Stroke

CLINICAL AND POPULATION SCIENCES

Intravenous Thrombolysis Before Endovascular Treatment in Posterior Circulation Occlusions: A MR CLEAN Registry Study

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BACKGROUND: The effectiveness of intravenous thrombolysis (IVT) before endovascular treatment (EVT) has been investigated in randomized trials and meta-analyses. These studies mainly concerned anterior circulation occlusions. We aimed to investigate clinical, technical, and safety outcomes of IVT before EVT in posterior circulation occlusions in a nationwide registry.

METHODS: Patients were included from the MR CLEAN Registry (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands), a nationwide, prospective, multicenter registry of patients with acute ischemic stroke due to a large intracranial vessel occlusion receiving EVT between 2014 and 2019. All patients with a posterior circulation occlusion were included. Primary outcome was a shift toward better functional outcome on the modified Rankin Scale at 90 days. Secondary outcomes were favorable functional outcome (modified Rankin Scale scores, 0–3), occurrence of symptomatic intracranial hemorrhages, successful reperfusion (extended Thrombolysis in Cerebral Ischemia ≥2B), first-attempt successful reperfusion, and mortality at 90 days. Regression analyses with adjustments based on univariable analyses and literature were applied.

RESULTS: A total of 248 patients were included, who received either IVT (n=125) or no IVT (n=123) before EVT. Results show no differences in a shift on the modified Rankin Scale (adjusted common odds ratio, 1.04 [95% CI, 0.61–1.76]). Although symptomatic intracranial hemorrhages occurred more often in the IVT group (4.8% versus 2.4%), regression analysis did not show a significant difference (adjusted odds ratio, 1.65 [95% CI, 0.33–8.35]). Successful reperfusion, favorable functional outcome, first-attempt successful reperfusion, and mortality did not differ between patients treated with and without IVT.

CONCLUSIONS: We found no significant differences in clinical, technical, and safety outcomes between patients with a large vessel occlusion in the posterior circulation treated with or without IVT before EVT. Our results are in line with the literature on the anterior circulation.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: posterior circulation ■ stroke ■ thrombectomy ■ thrombolytic therapy

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*A list of all MR CLEAN Registry participants is given in the Appendix.
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For Sources of Funding and Disclosures, see page 409.

Nonstandard Abbreviations and Acronyms

aOR	adjusted odds ratio
BAO	basilar artery occlusion
CT	computed tomography
eTICI	extended Thrombolysis in Cerebral Ischemia
EVT	endovascular treatment
IV r-tPA	intravenous recombinant tissue-type plasminogen activator
IVT	intravenous thrombolysis
LVO	large vessel occlusion
MR CLEAN	Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands
mRS	modified Rankin Scale
sICH	symptomatic intracranial hemorrhage

Intravenous thrombolysis (IVT) before endovascular treatment (EVT) is recommended in all patients with ischemic stroke due to an intracranial large vessel occlusion (LVO) in the anterior circulation within 4.5 hours after symptom onset.[1] Although treatment with IVT between 4.5 and 9 hours may be considered in the presence of a mismatch on computed tomography (CT) perfusion in the anterior circulation, there is no consensus about the indication for IVT before EVT in this late time window.[1]

Recent meta-analyses and randomized clinical trials found no superiority or noninferiority in functional outcome and mortality at 90 days between patients with an LVO treated with and without IVT before EVT.[2–8] These studies mainly concerned patients with anterior circulation occlusions.

The BEST (Basilar Artery Occlusion Endovascular Intervention Versus Standard Medical Treatment), BASICS (Basilar Artery International Cooperation Study), ATTENTION (Endovascular Treatment for Acute Basilar Artery Occlusion: A Multicentre Randomised Clinical Trial), and BAOCHE (Basilar Artery Occlusion Chinese Endovascular) trials are randomized clinical trials on the effectiveness of EVT in patients with basilar artery occlusion (BAO).[9–12] ATTENTION and BAOCHE showed a beneficial effect of EVT in patients treated within 12 hours and between 6 and 24 hours of symptom onset, respectively. However, no randomized clinical trials are available on the effectiveness of IVT in posterior circulation occlusions.[13] Two meta-analyses, based on cohort studies, showed lower incidences of intracranial hemorrhage in patients treated with IVT alone for posterior circulation stroke as compared with anterior circulation stroke. These meta-analyses included all posterior circulation occlusions (intracranial vertebral, basilar, and posterior cerebral artery occlusions).[14,15] In patients with posterior circulation stroke compared with anterior circulation stroke treated with IVT, but without EVT, higher mortality rates were found.[15] When patients were treated with IVT before EVT, symptomatic intracranial hemorrhage (sICH) rates were comparable and mortality rates were higher in the posterior circulation occlusion as compared with anterior circulation occlusion.[15]

Because the available data from the literature is limited, our study aimed to investigate the outcomes of patients with posterior circulation occlusion treated with EVT, with or without prior IV r-tPA (intravenous recombinant tissue-type plasminogen activator) in a large nationwide registry MR CLEAN Registry (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands).[16]

METHODS

The corresponding author had full access to all the data in this study and takes responsibility for its integrity and the data analysis. Source data will not be made available because of legislative issues on patient privacy. Detailed statistical analyses and analytic methods will be made available on reasonable request to the corresponding author. This study was conducted using the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Design and Participants

Patients were included from the MR CLEAN Registry: a prospective, observational study in all EVT performing centers (n=18) in the Netherlands. The registry included patients treated with EVT for acute ischemic stroke due to LVO between March 2014 and December 2018. The MR CLEAN Registry study protocol was evaluated by the medical ethics committee of the Erasmus University Medical Center and permission was granted to carry out the study as a registry. The need for obtaining informed consent was waived. For the current study, the following inclusion criteria were used: age ≥18 years, National Institutes of Health Stroke Scale score ≥2, and an occlusion in the posterior circulation (intracranial vertebral artery, basilar artery, or posterior cerebral artery) confirmed by CT angiography. Patients in whom only a catheterization was performed due to no intracranial access of the materials were excluded.

The time of symptom onset was defined as the first moment of start symptoms when witnessed or the time the patient was last seen well if the onset was unwitnessed. In patients with mild neurological symptoms with secondary clinical worsening, the time of deterioration was considered as the estimated time of the LVO.

Treatment

Because EVT was not yet been proven to be effective in BAO patients, EVT was not performed routinely and was not supported by national guidelines. Its use was based on the clinical judgment of the treating physician. All patients with BAO treated with EVT in the Netherlands outside the BASICS trial were registered. IV r-tPA (alteplase) could be administered within 4.5 hours after the estimated time of the LVO but also

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after 4.5 hours. Treating physicians were free to choose which materials and thrombectomy techniques they used during EVT.

Outcome Measures

The primary outcome was the modified Rankin Scale (mRS) score at 90 days follow-up, ranging from 0 (no disability) to 6 (death). In the MR CLEAN Registry, the mRS score at 90 days was scored by trained nurses during an in-person or telephonic interview. Secondary outcomes were favorable functional outcome (defined as mRS scores, 0–3), functional independent outcome (defined as mRS scores, 0–2), and the National Institutes of Health Stroke Scale score at 24 to 48 hours. Technical outcomes included procedure duration (defined as groin puncture to reperfusion), first-attempt successful reperfusion, and successful reperfusion. Safety outcomes were the occurrence of sICH within 3 days after EVT, mortality at 90 days, and serious adverse events (eg, stroke progression and pneumonia).

Imaging Assessment

Intracranial hemorrhage was defined as symptomatic when the patient had neurological deterioration (at least 4 points increase on the National Institutes of Health Stroke Scale) in combination with a hemorrhage (according to the Heidelberg criteria), which was related to the clinical deterioration. An adverse event committee evaluated the medical reports and imaging to determine a sICH.

Reperfusion status was scored on digital subtraction angiography according to the extended Thrombolysis in Cerebral Ischemia (eTICI) by an independent core laboratory. This core laboratory consisted of 8 interventional radiologists or neuroradiologists, all blinded to the clinical findings. The neuroimaging scoring was centrally conducted and the core laboratory had access to all available neuroimaging per patient, this included digital subtraction angiography, noncontrast CT, CT angiography, and CT perfusion when available. The eTICI ranges from 0 (no reperfusion) to 3 (complete reperfusion). In this study, successful reperfusion was defined as eTICI ≥2B (50%–90% reperfusion of affected area), excellent reperfusion as eTICI 3, and first-attempt successful recanalization as eTICI ≥2C (90%–99% reperfusion of affected area) in combination with 1 attempt. When only a digital subtraction angiography was performed because of recanalization, it was registered as early recanalization. When the digital subtraction angiography was made in only 1 direction, the maximum eTICI score was set at 2A. The posterior circulation Acute Stroke Prognosis Early Computed Tomography Score was scored on noncontrast CT, while the posterior circulation collateral score was scored on baseline CT angiography by the core laboratory.

Statistical Analysis

Baseline characteristics were presented using descriptive statistics. Dichotomous and ordinal parameters were compared using Pearson χ^2 test or Fisher exact test. Continuous variables were tested using independent-samples *t* test or Mann-Whitney *U* test, after checking for the normality using histograms.

For the primary outcome, a multivariable ordinal logistics regression model was used to compare the use of IVT for a 1-step shift on the mRS score at 90 days follow-up. Continuous variables were checked on normality of distribution of the residuals using Q-Q plots. When no normality was seen, the variable

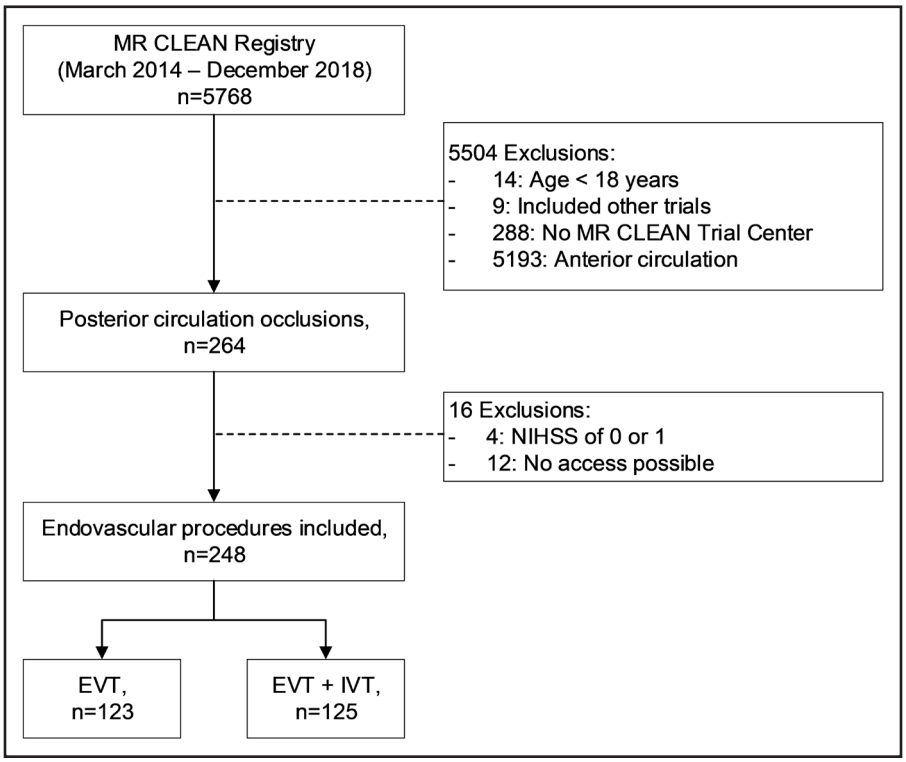

Figure 1. Flow-chart of included patients in this study.
EVT indicates endovascular treatment; IVT, intravenous thrombolysis; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and NIHSS, National Institutes of Health Stroke Scale.

Table 1. Baseline Characteristics of Included Patients

	Treated without IVT (n=123)	Treated with IVT (n=125)	*P* value
Age, y; median (IQR)	69 (56–76)	62 (52–71)	0.14
Male, n (%)	64 (52)	78 (62)	0.13
BMI, kg/m^2; median (IQR)*	26 (23–29)	26 (24–29)	0.34
Patient's history, n (%)			
Previous stroke	27/120 (23)	19/125 (15)	0.19
Atrial fibrillation	23/120 (19)	14/125 (11)	0.12
Hypertension	63/118 (53)	61/124 (49)	0.60
Hypercholesterolemia	27/116 (23)	26/122 (21)	0.84
Myocardial infarction	20/120 (17)	11/123 (8.9)	0.11
Diabetes	20/121 (17)	23/125 (18)	0.83
Current smoking	27/84 (32)	26/93 (28)	0.66
Medication, n (%)			
Antiplatelet	36/119 (30)	32/123 (26)	0.56
Anticoagulation	24/118 (20)	6/122 (4.9)	<0.00
Antihypertensive medication	68/116 (59)	56/122 (46)	0.07
Statin	36/118 (31)	34/121 (28)	0.79
Clinical			
NIHSS baseline, median (IQR)†	17 (9.3–29)	15 (7.5–31)	0.81
Pre-mRS, n (%)			0.02
0	73/122 (60)	88/121 (73)	
1	17/122 (14)	20/121 (17)	
2	14/122 (12)	8/121 (6.6)	
3	6/122 (4.9)	3/121 (2.5)	
>3	12/122 (9.8)	2/121 (1.7)	
Systolic blood pressure; median mm Hg (IQR)‡	150 (130–170)	149 (130–163)	0.25
Course symptoms, n (%)			0.74
Maximum from onset	56/116 (48)	65/123 (53)	
Progressive deficit	44/116 (38)	41/123 (33)	
Fluctuating deficit	16/116 (14)	17/123 (14)	
Imaging			
Occlusion location, n (%)			0.11
Intracranial VA	6/120 (5.0)	8/123 (6.5)	
BA	57/120 (48)	38/123 (31)	
BA extending in PCA	38/120 (32)	54/123 (44)	
PCA	15/120 (13)	17/123 (14)	
Non-occlusive thrombosis	4/120 (3.3)	6/123 (4.9)	
PC-ASPECTS, n (%)			0.33
0–4	4/121 (3.3)	2/124 (1.6)	
5–7	11/121 (9.1)	6/124 (4.8)	
8–10	106/121 (88)	116/124 (94)	
PC-collaterals, n (%)			0.67
0–4	14/120 (12)	19/122 (16)	
5–7	64/120 (53)	61/122 (40)	
8–10	42/120 (35)	42/122 (34)	
Procedure			
Duration onset symptoms to groin, min; median (IQR)	360 (228–565)	234 (169–311)	<0.00
Duration eLVO to groin, min; median (IQR)‖	300 (195–438)	207 (157–290)	<0.00
Door to groin in minutes, median, (IQR)]¶	89 (48–146)	79 (57–105)	0.14
Performed procedure, n (%)			0.01
DSA	7 (5.7)	21 (17)	
EVT	116 (94)	104 (83)	
Technique first attempt, n (%)			
Stent retriever	65/115 (57)	66/100 (66)	0.20
Direct aspiration	41/115 (36)	30/100 (30)	0.46
Transfer from primary stroke center, n (%)	45 (37)	59 (47)	0.12

BA indicates basilar artery; BMI, body mass index; DSA, digital subtraction angiography; eLVO, estimate large vessel occlusion; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PC, posterior circulation; PCA, posterior cerebral artery; PC-ASPECTS, posterior circulation-Alberta Stroke Program Early Computed Tomography Score; and VA, vertebral artery.

*n=137, missing in 111 patients.
†n=245, missing in 3 patients.
‡n=240, missing in 8 patients.
‖n=231, missing in 17 patients.
¶n=235, missing in 13 patients.

was transformed using a natural logarithm. After exponentiating the regression coefficient, relative percentages were calculated using the following formula: (exponentiate [coefficient] −1)×100%. Adjusted odds ratios (aORs) or beta estimates with 95% CIs were used to present the regression model results.

All regression models were adjusted for potential confounders: age, sex, baseline National Institutes of Health Stroke Scale score, pre-mRS score (dichotomized 0–2 versus 3–5), diabetes, hypertension in patients' history, systolic blood pressure when entering the hospital, the use of anticoagulation medication, the collaterals at CT angiography baseline, and the time between estimated LVO and groin puncture. These confounders were chosen based on univariable analyses complemented with parameters observed in previous literature and baseline differences. All analyses were performed using R (version 4.1.2.). A *P* value of <0.05 was defined as statistically significant for all analyses.

Missing Values

Original data were used for the descriptive analyses, whereas multiple imputations with chained equitation were used for the missing data before conducting the regression analyses. The number of imputations was set at 50. The complete list of variables used for imputation is described in Supplemental S1.

Subgroup Analyses

An interaction term was calculated to assess the interaction between occlusion location and IVT on the mRS score at 90

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days. Exploratory subgroup analyses by occlusion location were performed. The same variables for adjustment were used as for the primary analysis, regardless of the group sizes.

RESULTS

Baseline Characteristics

A total of 5768 patients were included in the MR CLEAN Registry, of which 264 patients had a posterior circulation occlusion. After applying the inclusion and exclusion criteria, a total of 248 patients were analyzed in the current study (Figure 1). Patients with IVT less often used anticoagulation before EVT, had lower pre-mRS scores, had faster onset to groin puncture times, and more often showed early recanalization compared with the patients treated without IVT (Table 1).

Clinical Outcome

There was no significant difference in the mRS score at 90 days between patients treated with IVT and without IVT (adjusted common odds ratio, 1.04 [95% CI, 0.61–1.76]; Figure 2). Also, no differences were seen in mortality and favorable functional outcome at 90 days, aOR, 0.93 (95% CI, 0.50–1.74), and aOR, 0.80 (95% CI, 0.43–1.49), respectively (Tables 2 and 3).

Technical Outcome

Although patients treated with IVT before EVT had an on average shorter procedure time (56 versus 65 minutes, *P*=0.13; Table 2), no significant differences were seen in the adjusted regression analysis after transforming the data (−13% [95% CI, −27 to 3.7]). Additionally, no differences were seen in first-attempt successful recanalization rates and successful recanalization rates (aOR, 1.26 [95% CI, 0.57–2.77 and aOR, 0.70 [95% CI, 0.37–1.32], respectively; Tables 2 and 3).

Safety Outcome

In 47% of the patients treated without IVT and in 54% with IVT before EVT any SAE occurred (*P*=0.31). Symptomatic ICH was twice as often seen in patients treated with IVT before EVT (4.8% versus 2.4%) (Table 2); however, this difference was not statistically significant in regression analysis (aOR, 1.65 [95% CI, 0.33–8.35]; Table 3).

Subgroup Analysis

There was a significant interaction between occlusion location and IVT on the mRS score at 90 days (*P*<0.00). In the subgroup analyses, IVT had a negative association with mRS score at 90 days (meaning higher mRS scores) in patients with an isolated posterior cerebral artery occlusion (adjusted common odds ratio, 0.08 [95% CI, 0.00–0.72]; Figure S1). There was no significant difference in favorable functional outcome in patients with isolated basilar artery occlusions treated with or without prior IVT (adjusted common odds ratio, 2.28 [95% CI, 0.95–5.49]).

DISCUSSION

In this study, the use of IVT before EVT in patients with a posterior circulation occlusion did not lead to significant differences in clinical, technical, and safety outcomes.

Literature is scarce about the impact of IVT before EVT in patients with ischemic stroke due to posterior circulation occlusion. In the anterior circulation, multiple studies, including trials and registries, showed no

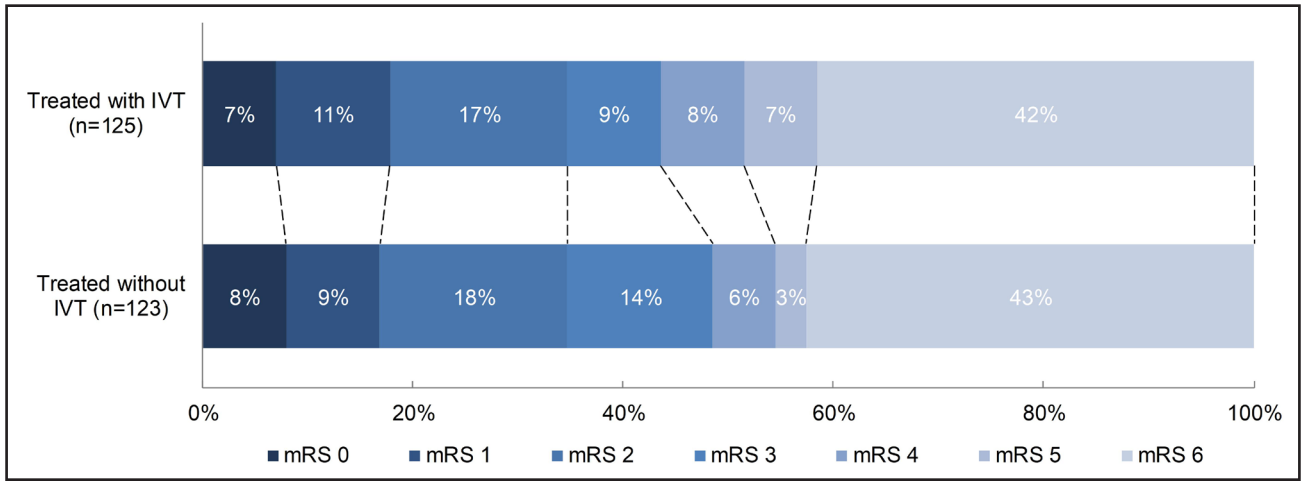

Figure 2. Distribution of the modified Rankin Scale.
Multiple logistic regression with adjustment showed no significant difference between patients treated with intravenous thrombolysis (IVT) prior endovascular treatment (EVT) compared to patients treated with IVT prior EVT (adjusted common odds ratio, 1.04 [95%CI:0.61 – 1.76]). mRS indicates modified Rankin Scale.

Table 2. Outcomes Between Patients Treated With and Without IVT

	Treated without IVT (n=123)	Treated with IVT (n=125)	*P* value
mRS scores at 90 d, n (%)			0.59
0	9/118 (7.6)	8/118 (6.8)	
1	10/118 (8.5)	13/118 (11)	
2	21/118 (18)	20/118 (17)	
3	17/118 (14)	10/118 (8.5)	
4	7/118 (5.9)	9/118 (7.6)	
5	3/118 (2.5)	8/118 (6.8)	
6	51/118 (43)	50/118 (42)	
mRS scores; 0–2 at 90 d, n (%)	40/118 (34)	41/118 (35)	1.00
mRS scores, 0–3 at 90 d; n (%)	57/118 (48)	51/118 (43)	0.51
Mortality at 90 d, n (%)	51/118 (43)	50/118 (42)	1.00
NIHSS scores at 24–48 h; median (IQR)*	9 (3–28)	8 (3–21)	0.33
Post-eTICI, n (%)			0.32
0	13/118 (11)	15/113 (13)	
1	7/118 (5.9)	2/113 (1.8)	
2A	7/118 (5.9)	14/113 (12)	
2B	28/118 (24)	28/113 (25)	
2C	13/118 (11)	10/113 (8.9)	
3	50/118 (42)	44/113 (39)	
Post-eTICI ≥2B, n (%)	91/118 (77)	82/113 (73)	0.52
Post-eTICI ≥2C, n (%)	63/118 (53)	54/113 (48)	0.47
Post-eTICI 3, n (%)	50/118 (42)	44/113 (39)	0.69
sICH, n (%)	3 (2.4)	6 (4.8)	0.50
Stroke progression, n (%)	22 (18)	21 (17)	0.95
Any SAE, n (%)	58 (47)	68 (54)	0.31
Pneumonia, n (%)	14 (11)	17 (14)	0.74
Duration of procedure, min; median (IQR)†	65 (38–93)	56 (36–83)	0.13

eTICI indicates extended Thrombolysis in Cerebral Ischemia; IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SAE, serious adverse event; and sICH, symptomatic intracranial hemorrhage.

*n=235, missing in 13 patients.

†n=232, missing in 16 patients.

superiority or noninferiority in patients treated with IVT before EVT on functional outcome at 90 days.[2,6,17] No trials are performed yet on the effect of IVT before EVT in the posterior circulation.

In the BAOCHE, ATTENTION, and BEST trials 15%, 34%, and 27% of the patients received IVT, respectively,[9,11,12] while 79% of patients in the BASICS trial received IVT.[10] Main reason for the difference is the treatment window. BAOCHE included patients between 6 and 24 hours after symptom onset, the ATTENTION up to 12 hours of estimated time of BAO, and the BEST up to 8 hours after estimated time of BAO, while patients in the BASICS trial were included within 6 hours of estimated time of BAO. Another reason may be that BAOCHE, ATTENTION, and BEST included patients from China, where, to receive IVT, payment in advance is required.[9,11,12] In the Netherlands, IVT is reimbursed, which may explain the higher rates of IVT in the MR CLEAN Registry.

The 4 above-mentioned trials showed ≈45% favorable functional outcome (mRS scores, 0–3) in the EVT group. Similar results are presented in the current study, Table S1 gives an overview of favorable functional outcome in patients with only a BAO. Favorable functional outcome was seen in 44% in patients with BAO treated with IVT and 42% in patients not treated with IVT. Despite the lower pre-mRS in patients treated with IVT, no differences in favorable functional outcome were seen.

Subgroup analysis on occlusion location (Figure S1) suggests that the potential benefit of IVT diminishes as the occlusion is more distally located when combined with EVT. It is known that IVT may more often lead to thrombus migration and, therefore, to more clot

Table 3. Outcomes of Regression Analyses on Clinical, Technical, and Safety Outcomes

Patients treated without IVT as first modality	EE	Unadjusted (95% CI)	Adjusted (95% CI)
mRS scores at 90 d*	cOR	0.99 (0.62 to 1.57)	1.04 (0.61 to 1.76)
mRS scores, 0–2 at 90 d	OR	1.09 (0.64 to 1.84)	1.02 (0.54 to 1.93)
mRS scores, 0–3 at 90 d	OR	0.84 (0.51 to 1.39)	0.80 (0.43 to 1.49)
Mortality at 90 d	OR	0.93 (0.56 to 1.55)	0.93 (0.50 to 1.74)
Post-EVT eTICI	cOR	0.76 (0.48 to 1.19)	0.78 (0.47 to 1.28)
Successful recanalization (eTICI ≥2B)	OR	0.67 (0.38 to 1.19)	0.70 (0.37 to 1.32)
Excellent recanalization (eTICI 3)	OR	0.79 (0.47 to 1.33)	0.74 (0.41 to 1.34)
Any serious adverse event	OR	1.34 (0.81 to 2.21)	1.44 (0.82 to 2.54)
Symptomatic ICH	OR	2.02 (0.49 to 8.31)	1.65 (0.33 to 8.35)
Stroke progression	OR	0.93 (0.48 to 1.80)	0.98 (0.45 to 2.10)
Pneumonia	OR	1.23 (0.57 to 2.62)	1.09 (0.47 to 2.52)
First-attempt successful recanalization	OR	0.98 (0.50 to 1.94)	1.26 (0.57 to 2.77)
NIHSS scores at 24–48 h	%	−6.8 (−30 to 25)	−1.5 (−26 to 31)
Procedure time	%	−13 (−26 to 2.2)	−13 (−27 to 3.7)

cOR indicates common odds ratio; EE, effect estimate; eTICI, extended Thrombolysis in Cerebral Ischemia; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and OR, odds ratio.

*Shift toward a better functional outcome on the full scale.

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inaccessibility for thrombectomy.[18] This may be a reason why the isolated patients with PCA are performing worse in our subgroup analysis. Additionally, treatment of PCA occlusion with EVT appears to be less established than treatment of BAO leading to a difference in treatment strategy which may have influenced outcome.[19] IVT may have an effect on clot composition and size which may lead to easier clot extraction. Although review of the literature did not show fewer thrombectomy attempts when treated with IVT before EVT, 1 study suggested significantly reduction of thrombus size after IVT.[20] In combination with a more aggressive treatment approach in patients with BAO, this could substantiate our subgroup analyses. However, analyses were performed on a limited number of patients with the same adjustments as for our primary analysis precluding strong conclusions, indicating the need for pooling data with other similar studies to increase power.

In 4.8% of the patients treated with IVT before EVT a sICH was seen. Comparable sICH rates were seen in the EVT groups of the BASICS (4.5%), ATTENTION (6%), BEST (8%), and BAOCHE (5%) trials.[9–12] However, these EVT groups include patients treated with and without IVT before EVT, while different sICH criteria were used. IVT in combination with EVT could potentially increase the rates of sICH compared with EVT alone, especially because of the concomitant periprocedural use of anticoagulation potential vessel wall damage due to the thrombectomy materials. However, we did not observe this in our results. Explanations are at the moment purely hypothetical. Literature suggests better collateral circulation in the posterior circulation compared with the anterior circulation as a possible explanation for the lower sICH rates.[13]

One reason to start EVT directly, before administering IVT, is because of the potential time delay. Especially when patients are directly presented at a stroke center. However, another MR CLEAN Registry study did not show a delay in door-to-groin times when IVT was given before EVT.[21] Additionally, patients treated with IVT before EVT showed higher rates of early recanalization (17%) compared with patients treated without IVT before EVT (5.7%). These higher rates did not lead to differences in clinical outcome. The clinical outcome measure (mRS score at 90 days) may not be optimal to detect small differences in clinical outcomes, and a more sensitive outcome measure may be needed.

Our study has limitations. First of all, patients who recanalized after treatment with IVT alone were not included in the MR CLEAN Registry, potentially causing an underestimation of the effect of IVT before EVT in patients with a BAO. Furthermore, we excluded patients (n=12) in whom no intracranial access was obtained with thrombectomy materials. Second, during the MR CLEAN Registry, many patients with basilar artery occlusion were included (when eligible) in the BASICS trial, causing also potential selection bias. However, this selection bias was probably limited, since a previous publication showed similar favorable functional outcome in patients treated within the MR CLEAN Registry compared with the BASICS trial.[22] Third, our registry based on real-world data has the limitations of a nonrandomized study: use of IVT was left to the treating physician and the numbers are small. In the American Heart Association guidelines IVT is contraindicated in some patients using anticoagulation and with high systolic blood pressures[23]; to minimize this effect analyses were adjusted for these potential confounders. Finally, in this study, thrombus characteristics, such as the length of the occlusion and thrombus density, were not taken into account in the analysis. However, the impact of these characteristics seems to be limited.[24]

CONCLUSIONS

We found no significant differences in clinical, technical, and safety outcomes between patients with an LVO in the posterior circulation treated with or without IVT before endovascular therapy. Our results are in line with the literature about the anterior circulation.

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Supplemental Material

Supplemental S1
Table S1
Figure S1

APPENDIX

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