

Endovascular versus medical therapy in posterior cerebral artery stroke: role of baseline NIHSS and occlusion site

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Stroke

Abstract

Background: Acute ischemic stroke (AIS) with isolated posterior cerebral artery occlusion (iPCAO) lacks management evidence from randomized trials. We aimed to evaluate whether the association between endovascular treatment (EVT) and outcomes in iPCAO-AIS is modified by initial stroke severity (baseline NIHSS) and arterial occlusion site.

Methods: Based on the multicenter, retrospective, case-control study of consecutive iPCAO-AIS patients (PLATO study), we assessed the heterogeneity of EVT outcomes compared to medical management (MM) for iPCAO, according to baseline NIHSS (≤ 6 vs. >6) and occlusion site (P1 vs. P2), using multivariable regression modelling with interaction terms. The primary outcome was the favorable shift of 3-month mRS. Secondary outcomes included excellent outcome (mRS 0-1), functional independence (mRS 0-2), symptomatic intracranial hemorrhage (sICH) and mortality.

Results: From 1344 patients assessed for eligibility, 1,059 were included (median age 74 years, 43.7% women, 41.3% had intravenous thrombolysis), 364 receiving EVT and 695 MM. Baseline stroke severity did not modify the association of EVT with 3-month mRS distribution ($p_{\text{int}}=0.312$), but did with functional independence ($p_{\text{int}}=0.010$), with a similar trend on excellent outcome ($p_{\text{int}}=0.069$). EVT was associated with more favorable outcomes than MM in patients with baseline NIHSS >6 (mRS 0-1: 30.6% vs. 17.7%, aOR=2.01, 95%CI=1.22-3.31; mRS 0-2: 46.1% vs. 31.9%, aOR=1.64, 95%CI=1.08-2.51), but not in those with NIHSS ≤ 6 (mRS 0-1: 43.8% vs. 46.3%, aOR=0.90, 95%CI=0.49-1.64; mRS 0-2: 65.3% vs. 74.3%, aOR=0.55, 95%CI=0.30-1.0). EVT was associated with more sICH regardless of baseline NIHSS ($p_{\text{int}}=0.467$), while the mortality increase was more pronounced in patients with NIHSS ≤ 6 ($p_{\text{int}}=0.044$, NIHSS ≤ 6 : aOR=7.95, 95%CI=3.11-20.28, NIHSS >6 : aOR=1.98, 95%CI=1.08-3.65). Arterial occlusion site did not modify the association of EVT with outcomes compared to MM.

Conclusion: Baseline clinical stroke severity, rather than the occlusion site, may be an important modifier of the association between EVT and outcomes in iPCAO. Only severely affected patients with

iPCAO (NIHSS>6) had more favorable disability outcomes with EVT than MM, despite increased mortality and sICH.

Non-standard Abbreviations and Acronyms

AIS= Acute ischemic stroke

CI= Confidence intervals

ER= Emergency room

EVT= Endovascular treatment

iPCAO= Isolated posterior cerebral artery occlusion

IQR= Interquartile range

IVT= Intravenous thrombolysis

IPTW= Inverse probability of treatment weighting

LPGH= Last proof of good health

MM= Medical management

mRS= modified Rankin Scale

OR= Odds ratio

PCA= Posterior cerebral artery

PCAO= Posterior cerebral artery occlusion

PLATO= Posterior CerebraL ArTery Occlusion Stroke

sICH= Symptomatic intracerebral hemorrhage



Stroke

Introduction

The optimal management of patients presenting with acute ischemic stroke (AIS) resulting from isolated posterior cerebral artery occlusion (iPCAO) remains uncertain. Although endovascular treatment (EVT) shows a higher likelihood of arterial recanalization,¹ its net clinical benefit over medical management (MM) in this context has yet to be established. Current knowledge regarding the association of EVT with safety and clinical outcomes for iPCAO stems from several retrospective studies yielding heterogeneous results.¹⁻⁷ Two study-level meta-analyses did not show significant differences in 3-month disability, rates of symptomatic intracranial hemorrhage (sICH) or mortality between iPCAO patients treated with EVT and those with MM.^{8,9} The largest patient-level analysis, involving 1,023 iPCAO patients from the Endovascular therapy of Posterior Cerebral Artery Occlusion Stroke (PLATO) collaboration, found that patients treated with EVT and MM had similar 3-month disability, without any significant difference on the distribution of the modified Rankin Scale (mRS). However, a higher proportion of patients treated with EVT had early neurological improvement and achieved excellent 3-month outcome (mRS 0-1), yet with higher rates of sICH.⁶ These findings do not lead to definitive conclusions but suggest that the effect size of EVT in unselected AIS from PCAO might be small or even absent. Furthermore, it remains unclear whether certain subgroups of PCAO patients, such as those defined by stroke severity or by the occluded arterial segment, might benefit or be harmed from EVT.

Such heterogeneity of EVT's effect, contingent upon clinical stroke severity and the occluded arterial segment, exists in other AIS settings. For instance, in anterior circulation stroke, the efficacy of EVT is established for proximal arterial segment occlusions (internal carotid artery, M1 segment of the middle cerebral artery) but remains under investigation for more distal occlusions. Regarding basilar artery occlusion, the effect of EVT seems to vary with clinical stroke severity, as there are indications of its efficacy in patients with moderate to severe stroke, but evidence is less conclusive in those with mild deficits.¹⁰⁻¹³

In this secondary analysis of the PLATO cohort, our aim was to assess if, in AIS from iPCAO the association of EVT with 3-month disability and safety outcomes is modified by baseline stroke clinical severity (measured by NIHSS) and the site of arterial occlusion within the PCA.

Methods

Ethics

Ethics committee or local institutional review board approval was obtained from all sites. Patient written informed consent was waived due to the retrospective nature of this study with anonymized data. The lead authors (T.N.N., D.S., S.N.) and the statistician (M.M.Q.) had password-protected access to all data centralized in the Helsinki University research platform. This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Anonymized data not published in this article will be made available on request by a qualified investigator.

Study population

The PLATO study (NCT05291637) was an international, multicenter, retrospective case-control study of consecutive patients aged 18 years or older with iPCAO treated between January 1, 2015, to August 1, 2022. Since the main publication, the PLATO study expanded with an additional 4 sites, totaling 31 sites across 9 countries included in this analysis.

The inclusion criteria for this secondary analysis were: 1) patients ≥ 18 years diagnosed with ischemic stroke resulting from an isolated, unilateral, occlusion of non-fetal PCA in the P1, P2 segment of the artery; 2) patient presentation within 24 hours of symptom onset; and 3) pre-stroke modified Rankin Scale (mRS) of 0 to 3. Patients were excluded if there was concomitant basilar artery occlusion or multiple vessel occlusion outside the PCA territory. In addition, we excluded patients with missing data in the covariates used in the analyses.

Patients were divided based on the treatment received: EVT versus MM, with or without IVT. The decision to treat patients with EVT or MM was made by the treating medical team according to local treatment recommendations and the technical feasibility of performing EVT.

Data Collection

We collected baseline demographics, clinical presentation, imaging parameters, and clinical and safety outcomes as described in the primary publication.⁶ Outcome at 3 months was part of each site's stroke registry. The 3-month mRS was prospectively collected during the routine clinical examination in the outpatient clinic, or by a structured telephone interview by site investigators or coordinators, who could have been unblinded to the treatment received.

Outcome Variables

The primary outcome of this analysis was the distribution of the 3-month mRS. Secondary outcomes included 3-month functional independence (defined as mRS 0-2, or, in patients with pre-stroke mRS >2 , return to baseline mRS), 3-month excellent outcome (defined as mRS 0-1, or, in patients with pre-stroke mRS >1 , return to baseline mRS), early neurological improvement (NIHSS improvement by 2 or more

points at 24 hours or at hospital discharge)^{1,6}, symptomatic intracranial hemorrhage (sICH; defined as local or remote parenchymal hemorrhage type 2, subarachnoid hemorrhage, and/or intraventricular hemorrhage, combined with a neurological deterioration of 4 points or more on the NIHSS from baseline or leading to death, both judged causative by the attending physician), and 3-month mortality.

Subgroup definition

The heterogeneity of the association between EVT and outcomes was assessed by evaluating subgroups based on baseline NIHSS and occlusion site. Regarding baseline NIHSS, we defined two subgroups by dichotomization of baseline NIHSS as ≤ 6 and > 6 . The lead investigators chose the selection of the 6-point cut-off because it approximated the median of the overall cohort and given the absence of data on a NIHSS treatment threshold in the published literature. In addition, we performed the same interaction analysis using NIHSS as a continuous variable. As for the occlusion site, we defined two subgroups: patients with P1 segment occlusion and those with P2 segment occlusion. These were defined as follows: P1 segment, from the branching point of the distal basilar artery to the branching point of the posterior communicating artery; P2 segment, from the PCA branching point of the posterior communicating artery, coursing around the midbrain to the quadrigeminal cistern.⁶ The PCA was considered as “fetal” (and patients excluded from the study) if the P1 segment was absent or hypoplastic, and the P2 segment was supplied primarily by the posterior communicating artery supplied by the internal carotid artery. Imaging assessment was conducted following local protocols, and the site of the arterial occlusion was determined through CT angiography or MR angiography. Each center’s investigators evaluated the site of arterial occlusion according to these predefined criteria.

Statistical Analysis

We present continuous variables as median values with interquartile ranges (IQR) and categorical variables as absolute numbers and percentages. We compared baseline and outcome variables by treatment (MM and EVT), baseline NIHSS (NIHSS ≤ 6 and > 6), and occlusion site (P1 and P2 segment occlusions), using the Pearson’s chi-squared test for categorical variables and Mann–Whitney U test for continuous variables, as appropriate.

To assess the association between EVT and each outcome, we used multivariable regression models entering as independent variables the type of treatment together with prespecified baseline clinical and radiological variables known to be associated with the outcome. The following covariates were considered for different analyses: age, sex, baseline NIHSS, year of treatment, pre-stroke mRS, hypertension, diabetes, atrial fibrillation, treatment with IVT, pc-ASPECTS, and occlusion location. To

account for the evolution of revascularization treatment over time, we included the year of stroke in the statistical models. The exact model for each analysis is described in Figure and Table footnotes.

For the primary ordinal outcome, we utilized the PROC GENMOD in SAS 9.4, with the cumulative logit link function and multinomial distribution. For the secondary binary outcomes, logistic regression models with logit link function and binomial distribution specifications were used. Clustering by sites was accounted for using a generalized estimating equation approach. An independent correlation structure with the smallest quasi-likelihood independence criterion value was assumed for the within-site clustering. To assess for potential heterogeneity in EVT association with outcomes, based on baseline NIHSS and occlusion site, we entered an interaction term between the treatment variable and the subgroup variable in the regression models for each outcome. P-values of the interaction term (p for interaction) were calculated.

The analyses were repeated using the propensity score-based inverse probability of treatment weighting (IPTW) method as an alternative model correcting for the same covariates. Using a multivariable logistic regression model, we first estimated the probability of EVT assignment (propensity score) conditional on the above covariates. For IPTW, the EVT group received weights of $[1/\text{propensity score}]$, and MM received weights of $[1/(1-\text{propensity score})]$. The weights for the EVT and MM groups were stabilized by replacing the numerator 1 with the proportion of patients receiving EVT and MM, respectively. These weights were then used in the regression models with interaction terms described above. All associations between predictors and outcomes are expressed as odds ratios (OR) and 95% confidence intervals (CI). All patients included in the above analyses had complete data on the covariates and the outcome variable included in the models. In instances of missing outcome data, we limited the analysis to patients with complete outcome data and reported the relative numbers. All tests were two-sided, and P -values < 0.05 were considered significant. No adjustment for multiple testing was performed. We performed statistical analysis with SAS 9.4 (SAS Institute, Cary, NC) and R statistical software, version 4.3.1 (R Core Team 2023. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria).

Results

Out of 1344 patients assessed for eligibility in the PLATO cohort, 239 did not meet the study inclusion criteria, and 46 were excluded because of missing covariate data, leaving 1059 patients for the current study (patient's selection process in **Figure S1**; excluded patients had similar characteristics as patients included in the study, as shown in **Table S1**). The median (IQR) age of the study cohort was 74 (64-82)

years, and 42.7% were women. Overall, 695 patients were treated with MM and 364 with EVT, and approximately 40% of patients were treated with IVT in both groups. Median NIHSS was 3 points lower in the MM than in the EVT group (respectively 5 vs. 8 points, $p < 0.001$). Baseline clinical and radiological features and outcomes of the overall cohort, the EVT and MM groups are displayed in **Table S2**. Of the 1059 patients initially included, 100 (9.4%) had missing data on the 3-month mRS and were therefore excluded from analyses on the primary outcome, excellent outcome, and functional independence. The number of patients with missing information for each outcome, along with those included in each respective analysis, is detailed in **Figure S1**.

Patients with baseline NIHSS > 6 , compared to those with NIHSS ≤ 6 , were older (median [IQR] 76 [67-83] vs. 72 [61-80], $p < 0.0001$), more frequently female (46.9% vs. 38.8%, $p = 0.009$), had higher pre-stroke disability, more visual field defect (74.2% vs. 65.6%, $p = 0.004$), more vascular risk factors, and higher frequency of P1 occlusion (54.9% vs. 34.5%, $p < 0.0001$). They were more frequently treated with EVT (45.5% vs. 24.1%, $p < 0.0001$), and EVTs were more often performed within 6 hours (72.4% vs. 65.6%, $p = 0.027$). (**Table 1**). Patients with baseline NIHSS > 6 had higher likelihood of early neurological improvement (NIHSS change ≥ 2 : MVA-aOR 4.24, 95%CI 3.22-5.58), but less favorable 3-month disability outcomes (3-month mRS favorable shift: MVA-aOR 0.33, 95%CI 0.27-0.41), and higher mortality (MVA-aOR 3.93, 95%CI 2.05-7.52) compared to patients with baseline NIHSS 0 to 6 (**Table 2**). The interaction analysis between baseline NIHSS and EVT showed that the baseline NIHSS did not modify the association of EVT with the distribution of 3-month mRS ($p_{\text{int}} = 0.312$). However, baseline NIHSS modified the association of EVT with functional independence ($p_{\text{int}} = 0.010$) and mortality ($p_{\text{int}} = 0.044$), and a similar yet non-significant trend was observed for excellent outcome ($p_{\text{int}} = 0.069$) (**Figure 1A**, and **Table S3** for IPTW analysis). Specifically, EVT was associated with more excellent outcome and functional independence than MM in patients with baseline NIHSS > 6 (mRS 0-1: 30.6% vs. 17.7%, aOR=2.01, 95%CI=1.22-3.31; mRS 0-2: 46.1% vs. 31.9%, aOR=1.64, 95%CI=1.08-2.51), while in patients with baseline NIHSS ≤ 6 , the difference was absent or less favorable for EVT (mRS 0-1: 43.8% vs. 46.3%, aOR=0.90, 95%CI= 0.49-1.64; mRS 0-2: 65.3% vs. 74.3%, aOR=0.55, 95%CI=0.30-1.0). SICH and mortality were higher in patients treated with EVT compared to those receiving MM, regardless of baseline NIHSS being ≤ 6 or > 6 ($p_{\text{int}} = 0.467$), but the mortality increase was significantly more pronounced in the former group ($p_{\text{int}} = 0.044$, NIHSS ≤ 6 : aOR=7.95, 95%CI=3.11-20.28, NIHSS > 6 : aOR=1.98, 95%CI=1.08-3.65). Similarly, we detected an interaction between EVT and NIHSS as continuous variable for excellent outcome ($p_{\text{int}} = 0.047$), functional independence ($p_{\text{int}} < 0.001$) and mortality ($p_{\text{int}} = 0.005$) (**Figure 2A-F** and **Figure S2A-F** for IPTW analysis). In the

multivariable analysis, EVT was associated with more excellent outcome and functional independence starting from baseline NIHSS >6 and >11 respectively (as indicated by the point at which the lower boundary of the 95% CI of the OR crossed 1, indicating no association) (**Figure 2B-C**). Similar results were obtained in the IPTW analysis, where the association of EVT with excellent outcome and functional independence was present starting from baseline NIHSS >4 and >8 respectively (**Figure S2B-C**).

When comparing patients with occlusions in the P1 and P2 segments of the PCA, those with P1 segment occlusion presented with higher baseline NIHSS (median [IQR]= 8 [4-13] vs. 5 [3-8], $p<0.0001$), less frequent visual field deficits (63.9% vs. 74.1%, $p=0.001$), and lower baseline pc-ASPECTS (median [IQR]= 9 [8-10] vs. 9 [9-10], $p=0.004$, **Table S4**). They had similar rates of IVT administration (38.4 % vs. 43.6%, $p=0.089$) but underwent EVT more frequently (44.8% vs. 25.6%, $p<0.001$). Procedural metrics among EVT-treated patients were comparable between patients with P1 and P2 occlusions. While univariable analysis showed that P2 occlusion was associated with a more favorable mRS distribution, a higher proportion of excellent outcome and functional independence, and lower mortality, these differences were not significant when adjusting for potential confounders in multivariable and IPTW analyses (**Table 3**). We did not detect an interaction between EVT and the occluded arterial segment with regard to any of these outcomes. EVT was associated with a higher likelihood of early neurological improvement but also higher rates of sICH and mortality without a significant association with the overall 3-month mRS distribution. These findings were consistent across the entire cohort and within the P1 and P2 occlusions both in multivariable and IPTW analyses (**Figure 1B, Table S5**).

Discussion

This secondary analysis of the international multicenter PLATO cohort demonstrated that among patients presenting with iPCAo within 24 hours of symptom onset, baseline NIHSS significantly modified the association of EVT with outcomes. In moderate to severe iPCAo stroke, EVT was associated with a higher rate of excellent outcome and functional independence, despite higher mortality and sICH. In mild iPCAo stroke, the increased mortality associated with EVT compared to MM was more pronounced, sICH was similarly increased, and the difference on disability outcomes was absent or less in favor of EVT. The site of arterial occlusion in P1 or P2 segments of the PCA did not modify the association of EVT with any of the clinical or safety outcomes.

According to our findings, initial stroke severity measured by NIHSS emerges as an important parameter in guiding EVT selection for iPCAo patients. In patients with mild deficits at baseline, the potential advantages of arterial recanalization with EVT may be outweighed by procedural complications and a

higher risk of sICH. Indeed, these complications usually yield a pronounced impact on outcomes,¹⁴ which is likely to weigh even more in the population with baseline mild deficits. Conversely, in patients presenting with more severe strokes, the advantage of revascularization may balance or outweigh the risks associated with EVT, and the impact of procedural complications might be comparatively less significant. Our analysis of baseline NIHSS as a continuous variable provides results consistent with those from the dichotomized NIHSS approach. It also suggests that the NIHSS threshold at which the treatment-outcome association becomes evident varies depending on the outcome measure. For instance, the outcomes association with EVT compared to MM became apparent at lower NIHSS values for the mRS 0-1 endpoint, whereas a higher NIHSS threshold was required to show better EVT outcomes when mRS 0-2 was used as outcome measure. In other words, patients with a lower baseline NIHSS may have less likelihood of showing EVT benefit compared to MM on higher Rankin disability endpoints, such as mRS 0-2. Our findings on the role of baseline NIHSS are rather novel, as previous observational studies on iPCAO either did not perform subgroup analysis evaluating 3-month outcome as stratified by baseline NIHSS,^{3,7} or did not detect better 3-month outcomes (mRS 0-1, mRS 0-2) with EVT compared to MM in patients with NIHSS >10, possibly due to lower sample size.⁵ Nevertheless, the TOPMOST and EaT-PeCANpIeS studies reported results on short-term outcome consistent with ours,^{3,7} revealing a greater probability of neurological improvement and better mRS at hospital discharge with EVT in iPCAO patients with more severe stroke. Similar trends regarding the influence of baseline NIHSS have been observed in studies looking at other intracranial occlusions, particularly in basilar artery occlusions, where potential benefits have been suggested in patients with baseline NIHSS ≥ 6 , whereas outcomes are less certain for those with mild clinical stroke severity.^{10,11,13} Similarly, in anterior circulation occlusion, the benefit of EVT has been established primarily for AIS with moderate to severe strokes, while its efficacy in patients presenting with mild deficits remains under debate.^{15,16} Notably, anterior circulation LVOs with initial minor deficit not receiving EVT often result in early neurological deterioration, significantly impacting medium-term outcomes. This deterioration is commonly attributed to a breakdown of collateral supply and is potentially preventable by immediate EVT.¹⁷ Interestingly, PCAOs receiving MM appear to have a lower rate of early neurological deterioration,^{5,17} which could further diminish the potential benefit of EVT.

The absence of influence of arterial occlusion site on EVT outcomes might appear unexpected but has already been reported in previous studies.³⁻⁵ This probably indicates that the distinction between the P1 and P2 segments may not comprehensively capture the different aspects of PCAO. Indeed, distal P1 occlusions could resemble proximal P2 occlusions in many aspects, such as functional impact, stroke

clinical severity, and technical accessibility. Conversely, within the P1 segment, occlusions might exhibit substantial heterogeneity depending on the involvement of thalamic or mesencephalic structures, mesiotemporal areas, the visual cortex, and the presence (or absence) of the posterior communicating artery supply of the P2 segment. Similarly, P2 occlusions may significantly vary in functional impact, depending on the involvement of the visual cortex and accessibility to EVT, which pivots on whether the occlusion is more proximal or distal within the P2 segment.¹⁸ Consequently, owing to the similarities between P1 and P2 occlusions and the clinical heterogeneity within each segment, the P1 versus P2 distinction might bear less relevance in the acute ischemic stroke setting and the selection of acute revascularization treatments. As an alternative explanation, our adjustment of this analysis with baseline NIHSS could have eliminated a possible effect of EVT on occlusion location.

Our study has limitations. First, the observational design, where patient allocation to treatment groups relied on the discretion of treating physicians, incurs selection bias. Second, patients were included from routine clinical practice, potentially leading to reporting bias due to unblinded outcome assessment. Third, the EVT group presented with a more severe baseline neurological deficit, which we adjusted for by conducting multivariable and IPTW analyses. The congruence of results across these analyses reinforces the validity of our findings. Additionally, we acknowledge that the NIHSS might not be the most suitable scale for assessing deficits resulting from posterior cerebral artery territory infarction.^{19,20} Besides, while the pc-ASPECTS was developed to quantify ischemic changes in the posterior circulation, i.e., basilar artery occlusion,²¹ it might not best capture the extent of stroke in iPCAO. Therefore, it is not surprising that both treatment groups in our study had high median pc-ASPECTS. Also, no central reading to ascertain site of occlusion or pc-ASPECTS score was performed. Furthermore, although our study documented follow-up NIHSS, 3-month mRS, sICH, and mortality, vision examination at 3 months was missing in a substantial proportion of patients with baseline visual field defects. Consequently, we could not perform an analysis of this outcome. Finally we did not evaluate cognitive outcomes, which may be a clinically meaningful consequence of PCA occlusion.⁴

In conclusion, our findings suggest that baseline NIHSS, rather than the site of arterial occlusion, appears to be an important modifier of the association of EVT versus MM and outcomes in iPCAO. EVT was associated with more favorable disability outcomes than MM in moderate to severe iPCAO strokes, while this difference was absent or less in favor of EVT in minor strokes. Mortality was higher with EVT compared to MM in both minor and severe stroke, but to a greater extent in the latter group. sICH was

increased with EVT irrespectively of baseline NIHSS. These observations might be important for hypothesis generation in future randomized studies exploring the efficacy of EVT for iPCAO.

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Supplementary Material

Table S1

Table S2

Table S3

Table S4

Table S5

Figure S1

Figure S2



Stroke

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Figures legend

Figure 1. Forest plot summarizing the odds ratio (OR) and their 95% confidence intervals (CI) obtained from multivariable regression analysis for comparison of endovascular treatment (EVT) and medical management (MM) on ordinal modified Rankin Scale (mRS) favorable shift, excellent outcome, functional independence, NIHSS decrease ≥ 2 points, symptomatic intracranial hemorrhage (sICH), and mortality, stratified by (A) baseline NIHSS (0-6 vs. >6) and (B) posterior cerebral artery (PCA) segment occluded (P1 vs. P2). The regression models were adjusted for the following covariates, in addition to baseline NIHSS, segment occluded and treatment: age, sex, baseline mRS, year of treatment, pc-ASPECTS, hypertension, atrial fibrillation, diabetes mellitus, IV tPA.

Figure 2. Association of endovascular treatment (EVT) versus medical management (MM) and outcomes expressed as odds ratio (OR) and their 95% confidence intervals (CI), depending on continuous baseline NIHSS. An OR greater than 1 indicates that the outcome is more likely with EVT, whereas for $OR < 1$ the outcome is more likely with MM. The outcomes displayed are: (A) ordinal modified Rankin Scale (mRS) favorable shift, (B) excellent outcome, (C) functional independence, (D) NIHSS decrease ≥ 2 points, (E) symptomatic intracranial hemorrhage (sICH), and (F) mortality. The continuous dark line indicates the point estimate of the OR associated with EVT vs MM at each NIHSS value. The shaded gray area reflects the 95% CI of the odds ratio. The vertical dotted lines indicate the NIHSS value at which the point estimate and the lower bound of the 95% CI crosses 1 (displayed only in case of statistically significant interaction between baseline NIHSS and treatment). ORs are obtained from multivariable regression analysis (MVA) with interaction term between treatment and baseline NIHSS. Models were adjusted for: age, sex, baseline mRS, year of treatment, pc-ASPECTS, hypertension, atrial fibrillation, diabetes mellitus, IV tPA, and segment occluded.

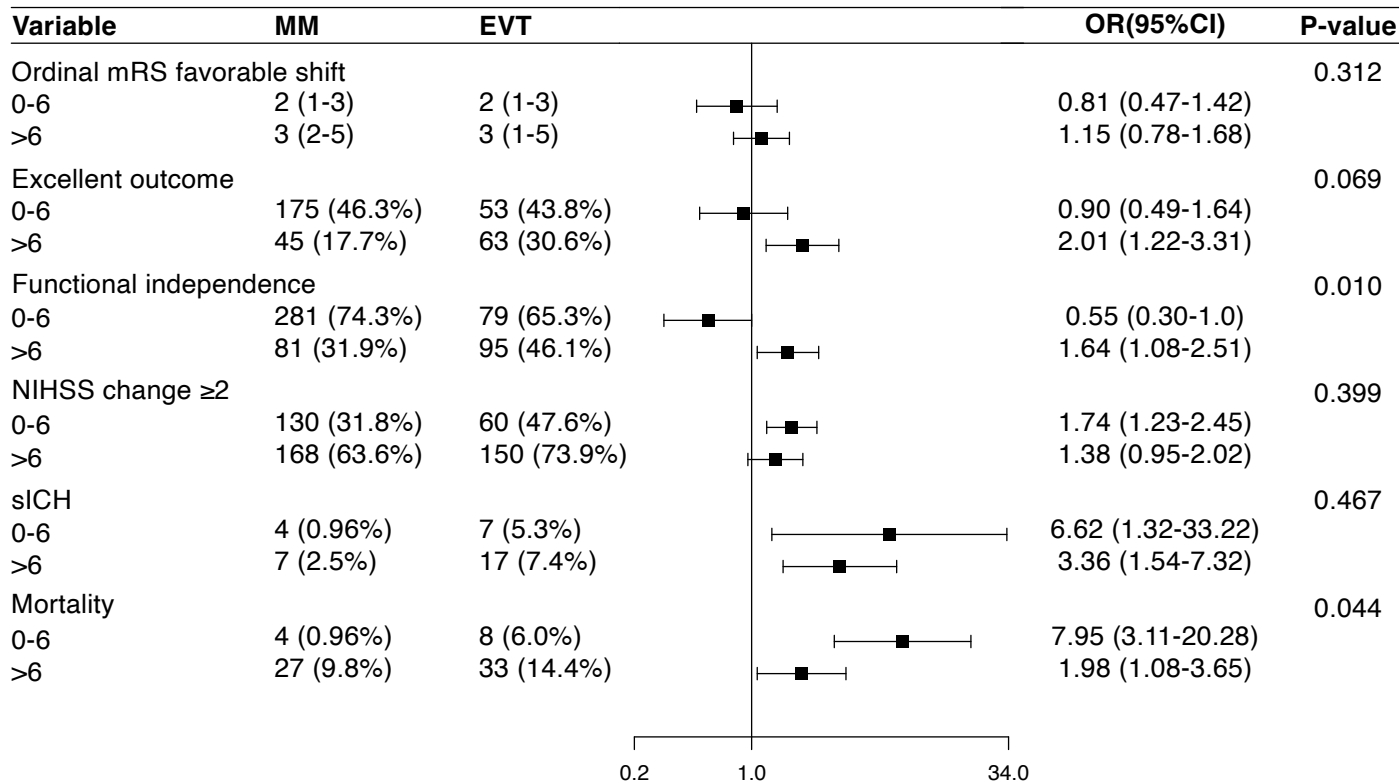
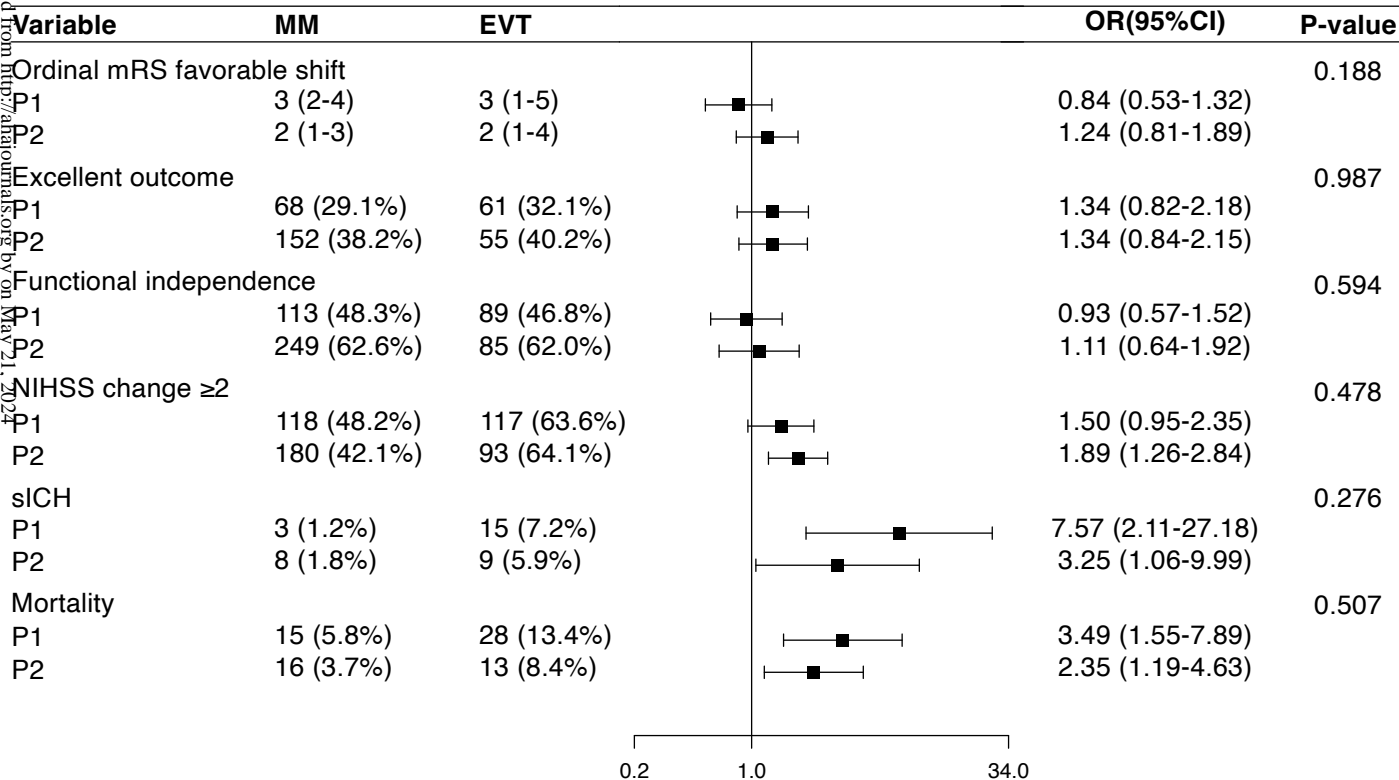
A**B**

Figure 2. Interaction between treatment and NIHSS as continuous variables (multivariable adjusted models)

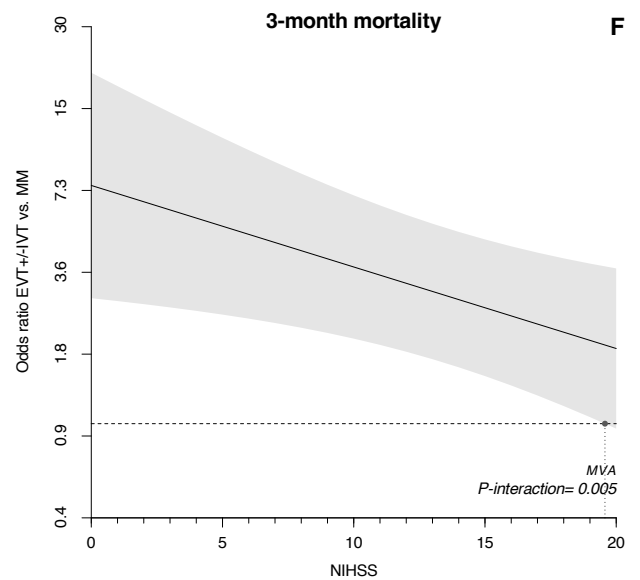
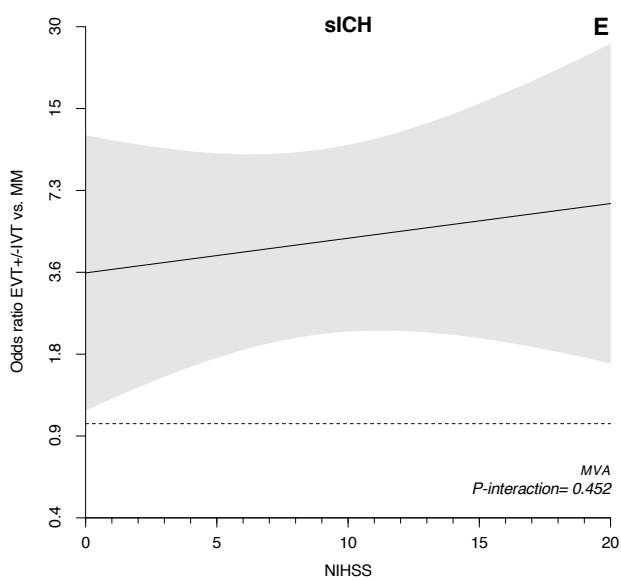
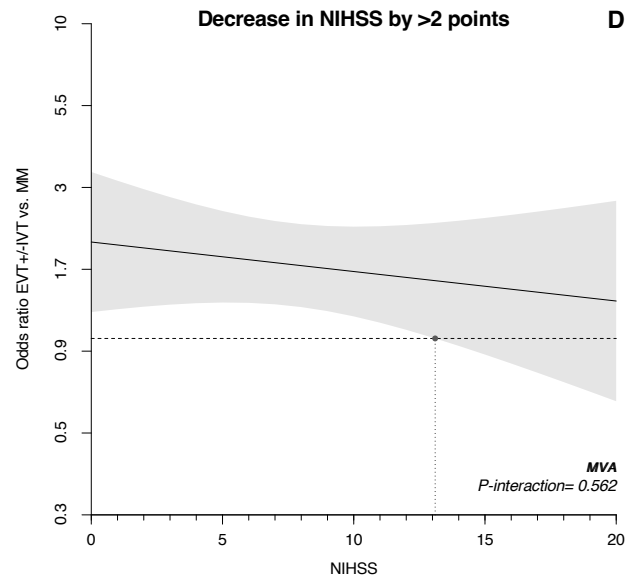
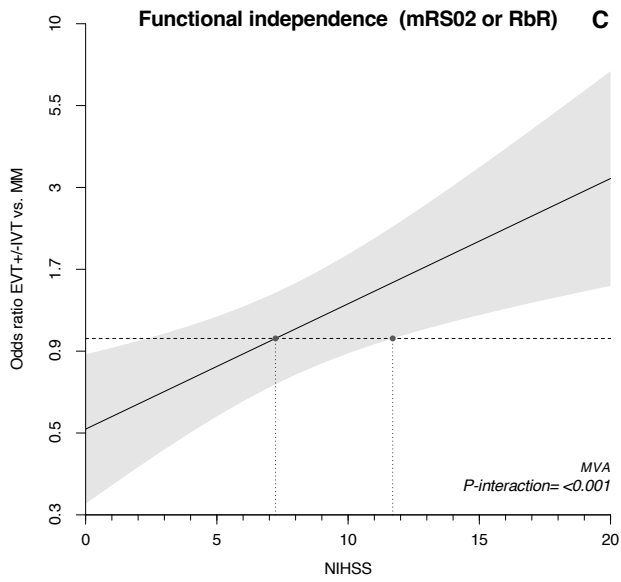
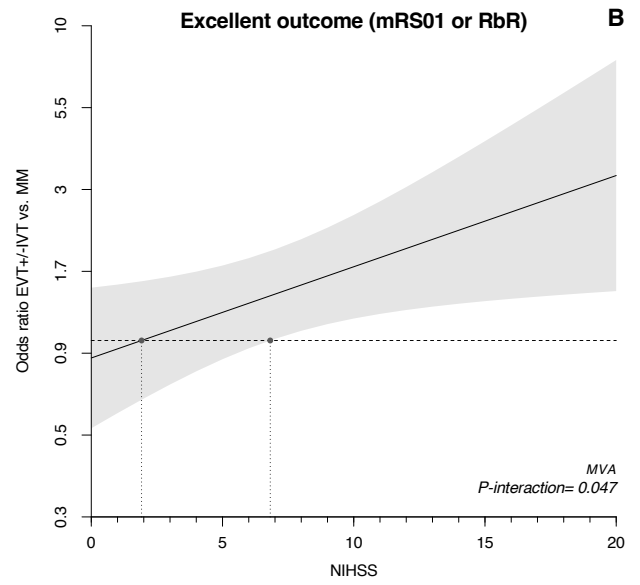
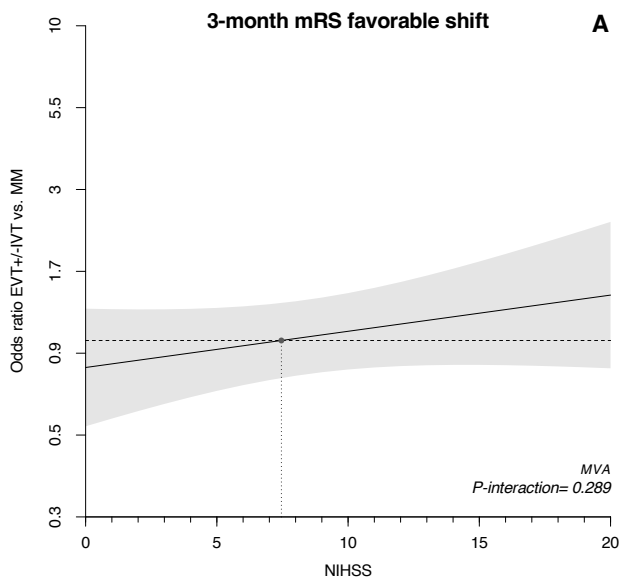


Table 1. Baseline characteristics and metrics of patients with posterior cerebral artery (PCA) occlusion by baseline NIHSS.

	Baseline NIHSS 0-6 (N=551)	Baseline NIHSS >6 (N=508)	<i>P</i>
Demographics			
Age, years	72 (61-80)	76 (67-83)	<0.0001
Sex			0.009
Male	337 (61.2)	270 (53.2)	
Female	214 (38.8)	238 (46.9)	
Year of treatment (2000s)	19 (17-20)	19 (17-20)	0.317
Clinical characteristics			
Transfer (N=913)			0.022
Local	397 (86.7)	369 (81.1)	
Transfer	61 (13.3)	86 (18.9)	
Baseline mRS			<0.0001
0	351 (63.7)	252 (49.6)	
1	103 (18.7)	109 (21.5)	
2	63 (11.4)	76 (15.0)	
3	34 (6.2)	71 (14.0)	
Baseline visual field deficit (N=941)			0.004
No	173 (34.4)	113 (25.8)	
Yes	330 (65.6)	325 (74.2)	
Admission SBP, mmHg (N=953)	158 (140-174)	155 (137-174)	0.204
Admission DBP, mmHg (N=948)	86 (76-96)	84 (75-95)	0.239
Vascular risk factors			
Hypertension	399 (72.4)	417 (82.1)	0.0002
Atrial fibrillation	134 (24.3)	173 (34.1)	0.001
Diabetes mellitus	131 (23.8)	163 (32.1)	0.003
Hyperlipidemia (N=1,057)	292 (53.0)	229 (45.3)	0.012
Current Smoker (N=981)	107 (20.7)	80 (17.2)	0.169
Prior Stroke (N=1,045)	99 (18.2)	92 (18.3)	0.968
Peripheral Artery Disease (N=958)	26 (5.2)	31 (6.8)	0.290
Dialysis (N=979)	16 (3.1)	22 (4.7)	0.195
Oral anticoagulation (N=1,036)	72 (13.4)	80 (16.1)	0.213
Statin (N=999)	176 (33.7)	164 (34.4)	0.825
Imaging and clot location			
pc-ASPECTS	9 (9-10)	9 (8-10)	0.426
Baseline imaging modality (N=1,048)			
CT	487 (89.4)	466 (92.6)	0.064
MRI	159 (29.2)	95 (18.9)	0.0001
Perfusion-imaging done (CT or MRI)	249 (45.7)	285 (56.7)	0.0004
Mismatch ratio > 1.2 ⁺ (N=408)	164 (84.1)	178 (83.6)	0.884
Occlusion site			<0.0001
P1	190 (34.5)	279 (54.9)	
P2	361 (65.5)	229 (45.1)	

Table 1. Baseline characteristics and metrics of patients with posterior cerebral artery (PCA) occlusion by baseline NIHSS continued.

	Baseline NIHSS 0-6 (N=551)	Baseline NIHSS >6 (N=508)	<i>P</i>
Time metrics and procedural factors			
IV tPA			0.155
No	335 (60.8)	287 (56.5)	
Yes	216 (39.2)	221 (43.5)	
Treatment			<0.0001
MM	418 (75.9)	277 (54.5)	
EVT	133 (24.1)	231 (45.5)	
Time to treatment*, h (N=894)	3.5 (2.0-9.2)	3.3 (1.9-6.8)	0.060
Time to treatment*, h (N=894)			0.027
0 to <6	301 (65.6)	315 (72.4)	
6 to 24	158 (34.4)	120 (27.6)	
Number of passes (N=331)	1 (1-2)	1 (1-2)	0.921
Recanalization (N=406)			0.859
TICI 0-2a	41 (26.8)	62 (24.5)	
TICI 2b	20 (13.1)	39 (15.4)	
TICI 2c	14 (9.2)	20 (7.9)	
TICI 3	78 (51.0)	132 (52.2)	
First pass EVT method (N=320)			0.035
Stent retriever	11 (9.1)	30 (15.1)	
Contact Aspiration	47 (38.8)	58 (29.2)	
Combined technique	59 (48.8)	110 (55.3)	
IA lytic	4 (3.3)	1 (0.50)	
Other			
Stroke etiology (N=1,054)			0.083
Large artery atherosclerotic	85 (15.5)	77 (15.3)	
Cardioembolic	209 (38.1)	223 (44.2)	
Small vessel atherosclerotic	9 (1.6)	15 (3.0)	
Other determined	51 (9.3)	34 (6.7)	
Undetermined	195 (35.5)	156 (30.9)	

Continuous variables are reported as median and interquartile range, categorical variables as number of patients and column percentages.

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; N, the total number of patients; mRS, modified Rankin Scale; SBP, systolic blood pressure; DBP, diastolic blood pressure; pc-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT Score; CT, computed tomography; MRI, Magnetic resonance imaging; IV tPA, intravenous tissue-type plasminogen activator; MM, Medical Management; EVT, Endovascular Therapy; TICI, Treatment in Cerebral Infarction; IA, intra-arterial.

†Calculated as the ratio between hypoperfusion volume and core volume.

*Time from symptom onset or last known well if unwitnessed onset, to administration of IVT or groin puncture for those treated with EVT.

Table 2. Outcomes of patients with posterior cerebral artery (PCA) occlusion by baseline NIHSS.

	Baseline NIHSS 0-6 (N=551)	Baseline NIHSS >6 (N=508)	Univariable comparison P	Univariable model OR (95% CI)	Multivariable model OR (95% CI)	IPTW model OR (95% CI)
mRS, 3 months (N=959)	2 (1-3)	3 (2-5)	<0.0001	0.27 (0.22-0.33)*	0.33 (0.27-0.41)*	0.39 (0.32-0.47)*
mRS 0-1 or RbR, 3 months (N=959)	228 (45.7)	108 (23.5)	<0.0001	0.36 (0.27-0.49)*	0.37 (0.28-0.50)*	0.40 (0.29-0.54)*
mRS 0-2 or RbR, 3 months (N=959)	360 (72.1)	176 (38.3)	<0.0001	0.24 (0.19 -0.30)*	0.27 (0.20-0.36)*	0.33 (0.26-0.41)*
NIHSS change ⁺ (continuous) (N=1,002)	1 (0-2)	4 (0-8)	<0.0001			
NIHSS change ≥ 2 (N=1,002)	190 (35.5)	318 (68.1)	<0.0001	3.88 (2.90-5.18)*	4.24 (3.22-5.58)*	3.37 (2.81-5.04)*
HBC ICH (N=856)	73 (16.6)	96 (23.1)	0.016			
Fatal ICH (N=1,001)	3 (0.57)	8 (1.7)	0.086			
sICH (N=1,054)	11 (2.0)	24 (4.8)	0.013	2.44 (1.46-4.08)*	1.42 (0.87-2.32)	1.59 (1.02-2.49)*
Vision recovery (N=233/655) [†]			0.474			
Complete	60 (43.5)	47 (49.5)				
Partial	15 (10.9)	5 (5.3)				
Same	53 (38.4)	36 (37.9)				
Worse	10 (7.3)	7 (7.4)				
Mortality (1,058)	12 (2.2)	60 (11.8)	<0.0001	6.03 (3.30-11.1)*	3.93 (2.05-7.52)*	3.23 (1.75-5.97)*

Continuous variables are reported as median and interquartile range, categorical variables are reported as number of patients and column percentages.

Abbreviations: NIHSS, National Institutes of Health Stroke Scale; N, the total number of patients; OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment weighting; mRS, modified Rankin Scale; RbR=Return to baseline Rankin; HBC, Heidelberg Bleeding Classification; ICH, Intracerebral hemorrhage; sICH, symptomatic intracranial hemorrhage.

Note: The multivariable model and IPTW analysis account for the following variables: age, sex, baseline mRS, year of treatment, pc-ASPECTS, hypertension, atrial fibrillation, diabetes mellitus, IV tPA, occlusion site, and treatment.

* Significant at $p < 0.05$ level

⁺Change in NIHSS is defined as NIHSS at admissions – NIHSS at discharge. A positive score means NIHSS at discharge is $<$ NIHSS at admission.

[†]Of 655 with visual field defects at baseline, information on vision recovery was available for 233. There were 57 deceased, while 365 were missing information.

Table 3. Outcomes of patients with posterior cerebral artery (PCA) occlusion by segment of arterial occlusion.

	P1 (N=469)	P2 (N=590)	Univariable compariso	Univariable model OR (95% CI)	Multivariable model OR (95% CI)	IPTW model
mRS, 3 months (N=959)	3 (2-4)	2 (1-3)	<0.0001	1.73 (1.36-2.21)*	1.12 (0.86-1.46)	1.08 (0.77-1.51)
mRS 0-1 or RbR, 3 months (N=959)	129 (30.4)	207 (38.7)	0.008	1.44 (1.13-1.84)*	1.16 (0.91-1.50)	1.09 (0.81-1.47)
mRS 0-2 or RbR, 3 months (N=959)	202 (47.6)	334 (62.4)	<0.0001	1.83 (1.37-2.44)*	1.27 (0.91-1.77)	1.14 (0.80-1.63)
NIHSS change ⁺ (continuous)	2 (0-5)	1 (0-4)	0.019			
NIHSS change ≥ 2 (N=1,002)	235 (54.8)	273 (47.6)	0.025	0.75 (0.54-1.05)	0.94 (0.70-1.28)	0.92 (0.63-1.34)
HBC ICH (N=856)	76 (19.7)	93 (19.8)	0.999			
Fatal ICH (N=1,001)	5 (1.2)	6 (1.1)	0.856			
sICH (N=1,054)	18 (3.9)	17 (2.9)	0.395	0.75 (0.38-1.47)	1.13 (0.48-2.67)	1.07 (0.49-2.36)
Vision recovery (N=233/655) [†]			0.080			
Complete	40 (55.6)	67 (41.6)				
Partial	2 (2.8)	18 (11.2)				
Same	26 (36.1)	63 (39.1)				
Worse	4 (5.6)	13 (8.1)				
Mortality (1,058)	43 (9.2)	29 (4.9)	0.007	0.51 (0.31-0.85)*	0.88 (0.54-1.43)	1.47 (0.68-3.17)

Continuous variables are reported as median and interquartile range, categorical variables are reported as number of patients and column percentages.

Abbreviations: N, the total number of patients; OR, odds ratio; CI, confidence interval; IPTW, inverse probability of treatment weighting; mRS, modified Rankin Scale; RbR=Return to baseline Rankin; NIHSS, National Institutes of Health Stroke Scale; HBC, Heidelberg Bleeding Classification; ICH, Intracerebral hemorrhage; sICH, symptomatic intracranial hemorrhage.

Note: The multivariable model and IPTW analysis account for the following variables: age, sex, baseline mRS, baseline NIHSS, year of treatment, pc-ASPECTS, hypertension, atrial fibrillation, diabetes mellitus, IV tPA, and treatment

* Significant at $p < 0.05$ level

⁺Change in NIHSS is defined as NIHSS at admissions – NIHSS at discharge. A positive score means NIHSS at discharge is $<$ NIHSS at admission.

[†]Of 655 with visual field defects at baseline, information on vision recovery was available for 233. 57 were deceased, while 365 were missing information.