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► To cite this version:

F. Clarençon, F. Baronnet, E. Shotar, V. Degos, C. Rolla-Bigliani, et al.. Should posterior cerebral artery occlusions be recanalized? Insights from the Trevo Registry. *European Journal of Neurology*, 2020, 27 (5), pp.787-792. 10.1111/ene.14154 . hal-02512399

HAL Id: hal-02512399

<https://hal.sorbonne-universite.fr/hal-02512399>

Submitted on 29 Jun 2020

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Should posterior cerebral artery occlusions be recanalized? Insights from the Trevo Registry

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Abstract

Background and Aims

The purpose of this study was to evaluate the safety and effectiveness of mechanical thrombectomy (MT) in patients with acute ischemic stroke (AIS) related to isolated and primary posterior cerebral artery (PCA) occlusions among the patients enrolled in the multicentre post-market Trevo Registry.

Method

Among the 2008 patients enrolled in the Trevo Registry with AIS due to large vessel occlusion (LVO) treated by MT, 22 (1.1%) (10 females [45.5%], mean age: 66.2±14.3 years [range 28-91]) had a PCA occlusion (17 P1 [77.3%] and five P2 occlusions [22.7%]). Recanalization after the first Trevo (Stryker, Fremont, CA) pass and at the end of the procedure was rated using the mTICI score. Procedure-related complications (i.e.: groin puncture complication, perforation, symptomatic hemorrhage, embolus in a new territory) were also recorded. Modified Rankin Scale (mRS) at 90 days was assessed.

Results

Median NIHSS at admission was 14 [IQR, 8-16]. Stroke etiology was cardio-embolic in 68.2% of cases. Half of the patients (11/22) received IV tPA. 54.5% of the patients were treated under general anesthesia. Reperfusion (i.e.: mTICI2b or 3) after first pass was obtained in 65% of cases. Final TICI2b-3 reperfusion was obtained in all cases. Only one (4.5%) procedure-related complication was recorded (puncture site), that resolved after surgery. At 90-day follow-up, mRS 0-2 was obtained in 59% of the patients and 9.1% died within the first 3 months after MT.

Conclusion

Mechanical thrombectomy for PCA occlusions seem to be safe (< 5% procedure-related complications) and effective. Larger repository datasets are needed.

Introduction

Acute ischemic strokes (AIS) involving the posterior cerebral artery (PCA)'s territory are rare; they account for approximately 5-10% of all AIS (1-3). Most of these PCA strokes are caused by a cardio-embolic pathomechanism (4). AIS related to PCA occlusion are even rarer; they have been reported accounting for about 0.5% of all AIS with large vessel occlusion (LVO) (5). This specific subtype of AIS is usually responsible for lower NIHSS strokes (1), but with potential life altering consequences such as inability to drive due to a visual impairment or alexia. These strokes are felt to be less severe compared to basilar artery occlusion or anterior circulation strokes (4). Additionally, the clinical symptoms revealing PCA infarcts are less recognized; which could be responsible for a delayed diagnosis, out of the time-window for intravenous (IV) thrombolysis (6).

Recent randomized control trials (RCTs) have proven the effectiveness of mechanical thrombectomy (MT), combined with the best medical treatment, in AIS with LVO involving the anterior circulation (7). However, data regarding the safety and effectiveness of MT in patients with AIS related to PCA occlusion are lacking. There have been limited reports for treating this condition to date (8, 9).

The purpose of our study was to evaluate the safety and recanalization rates of MT in PCA occlusions.

Materials and Methods

Study design:

Post-hoc analysis of a prospective multicentre post-market registry (the Trevo Retriever Registry; *ClinicalTrials.gov identifier: NCT02040259*). The Trevo Retriever Registry is a prospective, open-label, consecutive enrolment, multi-center, international registry aiming to collect real world performance data of the Trevo Retriever (Stryker, Fremont, CA) which is intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing AIS (10).

Patients' demographics/Inclusion criteria:

From November 11, 2013 to May 1, 2017, a total of 2008 patients were enrolled in the TREVO Retriever Registry (1041 females, 51.8%; mean age: 68.3 ± 14.4 years with a range of 19 to 99 years).

Among the patients enrolled in the Trevo Retriever Registry, only those with DSA proven isolated and primary PCA occlusion(s), from P1 to P4 (11), were included. Location of the occlusion site was evaluated by an independent core-lab. Patients with basilar artery occlusion associated with PCA occlusion were excluded. Patients with secondary PCA occlusions (i.e.: thrombus migration in PCA during basilar artery MT) were also excluded.

For each patient retained with a PCA occlusion, demographic data, time of symptoms' onset, and past medical history (history of coronary artery disease, atrial fibrillation, previous transient ischemic attack [TIA], or ischemic stroke) were systematically

recorded. The following cardiovascular risk factors were collected: blood hypertension, diabetes mellitus, current cigarette smoking, dyslipidemia, coronary artery disease.

Patients' management

In all cases, the patient was examined at admission by a stroke-trained provider who graded the NIHSS (National Institutes of Health Stroke Scale). After clinical examination, all patients had a standard investigation protocol including blood tests, electrocardiography, brain computed tomography (CT) scan, and/or magnetic resonance imaging (MRI). LVO was documented noninvasively by a CT angiography (CTA) and/or a magnetic resonance angiography (MRA). Cervical vessel evaluation was performed at the discretion of the team in charge of the patient.

Patients who were admitted within the appropriate time-window, and without contraindication, received intravenous (IV) rt-PA (recombinant tissue plasminogen activator) (0.9 mg/kg) as per their local institutional protocol. Patients were treated either under general anesthesia (GA) or under conscious sedation/local anesthesia, at the discretion of the operator.

Occlusion site/stroke subtype classification

The arterial occlusion site was evaluated on DSA in anteroposterior (AP) and lateral projections and graded according to the Fischer's segmentation (from P1 to P4) (11). Stroke aetiology was classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria (12).

Safety/intracranial hemorrhage

Procedure-related complications were divided into 1) minor complications: groin puncture minor complications that did not require blood transfusion or surgical repair, minor intracranial hemorrhage that did not lead to clinical worsening; and 2) major complications: intracranial arterial perforation, embolus in a new territory (ENT) leading to clinical worsening, symptomatic intracranial hemorrhage (i.e.: intracranial hemorrhage leading to a clinical worsening [4-point increasing on the NIHSS score]), cervical arterial dissection responsible for clinical worsening, groin puncture complications requiring blood transfusion or surgical repair.

Identification and classification of intracranial hemorrhage was performed routinely on brain MRI or CT within 24h after MT or in case of any clinical deterioration. ICH was classified as “symptomatic” if a parenchymal hematoma type 2 (according to the ECASS criteria) was accompanied by a 4-point or greater increase in the NIHSS score or if leading to death (13, 14).

Angiographic and clinical outcomes

Recanalization after the first Trevo pass and at the end of the procedure was rated using the mTICI score (15) on AP and lateral projections DSA by an independent core lab. Successful reperfusion was defined as mTICI 2B/3. mRS at 90 days was systematically recorded by a certified physician for mRS assessment. A mRS ≤ 2 at 3 months’ follow-up was considered as a good clinical outcome.

Statistical analysis:

We compiled descriptive statistics for parameters of interest for our analysis.

Reported p-values are two-sided and are not adjusted for multiple comparisons considering the exploratory nature of the analyses. All analyses were conducted using SAS software (SAS, Version 9.4, SAS Institute Inc., Cary, NC).

Ethical statement:

The registry was approved by the institutional review board at each site. Patients or their designee provided written informed consent within 7 days of the procedure.

Results

Out of the 2008 patients included in the Trevo Retriever registry, 22 (1.1%; 10 females [45.5%], mean age: 66.2 ± 14.3 y [range 28-91]) presented an AIS related to a primary and isolated PCA occlusion treated by MT with the Trevo Retriever device as first line strategy. Occlusion sites were distributed as follows: 17 P1 occlusions [77.3%] and 5 P2 occlusions [22.7%]. Neither P3 nor P4 occlusions were included in our study cohort. Median NIHSS at admission was 14 (Q1-Q3: 8-16; range: 1-26). Stroke etiology was cardio-embolic in most cases (68.2%), followed by large artery atherosclerosis (13.6%). Half of the patients (50%) received IV rt-PA. Interestingly, half of the patients (11/22) underwent the MT over the 4h30 time-window after the symptoms' onset. In 54.5% of the cases, the patients were treated under general anesthesia (*Baseline patient characteristics are summarized in **Additional Material # 1**; Procedural characteristics are summarized in **Additional Material # 2***).

Reperfusion (i.e.: mTICI2b or 3) after first pass with the Trevo Retriever was obtained in 65% of cases (mTICI 3 in 50% of the cases). Final mTICI 2b-3 reperfusion was obtained in 100% of the cases. In average 1.3 ± 0.5 passes (range: 1-2) of the Trevo Retriever were performed; 1.6 ± 0.9 (range: 1-4) for all thrombectomy devices (*Clinical assessment and efficacy outcomes are displayed in **Table 1***).

Only one (3.7%) severe procedure-related complication was recorded (puncture site), that resolved after surgery. No device (Trevo)-related complication occurred. One case (4.5%) of clinical worsening during the 24h after the MT was observed due to increased of the mass effect related to the infarct and which was not a procedure-related complication. Additionally, no embolus migration in another territory was recorded. No vessel perforation was observed, as well. Intracranial hemorrhages were

observed in 18.2% of the cases (3 HI 1 and 1 subarachnoid hemorrhage). No symptomatic hemorrhages according to the ECASS 3 study classification were recorded; asymptomatic hemorrhages were observed in 18.2% (4/22) of the cases.

Median NIHSS at 24h after the MT was 3 (Q1-Q3: 1-8; range: 0-27). At 90-day follow-up, 59.1% (13/22) of the patients had a mRS 0-2; 9.1% (2/22) died within the first 3 months after the MT.

Discussion

Acute ischemic strokes related to PCA occlusion are difficult to diagnose due to a frequent non-specific clinical presentation, which can explain the delay in their management, sometimes beyond the time-window for IV rt-PA. Since the symptoms and sequelae of AIS related to PCA occlusion are usually less severe, one may ask if MT is a suitable option for patients with PCA occlusion. Indeed, compared to middle cerebral artery (MCA) or anterior cerebral artery (ACA), sequelae after PCA occlusions are usually milder. However, P1 or P2 occlusions may involve perforating branches feeding the thalamus (16) which could lead to severe sequelae. Additionally, infarct the PCA's cortical territory may be responsible for severe hemianopia, which could be severely disabling, especially in young patients.

The aim of our study was to evaluate the safety and effectiveness of MT for AIS with PCA occlusions. Our sub-group analysis of MT for PCA occlusions from the Trevo Retriever registry showed the safety of this procedure for this specific occlusion site. Indeed, only one (< 5%) major procedure-related complication was recorded, which consisted in a groin puncture complication requiring surgical management, but which did not lead to clinical sequelae. It is noteworthy that this major complication rate is within the range of the ones reported in the literature for anterior circulation MT (17). Technically, there was a 100% successful reperfusion rate. Moreover, there were 18.2% of patients with asymptomatic hemorrhages and 81.8% (18/22) with improvement in their NIHSS at discharge. At 3-months follow-up, 59.1% of the patients had a good clinical outcome ($mRS \leq 2$). All these results are within the ranges of the ones reported for comparable-size arterial occlusions (i.e.: distal occlusions) of the anterior circulation (18).

Interestingly, admission NIHSS scores were higher in our study population (median: 14) than reported in series with patients treated by IV thrombolysis for PCA territory AIS ²¹. However, one should keep in mind that all the patients involved in our study had a proximal (P1 or P2) PCA occlusion, which may explain this discrepancy. Only limited data are available in the literature on the safety and effectiveness of MT in PCA occlusions; mainly case reports, either of regular (8) or fetal (19) PCA configurations, and short case series in which PCA occlusions were merged with other posterior circulation occlusions (20). In a recent study comparing anterior and posterior circulation strokes (20), only 6 (4.3%) isolated PCA occlusions were reported and 23 cases (16.5%) of PCA or vertebral artery occlusions combined with basilar artery occlusion. No sub-group analysis was available in this study on PCA occlusions (either isolated or combined) (20).

A short case series (21) comparing intra-arterial (IA) thrombolysis with IV rt-PA has shown no superiority of IA over IV thrombolysis in PCA occlusions in terms of good clinical outcome (mRS ≤ 2 in 67% of the cases for IA thrombolysis and 89% with IV thrombolysis). However, the number of patients included in this case series was very low (9 patients in each group [IA and IV]). Additionally, no randomization was performed for the technique used.

Limitations

The main limitation of our sub-group study analysis is the low volume of the patients with a PCA occlusion included. However, the Trevo Retriever Registry is a very large registry reflecting the real life daily practice in MT. The second limitation is the lack of randomization to compare MT to the best medical treatment. Indeed, PCA being a

relatively small artery, one could assume that rt-PA may be more effective in this specific localisation, compared to ICA terminus or proximal M1. Additionally, our study lacks specific data on visual evaluation, like visual field defects, as well as on neuropsychological examination. Such more specific evaluation would have been valuable for the assessment of sequelae related to the PCA's territory AIS. Finally, only P1 to P2 occlusions were included. The good results obtained in our case series in terms of recanalization and low complication rate may probably not be extrapolated to more distal (i.e.: P3 or P4) occlusions.

Summary

The post-hoc analysis of patients included in the Trevo Retriever Registry who underwent a MT for an isolated and primary PCA occlusion shows the safety of this technique with a low rate of major complication ($< 5\%$). MT in PCA occlusion seems effective with a high recanalization rate (100%). However, only a randomized controlled trial could prove the superiority of MT associated with the BMT over the BMT alone in terms of good neurological outcome for this specific subtype of acute ischemic stroke.

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Table 1. Clinical assessment and efficacy outcomes

ITT P1 P2 (N=22)	
First Trevo Pass Modified TICI $\geq$ 2b	65% (12/20)
First Trevo Pass Modified TICI	
Grade 0	25.0% (5/20)
Grade 1	10.0% (2/20)
Grade 2a	0% (0/20)
Grade 2b	15% (3/20)
Grade 3	50.0% (10/20)
Not available	9% (2/22)
Post-procedure Modified TICI $\geq$ 2b	100% (22/22)
Pre-stroke mRS	
0	85.7% (18/21)
1	4.8% (1/21)
2	9.5% (2/21)
90-day mRS 0 – 2	59.1% (13/22)
90-day mRS	
0	22.7% (5/22)
1	22.7% (5/22)
2	13.6% (3/22)
3	18.2% (4/22)
4	13.6% (3/22)

5	0% (0/22)
6	9.1% (2/22)

Pre-procedure NIHSS

Mean $\pm$ SD	12.6 $\pm$ 6.6 (21)
Median (Q1-Q3)	14 (8-16)
Range (Min-Max)	1-26

24-hour NIHSS

Mean $\pm$ SD	6.6 $\pm$ 7.3 (26)
Median (Q1-Q3)	3 (1-8)
Range (Min-Max)	0-27

NIHSS at Discharge or Day 5-7, whichever is earlier

Mean $\pm$ SD	5.2 $\pm$ 7.8 (20)
Median (Q1-Q3)	1.5 (1-7)
Range (Min-Max)	0-27

ITT indicates intention to treat, **N**: number, **TICI**: thrombolysis in cerebral infarction, **SD**: standard deviation, **Min**: minimum, **Max**: maximum