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Endovascular therapy or medical management alone for isolated posterior cerebral artery occlusion: a multicenter study

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ABSTRACT

Background: Whether endovascular therapy (EVT) added on best medical management (BMM), as compared to BMM alone, is beneficial in acute ischemic stroke with isolated posterior cerebral artery (PCA) occlusion is unknown.

Methods: We conducted a multicenter international observational study of consecutive stroke patients admitted within 6hrs from symptoms onset in 26 stroke centers with isolated occlusion of the first (P1) or second (P2) segment of the PCA and treated either with BMM + EVT or BMM alone. Propensity score with inverse probability of treatment weighting was used to account for baseline between-groups differences. The primary outcome was 3-month good functional outcome (modified Rankin score [mRS] 0-2 or return to baseline mRS). Secondary outcomes were 3-month excellent recovery (mRS 0-1), symptomatic intracranial hemorrhage (sICH), and early neurological deterioration.

Results: Overall, 752 patients were included (167 and 585 patients in the BMM + EVT and BMM alone groups, respectively). Median age was 74 (IQR 63-82) years, 329 (44%) patients were female, median NIHSS was 6 (IQR 4-10), and occlusion site was P1 in 188 (25%) and P2 in 564 (75%) patients. Baseline clinical and radiological data were similar between the two groups following propensity-score weighting. EVT was associated with a trend towards lower odds of good functional outcome (OR=0.81; 95%CI: 0.66-1.01; *P*=0.06) and was not associated with excellent functional outcome (OR=1.17; 95%CI: 0.95-1.43; *P*=0.15). EVT was associated with a higher risk of sICH (OR=2.51; 95%CI: 1.35-4.67; *P*=0.004) and early neurological deterioration (OR=2.51; 95%CI: 1.64-3.84; *P*<0.0001).

Conclusions: In this observational study of patients with proximal PCA occlusion, EVT was not associated with good or excellent functional outcome as compared to BMM alone. However, EVT was associated with higher rates of sICH and early neurological deterioration. EVT should not be routinely recommended in this population, but randomization into a clinical trial is highly warranted.

NON-STANDARD ABBREVIATIONS AND ACRONYMS

ASMD, absolute standardized mean difference
BMM, best medical management
END, early neurological deterioration
EVT, endovascular therapy
IVT, intravenous thrombolysis
mRS, modified Rankin Score
NIHSS, National Institutes of Health Stroke Scale
P1, first segment of the posterior cerebral artery
P2, second segment of the posterior cerebral artery
PCA, posterior cerebral artery
sICH, symptomatic intracranial hemorrhage

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INTRODUCTION

Approximately 2% of acute ischemic stroke patients harbor an isolated occlusion of the posterior cerebral artery (PCA).[1,2] Even though these patients commonly present with apparent mild-to-moderate deficits in the acute phase, more than half of them are substantially disabled at 3-month owing to visual field defects, cognitive dysfunction, hemiparesis or neuropathic pain.[3-5]

In this population, international guidelines recommend intravenous thrombolysis (IVT) in the 0-4.5hr time window in the absence of contraindication.[6,7] However, the benefit of endovascular therapy (EVT) – either as a stand-alone therapy or in addition to IVT – over best medical management (BMM) alone is uncertain because these patients were excluded from the pivotal EVT trials. Consequently, the European Stroke Organization provides no specific recommendation regarding EVT in this population,[8] while the American Heart Association/American Stroke Association guidelines state that EVT may be reasonable for carefully selected patients.[7]

Currently, a few observational studies have compared BMM + EVT and BMM alone in this population, all reporting similar 3-month functional outcome in the two treatment groups.[3,4,9-11] However, these studies were limited by moderate sample sizes,[3,9,10] or the exclusion of patients with the most proximal occlusion (ie, first segment of the PCA) where a benefit of EVT may be more likely.[4]

Here, we studied the clinical efficacy and safety of BMM + EVT as compared to BMM alone in a large international multicenter cohort of acute stroke patients with primary proximal isolated PCA occlusion admitted in the early time window.

METHODS

This report was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines.[12] The study was approved by the local ethic committee of the Rothschild Foundation hospital (IRB 00012801) and declared on clinicaltrials.gov (NCT04823481). Each patient was informed of their participation in the study and was offered the possibility to withdraw, if required by the local legislations. The data supporting the study findings are available upon reasonable request.

Study cohort

This international multicenter retrospective study collected data from all consecutive acute stroke patients admitted to 26 stroke centers (France, n=22; Switzerland, n=3; USA, n=1) between February 2003 and January 2022 (inclusion dates varied across centers, see **Supplemental Table 1**), who met the following criteria: (1) baseline non-invasive imaging performed within 6 hours from symptom onset and showing an isolated occlusion of the first (P1) or second (P2) segment of the PCA, (2) treated either with BMM alone (IVT unless contraindicated) or BMM + EVT, and (3) with available 3-month modified Rankin scale (mRS) score. Patients with any associated intracranial occlusion (ie, basilar, carotid, middle or anterior cerebral arteries) were excluded, as well as 'secondary' PCA occlusion after reperfusion of a basilar artery occlusion. In each center, eligibility for EVT was at the discretion of the treating physician. Eleven participating centers were unable to retrieve data from patients receiving neither IVT nor EVT.

Study treatment groups

Patients were classified in two treatment groups, according to the initial treatment decision: (1) BMM alone: patients intended for BMM alone (IVT unless contraindicated), including those who eventually received rescue EVT because of early neurological deterioration, and (2) BMM + EVT: patients immediately intended for additional EVT following BMM, including those who eventually did not receive EVT (eg, because of early post-IVT recanalization or distal thrombus migration). This approach

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was deliberate, to reflect the real-world dilemma facing the clinician in-charge.[13] For each patient, the treatment group was determined based on a careful analysis of medical notes on patient admission.

Clinical variables

The following variables were collected: age, sex, pre-stroke mRS, vascular risk factors, previous vascular events, previous antithrombotic treatments, National Institutes of Health Stroke Scale (NIHSS) score on admission and at 24 hrs, EVT facility in the admission center, time between symptoms onset and admission imaging, and 3-month mRS. For patients receiving EVT, we additionally collected time between (1) symptoms onset and groin puncture; (2) imaging start and groin puncture; and (3) groin puncture and reperfusion, as well as the device used for EVT.

Radiological variables

All included patients underwent either non contrast CT with CT-angiography or MRI with MR-angiography on admission, and follow-up MRI or CT within ~24 hours following admission. To ensure homogeneity in radiological evaluation, one neuroradiologist with 15 years of experience (FC) reviewed all baseline and follow-up imaging using a structured form, blinded to treatment group and clinical outcomes. Several variables were collected. First, the topography of the PCA infarct on non-contrast CT or diffusion-weighted imaging, categorized as superficial, deep (ie, thalamus involvement), both superficial and deep, and no visible infarct. Second, PCA occlusion side and site on CT-angiography or MR-angiography. The P1 segment was defined as the first portion of the PCA up to the posterior communicating artery, and the P2 segment from the posterior communicating artery to the posterior edge of lateral part of the midbrain, until the entrance into the quadrigeminal cistern.[4] Last, on 24 hr imaging, evidence of intracranial hemorrhage according to the European Cooperative Acute Stroke Study (ECASS) II classification.[14] For patients receiving EVT, recanalization was evaluated centrally by one interventional neuroradiologist (FD), blinded from outcomes, on the final intracranial run using the modified Thrombolysis in Cerebral Infarction (mTICI) scale. mTICI 2b to 3 was considered as successful reperfusion (ie, reperfusion ≥50% of the initially affected PCA territory).

Study outcomes

The primary efficacy outcome was 3-month good functional outcome, defined as mRS 0 to 2, or return to pre-stroke mRS. The secondary efficacy outcome was excellent functional recovery (3-month mRS 0 to 1 or return to pre-stroke mRS). The primary safety outcome was symptomatic intracranial hemorrhage (sICH) according to the ECASS II definition, namely any ICH associated with clinical worsening ≥ 4 points on the NIHSS score at 24 hrs.[14] The secondary safety outcome was early neurological deterioration (END), defined as an NIHSS score increase of 4 points or more at 24 hrs after admission.

Statistical analysis

Continuous variables were described as mean± standard deviation or median (interquartile range, IQR), as appropriate, and categorical variables as numbers and percentages. In order to account for imbalance in potential confounders for the associations between treatment group and outcome, we chose *a priori* to use a propensity-score weighted approach. The propensity score was estimated using a non-parsimonious multivariable logistic regression model, with the treatment group as dependent variable and all variables listed in **Table 1** as covariates. Multiple imputations for missing data were not performed considering the low number of missing variables (3.1%). The few patients (n=23) with missing data were therefore excluded. No further patients were excluded to derive the propensity score (i.e., the lower and upper limits for the propensity score support region were equal to 0.0 and 1.0, respectively). Balance of baseline characteristics between the two treatment groups was assessed before and after propensity-score weighting by calculation of absolute standardized mean differences (ASMD). An ASMD ≤10% was interpreted as a negligible difference (i.e. satisfactory balance between treatment

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groups).[15] The association between treatment group and each outcome was estimated through odds ratios (OR) and their 95% confidence intervals (CI), calculated in binary logistic regression with inverse probability of treatment weighting. Potential heterogeneity in treatment effect depending on occlusion site (P1 vs. P2), NIHSS score (<10 vs. ≥10) and IVT use, was assessed in logistic models with calculation of *P* for interaction ($P_{interaction}$). Last, sensitivity analyses limited to patients treated since 2015 were conducted. All tests were 2-tailed, and the threshold for statistical significance was set to $P<0.05$. Statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Of the 930 patients screened, a total of 752 patients were included, 585 (78%) and 167 (22%) in the BMM alone and BMM + EVT groups, respectively (**Figure 1**). Median age was 74 (IQR 63-82) years, 329 (44%) patients were female, median NIHSS score was 6 (IQR 4-10), and 557 (74%) patients received IVT. Baseline imaging was CT for 226 (30%) patients and MRI for 526 (70%) patients, with a median symptom onset-to-imaging time of 138 (IQR, 100-190) minutes. Occlusion site was P1 for 188 (25%) patients and P2 for 564 (75%) patients. The rate of infarct core visualization was 78% (587/752), 38% (86/226) in patients imaged with CT and 95% (501/526) among those imaged with MRI. Among the 587 patients with visible infarct core on baseline imaging, infarct topography was deep, superficial, and both deep and superficial in 179 (30%), 95 (16%) and 313 (53%) patients, respectively. Most patients were treated since 2015 (609/752, 81%). Details regarding the number of patients treated per year are presented in **Supplemental Figure 1**. In the BMM + EVT group, 21/167 (13%) patients did not receive EVT due to distal thrombus migration/complete recanalization, early clinical improvement or catheterization failure (see details in **Figure** 1). In the BMM alone group, 10/585 (2%) patients received rescue EVT because of END.

Characteristics of treatment groups

Table 1 summarizes patients' characteristics in the two treatment groups. Before propensity-score weighting several meaningful differences (ASMD >10%) were observed: in the BMM alone group, patients less frequently were female, had previous atrial fibrillation and anticoagulant therapy, more frequently had previous stroke and antiplatelet therapy, had lower NIHSS score on admission, more distal occlusions and received more frequently IVT (**Table 1**). They were also less likely to have CT imaging, to be treated since 2015 and in a stroke center without on-site EVT facility. These differences were effectively reduced following propensity-score weighting (**Table 1**), with absolute standardized mean differences now ≤10% for all baseline variables, indicating satisfactory balance between the two groups.

Data regarding the EVT procedure for the 160 patients in the BMM + EVT group who underwent groin puncture are presented in **Table 2**. EVT procedures occurred since 2015 in 151/160 (94%) patients, and were mostly performed by means of stent retriever, aspiration catheter, or both (90%). Successful recanalization was obtained in 119/160 (74%) patients. Iatrogenic vessel perforation occurred in 3 patients (P2 occlusion, n=1; and P1 occlusion, n=2).

Efficacy Outcomes

In the entire cohort (ie, regardless of treatment group), good and excellent functional outcomes occurred in 480/752 (64%) and 324/752 (43%) patients, respectively. Crude rates of good and excellent outcome in each treatment group are presented in **Table 3**. After propensity-score weighting (n=729 without any missing baseline data), BMM + EVT was not associated with higher rates of good (OR=0.81; 95%CI: 0.66-1.01; *P*=0.06) or excellent functional outcome (OR=1.17; 95%CI: 0.95-1.43; *P*=0.15). The sensitivity analyses limited to patients treated since 2015 showed similar results (**Supplemental Table 2**). No significant interaction was observed between BMM + EVT effect and occlusion site (P1 vs. P2), NIHSS score (<10 vs. ≥10), or IVT use for either outcome (**Figures 2A** and **2B**).

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Safety Outcome

In the entire cohort, the rate of sICH was 3% (20/742), and the rate of END was 7% (50/732). Crude rates of sICH and END in each treatment group are presented in **Table 3**. Following propensity-score weighting (n=729 without any missing baseline data), BMM + EVT was significantly associated with higher odds of sICH (OR=2.51; 95%CI: 1.35-4.67; *P*=0.004) and END (OR= 2.51; 95%CI: 1.64-3.84; *P*<0.0001). The sensitivity analyses limited to patients treated since 2015 showed similar results (**Supplemental Table 2**). No significant interaction was observed between BMM + EVT effect and occlusion site, NIHSS score, or IVT use regarding the risk of sICH (**Figure 3A**). However, there was an interaction (*P*<0.01) between BMM + EVT effect and IVT use regarding END: EVT was associated with higher risk of END in both IVT-treated and untreated subgroups, but this risk was greater without IVT (**Figure 3B**).

DISCUSSION

The aim of this observational study was to compare functional and safety outcomes in acute ischemic stroke patients with proximal PCA occlusion treated with BMM + EVT or BMM alone. Three salient findings emerged. First, the prevalence of severe disability in the entire cohort was high (36% of 3-month mRS above 2). Second, BMM + EVT was not associated with higher rates of good or excellent functional outcome as compared to BMM alone. Third, EVT was independently associated with higher rates of sICH and early neurological deterioration.

More than one third of our cohort was unable to live independently at 3-month (mRS above 2), and 57% of patients had some degree of disability (mRS above 1), in line with previous reports.[11] This indicates that despite relatively low NIHSS scores on admission (median value of 6), proximal PCA occlusion stroke is a disabling condition. This apparent discrepancy between moderate baseline NIHSS scores and a high rate of poor functional outcome is likely due the poor sensitivity of the NIHSS to assess posterior circulation-related neurologic deficits.[16] Indeed, several studies have reported a lower NIHSS cutoff to accurately predict poor outcome in posterior as compared to anterior circulation strokes; the former being at high risk of substantial 3-month disability despite relatively low NIHSS scores.[16,17] Several symptoms frequently seen following PCA infarctions such as visual field defects, cognitive dysfunction or neuropathic pain are poorly captured by the NIHSS, yet can be highly disabling. This high rate of poor functional outcome highlights the urgent need to improve treatment options, particularly in the acute setting.

EVT was not associated with higher rates of good or excellent functional outcome as compared to BMM alone in our dataset and was even associated with a trend towards lower rate of good functional outcome. The rate of good functional outcome in the EVT + BMM group was similar in our cohort than in a previous study-level meta-analysis in a similar population (58% in both studies) but was markedly higher in the BMM group of our study (65% vs 48%, respectively).[11] However, the low rate of good functional outcome following BMM in this meta-analysis is mainly driven by three studies with unusually low rates of IVT.[11] Nevertheless, the lack of benefit of EVT over BMM alone found in our study is in line with the few other observational studies comparing the two treatment strategies in PCA occlusion strokes,[3,4,9,10] as well as with their study-level meta-analysis.[11] Importantly, in our cohort the association between EVT and 3-month functional outcome –as compared to BMM alone– did not significantly differ according to occlusion site, baseline NIHSS, or IVT use (ie, no significant interaction was observed). A multicenter retrospective international study focusing on patients with P2 or P3 occlusions recently suggested better outcomes in EVT treated patients (as compared to BMM alone) for early clinical improvement in the subgroups of patients with admission NIHSS >10 and those not treated with IVT.[4] However, this early clinical improvement did not translated into better 3-month functional outcome,[4] in line with our results.

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We found that EVT was associated with an approximately two-fold higher risk of sICH and END. The absolute rate of sICH was small in both groups (2.1% and 4.8% in the BMM alone and EVT groups, respectively), but the incidence rate of END rate was substantial (4.7% and 14.2%, respectively). We opted to use the ECASSII definition for sICH (namely, any ICH associated with END) because it is widely used, and robustly predicts 3-month poor outcome.[18] However, as it encompasses minor ICH, sometimes unlikely to cause the deterioration, this classification mixes two distinct causes of poor outcome, true sICH and 'ischemic worsening' associated with asymptomatic hemorrhagic transformation. The higher rate of sICH following EVT was not significant in the four previous observational studies in this population,[3,4,9,10] yet one of them reported a numerically higher rate of sICH (1.6% vs. 4.1% in the BMM and EVT groups, respectively).[3] In our population, the higher sICH risk following EVT seems primarily present in the subgroups of patients with P2 occlusion and NIHSS <10. This may be due to the higher risk of EVT-related complications in distal occlusions. Also, the detrimental effects of even a medium-size intracranial hemorrhage on neurological deficit may be more visible in case of low NIHSS score. Regarding END, our study is the first to describe a higher rate following EVT in this population; previous observational studies did not report this outcome.[3,4,9,10] The majority of post-EVT ENDs were not associated with any ICH, and may therefore be primarily due to 'ischemic worsening' related to the procedure, yet their exact mechanisms is somewhat unclear and warrants further investigation.[19]

The rate of successful recanalization following EVT in our cohort was similar than reported by others on similar populations (74% vs. 79% in a recent meta-analysis).[20] This relatively low rate of post-EVT successful recanalization may partly explain the lack of association between EVT and favorable outcomes in our study. Even though the vast majority (94%) of EVT were have been performed since 2015, rapid technical innovations have resulted in safer and more effective procedures in most recent years.[21]

Because PCA occlusion was an exclusion criterion in most of the pivotal EVT trials, the benefit of EVT over BMM alone in this setting has remained uncertain. With advances in thrombectomy devices and techniques, the use of EVT is expanding to medium and distal vessel occlusions –including PCA occlusions–, and several randomized trials comparing BMM+ EVT and BMM alone are currently ongoing (NCT05030142, NCT05029414, NCT05151172).[2] Our findings suggest that EVT should not be routinely recommended for proximal PCA occlusion strokes. However, despite the several signals of EVT harm found in our study we believe that randomization into a trial is highly warranted whenever feasible considering the retrospective nature of the present study and the rapid advances in EVT techniques that may provide safer interventions. Note however that ongoing trials merge different type of medium vessel occlusion (P1, P2, third segment of the PCA, as well as the second and third segment of the middle and anterior cerebral arteries) where different benefit/risk profile of EVT may exist. Consequently, these trials may not provide a definitive answer regarding the benefit of EVT in isolated PCA occlusion. Dedicated trials for PCA occlusion patients may be warranted but will require large sample sizes considering the possibly small additional benefit of EVT –if any– in this population, which is challenging considering the relatively rare prevalence of proximal PCA occlusions.

Our study has several strengths. First, even though they are relatively uncommon,[1,2] we were able to collect a large population of acute stroke with proximal PCA occlusion owing to the multicenter international design. Second, the central reading of the imaging datasets ensured a uniform assessment of key variables such as occlusion site, infarct topography, post-EVT recanalization and intracranial hemorrhage for the entire population. Last, despite the retrospective design, the rate of missing 3-month mRS was relatively low (7%, **Figure** 1).

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This study also has limitations. The main limitation is the observational design leading to the possibility of confounding by indication. Although propensity-score weighted analysis dramatically reduced between-group differences in baseline characteristics, unmeasured or unknown confounding factors may have been overlooked. For instance, the type of neurological deficit and imaging characteristics, such as infarct volume, penumbral volume, and collaterals assessment, could impact both decision making and 3-month mRS. Second, the mRS is a global functional outcome scale which may not capture all clinically relevant neurological deficits. More specific neurological outcomes such as visual field defects and cognitive dysfunction seem highly relevant in this population,[3] but were not available. Prospective studies should consider evaluating such additional outcomes in a standardized manner and involve neuro-ophthalmologists. Third, this study was retrospective, and even though the medical records were carefully reviewed to determine the initial treatment decision at the individual level (ie, BMM alone or BMM + EVT), classification errors might have occurred in some patients. Fourth, considering the retrospective nature of the study, 3-month mRS assessment was not centralized, and was not blinded to treatment group. Also, the precise date of assessment was not retrieved. Last, the inclusion period was large, and patients' clinical management and endovascular techniques may have changed over time, which might impact clinical outcomes. However, the sensitivity analyses limited to patients treated since 2015 showed similar results.

CONCLUSION

In our population of acute ischemic stroke patients with isolated P1 or P2 occlusion, more than one third were functionally dependent at 3-month, highlighting the urgent need to improve treatment options for this population. EVT added to BMM was not associated with higher rates of good or excellent functional outcome as compared to BMM alone. However, EVT was associated with higher rates of symptomatic intracranial hemorrhage and END. Our data suggest that EVT should not be routinely recommended in this population, and that randomization into a clinical trial is highly warranted whenever feasible.

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Appendix: ACAPULCO collaborators: Kateryna Antonenko, Caroline Arquizan, Lynda Benammar, Claire Boutet, Frédéric Clarençon, Pierre-Olivier Comby, Hubert Desal, Olivier Detante, François Eugene, Emmanuel Gerardin, Benjamin Gory, Stéphane Kremer, Sylvain Ledure, Mathieu Krug, Bertrand Lapergue, Philippe Niclot, Christophe Magni, Michael Obadia, Canan Ozsancak, Fernando Pico, Sara Pilgram-Pastor, Raoul Pop, Sébastien Richard, Charlotte Rosso, Julien Savatovsky, Solène Moulin, Clément Tracol, Martin Zbinden.

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Figure legends

Figure 1: Study flow chart.
Abbreviations: PCA: posterior cerebral artery; BMM: best medical management; EVT: endovascular therapy.

Figure 2: Comparison of efficacy outcomes in each treatment group according to occlusion site, intravenous thrombolysis use and NIHSS (propensity-score weighted analyses)

Forest plot summarizes the odds ratio obtained for comparison of BMM + EVT and BMM alone on (**A**) good functional outcome (mRS 0-2 or return to baseline mRS) and (**B**) excellent functional outcome (mRS 0–1 or return to baseline mRS), according to occlusion site, intravenous thrombolysis use and dichotomized baseline NIHSS.

Figure 3: Comparison of safety outcomes in each treatment group according to occlusion site, intravenous thrombolysis use and NIHSS (propensity-score weighted analyses)

Forest plot summarizes the odds ratio obtained for comparison of BMM + EVT and BMM alone on (**A**) symptomatic intracerebral hemorrhage, and (**B**) early neurological deterioration, according to occlusion site, intravenous thrombolysis use and dichotomized baseline NIHSS.

***** Firth's penalized likelihood was used to reduce the risk of bias caused by rare events (among patients not treated with intravenous thrombolysis, only one experienced END in the BMM group).

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Table 1. Baseline Characteristics and Comparison of Both Treatment Groups*

	BMM alone (n=585)	BMM + EVT (n=167)	ASMD before propensity-score weighting†	ASMD after propensity-score weighting†
Age, years	74 (63, 83)	72 (62, 82)	7%	5%
Female gender	250 (42.7%)	79 (47.3%)	13%	2%
mRS before stroke	0 (0, 1)	0 (0, 1)	8%	9%
Patient history				
Hypertension	377 (64.4%)	108 (64.7%)	1%	10%
Diabetes mellitus	99 (16.9%)	30 (18.0%)	4%	2%
Current smoker	98 (16.9%)	30 (18.0%)	5%	5%
Previous stroke	89 (15.3%)	16 (9.8%)	16%	9%
Previous atrial fibrillation	118 (20.2%)	43 (25.9%)	14%	4%
Antiplatelet therapy	184 (31.5%)	48 (28.7%)	11%	6%
Anticoagulant therapy	49 (8.4%)	21 (12.6%)	15%	2%
Characteristics on admission				
NIHSS	6 (3, 10)	8 (5, 11)	31%	9%
Treatment since 2015	451 (77.1%)	158 (94.6%)	50%	1%
Use of IVT	467 (79.8%)	90 (53.9%)	57%	1%
On-site EVT facility‡	477 (81.5%)	116 (69.5%)	24%	4%
Baseline imaging characteristics				
Onset-to-imaging time, minutes	140 (102, 190)	128 (93, 191)	1%	9%
Imaging type			10%	8%
CT	170 (29.1%)	56 (33.5%)		
MRI	415 (70.9%)	111 (66.5%)		
Occlusion side			9%	10%
Left	314 (53.7%)	84 (50.3%)		
Right	257 (43.9%)	74 (44.3%)		
Bilateral	14 (2.4%)	9 (5.4%)		
Occlusion site			31%	6%
P1	128 (21.9%)	60 (35.9%)		
P2	457 (78.1%)	107 (64.1%)		
Infarct topography			9%	5%
Superficial	144 (24.6%)	35 (21.0%)		
Deep	76 (13.0%)	19 (11.4%)		
Superficial and deep	236 (40.3%)	77 (46.1%)		
No visible infarct	129 (22.1%)	36 (21.6%)		

Abbreviations: ASMD: absolute standardized mean difference; BMM: best medical management; EVT: endovascular treatment; IVT: intravenous thrombolysis; P1 and P2: first and second segment of the posterior cerebral artery.

*Categorical variables are expressed as numbers (%) and continuous variables as median (IQR) or mean (SD).

†An ASMD ≤10% corresponds to a small difference (ie, well-balanced groups regarding the variable of interest).

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‡Baseline imaging performed in a stroke center with on-site thrombectomy capability.

Table 2: Characteristics of Endovascular Procedures in the BMM + EVT group*

	N=160 with groin puncture†
Onset-to-puncture time, min	237 (182-307)
Imaging-to-puncture time, min	87 (56-137)
On-site EVT facility (n=112)	70 (46-95)
No EVT facility (n=48)	154 (118-180)
Puncture-to-reperfusion time, min	50 (30-85)
Material used	
Aspiration	38 (25.5%)
Strentriever	44 (29.5%)
Aspiration + stentriever	40 (26.8%)
Intra-arterial thrombolysis	11 (7.3%)
Other devices	2 (1.3%)
None#	14 (9.4%)
mTICI 2b-3	119 (74.4%)
mTICI 2c-3	103 (64.4%)

*: Categorical variables are expressed as numbers (%) and continuous variables as median (IQR).

†: 7/167 patients did not have groin puncture because of early neurological improvement or early recanalization evidenced on a non-invasive imaging

#: These patients had distal thrombus migration or complete recanalization on angiographic first run (n=8) or had catheterization failure (n=6).

Abbreviations: mTICI: modified thrombolysis in cerebral infarction.

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Table 3: Crude Rates of Each Clinical Outcome according to Treatment Group

	Overall (n=752)	BMM alone (n=585)	BMM + EVT (n=167)
Good functional outcome (mRS 0-2)	480 (63.8%)	383 (65.5%)	97 (58.1%)
Excellent functional outcome (mRS 0-1)	324 (43.1%)	254 (43.4%)	70 (41.9%)
Symptomatic intracerebral hemorrhage*	20/742 (2.7%)	12/577 (2.1%)	8/165 (4.8%)
Early neurological deterioration†	50/732 (6.8%)	27/570 (4.7%)	23/162 (14.2%)

* Symptomatic intracerebral hemorrhage was not available in 10 patients (8 in the BMM and 2 in the BMM + EVT groups, respectively)

† Early neurological deterioration was not available in 20 patients (15 in the BMM and 5 in the BMM + EVT groups, respectively)

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References:

1. Duloquin G, Graber M, Garnier L, Crespy V, Comby PO, Baptiste L, Mohr S, Delpont B, Guéniat J, Blanc-Labarre C*, et al.* Incidence of acute ischemic stroke with visible arterial occlusion: A population-based study (Dijon Stroke Registry). *Stroke*. 2020;51:2122-2130
2. Saver JL, Chapot R, Agid R, Hassan A, Jadhav AP, Liebeskind DS, Lobotesis K, Meila D, Meyer L, Raphaeli G*, et al.* Thrombectomy for distal, medium vessel occlusions: A consensus statement on present knowledge and promising directions. *Stroke*. 2020;51:2872-2884
3. Strambo D, Bartolini B, Beaud V, Marto JP, Sirimarco G, Dunet V, Saliou G, Nannoni S, Michel P. Thrombectomy and thrombolysis of isolated posterior cerebral artery occlusion: Cognitive, visual, and disability outcomes. *Stroke*. 2020;51:254-261
4. Meyer L, Stracke CP, Jungi N, Wallocha M, Broocks G, Sporns PB, Maegerlein C, Dorn F, Zimmermann H, Naziri W*, et al.* Thrombectomy for primary distal posterior cerebral artery occlusion stroke: The TOPMOST study. *JAMA Neurol*. 2021;78:434-444
5. Brandt T, Steinke W, Thie A, Pessin MS, Caplan LR. Posterior cerebral artery territory infarcts: Clinical features, infarct topography, causes and outcome. Multicenter results and a review of the literature. *Cerebrovasc Dis*. 2000;10:170-182
6. Berge E, Whiteley W, Audebert H, De Marchis GM, Fonseca AC, Padiglioni C, de la Ossa NP, Strbian D, Tsivgoulis G, Turc G. European stroke organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J*. 2021;6:I-lxii
7. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B*, et al.* 2018 guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2018;49:e46-e110
8. Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M, Schellinger PD, Toni D, de Vries J, White P*, et al.* European stroke organisation (ESO)- european society for minimally invasive neurological therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke. *J Neurointerv Surg*. 2019;11:535-538
9. Cunha B, Baptista M, Pamplona J, Carvalho R, da Câmara CP, Alves M, Papoila AL, Nunes AP, Reis J, Fragata I. Acute treatment of isolated posterior cerebral artery occlusion: Single center experience. *J Stroke Cerebrovasc Dis*. 2022;31:106239
10. Herweh C, Abdalkader M, Nguyen TN, Puetz V, Schöne D, Kaiser D, Chen CH, Jeng JS, Möhlenbruch MA, Ringleb PA*, et al.* Mechanical thrombectomy in isolated occlusion of the proximal posterior cerebral artery. *Front Neurol*. 2021;12:697348
11. Berberich A, Finitsis S, Strambo D, Michel P, Herweh C, Meyer L, Hanning U, Strbian D, Abdalkader M, Nogueira RG*, et al.* Endovascular therapy versus no endovascular therapy in patients receiving best medical management for acute isolated occlusion of the posterior cerebral artery: A systematic review and meta-analysis. *Eur J Neurol*. 2022;29:2664-2673
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Int J Surg*. 2014;12:1495-1499
13. Nagel S, Haussen DC, Nogueira RG. Importance of the intention-to-treat principle. *JAMA Neurol*. 2020;77:905-906
14. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, Larrue V, Bluhmki E, Davis S, Donnan G*, et al.* Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second european-australasian acute stroke study investigators. *Lancet*. 1998;352:1245-1251
15. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Stat Med*. 2009;28:3083-3107
16. Sato S, Toyoda K, Uehara T, Toratani N, Yokota C, Moriwaki H, Naritomi H, Minematsu K. Baseline nih stroke scale score predicting outcome in anterior and posterior circulation strokes. *Neurology*. 2008;70:2371-2377
17. Inoa V, Aron AW, Staff I, Fortunato G, Sansing LH. Lower nih stroke scale scores are required to accurately predict a good prognosis in posterior circulation stroke. *Cerebrovasc Dis*. 2014;37:251-255

DOI: 10.1161/STROKEAHA.122.042283

18. Rao NM, Levine SR, Gornbein JA, Saver JL. Defining clinically relevant cerebral hemorrhage after thrombolytic therapy for stroke: Analysis of the national institute of neurological disorders and stroke tissue-type plasminogen activator trials. *Stroke*. 2014;45:2728-2733
19. Girot JB, Richard S, Gariel F, Sibon I, Labreuche J, Kyheng M, Gory B, Dargazanli C, Maier B, Consoli A*, et al.* Predictors of unexplained early neurological deterioration after endovascular treatment for acute ischemic stroke. *Stroke*. 2020;51:2943-2950
20. Abdelnaby R, Mohamed KA, A EL, Sonbol YT, Bedewy MM, Aboutaleb AM, Dardeer KT, Heikal HA, Gawish HM, Nikoubashman O*, et al.* Endovascular therapy in acute isolated posterior cerebral artery occlusion : Systematic review and meta-analysis. *Clin Neuroradiol*. 2022
21. Compagne KCJ, Kappelhof M, Hinsenveld WH, Brouwer J, Goldhoorn RB, Uyttenboogaart M, Bokkers RPH, Schonewille WJ, Martens JM, Hofmeijer J*, et al.* Improvements in endovascular treatment for acute ischemic stroke: A longitudinal study in the MR CLEAN registry. *Stroke*. 2022;53:1863-1872