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Stroke with large vessel occlusion in the posterior circulation: IV thrombolysis plus thrombectomy versus IV thrombolysis alone

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Abstract

Efficacy and safety of mechanical thrombectomy (MT) for stroke with posterior circulation large vessel occlusion (LVO) is still under debate. We aimed to compare the outcomes of stroke patients with posterior circulation LVO treated with intravenous thrombolysis (IVT) (< 4.5 h after symptom onset) plus MT < 6 h after symptom onset with those treated with IVT alone (< 4.5 h after symptom onset). Patients enrolled in the Italian Registry of Endovascular Treatment in Acute Stroke (IRETAS) and in the Italian centers included in the SITS-ISTR were analysed. We identified 409 IRETAS patients treated with IVT plus MT and 384 SITS-ISTR patients treated with IVT alone. IVT plus MT was significantly associated with higher rate of sICH (ECASS II) compared with IVT alone (3.1 vs 1.9%; OR 3.984, 95% CI 1.014–15.815), while the two treatments did not differ significantly in 3-month mRS score ≤ 3 (64.3 vs 74.1%; OR 0.829, 95% CI 0.524–1.311). In 389 patients with isolated basilar artery (BA) occlusion, IVT plus MT was significantly associated with higher rate of any ICH compared with IVT alone (9.4 vs 7.4%; OR 4.131, 95% CI 1.215–14.040), while two treatments did not differ significantly in 3-month mRS score ≤ 3 and sICH per ECASS II definition. IVT plus MT was significantly associated with higher rate mRS score ≤ 2 (69.1 vs 52.1%; OR 2.692, 95% CI 1.064–6.811) and lower rate of death (13.8 vs 27.1%; OR 0.299, 95% CI 0.095–0.942) in patients with distal-segment BA occlusion, while two treatments did not differ significantly in 3-month mRS score ≤ 3 and sICH per ECASS II definition. IVT plus MT was significantly associated with lower rate of mRS score ≤ 3 (37.1 vs 53.3%; OR 0.137, 0.009–0.987), mRS score ≤ 1 (22.9 vs 53.3%; OR 0.066, 95% CI 0.006–0.764), mRS score ≤ 2 (34.3 vs 53.3%; OR 0.102, 95% CI 0.011–0.935), and higher rate of death (51.4 vs 40%; OR 16.244, 1.395–89.209) in patients with proximal-segment BA occlusion. Compared with IVT alone, IVT plus MT was significantly associated with higher rate of sICH per ECASS II definition in patients with stroke and posterior circulation LVO, while two treatment groups did not differ significantly in 3-month mRS score ≤ 3. IVT plus MT was associated with lower rate of mRS score ≤ 3 compared with IVT alone in patients with proximal-segment BA occlusion, whereas no significant difference was found between the two treatments in primary endpoints in patients isolated BA occlusion and in the other subgroups based on site occlusion.

Keywords Stroke · Thrombolysis · Thrombectomy · Posterior · Large vessel occlusion

Highlights

- IVT plus MT was associated with higher rate of sICH in strokes with posterior circulation LVO.
- IVT plus MT was associated with higher rate of any ICH in strokes with isolated BA occlusion.
- IVT plus MT was associated with better outcomes in strokes with distal BA occlusion.
- IVT plus MT was associated with worse outcomes in strokes with proximal BA occlusion.

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Introduction

While mechanical thrombectomy (MT) with or without intravenous thrombolysis (IVT) is established as first-line treatment for stroke with large vessel occlusion (LVO) in the anterior circulation, its efficacy and safety for stroke with LVO in the posterior circulation is still under debate. The first two randomized controlled trials (RCTs)—the BASICS (Basilar Artery International Cooperation Study; international study) [1] and the BEST (Endovascular Intervention vs Standard Medical Treatment; Chinese study) [2]—did not show the superiority of endovascular thrombectomy (EVT) plus best medical treatment (BMT) over BMT alone in stroke patients presenting up to the 6- and 8-h window of estimated time of basilar artery (BA) occlusion. A meta-analysis of the two RCTs suggested an increased rate of functional independence in patients randomized to EVT using a Bayesian random-effects meta-analysis, but not using classical estimates [3]. Recently, two Chinese RCT—the ATTENTION [4] and the BAOCHE [5]—reported that EVT plus BMT within 12 h of estimated time of BA occlusion and in the 6- to 24- h time window led to better functional outcomes at 90 days than BMT, but was associated with procedural complications and intracerebral hemorrhage (ICH). However, only a small proportion of patients enrolled in Chinese trials received IVT because the time from stroke onset to randomization was often beyond 4.5 h after symptom onset, and rate of mortality was very high. To date, differences between EVT plus IVT and IVT alone for ischemic stroke due to BA occlusion are not demonstrated in the classical time window for treatment.

In patients with stroke and isolated posterior cerebral artery (PCA) occlusion [6] or posterior circulation tandem occlusions [7], EVT appears safe and feasible but data from prospective or randomized studies are lacking.

We aimed to compare the outcomes of patients with stroke and posterior circulation LVO treated with IVT (within 4.5 h after symptom onset) plus MT within 6 h after symptom onset, with those treated with IVT alone (within 4.5 h after symptom onset).

Methods

Study design, participants, and procedures

We conducted a study on prospectively collected data of 16,031 patients registered in the Italian Registry of Endovascular Treatment in Acute Stroke (IRETAS, an ongoing, multicenter, observational internet-based registry) [8] between January 2011 and December 2020 for treatment with IVT plus MT and of 112,499 patients registered by the Italian centers included in the Safe Implementation of Thrombolysis- International Stroke Registry (SITS-ISTR), an ongoing, multicenter, observational internet-based registry [9, 10], between May 2001 and December 2021 for treatment with IVT alone.

Inclusion and exclusion criteria

We included stroke patients receiving IVT within 4.5 h after symptom onset plus MT within 6 h after symptom onset and patients receiving IVT alone within 4.5 h after symptom onset, with complete data on site occlusion in the posterior circulation detected by computed tomography angiography or magnetic resonance angiography.

We excluded patients with concomitant occlusions in the posterior and anterior circulation or multiple occlusions in the left and right side in the posterior circulation.

Since data are extracted from national registries, the choice of treatment (IVT plus MT or IVT alone or) was at the discretion of the neurologist and neuroradiologist according to current national [11] and international guidelines [12].

Data collection

The following data were prospectively collected and included in the analysis: age, sex, hypertension, diabetes mellitus, hyperlipidemia, previous stroke or transient ischemic attack, atrial fibrillation, prior use of antiplatelet, prior use of oral anticoagulant with INR < 1.7, pre-stroke mRS score, NIHSS score at baseline and at 24 h, occlusion site on CT or MR angiography before IVT (isolated distal-, middle-, or proximal-segment BA occlusion, isolated P1-segment PCA occlusion, combination of BA occlusion with P1-segment PCA occlusion, combination of BA occlusion with VA occlusion, onset-to-needle time, onset-to-groin time, type of procedure (stent retriever alone, aspiration alone, and combination of stent retriever and aspiration), and recanalization according to Thrombolysis In Cerebral Infarction (TICI) scale for IRETAS cohort, types of ICH at 24 h according to the European Cooperative Acute Stroke Study (ECASS) II classification [13], and mRS score at 3 months.

Outcomes

The primary efficacy endpoint was defined as a score of 0 to 3 on the mRS score at 3 months according to the other RCTs [1, 2, 4, 5]. The primary safety endpoint was defined as symptomatic ICH (sICH) according to the European Cooperative Acute Stroke Study (ECASS) II definition (any ICH combined with a neurological deterioration of 4 points or more on the NIHSS from baseline not attributable to general anesthesia, or leading to death). Secondary functional outcome measures at 3 months were: (a) excellent outcome (mRS score ≤ 1), (b) favorable outcome (mRS score ≤ 2), and (c) mortality. Secondary intracranial bleeding measures at 24 h were: (a) any ICH, (b) parenchymal hemorrhage (PH), and (c) ICH according to the National Institute of Neurological Disorders and Stroke (NINDS) definition (any ICH combined with a neurological deterioration of 1 point or more on the NIHSS from baseline not attributable to general anesthesia, or leading to death).

Statistical analysis

We performed statistical analyses using SPSS 22.0 statistical package and STATA-16 software. Normally distributed continuous variables were presented as means and standard deviation (SD) and compared using Student's *t*-tests. Not-normally distributed continuous variables were presented as median and IQR and compared using Mann–Whitney U-test. Categorical variables were expressed as frequency and percentage and compared using $\chi 2$ test. Proportions were calculated for categorical variables, dividing the number of events by the total number excluding missing/unknown cases.

Descriptive analysis was used to identify differences in characteristics between the treatments (IVT plus MT and IVT alone).

Using the entire cohort and the cohort of patients with isolated BA occlusion, binary regression was performed to estimate the association of IVT plus MT (vs IVT alone) with outcomes by calculating the crude odds ratios (OR)s with two-sided 95% confidence intervals (CI) and the ORs with two-sided 95% CI after adjustment for pre-defined variables (age, baseline NIHSS score, and occlusion site) and group differences in baseline characteristics (probability value < 0.05). Using the cohort of patients with isolated distal-, middle-, or proximal-segment BA occlusion, isolated P1-segment PCA occlusion, combination of BA occlusion with P1-segment PCA occlusion, combination of BA occlusion with VA occlusion, the ORs with two-sided 95% CI were presented after adjustment for pre-defined variables (age and baseline NIHSS score) and group differences in baseline characteristics (probability value < 0.05).

Results

We identified 409 patients registered in the IRETAS cohort by 45 centers who received IVT plus MT and 384 patients registered in the SITS cohort by 101 centers who received IVT alone. Centers that have treated both patients with IVT plus MT and patients with IVT alone are reported in Supplemental Table 1.

Characteristics per treatment of patients of the IRETAS and SITS-ISTR cohorts are reported in Table 1. Patients of the SITS-ISTR group were significantly older and had a significantly lower NIHSS score at baseline. Previous ischemic stroke/TIA and prior use of antiplatelet therapy were significantly more frequent in the SITS-ISTR group. The groups were significantly different in distribution of occlusion site. The rate of TICI 2b/3 was reported in 81.2% of the patients treated with IVT plus MT. Data on 3-month functional outcomes were available in 627 patients, data on ICH types in 727 patients, and data on sICH in 707 patients. Associations of IVT plus MT (vs IVT alone) with outcomes in the IRETAS and Italian SITS-ISTR cohorts are reported in Table 2. After adjustment, IVT plus MT group was significantly associated with higher rate of sICH per ECASS II definition compared with IVT alone (3.1 vs 1.9%; OR 3.984, 95% CI 1.014–15.815) Two treatments did not differ significantly in 3-month mRS score ≤ 3 (64.3 vs 74.1%; OR 0.829, 95% CI 0.524–1.311).

Characteristics per treatment of patients with isolated BA occlusion are reported in Table 1. Patients receiving IVT alone were significantly older and had a higher rate of previous ischemic stroke/TIA and prior use of antiplatelet therapy. No difference was found in distribution for different BA segments. The rate of TICI 2b/3 was reported in 81.4% of the patients treated with IVT plus MT. Data on 3-month functional outcomes were available in 319 patients, data on ICH types in 346 patients, and data on sICH in 338 patients. Associations between IVT plus MT (vs IVT alone) and outcomes in patients with isolated BA occlusion are reported in Table 3. After adjustment, IVT plus MT was significantly associated with higher rate of any ICH compared with IVT alone (9.4 vs 7.4%; OR 4.131, 95% CI 1.215–14.040). Two treatments did not differ significantly in 3-month mRS score ≤ 3 (60.8 vs 64.7%; OR 1.055, 95% CI 0.558–1.994) and sICH per ECASS II definition (3.2 vs 1.7%; OR NA).

Characteristics per treatment of patients with isolated distal-, middle-, and proximal-segment BA occlusion, and P1-segment PCA occlusion are reported in Supplemental Table 2. Associations between IVT plus MT (vs IVT alone) and outcomes in patients with isolated distal-, middle-, and proximal-segment BA occlusion, and P1-segment PCA occlusion are reported in Supplemental Table 3. After adjustment, IVT plus MT was significantly associated with higher rate of mRS score ≤ 2 (69.1 vs 52.1%; OR 2.692, 95% CI 1.064–6.811) and lower rate of death (13.8 vs 27.1%; OR 0.299, 95% CI 0.095–0.942) in patients with distal-segment BA occlusion. Two treatments did not differ significantly in 3-month mRS score ≤ 3 (75.5 vs 64.6%; OR 2.487, 95% CI 0.905–6.836) and sICH per ECASS II definition (1.1 vs 1.8%; OR NA). After adjustment, IVT plus MT was

Table 1 Characteristics per treatment of the IRETAS and Italian SITS-ISTR cohorts and patients with isolated basilar artery occlusion

	All patients (*n* = 793)	All patients			Isolated basilar artery occlusion		
		IVT plus MT (*n* = 409)	IVT alone (*n* = 384)	*P* value	IVT plus MT (*n* = 231)	IVT alone (*n* = 158)	*P* value
Demographics							
Age (years)	71.1 (12.9)	69.8 (12.5)	72.5 (13.2)	0.004	70.4 (12.3)	73.3 (13.1)	0.028
Male sex	471 (59.4)	245 (59.9)	226 (58.9)	0.773	135 (58.4)	103 (65.2)	0.204
Medical history							
Hypertension	526 (69.5) [757]	251 (67.1) [374]	275 (71.8) [383]	0.180	132 (64.1) [206]	110 (70.1) [157]	0.261
Diabetes mellitus	131 (17.3) [757]	63 (16.8) [374]	68 (17.8) [383]	0.774	30 (14.6) [206]	23 (14.6) [157]	1.000
Atrial fibrillation	176 (23.4) [752]	82 (21.9) [374]	94 (24.9) [378]	0.345	38 (18.4) [206]	38 (24.4) [156]	0.193
Previous ischemic stroke/TIA	84 (11.1) [756]	9 (2.4) [374]	75 (19.6) [382]	< 0.001	6 (2.9) [206]	39 (25) [156]	< 0.001
Hyperdyslipidemia	199 (26.4) [754]	96 (25.7) [374]	103 (27.1) [380]	0.680	54 (26.2) [206]	45 (28.7) [157]	0.635
Antiplatelet therapy	231 (30.9) [747]	95 (23.2)	136 (40.2) [338]	< 0.001	42 (18.2)	62 (41.9) [148]	< 0.001
Oral anticoagulant therapy	36 (4.6) [781]	22 (5.5) [401]	14 (3.7) [380]	0.238	12 (5.2) [229]	6 (3.8) [156]	0.627
Baseline data							
Pre-stroke mRS score 0–1	666 (91.4) [729]	325 (91.8) [354]	341 (90.9) [375]	0.694	192 (92.3) [208]	141 (91.6) [154]	0.846
NIHSS score	10 (6–18) [705]	12 (7–20) [335]	8 (5–16) [370]	< 0.001	13 (7–22) [183]	12 (6–22) [150]	0.601
Occlusion site				< 0.001			
Isolated distal BA	175 (22.1)	101 (24.7)	74 (19.3)		101 (43.7)	74 (46.8)	0.629
Isolated middle BA	157 (19.8)	93 (22.7)	64 (16.7)		93 (40.3)	64 (40.5)	
Isolated proximal BA	57 (7.2)	37 (9)	20 (5.2)		37 (16)	20 (12.7)	
Isolated P1-segment PCA	285 (35.9)	92 (22.5)	193 (50.3)		–	–	
PCA-BA	59 (7.4)	43 (10.5)	16 (4.2)		–	–	
VA-BA artery	60 (7.6)	43 (10.5)	17 (4.4)		–	–	
Onset-to-needle time (minutes)	165 (130–210)	160 (120–210)	170 (135–210)	0.125	165 (130–215)	165 (130–206)	0.956
Onset-to-groin time (minutes)	–	240 (175–295)	–	NA	250 (185–303)	–	NA
Type of procedure		[310]		NA	[174]		NA
Stent retriever alone	–	64 (20.6)	–		37 (21.3)	–	
Aspiration alone	–	165 (53.2)	–		95 (54.6)	–	
Combination of stent retriever and aspiration	–	81 (26.1)	–		42 (24.1)	–	
TICI 2b/3	–	323 (81.2) [398]		NA	–	187 (82.4) [227]	NA

Continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables are expressed as frequency and percentage. Proportions were calculated for categorical variables, dividing the number of events by the total number excluding missing/unknown cases. Numbers within square brackets indicate number of patients for which data were known. Statistical significance was established at two-tailed 0.05 level ($P < 0.05$)

associated with lower rate of mRS score ≤ 3 (37.1 vs 53.3%; OR 0.137, 0.009–0.987), mRS score ≤ 1 (22.9 vs 53.3%; OR 0.066, 95% CI 0.006–0.764), mRS score ≤ 2 (34.3 vs 53.3%; OR 0.102, 95% CI 0.011–0.935), and higher rate of death (51.4 vs 40%; OR 16.244, 1.395–89.209) in patients with proximal-segment BA occlusion. Two treatments did not differ significantly in sICH per ECASS II definition (2.8 vs 6.7%; OR NA). No difference was found between the two groups in patients with isolated middle-segment BA occlusion and isolated P1-segment PCA occlusion.

Characteristics per treatment of patients with combination of BA occlusion with P1-segment PCA occlusion, combination of BA occlusion with VA occlusion are reported in Supplemental Table 4. No significant association between IVT plus MT (vs IVT alone) and outcomes was found in patients with BA occlusion in combination with P1-segment PCA occlusion and in patients with BA occlusion in combination with VA occlusion (Supplemental Table 5).

Discussion

Our study shows that patients receiving IVT plus MT in the entire IRETAS cohort had a significant higher rate of sICH per ECASS II definition, when compared to stroke patients receiving IVT alone in the SITS-ISTR cohort, while two treatment groups did not differ significantly in 3-month mRS score ≤ 3. In patients with isolated BA occlusion, IVT

Table 2 Binary regression: association of IVT plus MT (vs IVT alone) with outcomes in the IRETAS and Italian SITS-ISTR cohorts

	All patients					
	IVT plus MT ($n=409$)	IVT alone ($n=384$)	Crude OR (95 CI)	*P* value	Adjusted OR (95 CI)	*P* value
Functional outcomes						
mRS score ≤ 3	245 (64.3) [381]	177 (74.1) [239]	0.631 (0.441–0.902)	0.012	0.829 (0.524–1.311)	0.423
mRS score ≤ 1	162 (42.5) [381]	115 (48.1) [239]	0.798 (0.576–1.104)	0.173	0.798 (0.528–1.206)	0.284
mRS score ≤ 2	213 (55.9) [381]	148 (61.9) [239]	0.780 (0.560–1.085)	0.139	0.983 (0.648–1.492)	0.936
Death	82 (21.5) [381]	41 (17.2) [239]	1.324 (0.874–2.007)	0.185	1.023 (0.604–1.735)	0.932
Intracranial bleedings						
sICH (ECASS II definition)	12 (3.1) [388]	6 (1.9) [319]	1.665 (0.618–4.487)	0.314	3.984 (1.014–15.815)	0.048
Any ICH	42 (10.6) [396]	27 (8.2) [331]	1.336 (0.804–2.218)	0.263	1.839 (0.966–3.499)	0.063
PH	12 (3) [396]	6 (1.8) [331]	1.693 (0.628–4.560)	0.298	3.330 (0.821–13.510)	0.092
sICH (NINDS definition)	13 (3.4) [388]	7 (2.2) [319]	1.545 (0.609–3.920)	0.360	3.145 (0.930–10.632)	0.065

Categorical variables are expressed as frequency and percentage. Proportions were calculated for categorical variables, dividing the number of events by the total number excluding missing/unknown cases. Numbers within square brackets indicate number of patients for which data were known. Statistical significance was established at two-tailed 0.05 level ($P<0.05$). Adjustment for age, NIHSS score, site occlusion, previous ischemic stroke/TIA, and antiplatelet therapy

Table 3 Binary regression: association of IVT plus MT (vs IVT alone) with outcomes of the patients with isolated basilar artery occlusion

	Isolated basilar artery occlusion					
	IVT plus MT ($n=231$)	IVT alone ($n=158$)	Crude OR (95 CI)	*P* value	Adjusted OR (95 CI)	*P* value
Functional outcomes						
mRS score ≤ 3	132 (60.8) [217]	66 (64.7) [102]	0.847 (0.519–1.381)	0.506	1.055 (0.558–1.994)	0.869
mRS score ≤ 1	90 (41.5) [217]	41 (40.2) [102]	1.054 (0.653–1.702)	0.829	0.800 (0.430–1.488)	0.481
mRS score ≤ 2	120 (55.3) [217]	55 (53.9) [102]	1.057 (0.659–1.696)	0.818	1.211 (0.661–2.218)	0.535
Death	51 (23.5) [217]	28 (27.5) [102]	0.812 (0.475–1.388)	0.446	0.786 (0.389–1.589)	0.503
Intracranial bleedings						
sICH (ECASS II definition)	7 (3.2) [218]	2 (1.7) [120]	1.957 (0.400–9.575)	0.407	–	NA
Any ICH	21 (9.4) [224]	9 (7.4) [122]	1.299 (0.575–2.932)	0.529	4.131 (1.215–14.040)	0.023
PH	4 (1.8) [224]	2 (1.6) [122]	1.091 (0.197–6.043)	0.921	9.446 (0.375–37.925)	0.173
sICH (NINDS definition)	7 (3.2) [218]	2 (1.7) [120]	1.957 (0.400–9.575)	0.407	–	NA

Categorical variables are expressed as frequency and percentage. Proportions were calculated for categorical variables, dividing the number of events by the total number excluding missing/unknown cases. Numbers within square brackets indicate number of patients for which data were known. Statistical significance was established at two-tailed 0.05 level ($P<0.05$)

Adjustment for age, NIHSS score, previous ischemic stroke/TIA, and antiplatelet therapy

plus MT was significantly associated with higher rate of any ICH, but no significant difference was found between the two treatments in primary efficacy and safety endpoints. In patients with proximal-segment BA occlusion, IVT plus MT was associated with lower rate of mRS score ≤ 3 compared with IVT alone, while the two treatments did not differ significantly in sICH per ECASS II definition. In the other subgroups based on site occlusion, IVT plus MT was significantly associated with higher rate of any ICH in patients with isolated BA occlusion, with worse functional outcomes (mRS score ≤ 1, mRS score ≤ 2, mRS score ≤ 3, and death) in patients with proximal-segment BA occlusion, and with better functional outcomes in patients with distal-segment BA occlusion (mRS score ≤ 2 and death). However, no significant difference was found between the two treatments in primary endpoints.

When compared to the BASICS cohort including non-Asian stroke patients receiving EVT within 6 h from the estimated time of BA occlusion [1], the IRETAS cohort including patients with isolated BA occlusion had higher rates of TICI 2b/3 (82.4 vs 72%) and 3-month mRS score ≤ 3 (60.8 vs 44.4%). Similarly, the control group of the SITS-ISTR cohort had a higher rate of 3-month mRS ≤ 3 than the control group of the BASICS cohort (64.7 vs 37.7%). The differences between BASICS cohort and our study cohort could be explained because median NIHSS score at baseline was higher in the BASICS trial (21 vs 13 for EVT groups and 22 vs 12 for control group), but also because more than a quarter of the patients of the BASICS trial did not receive IVT (20.5% in the control group and 21.4% in the EVT group) and some patients received IVT beyond 4.5 h after symptom onset.

Our study shows that rates of intracranial bleedings were higher in the EVT group than control group. However, rate of sICH in the EVT arms in the RCTs enrolling patients with BA occlusion [14] was similar to that in the EVT arms in the RCTs enrolling patients within 6 h afters symptom onset with anterior circulation LVO [15] (5.5 vs 4%).

A recent meta-analysis of RCTs enrolling patients with BA occlusion showed that EVT effect on 3-month mRS score ≤ 3 might be modified by occlusion location of the BA, with greatest benefit for proximal, intermediate benefit for middle, and least benefit for distal occlusions [14]. Instead, our study suggests that functional outcomes were better in patients receiving IVT plus MT for distal-segment BA occlusion than in those treated for middle and proximal segments (mRS score ≤ 1: 48.9 vs 40.9 vs 22.9%, mRS score ≤ 2: 69.1 vs 48.9 vs 34.3%, mRS score ≤ 3: 75.5 vs 54.4 vs 37.1%, death: 13.8 vs 22.7 vs 51.4%). The differences between our study and recent meta-analysis of the RCTs could be explained because aspiration alone was used during EVT in more than half of our cohort and most frequently in patients with distal-segment BA occlusion, whereas stent retriever alone and combination of stent retriever and aspiration were more frequently used in patients with middle and proximal segments. Instead, stent retriever was used during EVT in most of the RCTs [14]. Aspiration alone might be advantageous over stent retriever alone in patients with distal-segment BA occlusion and embolic occlusion. To date, little is known about whether occlusion site is a prognostic factor for BA occlusion. Previous findings suggest that patients with distal occlusion have a more favorable outcome following EVT [16–18]. An ischemic stroke occurring at the top of the BA often causes infarction of the midbrain, thalamus, and portions of the temporal and occipital lobes supplied by the posterior communicating and posterior cerebral branches of the BA. These territories regulate the consciousness level, vision, and other functions, and patients with distal BAO can show various clinical signs and symptoms, including consciousness disorder, hemianopia, oculomotor disorders, and behavioral abnormalities rather than prominent motor dysfunction. Therefore, patients receiving MT for distal-segment BA occlusion may achieve better mRS score at 3 months than those treated with MT for middle- or proximal-segment BA occlusion. Some studies have shown that atherosclerosis often leads to occlusion of the proximal and middle segments of the BA, whereas embolic BA occlusion often manifests in the distal segment [16, 19, 20]. Patients with atherosclerosis require a longer procedural time than those with emboli [21]. Moreover, atherosclerotic lesions frequently cause acute arterial re-occlusion after EVT [22, 23]. In contrast, the proportion of re-occlusion in the embolism group is lower than that in the atherosclerosis group due to mild or no arterial wall injury, less damage to perforating branches, and reduced thrombectomy time. However, each of these hypotheses would require full investigations.

In line with previous retrospective studies [6, 7], our study shows that EVT appears safe and feasible in patients with isolated occlusions of the PCA and posterior circulation tandem occlusions, but it does not seem to be associated with higher rates of 3-month good outcome compared to IVT alone.

While ATTENTION [4] and BAOCHE [5] trials showed that EVT was superior to BMT—IVT in only 34% and 21% of patients—in late-window patients until 24 h without requiring advanced imaging in a Chinese population, our study confirms that EVT after IVT was not superior to IVT alone in early-window patients as shown by ATTENTION and BEST trials [1, 2]. Therefore, as recommended by current national [11] and international guidelines [12], large RCTs are needed to determine the efficacy and safety of IVT plus MT vs IVT alone in non-Asian patients with posterior circulation LVO occlusion.

We are aware that our study has some limitations. First, the present study did not randomize patients by treatment, but it is based on a retrospective analysis of prospectively collected data. Second, the number of missing data for outcome measures and variables of adjustment might have influenced the final outcome. Third, reasons for the treatment were not recorded. It is likely that these choices were influenced by center-specific standards regarding the treatment of stroke patients with LVO in the posterior circulation and unmeasurable factors related to individual physician's decision, which might have influenced our key findings, considering also the extended recruitment period. However, the group of patients included in the present study for receiving IVT alone in the pre-EVT era, although possible candidates for both treatments in the EVT era, represents a reasonable comparison group for patients who received IVT plus MT. Finally, data on collateral circulation status and stroke etiology are not available.

Conclusions

Our study shows that IVT plus MT within 6 h after symptom onset was significantly associated with higher rate of 24-h sICH per ECASS II definition in stroke patients with posterior circulation LVO when compared to IVT alone, while two treatment groups did not differ significantly in 3-month mRS score ≤ 3. IVT plus MT was associated with lower rate of mRS score ≤ 3 compared with IVT alone in patients with proximal-segment BA occlusion, whereas no significant difference was found between the two treatments in primary endpoints in patients isolated BA occlusion and in the other subgroups based on site occlusion.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11239-023-02844-4.

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Data availability Anonymized data will be shared upon reasonable request from any qualified investigator.

Declarations

Conflict of interest MC: consultancy or advisory board fees or speaker's honoraria from Boehringer Ingelheim, Pfizer/Bristol Meyer Squibb, and Daiichi Sankyo. AZ: consultancy and speaker's honoria fees from Boehringer-Ingelheim, Medtronic, Cerenovus and advisory board from Daiichi Sankyo and Boehringer-Ingelheim and Stryker. LR: speaker's honoraria from stryker, penumbra. EL: consultancy fees from Stryker. ADV: consultancy from Boehringer Ingelheim, Daichi Sankyo. MB: consultancy fees from Stryker, Penumbra. SC: advisory board fees or speaker's honoraria from Abbott, Allergan-Abbvie, AstraZeneca, Eli Lilly, Lundbeck, Novartis, NovoNordisk, Pfizer, Teva. All other authors report no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Standard protocol approvals, registrations, and patient consents The present study was in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Need for ethical approval or patient consent for participation in the IRETAS varied among participating hospitals. Informed consent to use of anonymized and aggregated data for participation in the IRETAS was obtained in all patients of each center.

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