Effectiveness of very low profile thrombectomy device in primary distal medium vessel occlusion, as rescue therapy after incomplete proximal recanalization or following iatrogenic thromboembolic events

Reza Rikhtegar,1 Pascal John Mosimann Ⓡ,1 Ralph Weber,2 Marta Wallocha,1 Elfı Yamac,1 Mohammad Mirza-Aghazadeh-Attari Ⓡ,1 René Chapot Ⓡ1

ABSTRACT
Background Recent progress with smaller retrievers has expanded the ability to reach distal brain arteries. We herein report recanalization, bleeding complications and short-term clinical outcomes with the smallest currently known low profile thrombectomy device in patients with primary or secondary distal medium vessel occlusion (DMVO).

Methods We performed a retrospective analysis of 115 patients receiving mechanical thrombectomy (MT) in DMVO using the extended Thrombolysis in Cerebral Infarction (eTICI), European Cooperative Acute Stroke Study (ECASS) II classification, The National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) scores at admission and discharge to evaluate outcomes. Patients were stratified into three groups: (1) primary isolated distal occlusion (n=34), (2) secondary distal occlusion after MT of a proximal vessel occlusion (n=71), or (3) during endovascular treatment of aneurysms or arteriovenous malformations (AVMs) (n=10).

Results Successful distal recanalization, defined as an eTICI score of 2b67, 2c and 3, was achieved in 74.7% (86/115) of patients. More specifically, it was 70.5% (24/34), 73.2% (52/71), and 100% (10/10) of primary DMVO, secondary DMVO after proximal MT, and rescue MT during aneurysm or AVM embolization, respectively. Symptomatic intraparenchymal bleeding occurred in 6.9% (eight patients). In-hospital mortality occurred in 18.1% (19/105) of patients with stroke. The most common cause of death was large infarct, old age, and therapy limitation.

Conclusion Direct or rescue MT of DMVO using a very low profile thrombectomy device is associated with a high rate of successful recanalization and a reasonable rate of symptomatic hemorrhagic complication, despite a risk of 18.1% hospital mortality in elderly patients. Further trials are needed to confirm our results and assess long-term clinical outcomes.

INTRODUCTION
Bridging therapy, consisting of combined intravenous thrombolysis (IVT) and mechanical thrombectomy (MT), is the current gold standard treatment in patients with acute ischemic stroke (AIS) presenting with an emergent proximal large vessel occlusion (PLVO) in the anterior brain circulation.1 Although distal, medium vessel occlusions (DMVOs) tend to be less devastating than PLVOs, occlusion of an eloquent peripheral brain vessel may substantially degrade functional outcome and quality of life.1 2 It is estimated that DMVO accounts for 25–40% of all brain vessel occlusions.3 While IVT remains the primary therapy of choice, many contraindications limit its use in clinical practice. Moreover, IVT fails to recanalize one-half to two-thirds of DMVOs.1 4 Furthermore, secondary DMVOs frequently occur after IVT or MT of PLVOs.5 While MT is deemed safe and effective in proximal M2 occlusions of the middle cerebral artery (MCA), its benefit in more distal locations remains unclear.6 Considering the impact of rapid and full or near-complete recanalization on clinical outcome,7 exploring the benefit of MT for primary or secondary DMVO is warranted.8 Moreover, thromboembolic complications during embolization of brain aneurysms or arteriovenous malformations may also benefit from DMVO thrombectomy,9 especially in patients receiving dual anti-platelet medication, where thrombosis may result in or worsen hemorrhagic complications.

Devices used in PLVO trials require microcatheters with a lumen of 0.021–0.027 inch, which can be difficult to be safely navigated in tortuous sulcal or gyral distal brain arteries measuring 1.5 mm or less in diameter.9 This is especially true when triaxial systems with guiding and intermediate catheters are used. Low profile stent retrievers adapted for DMVO that fit through a 0.017-inch lumen microcatheter include the Catchview mini (Balt, Montmorency, France) and the Mindframe Capture (Medtronic, Dublin, Ireland).10 Lately, a thinner, soft, and adaptive mesh-like stent retriever fitting through a 0.013–0.0165-inch lumen microcatheter was developed (Tigertriever 13, Rapid Medical, Yokneam, Israel). In the present study, we investigated the technical feasibility to perform distal thrombectomy in patients with stroke who were relevantly disabled and in patients who experienced DMVO as a thromboembolic complication during aneurysm or AVM embolization. We assessed recanalization and bleeding rates, as well as short-term clinical outcome in patients with stroke in a consecutive series of patients treated with the Tigertriever 13 device.
Acquisition of data
Demographic and clinical data were gathered from electronic medical records. Images were reviewed via the Agfa IMPAX picture archiving and communication system and randomly presented to two experienced interventional neuroradiologists (RC, PJM) blinded to the patient’s clinical characteristics. The following DMVOs were included in the present study: A3 segment of the anterior cerebral artery, M3 and M4 segments of the MCA, P2, and P3 segments of the posterior cerebral artery, as well as cerebellar arteries. Occlusions of the proximal and distal M2 segment were excluded because these are generally treated with conventional stent retrievers through 0.021 microcatheters (mostly the Solitaire 6×40 Platinum device; Medtronic). No manual or pump-assisted distal aspiration was performed.

Angiographic results after the MT procedure were interpreted according to the extended Thrombolysis in Cerebral Infarction (eTICI) classification. Discrepancy between the two blinded readers was resolved by consensus reading. Technical variables such as type of device, number of passes, and time from groin puncture to reperfusion were collected from the interventional reports. The primary endpoint was successful recanalization with conventional stent retrievers through 0.021 microcatheters (mostly the Solitaire 6×40 Platinum device; Medtronic). No manual or pump-assisted distal aspiration was performed.

Statistical analysis
Statistical analysis was performed using SPSS version 23. Qualitative data were represented as frequencies and medians, while quantitative data were presented as mean±SD. Paired Student t-test and Wilcoxon signed-rank tests were used to compare means of variables. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS
During the 21 month study period, intracranial endovascular treatment was performed in 2056 patients, of whom 690 received MT. A total of 115 patients with DMVO were consecutively
treated with the Tigertriever 13 device, 105 in the context of AIS (see table 1).

Of the 115 patients, 34 had a primary isolated DMVO (group 1), while 71 presented with a secondary DMVO after failed or incomplete MT of a PLVO (group 2). The remaining 10 patients experienced distal thromboembolic events during elective aneurysm or arteriovenous malformation embolization (group 3). Mean age was 72±16.5 years (range 23–99, median 77 years), 63 patients (54.8%) were female. Fifty patients with AIS (48%) received IVT prior to MT. The mean number of passes with the Tigertriever 13 device alone. In these cases, the Solitaire and the device was necessary after two unsuccessful retrievals with the Tigertriever 13 device was necessary after two unsuccessful retrievals with the Tigertriever 13 device alone. In these cases, the Solitaire and the Tigertriever 13 device were placed in the larger and smaller division branch, respectively. Successful recanalization was achieved in four (57%) of these seven patients without peri-interventional complications. Median NIHSS at admission, after 24 hours, and at discharge was 11, 8, and 5, respectively (p=0.001 for change from admission to discharge). A good functional outcome was observed in 28 of the 71 patients (39.4%) in the combined PLVO/DMVO thrombectomy group.

All patients with distal vessel thromboembolic complications during cerebral aneurysm or AVM embolization (group 3) were successfully recanalized (10/10). The most common clot location was M3 (80%). There were no deaths or thrombectomy-related morbidity.

Active SAH caused by guidewire perforation or after a thrombectomy attempt was angiographically identified during the MT procedure in seven (6.7%) of the 105 patients with AIS. Three ceased spontaneously within 10 min after systolic blood pressure reduction below 80 mm Hg. Two needed temporary coiling, while the remaining two required definitive coil occlusion.

Subarachnoid contrast medium extravasation after DMVO MT was observed on immediate postoperative cone-beam CT.

### Table 1: Demographic, clinical characteristics and treatment outcome

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Primary isolated distal occlusion (group 1)</th>
<th>Secondary DMVO following MT of a proximal vessel occlusion (group 2)</th>
<th>Distal thrombectomy during elective AVM or aneurysm embolization (group 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>76 (12)</td>
<td>74 (15)</td>
<td>46 (17)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>17 (50)</td>
<td>41 (57.8)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Prior IVT, n (%)</td>
<td>23 (67.6)</td>
<td>27 (38.0)</td>
<td>NA</td>
</tr>
<tr>
<td>NIHSS at admission, median (range)</td>
<td>7 (0–22)</td>
<td>11 (0–31)</td>
<td>NA</td>
</tr>
<tr>
<td>NIHSS at 24 hours, median (range)</td>
<td>6 (0–31)</td>
<td>8 (0–31)</td>
<td>NA</td>
</tr>
<tr>
<td>NIHSS at discharge, median (range)</td>
<td>3 (0–31)</td>
<td>5 (0–23)</td>
<td>NA</td>
</tr>
<tr>
<td>Successful recanalization (eTICI 2b–3), n (%)</td>
<td>24 (70.5)</td>
<td>52 (73.2)</td>
<td>10 (100)</td>
</tr>
<tr>
<td>No of passes with Tigertriever 13, median (range)</td>
<td>2 (1–4)</td>
<td>1 (1–5)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Duration of MT procedure (min), mean (SD)</td>
<td>71 (50.1)</td>
<td>104 (68.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Contrast agent extravasation in CBCT immediately after thrombectomy, n (%)</td>
<td>16 (47.0)</td>
<td>31 (43.6)</td>
<td>0</td>
</tr>
<tr>
<td>Asymptomatic intracranial bleeding, n (%)</td>
<td>7 (20.6)</td>
<td>12 (16.9)</td>
<td>0</td>
</tr>
<tr>
<td>Symptomatic intraparenchymal bleeding, n (%)</td>
<td>3 (8.8)</td>
<td>5 (7.0)</td>
<td>0</td>
</tr>
<tr>
<td>In-hospital mortality, n (%)</td>
<td>4 (11.8)</td>
<td>15 (21.1)</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Including subarachnoid and intra-parenchymal.

DMVO, distal medium vessel occlusion; MT, mechanical thrombectomy; PLVO, proximal large vessel occlusion.

### Table 2: Clot location in DMVO

<table>
<thead>
<tr>
<th></th>
<th>A3 (%)</th>
<th>M3 (%)</th>
<th>M4 (%)</th>
<th>P2 (%)</th>
<th>P3 (%)</th>
<th>PICA (%)</th>
<th>SCA (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary isolated DMVO, n (%)</td>
<td>1 (2.9)</td>
<td>28 (82.4)</td>
<td>0 (0)</td>
<td>2 (5.9)</td>
<td>1 (2.9)</td>
<td>0 (0)</td>
<td>2 (5.9)</td>
<td>34</td>
</tr>
<tr>
<td>Secondary DMVO after MT in proximal PLVO, n (%)</td>
<td>9 (12.7)</td>
<td>48 (67.6)</td>
<td>6 (8.5)</td>
<td>0 (0.0)</td>
<td>2 (2.8)</td>
<td>1 (1.4)</td>
<td>5 (7.0)</td>
<td>71</td>
</tr>
<tr>
<td>DMVO related to secondary causes, n (%)</td>
<td>0 (0)</td>
<td>8 (80.0)</td>
<td>1 (10)</td>
<td>1 (10)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0)</td>
<td>10</td>
</tr>
</tbody>
</table>

DMVO, distal medium vessel occlusion; MT, mechanical thrombectomy; PLVO, proximal large vessel occlusion.


Ischemic stroke (CBCT) in 47 (44.7%) of the 105 patients with AIS (groups 1 and 2). No bleeding occurred in elective patients with thromboembolic events treated by distal thrombectomy (group 3).

Symptomatic and asymptomatic intracranial hemorrhage on control brain imaging was observed in 8 (7.6%) and 19 (18.1%) of the 105 patients with AIS, respectively, independently of prior use of IVT (p=0.9).

Nineteen patients with AIS (18.1%) died during their hospital stay (table 4). Mean age at death was 81.1±11.9 years (range 54–99 years; 13 (68%) older than 80 years). The mean duration of intervention in the deceased patients with AIS was 146±83.6 min compared with 82.4±53.6 in stroke survivors. The difference was statistically significant (p=0.001). Only six of the 19 deceased patients with AIS received IVT, the remainder having presented outside of the eligible time window. Two died due to a symptomatic brain hemorrhage, one having received prior IVT.

Figure 2 shows representative examples of different contrast extravasation or bleeding types observed.

**DISCUSSION**

The main finding of our study is that stent retriever thrombectomy in DMVO is technically feasible by experienced neurointerventionalists, as successful mechanical recanalization was achieved in 74.7% of patients overall, matching the results of PLVO thrombectomy studies.14

The literature on distal MT is scarce. Piergallini and colleagues15 reported a series of eight patients (mean age 84±11 years) with distal occlusions successfully recanalized with a Catchview Mini stent-retriever through a Headway Duo microcatheter. No treatment-related complications were reported, and only one patient underwent general anesthesia while the remainder received conscious sedation. Our cohort represents a more diverse set of patients, including rescue therapy for distal iatrogenic emboli after LVO thrombectomy and patients with distal thromboembolic complications during elective embolization procedures. Our results show that mechanically removing the distal clots resulted in a high rate of successful recanalization, which is known to be one of the strongest predictors for good functional outcome.16 Similarly, Dobrocky and colleagues 17 reported on 38 patients with isolated M2 occlusions using the low profile Mindframe Capture retriever under balanced general anesthesia and conscious sedation. Successful recanalization was achieved in 74% (28 patients) and only a single case of symptomatic intracranial hemorrhage was observed. An adjusted mRS

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**Table 3** Recanalization results after distal thrombectomy according to eTICI score

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2A</th>
<th>2B</th>
<th>2C</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary isolated DMVO, n (%)</td>
<td>7 (20.6)</td>
<td>0 (0.0)</td>
<td>3 (8.8)</td>
<td>4 (11.8)</td>
<td>7 (20.6)</td>
<td>13 (38.2)</td>
<td>34</td>
</tr>
<tr>
<td>Secondary DMVO after MT in proximal PLVO, n (%)</td>
<td>10 (14.1)</td>
<td>1 (1.4)</td>
<td>8 (11.3)</td>
<td>10 (14.1)</td>
<td>16 (22.5)</td>
<td>26 (36.6)</td>
<td>71</td>
</tr>
<tr>
<td>DMVO related to secondary causes, n (%)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1 (10.0)</td>
<td>9 (90.0)</td>
<td>10</td>
</tr>
</tbody>
</table>

DMVO, distal medium vessel occlusion; eTICI, extended Thrombolysis in Cerebral Infarction; MT, mechanical thrombectomy; PLVO, proximal large vessel occlusion.

**Table 4** Cause of death in patients with acute ischemic stroke (groups 1 and 2)

<table>
<thead>
<tr>
<th>Cause</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large infarction due to proximal LVO (ICA, carotid T, basilar artery, combined MCA/AC), age ≥80 years, and therapy limitation (palliative care)</td>
<td>9</td>
</tr>
<tr>
<td>Failed mechanical thrombectomy</td>
<td>5</td>
</tr>
<tr>
<td>Symptomatic ICH</td>
<td>2</td>
</tr>
<tr>
<td>Other reason (acute coronary syndrome with pulmonary edema, sepsis)</td>
<td>3</td>
</tr>
</tbody>
</table>

ICA, internal carotid artery; ICH, intracranial hemorrhage; LVO, large vessel occlusion; MCA, middle cerebral artery.

Figure 2 Column A (left) and B (right) displaying CBCT immediately after thrombectomy and regular CT scan after 24 hours, respectively. Upper row: minimal contrast agent extravasation in the left sylvian fissure initially with complete resolution on follow-up. Middle row: moderate contrast agent extravasation in the right sylvian fissure with marked but incomplete resorption at 24 hours (rated as asymptomatic intracranial bleeding). Lower row: important contrast agent extravasation in the left sylvian fissure with an associated temporal parenchymal hemorrhage and intraventricular extension on the control CT the following day (rated as symptomatic intraparenchymal hemorrhage). CBCT=flat panel cone-beam CT.
score of 0–2 at 3 months was observed in 65% of the 38 patients when taking pre-stroke disability into account. We observed a favorable short-term clinical outcome with an adjusted mRS score of 0–2 at discharge in only 41% of our patients with AIS. Since more than half of our patients with AIS (56/105) were transferred back to the referring hospitals within 72 hours after the MT procedure, it is possible that we underestimated the rate of favorable outcomes.

Interestingly, eight patients (21%) presented minor focal SAH on follow-up imaging at 24 hours in the study by Dobrocky and colleagues. In our cohort, cone-beam CT was systematically performed and disclosed a higher rate of immediate postoperative contrast extravasation in more than a third of patients with AIS. Nonetheless, this should be considered as a benign epiphenomenon related to the mechanical straightening of the distal sulcal vessels due to the tearing of some cortical arterioles during device retraction. Indeed, these short-lived SAHs either resolved or remained stable at 24 hours. More importantly, the rate of symptomatic intracranial hemorrhage remains acceptably low. While the incidence of minor SAH reported here is higher than on CT following PLVO thrombectomy, immediate postoperative cone-beam CT in PLVO studies was rarely performed and virtually never reported. No immediate or delayed vasospasm was observed in our series and no patient experienced further related cerebral infarction no received preventive or therapeutic oral nimodipine, further illustrating the benign nature of contrast extravasation after DMVO MT.

Of all the patients presenting with AIS (groups 1 and 2), 47.6% received intravenous thrombolysis prior to distal thrombectomy. While this did not statistically influence the rate of hemorrhagic complications in our series, it is too early to conclude that prior use of intravenous thrombolysis is safe whenever distal thrombectomy is considered. Furthermore, a recent study covering 21 hospitals showed that DMVO occurred in one in four patients receiving intravenous tissue plasminogen activator in whom distal MT was not attempted in 41.3%, thereby depriving a significant number of patients of a possible better clinical outcome.

Intra-arterial thrombolysis may be achieved as an alternative to DMVO. In the Bernese experience, the TICI rate was improved in 34% of patients treated by adjunctive intra-arterial Urokinase after incomplete or failed thrombectomy. However, the absence of hemorrhagic complications in both studies does not reflect the 10% risk of symptomatic hemorrhage reported in PROACT 2.

Distal aspiration techniques focused on DMVO have also been reported. Grieb and colleagues used contact aspiration (ADAPT) with the Sofia French and Catalyst six access catheters for M2 occlusions in 52 patients. Additional stent retriever use increased their rate of successful recanalization from 86.5% to 92.3%. Haussen and colleagues used another retriever named the Trevo XP 3×20 mm retriever (Baby Trevo), studying eight patients with distal occlusions. After one to three passes, recanalization was achieved in all cases. One of the patients had a parenchymal hemorrhage type 1, and the other had a parenchymal hemorrhage type 2. None of the patients had SAH or vessel perforation. Five patients experienced intraoperative vasospasm.

The same authors also conducted an observational study where they compared 3MAX aspiration with 3 mm Trevo retriever in patients with AIS and distal occlusions. They included 92 vessels that were treated with the Trevo retriever and 52 vessels with the 3MAX device. Of all the patients treated with the Trevo retriever, 58 patients (62%) had an mTICI 2b-3 grade compared with only 23 patients (44%) in the distal aspiration group, which was statistically significant. Similarly, mortality was lower in the stentretriever group (19% compared with aspiration at 24%) despite a lack of statistical significance. In contrast to the aforementioned studies, we did not perform additional distal aspiration in our study.

Anesthesia management during MT remains controversial. Based on our experience and encouraging results of prospective trials, the overwhelming majority of our patients having thrombectomy underwent general anesthesia. In the present cohort, only one patient was treated under conscious sedation. While respiratory complications remain a concern, particularly in older patients, we are convinced that general anesthesia improves the safety of distal thrombectomy by reducing the risk of wire perforation due to optimal roadmap imaging without patient movement. Nevertheless, SAH caused by guidewire perforation or after a thrombectomy attempt occurred in 6.7% patients. It is not known whether these SAHs are associated with a higher rate of post-stroke seizures or other complications as we are not able to provide long-term outcome data in our patient cohort. The rate of symptomatic brain hemorrhage in our study (7.6%) was higher compared with the rates reported in PLVO thrombectomy (HERMES, ASTER) but lower compared with the study by Haussen and colleagues using the ‘Baby Trevo’ device.

It is therefore important to acknowledge that MT of distal brain arteries is technically challenging and should be performed only by experienced neurointerventionalists at higher volume centers. This is especially true with the Tiger Trevo 13 device which requires a different learning curve than the more classical stent retrievers.

In our study, 19 patients with AIS and DMVO died during hospitalization (18.0%). This number is similar to the reports of previous large vessel occlusion studies. It should be noted that the majority of deaths in our study occurred in patients who were at least 80 years old and mostly with pre-existing conditions. Since it is known that octogenarians are at greater risk of mortality, the safety profile of the Tiger Trevo 13 device may be higher in younger patients.

Finally, we previously reported the use of Tiger Trevo 13 device to retrieve misplaced embolic agents during brain AVM embolization. We herein confirm the usefulness of this device in 10 patients with iatrogenic thromboembolic complications during elective embolization of arteriovenous malformations in whom full recanalization was obtained, followed by an eventful clinical course.

The limitations of our study are its retrospective nature with inherent biases but also the self-adjudicated imaging results (no core lab evaluation) and many confounding factors that prevented us to correlate angiographic data with long-term clinical outcome (that was also lacking), although the 24-hour NIHSS appears to be an acceptable surrogate marker. Another concern is the learning curve and the possible over-expansion of the mesh during clot pinching and retrieval, which may increase the hemorrhagic risk compared with the usual stent retrievers. Despite these limitations, our data indicate that the Tiger Trevo 13 device may improve the rate of full or near-complete recanalization in patients with primary or secondary DMVO without exposing them to significant symptomatic hemorrhagic complications.

**CONCLUSION**

Direct or rescue thrombectomy of distal, medium vessel occlusion with a very low profile adaptive mesh device seems to be associated with a high rate of successful recanalization and a reasonable rate of symptomatic hemorrhagic complications.
Multicenter trials are needed to confirm these results and better assess long-term clinical outcome.

Contributors RR: writing of the manuscript, a systemic search of the literature, acquisition of data, study concept, statistical analysis. PJM: gathering of information, a systemic search of the literature, writing of the manuscript, interpretation of imaging findings, acquisition of data, statistical analysis. MW: gathering of information, a systemic search of the literature, writing of the manuscript, interpretation of imaging findings. EY: gathering of information, acquisition of data, study concept, statistical analysis. PJM: gathering of information, acquisition of data, study concept, overall supervision, final edit of the manuscript, interpretation of imaging findings.

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