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ORIGINAL RESEARCH

Optimal endovascular therapy technique for isolated intracranial atherothrombotic stroke-related large vessel occlusion in the acute to subacute stage

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ABSTRACT

BACKGROUND AND PURPOSE: Reocclusion after treatment is a concern in endovascular therapy (EVT) for isolated intracranial atherothrombotic stroke-related large vessel occlusion (AT-LVO). However, the optimal EVT technique for AT-LVO has not yet been investigated. This study evaluated the optimal EVT technique for AT-LVO in a real-world setting.

MATERIALS AND METHODS: We conducted a historical multicenter registry study at 51 centers that enrolled patients with AT-LVO. We divided the patients into three groups based on the EVT technique: mechanical thrombectomy alone (MT-only), percutaneous transluminal angioplasty (PTA), and stent deployment (Stent). MT alone was classified into the MT-only group, PTA and MT-PTA into the PTA group, and MT-Stent, MT-PTA-Stent, PTA-Stent, and Stent-only into the Stent group. The primary outcome was the incidence of reocclusion of the treated vessels within 90 days of EVT completion.

RESULTS: We enrolled 770 patients and analyzed 509 patients. The rates in the MT-only, PTA, and Stent groups were 40.7, 44.4, and 14.9%, respectively. The incidence rate of residual stenosis >70% of final angiography was significantly higher in the MT-only group than in the PTA and Stent groups (MT-only vs. PTA vs. Stent: 34.5% vs. 26.3% vs. 13.2%, p=0.002). The reocclusion rate was significantly lower in the PTA group than in the MT-only group (adjusted hazard ratio [95% confidence interval], 0.48 [0.29–0.80]). Of the patients, 83.5% experienced reocclusion within 10 days after EVT. Alarmingly, a substantial subset (approximately 62.0%) of patients underwent reocclusion within 2 days of EVT. The incidence of modified Rankin scale scores of 0–2 90 days after EVT was not significantly different among the three groups. The incidences of symptomatic intracranial hemorrhage (ICH), any other ICH, and death were not significantly different.

CONCLUSIONS: The incidence rate of reocclusion was significantly lower in the PTA group than in the MT-only group. We found no significant difference in reocclusion rates between the Stent and MT-only groups. In Japan, GP IIb/IIIa inhibitors are not reimbursed. Therefore, PTA might be the preferred choice for AT-LVOs due to the higher reocclusion risk with MT-only. Reocclusion was likely to

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occur within 10 days, particularly within 2 days post-EVT.

ABBREVIATIONS: EVT = endovascular treatment; LVO = large vessel occlusion; MT = mechanical thrombectomy; PTA = percutaneous transluminal angioplasty; ICH = intracranial hemorrhage; SD = standard deviation; IQR = interquartile range; HRs = hazard ratios; BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein; DAPT = dual antiplatelet therapy; TAPT = triple antiplatelet therapy

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SUMMARY SECTION

PREVIOUS LITERATURE: Atherosclerosis is the second leading cause of large vessel occlusion (LVO). The incidence of atherothrombotic stroke-related LVO (AT-LVO) is significantly higher in Asian groups. Patients with AT-LVO tend to be refractory to endovascular treatment (EVT) due to atherosclerotic stenosis, which leads to vessel dissections and increased reocclusion after EVT. Owing to the specificity of the lesion, the optimal treatment for patients with AT-LVO remains unknown. In addition, GP IIb/IIIa inhibitors, which are indispensable for the treatment of AT-LVO, are not reimbursed in Japan.

KEY FINDINGS: We showed that reocclusion was lower in the percutaneous transluminal angioplasty (PTA) group than that in the mechanical thrombectomy alone (MT-only) group and was likely to occur within 10 days post-EVT for AT-LVO. Reocclusion is particularly prone to occur within 2 days post-EVT.

KNOWLEDGE ADVANCEMENT: Our findings based on a large multicenter real-world registry suggested the optimal EVT technique for AT-LVO and revealed a high incidence of reocclusion within 10 days, particularly within 2 days post-EVT. Further additional prospective studies are warranted to investigate the optimal EVT technique and antiplatelet agent use for AT-LVO.

INTRODUCTION

Endovascular therapy (EVT) has become an established therapy for treating acute ischemic stroke caused by large vessel occlusion (LVO).[1, 2] Atherosclerosis is the second leading cause of LVO. The incidence of atherothrombotic stroke-related LVO (AT-LVO) is significantly higher in Asian groups, such as the Japanese population, compared with that in other groups,[3] making its treatment a global concern.[4] The etiology of AT-LVO can be categorized into two main mechanisms: acute in situ occlusion due to intracranial arterial atherosclerotic stenosis and embolic mechanisms originating from extracranial artery stenosis or occlusion. Thrombectomy is often the principal EVT for AT-LVO. Nevertheless, patients with AT-LVO tend to be refractory to EVT due to atherosclerotic stenosis, which leads to vessel dissections and increased reocclusion after EVT.[3-5] In particular, reocclusion after treatment is as high as 22.2%, so it is important to reduce reocclusion rates and improve treatment outcomes.[6] Owing to the specificity of the lesion, the optimal choice of EVT for AT-LVO also differs from that made for non-atherosclerotic etiologies.[7] However, with recent advancements in devices and antiplatelet agents, the optimal treatment for patients with AT-LVO remains unknown. GP IIb/IIIa inhibitors, which can inhibit platelet aggregation capacity in a short time, are not reimbursed in Japan. However, dual antiplatelet therapy (DAPT) and loading doses are frequently used for percutaneous transluminal angioplasty (PTA) and stent deployment.

Thus, we conducted a post hoc study using a nationwide registry of patients with AT-LVO treated with EVT in a real-world setting to compare the prognosis of AT-LVO in the three different treatment categories.

MATERIALS AND METHODS

2.1. Data collection and definitions

The data supporting the findings of this study are available from the corresponding author upon request. Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolic and Atherothrombotic Stroke with LVO (RESCUE AT-LVO) was a historical multicenter registry study conducted in 51 facilities in Japan that enrolled patients with acute intracranial occlusion caused by intracranial or extracranial carotid atherosclerosis from January 2017 to December 2019. We showed the number of facilities performing EVT over a 2-year period stratified by the number of AT-LVO cases (0 to 4, 5 to 9, 10 to 19, 20 to 39, and 40 or more) (Figure 2). In this study, we investigated AT-LVO caused by in situ occlusion of the intracranial arteries. The eligibility criteria were as follows: (1) acute ischemic stroke with in situ occlusion of the intracranial artery; (2) EVT performed for intracranial occlusion within 7 days from the time the patient was last known to be well; (3) a final diagnosis of atherosclerotic disease[8]; and (4) occlusion site at the intracranial internal carotid artery, M1 or M2 segment of the middle cerebral artery, basilar artery, or intracranial vertebral artery. Patients were excluded if they had (1) stenosis caused by a non-atherosclerotic etiology, such as the Moyamoya disease, arterial dissection, or vasculitis; (2) multiple acute infarctions in multiple vascular territories, excluding artery-to-artery embolism due to cervical artery occlusion or stenosis; (3) EVT performed only for cervical lesions; and (4) artery-to-artery embolism due to occlusion or stenosis of the vertebral artery origin. Based on the eligibility and exclusion criteria, we have comprehensively assessed preoperative, intraoperative, and postoperative information and determined the lesions to be consistent with AT-LVO.

The patients were categorized into three groups based on the EVT technique: mechanical thrombectomy (MT), including local intra-arterial fibrinolysis and mechanical clot disruption; PTA; and stent deployment (Stent). MT alone was classified into the MT-only group; PTA and MT-PTA into the PTA group; and MT-Stent, MT-PTA-Stent, PTA-Stent, and Stent-only into the Stent group.

This study was conducted in accordance with the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan. The study protocol was approved by the Institutional Review Board of the Hyogo College of Medicine (approval number 3727) and all participating facilities. The requirement for written informed consent was waived because we used clinical information obtained from routine clinical practice. Clinical data were collected at each facility through chart reviews or contact with the patients or their relatives.

The collected variables included age, sex, mRS score before onset,[9] medical history, prior medication, initiating additional antiplatelet medication, vital signs, National Institutes of Health Stroke Scale (NIHSS) score on admission,[10] laboratory data, imaging studies, use of recombinant tissue plasminogen activator (rt-PA), and time. Imaging studies evaluated the ischemic volume on admission using the Alberta Stroke Program Early CT Score (ASPECTS) and the occluded vessels. We evaluated the ASPECTS using diffusion-weighted image (DWI) in MRI or non-contrast CT.[11, 12] and defined the ASPECTS of each patient as ASPECTS on non-contrast CT or ASPECTS on DWI. The degree of reperfusion by EVT was classified using the modified TICI grading system based on digital subtraction angiography findings immediately after EVT procedures.[13] The preoperative and postoperative stenosis rates of the lesion were determined using the Warfarin-Aspirin Symptomatic Intracranial Disease criteria for intracranial stenosis.[14] Intraoperative complications encompass vessel perforation, vessel rupture, vascular dissection, distal embolism, cholesterol crystal embolization, and puncture site complications.

We routinely performed non-contrast CT or MRI 24±8 h after EVT. To evaluate hemorrhagic complications, we defined any intracranial hemorrhage (ICH) as any new hemorrhage on imaging irrespective of symptoms and symptomatic ICH as any exacerbation of four or more points on the NIHSS score, according to the Heidelberg classification.[15] The presence of reocclusion was confirmed using digital subtraction angiography or MRI. When employing digital subtraction angiography, reocclusion was defined as mTICI 0 or 1. When utilizing MRI, the presence of reocclusion was confirmed using the modified Mori grade. Reocclusion was defined as a modified Mori grade of 0 or 1.

2.2 Outcomes

The primary outcome was the incidence of reocclusion of the treated vessels within 90 days of EVT completion. The secondary outcomes were as follows: (1) incidence of modified TICI 2b–3 immediately after EVT, (2) incidence of mRS 0–2 90 days after EVT, (3) incidence of any ICH within 90 days after EVT, (4) incidence of symptomatic ICH within 90 days after EVT, (5) incidence of death within 90 days after EVT, and (6) mRS score 90 days after EVT.

2.3. Statistical analyses

We analyzed the characteristics of patients in the MT-only, PTA, and Stent groups. Categorical variables are expressed as frequencies and percentages, and continuous variables are reported as means±standard deviations or medians with interquartile ranges. Variables between patients with different groups were compared using ANOVA and the Kruskal–Wallis test, as appropriate, and categorical variables were analyzed using the X^2 test. The cumulative incidence was calculated using the Kaplan–Meier method, and variances among the groups were evaluated using the log-rank test. The period until reocclusion of the treated vessel was identified as the first day reocclusion was observed in the treated vessel, subtracting the day of the initial treatment and adding an extra day within a timeframe of 90±30 days after the initial treatment.

To assess the effects of the MT-only group compared with that of the other groups on primary and secondary outcomes, we used two statistical methods. First, we applied Cox proportional hazards models to estimate the primary and secondary outcomes as hazard ratios (HRs) with 95% confidence intervals (CIs). Second, we used binary logistic regression models to estimate the modified TICI 2b–3 and

mRS scores 0–2 at 90 days after EVT as odds ratios (ORs) with 95% CIs. We constructed crude and adjusted models with adjustments for age, initial NIHSS score on admission, premorbid mRS score, ASPECTS before the procedure, onset to puncture (days), site of occlusion (anterior or posterior circulation), and use of intravenous rt-PA. Subsequently, we compared the frequencies of the outcomes according to the technique using the X^2 test.

We conducted subgroup analyses to evaluate the efficacy of PTA and Stent compared to the MT-only group in preventing reocclusion. Subgroups were defined by age (≥75 or <75 years), sex, presence of anterior circulation, residual stenosis rate (≥70 or <70%), use of DAPT/TAPT, and administration of rt-PA.

All statistical analyses were performed using JMP 16.0 (SAS Institute Inc., Cary, NC, USA). All reported p-values were two-tailed, and p-values <0.05 were considered statistically significant.

RESULTS

3.1

Among the 783 enrolled patients in RESCUE AT-LVO, 514 were assigned to the intracranial group, and 509 were included in this study (Figure 1).

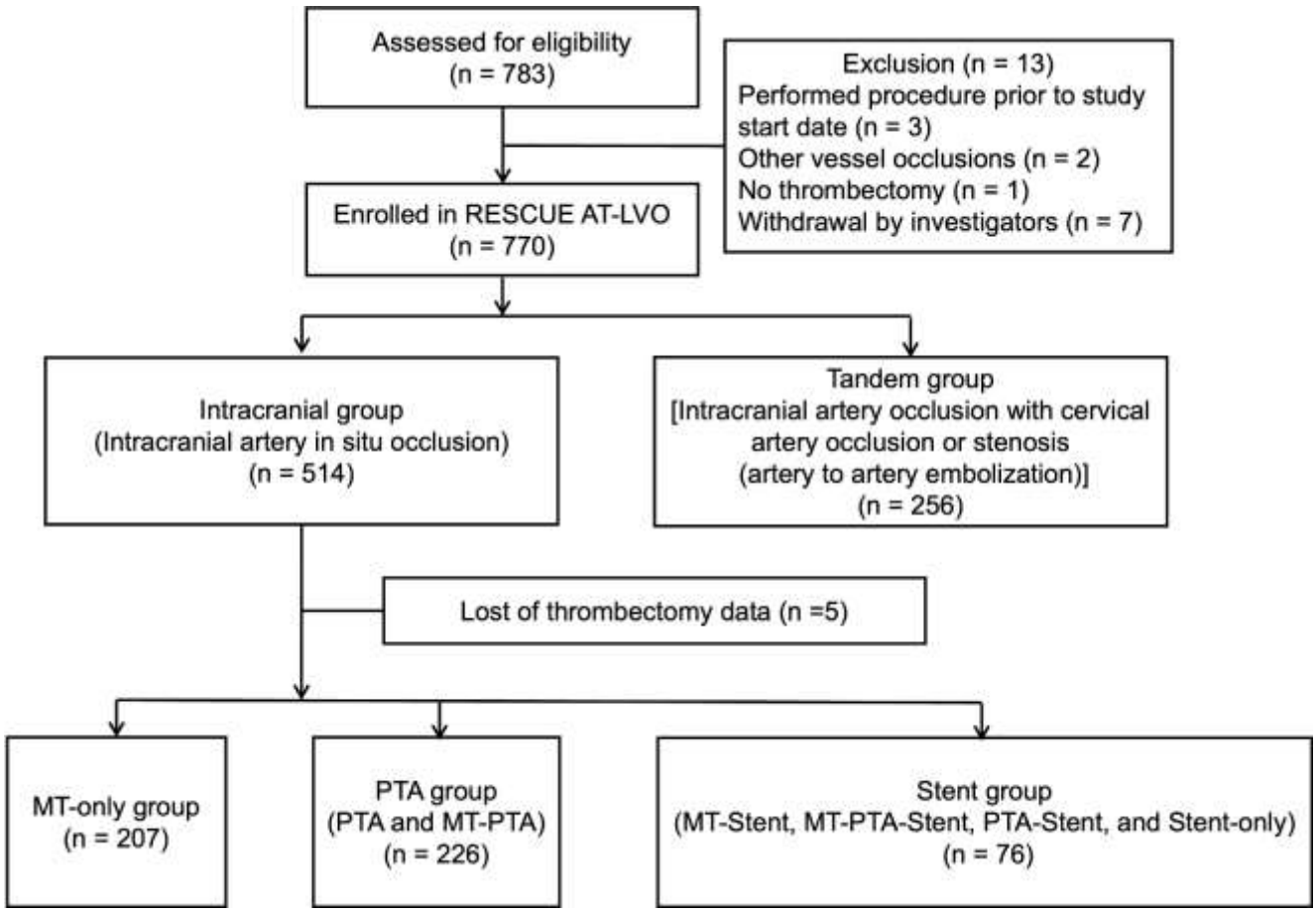


Figure 1. Study flowchart. Abbreviations: RESCUE AT-LVO, Recovery by Endovascular Salvage for Cerebral Ultra-Acute Embolic and Atherothrombotic Stroke with Large Vessel Occlusion; MT, mechanical thrombectomy; PTA, percutaneous transluminal angioplasty; Stent, stent deployment. MT alone was classified into the MT-only group. PTA and MT-PTA were classified into the PTA group. MT-Stent, MT-PTA-Stent, PTA-Stent, and Stent-only were classified into the Stent group.

Among the 51 facilities, 47 facilities enrolled under 19 patients (Figure 2). The distribution of each category was as follows: MT-only, 207 (40.7%); PTA, 226 (44.4%); and Stent, 76 (14.9%). The baseline characteristics were predominantly consistent across the different groups, with minor deviations in specific parameters (Table 1).

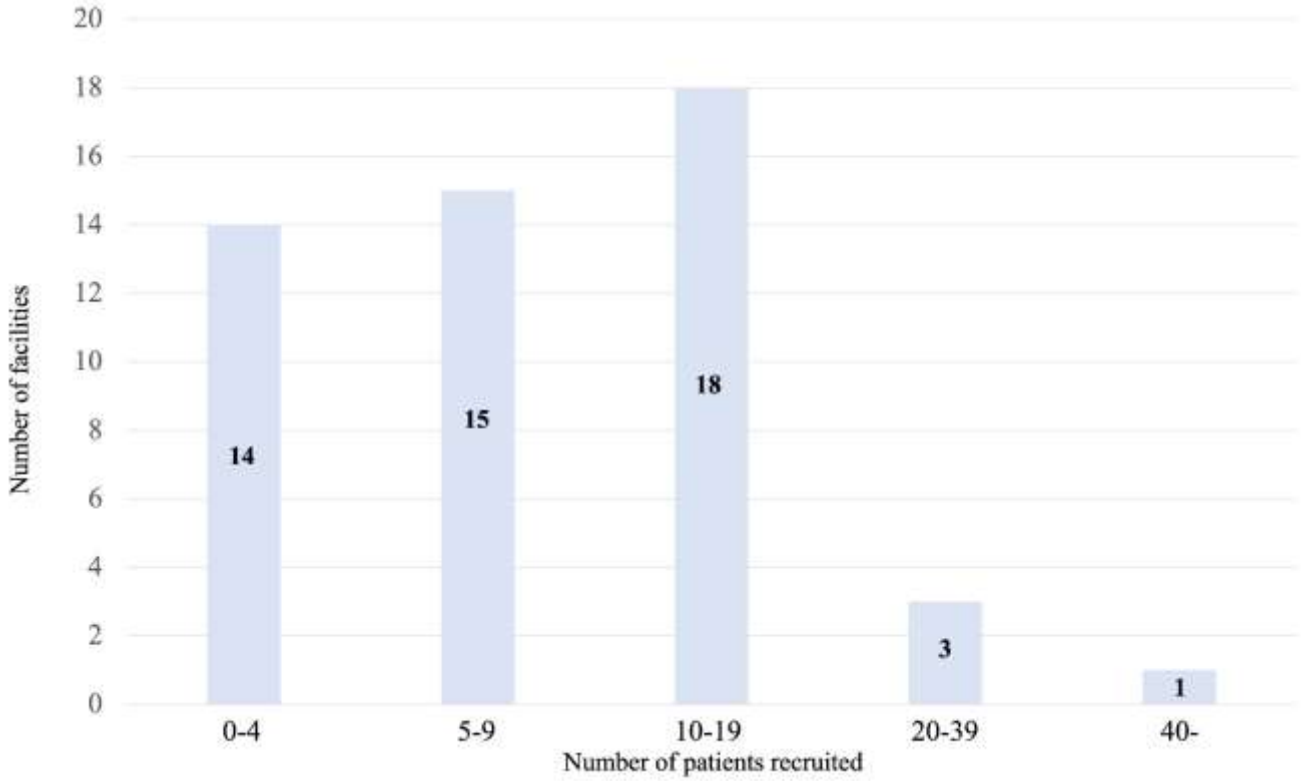


Figure 2. The number of recruited patients and the number of facilities

Patients in the MT-only group had a higher rate of medical history of ischemic heart disease than patients in the PTA and Stent groups (MT-only, 11.1%; PTA, 3.5%; and Stent, 7.9%). Occlusion of the M2 segment of the MCA was frequently observed in the MT-only group (MT-only, 16.4%; PTA, 4.4%; and Stent, 5.3%), and vertebral artery occlusion was frequently observed in the Stent group (MT-only, 4.8%; PTA, 5.8%; and Stent, 10.5%). The rate of puncture onset within 72 h was not significantly different among the three groups (MT-only, 98.6%; PTA, 95.1%; Stent, 96.1%) (Table 1).

3.2 Antiplatelet therapy and treatment efficacy and complications

The rates of antiplatelet therapy in the MT-only, PTA, and Stent groups were 54.6%, 76.1%, and 92.1% for the entire study period, respectively. The rate of antiplatelet therapy before onset was not significantly different among the three groups. However, the PTA and Stent groups had a higher rate of initiating additional antiplatelet medication than that of the MT-only group (MT-only, 38.7%; PTA, 70.4%; and Stent, 89.5%; $p<0.0001$). Specifically, the initiation of additional antiplatelet medication was more frequent after onset-before EVT (MT-only, 13.0%; PTA, 20.4%; and Stent, 26.3%; $p<0.0001$) and during EVT (MT-only, 9.2%; PTA, 38.9%; and Stent, 54.0%; $p<0.0001$) (Table 2).

Table 1. Antiplatelet therapy and treatment efficacy and complications

	MT-only	PTA	Stent	P-value
Number of patients, n (%)	207 (40.7)	226 (44.4)	76 (14.9)	NA
Antiplatelet, therapy, n (%)	112 (54.6) (n=205)	172 (76.1)	70 (92.1)	< 0.001
Before onset, n (%)	46 (22.4) (n=205)	46 (20.5) (n=224)	10 (13.5)	0.26
After onset, n (%)	80 (38.7)	159 (70.4)	68 (89.5)	< 0.001
After onset – before EVT, n (%)	27 (13.0)	46 (20.4)	20 (26.3)	< 0.001
During EVT, n (%)	19 (9.2)	88 (38.9)	41 (54.0)	< 0.001
Just after EVT, n (%)	34 (16.4)	25 (11.1)	7 (9.2)	< 0.001
Residual stenosis (WASID) – %, median [IQR]	64 [50–80] (n=200)	57 [40–71] (n=224)	47 [20–61]	< 0.001

Residual stenosis (WASID) >70%, n (%)	69 (34.5) (n=200)	59 (26.3) (n=224)	10 (13.2)	0.002
Intraoperative Complications, n (%)	10 (4.8)	21 (9.3)	11 (14.5)	0.03
vessel perforation	3 (1.5)	4 (1.8) (n=225)	0 (0)	0.51
vessel rupture	0 (0)	1 (0.4) (n=225)	1 (1.3)	0.29
vascular dissection	5 (2.4)	9 (4.0) (n=225)	5 (6.6)	0.25
distal embolism	0 (0)	3 (1.3) (n=225)	6 (7.9)	< 0.001
cholesterol crystal embolization	0 (0)	0 (0)	0 (0)	NA
puncture site complications	2 (1.0)	4 (1.8) (n=225)	1 (1.3)	0.77

Moreover, the PTA and Stent groups had a higher rate of initiating additional antiplatelet medication during EVT with aspirin and clopidogrel compared to that in the MT-only group (Aspirin: MT-only, 7.3%; PTA, 30.1%; Stent, 46.1%; p<0.001; Clopidogrel: MT-only, 6.3%; PTA, 24.3%; Stent, 40.8%; p<0.001). The use of DAPT or TAPT was also more frequent in the PTA and Stent groups compared to that in the MT-only group (DAPT/TAPT: MT-only, 28.5%; PTA, 62.2%; Stent, 76.3%; p<0.001) (Table 3).

Table 2: Detailed antiplatelet therapy after onset

	MT-only	PTA	Stent	P vale
Number of patients, n (%)	207 (40.7)	226 (44.4)	76 (14.9)	NA
Antiplatelet therapy after onset, n (%)	80 (38.7)	159 (70.4)	68 (89.5)	< 0.001
Aspirin, n (%)	68 (32.9)	149 (65.9)	63 (82.9)	< 0.001
Before EVT, n (%)	25 (12.1)	50 (22.1)	24 (31.6)	< 0.001
During EVT, n (%)	15 (7.3)	68 (30.1)	35 (46.1)	< 0.001
Just after EVT, n (%)	28 (13.5)	31 (13.7)	4 (5.3)	< 0.001
Clopidogrel, n (%)	55 (26.6)	122 (54.0)	55 (72.4)	< 0.001
Before EVT, n (%)	21 (10.1)	42 (18.6)	19 (25.0)	< 0.001
During EVT, n (%)	13 (6.3)	55 (24.3)	31 (40.8)	< 0.001
Just after EVT, n (%)	21 (10.1)	25 (11.1)	5 (6.6)	< 0.001
Prasugrel, n (%)	3 (1.5)	9 (4.0)	6 (7.9)	< 0.001
Before EVT, n (%)	1 (0.5)	1 (0.4)	1 (1.3)	< 0.001
During EVT, n (%)	2 (1.0)	6 (2.6)	5 (6.6)	< 0.001
Just after EVT, n (%)	0 (0)	2 (0.9)	0 (0)	< 0.001
Cilostazol, n (%)	13 (6.3)	41 (18.1)	13 (17.1)	< 0.001
Before EVT, n (%)	5 (2.4)	12 (5.3)	1 (1.3)	< 0.001
During EVT, n (%)	1 (0.5)	19 (8.4)	9 (11.8)	< 0.001
Just after EVT, n (%)	7 (3.4)	10 (4.4)	3 (4.0)	< 0.001
Ozagrel sodium, n (%)	3 (1.5)	20 (8.9)	6 (7.9)	< 0.001
Before EVT, n (%)	0 (0)	1 (0.4)	0 (0)	< 0.001
During EVT, n (%)	2 (1.0)	19(8.4)	5 (6.6)	< 0.001
Just after EVT, n (%)	1 (0.5)	0 (0)	1 (1.3)	< 0.001
DAPT or TAPT, n (%)	59 (28.5)	141 (62.4)	58 (76.3)	< 0.001

Residual stenosis >70% was higher in the MT-only group than in the PTA and Stent groups (MT-only, 34.5%; PTA, 26.3%; Stent, 13.2%; p<0.002). The intraoperative complication rate increased approximately twice for the PTA group and thrice for the Stent group

compared with that for the MT-only group (MT-only, 4.8%; PTA, 9.3%; and Stent, 14.5%; p=0.03). Distal embolism was more frequent in the PTA group (MT-only, 0%; PTA, 1.3%; Stent, 7.9%; p<0.001). However, the rates of other intraoperative complications were not significantly different among the three groups (Table 2).

3.3 Outcomes

Reocclusion occurred in 80 (15.7%) of the patients. The cumulative incidence rates of reocclusion in the MT-only, PTA, and Stent groups were 20.3% (42), 10.6% (24), and 18.4% (14), respectively. The cumulative incidence rate of reocclusion was lower in the PTA group than in the MT-only group (adjusted HR [95% CI], 0.48 [0.29–0.80]) (Table 4).

Table 3. Outcomes

Variables	Incidence, n (%)	Crude HR (95% CIs)	P-value	Adjusted HR (95% CIs)	P-value
Reocclusion, n (%)					
MT-only	42 (20.3)	Reference			
PTA	24 (10.6)	0.48 (0.29–0.80)	0.005	0.48 (0.29–0.80)	0.005
Stent	14 (18.4)	0.88 (0.48–1.61)	0.68	0.89 (0.48–1.65)	0.72
Variables	Incidence, n (%)	Crude OR (95% CIs)	P Value	Adjusted OR (95% CIs)	P-value
Modified TICI2b-3, n (%)					
MT-only	158 (76.3)	Reference			
PTA	193 (85.4)	1.81 (1.11–2.96)	0.02	1.87 (1.12–3.11)	0.02
Stent	69 (90.8)	3.06 (1.32–7.09)	0.01	2.83 (1.20–6.71)	0.02
mRS score 0–2 at 90 days, n (%)					
MT-only (n=190)	70 (36.8)	Reference			
PTA (n=214)	88 (41.1)	1.19 (0.80–1.79)	0.38	1.35 (0.85–2.15)	0.21
Stent (n=73)	32 (43.8)	1.34 (0.77–2.32)	0.30	1.31 (0.70–2.46)	0.39
Variables	Incidence, n (%)	Crude HR (95% CIs)	P-value	Adjusted HR (95% CIs)	P-value
Any ICH, n (%)					
MT-only	13 (6.3)	Reference			
PTA	13 (5.8)	0.91 (0.42–1.96)	0.81	0.89 (0.40–1.97)	0.77
Stent	2 (2.6)	0.41 (0.09–1.84)	0.25	0.50 (0.11–2.24)	0.36
Symptomatic ICH, n (%)					
MT-only	3 (1.5)	Reference			
PTA	4 (1.8)	1.22 (0.27–5.44)	0.80	0.90 (0.17–4.74)	0.91
Stent	1 (1.3)	0.91 (0.09–8.74)	0.93	1.07 (0.11–10.8)	0.95
Death, n (%)					
MT-only	15 (7.3)	Reference			
PTA	14 (6.2)	0.78 (0.38–1.63)	0.51	0.73 (0.34–1.57)	0.43
Stent	4 (5.3)	0.69 (0.23–2.09)	0.51	0.38 (0.09–1.68)	0.20

Of the 79 patients, 66 (83.5%) experienced reocclusion within 10 days following EVT; specifically, 49 of 79 (62.0%) patients experienced reocclusion within 2 days (Figure 3A). A modified TICI 2b–3 was achieved in 420 (82.5%) patients. Among these patients,

modified TICI2b-3 was more frequent in the PTA and Stent groups than in the MT-only group (aOR, 1.87 [1.12–3.11] and 2.83 [1.20–6.71], respectively) (Table 4). A total of 190 patients (39.8%) achieved an mRS score of 0–2 at 90 days after EVT (Table 4, Figure 4). The incidence of mRS scores of 0–2 at 90 days after EVT was not significantly different among the three groups (Table 4). The cumulative incidences of symptomatic ICH, ICH, and death were not significantly different among the groups (Table 4, Figure 3B–D). The distribution of mRS scores at 90 days was also not significantly different among the three groups (Figure 4).

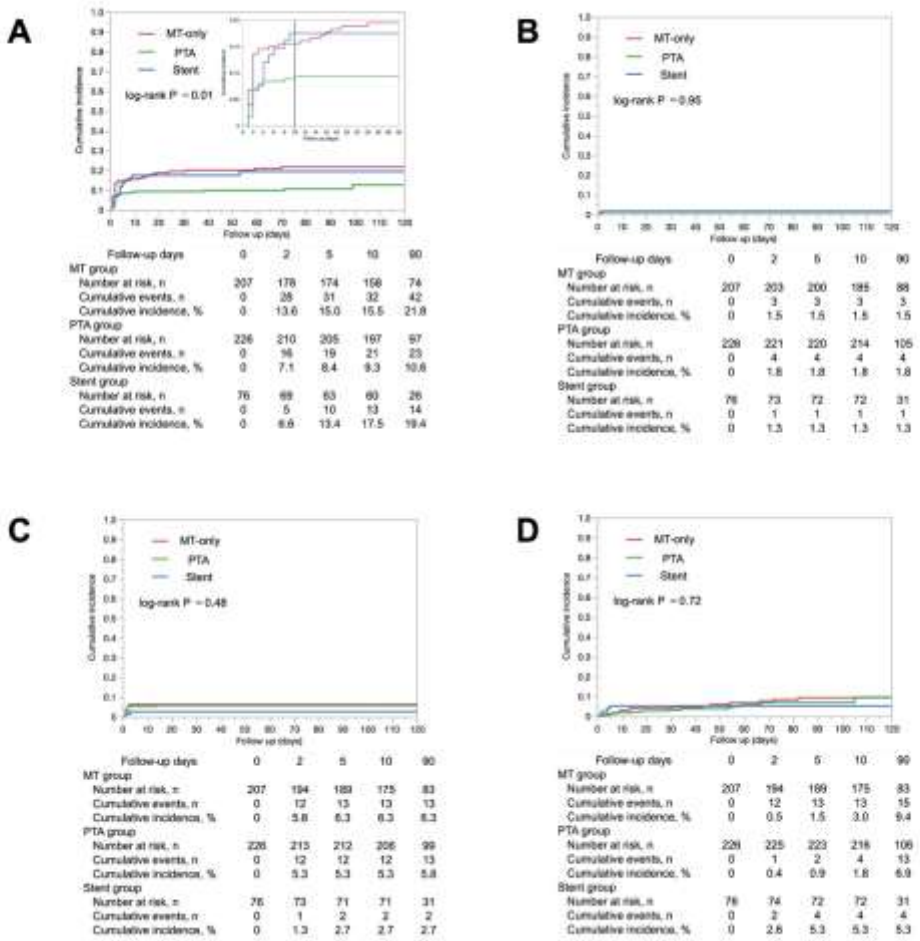
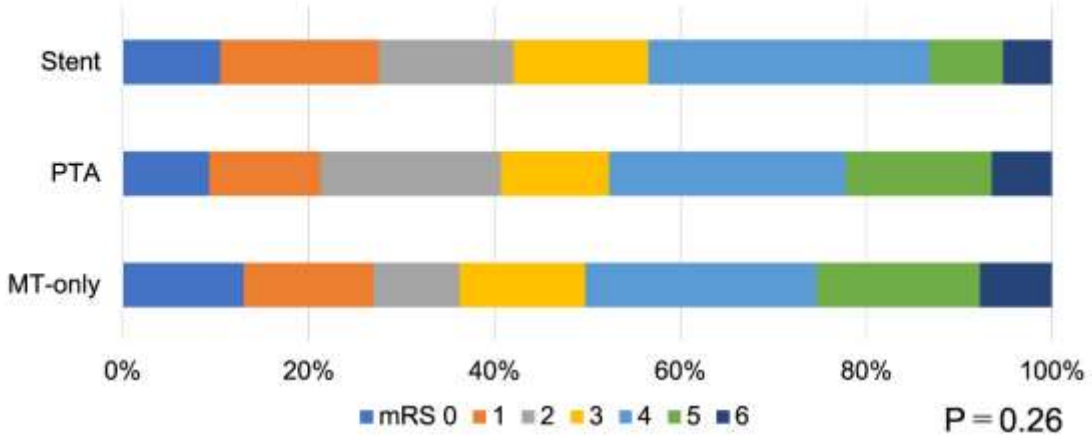


Figure 3. Cumulative incidences of outcomes. A: Reocclusion. B: Symptomatic ICH. C: Any ICH. D: Death
ICH, intracranial hemorrhage; MT, mechanical thrombectomy; PTA, percutaneous transluminal angioplasty; Stent, stent deployment



	mRS at 90 days	0	1	2	3	4	5	6
MT-only (n = 193)	n (%)	25 (13,0)	27 (14.0)	18 (9.3)	26 (13.5)	48 (24.9)	34 (17.6)	15 (7.8)
PTA (n = 216)	n (%)	20 (9.3)	26 (12.0)	42 (19.4)	25 (11.6)	55 (25.5)	34 (15.7)	14 (6.5)
Stent (n = 76)	n (%)	8 (10.5)	13 (17.1)	11 (14.5)	11 (14.5)	23 (30.3)	6 (7.9)	4 (5.3)

Figure 4. Distribution of mRS scores at 90 days
MT, mechanical thrombectomy; PTA, percutaneous transluminal angioplasty; Stent, stent deployment; mRS, modified Rankin scale

3.4 Subgroup analyses

In subgroup analyses, PTA was associated with significantly fewer cases of reocclusion compared to the MT-only group in the following groups: patients aged 75 years and older, male patients, patients with anterior circulation, those with residual stenosis less than 70%, those without the use of DAPT/TAPT, and patients treated with rt-PA. However, these differences were not significant (Figure 5).

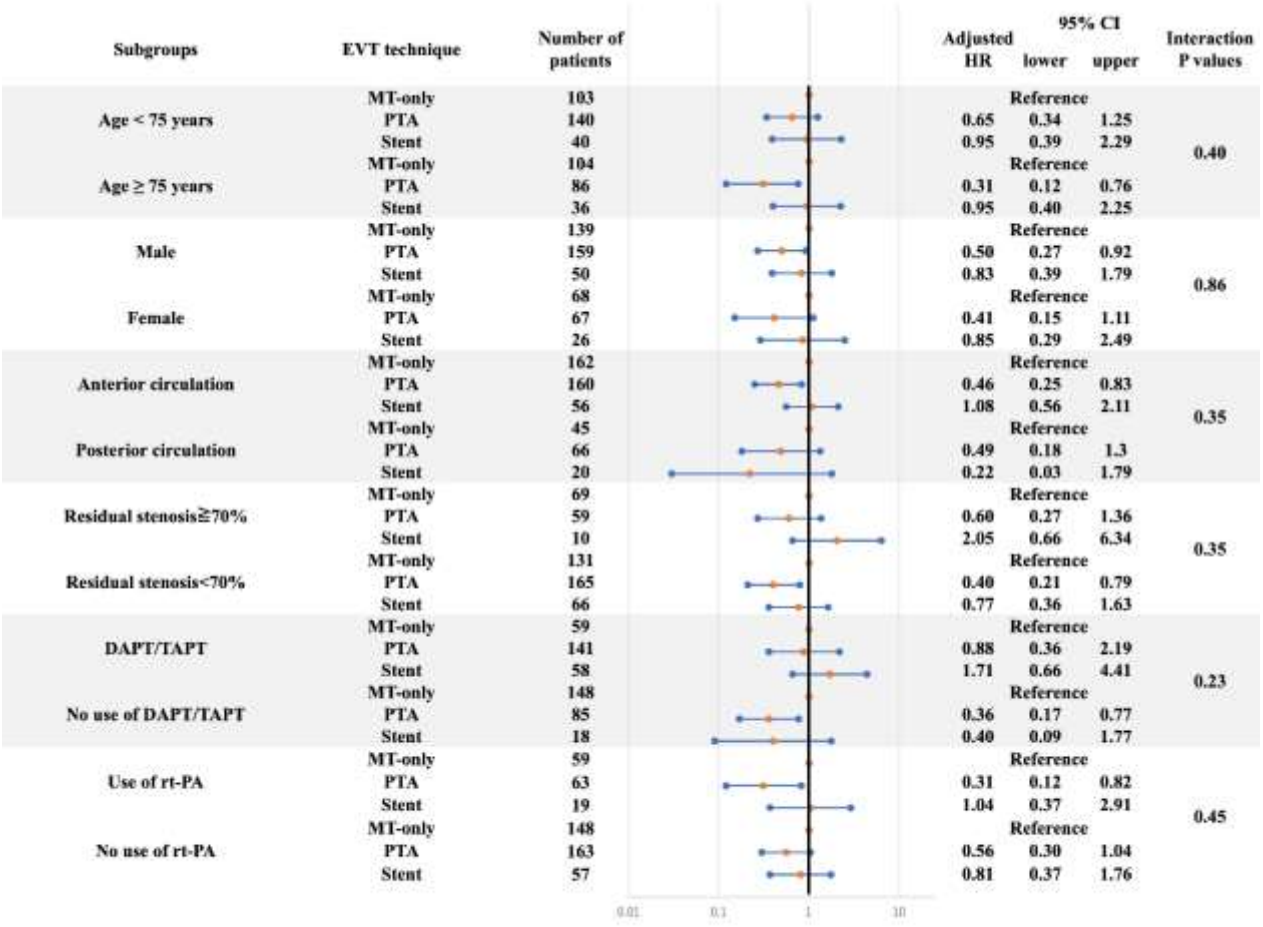


Figure 5. Subgroup analyses of reocclusion

DISCUSSION

Our study showed that the reocclusion rate was lower in the PTA group than in the MT-only group. In addition, all three groups had a high incidence of reocclusion within 10 days of EVT. A substantial subset (approximately 62.0%) encountered reocclusion within 2 days. In the PTA and Stent groups, a high percentage of patients received antiplatelet drugs administered immediately before or during EVT. This suggested that AT-LVO was suspected and administered immediately before or during the procedure. Regarding intraoperative complications, the rate increased by approximately twice for the PTA group and thrice for the Stent group compared with that for the MT-only group. In contrast, symptomatic ICH, ICH, and death rates were not significantly different among the three groups.

AT-LVO can be an occult cause of reocclusion following MT.[3] In a recent study using stent retrievers as first-line treatment, there was no difference in the first-pass effect between the AT-LVO and other groups, but there was a significant difference in the final modified TICI (80.0% vs. 92.5; aOR, 0.21 [0.09–0.50]), suggesting that the AT-LVO group is more likely to experience reocclusion during the procedure.[16] Some studies have indicated that PTA and/or Stent is safe and yield positive results in patients with AT-LVO.[17,18] These results are consistent with the findings of our present study. In addition, the restenosis rates after balloon angioplasty for symptomatic intracranial artery stenosis were 6.3% with the use of a drug-coated balloon and 31.3% with the use of a conventional balloon.[19] Therefore, we believe that the use of drug-coated balloons will improve the outcomes of patients with AT-LVO in the future. Our study found that >70% residual stenosis was higher in the MT-only group than in the PTA and Stent groups. Considering the higher reocclusion rate in the MT-only group, additional procedures, including PTA or Stent, may yield greater benefits for patients with severe stenosis after recanalization with MT-only. In the present study, we did not observe a significant difference in reocclusion rates between the Stent and MT-only groups. The primary reason, which may be subject to selection bias, is that the Stent group comprised patients with refractory occlusion or dissection who had undergone rescue stenting. This bias may have influenced the results. It has been suggested that even in difficult-to-treat cases, stent placement can potentially achieve treatment outcomes comparable to those of MT-only.[20] A secondary consideration is that platelet aggregation screening is not universally conducted across all institutions, and these data were not collected in this study. Additionally, in Japan, GP IIb/IIIa inhibitors such as abciximab, eptifibatide, and tirofiban are not reimbursed. This policy applies to all formulations, including intravenous and oral. However, DAPT or loading doses are frequently used for PTA and stent replacement. These may affect the interpretation of reocclusion rates and the generalizability of the findings of this study. We consider that the use of antiplatelet agents in patients with AT-LVO is essential for preventing reocclusion. If a patient presents with a score that predicts AT-LVO, antiplatelet agents should be administered as soon as possible to reduce reocclusion.[21]

The new ANGEL-REBOOT trial, a randomized controlled study examining the effectiveness of angioplasty as a secondary intervention

in patients with AT-LVO, has been fully registered, and its findings are anticipated (NCT05122286). This trial, formally known as a randomized study of bailout intracranial angioplasty following thrombectomy for acute large vessel occlusion, aims to provide new insights into this treatment approach. Our study included the largest registry of patients who underwent EVT for AT-LVO in a real-world setting.

Some limitations of this study should be considered when interpreting our findings. First, we did not have a standardized EVT protocol specifying balloon and stent sizes and length or perioperative antiplatelet therapy. Therefore, these decisions were left to the discretion of the physician in charge. Consequently, selection bias might have occurred. The Stent group included patients with refractory occlusion or dissection who underwent rescue stenting. Second, this study lacked a core laboratory. Typically, a core laboratory provides standardized, unbiased analysis and interpretation of clinical data, particularly in studies involving complex imaging or procedural outcomes. The absence of such facilities may lead to variability in data interpretation and can potentially affect the study's overall reliability and validity. Third, reocclusion was assessed without a standardized imaging follow-up protocol. Evaluations were primarily based on symptom deterioration or incidental findings of occlusion on follow-up MRI. This approach may have led to an underestimation of asymptomatic reocclusion. Fourth, we systematically registered patients with AT-LVO at 51 centers, and this study is, to the best of our knowledge, the largest study to evaluate the outcomes of EVT for AT-LVO. However, the sample size was significantly small to evaluate the outcomes in the different groups. Further large-scale studies are required to accurately assess the optimal EVT technique for AT-LVO. Finally, this registry study was conducted in Japan, where GP IIb/IIIa inhibitors are not reimbursed. In addition, the risk of bleeding events differs among ethnicities.[22] Thus, the generalizability of our findings to the rest of the world should be carefully considered.

CONCLUSIONS

The reocclusion rate is lower with PTA than with MT-only. We did not observe a significant difference in reocclusion rates between the Stent and MT-only groups. In Japan, where GP IIb/IIIa inhibitors are not reimbursed, DAPT or loading doses are frequently used for PTA and stent replacement. PTA may be considered a first-line strategy for AT-LVOs because reocclusion is more likely to occur if the procedure is terminated with MT alone. Randomized controlled trials are necessary to accurately determine the optimal EVT technique for AT-LVO. Reocclusion is likely to occur within 10 days of EVT in patients with AT-LVO. It is especially prone to occur within 2 days post-EVT. The preoperative and intraoperative administration of antiplatelet agents should be administered as soon as possible to reduce reocclusion.

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SUPPLEMENTAL FILES

Online Supplemental Data. Patient characteristics

	MT-only	PTA	Stent	P-value
Number of patients, n (%)	207 (40.7)	226 (44.4)	76 (14.9)	NA
Age – years, mean (SD)	73.4 (10.6)	71.8 (11.1)	70.3 (12.4)	0.07
Men, n (%)	139 (67.2)	159 (70.4)	50 (65.8)	0.67
mRS before onset, median [IQR]	0 [0–1]	0 [0–1]	0 [0–0]	0.18
NIHSS score on admission, median [IQR]	12 [8–20]	13 [6–21]	13 [6–19]	0.65
NIHSS score before EVT, median [IQR]	14 [8–22]	14 [8–22]	14 [8–20]	0.65
Medical history				
Hypertension, n (%)	128 (61.8)	154 (68.1)	50 (65.8)	0.39
Diabetes mellitus, n (%)	70 (33.8)	65 (28.8)	27 (35.5)	0.40
Hyperlipidemia, n (%)	75 (36.2)	65 (28.8)	24 (31.6)	0.25
Statin use, n (%)	38 (18.5)	38 (17.0)	9 (12.2)	0.46

Atrial fibrillation, n (%)	11 (5.3)	8 (3.5)	4 (5.3)	0.64
Ischemic heart disease, n (%)	23 (11.1)	8 (3.5)	6 (7.9)	0.01
Cerebral infarction, n (%)	38 (18.4)	44 (19.5)	18 (23.7)	0.83
Cerebral hemorrhage, n (%)	5 (2.4)	7 (4.6)	1 (9.1)	0.60
Current smoker, n (%)	52 (28.0)	60 (29.3)	20 (29.4)	0.94
Systolic blood pressure – mmHg, mean (SD)	162.4 (28.4)	165.5 (27.7)	163.3 (34.3)	0.55
Diastolic blood pressure – mmHg, mean (SD)	88.8 (16.8)	89.9 (17.8)	90.1 (19.0)	0.76
BMI – kg/m^2, mean (SD)	23.1 (3.9)	23.4 (3.7)	23.3 (3.8)	0.67
Laboratory results				
LDL cholesterol – mg/dL, mean (SD)	129.7 (43.7)	122.6 (39.9)	124.5 (35.8)	0.27
HDL cholesterol – mg/dL, mean (SD)	49.7 (15.8)	48.0 (14.2)	49.9 (14.6)	0.53
Creatinine – mg/dL, median [IQR]	0.85 [0.67–1.03]	0.81 [0.66–0.98]	0.75 [0.62–0.93]	0.24
CRP – mg/dL, median [IQR]	0.18 [0.08–0.96]	0.18 [0.09–0.55]	0.15 [0.06–0.65]	0.38
Hemoglobin – g/dL, median [IQR]	14.0 [12.7–15.5]	14.2 [13.0–15.6]	13.8 [12.8–14.9]	0.22
Platelet – 10^4/μL, median [IQR]	21.2 [18.2–25.8]	21.8 [17.5–25.1]	21.8 [18.8–24.9]	0.60
Blood glucose – mg/L, median [IQR]	127 [110–170]	130 [111–172]	124[106–167]	0.15
ASPECTS, median [IQR]	8 [7–9]	8 [7–10]	8 [7–9]	0.65
pc-ASPECTS, median [IQR]	7 [6–8]	7 [5–8]	7 [4–9]	0.96
ALL ASPECTS, median [IQR]	8 [6–9]	8 [6–9]	8 [6–9]	0.92
Intracranial occlusion site				
Anterior circulation, n (%)	162 (78.3)	160 (70.8)	56 (73.7)	0.21
Intracranial ICA, n (%)	26 (12.6)	35 (15.5)	13 (17.1)	0.001
M1 segment of MCA, n (%)	102 (49.3)	115 (50.9)	39 (51.3)	
M2 segment of MCA, n (%)	34 (16.4)	10 (4.4)	4 (5.3)	
Basilar artery, n (%)	35 (16.9)	53 (23.5)	12 (15.8)	
Vertebral artery, n (%)	10 (4.8)	13 (5.8)	8 (10.5)	
Intravenous rtPA use, n (%)	59 (28.5)	63 (27.9)	19 (25.0)	0.84
Onset to puncture time – days, median [IQR]	1 [1–1]	1 [1–2]	1 [1–2]	0.01
Onset to puncture time < 72 h, n (%)	204 (98.6)	215 (95.1)	73 (96.1)	0.13