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Thrombectomy for Primary Distal Posterior Cerebral Artery Occlusion Stroke
The TOPMOST Study

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Supplemental content

IMPORTANCE Clinical evidence of the potential treatment benefit of mechanical thrombectomy for posterior circulation distal, medium vessel occlusion (DMVO) is sparse.

OBJECTIVE To investigate the frequency as well as the clinical and safety outcomes of mechanical thrombectomy for isolated posterior circulation DMVO stroke and to compare them with the outcomes of standard medical treatment with or without intravenous thrombolysis (IVT) in daily clinical practice.

DESIGN, SETTING, AND PARTICIPANTS This multicenter case-control study analyzed patients who were treated for primary distal occlusion of the posterior cerebral artery (PCA) of the P2 or P3 segment. These patients received mechanical thrombectomy or standard medical treatment (with or without IVT) at 1 of 23 comprehensive stroke centers in Europe, the United States, and Asia between January 1, 2010, and June 30, 2020. All patients who met the inclusion criteria were matched using 1:1 propensity score matching.

INTERVENTIONS Mechanical thrombectomy or standard medical treatment with or without IVT.

MAIN OUTCOMES AND MEASURES Clinical end point was the improvement of National Institutes of Health Stroke Scale (NIHSS) scores at discharge from baseline. Safety end point was the occurrence of symptomatic intracranial hemorrhage and hemorrhagic complications were classified based on the Second European-Australasian Acute Stroke Study (ECASSII). Functional outcome was evaluated with the modified Rankin Scale (mRS) score at 90-day follow-up.

RESULTS Of 243 patients from all participating centers who met the inclusion criteria, 184 patients were matched. Among these patients, the median (interquartile range [IQR]) age was 74 (62-81) years and 95 (51.6%) were female individuals. Posterior circulation DMVOs were located in the P2 segment of the PCA in 149 patients (81.0%) and in the P3 segment in 35 patients (19.0%). At discharge, the mean NIHSS score decrease was −2.4 points (95% CI, −3.2 to −1.6) in the standard medical treatment cohort and −3.9 points (95% CI, −5.4 to −2.5) in the mechanical thrombectomy cohort, with a mean difference of −1.5 points (95% CI, 3.2 to −0.8; *P* = .06). Significant treatment effects of mechanical thrombectomy were observed in the subgroup of patients who had higher NIHSS scores on admission of 10 points or higher (mean difference, −5.6; 95% CI, −10.9 to −0.2; *P* = .04) and in the subgroup of patients without IVT (mean difference, −3.0; 95% CI, −5.0 to −0.9; *P* = .005). Symptomatic intracranial hemorrhage occurred in 4 of 92 patients (4.3%) in each treatment cohort.

CONCLUSIONS AND RELEVANCE This study suggested that, although rarely performed at comprehensive stroke centers, mechanical thrombectomy for posterior circulation DMVO is a safe, and technically feasible treatment option for occlusions of the P2 or P3 segment of the PCA compared with standard medical treatment with or without IVT.

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Given the latest advances in catheter technology and the development of smaller thrombectomy devices together with increasing neuroendovascular expertise, distal, medium vessel occlusion (DMVO) has been declared as a potential frontier in endovascular treatment (EVT) of acute ischemic stroke.[1,2] Although results from several past pivotal thrombectomy trials support the benefit of mechanical thrombectomy for DMVO within the anterior circulation,[3] clinical evidence of EVT for posterior circulation DMVO is still sparse,[4] even though isolated occlusions of the posterior cerebral artery (PCA) account for approximately 5% to 10% of all ischemic strokes.[5]

Because of the variability of vascular anatomy, isolated posterior circulation DMVO may be associated with wide-ranging neuropsychological symptoms[6] that lead to delayed hospital admission and subsequent ineligibility for thrombolytic therapy options, especially in patients presenting with minor deficits.[7] However, because of the vascular supply of eloquent brain areas (eg, the primary visual cortex and the thalami), stroke caused by posterior circulation DMVO can lead to acute, severe, and permanent disability with substantial impact on quality of life.[6,8,9]

In the absence of clear, guideline-based treatment recommendations for posterior circulation DMVO stroke,[10-12] a multi-institutional, international consensus statement was recently published that highlights the clinical relevance and urgent need for evidence of the potential benefit of mechanical thrombectomy in this subgroup of patients.[13]

This international, retrospective multicenter case-control study aimed to investigate the frequency as well as clinical and safety outcomes of mechanical thrombectomy for isolated posterior circulation DMVO stroke of the PCA P2 and P3 segments and to compare them with the outcomes of standard medical treatment with or without intravenous thrombolysis (IVT) in daily clinical practice.

Key Points

Question Is mechanical thrombectomy for ischemic stroke attributed to primary distal occlusion of the posterior cerebral artery of the P2 or P3 segment safe, technically feasible, and associated with clinical benefits compared with standard medical treatment alone?

Findings In this case-control study of 184 patients, endovascular treatment appeared to be safe (symptomatic intracerebral hemorrhage) and technically feasible (proportion of successful recanalization) and showed early clinical treatment benefits on the National Institutes of Health Stroke Scale, compared with standard medical treatment alone.

Meaning Results of this study suggest that, among patients who experienced stroke attributed to primary distal occlusion of the posterior cerebral artery of the P2 or P3 segment, mechanical thrombectomy is a reasonable, safe and technically feasible therapy option.

Methods

The study was approved by the ethics committee of Hamburg, Germany (Chamber of Physicians, Hamburg), in accordance with the Declaration of Helsinki.[14] The requirement for patient informed consent was waived by the ethics committee because of the retrospective nature of the study design. Each of the 23 participating centers obtained ethical approval according to their local protocol for sharing retrospective and fully anonymized data.

Study Cohort

This retrospective, multicenter, case-control study included patients who were treated between January 1, 2010, and June 30, 2020, at 1 of the 23 comprehensive stroke centers in Europe, United States, and Asia (University Medical Center Hamburg-Eppendorf, Hamburg, Germany; University Hospital Muenster, Muenster, Germany; Alfried-Krupp Hospital Essen, Essen, Germany; University Hospital Basel, Basel, Switzerland; Klinikum Rechts der Isar, School of Medicine, Technical University Munich, Munich, Germany; University Hospitals, Ludwig-Maximilians-Universität München, Munich, Germany; University of Cologne, Cologne, Germany; University Hospital Goettingen, Goettingen, Germany; Universitätsklinikum Knappschaftskrankenhaus Bochum, Universitätsklinik der Ruhr-Universität Bochum, Bochum, Germany; Heidelberg University Hospital, Heidelberg, Germany; University Hospital Rostock, Rostock, Germany; Johanna-Étienne-Hospital, Neuss, Germany; Charité Universitätsmedizin Berlin, Berlin, Germany; Klinikum Osnabrück, Osnabrück, Germany; National University Health System, Singapore; Centre Hospitalier Régional Universitaire de Nancy, Nancy, France; Hospital Clínico Universitario de Valladolid, Valladolid, Spain; New York Langone Medical Center, New York; Karolinska Institutet, Stockholm, Sweden; Hospital Bremen-Mitte, Bremen, Germany; Westpfalz-Klinikum, Kaiserslautern, Germany; Hospital Universitario La Paz, Madrid, Spain; and Inselspital, Bern University Hospital, Bern, Switzerland). All participating centers were invited to review their prospectively collected stroke databases and provide data on all consecutively treated patients who received mechanical thrombectomy or standard medical treatment with or without IVT for primary distal occlusions of the PCA for inclusion in the TOPMOST (treatment for primary distal, medium vessel occlusion stroke) registry.

The main inclusion criteria were as follows: (1) diagnosis of an acute ischemic stroke attributed to an isolated occlusion within distal medium-sized vessel segments of the PCA; (2) stroke involving the P2 segment (from the PCA branch point of the posterior communicating artery, curving around the midbrain within the ambient cistern, to the beginning of the quadrigeminal cistern) and P3 segment (from the entrance point of the quadrigeminal cistern through its lateral aspect to the anterior limit of the calcarine fissure)[15-17]; and (3) receipt of either mechanical thrombectomy with approved devices (ie, aspiration catheters or stent retrievers) or standard medical treatment with or without IVT, in accordance with guideline recommendations. eFigure 1 in the Supplement provides a flowchart of the patient inclusion criteria.

Of the 313 patients who were treated for posterior circulation DMVO, 243 met the inclusion criteria. After 1:1 propensity score matching (PSM), 184 patients were compared by treatment group.

Baseline data, including age, sex, initial National Institutes of Health Stroke Scale (NIHSS) score, and administration of IVT and detailed therapeutic parameters, were obtained from patients' clinical records and imaging at admission and follow-up. The cause of stroke was ascertained using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification.[18]

Diagnostic Imaging and Procedural Analysis

Imaging workflows for detecting posterior circulation DMVO, excluding intracerebral hemorrhage, depended on the local centers' acute stroke imaging protocol and included magnetic resonance imaging or computed tomography with computed tomography angiography and perfusion. Endovascular reperfusion was assessed through angiography, with the modified Thrombolysis in Cerebral Infarction (mTICI) scale-graded analogue to the anterior circulation defining an mTICI score of 2b as at least 50% reperfusion of the hypoperfused territory distal to the target occlusion.[19] The number of thrombectomy maneuvers were counted and their outcomes and complications were analyzed. In addition, a first-pass effect was defined as an mTICI score of 3 after the first endovascular reperfusion maneuver.[20] Further procedural feasibility assessment included the procedural time (groin puncture to final reperfusion status); the rate of intervention-related serious adverse events, such as iatrogenic dissections or perforations; and the distal embolization within and without the treated vascular territory.

Clinical and Safety Outcomes

Early clinical benefits of treatment were evaluated by the mean and median changes of NIHSS scores from baseline to discharge. Adjusted for moderately severe stroke, early neurological improvement (ENI) was specified in a binary fashion as an improvement in NIHSS scores of at least 4 points or reaching 0 points.[21] Functional outcome was assessed with the modified Rankin Scale (mRS) score at the 90-day follow-up, with excellent functional outcome defined as an mRS score of 1 point or lower and favorable functional outcome as an mRS score of 2 points or lower. Mortality rates were assessed during hospitalization and at the 90-day follow-up. The occurrence of intracerebral hemorrhage was analyzed, and hemorrhagic complications were classified as symptomatic in accordance with the Second European-Australasian Acute Stroke (ECASS II) Study.[22]

Statistical Analysis

Standard descriptive statistics were used for all study end points. Univariable distribution of metric variables was described with median and interquartile range (IQR) and categorical variables with absolute and relative frequencies. Bootstrapping was used to calculate the CI of the relative frequency of performed endovascular procedures for posterior circulation DMVO.

To reduce the possibility of selection bias, we performed PSM to adjust for covariates of baseline variables. The propensity score was estimated using a logistic regression model adjusted for age, sex, and NIHSS score on admission (eMethods in the Supplement). We performed 1:1 propensity score matching without replacement based on the nearest-neighbor matching algorithm with a caliper width of 0.2. Before and after PSM, we used a graphical comparison to assess the distributional similarity between propensity score distributions (eFigure 2 in the Supplement). A sensitivity analysis was performed and each adjusted covariate was plotted against the estimated propensity score, stratified by treatment status (eFigure 3 in the Supplement).

After PSM, we compared baseline characteristics and outcome variables by using the χ^2 tests for categorical variables and the Mann-Whitney test (non-normally distributed data) and unpaired, 2-tailed *t* test (normally distributed data) for ordinal and continuous variables. Early clinical improvement was analyzed by mean differences using the 2-sample *t* test based on original data and stratified by baseline NIHSS score (≥10, 9-6, or ≤5 points), age (<70 years or ≥70 years), sex (male or female), and IVT (yes or no). Multivariable logistic regression analysis was performed to identify the independent factors in early neurological recovery. Odds ratio (OR) with 95% CI and *P* value of likelihood ratio test were calculated for selected variables. No adjustment for multiple testing was performed, and the analyses were regarded as explorative. Local, unadjusted 2-sided $P < .05$ was considered to be statistically significant. Statistical analyses were carried out with SPSS, version 26 (IBM Corporation), and R (R Foundation for Statistical Computing).

Results

Baseline Characteristics

A total of 243 patients from all participating centers were included in the study, of whom 143 (58.8%) received mechanical thrombectomy and 100 (41.2%) received standard medical treatment with or without IVT. **Table 1** provides a detailed overview of patients' baseline characteristics before and after PSM with adjustment for age, sex, and NIHSS scores on admission. After PSM (n = 184), the median (IQR) age of participants was 74 (62-81) years, and 89 male (48.4%) and 95 female (51.6%) individuals were included. At hospital admission, the median (IQR) NIHSS score was 5 (3-10) points.

The most common cardiovascular risk factors were arterial hypertension (144 of 184 [78.3%]) and atrial fibrillation (66 of 184 [35.9%]). Diabetes as a cardiovascular risk factor was significantly higher in the standard medical treatment cohort vs the mechanical thrombectomy cohort (30 of 92 [32.6%] vs 14 of 92 [15.2%]; *P* = .006). The most frequently observed cause of stroke was cardioembolic (68 of 184 [37.4%]). Posterior circulation DMVOs were located in the P2 segment of the PCA in 149 patients (81.0%) and in the P3 segment in 35 patients (19.0%), including 8 patients (4.3%) with fetal variants and 7 patients (3.8%) with bilateral occlusions. Additional basilar artery branch occlusions occurred in 4 cases involving the

Table 1. Baseline and Procedural Patient Characteristics Compared by Treatment Arm Before and After Propensity Score Matching

Baseline characteristic	Before PSM No. (%) All patients (n = 243)	Before PSM No. (%) Mechanical thrombectomy cohort (n = 143)	Before PSM No. (%) Standard medical treatment cohort (n = 100)	Before PSM *P* value	After PSM No. (%) All patients (n = 184)	After PSM No. (%) Mechanical thrombectomy cohort (n = 92)	After PSM No. (%) Standard medical treatment cohort (n = 92)	After PSM *P* value
Patient characteristics								
Age, median (IQR), y	75 (62-81)	75 (62-81)	75 (62-81)	.92	74 (62-81)	74 (62-81)	74 (62-81)	.95
Female sex	114 (46.9)	64 (44.8)	50 (50.0)	.42	95 (51.6)	45 (48.9)	50 (54.3)	.46
Cardiovascular risk factors								
Atrial fibrillation	88 (36.2)	52 (36.4)	36 (36.0)	.95	66 (35.9)	33 (35.9)	33 (35.9)	.99
Arterial hypertension	189 (77.8)	107 (74.8)	82 (82.0)	.18	144 (78.3)	70 (76.1)	74 (80.4)	.47
Diabetes	59 (24.3)	26 (18.2)	33 (33.0)	.008[a]	44 (23.9)	14 (15.2)	30 (32.6)	.006[a]
Dyslipidemia	109 (44.9)	60 (42.0)	49 (49.0)	.27	78 (42.4)	35 (38)	43 (46.7)	.23
Prestroke mRS score, median (IQR)	0 (0-1)	0 (0-1)	0 (0-2)	.48	0 (0-3)	0 (0-2)	0 (0-3)	.62
Missing data, No.	25	25	11	NA	NA	NA	NA	NA
Admission NIHSS score, median (IQR)	6 (3-10)	7 (4-11)	5 (2-10)	.02[a]	5 (3-10)	5.5 (3-10)	5 (2-10)	.44
Occlusion site								
P2 segment[b]	199 (81.9)	120 (83.9)	79 (79.0)	.32	149 (81.0)	75 (81.5)	74 (80.4)	.85
P3 segment[c]	44 (18.1)	23 (16.1)	21 (21.0)		35 (19.0)	17 (18.5)	18 (19.6)	NA
Fetal variant	15 (6.2)	14 (9.8)	1 (1.0)		8 (4.3)	7 (7.6)	1 (1.1)	NA
Bilateral	8 (3.3)	7 (4.9)	1 (1.0)		7 (3.8)	6 (6.5)	1 (1.1)	NA
TOAST classification								
Large-artery atherosclerosis	36 (18.0)	15 (13.2)	21 (24.4)	.06	32 (21.5)	11 (15.5)	21 (26.9)	.98
Cardioembolic	95 (47.5)	57 (50.0)	38 (44.2)	.41	68 (37.4)	33 (46.9)	35 (44.9)	.84
Small-artery occlusion	NA	NA	NA	NA	NA	NA	NA	NA
Other determined cause	13 (6.5)	7 (6.1)	6 (7.0)	.81	11 (7.4)	11 (8.5)	5 (6.4)	.07
Undetermined cause	56 (28.0)	35 (30.7)	21 (24.0)	.16	38 (25.5)	21 (29.6)	17 (21.8)	.27
Missing data, No.	NA	29	14	NA	35	21	14	NA
Time from symptom onset to groin puncture, median (IQR), min								
Groin puncture	NA	197 (148-277)	NA	NA	NA	197 (148-277)	NA	NA
Imaging	NA	NA	145 (102-216)	NA	NA	NA	141 (104-216)	NA
IVT	NA	NA	154 (120-218)	NA	NA	NA	151 (120-201)	NA
Missing data, No.	NA	30 (onset to groin puncture)	Imaging: 17; IVT: 45	NA	NA	NA	Imaging: 17; IVT: 45	NA
Procedural characteristics								
IVT	113 (46.5)	57 (39.9)	56 (56.0)	.01[a]	45 (48.9)	37 (40.2)	53 (57.6)	.01[a]
Anesthesia								
Local anesthesia	NA	18 (12.8)	NA	NA	NA	NA	NA	NA
Conscious sedation	NA	62 (43.4)	NA	NA	NA	NA	NA	NA
General anesthesia	NA	61 (43.3)	NA	NA	NA	NA	NA	NA
Missing data	NA	2	NA	NA	NA	NA	NA	NA
Interventional duration, median (IQR), min	NA	38.5 (23-62)	NA	NA	NA	NA	NA	NA
No. of recanalization attempts, median (IQR)	NA	1 (1-2)	NA	NA	NA	NA	NA	NA

(continued)

Table 1. Baseline and Procedural Patient Characteristics Compared by Treatment Arm Before and After Propensity Score Matching (continued)

Baseline characteristic	Before PSM, No. (%): All patients (n = 243)	Mechanical thrombectomy cohort (n = 143)	Standard medical treatment cohort (n = 100)	P value	After PSM, No. (%): All patients (n = 184)	Mechanical thrombectomy cohort (n = 92)	Standard medical treatment cohort (n = 92)	P value
Recanalization degree								
mTICI score ≤2a	NA	18 (12.6)	NA	NA	NA	NA	NA	NA
mTICI score ≥2b/3	NA	125 (87.4)	NA	NA	NA	NA	NA	NA
First-pass thrombectomy method	NA							
Stent retriever (+/− aspiration)	NA	103 (72.0)	NA	NA	NA	NA	NA	NA
Primary aspiration	NA	38 (26.6)	NA	NA	NA	NA	NA	NA
Intra-arterial recombinant tPA administration	NA	2 (1.4)	NA	NA	NA	NA	NA	NA

Abbreviations: IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; NA, not applicable; NIHSS, National Institutes of Health Stroke Scale; PSM, propensity score matching; tPA, tissue plasminogen activator; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

[a] Indicating statistical significance.

[b] P2 segment begins from the posterior cerebral artery branch point of the posterior communicating artery, curving around the midbrain within the ambient cistern, to the beginning of the quadrigeminal cistern.

[c] P3 segment begins from the entrance point of the quadrigeminal cistern, through its lateral aspect, to the anterior limit of the calcarine fissure.

superior cerebellar artery and the posterior inferior cerebellar artery (eTable in the Supplement).

In comparison to the mechanical thrombectomy cohort, the standard medical treatment cohort received significantly more IVT before PSM (57 of 143 [39.9%] vs 56 of 100 [56.0%]; *P* = .01) and after PSM (37 of 92 [40.2%] vs 53 of 92 [57.6%]; *P* = .01). In the mechanical thrombectomy cohort, the median (IQR) time from onset to groin puncture was 197 (148-277) minutes. In the standard medical treatment cohort, the median (IQR) time from onset to imaging was 141 (104-216) minutes and to IVT application was 151 (120-201) minutes.

Endovascular Outcome and Complications

The frequency of patients who received mechanical thrombectomy for posterior circulation DMVO vs all stroke thrombectomies during the study period at the participating center was 1.6% (143 of 9184; 95% CI, 1.33-1.83). Mechanical thrombectomy was performed under general anesthesia in 61 of 141 patients (43.3%). Intra-arterial thrombolysis was administered with mechanical thrombectomy in 4 cases and without mechanical thrombectomy as a primary treatment strategy in 2 cases. The first-pass thrombectomy technique was a stent retriever with or without additional aspiration in 103 of 143 patients (72.0%) and with distal direct aspiration in 38 of 143 patients (26.6%). The median (IQR) time from groin puncture to the final recanalization result was 38.5 (23-62) minutes.

In 65 of 143 patients (45.5%), a successful first-pass effect led to complete reperfusion (mTICI 3). Additional endovascular reperfusion attempts increased the overall rate of an mTICI 3 score to 76.2% (109 of 143) with a median (IQR) number of 1 (1-2) mechanical thrombectomy maneuver. The angiographic outcomes of an mTICI 2b score were reported in 16 of 143 patients (11.2%) and of an mTICI 2a or lower score in 18 of 143 patients (12.6%). In cases with bilateral occlusions, complete reperfusion was achieved in all patients. One case (1 of 143 [0.7%]) of iatrogenic dissection within the P2 segment became hemodynamically relevant and was treated with emergency stenting the day after the intervention (**Figure 1**). Additional iatrogenic dissections (3 cases) were located in proximal arteries of the posterior circulation (eTable in the Supplement). Two cases (1.4%) of iatrogenic perforation occurred (1 in P2 segment and 1 in P3 segment).

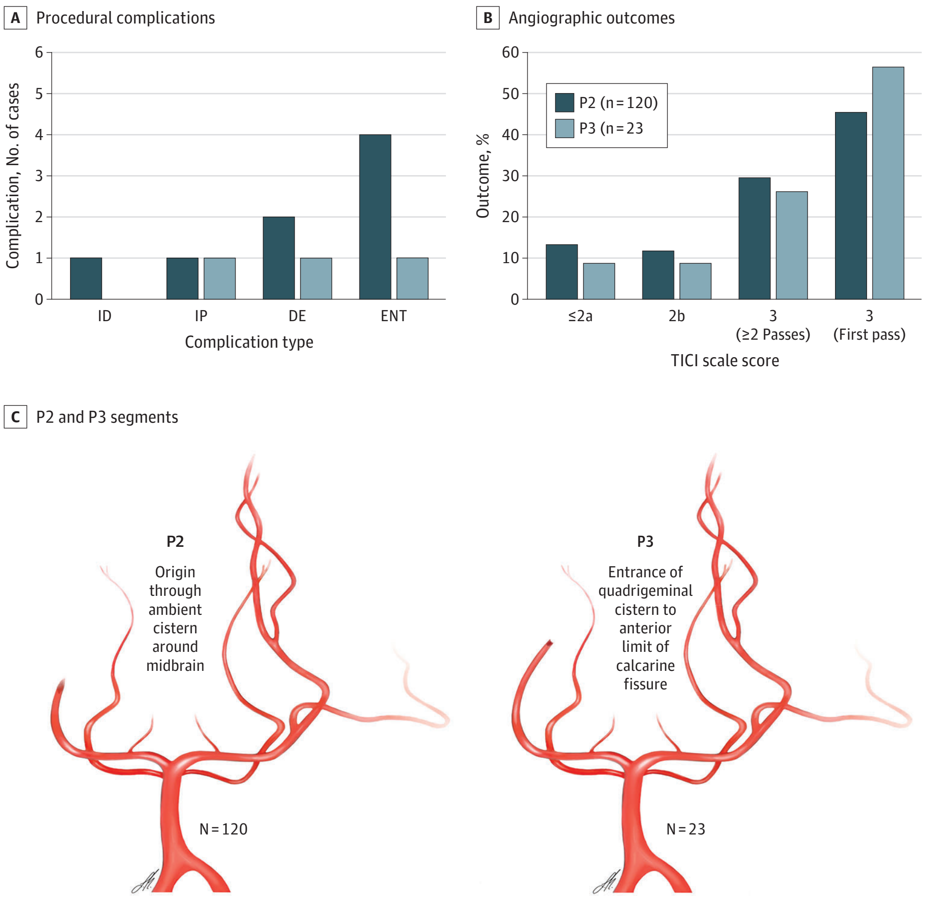
In 5 of 143 patients (3.5%), a distal embolization to a new vessel territory occurred, of which 2 occlusions of the superior cerebellar artery and 1 occlusion of the posterior inferior cerebellar artery were successfully recanalized with mechanical thrombectomy. Periprocedural downstream emboli occurred in 3 cases (2.1%). Figure 1 provides an overview of the complications and angiographic outcomes grouped by occlusion site.

Clinical and Functional End Points

After PSM (**Table 2**), the median (IQR) baseline NIHSS score had decreased at discharge to −2 (−5 to −1) points in the mechanical thrombectomy cohort and −1.5 (−4.2 to 0) points in the standard medical treatment cohort (*P* = .06). The binary ENI was observed in 36 of 85 patients (42.4%) in the mechanical thrombectomy cohort and 32 of 86 (37.2%) in the standard medical treatment cohort (*P* = .49) (Table 2).

Figure 2 shows the mean differences in NIHSS score decrease from admission to discharge within and across each cohort, stratified by sex (female or male), age (<70 or ≥70 years), occlusion site (P2 or P3), stroke severity (NIHSS score ≥10, 9-6, or ≤5 points), and application of IVT (yes or no). At discharge, the mean NIHSS score decrease was −2.4 points (95% CI, −3.2 to −1.6) in the standard medical treatment cohort and −3.9

Figure 1. Endovascular Complications and Angiographic Outcomes Stratified by Vessel Segment



The P2 vessel segment begins from the posterior cerebral artery branch point of the posterior communicating artery, curving around the midbrain within the ambient cistern, to the beginning of the quadrigeminal cistern. The P3 vessel segment begins from the entrance point of the quadrigeminal cistern, through its lateral aspect, to the anterior limit of the calcarine fissure. DE indicates downstream emboli; ENT, emboli to new territory; ID, iatrogenic dissection; IP, iatrogenic perforation; and TICI, Thrombolysis in Cerebral Infarction.

points (95% CI, −5.4 to −2.5) in the mechanical thrombectomy cohort, with a mean difference of −1.5 points (95% CI, 3.2 to −0.8; *P* = .06). The mean difference in NIHSS score decrease was significantly higher in the mechanical thrombectomy cohort vs standard medical treatment cohort for the subgroup of patients with NIHSS score of 10 points or higher on admission (mean difference, −5.6; 95% CI, −10.9 to −0.2; *P* = .04) and for patients who were not eligible for IVT (mean difference, −3.0; 95% CI, −5.0 to 0.9; *P* = .005).

In other cohort subgroup analysis, the median (IQR) NIHSS score did not decrease significantly from admission to discharge in patients with an mTICI of 2a or lower reperfusion in the mechanical thrombectomy cohort (from 9 [5-13] to 5 [2-11] points; *P* = .13) (eFigure 4 in the Supplement) and in patients who were not eligible for IVT in the standard medical treatment cohort (from 2 [1-4] to 2 [0-4] points; *P* = .39) (eFigure 5 in the Supplement).

In multivariable logistic regression analysis for ENI within the mechanical thrombectomy cohort, higher NIHSS scores on admission (adjusted OR [aOR], 1.19; 95% CI, 1.08-1.31; *P* < .001) and a successful first-pass effect (aOR, 2.32; 95% CI, 1.03-5.20; *P* = .04) were independent factors in reaching ENI (eFigure 6 in the Supplement). In multivariable logistic regression analysis for ENI within the standard medical treatment cohort, P3 occlusions were independently significant (aOR, 4.25; 95% CI, 1.27-14.22; *P* = .02), and IVT showed an association with reaching ENI (aOR, 2.69; 95% CI, 0.98-7.37; *P* = .054) (eFigure 7 in the Supplement).

At 90-day follow-up, excellent functional outcomes (mRS ≤1) were observed in 51 of 77 patients (66.2%) in the mechanical thrombectomy cohort and 31 of 57 patients (54.4%) in the standard medical treatment cohort. Overall, mRS score distributions did not differ significantly between the 2 cohorts at 90-day follow-up (median [IQR] mRS score, 1 [0-2] points vs 0 [1-2.5] points; *P* = .26) (**Figure 3**).

Safety End Points

Postinterventional complications included 4 of 92 patients (4.3%) with symptomatic intracerebral hemorrhage in each of the cohorts. After PSM, the overall mortality in both cohorts was 4.9% (9 of 183) for in-hospital rates and 13.4% (18 of 134) at 90-day follow-up, including 3 patients in the mechanical thrombectomy cohort who died from a non-stroke-related causes (eTable in the Supplement). Mortality rates did not differ significantly between the treatment groups (Table 2). The highest relative mortality rates were observed in patients who had an NIHSS score of 10 or higher on admission, had an mTICI score of 2a or lower, and received standard medical treatment with ineligibility for IVT (eFigures 2 and 3 in the Supplement).

Table 2. Main Outcome and Safety Parameter Compared by Treatment Group Before and After Propensity Score Matching

	Before PSM			After PSM		
	No. (%)			No. (%)		
Outcome	Mechanical thrombectomy cohort (n = 143)	Standard medical treatment cohort (n = 100)	*P* value	Mechanical thrombectomy cohort (n = 92)	Standard medical treatment cohort (n = 92)	*P* value
NIHSS score change						
Mean (SD)	−4.0 (6.4)	−2.4 (3.9)	.02[a]	−3.9 (6.7)	−2.4 (3.6)	.06
Median (IQR)	−3 (−6 to −1)	−1 (−4 to 0)	.005[a]	−2 (−5 to −1)	−1.5 (−4.2 to 0)	.06
Binary ENI	73 (56.6)	41 (43.6)	.056	36 (42.4)	32 (37.2)	.49
mRS score at 90-d follow-up						
0-1	72 (66.1)	29 (50.9)	.057	51 (66.2)	31 (54.4)	.16
0-2	86 (78.9)	41 (71.9)	.31	59 (76.6)	43 (75.4)	.87
Safety outcomes						
sICH	5 (3.5)	4 (4)	.83	4 (4.3)	4 (4.3)	>.99
Mortality						
In-hospital	7 (5.6)	5 (9.1)	>.99	4 (4.4)	5 (5.4)	>.99
At 90-d follow-up	12 (11)	9 (17.5)	.23	9 (11.8)	9 (15.8)	.40

Abbreviations: ENI, early neurological improvement; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PSM, propensity score matching; sICH, symptomatic intracerebral hemorrhage.

[a] Indicating statistical significance.

Discussion

This retrospective, multicenter case-control study investigated the frequency as well as clinical and safety outcomes of mechanical thrombectomy compared with those of standard medical treatment for isolated posterior circulation DMVO. The study has several findings: (1) mechanical thrombectomy for posterior circulation DMVO within the P2 and P3 segments was rarely performed in daily clinical practice; (2) the endovascular procedure seemed to be safe and showed no increased risks for intracerebral hemorrhage in comparison to standard medical treatment; (3) a pattern of substantial early clinical recovery after thrombectomy was observed across most subgroups, including patients with mild deficits (NIHSS score of 0-5 points) and especially patients with higher NIHSS scores (≥10 points) on admission vs those who were not eligible for IVT within the standard medical treatment cohort; and (4) if eligible for IVT, patients in the standard medical treatment cohort also had a substantial improvement in NIHSS scores.

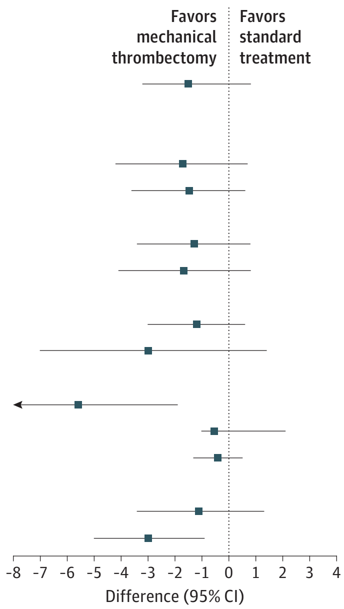
Patients who experienced acute ischemic stroke associated with distal occlusions in medium-sized vessel segments appear to be (until randomized results become available) one of the last subgroups of patients who may benefit from EVT.[1] Despite case reports[23] and a small case series (n = <20),[4,24-26] a large systematic analysis of consecutively treated patients with posterior circulation DMVO has not been published yet. Accordingly, we observed a comparatively low prevalence (1.6%) of mechanical thrombectomy for posterior circulation DMVO as measured by the total number of thrombectomy cases from all participating comprehensive stroke centers during the inclusion period of this study. This finding has a likely 4-fold explanation: (1) the absence of clear guideline recommendations for patients with DMVO and (2) patients with relatively mild stroke deficits (NIHSS score of ≤5 points) commonly seen in posterior circulation DMVO, as well as (3) the overall low incidence of patients presenting at neuroendovascular centers with isolated posterior circulation DMVO that is partially associated with (4) a variety of symptoms, which often lead to delayed hospital admissions outside of currently applied time windows for therapeutic reperfusion options.

Currently in daily clinical practice, substantial restraint remains in providing EVT to patients with mild deficits, particularly patients who are eligible for IVT.[27] However, typical symptoms of infarcts in the territory of the PCA, such as hemianopia, may be associated with substantial restrictions in quality of life.[9] The NIHSS score is weighted toward anterior circulation deficits and does not represent the entire spectrum of posterior circulation stroke symptoms that substantially lower NIHSS cutoff values for estimating long-term outcomes compared with the anterior circulation.[28] On the basis of this systematic exclusion of patients for whom acute reperfusion therapies could be beneficial,[29] a considerable number of patients are discharged with poor outcomes despite low NIHSS scores.[30]

The data from this study suggested the potential clinical benefit of mechanical thrombectomy compared with standard medical treatment (mean NIHSS score difference, −1.5; 95% CI, −3.2 to 0.8; *P* = .06). This possibility was especially visible in patients in the standard medical treatment cohort who were not eligible for IVT (mean NIHSS score difference, −3.0; 95% CI, −5.0 to 0.9; *P* = .005) and was an important finding given that patients who experienced posterior circulation DMVO often present at the hospital later than 4.5 hours after onset.[5] However, patients from the standard medical treatment cohort who were eligible for IVT, as the current standard of care for DMVOs, did gain a substantial benefit from the treatment. Nevertheless, even in patients with initial NIHSS scores of 5 points or lower, we did not observe a potential harmful treatment effect associated with mechanical thrombec-

Figure 2. Early Clinical Outcome at Discharge

Group	No. of patients		Change in NIHSS score			P value
	Mechanical thrombectomy	Standard treatment	Mechanical thrombectomy (95% CI)	Standard treatment 95% CI)	Difference (95% CI)	
All patients	85	86	-3.9 (-5.4 to -2.5)	-2.4 (-3.1 to -1.2)	-1.5 (-3.2 to 0.8)	.06
Subgroup						
Sex						
Female	41	37	-3.8 (-6.1 to -1.5)	-2.1 (-3.1 to -1.1)	-1.7 (-4.2 to 0.7)	.16
Male	44	49	-4.0 (-5.9 to -2.1)	-2.6 (-3.8 to -1.4)	-1.4 (-3.6 to 0.8)	.19
Age, y						
<70	36	33	-4.3 (-6.0 to -2.6)	-3.0 (-4.3 to -1.6)	-1.3 (-3.4 to 0.8)	.23
≥70	49	53	-3.7 (-5.9 to -1.4)	-2.0 (-3.0 to -1.0)	-1.7 (-4.1 to 0.8)	.18
Occlusion site						
P2	70	69	-3.6 (-5.2 to -2.1)	-2.4 (-3.3 to -1.5)	-1.2 (-3.0 to 0.6)	.18
P3	15	17	-5.2 (-9.3 to -1.1)	-2.2 (-4.0 to -0.4)	-3.0 (-7.0 to 1.1)	.14
NIHSS score						
≥10	21	22	-9.5 (-14.3 to -4.6)	-3.9 (-6.4 to -1.4)	-5.6 (-10.9 to -0.2)	.04
9-6	19	17	-4.2 (-5.3 to -3.0)	-4.7 (-5.8 to -3.6)	-0.5 (-1.0 to 2.1)	.48
≤5	45	47	-1.2 (-2.1 to -0.3)	-0.8 (-1.3 to -0.4)	-0.4 (-1.3 to 0.6)	.40
IVT						
Yes	33	48	-5.3 (-7.4 to -3.1)	-4.2 (-5.3 to -3.2)	-1.1 (-3.4 to 1.3)	.37
No	52	38	-3.1 (-5.0 to -1.1)	-0.5 (-0.7 to -6.0)	-3.0 (-5.0 to -0.9)	.005



Improvement of National Institutes of Health Stroke Scale (NIHSS) scores and differences were compared by treatment group and stratified by subgroups. IVT indicates intravenous thrombolysis.

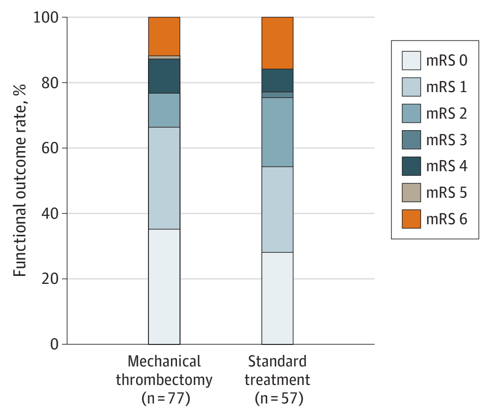
tomy, and accordingly only 6 of 58 patients experienced an NIHSS score relevant to worsening of symptoms in this subgroup (eTable in the Supplement).

These findings suggest that mechanical thrombectomy for posterior circulation DMVO should not be withheld from this subgroup solely on the basis of NIHSS score on admission. Contrary to the generally expected clinical presentation of patients with posterior circulation DMVO, in 71 cases (43 in the EVT cohort, and 23 in the standard medical treatment cohort) the NIHSS score on admission was higher than 9 points. This finding seemed to be partially associated with the angioarchitectural variability of perforators supplying the thalamic nuclei from the P2 and P3 segments, underlining the potential clinical severity of isolated posterior circulation DMVO stroke. Although considered as an exclusion criterion, an initial large vessel occlusion (LVO) with preimaging clot migration ultimately cannot be excluded in these cases. However, in this LVO-alike subgroup, we observed a significant treatment effect of mechanical thrombectomy over standard medical treatment.

Corroborating the results of previous studies, a successful first-pass effect associated with complete reperfusion was an independent factor (aOR, 2.32; 95% CI, 1.03-5.20; $P = .04$) for ENI in the mechanical thrombectomy cohort. This finding emphasizes once more that technical success is associated with high treatment effects (compared with achieving complete reperfusion after multiple attempts) and that first-pass effect remains one of the most valuable therapy goals in endovascular stroke treatment, regardless of the occlusion site.[20,31]

In this study, rates of excellent functional outcome did not differ significantly in both treatment groups at 90-day follow-up but exceeded the results of previous randomized clinical trials (RCTs).[32] This finding is explained by the mild stroke symptoms of posterior circulation DMVO compared with proximal LVO stroke. In addition, the mRS as a global functional outcome scale, with a focus on motor deficits, does not appropriately reflect neurological recovery after a posterior circulation stroke. Currently, defining a valid mRS-based study end point for DMVO seems complicated without the results of RCTs that are stratified by vessel segment.[13] Despite having clear enrollment criteria, future DMVO RCTs will need to have detailed circulation adjustments in stroke assessment and outcome scales,

Figure 3. Modified Rankin Scale (mRS) Scores at 90 Days



Functional outcome rates (mRS) at 90 days were stratified and compared by treatment status after propensity score matching.

especially for posterior circulation DMVO, to better capture and compare the treatment effects in subgroups who are at risk for a neutral trial result.[33] Emphasizing the safety of the endovascular procedure, no differences were found between the in-hospital (4.9%) and 90-day follow-up (11.0%) mortality rates in this study and the mortality rates in the registry data of the Athens Stroke Outcome Project, which reported on isolated PCA stroke treated with standard medical treatment only (10% mortality).[5] We observed in both treatment cohorts the highest mortality rates in patients with higher NIHSS scores on admission and partial reperfusion after mechanical thrombectomy, which supports previous findings (eFigures 2 and 3 in the Supplement).[34,35]

The fragility of distal smaller-sized vessels has always been a major concern in endovascular stroke treatment because of its increased risk for complications that lead to intracerebral hemorrhage and are associated with poor outcomes, especially in patients who are eligible for IVT.[36] The present multicenter analysis did not substantiate this concern. Conversely, we observed similar rates of symptomatic bleeding events in both treatment cohorts (4.3%) that did not exceed the results of previous thrombectomy RCTs and large registry data on anterior LVO strokes.[3,32,37] Furthermore, underlining the safety of EVT, the frequencies of iatrogenic complications (ie, dissections), and perforations or periprocedural thrombi fragmentation leading to new distal emboli inside and outside of the treated territory were comparable to those in previous studies on LVO stroke.[38-41] The final numbers of emboli to new territory even decreased from 5 to 2 after successful endovascular reperfusion of 3 basilar artery branch occlusions (eTable in the Supplement), which may be considered as an endovascular target, as recently reported.[42] An RCT that compares mechanical thrombectomy with standard medical treatment is warranted to evaluate thrombectomy for posterior circulation DMVO and to resolve clinical equipoise in acute therapeutic decision-making.

Limitations

This study has limitations that are associated with its retrospective nonrandomized design and missing data. Furthermore, the exact extent and location of infarcted tissue on initial imaging as well as clinical information that is specific to symptoms of distal occlusions of the posterior circulation were not available for specified outcome assessment either at discharge or at long-term follow-up. Future studies will need to address this limitation with a detailed comparison of the long-term treatment effects of both mechanical thrombectomy and standard medical treatment cohorts. Furthermore, follow-up vessel imaging that evaluated the posttreatment recanalization status was not performed in the standard medical treatment group and therefore was not available for subgroup analysis and comparison.

Conclusions

In this case-control study, mechanical thrombectomy for primary posterior circulation DMVO appeared to be reasonable, safe, and technically feasible for therapeutic management of occlusions of the P2 or P3 segment compared with standard medical treatment, especially if patients were not eligible for IVT or presented with high NIHSS scores (≥10 points). The study results did not allow general treatment recommendations. An RCT that compares mechanical thrombectomy with standard medical treatment is warranted to evaluate the use of thrombectomy for posterior circulation DMVO and to resolve clinical equipoise in acute therapeutic decision-making.

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