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Thrombus migration in patients with acute ischaemic stroke undergoing endovascular thrombectomy

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ABSTRACT

Objective The impact of thrombus migration (TM) prior to endovascular thrombectomy (EVT) on clinical outcomes and revascularisation rates remains unknown. We aimed to examine whether preinterventional TM modifies the treatment effects of direct EVT versus bridging EVT in acute large vessel occlusion patients.

Methods All patients undergoing catheter angiography in the Direct Intra-arterial thrombectomy in order to Revascularise acute ischaemic stroke patients with large vessel occlusion Efficiently in Chinese Tertiary hospitals: A Multicentre randomised clinical Trial were included. TM was determined by radiologists unaware of the study by analysing discrepancies between computed tomographic angiography at baseline and first-run digital subtraction angiography before EVT. The primary outcome was the score on the modified Rankin scale (mRS) assessed at 90 days.

Results Of 627 included patients, the TM rate was 11.3% (71/627). In the multivariable logistic regression model, baseline National Institutes of Health Stroke Scale score (adjusted OR 0.956, 95% CI 0.916 to 0.999; p=0.043) and intravenous thrombolysis (adjusted OR 2.614, 95% CI 1.514 to 4.514; p<0.001) were independently associated with TM. The patients with TM were less likely to be completely recanalised than those without TM (21.27% vs 36.23%, p=0.040). The interaction of TM and the EVT treatment effect did not significantly affect mRS shift analysis (p=0.687) or mRS scores of 0 to 1 (p=0.436).

Conclusion Preinterventional TM does not modify the treatment effects of direct versus bridging EVT on functional outcomes in patients with acute ischaemic stroke with anterior large vessel occlusion. TM leads to a lower complete recanalisation rate.

Trial registration number

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Uncertainties remain about whether thrombus migration (TM) modify the effect of intravenous alteplase prior to thrombectomy in patients with anterior circulation large vessel occlusion.

WHAT THIS STUDY ADDS

⇒ After adjustment for potential confounders, preinterventional TM does not modify the treatment effect on functional outcomes in patients with acute ischaemic stroke (AIS) who underwent thrombectomy. TM leads to a lower complete recanalisation rate.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study found no evidence of preinterventional TM modify the treatment effect on functional outcomes in patients with AIS who underwent thrombectomy.

INTRODUCTION

Thrombus migration (TM) was commonly seen in intravenous thrombolysis (IVT) patients with large vessel occlusion (LVO) and was also confirmed in the vivo model.[1 2] Preinterventional TM was also reported to be prevalent between 17% and 30% in individuals treated with endovascular thrombectomy (EVT).[3–7] However, the data from previous studies were mainly derived from the relatively small scale of single-centre cohort studies. The disintegration of a pre-existing clot, whether postthrombolysis or not, might increase the challenge in EVT procedure. A migrated clot in a distal vessel may make the EVT procedure more complex and thus affect successful recanalisation. When thrombus fragments migrate to more than one location, retrieving all the clots might also cost more time. However, the association between pr-interventional TM and clinical outcomes remains uncertain.

We aimed to explore whether preinterventional TM affects successful EVT and modify clinical outcomes using data from the 'Direct Intra-arterial thrombectomy in order to Revascularise acute ischaemic stroke patients with large vessel occlusion Efficiently in Chinese Tertiary hospitals: A Multicentre randomised clinical Trial (DIRECT-MT)'.[8]

MATERIALS AND METHODS

Study design and participants

DIRECT-MT trial was a multiple-centre, randomised, open-label trial with blinded

outcome assessment involving patients with acute ischaemic stroke (AIS), which assessed whether direct mechanical thrombectomy is non-inferior to intravenous rt-PA combined with mechanical thrombectomy in patients with large vascular occlusion of the anterior circulation (ClinicalTrials.gov Identifier: NCT03469206). We conducted a post hoc analysis based on DIRECT-MT database.

The methods and results of the DIRECT-MT trial have been reported.[8 9] Briefly, patients in the DIRECT-MT trial who met the following inclusion criteria were included: (1) they had AIS with anterior LVO (within 4.5 hours after symptom onset), (2) had undergone catheter angiography in the DIRECT-MT trial and (3) had complete imaging data, including a baseline CT angiography (CTA), a first-run digital subtraction angiography (DSA) before thrombectomy, final post-EVT angiography images and follow-up images.

For patients with tandem lesions, no specific EVT procedure was recommended in the protocol of the DIRECT MT trial and the appropriate procedure was left to the clinician's discretion.

Assessment of TM

For all included patients, we recorded CTA images (including a thin slice series) at baseline and the first DSA run before EVT. The site of thrombus on CTA and DSA and the occurrence of TM were evaluated by trained radiologists or qualified personnel in the core lab of the DIRECT MT trial.[9] For discrepancies between the two readers, another neurologist with neuroimaging expertise, re-evaluated the images and helped reach a consensus. Detailed information on image evaluation was published in the protocol and online supplemental file of the DIRECT-MT trial(online supplemental file 3).[8 9]

The initial location of the thrombus was determined based on the baseline CTA findings before the patient was enrolled. The position of the thrombus was categorised into different groups based on its location in the cerebral circulation, including the internal carotid artery (ICA); proximal middle cerebral artery (MCA) M1 segment; distal MCA M1, M2, M3, M4 or M5 segment; anterior cerebral artery (ACA), and segments A1 and A2. Of note, M1 segment of MCA was defined as the origin of MCA to the bifurcation/trifurcation or the genu adjacent to the limen insulae.[9] The length of MCA-M1 was measured from the M1 portion of MCA, which was defined as the segment between the ACA-MCA bifurcation point and the MCA -M2 bifurcation point or the genu adjacent to the limen insulae. MCA-M1 was dichotomised into proximal and distal at the midpoint of the course. The distal end of M1 segment refers to either of two locations: (1) at the genu adjacent to the limen insulae or (2) at the main bifurcation. Tandem lesions refer to simultaneous stenosis of the cervical and intracranial internal carotid arteries (or M1 segment of MCA). TM was defined as a thrombus moving from one segment to another downstream segment. Based on data from DIRECT MT trial, 99% of ICA thrombi at baseline were in the distal segment; therefore, this study did not define thrombus movement within the ICA as TM. According to the presence of TM, the patients were divided into two groups: TM groups and non-TM groups. A migrated thrombus beyond the distal end of the M1 segment or in ACA was designated a 'distal TM (DTM)'. When thrombus fragments migrate to more than one location, the most proximal location is defined as the location of the thrombus.

Outcomes

The primary outcome was measured by the modified Rankin scale (mRS) assessed at 90 days. The secondary outcome was a 90-day mRS score of 0–1, significant neurological improvement (SNI), and an expanded Thrombolysis In Cerebral Infarction scale (eTICI) score on final angiography ≥2b. The SNI was defined as an 8-point improvement on the National Institutes of Health Stroke Scale (NIHSS) or an NIHSS score of 0 or 1 on day 7 or discharge. The secondary safety outcomes included all-cause mortality, symptomatic intracranial haemorrhage or asymptomatic ICH, arterial dissection, embolism in new areas and EuroQol-5 Dimension scores. Detailed descriptions of primary and secondary outcomes and safety outcomes were provided in the DIRECT MT protocol.[9]

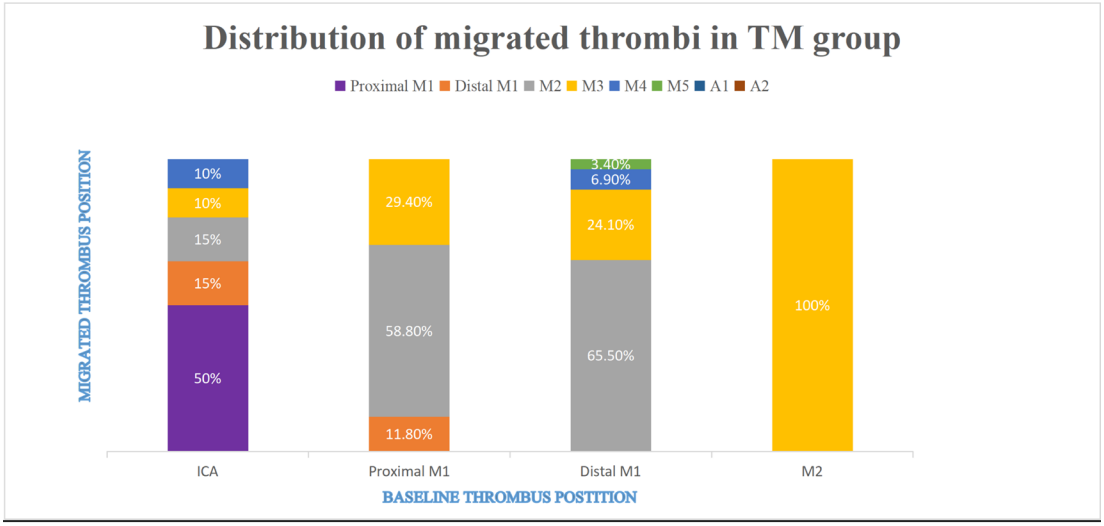
Statistical analyses

Baseline characteristics and laboratory data according to the presence or absence of TM before EVT were illustrated. Categorical variables in each group using the χ^2 test and continuous variables using the Student's t-test. We used univariable regression analysis to identify potential factors of TM. To obtain independent risk factors for TM, we included variables with significant differences in univariable regression analysis and other relevant variables (age, baseline NIHSS score, onset date of groin puncture, occlusion site) in multiple regression analysis. Missing data for baseline characteristics were imputed with multiple imputations by fully conditional specification regression for continuous variables or fully conditional specification logistic regression for binary and ordinal variables.

The Cochran-Mantel-Haenszel tests were also performed to compare the differences in the incidence of TM and DTM between the thrombectomy-alone group and the combination therapy group. We evaluated the interaction between TM and treatments on the primary outcome before and after adjusting for imbalances in baseline important prognostic factors.

All analyses were then adjusted for certain variables in the model: age, the baseline NIHSS score, the mRS score before stroke onset, cerebral collateral status and the time from stroke onset to randomisation.

A two-sided $p<0.05$ was considered statistically significant. All analyses were conducted using SPSS, V.22 (SPSS).



Baseline thrombus position (n)	Distribution of migrated thrombus by DSA（n）							
	Proximal M1	Distal M1	M2	M3	M4	M5	A1	A2
ICA(20)	10	3	3	2	2	0	0	0
Proximal M1(17)		2	10	5	0	0	0	0
Distal M1(29)			19	7	2	1	0	0
M2(2)				2	0	0	0	0

Figure 1 Trial flow diagram. DSA, digital subtraction angiography; ICA, internal carotid artery; TM, thrombi migration.

Data availability

Anonymised data will be shared by request from any qualified investigator.

RESULTS

Patient characteristics

Overall, 656 patients were enrolled in DIRECT-MT, 327 patients in the thrombectomy-alone group and 329 patients in the combination therapy group. Among them, those who did not undergo catheter angiography, with incomplete imaging data or lost to follow-up for other reasons were excluded (figure 1). A total of 627 cases were included in the subgroup analysis, including 310 cases in the thrombectomy-alone group and 317 cases in the combination therapy group (figure 1). There are 12 patients developed reocclusion after EVT; however, a non-significant difference was found between TM (1.41%) and non-TM groups (1.98%) (p=1.000). (online supplemental table 1) The tandem lesion rate was 9.73% (61 cases), and no significant difference was found between TM (11 cases) and non-TM group (50 cases) (15.49% vs 8.99%, p=0.082, respectively) (online supplemental table 2). The detailed baseline characteristics of the TM subgroups are shown in table 1.

Incidence of TM and associated factors

TM rate in this study was 11.3% (71/627). The baseline thrombus position and distribution of TM were illustrated in figure 2. Most M1 thrombi (15, 88.2%) migrated to the M2 or M3 segment. More than half of thrombi from the ICA ended in the proximal M1 segment (50%) or the distal bifurcation of the M1 segment (15%) (figure 2).

Patients with atrial fibrillation (33.80% vs 48.02%, p=0.024) and those treated with IVT (70.42% vs 48.02%, p<0.001) had a higher rate of TM (table 1). In the multivariable logistic regression model, baseline NIHSS score (adjusted OR 0.956, 95% CI 0.916 to 0.999; p=0.043) and IVT (adjusted OR 2.614, 95% CI 1.514 to 4.514; p<0.001) were independently associated with TM (table 2).

TM and DTM with recanalisation

Patients with TM were less likely to have eTICI3 reperfusion on the final angiogram (21.27% vs 36.23%, p=0.04), and they had fewer attempts during the EVT procedure (medians 1 vs 2, p<0.001) (table 1). Similarly, the eTICI3 recanalisation rate was significantly lower in the DTM group (15.09%) than in the non-DTM group (33.27%) (p=0.0065); the eTICI≥2b recanalisation rate was also lower in the DTM group (50.94%) than in the non-DTM group (80.21%) (p<0.001) (online supplemental table 3).

Interaction between TM and successful recanalisation

Among patients with TM, a higher rate of successful recanalisation (eTICI≥2b) was observed in the bridging group compared with EVT-only (89.4% vs 75.0%, adjusted OR 0.190, 95% CI 0.037 to 0.965) (table 3). Among patients without TM, successful recanalisation (eTICI≥2b) did not differ significantly between thrombectomy alone and combination therapy (OR 0.757, 95% CI 0.489 to 1.173) (table 3). However, TM did not modify the rate of successful recanalisation (p for interaction=0.259).

Table 1 Baseline characteristics of patients by thrombus migration or non-thrombus migration

Characteristics	TM (N=71)	Non-TM (N=556)	P value
Age (IQR)	66 (59–77)	70 (61–76)	0.321
Sex (male, %)	45 (63.38)	309 (55.58)	0.332
Baseline NIHSS score (IQR)	16 (12–21)	17 (13–22)	0.037
Medical history, n (%)			
Hypertension	45 (63.38)	331 (59.53)	0.533
Diabetes mellitus	14 (19.72)	105 (18.88)	0.866
Atrial fibrillation	24 (33.80)	267 (48.02)	0.024
Previous ischaemic stroke	11 (15.49)	75 (13.49)	0.644
Cause of emboli, n (%)			0.108
Cardio embolic	25 (35.21)	255 (45.86)	
Intracranial atherosclerosis	3 (4.23)	41 (7.37)	
Ipsilateral extracranial	11 (15.49)	50 (8.99)	
Undetermined	32 (45.07)	210 (37.77)	
Treatment with rtPA, n (%)	50 (70.42)	267 (48.02)	<0.001
Procedure and median duration (minutes)			
Hospital admission to CT	18 (7–28)	21 (12–32)	0.101
CT to groin puncture	72 (54–92)	64 (47–86)	0.063
Onset to groin puncture	202 (155–240)	205 (160–250)	0.717
Onset to rtpa	194 (142–232)	183 (135–224)	0.480
EVT procedure			
Groin puncture to recanalisation	55 (38–85)	63 (43–95)	0.226
First-pass recanalisation	26 (38.24)	265 (47.66)	0.141
Stroke onset to recanalisation	271 (239, 320.5)	275 (225, 329)	0.911
eTICI on final angiogram, n (%)			
eTICI 3	10 (21.27)	192 (36.23)	0.040
eTICI≥2b	57 (83.82)	449 (80.76)	0.498
Attempt times (N)	1 (0.00–2.00)	2 (1.00–3.00)	<0.001

Data are n (%), mean (SD), or median (IQR).
First pass recanalisation: first attempt eTICI≥2b.
AF, atrial fibrillationeTICI, The expanded treatment in cerebral infarction; EVT, endovascular thrombectomy; NIHSS, National Institutes of Health Stroke Scale; rtPA, recombinant tissue plasminogen activator; TM, thrombus migration.

Interaction between TM and clinical outcome

Patients with TM had a similar distribution of mRS at 90 days compared with those without (adjusted OR 1.584, 95% CI 0.595 to 4.217 vs 1.111, 95% CI 0.827 to 1.473, interaction p=0.687) (table 3). Among patients with TM, favourable functional outcome (mRS 0–1) was no significant difference between the thrombectomy-alone group and combination therapy group (45.0% vs 25.0%, adjusted OR 1.58, 95% CI 0.60 to 4.22), as well as in the patients without TM (23.3% vs 21.0% adjusted OR 1.11, 95% CI 0.82 to 1.47) (table 3). There were similar Euro-Qol-5 Dimension scores in both treatment groups among patients with or without TM (table 3).

We also found no significant interaction between TM and EVT treatment regimens on the safety outcomes (all-cause mortality, symptomatic ICH, asymptomatic ICH, embolism in a new area and vessel dissection; adjusted p for the interaction=0.602, 0.127, 0.054, 0.951 and 0.998, respectively). Vascular dissection occurred in eight patients (2.8%) in the thrombectomy-alone group and five patients (1.9%) in the combination therapy group (adjusted OR 1.60, 95% CI 0.51 to 4.99) in patients without TM (table 3).

DISCUSSION

This study found that the TM rate was 11.3% (71/627), and there was no interaction between TM and direct EVT or bridging EVT treatment in the 90-day distribution of mRS and other clinical outcomes. Further, we also found that TM was associated with IVT therapy and lower baseline NIHSS.

There was no interaction between TM and direct or bridging EVT in clinical outcomes in this study. Our

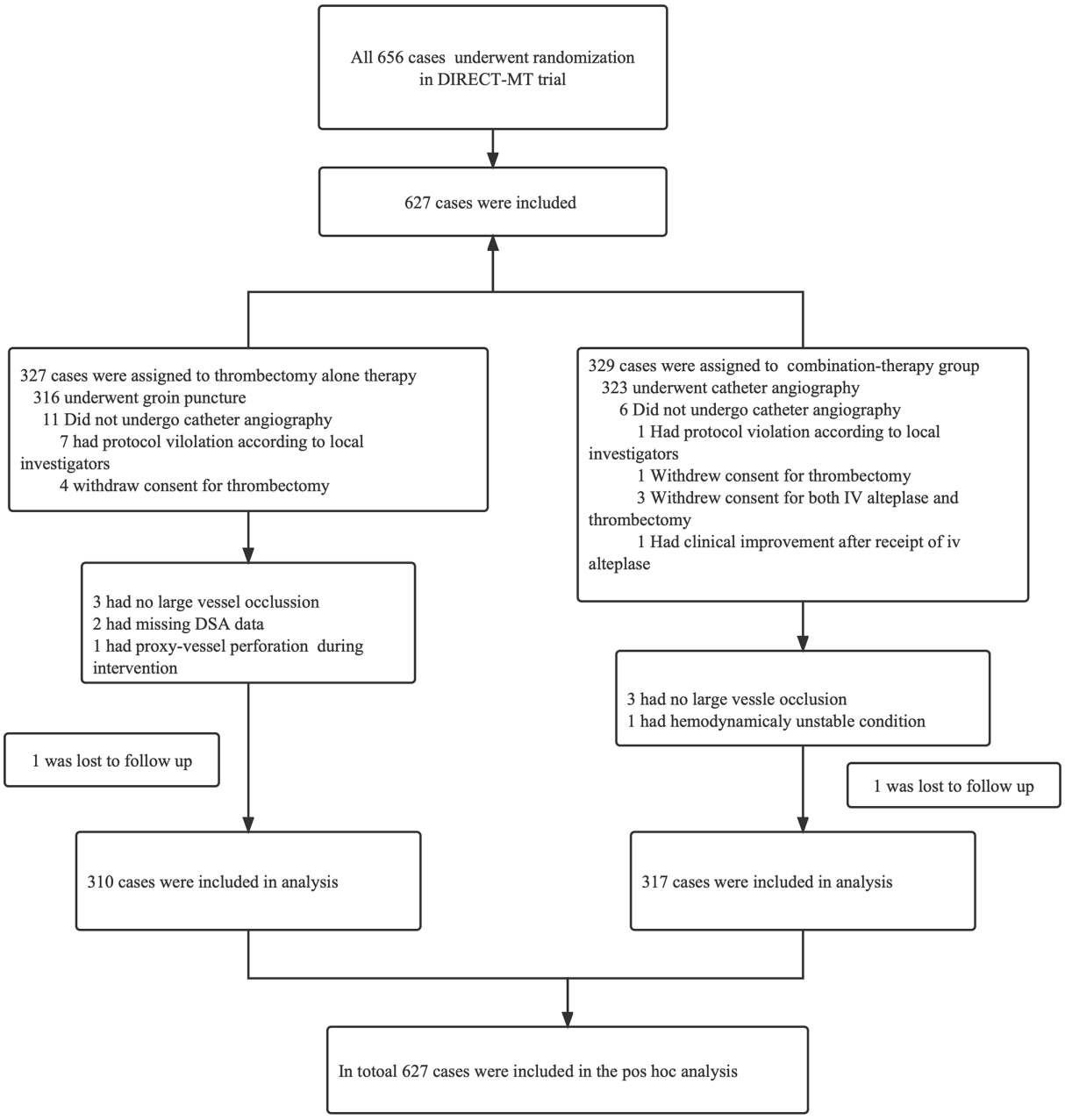


Figure 2 Distribution of migrated thrombi in TM group. DSA, digital subtraction angiography; DIRECT-MT, Direct Intra-arterial thrombectomy in order to Revascularise acute ischaemic stroke patients with large vessel occlusion Efficiently in Chinese Tertiary hospitals: A Multicentre randomised clinical Trial (DIRECT-MT); TM, thrombi migration.

finding was consistent with previous single-centre retrospective studies by Bernard *et al*.[6] Further, the data from the MR CLEAN registry (Multicentre Randomised Clinical Trial of Endovascular Treatment of Acute Ischaemic Stroke) also found a similar result[10] Although patients with TM were less likely to be completely recanalised (eTICI3) and had fewer attempts during EVT in our study. (table 1) However, a previous study found that TM led to a better functional outcome (adjusted OR 1.49; 95% CI 1.02 to 2.17) in patients with MCA M1 occlusion.[10] Another small-scale study (98 cases) using Penumbra 4 or 5 MAX reperfusion catheters to treat acute MCA occlusion also found a trend of more favourable clinical outcomes in the migrated thrombus group than in the non-migrated thrombus group (78.9% vs 60.8%, p=0.231).[3] Therefore, the influence of TM on 90 days functional outcome might relate to the location of the occluded artery. We need a larger scale of prospective studies focused on M1 occlusion patients to answer this question.

Furthermore, we also have done analysis to determine whether TM is directly associated with clinical outcomes. After adjusting for other related factors, including treatment options (direct or bridging therapy), the results showed that TM is associated with a better 90-day clinical outcome (mRS 0–2) (p=0.0281, aOR 1.360 (95% CI 0.767 to 2.41)) (online supplemental table 4). However,

Table 2 Multivariable analysis for factors associated with thrombus migration

	Adjusted* OR for TM	P value
Age (year)	1.003 (0.981–1.025)	0.823
Atrial fibrillation	0.598 (0.344–1.039)	0.068
IVT	2.614 (1.514–4.514)	<0.001
Baseline NIHSS score (per point)	0.956 (0.916–0.999)	0.043
Onset to groin puncture (minutes)	0.999 (0.990–1.008)	0.870
Occlusion site		
ICA	Ref	
M1	1.477 (0.831–2.624)	0.183
M2	0.405 (0.114–1.443)	0.164

*Values were adjusted for age, atrial fibrillation, treatment with rtPA, baseline NIHSS score, time from onset to groin puncture and occlusion site.
ICA, internal carotid artery; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; NIHSS, National Institutes of Health Stroke Scale; rtPA, recombinant tissue plasminogen activator; TM, thrombus migration.

TM is not associated with 90 days of excellent outcome (mRS 0–1) (p=0.1074, aOR 1.262 (95% CI 0.69 to 2.311)) (online supplemental table 4). Therefore, we assume that TM might be associated with the good clinical outcome independent of treatment options (direct or bridging therapy). Further well-designed prospective study to analysis the association between TM and clinical outcome is needed.

The preintervention TM rate in previous studies was between 17% and 30%,[3–7] which was relatively higher than our study (11.3%). The relatively low incidence of TM in this study may be associated with several reasons. First, in this study, most patients enrolled in the DIRECT MT trial accepted IVT and EVT at one centre without interhospital transfer. Therefore, the median time from baseline CTA to groin puncture was 65 min, much shorter than in previous registry studies (120 min).[11] Studies have shown that the time between the completion of IVT and the EVT procedure is related to the incidence of TM.[2] The shorter time interval between IVT and EVT treatment in our study may contribute to the low incidence of TM. Second, among the thrombolytic patients, the intravenous infusion was not completed before the procedure, which may affect the incidence of TM.

In line with previous studies,[6 10] our study showed that IVT therapy was independently associated with TM after adjusting for other factors. As reported by Bernard *et al*, the clot migration rate was significantly lower among the direct EVT group compared with the IVT group (3.8% vs 18.7%, OR 5.79; 95% CI 2.01 to 16.69; p=0.001).[6] In the MR CLEAN registry, alteplase treatment was associated with increased TM (adjusted OR, 2.01; 95% CI 1.29 to 3.11).[10] Although some studies showed no association between TM and IVT,[3 4 7] we assume this discrepancy might be due to the size of studies and the time interval between the assessment of thrombus location at baseline and the first run of DSA.

A lower baseline NIHSS score was associated with TM in this study. In light of the fact that the difference in NIHSS scores is minimal (only one point different), we should interpret this result with more caution. The impact of slight differences in NHISS scores on TM will need to be confirmed by subsequent studies. Previous studies have reported that TM was associated with shorter and blood cell-enriched thrombi.[5 7] We assume that extensive and firm thrombi are usually less likely to move and might cause more severe clinical symptoms than fragile and smaller thrombi.

This study has several limitations. First, the DIRECT-MT trial was conducted in advanced stroke centres. Currently, the extraction of thrombi beyond the M1 segment is only available in some primary centres or centres with experienced neurointerventionists. Even though evidence from a meta-analysis of several randomised trials, guidelines and clinical data did not widely support thrombectomy beyond the M1 segment.[12] Therefore, cautiously applying the result in centres without adequate thrombectomy experience is encouraged. The results of the recently published A Randomised Controlled Trial of DIRECT Endovascular Clot Retrieval vs Standard Bridging Thrombolysis With Endovascular Clot Retrieval study also did not suggest a non-inferiority of direct EVT versus bridging therapy.[13] For this reason, IVT before EVT was still warranted by most specialists, especially in rural areas without access to timely EVT.[14]

Another limitation of this study, only 6.9% of the patients in the DIRECT MT study had intracranial atherosclerotic disease, although studies have reported that this is a common cause in Asia, which may hinder the generalisation of our findings to the Asian population. In addition, this study did not consider the TM within the ICA. Thrombi might occlude the anterior choroidal artery by moving from the initial segment to the distal end within the ICA. However, based on data from DIRECT MT trial, 99% of ICA thrombi at baseline were in the distal segment; therefore, this study did not define thrombus movement within the ICA as TM.

Furthermore, there were no data on the histological composition or size of the thrombus. Several studies have shown significant impacts of clot size and histological composition on their stability and accessibility. Blood cell enrichment and shorter thrombi were more easily broken down and were associated with a better clinical response.[10–12 14]

CONCLUSION

Preinterventional TM does not modify the treatment effects of direct versus bridging EVT on functional outcomes in patients with AIS with anterior LVO. TM leads to a less complete recanalisation rate.

Table 3 Interaction between TM and thrombectomy-alone or combination-therapy on the clinical outcomes

	TM			NTM			
	Thrombectomy-alone (n=20)	Combination therapy (n=48)	Adjusted value	Thrombectomy-alone (n=289)	Combination therapy (n=267)	Adjusted value	P for interaction
mRS 90days (IQR)	2 (0–4.5)	3 (1.5–5)	1.584 (0.595, 4.217)	3 (2–5)	4 (2–5)	1.111 (0.827,1.473)	0.687
mRS (0–1)	9 (45.00%)	12 (25.00%)	2.559 (0.688, 9.519)	67 (23.30%)	56 (21.00%)	1.167 (0.763,1.785)	0.438
mRS (0–2)	11 (55.00%)	22 (45.83%)	1.024 (0.275, 3.807)	101 (35.07%)	93 (34.83%)	1.052 (0.718,1.540)	0.955
Death	3 (15.00%)	7 (14.58%)	1.180 (0.221, 6.306)	54 (18.7%)	51 (19.1%)	0.938 (0.602,1.463)	0.602
SNI at day7 or discharge	12 (60.00%)	27 (56.3%)	1.361 (0.414, 4.473)	156 (54.0%)	146 (54.7%)	0.988 (0.696,1.402)	0.899
eTICI on final angiogram≥2b	15 (75.00%)	42 (89.4%)	0.190 (0.037, 0.965)	225 (79.5%)	221 (83.7%)	0.757 (0.489,1.173)	0.259
Outcome lesion volume on CT—median (IQR)—mL	21.99 (2.38,91.11)	32.11 (9.57, 83.35)	16.791 (–32.481, 66.063)	37.15 (10.07, 114.77)	39.45 (10.53, 101.84)	0.447 (–13.821, 14.715)	0.512
NIHSS score at 5–7 days or discharge—median (IQR)	3.00 (0.50, 11.00)	5.00 (1.00, 12.00)	1.081 (–5.636, 7.799)	8.00 (2.00, 17.00)	9.00 (2.00,19.00)	–1.475 (–3.540, 0.580)	0.299
EQ-5D score at 90 days—median (IQR)	0.94 (0.57, 1.00)	0.95 (0.75, 1.00)	0.057 (–0.164, 0.278)	0.84 (0.33, 0.95)	0.84 (0.33, 0.95)	0.018 (–0.062, 0.093)	0.899
Vascular dissection	0.00 (0.00)	0.00 (0.00%)		8 (2.80%)	5 (1.90%)	1.597 (0.512,4.986)	0.998
Symptomatic ICH	2 (10.00%)	2 (4.20%)	3.462 (0.318, 37.735)	12 (4.20%)	18 (6.70%)	0.580 (0.272, 1.236)	0.127
Asymptomatic ICH	1 (5.00%)	16 (33.30%)	0.118 (0.014, 0.996)	104 (36.00%)	102 (38.20%)	0.919 (0.647, 1.307)	0.054
Embolism in new area	0.00 (0.00%)	2 (4.20%)	0.000 (0.000, 2.263)	35 (12.10%)	29 (10.90%)	1.107 (0.648, 1.892)	0.951

*Values were adjusted for baseline NIHSS score, mRS score before stroke, cerebral collateral blood-flow status, time from stroke onset to randomisation reported.
EQ-5D, EuroQol-5 Dimension; eTICI, expanded thrombolysis in cerebral infarction grading system; ICH, intracranial haemorrhage; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale Score; SNI, significant neurological improvement; TM, thrombus migration.

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Contributors Contributors ZT, AX, WC formulated the study concept. LZ, HL, HQ, MG, BY, PY YZ, HS, YZ, BH, HS, HH, CL and WC performed the experiments. LZ, and ZT analysed the data and interpreted the results. LX and YD assisted in the revision of the manuscript. ZT, LZ, and AX wrote the paper. AX and JL accepts full responsibility for the work and the conduct of the study as the guarantor, had access to the data, and controlled the decision to publish.

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