Ischemic stroke

Endovascular therapy in the distal neurovascular territory: results of a large prospective registry

Raul G Nogueira,1 Mahmoud H Mohammaden ,1 Diogo C Haussen,1 Ronald F Budzik,2 Rishi Gupta,3 Antonin Krajina,4 Joey D English,7 Ali R Malek,6 Amrou Sarraj ,5 Ana Paula Narata,8 Muhammad Asif Taqi,9 Michael R Frankel,1 Timothy Ryan Miller,10 Thomas Grobelny,11 Blaise W Baxter,12 Bruno Mario Bartolini,13 Paul Jenkins,14 Laurent Estrade,15 David Liebeskind,16 Erol Veznedaroglu,17 on behalf of the Trevo Registry Investigators

ABSTRACT

Background There is a paucity of data regarding mechanical thrombectomy (MT) in distal arterial occlusions (DAO). We aim to evaluate the safety and efficacy of MT in patients with DAO and compare their outcomes with proximal arterial occlusion (PAO) strokes.

Methods The Trevo Registry was a prospective open-label MT registry including 2008 patients from 76 sites across 12 countries. Patients were categorized into: PAO: intracranial ICA, and MCA–M1; and DAO: MCA–M2, MCA–M3, ACA, and PCA. Baseline and outcome variables were compared across the PAO vs DAO patients with pre-morbid mRS 0–2.

Results Among 407 DAOs including 350 (86.0%) M2, 25 (6.1%) M3, 10 (2.5%) ACA, and 22 (5.4%) PCA occlusions, there were 376 DAO with pre-morbid mRS 0–2 which were compared with 1268 PAO patients. The median baseline NIHSS score was lower in DAO (13 [8–18] vs 16 [12–20], P<0.001). There were no differences in terms of age, sex, IV-TPA use, co-morbidities, or time to treatment across DAO vs PAO. The rates of post-procedure reperfusion, symptomatic intracranial hemorrhage (sICH), and 90-mortality were comparable between both groups. DAO showed significantly higher rates of 90-day mRS 0–2 (68.3% vs 56.5%, P<0.001). After adjustment for potential confounders, the level of arterial occlusion was not associated with the chances of excellent outcome (DAO for 90-day mRS 0–1: OR; 1.18, 95% CI [0.90 to 1.54], P=0.225), successful reperfusion or sICH. However, DAO patients were more likely to be functionally independent (mRS 0–2: OR; 1.45, 95% CI [1.09 to 1.92], P=0.01) or dead (OR; 1.54, 95% CI [1.06 to 2.27], P=0.02) at 90 days.

Conclusion Endovascular therapy in DAO appears to result in a comparable safety and technical success profile as in PAO. The potential benefits of DAO thrombectomy should be investigated in future randomized trials.

INTRODUCTION

There is a paucity of data regarding mechanical thrombectomy (MT) in patients presenting with acute ischemic strokes (AIS) due to distal arterial occlusions (DAO). Even though over one-third of patients presenting within 24 hours of stroke symptoms have a DAO, very few DAO are currently treated with MT.1 2 Thrombectomy in the distal vascular territory is theoretically associated with higher risks since more distal vessels have smaller calibers, thinner walls, and more tortuous courses which make them more prone to endovascular complications including perforation, dissection, and vasospasm. Moreover, as distal vessels inherently supply smaller volumes of the brain, their reperfusion is presumably associated with a lower range of benefit given the more restricted areas of tissue at risk. Therefore, DAO patients are not typically considered ideal candidates for endovascular reperfusion. Nonetheless, DAO thrombectomy may be a reasonable option, in particular, for patients with DAO involving areas of high eloquence and resulting in disabling deficits. Indeed, the current AHA Guidelines state that middle cerebral artery (MCA) M2, MCA–M3, anterior cerebral artery (ACA), and posterior cerebral artery (PCA) thrombectomy may be reasonable for carefully selected patients with AIS within 6 hours of symptom onset (level IIb).3

DAOs are highly underrepresented in randomized clinical trials (RCTs). For example, in the Interventional Management of Stroke III (IMS-III) trial, among subjects who underwent endovascular treatment only 8% had M3/M4 occlusions.4 Similarly, in the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) trial, only three subjects had ACA and none had MCA–M3 occlusions.5 Despite the growing evidence supporting the broader use of MT including the recent trials expanding its indications up to 24 hours from time last seen well and a meta-analysis suggesting the potential for a retained benefit even in the setting of large infarct sizes,6–8 there is essentially no evidence to either support or refute endovascular treatment of DAOs.

Herein, we aim to evaluate the safety and efficacy of MT in a large prospective cohort of patients presenting with AIS in the setting of DAO and to compare their outcomes with those seen in proximal arterial occlusion (PAO) strokes.
METHODS

Trevo Retriever Registry

The Trevo Retriever Registry (ClinicalTrials.gov identifier: NCT02040259) was an international, multicenter, prospective, open-label, registry of patients who underwent MT with the Trevo stent-retriever (Stryker, Fremont, CA) as first-line therapy. The registry recruited a total of 2008 patients at 76 sites across 12 countries between November 11, 2013, and May 1, 2017. Pretreatment imaging and other entry criteria were based on local institutional protocols. The protocol was amended on March 26, 2015, to include an imaging core laboratory that was then used for central adjudication in 1599 of the 2008 (79.6%) patients of the site of vessel occlusion, pre- and posttreatment modified Thrombolysis in Cerebral Infarction (mTICI), and post-treatment imaging for hemorrhagic complications. The modified Rankin scale (mRS) assessment at 90 days was obtained in person or by telephone by a certified examiner at each site. All subjects in whom the Trevo retriever was deployed were computed in the intention-to-treat analysis. The study was funded by Stryker Neurovascular (Fremont, CA). A steering committee including academic investigators and representatives of the sponsor designed the study and led its execution. The registry was approved by the institutional review board at each site. Written informed consent was required from all enrolled patients or their designee. Additional details about the Trevo Retriever Registry methodology have been previously published elsewhere.9

Patient population and study analysis

The current analysis categorized Trevo Retriever Registry patients into PAO: intracranial internal carotid artery (ICA) and MCA–M1 and DAO: MCA–M2, MCA–M3, ACA, and PCA according to their primary site of occlusion (eg, patients initially presenting with PAO who subsequently had intra-procedural clot migration or embolization into the distal territory were still considered PAO). Patients’ demographic data, cardiovascular risk factors such as hypertension, atrial fibrillation and diabetes mellitus, baseline National Institute of Health Stroke Scale (NIHSS) score, pre-morbid mRS, administration of intravenous tissue plasminogen activator (IV-tPA), time-from-last-seen-well (TLSW), and arterial puncture were analyzed. Descriptive analysis was provided for the overall DAO population. Baseline and outcome variables were compared across the PAO vs DAO patients with pre-morbid mRS 0–2.

Definitions for site of arterial occlusion

The MCA–M1 segment was defined as the proximal stem of the MCA including the lenticulostriate arteries and the anterior temporal artery branch. The MCA–M2 segment begins with first non-penetrator branching occurring distally to the origin of the anterior temporal artery. The anterior temporal artery is the branch of the M1 that can be identified by the confinement of its course to the anterior temporal lobe. If a branch artery exits the Sylvian fissure and supplies territory beyond the anterior temporal lobe (including the posterior temporal or inferior parietal areas), it was considered a MCA–M2 segment as opposed to an anterior temporal artery branch.10 The MCA–M2 segment continues through the entire vertical course of branches up the Sylvian fissure. The MCA–M3 vessels start as the MCA branches exit from the Sylvian fissure and turn to run horizontally in the opercular regions.

Procedural characteristics

According to the inclusion criteria of the Trevo Retriever Registry, all included patients underwent MT with the Trevo stent-retriever as first-line therapy. Patients were treated either under general anesthesia or under conscious sedation according to the operator’s preference.

Outcome and safety measures

Outcome variables included the rates of successful reperfusion defined as a grade 2b or more on the mTICI scale,11 rapid neurological improvements (RNI) defined as a reduction of ≥10 on the NIHSS score or NIHSS score zero to 1, 24 hours after MT, favorable outcome (90-day mRS 0–1), and functional independence (90-day mRS 0–2). Safety measures included the rates of symptomatic intracranial hemorrhage (sICH) defined as per the ECASS 3 Trial definition (eg, any apparently extravascular blood in the brain or within the cranium associated with deterioration in NIHSS score of ≥4 points, or that led to death and that was identified as the predominant cause of the neurologic deterioration),12 vessel perforation, emboli to a new territory, and 90-day mortality.

The first author wrote the first draft of the manuscript with the subsequent input of all co-authors. Stryker Neurovascular supplied the data and analytic support, but the company was not involved in the study design or in the preparation of the manuscript. This study is reported in accordance with the STrengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

Statistical analysis

Continuous variables were reported as mean±SD or median (IQR) after normality testing with the Shapiro–Wilks test and were compared using the Mann–Whitney U test or t-test as appropriate. Categorical variables were reported as frequencies and percentages. Comparisons of categorical variables were made with Pearson X² or Fisher’s exact tests as appropriate. Univariable analysis was performed to compare the baseline and outcome variables in patients with DAO vs those with PAO. Multivariable regression analyses were performed to evaluate the association of different variables with outcomes (90-day mRS 0–1, 90-day mRS 0–2, 90-day mortality, sICH within 48 hours post-procedure, and final mTICI 2b–3) in both the overall population and patients with DAO only. Variables with P<0.20 in the univariate analysis and those previously described to be associated with each outcome, were entered into multiple logistic regression equations with backward variable selection. All models retained the binary covariate representing PAO vs DOA. The final models included any variable with P≤0.10. Statistical analyses were performed with SAS software (version 9.4; SAS Institute Inc, Cary, NC).

RESULTS

Overall, there were 407 DAOs including 350 (86.0%) M2, 25 (6.1%) M3, 10 (2.5%) ACA, and 22 (5.4%) PCA occlusions vs 1392 PAOs including 294 (21.1%) intracranial ICA and 1098 (78.9%) M1 occlusions. Baseline characteristics, and procedural and clinical outcomes for the different subsets of the overall DAO population can be found in table 1.

A total of 376 DAO (M2: 324, 86.2%; M3: 23, 6.1%; ACA, 8, 2.1%; PCA, 21, 5.6%) and 1268 PAO (ICA: 332, 23.1%; M1: 1107, 76.9%) patients had pre-morbid mRS 0–2. Among these, DAOs had lower median baseline NIHSS score (13 [8–18] vs 16 [12–20], P<0.001) compared with PAO patients. There were no differences in terms of age (68.3 vs 67.9 years, P=0.747), sex (female, 51.1% vs 52.9%, P=0.527), IV-tPA use (51.1% vs 56.3%, P=0.724), major stroke-related risk factors, and pre-morbid mRS 0–1. Median TLSW to arterial puncture was comparable between DAO and PAO (4.2 vs 4.2 hours, P=0.853). There

Ischemic stroke

Ischemic stroke was a significantly higher use of general anesthesia in patients with DAO (46.6% vs 39.1%, P = 0.017) and lower median number of device passes (1 [1–2] vs 1 [1–3], P = 0.002) as compared with those with PAO (table 2).

The rates of successful reperfusion (mTICI 2b–3) and full reperfusion (mTICI 3) were comparable between DAO and PAO (92.6% vs 92.7%, P = 0.90% and 55.1% vs 56.2%, P = 0.706, respectively).

Table 1  Baseline characteristics, procedural and clinical outcomes for the overall DAO population

<table>
<thead>
<tr>
<th>Baseline characteristics % (n)</th>
<th>MCA–M2 (n=350)</th>
<th>MCA–M3 (n=25)</th>
<th>ACA (n=10)</th>
<th>PCA (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD</td>
<td>69.1±13.5</td>
<td>66.7±13.9</td>
<td>65.9±12.8</td>
<td>66.2±14.3</td>
</tr>
<tr>
<td>Female</td>
<td>53.7 (188)</td>
<td>48 (12)</td>
<td>30 (3)</td>
<td>45.5 (10)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>75.4 (264)</td>
<td>72 (18)</td>
<td>88.9 (8/9)</td>
<td>73.3 (17)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>35.5 (124/349)</td>
<td>32 (8)</td>
<td>33.3 (3/9)</td>
<td>22.7 (5)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>23.5 (82/349)</td>
<td>32 (8)</td>
<td>22.2 (2/9)</td>
<td>31.8 (7)</td>
</tr>
<tr>
<td>Previous ICAD</td>
<td>0.0 (0/349)</td>
<td>0.0 (0)</td>
<td>0.0 (0/9)</td>
<td>0.0 (0)</td>
</tr>
<tr>
<td>Baseline NIHSS score, median (IQR)</td>
<td>13(8–18)</td>
<td>11.5(7–15)</td>
<td>17.5(12–20)</td>
<td>14.0(8–16)</td>
</tr>
<tr>
<td>Pre-morbid mRS 0–1</td>
<td>86.7 (300/346)</td>
<td>95.8 (23/24)</td>
<td>80 (8)</td>
<td>90.5 (19/21)</td>
</tr>
<tr>
<td>IV-tPA use</td>
<td>52.9 (185)</td>
<td>48 (12)</td>
<td>66.7 (6/9)</td>
<td>50 (11)</td>
</tr>
<tr>
<td>TLSW to puncture (hours), median (IQR)</td>
<td>4.1 (2.8–6.4)</td>
<td>5.2 (2.9–7.8)</td>
<td>2.6 (2.2–5.0)</td>
<td>4.7 (3.5–10.7)</td>
</tr>
<tr>
<td>Time from puncture to device deployment (minutes), median (IQR)</td>
<td>24.0 (17.0–36.0)</td>
<td>27.0 (16.5–40.0)</td>
<td>26.0 (14.0–35.0)</td>
<td>32.0 (21.0–40.0)</td>
</tr>
<tr>
<td>Total procedural duration (minutes), mean±SD</td>
<td>54.3±30.8</td>
<td>63.9±27.4</td>
<td>49.3±30.3</td>
<td>50.0 (11/22)</td>
</tr>
<tr>
<td>Trevo 3×20 mm</td>
<td>41.7% (144/345)</td>
<td>80.0% (20/25)</td>
<td>60.0% (6/9)</td>
<td>31.8% (7/22)</td>
</tr>
<tr>
<td>Trevo 4×20 mm</td>
<td>43.2% (149/345)</td>
<td>16.0% (4/25)</td>
<td>40.0% (4/10)</td>
<td>31.8% (7/22)</td>
</tr>
<tr>
<td>Trevo 4×30 mm</td>
<td>11.0% (38/345)</td>
<td>4.0% (1/25)</td>
<td>0.0% (0/10)</td>
<td>31.8% (7/22)</td>
</tr>
<tr>
<td>Trevo 6×25 mm</td>
<td>4.1% (14/345)</td>
<td>0.0% (0/25)</td>
<td>0.0% (0/10)</td>
<td>4.6% (1/22)</td>
</tr>
<tr>
<td>Intermediate catheter</td>
<td>47.0% (164/349)</td>
<td>40.0% (10/25)</td>
<td>70.0% (7/10)</td>
<td>59.1% (13/22)</td>
</tr>
<tr>
<td>Intra-arterial lytics</td>
<td>52.9% (185/350)</td>
<td>48.0% (12/25)</td>
<td>66.7% (6/9)</td>
<td>50.0% (11/22)</td>
</tr>
<tr>
<td>Number of device passes, median (IQR)</td>
<td>1(1–2)</td>
<td>2(1–2)</td>
<td>1(1–2)</td>
<td>1(1–2)</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>46.6% (163/350)</td>
<td>36.0% (9/25)</td>
<td>30 (3)</td>
<td>54.6 (12)</td>
</tr>
<tr>
<td>mTICI 2b–3 (Overall)</td>
<td>92.3% (323/350)</td>
<td>92.0% (23/25)</td>
<td>100% (10)</td>
<td>100% (22)</td>
</tr>
<tr>
<td>mTICI 2b–3 (IV tPA use)</td>
<td>93.0% (172/185)</td>
<td>83.3% (10/12)</td>
<td>100% (6/6)</td>
<td>100% (11/11)</td>
</tr>
<tr>
<td>mTICI 2b–3 (no IV tPA use)</td>
<td>91.5% (151/165)</td>
<td>100% (13/13)</td>
<td>100% (3/3)</td>
<td>100% (11/11)</td>
</tr>
<tr>
<td>mTICI 3 (overall)</td>
<td>53.7% (188)</td>
<td>60% (15/25)</td>
<td>80.0% (8)</td>
<td>63.6% (14)</td>
</tr>
<tr>
<td>mTICI 3 (IV tPA use)</td>
<td>52.4% (97/185)</td>
<td>41.7% (5/12)</td>
<td>66.7% (4/6)</td>
<td>63.6% (7/11)</td>
</tr>
<tr>
<td>mTICI 3 (No IV tPA use)</td>
<td>55.2% (91/165)</td>
<td>76.9% (10/13)</td>
<td>100.0% (3/3)</td>
<td>63.6% (7/11)</td>
</tr>
<tr>
<td>RNI</td>
<td>44.8% (151/337)</td>
<td>58.3 (14/24)</td>
<td>50 (5)</td>
<td>52.4 (11/21)</td>
</tr>
<tr>
<td>sICH (overall)</td>
<td>1.7% (6/350)</td>
<td>4% (1/25)</td>
<td>0.0% (0)</td>
<td>0.0% (0)</td>
</tr>
<tr>
<td>sICH (IV tPA use)</td>
<td>0.5% (1/185)</td>
<td>8.3% (1/12)</td>
<td>0.0% (0/6)</td>
<td>0.0% (0/11)</td>
</tr>
<tr>
<td>sICH (no IV tPA use)</td>
<td>3.0% (5/165)</td>
<td>0.0% (0/13)</td>
<td>0.0% (0/3)</td>
<td>0.0% (0/11)</td>
</tr>
<tr>
<td>Vessel perforation</td>
<td>0.4% (1/247)</td>
<td>5% (1/20)</td>
<td>0.0% (0)</td>
<td>0.0% (0)</td>
</tr>
<tr>
<td>Emboli to new territory</td>
<td>2% (7/350)</td>
<td>8.0% (2/25)</td>
<td>0.0% (0)</td>
<td>0.0% (0)</td>
</tr>
<tr>
<td>90-day mRS 0–2</td>
<td>64.9% (226/348)</td>
<td>72.0% (18/25)</td>
<td>50.0% (5)</td>
<td>59.1% (13)</td>
</tr>
<tr>
<td>90-day mRS 0–2 (overall)*</td>
<td>68.7% (222/323)</td>
<td>73.9% (17/23)</td>
<td>62.5% (5)</td>
<td>57.1% (12/21)</td>
</tr>
<tr>
<td>90-day mRS 0–2 (IV tPA use)*</td>
<td>63.4% (116/183)</td>
<td>75.0% (9/12)</td>
<td>50.0% (3/6)</td>
<td>54.6% (6/11)</td>
</tr>
<tr>
<td>90-day mRS 0–2 (no IV tPA use)*</td>
<td>66.7% (110/165)</td>
<td>69.2% (9/13)</td>
<td>33.3% (1/3)</td>
<td>63.6% (7/11)</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>14.3% (50)</td>
<td>16.0% (4)</td>
<td>20.0% (2)</td>
<td>9.1% (2)</td>
</tr>
<tr>
<td>90-day mortality (IV tPA use)</td>
<td>12.4% (23/185)</td>
<td>16.7% (2/12)</td>
<td>16.7% (1/6)</td>
<td>18.2% (2/11)</td>
</tr>
<tr>
<td>90-day mortality (No IV tPA use)</td>
<td>16.4% (27/165)</td>
<td>15.4% (2/13)</td>
<td>33.3% (1/3)</td>
<td>0.0% (0/11)</td>
</tr>
</tbody>
</table>

*Subsetted to only pre-stroke mRS 0–2.

ACA, anterior cerebral artery; IV-tPA, intravenous tissue plasminogen activator; MCA, middle cerebral artery; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; NIHSS, National Institute of Health Stroke Scale; PCA, posterior cerebral artery; RNI, rapid neurological improvement; SAE, serious adverse event; sICH, symptomatic intracerebral hemorrhage; TLSW, time last seen well.

was a significantly higher use of general anesthesia in patients with DAO (46.6% vs 39.1%, P = 0.017) and lower median number of device passes (1 [1–2] vs 1 [1–3], P = 0.002) as compared with those with PAO (table 2).
Likewise, the rates of SICH, vessel perforation, and RNI were similar across both groups. The group with DAO showed a significantly higher rate of 90-day mortality (12.8% vs 11%, P = 0.003) and similar rates of 90-day mRS 0–2 (68.3% vs 56.5%, P = 0.017) at 90 days. However, DAO patients were more likely to be functionally independent (90-day mRS 0–2: OR, 1.45, 95% CI [1.09 to 1.92], P = 0.01) or dead (OR, 1.45, 95% CI [1.06 to 2.27], P = 0.02) at 90 days.

Tables 3–5 and online supplemental tables I and II depict the multivariable analysis for the predictors of mRS 0–1, mRS 0–2, and mortality at 90 days as well as successful reperfusion (mTICI2b–3) and SICH within 48 hours post-procedure, respectively. The level of arterial occlusion was not associated with the chances of excellent outcome at 90 days (DAO OR for mRS 0–1: 1.18, 95% CI [0.90 to 1.54], P = 0.225), successful reperfusion (DAO OR for mTICI2b–3: 0.95, 95% CI [0.56 to 1.61], P = 0.865) or SICH within 48 hours (DAO OR: 0.89, 95% CI [0.33 to 2.44], P = 0.826). However, DAO patients were more likely to be functionally independent (mRS 0–2: OR, 1.45, 95% CI [1.09 to 1.92], P = 0.01) or dead (OR, 1.45, 95% CI [1.06 to 2.27], P = 0.02) at 90 days.

Online supplemental tables depict the multivariable analysis for the predictors of mRS 0–1, mRS 0–2, and mortality at 90 days.
days as well as successful reperfusion (mTICI2b–3) and sICH within 48 hours post-procedure in the overall DAO, and in the combined MCA–M3, ACA, and PCA patients only (note that the results in this latter category are merely exploratory given its small sample size). In the DAO population, age and pre-stroke mRS 0–1 were independently associated with both mRS 0–2 and death at 90 days, whereas the baseline NIHSS score was significantly associated with 90-day functional independence and showed a strong trend toward an association with mortality. Interestingly, there was a trend toward better reperfusion (mTICI2b–3) in DAO treated under general anesthesia (OR: 2.95, 95% CI [0.95 to 9.09], P=0.061).

DISCUSSION

The Trevo Retriever Registry remains one of the largest thrombectomy registries to date. As there were no restrictions on inclusion other than the requirement of informed consent and Trevo for first-device use, it provides an unique opportunity to explore various treatment paradigms and trends, including those not properly evaluated in the recent randomized trials. The present analyses demonstrated that MT in the distal arterial territory was technically feasible and safe. Similar rates of successful reperfusion, vessel perforation, and sICH were found when compared with MT in PAOs. Despite the relatively higher rates of 90-day functional independence, our study demonstrated that DAO are not necessarily a “benign” condition. This was illustrated by the similar 90-day mortality across the two levels of arterial occlusion and poor outcomes (mRS >2) in almost one-third of the DAO patients. Moreover, the degrees of 90 day excellent outcome (mRS 0–1) were comparable across DAO and PAO after adjustment for clinical severity (eg, baseline NIHSS).

Notably, DAO was associated with 90-day mortality on multivariable analysis. This is presumably related to a selection bias in the treatment decision-making process as, in general, DAO patients will have lower NIHSS scores and will only be treated properly evaluated in the recent randomized trials. The present analyses demonstrated that MT in the distal arterial territory was technically feasible and safe. Similar rates of successful reperfusion, vessel perforation, and sICH were found when compared with MT in PAOs. Despite the relatively higher rates of 90-day functional independence, our study demonstrated that DAO are not necessarily a “benign” condition. This was illustrated by the similar 90-day mortality across the two levels of arterial occlusion and poor outcomes (mRS >2) in almost one-third of the DAO patients. Moreover, the degrees of 90 day excellent outcome (mRS 0–1) were comparable across DAO and PAO after adjustment for clinical severity (eg, baseline NIHSS).

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et al adopted the definition of medium-vessel occlusions for occlusions that meet specific criteria related to vessel anatomy (involvement of MCA–M2/M3, ACA–A2/A3, and PCA–P2/P3), size (1–3 mm vessel diameter), and associated clinical deficit (NIHSS ≥ 5 and/or disabling deficit).24 Similarly, Saver et al have defined the level of occlusion on the basis of both vessel size and vessel distance/tortuosity with “medium vessels” operationally defined as cerebral arteries with lumen diameters between 0.75 and 2.0 mm, and distal vessels defined as those beyond the M1 segment of the MCA or the basilar artery.25

Although our findings are consistent with previous studies demonstrating the feasibility and safety of MT in DAO,26,27 it is important to again acknowledge that DAO MT is at least theoretically associated with higher risks, given the previously discussed anatomic peculiarities of the distal arteries. However, small distal vessels are safely navigated for the treatment of various cerebrovascular diseases in which the treatment benefit is presumably lower than that of AIS involving similar territory. For instance, flow diverters have been increasingly used to treat unruptured aneurysms in the distal arteries.28 29 Moreover, despite the fact that intravenous thrombolysis (IVT) is more effective in DAO than PAO, not all patients with DAO are eligible for IVT either due to its many contraindications or delayed presentation times. Notably, IVT trials in the extended window have either failed to demonstrate benefit (DIAS1-4, DEDAS, EPITHET)30 31 or had an underrepresentation of the DAO population (only ~30% of subjects in EXTEND-IV).32 These findings reinforce the need to further explore endovascular means for distal artery reperfusion. Finally, another interesting finding of our study was the association between the number of device passes with sICH (OR, 1.24, 95% CI [1.00 to 1.53], P = 0.047). This is consistent with a report from the ASTER trial demonstrating that more than three stent-retriever passes was an independent predictor of parenchymal hematoma (adjusted OR, 9.24; 95% CI, 2.65 to 32.13).33

Our study possesses all the limitations inherent to any analysis that is retrospective in nature. As approximately 86% of all DAO patients in our analysis had M2 occlusions, caution should be taken to not simply generalize all of our findings to the M3, ACA, and PCA territories. Moreover, the inclusion of all types of M2s may further dilute the significance of our findings as dominant M2 vessels may more closely approximate to PAO/ MCA-M1 occlusions rather than DAOs. Since the ASPECTS system does not compute lesions in the ACA or PCA territories, we were not able to properly quantify or make adjustments for baseline infarct burden. The lack of a control medical treatment arm does not allow for the exploration of treatment benefit. Other limitations of the Trevo Retriever Registry, including the potential for selection bias, have been previously detailed elsewhere.9 The main strength of the present study is the inclusion of a robust number of primary DAOs with the demonstration of a good safety profile, while also highlighting that stroke prognosis is dictated by the clinical severity on presentation rather than the level of occlusion in isolation.

CONCLUSIONS
Endovascular therapy may be safely performed in the distal cerebrovascular bed with no clear evidence of any additional safety concerns (including vessel perforation or sICH) as compared with PAO thrombectomy, while yielding similarly high rates of reperfusion (mTICI 2b–3: 93%). DAO can result in significant morbidity and mortality with a similar adjusted impact on outcomes as compared with PAO. The potential benefits of DAO thrombectomy should be investigated in future randomized trials.

Author affiliations
1. Department of Neurology, Marcus Stroke & Neuroscience Center, Grady Memorial Hospital, Emory University School of Medicine, Atlanta, Georgia, USA
2. Department of Neuroradiology, Riverside Methodist Hospital, Columbus, Ohio, USA
3. Department of Neurosurgery, WeillStar Health System, Atlanta, Georgia, USA
4. Department of Neuroradiology, University Hospital Hradec Kralove, Hradec Kralove, Czech Republic
5. Department of Neurology, California Pacific Medical Center, San Francisco, California, USA
6. Neurointerventional & Comprehensive Stroke Program, Saint Mary Medical Center, Long Beach, California, USA
7. Neurology, University of Texas McGeown Medical School, Houston, Texas, USA
8. Department of Radiology, Diagnostic and Interventional Neuroradiology Section, Regional University Hospital Centre Tours, Tours, Centre, France
9. Department of Neurology, Vascular Neurology of Southern California, Thousand Oaks, California, USA
10. Department of Radiology, University of Maryland School of Medicine, Baltimore, Maryland, USA
11. Advocate Neurovascular Center, Advocate Health Care Library Network, Park Ridge, Illinois, USA
12. Department of Radiology, University of Tennessee, Chattanooga, TN, USA
13. Department of Neuroradiology, CHUV, Lausanne, VS, Switzerland
14. Division of Biostatistics, Styrker Neuurovascular, Fremont, California, USA
15. Department of Interventional Neuroradiology, Centre Hospitalier Regional Universitaire de Lille, Lille, France
16. Department of Neurology, UCLA, Los Angeles, California, USA
17. Department of Neurosciences, Drexel University College of Medicine, Philadelphia, Pennsylvania, USA

Twitter: Amrou Nogueria <@amrounogueria>

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ORCID iDs
Mahmoud H Mohammaden http://orcid.org/0000-0002-7393-9989
Amrou Sarraj http://orcid.org/0000-0001-5726-4478
REFERENCES


