was advanced to the occlusion site. A distal aspiration was then attempted; in case of failure, a stentriever thrombectomy with distal aspiration was performed. Successful recanalization was defined when a modified treatment in cerebral infarction (mTICI) 2b or 3 score\textsuperscript{18} was persistent on at least a 10-minute delayed angiogram.

A brain CT scan was obtained on a rotational angiographer XperCT (Philips, Best, The Netherlands) at the end of the procedure, and a control CT scan was repeated at 4–6 hours to exclude hemorrhagic complications. Then 24-hour control DSA was performed to verify vessel patency.

Ultrasound Insionation Protocol

All patients presenting with an acute ischemic stroke were evaluated by specialized stroke neurologists experienced in the use of cerebrovascular ultrasound (C. B., F. V., and F. F.), who performed a
fast-track, clinically oriented cervical and intracranial ultrasound assessment aimed at diagnosing an LVO amenable to intravenous thrombolysis and/or mechanical thrombectomy. All cervical vessels were examined using high-resolution color-coded duplex sonography scanners with a high-frequency (5–10 MHz) linear probe. Examination was started on the affected side, in transverse B-mode planes followed by color mode sweep from proximal to distal carotid segments. Carotid plaques were rapidly recorded, and stenoses were graded according to validated criteria. The intracranial arteries were examined with a low-frequency (1–3 MHz) phased-array TCCS probe following a validated protocol with reference values of normal intracranial blood flow velocity ranges. The system settings were adjusted for the analysis of middle high-velocity signals, with an appropriate pulse repetition frequency for arterial vessel detection. Patients were examined in a supine position, first through the transtemporal bone window of the affected side, and then rapidly through the transtemporal window of the contralateral side. The MCA and anterior cerebral artery were examined through the temporal bone window in the mesencephalic plane, whereas the carotid syphon and terminal ICA were examined through the temporal bone window, in the anterior coronal plane. After correctly identifying all these vessels, hemodynamic data were collected (blood flow direction, peak systolic velocity [PSV], and end-diastolic velocity). The maximum achievable flow velocity without angle correction was recorded, unless a straight vessel segment of at least 1.5–2.0 cm was visualized. The pulsatility index, which reflects downstream intracranial arterial resistance, was calculated for all patients according to the following formula: PSV = end-diastolic velocity/mean flow velocity. Cerebral artery stenosis was diagnosed qualitatively based on aliasing phenomenon visible on TCCS in a short segment of the vessel, increased flow velocities in the area of the stenosis, and flow disturbances upstream and downstream from the lesion. Previously validated criteria were used to detect >50% intracranial stenosis and occlusion. In case of suspected anterior circulation LVO or unfavorable temporal bone window in eligible patients for reperfusion treatment, 1 cc of SonoVue, an ultrasound contrast agent made up of microbubbles stabilized by phospholipids and containing sulfur hexafluoride, was administered as a bolus via a 23-gauge sterile infusion catheter placed into an arm vein. After injection of the ultrasound contrast agent, the catheter was flushed with 5 mL of saline to ensure that the entire preparation had been administered. All EVT-treated patients were reassessed by TCCS soon after the endovascular procedure with the patient in supine position, and depending on the patient’s clinical condition, directly in the angiographic suite or after transferring the patient to the stroke unit or neurointensive care. The treated artery was ionized using a low-frequency probe (1–3 mHz) following a validated protocol which included the examination of the contralateral homologous artery. A mean middle cerebral artery peak systolic velocity (PSV_{MCA}) ratio (PSV of recanalized MCA/PSV of contralateral MCA) was calculated to account for interindividual variability of absolute PSV_{MCA} values and exclude factors that might affect PSV_{MCA}, such as heart rate, arterial blood pressure, or hematocrit. Moreover, to avoid any influence on intracranial velocity measurements, patients with ≥70% stenosis or occlusion of the extracranial ICA, or ≥50% stenosis of the contralateral MCA were also excluded.

Clinical and Radiologic Follow-Up
All patients underwent brain MRj/CT scan 24 hours after admission, and brain MRj was performed just before hospital discharge. In case of a neurologic deterioration (NIHSS score increase of ≥2 points in one category or >4 points in total), immediate CT scan or MRJ was obtained to check for ICH or recurrence. ICH was classified as hemorrhagic transformation, parenchymal hemorrhage, intraventricular hemorrhage, subarachnoid hemorrhage, and subdural hemorrhage.

Clinical and functional status was assessed with the NIHSS and mRS, respectively, at discharge and at 3 months. Vessel patency and cerebral hemodynamics were evaluated by TCCS at 48 hours, 1 week, and 1 and 3 months; in case of restenosis, the diagnosis was confirmed by CTA/magnetic resonance angiography.

Statistical Analysis
Statistical analyses were performed with SPSS version 17.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Patient demographics and clinical characteristics were recorded as means ± SDs, medians and ranges, or percentages. Mean values were compared with Student t test or analysis of variance test as appropriate. Frequencies and categorical data were compared with χ² test (or Fisher exact test when necessary). Multivariate linear logistic regression analysis was used to see which statistically significant factors at univariate analysis could influence outcomes, calculating the odds ratios with 95% confidence intervals. Significance was assumed at P < 0.05.

Results
Out of 241 consecutive patients hospitalized with their first-ever anterior circulation acute ischemic stroke because of LVO during the study period, 15 (6.2%) were excluded because of a ≥50% contralateral MCA stenosis (n = 4), a severe (>70%) extracranial ICA stenosis (n = 5), and an extracranial ICA occlusion (n = 6).

Consequently, 226 patients (130 men [57.5%]; mean age, 69.8 ± 12.5 years) were recruited into the study: 184 (81.4%) with an MCA occlusion, 19 (8.4%) with an intracranial ICA occlusion, and 23 (10.2%) with a combined intracranial ICA and MCA occlusion. The median NIHSS score at admission was 18 (range, 4–27). Before EVT, 130 (57.5%) received intravenous thrombolyis. A successful recanalization (mTICI scores 2b and 3) was obtained in 180 patients (79.6%).

Postinterventional brain CT examinations performed at ≥18 ± 5.6 hours showed ICH in 28 patients (15.5%) with successful EVT: hemorrhagic transformations (14 class 1a [7.8%], 8 class 1b [4.4%], 2 class 1c [1.1%]) or intracerebral hemorrhages (2 class 2 [1.1%], 2 class 3a [1.1%]) (Table 1). No other type of ICH was observed. ICH was symptomatic in 6 patients (3.5%); 4 with hemorrhagic transformations and 2 with intracerebral hemorrhages. The latter 2 underwent intracranial pressure monitoring; one of these patients had a large temporal
hematoma which was evacuated, but he died a few days later. After correction for multiple comparisons and taking into account the small number of symptomatic ICHs, no significant differences were found between nonsymptomatic and symptomatic ICH, and between symptomatic ICH and no ICH.

Patients with ICH had more often arterial hypertension (25/28 [89.3%] vs. 106/152 [69.7%], \( P = 0.04 \)), more severe stroke symptoms on admission (median, 18 vs. 16; \( P = 0.01 \)), greater intrahospital mortality (4/28 [14.3%] vs. 2/152 [1.3%]; \( P < 0.01 \)), and a worse clinical outcome at 90 days (mRS score 3–5: 16/28 [57.1%] vs. 42/152 [27.6%]) than patients without ICH, respectively (Table 2).

At the first ultrasound evaluation, patients with postinterventional ICH showed a significantly higher mean PSV\textsubscript{MCA} ratio (3.4 ± 0.1 vs. 2.4 ± 0.1, respectively; \( P < 0.0001 \)) than patients without ICH. However, no significant difference was observed in the pulsatility index between these 2 groups (1.13 ± 0.33 vs. 1.11 ± 0.32, respectively). At the 48-hour TCCS, patients with postinterventional ICH had persistently higher mean PSV\textsubscript{MCA} ratios (2.3 ± 0.1 vs. 1.9 ± 0.1, respectively; \( P < 0.0001 \)) than patients without ICH.

On multivariate analysis, only a higher PSV\textsubscript{MCA} ratio soon after EVT (odds ratio, 13.379; 95% confidence interval, 2.466–50.372; \( P < 0.01 \)) remained independently associated with postinterventional ICH (Table 4). At 1 week after EVT, the 19 of 28 patients with ICH (67.9%) who resumed normal PSV\textsubscript{MCA} values had a better outcome at 90 days than those with abnormal PSV\textsubscript{MCA} values

<table>
<thead>
<tr>
<th>Type</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1a (HI1)</td>
<td>14 (7.8)</td>
</tr>
<tr>
<td>Class 1b (HI2)</td>
<td>8 (4.4)</td>
</tr>
<tr>
<td>Class 1c (PH1)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Class 2 (PH2)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Class 3a (PHr)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>Total (N = 180)</td>
<td>28 (15.5)*</td>
</tr>
</tbody>
</table>

*Six patients (3.3%) were symptomatic (2 class 1b, 2 class 1c, 2 class 2).

Table 2. Demographic and Clinical Characteristics of Patients with Ischemic Stroke with Large Vessel Occlusion of the Anterior Circulation After Successful Endovascular Treatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Patients (N = 180)</th>
<th>No ICH (n = 152)</th>
<th>Post-EVT ICH (n = 28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD (years)</td>
<td>69.3 ± 11.4</td>
<td>69.1 ± 11.3</td>
<td>70.4 ± 11.6</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>101 (56.1)</td>
<td>85 (55.9)</td>
<td>16 (57.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>131 (72.8)</td>
<td>106 (69.7)</td>
<td>25 (89.3)</td>
<td>0.0372</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>24 (13.3)</td>
<td>20 (13.1)</td>
<td>4 (14.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>32 (17.8)</td>
<td>27 (17.8)</td>
<td>5 (17.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>39 (21.7)</td>
<td>33 (21.7)</td>
<td>6 (21.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary syndromes</td>
<td>30 (16.7)</td>
<td>25 (16.4)</td>
<td>5 (17.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>53 (29.4)</td>
<td>44 (28.9)</td>
<td>9 (32.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Antiplalet therapy</td>
<td>84 (46.7)</td>
<td>71 (46.7)</td>
<td>13 (46.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Anticoagulant therapy</td>
<td>16 (8.9)</td>
<td>13 (8.5)</td>
<td>3 (10.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Median basal NIHSS score (range)</td>
<td>16 (5–26)</td>
<td>16 (5–26)</td>
<td>18 (10–23)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mean time to revascularization ± SD (minutes)</td>
<td>220 ± 49</td>
<td>218 ± 48</td>
<td>228 ± 51</td>
<td>NS</td>
</tr>
<tr>
<td>EVT for ICA occlusion</td>
<td>16 (8.9)</td>
<td>13 (8.6)</td>
<td>3 (10.7)</td>
<td>NS</td>
</tr>
<tr>
<td>EVT for MCA occlusion</td>
<td>147 (81.7)</td>
<td>124 (81.6)</td>
<td>23 (82.1)</td>
<td>NS</td>
</tr>
<tr>
<td>EVT for ICA + MCA occlusion</td>
<td>17 (9.4)</td>
<td>14 (9.2)</td>
<td>3 (10.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Bridging thrombolysis</td>
<td>118 (65.6)</td>
<td>99 (65.1)</td>
<td>19 (67.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Intrahospital mortality</td>
<td>6 (3.3)</td>
<td>2 (1.3)</td>
<td>4 (14.3)</td>
<td>0.0058</td>
</tr>
<tr>
<td>mRS score 0–2 at 90 days</td>
<td>105 (58.3)</td>
<td>97 (63.8)</td>
<td>8 (28.6)</td>
<td>0.0007</td>
</tr>
<tr>
<td>mRS score 3–5 at 90 days</td>
<td>58 (32.2)</td>
<td>42 (27.6)</td>
<td>16 (57.1)</td>
<td>0.0037</td>
</tr>
<tr>
<td>mRS score 6 at 90 days</td>
<td>17 (9.4)</td>
<td>13 (8.6)</td>
<td>4 (14.3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are number of patients (%) or as otherwise indicated.
ICH, intracranial hemorrhage; EVT, endovascular treatment; NS, not significant; NIHSS, National Institutes of Health Stroke Scale; ICA, internal carotid artery; MCA, middle cerebral artery; mRS, modified Rankin Scale.
(mRS score 0—2, 8 vs. 0 [42.1% vs. 0%]; mRS score 3, 8 vs. 0; mRS score 4, 3 vs. 2; mRS score 5, 0 vs. 3; mRS score 6, 0 vs. 4) (Figure 1).

**DISCUSSION**

According to our study results, a high PSV<sub>MCA</sub> ratio detected by bedside TCCS soon after EVT indicates an increased risk of ICH and a poor outcome at 3 months in patients with ischemic stroke successfully treated for LVO of the anterior circulation, and cerebral hemodynamics normalization at 1 week after successful EVT predicts a relatively better prognosis at 90 days.

Different studies have shown that poststroke outcome is strictly dependent on the success of the endovascular procedure with better prognosis being observed in optimal (mTICI score 3) or suboptimal (mTICI score 2b) recanalized patients compared with those with partial (mTICI score 2a) or no recanalization (mTICI score 0—1).25,26 However, a significant number of patients have a poor outcome, despite angiographically successful recanalization, especially when hemorrhage occurs in the reperfused ischemic brain tissue. In particular, ICH is a common complication after EVT, having been reported in more than 40% of patients in clinical trials performed in experienced comprehensive stroke centers.27 This evidence highlights that factors other than simple artery recanalization might play a role in clinical recovery of patients with acute stroke, prompting further investigations on hemodynamic changes after EVT and possible hemodynamic predictors of ICH and clinical outcome.

In our study, about 1 in 7 patients with successful EVT (mTICI score 2b—3) developed an ICH; specifically, symptomatic ICH occurred in 3.3% of cases similarly to what is reported in randomized controlled trials (4.4%).2 ICH exacerbated the functional outcome at 90 days after EVT, regardless of being symptomatic or not.

In line with previous studies, we identified arterial hypertension and severe stroke syndrome as factors associated with postprocedural ICH.8,53 Consequently, EVT should be performed with special care under strict blood pressure control especially in critical patients. Other factors, such as hyperglycemia, atrial fibrillation, antithrombotic therapy, and systemic thrombolysis, although reported in previous studies,8,10,29,30 were not related to ICH in our analysis.

The detailed mechanism of ICH remains elusive. Possible mechanisms of ICH are a mechanical lesion of the vessel wall, BBB disruption, and/or hemodynamic damage because of cerebral hyperperfusion. A mechanical lesion of the recanalized vessel can occur during EVT, especially when multiple passes with the stent retriever device are made.5 In this situation, a subarachnoid hemorrhage is usually the end result, but we did not observe this type of intracranial bleeding in our study. This might be due not only to the experience and skillfulness of the neurointerventionalists but also to the use of new generation stent retriever devices that determine less traction of the vascular tree, resulting in less trauma than old generation devices. BBB disruption has been suggested as an underlying mechanism for postinterventional ICH17 causing increased mortality.23 The severity of BBB disruption was shown to be associated with worsening ICH because marked BBB compromise exhibited parenchymal hematoma.24 BBB disruption might result from rapid reperfusion after EVT in the setting of cerebral hyperperfusion syndrome causing vasogenic edema and ICH through microvascular and endothelial damage.22 Interestingly, in our study, we found that patients who experienced an ICH after recanalization had a higher PSV<sub>MCA</sub> ratio soon after EVT.

### Table 3. Postinterventional Ultrasound Findings in Patients with Ischemic Stroke Successfully Treated for Anterior Circulation Large Vessel Occlusion

<table>
<thead>
<tr>
<th></th>
<th>Total Patients (N = 180)</th>
<th>No ICH (n = 152)</th>
<th>ICH (n = 28)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean PSV ratio soon after EVT</td>
<td>2.6 ± 0.1</td>
<td>2.4 ± 0.1</td>
<td>3.4 ± 0.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PI values after EVT</td>
<td>1.11 ± 0.32</td>
<td>1.11 ± 0.32</td>
<td>1.13 ± 0.33</td>
<td>NS</td>
</tr>
<tr>
<td>Mean PSV ratio 48 hours after EVT</td>
<td>1.9 ± 0.1</td>
<td>1.9 ± 0.1</td>
<td>2.3 ± 0.1</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean ± SD or as otherwise indicated.

ICH, intracranial hemorrhage; PSV, peak systolic velocity; EVT, endovascular treatment; PI, pulsatility index; NS, not significant.

### Table 4. Association Between Postinterventional Intracranial Hemorrhage and Clinical/Ultrasound Parameters

<table>
<thead>
<tr>
<th></th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>3.616 (1.039—12.579)</td>
<td>2.801 (0.967—5.821) NS</td>
</tr>
<tr>
<td>NIHSS score at admission</td>
<td>5.022 (1.995—14.683)</td>
<td>2.099 (0.811—6.434) NS</td>
</tr>
<tr>
<td>Higher mean PSV ratio soon after EVT</td>
<td>10.864 (2.308—3.433)</td>
<td>13.379 (2.466—0.372) &lt;0.01</td>
</tr>
</tbody>
</table>

Values are odds ratio (95% confidence interval). P value.

NS, not significant; NIHSS, National Institutes of Health Stroke Scale; PSV, peak systolic velocity; EVT, endovascular treatment.
than those who did not have an intracranial bleeding. These results, consistent with a previous transcranial Doppler study, suggest that hyperperfusion after mechanical recanalization of LVO might have deleterious effects on several elements of the BBB in the ischemic tissue because of reperfusion mediated injury. Moreover, the persistence of abnormal hemodynamics at 48-hour evaluation of post-EVT patients with ICH might represent both a more severe impairment of cerebrovascular reactivity as a predisposing factor for ICH, or alternatively an abolished arteriolar wall tone within the ischemic brain tissue after hemorrhagic transformation.

Finally, even among post-EVT patients with ICH, bedside TCCS provided valuable prognostic clues because hemodynamics normalization at 1 week predicted a relatively better outcome at 3 months.

Altogether, our findings may modify the critical care management of patients with stroke right after recanalization. In particular, those with unfavorable baseline PSV\textsubscript{MCA} ratios should be followed more strictly in a stroke unit or neurointensive care unit, with special care for blood pressure control until normalization of cerebral hemodynamics. Early brain CT scan/MRI is also important in these patients for detecting ICH and tailoring antithrombotic therapy. These results should prompt a more extensive application of ultrasound because it could definitely improve the efficacy of treatment, potentially leading to better outcomes.

Although this study has the advantage of a consolidated diagnostic and interventional protocol performed in a large university hospital, it also has some limitations regarding sample size, with this being a single-center study. For this reason, we strongly promote a collaborative effort among international stroke centers.

**CONCLUSIONS**

This study has shown that a high PSV\textsubscript{MCA} ratio detected by bedside TCCS soon after EVT indicates an increased risk of ICH in patients with ischemic stroke successfully treated for LVO of the anterior circulation, and hemodynamics normalization at 1 week after successful EVT predicts a relatively better outcome at 3 months. These findings might help tailor blood pressure management right after recanalization and indicate when to safely start antithrombotic therapy.

**REFERENCES**


