Current status of aspiration thrombectomy for acute stroke patients in China: data from ANGEL-ACT Registry

Xu Tong (ID), Yilong Wang, Clayton T. Bauer, Baixue Jia, Xuelei Zhang, Xiaochuan Huo, Gang Luo, Anxin Wang, Ning Ma, Feng Gao, Dapeng Mo (ID), Ligang Song, Xuan Sun, Lian Liu, Yiming Deng, Xiaoqing Li, Bo Wang, Gaoting Ma, Yongjun Wang, Zeguang Ren and Zhongrong Miao, on behalf of ANGEL-ACT study group

Abstract

Background and Aims: Although noninferior to stent retriever (SR) as first-line approach for endovascular treatment (EVT) of acute large vessel occlusion (LVO) stroke, little is known about the current status of direct aspiration (DA) as first-line thrombectomy in China. This analysis of a prospective, nationwide registry (ANGEL-ACT) aimed to investigate the prevalence and comparative effectiveness of DA-first thrombectomy in a real-world practice in China.

Methods: All patients receiving thrombectomy were screened from a prospective cohort of LVO patients undergoing EVT at 111 hospitals in China between November 2017 and March 2019, and divided into two groups based upon which type of thrombectomy was attempted first ("DA-first" and "SR-first"). The following outcome measures were compared using logistic regression models with adjustment: successful recanalization after first-device alone and all procedures, use of rescue treatment, intracranial hemorrhage (ICH) within 24 h, and modified Rankin Scale (mRS) score at 90 days.

Results: A total of 1225 patients, 102 (8.3%) in DA-first group and 1123 (91.7%) in SR-first group, were included. Patients receiving DA-first had less often successful recanalization after first-device alone [30.4 *versus* 66.4%; odds ratio (OR) = 0.23, 95% confidence interval (CI) = 0.15–0.37], more frequent rescue treatment (62.8 *versus* 27.0%; OR = 4.55, 95% CI = 2.92–7.08) and ICH (35.4 *versus* 22.1%; OR = 1.78, 95% CI = 1.12–2.83) than those receiving SR-first; however, no significant difference was found in successful recanalization after all procedures (84.3 *versus* 90.3%; *p* = 0.18) and 90-day mRS (median: 3 *versus* 3 points; *p* = 0.90) between both groups.

Conclusion: This real-world registry suggested that DA-first thrombectomy for acute stroke patients lagged behind in China during the study period. Far fewer DA-first than SR-first thrombectomies were performed, and DA-first was associated with lower first-device recanalization, more frequently requiring rescue treatment, and increased ICH risk.

Clinical Trial Registration: ClinicalTrials.gov, NCT03370939.

Keywords: stroke, thrombectomy, aspiration, stent retriever, China

Correspondence to:
Zhongrong Miao
Department of Interventional Neuroradiology, Beijing Tiantan Hospital, Capital Medical University, No.119 South 4th Ring West Road, Fengtai District, Beijing, 100070, China
zhongrongm@163.com

Zeguang Ren
Department of Neurosurgery, University of South Florida, 2 Tampa General Circle, Tampa, FL 33606, USA
renzem@gmail.com

**Xu Tong
Baixue Jia
Xuelei Zhang
Xiaochuan Huo
Gang Luo
Ning Ma
Feng Gao
Dapeng Mo
Ligang Song
Xuan Sun
Lian Liu
Yiming Deng
Xiaoqing Li
Bo Wang
Gaoting Ma**
Department of Interventional Neuroradiology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Yilong Wang
Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Clayton T. Bauer
Department of Neurosurgery, University of South Florida, Tampa, FL, USA

**Anxin Wang
Yongjun Wang**
China National Clinical Research Center for Neurological Diseases, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Introduction

In the era of mechanical thrombectomy, there are two main modalities used to treat acute ischemic strokes with large vessel occlusion (LVO): direct aspiration (DA) and stent retriever (SR).[1] The angiographic and clinical outcomes of either DA

or SR as first-line thrombectomy have been reported to be similar in two recent randomized clinical trials.[2,3] Thus, DA as first-line thrombectomy is recommended by the 2019 updated guidelines as noninferior to SR first-line thrombectomy for appropriate patients with acute LVO.[4] DA thrombectomy techniques are being increasingly used in clinical practice in many developed countries,[5–7] and based on some observational data, potential advantages of DA first-line approach might include less injury to the vessel wall, earlier puncture-to-reperfusion and a lower cost compared with SR first-line thrombectomy.[3,5,6,8,9] However, the current status of DA as first-line approach in developing countries such as China are still rarely reported at present.

The current study utilized a prospective, nationwide registry to explore the prevalence and comparative effectiveness of DA-first thrombectomy in a real-world practice setting in China.

Methods

Study population

Data were derived from the ANGEL-ACT registry, a prospective nationwide registry of 1793 consecutive patients with acute LVO undergoing endovascular treatment (EVT) at 111 hospitals from 26 provinces in China between November 2017 and March 2019. Patients who met the following inclusion criteria were enrolled in the registry: (1) age ⩾18 years; (2) diagnosis of acute ischemic stroke caused by imaging-confirmed intracranial LVO, including internal carotid artery, middle cerebral artery (M1/M2), anterior cerebral artery (A1/A2), vertebral artery, basilar artery, and posterior cerebral artery (P1); (3) initiation of any type of EVT, including mechanical thrombectomy, intra-arterial thrombolysis, balloon angioplasty, stenting, and other mechanical fragmentation. The ANGEL-ACT registry aimed to reflect the current status of EVT for patients with acute LVO in real-world clinical practice in China. The protocol was approved by the ethics committees of Beijing Tiantan Hospital and each participating site. Each participant or his/her representative gave written informed consent before being enrolled in the study.

In this analysis, patients receiving thrombectomy with DA as first-line thrombectomy or SR as first-line thrombectomy were divided into two groups ("DA-first" and "SR-first", respectively). DA thrombectomy was performed with a distal access catheter [Navien 058/072 (Medtronic), Sofia/Sofia plus (Microvention), or Catalyst 5/6 (Stryker)] or Penumbra ACE60 reperfusion catheter (Penumbra). SR thrombectomy was performed by using a Solitaire FR (Medtronic), Trevo (Stryker), Revive (Cordis) or Reco (Jiangsu Nico) device. After failure of the first-line thrombectomy approach, the choice of devices for rescue treatment was left to the discretion of the operator.

Data collection

All variables, including demographic characteristics, vascular risk factors, vital signs, stroke severity [e.g. National Institutes of Health Stroke Scale (NIHSS)], laboratory tests, neurovascular images, endovascular procedural details, peri-procedural management and complications, functional outcome [e.g. modified Rankin Scale (mRS)] and adverse events within 90 days after the procedure, were prospectively collected. Only investigators trained and qualified to use NIHSS and mRS recorded the scores.

Baseline computed tomography (CT)/magnetic resonance (MR) and CT angiography (CTA)/MR angiography (MRA), digital subtraction angiography (DSA), and post-procedural CT were evaluated by an imaging core laboratory blinded to clinical data and outcomes. Follow-up CTs were performed immediately and 24 ± 2 h after the procedure, and an additional CT was obtained at any time of neurological deterioration. All images were independently assessed by two neuroradiologists, with a third available for adjudication when needed. Core laboratory image interpretation included early ischemic changes using Alberta Stroke Program Early CT Score (ASPECTS)[10] for anterior circulation strokes and posterior circulation ASPECTS (pc-ASPECTS)[11] for posterior circulation strokes, occlusion site, tandem lesions, underlying intracranial atherosclerotic disease (ICAD, defined as fixed stenosis degree >70% or >50% with distal blood flow impairment or evidence of repeated re-occlusion),[12] baseline and post-procedural modified Thrombolysis in Cerebral Infarction (mTICI),[13] and occurrence of intracranial hemorrhage (ICH) on post-treatment imaging. For patients of whom the images could not be obtained and intra-procedural complications found on DSA (e.g. distal

or new territorial embolization, arterial perforation, arterial dissection and vasospasm requiring treatment, etc.), site-reported data were used. The imaging review criteria of local investigators were the same as that of core laboratory, except that ICAD could also be determined according to previous images indicating stenotic lesion at the occlusion site.

Outcome measurement

The primary outcome was the successful recanalization (mTICI of 2b-3) of the occluded intracranial artery after first-device alone. The secondary outcomes included the complete recanalization (mTICI of 3) of the occluded intracranial artery after first-device alone, successful and complete recanalization after first-pass, number of passes, use of rescue treatment (switching to other thrombectomy devices/intra-arterial thrombolysis/balloon angioplasty/stenting), successful and complete recanalization after all procedures, procedure duration, 90-day mRS as an ordinal score, and mRS of 0–1, 0–2, 0–3 as dichotomous variables. The mRS score was assessed by trained investigators who were blinded to the baseline information *via* the telephone interview based on a standardized interview protocol. The safety outcomes included the distal or new territorial embolization during procedure, any ICH and symptomatic ICH within 24h according to the Heidelberg Bleeding Classification,[14] and death within 90 days.

Statistical analysis

All data were presented as the median (interquartile range [IQR]) for continuous and ordinal variables, and a number (percentage) for categorical variables. A comparison of the baseline characteristics between the two groups was performed using the Mann–Whitney *U* test for continuous and ordinal variables, and Pearson's chi-square test or Fisher's exact test for categorical variables. For comparing the outcome measures, the adjusted odds ratios (OR), common OR or β-coefficients with their 95% confidence intervals (CI) were analyzed using a binary or ordinal logistic regression model or generalized linear model, if applicable. All baseline variables with a significant difference of $p < 0.05$ as potential confounders were adjusted. In addition to conventional multivariable analysis, a propensity score was constructed for adjustment (the propensity

score was derived using a logistic regression model that included all baseline variables for first-line treatment options). Treatment effect modification on the primary outcome was explored in the following subgroups: occlusion site (internal carotid artery *versus* middle cerebral artery M1 segment *versus* vertebra-basilar artery), tandem lesions (yes *versus* no), ICAD (yes *versus* no), stroke subtype by Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria (large artery atherosclerosis *versus* cardioembolism *versus* other or unknown etiology),[15] and prior intravenous thrombolysis (yes *versus* no). Treatment effect size heterogeneity across the subgroups was tested by including the corresponding multiplicative interaction term into the logistic regression model with adjustment for the propensity score. All analyses were conducted with SAS software version 9.4 (SAS Institute Inc, Cary, NC). A two-sided *p*-value of <0.05 was considered to be statistically significant.

Results

A total of 1225 eligible patients were analyzed in this study. A flow chart of the patient selection is shown in Figure 1. Among the included patients, 755 (63.3%) were male, and the median age was 65 years (IQR: 55–73). The median baseline NIHSS score and onset-to-puncture time were 17 points (IQR: 13–22) and 301 min (IQR: 212–439). Successful recanalization at the final angiogram was achieved in 1100 patients (89.8%). Symptomatic ICH within 24h occurred in 89 (7.6%) out of 1164 patients. Of 1167 patients who attended a 90-day follow-up, the median mRS score was 3 points (IQR: 0–5), and the rate of the mRS 0–1, 0–2, 0–3, and death was 39.4%, 43.4%, 53.9%, and 16.8%, respectively.

Baseline characteristics

Of the 1225 patients included, 102 (8.3%) received DA-first, and 1123 (91.7%) received SR-first. The baseline characteristics are compared in Table 1. Patients of the DA-first group had higher rates of internal carotid artery occlusion (50.0% *versus* 23.4%), tandem lesions (35.3% *versus* 14.5%), cardioembolism (48.0% *versus* 35.4%), and prior intravenous thrombolysis (44.1% *versus* 25.9%) than those of the SR-first group (all *p*-values < 0.05). No significant differences existed between the two groups in the remaining baseline variables.
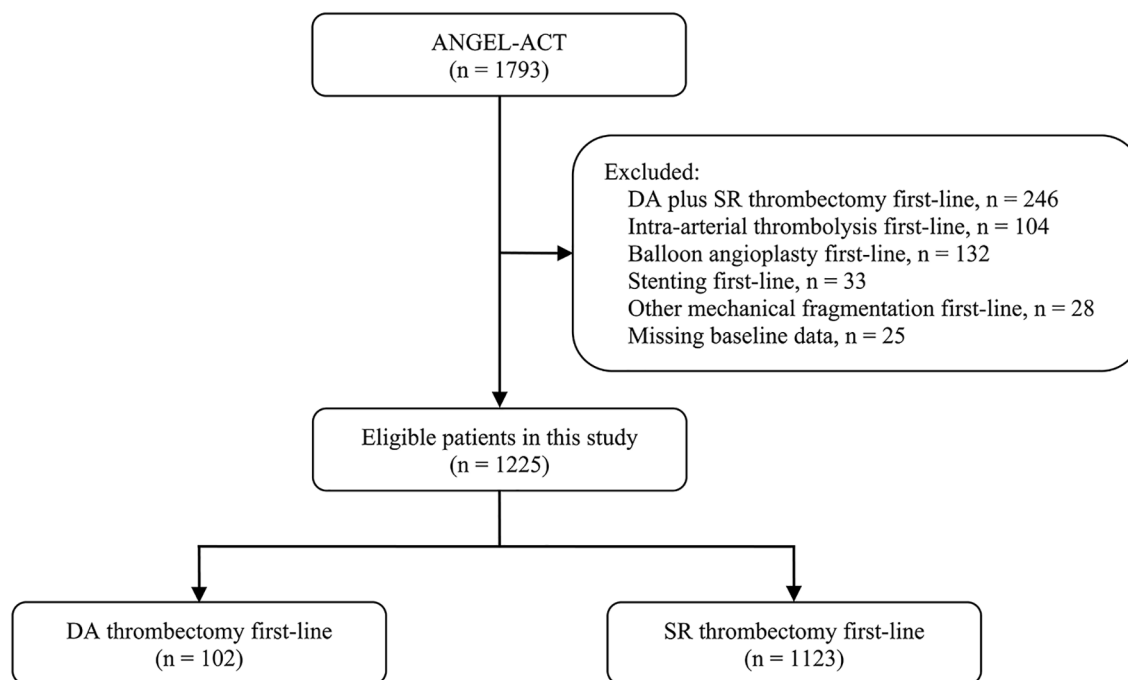
Figure 1. Flow chart of patient selection.
DA, direct aspiration; SR, stent retriever.

Outcome measures

A comparison of the outcome measures is presented in Table 2. Regarding the primary outcome, a multivariable analysis with adjustment for potential confounders showed that patients in the DA-first group had a lower rate of successful recanalization after first-device alone (30.4% *versus* 66.4%; OR = 0.23, 95% CI = 0.15–0.37; $p < 0.01$) compared with those in the SR-first group.

Regarding the secondary and safety outcomes, multivariable analyses demonstrated that patients who underwent DA-first had a lower chance of complete recanalization after first-device alone (24.5% *versus* 51.8%; OR = 0.33, 95% CI = 0.20–0.53; $p < 0.01$), more thrombectomy passes (median: 2 *versus* 1; β = 0.79, 95% CI = 0.53–1.05; $p < 0.01$), higher likelihood of rescue treatment (62.8% *versus* 27.0%; OR = 4.55, 95% CI = 2.92–7.08; $p < 0.01$), switching to other thrombectomy devices (56.9% *versus* 4.0%; OR = 27.67, 95% CI = 16.28–47.01; $p < 0.01$), and any ICH within 24h (35.4% *versus* 22.1%; OR = 1.78, 95% CI = 1.12–2.83; $p = 0.02$) than those who underwent SR-first. No significant differences were found between both groups in the remaining secondary and safety outcome measures.

As a sensitivity analysis, similar results were observed in the models with propensity score adjusted (Table 2).

Subgroup analysis

As shown in Figure 2, exploratory subgroup analyses showed significant heterogeneity in treatment effects on the primary outcome among the studied subgroups stratified by occlusion site, underlying ICAD, and TOAST subtype (p for interactions < 0.05); however, similar treatment effect sizes on the primary outcome were seen in the studied subgroups stratified by tandem lesions, and prior intravenous thrombolysis (p for interactions > 0.20).

Discussion

The major findings of this study were (1) the number of patients undergoing DA-first thrombectomy for acute LVO in China was far less than that of SR-first approach during the study period (ratio of DA-first to SR-first was approximately 1:11); (2) DA-first thrombectomy was associated with lower recanalization after first-device alone, more thrombectomy passes and requiring rescue treatment (specifically

Table 1. Baseline characteristics of patients undergoing thrombectomy with DA first-line *versus* SR first-line.

Baseline variable	DA first-line (*n* = 102)	SR first-line (*n* = 1123)	*p*-Value
Age, median (IQR), years	65 (54–74)	65 (55–73)	0.61
Male sex	63 (61.8)	712 (63.4)	0.74
History of hypertension	56 (54.9)	633 (56.4)	0.78
History of diabetes mellitus	21 (20.6)	194 (17.3)	0.40
History of dyslipidemia	10 (9.8)	98 (8.7)	0.71
History of coronary heart disease	17 (16.7)	175 (15.6)	0.77
History of atrial fibrillation	39 (38.2)	381 (33.9)	0.38
Prior stroke	20 (19.6)	234 (20.8)	0.77
Cigarette smoking			0.61
Never smoker	64 (62.8)	706 (62.9)	
Ex-smoker	9 (8.8)	72 (6.4)	
Current smoker	29 (28.4)	345 (30.7)	
Systolic blood pressure, median (IQR), mmHg	148 (135–160)	145 (130–161)	0.63
NIHSS score, median (IQR)	16 (12–19)	17 (13–22)	0.17
ASPECTS, median (IQR)[a]	9 (7–10)	9 (7–10)	0.21
Occlusion site			<0.01
Internal carotid artery	51 (50.0)	263 (23.4)	
Middle cerebral artery (M1)	34 (33.3)	510 (45.4)	
Vertebro-basilar artery	15 (14.7)	224 (20.0)	
Other intracranial arteries	2 (2.0)	126 (11.2)	
Tandem lesions	36 (35.3)	163 (14.5)	<0.01
Underlying ICAD			0.12
Yes	21 (20.6)	333 (29.7)	
No	66 (64.7)	666 (59.3)	
Undetermined	15 (14.7)	124 (11.0)	
Stroke subtype by TOAST criteria			0.02
Large artery atherosclerosis	33 (32.4)	506 (45.1)	
Cardioembolism	49 (48.0)	397 (35.4)	
Other or unknown etiology	20 (19.6)	220 (19.6)	
Prior use of antiplatelet agents	16 (15.7)	170 (15.1)	0.88

(Continued)

Table 1. (Continued)

Baseline variable	DA first-line (*n* = 102)	SR first-line (*n* = 1123)	*p*-Value
Prior use of anticoagulants	7 (6.9)	51 (4.5)	0.32
Prior intravenous thrombolysis	45 (44.1)	291 (25.9)	<0.01
Intra-procedural use of heparin	43 (42.2)	574 (51.1)	0.08
Type of anesthesia			0.11
Local anesthesia only	35 (34.3)	477 (42.5)	
Local anesthesia plus sedation	14 (13.7)	183 (16.3)	
General anesthesia	53 (52.0)	463 (41.2)	
Onset-to-puncture time, median (IQR), min	318 (210–425)	300 (212–440)	0.97

Values are numbers with percentages in parentheses, unless indicated otherwise.
aASPECTS for anterior circulation stroke; and pc-ASPECTS for posterior circulation stroke.
ASPECTS, Alberta stroke program early CT score; DA, direct aspiration; ICAD, intracranial atherosclerotic disease; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation Alberta stroke program early CT score; SR, stent retriever; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

switching to other thrombectomy devices), and increased risk of any ICH within 24h; (3) DA-first and SR-first modalities showed no significant difference in terms of the final recanalization rate after rescue treatment and 90-day functional outcomes; and (4) significant heterogeneity in the treatment effects on the first-device successful recanalization was found in the subgroups stratified by occlusion site, ICAD, and TOAST subtype.

The development of DA-first thrombectomy in China is much behind what one might expect compared with the published literature in the Western world. Five randomized trials have established thrombectomy as the standard of care for appropriate patients with LVO, and these trials predominantly used SR devices to do a thrombectomy.[16] As a result, established stroke guidelines in 2015 specifically recommend the use of SR to the exclusion of other thrombectomy techniques.[17] Since then, SR first-line thrombectomy has flourished and gained popularity in China, which has in turn limited the application of DA-first thrombectomy.

One of the notable findings from our study is that the DA-first group achieved a lower recanalization without the help of rescue treatment than the SR-first group after adjustment for potential confounders and propensity scores. In the real-practice setting, a failure of the first-line modality

to achieve satisfactory recanalization is not a rare instance. In such patients with LVO who were refractory to first-line modality, rescue treatment was often required. Because successful recanalization is one of the most important factors in achieving a favorable outcome,[18] it seems a reasonable strategy that rescue treatment is performed after the first-line modality failure rather than aborting further treatment. Various types of rescue treatment were used in this study. Switching to other thrombectomy devices was significantly higher in DA-first, while intra-arterial thrombolysis, balloon angioplasty, and permanent stenting were comparable in both. This seems to indicate that the causes of recanalization failure might differ between DA-first and SR-first. Specifically, SR was used as a rescue treatment in more than half of DA-first cases whereas DA was needed as rescue treatment in only 4% of SR-first cases. These data suggest that the performance of a DA-first approach was not as successful as a SR-first approach in the current study population. However, in light of the literature in total, it is unlikely that a DA-first approach has inherent technical disadvantages in clot retrieval. One possible explanation could be the experience and preference of the operators. These two thrombectomy modalities are quite different in the mechanisms of action and procedural details, and the experience and preference of operators may be the major determinant in the

Table 2. Outcome measures of patients undergoing thrombectomy with DA first-line *versus* SR first-line.

Outcome variable	DA first-line	SR first-line	Unadjusted model		Adjusted model 1[a]		Adjusted model 2[b]	
			Effect size (95% CI)	*p*-Value	Effect size (95% CI)	*p*-Value	Effect size (95% CI)	*p*-Value
Primary outcome								
Successful recanalization after first-device alone[f]	31/102 (30.4)	746/1123 (66.4)	0.22 (0.14–0.34)[c]	<0.01	0.23 (0.15–0.37)[c]	<0.01	0.24 (0.15–0.37)[c]	<0.01
Secondary outcomes								
Complete recanalization after first-device alone[g]	25/102 (24.5)	582/1123 (51.8)	0.30 (0.19–0.48)[c]	<0.01	0.33 (0.20–0.53)[c]	<0.01	0.31 (0.19–0.51)[c]	<0.01
Successful recanalization after first-pass[f]	29/102 (28.4)	404/1123 (36.0)	0.71 (0.45–1.11)[c]	0.13	0.82 (0.52–1.29)[c]	0.39	0.83 (0.52–1.31)[c]	0.42
Complete recanalization after first-pass[g]	24/102 (23.5)	325/1123 (28.9)	0.76 (0.47–1.22)[c]	0.25	0.84 (0.51–1.37)[c]	0.48	0.83 (0.51–1.37)[c]	0.47
Number of passes, median (IQR)	2 (1–4)	1 (1–2)	0.94 (0.68–1.20)[d]	<0.01	0.79 (0.53–1.05)[d]	<0.01	0.74 (0.48–1.01)[d]	<0.01
Use of rescue treatment	64/102 (62.8)	303/1123 (27.0)	4.56 (3.00–6.95)[c]	<0.01	4.55 (2.92–7.08)[c]	<0.01	4.51 (2.90–7.02)[c]	<0.01
Switching to other thrombectomy devices	58/102 (56.9)	45/1123 (4.0)	31.58 (19.30–51.67)[c]	<0.01	27.67 (16.28–47.01)[c]	<0.01	25.41 (15.18–42.53)[c]	<0.01
Intra-arterial thrombolysis	2/102 (2.0)	20/1123 (1.8)	1.10 (0.25–4.79)[c]	0.90	0.95 (0.21–4.37)[c]	0.95	1.15 (0.25–5.30)[c]	0.86
Balloon angioplasty	12/102 (11.8)	167/1123 (14.9)	0.76 (0.41–1.43)[c]	0.40	0.81 (0.42–1.55)[c]	0.53	0.88 (0.46–1.68)[c]	0.70
Stenting	11/102 (10.8)	158/1123 (14.1)	0.74 (0.39–1.41)[c]	0.36	0.79 (0.40–1.54)[c]	0.48	0.81 (0.41–1.58)[c]	0.54
Successful recanalization after all procedures[f]	86/102 (84.3)	1014/1123 (90.3)	0.58 (0.33–1.02)[c]	0.06	0.67 (0.37–1.21)[c]	0.18	0.74 (0.40–1.35)[c]	0.33
Complete recanalization after all procedures[g]	70/102 (68.6)	777/1123 (69.2)	0.97 (0.63–1.51)[c]	0.91	1.07 (0.68–1.68)[c]	0.77	1.02 (0.65–1.61)[c]	0.92
Procedure duration, median (IQR), min	84 (50–150)	80 (50–123)	6.81 (−5.30 to 18.91)[d]	0.27	4.39 (−8.02 to 16.81)[d]	0.49	4.30 (−8.32 to 16.91)[d]	0.50
mRS at 90d, median (IQR)	3 (0–5)	3 (0–5)	0.94 (0.65–1.36)[e]	0.73	1.03 (0.70–1.50)[e]	0.90	0.99 (0.67–1.44)[e]	0.94
mRS 0–1 at 90d	37/95 (39.0)	423/1072 (39.5)	0.98 (0.64–1.51)[c]	0.92	1.11 (0.71–1.73)[c]	0.65	1.02 (0.66–1.59)[c]	0.93

(Continued)

Table 2. (Continued)

Outcome variable	DA first-line	SR first-line	Unadjusted model		Adjusted model 1[a]		Adjusted model 2[b]	
			Effect size (95% CI)	p-Value	Effect size (95% CI)	p-Value	Effect size (95% CI)	p-Value
mRS 0–2 at 90d	40/95 (42.1)	467/1072 (43.6)	0.94 (0.62–1.44)[c]	0.78	1.03 (0.67–1.60)[c]	0.88	0.96 (0.62–1.49)[c]	0.86
mRS 0–3 at 90d	46/95 (48.4)	583/1072 (54.4)	0.79 (0.52–1.20)[c]	0.26	0.85 (0.55–1.31)[c]	0.45	0.81 (0.53–1.25)[c]	0.34
Safety outcomes								
Intra-procedural embolization	6/102 (5.9)	61/1123 (5.4)	1.09 (0.46–2.58)[c]	0.85	0.79 (0.32–1.94)[c]	0.61	0.68 (0.27–1.73)[c]	0.42
Any ICH within 24h	34/96 (35.4)	237/1074 (22.1)	1.94 (1.24–3.01)[c]	<0.01	1.78 (1.12–2.83)[c]	0.02	1.69 (1.06–2.69)[c]	0.03
Symptomatic ICH within 24h[h]	13/96 (13.54)	76/1068 (7.1)	2.05 (1.09–3.84)[c]	0.03	1.65 (0.84–3.26)[c]	0.15	1.51 (0.77–2.96)[c]	0.23
Death within 90d	15/95 (15.8)	181/1072 (16.9)	0.92 (0.52–1.64)[c]	0.78	0.82 (0.45–1.51)[c]	0.53	0.82 (0.45–1.48)[c]	0.51

Data are shown as the event number/total number (%), unless otherwise indicated.
[a]Adjusted for the baseline variables with a significant difference of $p < 0.05$ between both groups, including occlusion site, tandem lesions, TOAST subtype, intravenous thrombolysis.
[b]Adjusted for the propensity score.
[c]The OR values were calculated using a binary logistic regression model.
[d]The β-coefficients were calculated using a generalized linear model.
[e]The common OR values were calculated using an ordinal logistic regression model and indicated the odds of improvement of 1 point on the mRS at 90 days.
[f]Defined as mTICI of 2b–3.
[g]Defined as mTICI of 3.
[h]According to the Heidelberg Bleeding Classification.
CI, confidence interval; DA, direct aspiration; ICH, intracranial hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; OR, odds ratio; SR, stent retriever; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.
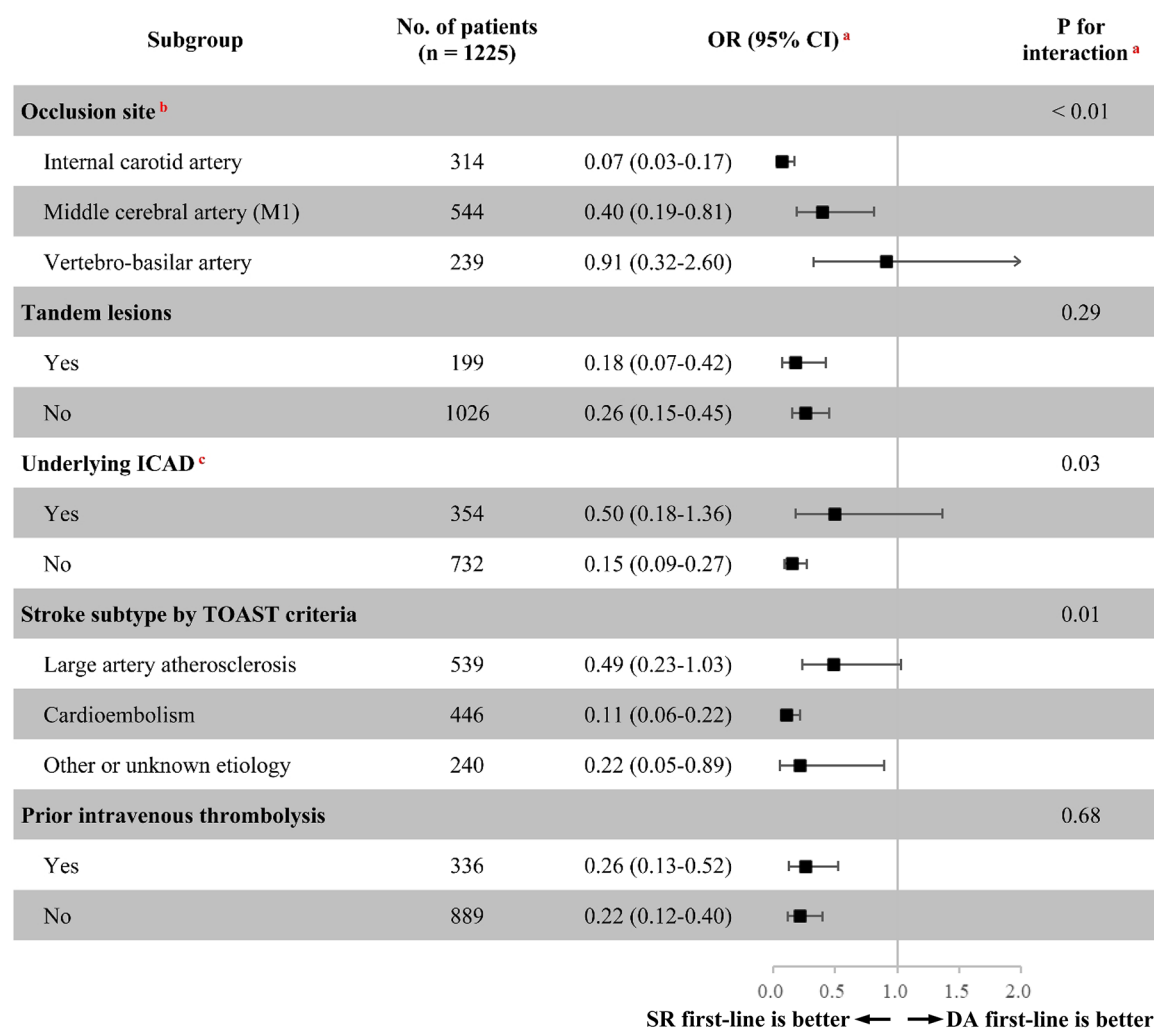
Subgroup	No. of patients (n = 1225)	OR (95% CI) [a]		P for interaction [a]
Occlusion site [b]				< 0.01
Internal carotid artery	314	0.07 (0.03-0.17)		
Middle cerebral artery (M1)	544	0.40 (0.19-0.81)		
Vertebro-basilar artery	239	0.91 (0.32-2.60)		
Tandem lesions				0.29
Yes	199	0.18 (0.07-0.42)		
No	1026	0.26 (0.15-0.45)		
Underlying ICAD [c]				0.03
Yes	354	0.50 (0.18-1.36)		
No	732	0.15 (0.09-0.27)		
Stroke subtype by TOAST criteria				0.01
Large artery atherosclerosis	539	0.49 (0.23-1.03)		
Cardioembolism	446	0.11 (0.06-0.22)		
Other or unknown etiology	240	0.22 (0.05-0.89)		
Prior intravenous thrombolysis				0.68
Yes	336	0.26 (0.13-0.52)		
No	889	0.22 (0.12-0.40)		

0.0   0.5   1.0   1.5   2.0

SR first-line is better ◄── ──► DA first-line is better

Figure 2. Treatment effects on the primary outcome according to exploratory subgroups.
[a]Adjusted for the propensity score.
[b]A total of 128 patients with other intracranial artery occlusions were excluded.
[c]A total of 139 patients with undetermined ICAD were excluded.
CI, confidence interval; DA, direct aspiration; ICAD, intracranial atherosclerotic disease; OR, odds ratio; SR, stent retriever; TOAST, Trial of ORG 10172 in Acute Stroke Treatment.

successful angiographic outcome, rather than differences in the thrombectomy devices themselves. During the study period, DA thrombectomy was only routinely performed in a few hospitals in China, and the annual volume of DA-first in these hospitals was very small. Accordingly, the annual volume of DA-first per operator would be even smaller, so most operators would likely have limited hands-on experience with DA thrombectomy. In this analysis, the operator's inexperience in DA may also be reflected in the fact that more thrombectomy passes and higher ICH rate were seen in the DA-first group than in the SR-first group.

The causes of recanalization failure may be various, including occlusion site, tandem lesions, preexisting ICAD, TOAST subtype, and added value of intravenous thrombolysis.[19] An exploratory subgroup analysis to investigate the difference in the causes of recanalization failure between DA-first and SR-first was completed. We found that DA-first was far less effective than SR-first in terms of first-device successful

recanalization for anterior circulation LVO as compared with posterior circulation LVO, possibly due to the different anatomical characteristics (tortuous access, vessel curvature or angulation), constituent ratio of stroke causes (ICAD or embolism), and proportion of thrombus components (hard or soft thrombi, red blood cell-rich or fibrin-rich clots) between anterior and posterior circulation.[20–22] We also found that the performance of DA-first was much poorer than SR-first in patients with embolic stroke, which corresponds well with previous studies.[23,24] SR-first thrombectomy may be a better option for acute LVO with susceptibility vessel sign (+) or CT thrombus hyperdense (+) suggesting embolic stroke; however, our unplanned subgroup analysis was unable to draw any definitive conclusions.[25,26] However, when choosing the modality of mechanical thrombectomy, we should comprehensively consider the thrombus burden, occlusion site, and anatomical access in addition to stroke etiology and thrombus component. From our point of view, DA-first thrombectomy may be suitable for the treatment of large-load soft thrombus (such as tandem lesions) and bifurcation occlusion (such as M1 bifurcation and basilar artery tip) with good access. The different causes of recanalization failure and optimizing the strategy of currently available EVT methods should be investigated in further studies.

This study has several inherent limitations that must be acknowledged. First, the results should be interpreted with the caution of selection bias caused by non-randomized treatment assignment, and measured or unmeasured variables (such as the aforementioned experience/preference of the operators) that may represent potential confounders that cannot be ruled out despite multiple adjustment models used. Second, since a relatively small number of patients were enrolled in the DA-first group, there was a possibility of a type II error in the statistical analysis. Third, as this was a retrospective analysis of a prospective registry, the number of passes determining a failure was not predefined, leading to potential heterogeneity in the use of rescue treatment between the two groups. However, the operators who participated in this study were experienced in when to perform rescue treatment. Fourth, thrombectomy for stroke is allowed in qualified tertiary and secondary hospitals in China. In the ANGEL-ACT registry, more than 90% of the patients were from tertiary hospitals, and in fact less DA first-line thrombectomy was done in secondary hospitals, so it is likely that the proportion of using DA-first could be even lower. Finally, we did not collect treatment costs, so it was not possible to compare the cost-effectiveness of the two modalities.

Conclusion

The study population from 111 hospitals across 26 (76.5%) of 34 provinces in China represents the real-world patients who received EVT between November 2017 and March 2019. Therefore, it is worthy of note that the results of this study reflect the current situation of DA as first-line thrombectomy for acute stroke patients in real clinical practice in China, suggesting that DA-first thrombectomy is less developed in China compared with the Western world. Specifically, far fewer DA-first than SR-first thrombectomies were performed during the study period, and DA-first thrombectomy was associated with lower first-device recanalization, more requiring rescue treatment, and increased risk of ICH.

Conflict of interest statement
The authors declare that there is no conflict of interest.

Data sharing
The data that support the findings of this study are available from the corresponding author Zhongrong Miao (zhongrongm@163.com) upon reasonable request.

ORCID iDs
Xu Tong 🔬 https://orcid.org/0000-0002-3277-6941

Dapeng Mo 🔬 https://orcid.org/0000-0002-1558-9626

Supplemental material

Supplemental material for this article is available online.

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