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ORIGINAL RESEARCH

Endovascular Thrombectomy Versus Bridging Thrombolysis: Real-World Efficacy and Safety Analysis Based on a Nationwide Registry Study

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BACKGROUND: It was uncertain if direct endovascular thrombectomy (ET) was superior to bridging thrombolysis (BT) for patients with acute ischemic stroke caused by large-vessel occlusions. We aimed to examine real-world clinical outcomes of ET using nationwide registry data in China and to compare the efficacy and safety between BT and direct ET.

METHODS AND RESULTS: Patients treated with ET from a nationwide registry study in China were included. Rapid neurological improvement, intracranial hemorrhage, and in-hospital mortality were compared between the 2 groups using multivariate logistic models and propensity-score matching analyses. A total of 7674 patients from 592 stroke centers were included. The median onset-to-puncture time, onset-to-door time, and door to puncture time were 290, 170, and 99 minutes, respectively. A total of 2069 (27.0%) patients received BT treatment. Patients in the BT group had a significantly shorter onset-to-puncture time (235 versus 323 minutes; $P<0.001$) and onset-to-door time (90 versus 222 minutes; $P<0.001$) compared with the direct ET group. The prior use of intravenous thrombolysis was associated with a higher rate of rapid neurological improvement (adjusted odds ratio [OR], 0.83; 95% CI, 0.71–0.96) and higher risk of intracranial hemorrhage (adjusted OR, 1.46; 95% CI, 1.18–1.80) in multivariate analyses and propensity-score matching analyses.

CONCLUSIONS: This study reflects the current application of ET in China. More patients received direct ET than BT. Our results suggested that favorable short-term outcomes could be achieved with BT compared with direct ET. Higher risk of intracranial hemorrhage was observed in the BT group.

Key Words: endovascular thrombectomy ■ ischemic stroke ■ outcome ■ thrombolysis

Stroke poses a substantial global challenge, with a growing economic burden and high morbidity, mortality, and disability rates.[1,2] In China, the prevalence, incidence, and mortality of stroke were reported to be 1114.8, 246.8, and 114.8 per 100 000 people/year, respectively, in 2013,[3] and the burden of stroke continues to increase.[4] Multiple clinical trials and meta-analyses have demonstrated the superiority of endovascular thrombectomy (ET) combined with standard medical management, including intravenous thrombolysis (IVT), in treating acute ischemic stroke (AIS) with anterior circulation large-vessel occlusion.[5–10] Because patients included in the clinical trials received IVT as standard treatment unless they had contraindications, current guidelines in many countries recommend offering IVT to eligible patients before ET.[11–13]

However, some studies have shown conflicting results on the additional benefits of bridging thrombolysis

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CLINICAL PERSPECTIVE

What Is New?

- Nationwide real-world data on the clinical application and outcomes of endovascular thrombectomy (ET) in China were provided in the study.
- Comparison of clinical outcomes of patients treated with bridging thrombolysis (BT) and direct ET in daily practice was performed in the study.
- A total of 27.0% patients in the study received BT, and the main reason for patients who received direct ET without intravenous thrombolysis was beyond time window; short-term favorable outcomes in BT-treated patients were achieved compared with direct ET, although a higher risk of intracranial hemorrhage was observed in the BT group.

What Are the Clinical Implications?

- A more efficient stroke management workflow in stroke units in China is indispensable to reduce prehospital delay, which may increase BT rates and improve functional outcomes.
- Our results support present guidelines that patients treated with BT have more favorable outcomes.
- More randomized trials to investigate whether intravenous thrombolysis should be administrated before ET are warranted.

Nonstandard Abbreviations and Acronyms

AIS	acute ischemic stroke
BOSC	Bigdata Observatory Platform for Stroke of China
BT	bridging thrombolysis
CSPPC-DEBATE	China Stroke Prevention Project Committee–Direct Endovascular Thrombectomy and Bridging Thrombolysis
DIRECT-MT	Direct Intraarterial Thrombectomy in Order to Revascularize Acute Ischemic Stroke Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: a Multicenter Randomized Clinical Trial
DPT	door-to-puncture time
ET	endovascular thrombectomy
ICH	intracranial hemorrhage
IVT	intravenous thrombolysis
NIHSS	National Institutes of Health Stroke Scale
OPT	onset-to-puncture time
PSM	propensity-score matching
RNI	rapid neurological improvement
TOAST	Trial of Org 10172 in Acute Stroke Treatment

(BT; which means IVT before ET) compared with direct ET.[10,14–20] IVT may dissolve thrombi before thrombectomy and improve reperfusion[21] but may also prolong the interval from disease onset to puncture, which decreases the recanalization rate[22] and may lead to a higher risk of intracranial hemorrhage (ICH).[10,23] However, these results on comparison of BT and direct ET were mainly based on clinical trials with highly selected patients. Data on clinical outcomes related to ET in real-world settings, and particularly nationwide representative data in East Asia, are lacking. When extending the application of ET to the real world and beyond trial conditions, possible prehospital delays and differences in the level of care provided by healthcare systems may affect the efficacy and safety outcomes.

Therefore, to provide insight into the current application of ET and compare the clinical outcomes between patients treated with BT and direct ET in China, we performed a study based on the CSPPC-DEBATE (China Stroke Prevention Project Committee–Direct Endovascular Thrombectomy and Bridging Thrombolysis) registry.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Design and Population

All data of enrolled patients were from BOSC (Bigdata Observatory Platform for Stroke of China) (http://pro.cnstroke.com), which is an ongoing, multicenter, internet-based registry platform regulated by CSPPC. Detailed descriptions of CSPPC and BOSC were published recently.[24,25] This study was approved by the Ethics Committee of Peking Union Medical College Hospital (No. S-K988), with a waiver of informed consent.

Established in July 2015, CSPPC has constructed a network of stroke centers, providing real-world clinical outcomes of stroke management in China. Until now, high-quality patient-level data of patients with AIS were collected on the basis of BOSC in >700 hospitals at 31 provinces in mainland China, including information about thrombolysis and endovascular treatment. Data quality was monitored by each stroke center, by project offices in each province, and by the national project committee. The CSPPC verified the quantity and quality of data reported by each center and reported the results on the website. Hospitals that fail to pass 3 consecutive inspections are disqualified from reporting data. *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) was applied in confirming the diagnosis of AIS.

For the CSPPC-DEBATE registry, the inclusion criteria were patients ≥18 years of age with a diagnosis of AIS who met the current guideline criteria for ET[13] between January 2018 and August 2019. Patients with incomplete data were excluded, such as cases without puncture records/onset-to-puncture time (OPT)/door-to-puncture time (DPT)/onset-to-needle time, and door-to-needle time for patients who underwent BT. We also excluded patients with OPT/DPT >24 hours or onset-to-needle time/door-to-needle time >4.5 hours, according to current guidelines in China.[26]

Demographic characteristics and procedural data collected in our study included age, sex, body mass index, systolic blood pressure, pulse, TOAST (Trial of Org 10172 in Acute Stroke Treatment), way to hospital, modified Rankin Scale score, National Institutes of Health Stroke Scale (NIHSS) score at admission and 0 hours, 24 hours, and 7 days after ET, OPT, DPT, onset-to-door time, onset-to-recanalization time, door-to-recanalization time, thrombolysis in cerebral infarction grade, ICH, length of hospitalization, and in-hospital mortality. For patients who received BT, additional data about IVT were collected: onset-to-needle time, door-to-needle time, reasons for not receiving IVT, and places for patients receiving IVT. More details are provided in Tables 1 and 2 and Table S1.

Clinical Assessment and Outcomes

Changes in NIHSS scores at different time points were calculated as follows: (NIHSS scores at admission)−(NIHSS scores at 0 hours, 24 hours, and 7 days after ET operation). Rapid neurological improvement (RNI) was defined as a reduction of the NIHSS score ≥8 or an NIHSS score of 0 to 1 at 24 hours after ET, and was regarded as an early indicator of a favorable outcome.[27–29] ICH, including both symptomatic and asymptomatic events after ET during hospitalization, detected by computed tomography, was reported by each center. In-hospital mortality was defined as death after ET during hospitalization for any causes.

Statistical Analysis

Categorical variables are displayed as frequencies and percentages, and Pearson χ^2 tests were used to compare these variables between the BT and direct ET groups. Continuous variables were compared using *t*-tests for normally distributed variables, and are displayed as average±SD. Mann-Whitney tests were used for nonnormal distributions, and data are presented as medians (interquartile ranges [IQRs]).

Using multivariate logistic regression analyses, we examined whether the prior use of IVT was associated with RNI, in-hospital mortality, and ICH rates by calculating the odds ratio (OR) and its 95% CI using binary logistic regression models. Continuous variables were transformed into categorical variables mainly according to clinical experience (eg, systolic blood pressure was classified into 4 groups: ≤89, 90–140, 141–180, and ≥181 mm Hg). We calculated the unadjusted ORs and adjusted ORs with respect to variables that are known to be associated with outcomes, such as age, sex, systolic blood pressure, body mass index, NIHSS score at admission, OPT, and thrombolysis in cerebral infarction grades after ET. Variables that were entered in each logistic model are summarized following each table. In a sensitivity analysis, we ran all multivariate analyses with all continuous variables not transformed into categorical variables.

Propensity-score matching (PSM) was conducted to help reduce the confounding effects of nonrandomized treatment assignment. Same covariates with multivariate logistic regression analyses were included in PSM analyses. The nearest-neighbor algorithm with 1:1 matching and a caliper width of 0.02 was applied. Balance of covariates was evaluated by standardized differences.[30] ORs of efficacy and safety outcomes were calculated. PSM analyses were performed using MatchIt and stddiff packages in R version 3.6.1.

P<0.05 was considered as statistically significant in this study. All analyses, except for PSM, were performed by SPSS version 25.0 (SPSS, Inc, Chicago, IL).

RESULTS

Study Population Characteristics

As shown in Figure 1, a total of 7674 patients from 592 stroke centers, located in 29 provinces in China, who were treated with ET from the BOSC database were included in the final analyses, according to the exclusion criteria. The median age of all patients was 68 (IQR, 58–76) years, and the median NIHSS score at admission was 16 (IQR, 12–21). Of all hospitals included, 97.5% (7477/7672) were tertiary hospitals with a large bed number (>500 beds). In terms of procedural characteristics, 72.9% (5594/7674) of patients received mechanical thrombectomy. The median OPT, onset-to-door time, and DPT were 290 (IQR, 207–389), 170 (IQR, 85–280), and 99 (IQR, 65–150) minutes,

Table 1. Basic Demographics and Hospital Data of Patients Receiving BT and ET, Before and After PSM

Characteristics	Unmatched Patients				PSM Patients*		
	All Patients (N=7674)	BT (N=2069)	Direct ET (N=5605)	*P* Value	BT (N=1539)	Direct ET (N=1539)	*P* Value
Basic demographics							
Age, median (IQR), y	68 (58–76), n=7674	68 (58–76), n=2069	67 (58–75), n=5605	0.04‡	68 (58–76), n=1539	69 (60–76), n=1539	0.47‡
Sex, men	60.0 (4604/7674)	60.0 (1242/2069)	60.0 (3362/5605)	0.97†	59.5 (915/1539)	58.9 (907/1539)	0.77†
Ethnicity, Han	98.5 (7559/7674)	98.0 (2027/2069)	98.7 (5532/5605)	0.02*	98.5 (1516/1539)	98.9 (1522/1539)	0.34†
BMI, median (IQR), kg/m^2	23.67 (21.72–25.61), n=7663	23.44 (21.22–25.71), n=2067	23.81 (21.97–25.54), n=5596	<0.001‡	23.44 (21.22–25.71), n=1539	23.44 (21.64–25.39), n=1539	0.45‡
SBP, median (IQR), mm Hg	145 (130–162), n=7664	147 (131–163), n=2067	145 (130–161), n=5597	0.15‡	146 (131–163), n=1539	146 (130–164), n=1539	0.80‡
DBP, median (IQR), mmHg	84 (75–95), n=7663	84 (75–95), n=2067	83 (75–94), n=5596	0.09‡	85 (75–95), n=1539	83 (75–94), n=1537	0.18‡
Pulse, median (IQR), bpm	78 (70–88), n=7563	78 (70–88), n=2034	78 (70–88), n=5529	0.62‡	78 (70–88), n=1539	146 (130–164), n=1539	0.91‡
TOAST				0.09†			0.05†
Large-artery atherosclerosis	53.5 (4104/7674)	55.2 (1142/2069)	52.8 (2962/5605)		53.5 (824/1539)	48.9 (752/1539)	
Cardioembolism	39.5 (3030/7674)	39.0 (807/2069)	39.7 (2223/5605)		40.7 (627/1539)	46.1 (709/1539)	
Small-artery occlusion	1.6 (126/7674)	1.4 (29/2069)	1.7 (97/5605)		1.0 (15/1539)	1.0 (15/1539)	
Stroke of other determined cause	1.3 (103/7674)	1.0 (21/2069)	1.5 (82/5605)		1.2 (18/1539)	1.2 (19/1539)	
Stroke of undetermined cause	4.0 (311/7674)	3.4 (70/2069)	4.3 (241/5605)		3.6 (55/1539)	2.9 (44/1539)	
Way to hospital				<0.001†			<0.001†
EMS	56.7 (4353/7674)	59.9 (1230/2069)	55.6 (3114/5605)		61.3 (943/1539)	58.8 (905/1539)	
Interhospital transfer	13.7 (1050/7674)	7.0 (144/2069)	16.2 (906/5605)		8.0 (123/1539)	12.5 (192/1539)	
Personal transport	29.6 (2271/7674)	33.1 (686/2069)	28.2 (1585/5605)		30.7 (473/1539)	28.7 (442/1539)	
NIHSS score at admission, median (IQR)	16 (12–21), n=7414	16 (12–20), n=2036	16 (12–21), n=5378	0.001‡	16 (12–20), n=1539	16 (12–20), n=1539	0.53‡
mRS scores at admission				0.09†			0.02†
Median (IQR)	4 (3–5), n=6458	4 (3–5), n=1785	4 (3–5), n=4673		4 (3–5).m=1410	4 (3–5), n=1344	
0	12.6 (814/6458)	15.2 (271/1785)	11.6 (543/4673)		15.5 (218/1539)	13.8 (186/1539)	
1	3.4 (220/6458)	2.6 (46/1785)	3.7 (174/4673)		2.2 (31/1539)	3.7 (50/1539)	
2	5.0 (324/6458)	4.1 (74/1785)	5.3 (250/4673)		4.1 (58/1539)	5.7 (77/1539)	
3	10.3 (667/6458)	9.1 (163/1785)	10.8 (504/4673)		9.3 (131/1539)	8.8 (118/1539)	
4	32.9 (2125/6458)	35.1 (627/1785)	32.1 (1498/4673)		36.0 (508/1539)	32.7 (439/1539)	
5	35.7 (2308/6458)	33.8 (604/1785)	36.5 (1704/4673)		32.9 (464/1539)	35.3 (474/1539)	
Hospital data							
Hospital level				<0.001†			0.02†
Secondary (100–500 beds)	2.5 (195/7672)	4.7 (98/2069)	1.7 (97/5603)		2.9 (44/1539)	1.6 (25/1539)	
Tertiary (>500 beds)	97.5 (7477/7672)	95.3 (1971/2069)	98.3 (5506/5603)		97.1 (1495/1539)	98.4 (1514/1539)	
Hospital region				<0.001†			<0.001†
Northeast	7.9 (609/7674)	7.9 (163/2069)	8.0 (446/5605)		7.9 (121/1539)	8.5 (131/1539)	

(*Continued*)

Table 1. Continued

Characteristics	Unmatched Patients				PSM Patients*		
	All Patients (N=7674)	BT (N=2069)	Direct ET (N=5605)	*P* Value	BT (N=1539)	Direct ET (N=1539)	*P* Value
North	9.8 (749/7674)	12.0 (248/2069)	8.9 (501/5605)		10.9 (167/1539)	6.4 (98/1539)	
East	42.3 (3246/7674)	40.1 (829/2069)	43.1 (2417/5605)		41.0 (631/1539)	46.1 (709/1539)	
Central	13.4 (1025/7674)	13.8 (286/2069)	13.2 (739/5605)		13.9 (214/1539)	12.8 (197/1539)	
South	11.4 (874/7674)	10.1 (210/2069)	11.8 (664/5605)		9.7 (149/1539)	11.7 (180/1539)	
Southwest	11.1 (853/7674)	12.1 (251/2069)	10.7 (602/5605)		13.1 (201/1539)	11.8 (181/1539)	
Northwest	4.1 (318/7674)	4.0 (82/2069)	4.2 (236/5605)		3.6 (45/1539)	2.8 (43/1539)	

Data are given as percentage (number/total), unless otherwise indicated. BMI indicates body mass index; BT, bridging thrombolysis; DBP, diastolic blood pressure; EMS, emergency medical services; ET, endovascular thrombectomy; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PSM, propensity-score matching; SBP, systolic blood pressure; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

*Matched on a propensity score with age, sex, SBP, BMI, pulse, hospital level, way to hospital, region, TOAST, NIHSS score at admission, thrombectomy, onset-to-puncture time, thrombolysis in cerebral infarction grade, and length of hospitalization.

†*P* value was calculated by Pearson χ^2 tests.

‡*P* value was calculated by Mann-Whitney tests.

respectively. A total of 83.6% (5152/7674) patients achieved thrombolysis in cerebral infarction grade 2b/3 after ET, while RNI occurred in 19.1% (1464/7674) of patients. ICH occurred in 9.4% (6956/7674) of patients. The median length of hospitalization was 11 (IQR, 6–16) days, and the in-hospital mortality was 4.7% (358/7674). Basic demographics, hospital data, and procedural characteristics of all patients are displayed in Tables 1 and 2.

In our study, 2069 patients (27.0%) were treated with BT, whereas 5605 patients (73.0%) were treated with direct ET. Beyond the thrombolysis time window (>4.5 hours) was the main reason (44.3%) patients did not receive IVT (Table S1). Characteristics were examined between patients treated with BT and direct ET (Tables 1 and 2), which showed significant differences between the 2 groups. The median OPT and onset-to-door time values were shorter in patients treated with BT (235 [IQR, 180–295] versus 323 [IQR, 225–430] minutes [*P*<0.001]; and 90 [IQR, 55–140] versus 222 [IQR, 120–320] minutes [*P*<0.001], respectively), whereas the median DPT was longer (125 [IQR, 88–181] versus 90 [60–135] minutes; *P*<0.001) compared with the direct ET group. After operation, 82.7% (1343/1623) and 84.0% (3809/4539) of patients achieved thrombolysis in cerebral infarction grade 2b/3 in the BT and direct ET groups, respectively, with no significant difference (*P*=0.34) between both groups. More patients achieved RNI in the BT group (22.0% versus 18.0%; *P*<0.001). Higher ICH rates (10.7% versus 8.8%; *P*=0.01) and longer length of hospitalization (12 [IQR, 7–17] versus 11 [IQR, 6–16] days; *P*<0.001) were observed in patients treated with BT compared with direct ET. No significant difference in in-hospital mortality was observed (5.2% versus 4.5%; *P*=0.16) between the 2 groups.

After PSM, 3078 patients were 1:1 matched in BT and direct ET groups. The distribution of the estimated propensity score of matched patients is shown in Figure S1. Standard differences of all covariates were <20%, representing well-balanced matching results (Figure S2). The OPT values were 231 (IQR, 180–290) and 225 (IQR, 170–300) minutes in BT and direct ET groups, respectively, with *P*=0.17.

Change in NIHSS Scores

Changes in NIHSS scores at 0 hours, 24 hours, and 7 days after operation in all patients and matched patients are shown in Figure 2 and Table S2. Patients receiving BT have a large median NIHSS score improvement compared with direct ET group in all patients and PSM patients, although this was not statistically significant. The percentage of patients with a change in NIHSS score ≥8 at 0 hours, 24 hours, and 7 days was significantly higher in the BT group (11.3%, 23.7%, and 44.3%, respectively) compared with the direct ET group (9.0%, 19.6%, and 41.5%, respectively) in all patients, whereas no statistically significant higher percentages were found in PSM patients.

Efficacy and Safety Outcomes

Results of multivariate analyses in all patients and PSM analyses are presented in Table 3. In multivariate models, BT was associated with higher rates of RNI

Table 2. Procedural Characteristics of Patients Receiving BT and ET, Before and After PSM

Characteristics	Unmatched Patients				PSM Patients*		
	All Patients (N=7674)	BT (N=2069)	Direct ET (N=5605)	*P* Value	BT (N=1539)	Direct ET (N=1539)	*P* Value
Thrombectomy				<0.001†			0.32†
MT	72.9 (5594/7674)	74.0 (1531/2069)	72.5 (4063/5605)		72.4 (1114/1539)	71.5 (1101/1539)	
AT	7.2 (552/7674)	8.7 (181/2069)	6.6 (371/5605)		7.8 (120/1539)	6.8 (105/1539)	
MT+AT	19.9 (1528/7674)	17.3 (357/2069)	20.9 (1171/5605)		19.8 (305/1539)	21.6 (333/1539)	
Time, median (IQR), min							
OPT	290 (207–389), n=7674	235 (180–295), n=2069	323 (225–430), n=5605	<0.001‡	231 (180–290), n=1539	225 (170–300), n=1539	0.17‡
DPT	99 (65–150), n=7674	125 (88–181), n=2069	90 (60–135), n=5605	<0.001‡	120 (85–175), n=1539	80 (55–113), n=1539	<0.001‡
ODT	170 (85–280), n=7674	90 (55–140), n=2069	222 (120–320), n=5605	<0.001‡	95 (59–142), n=1539	134 (75–210), n=1539	<0.001‡
DRT	222 (142–350), n=5055	229 (160–314), n=1312	220 (136–374), n=3743	0.58‡	227 (157–315), n=1273	182 (120–280), n=1290	<0.001‡
ORT	402 (290–583), n=5055	322 (246–425), n=1312	440 (317–655), n=3743	<0.001‡	327 (250–427), n=1243	330 (245–430), n=1270	0.763
TICI grade				0.34†			0.70†
0	4.9 (304/6164)	4.8 (79/1625)	4.9 (225/4539)		4.7 (73/1539)	5.0 (77/1539)	
1	3.4 (211/6164)	4.0 (65/1625)	3.2 (146/4539)		4.1 (63/1539)	3.2 (49/1539)	
2a	8.1 (497/6164)	8.5 (138/1625)	7.9 (359/4539)		8.4 (130/1539)	8.0 (123/1539)	
2b	25.3 (1560/7674)	25.2 (409/1625)	25.4 (1151/4539)		25.1 (387/1539)	25.3 (390/1539)	
3	58.3 (3592/7674)	57.5 (934/1625)	58.6 (2658/4539)		57.6 (886/1539)	58.5 (900/1539)	
RNI	19.1 (1464/7674)	22.0 (456/2069)	18.0 (1008/5605)	<0.001†	24.7 (380/1539)	21.4 (329/1539)	0.03†
ICH	9.4 (6956/7674)	10.7 (222/2069)	8.8 (496/5605)	0.01†	10.7 (164/1539)	7.0 (107/1539)	<0.001†
LOH, median (IQR), d	11 (6–16), n=7674	12 (7–17)	11 (6–16), n=5605	<0.001‡	11 (7–17), n=1539	12 (7–17), n=1539	0.90‡
In-hospital mortality	4.7 (358/7674)	5.2 (108/2069)	4.5 (250/5605)	0.16†	4.6 (71/1539)	5.1 (79/1539)	0.50†
NIHSS score after ET, median (IQR)	15 (10–20), n=5903	14 (10–20), n=1662	15 (10–20), n=4241	0.07‡	14 (10–19), n=1285	14 (9–19), n=1234	0.28‡
NIHSS score, 24 h after ET, median (IQR)	13 (7–20), n=6541	12 (6–19), n=1811	13 (7–20), n=4730	0.06‡	12 (6–18), n=1415	12 (6–18), n=1372	0.75‡
NIHSS score, 7 d after ET, median (IQR)	8 (3–15), n=5936	8 (3–15), n=1625	8 (3–15), n=4311	0.01‡	7 (3–14), n=1286	8 (3–14), n=1270	0.44‡

Data are given as percentage (number/total), unless otherwise indicated. AT indicates aspiration thrombectomy; BT, bridging thrombolysis; DPT, door-to-puncture time; DRT, door-to-recanalization time; ET, endovascular thrombectomy; ICH, intracranial hemorrhage; IQR, interquartile range; LOH, length of hospitalization; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; ODT, onset-to-door time; OPT, onset-to-puncture time; ORT, onset-to-recanalization time; PSM, propensity-score matching; RNI, rapid neurological improvement; and TICI, thrombolysis in cerebral infarction.

*Matched on a propensity score with age, sex, systolic blood pressure, body mass index, pulse, hospital level, way to hospital, region, Trial of Org 10172 in Acute Stroke Treatment, NIHSS score at admission, thrombectomy, OPT, TICI grade, and LOH.

†*P* value was calculated by Pearson χ^2 tests.

‡*P* value was calculated by Mann-Whitney tests.

(adjusted OR, 0.83; 95% CI, 0.71–0.96; *P*=0.01) and a higher risk of ICH (adjusted OR, 1.46; 95% CI, 1.18–1.80; *P*<0.001), but not with in-hospital mortality after adjusting for covariates. Other predictors for RNI, ICH, and in-hospital mortality are presented in Tables S3 through S5. When we did not transform continuous variables into categorical variables, the results were essentially the same (Table S6).

Similar results were yielded in PSM analyses. BT was associated with a higher ratio of RNI (OR, 0.83; 95% CI, 0.70–0.98) and a higher risk of ICH (OR, 1.62; 95% CI, 1.24–2.06), but not with in-hospital mortality.

DISCUSSION

Our study provides nationwide real-world data on the clinical application and outcomes of ET in Chinese patients with AIS. Our study included 7674 patients from 592 stroke centers located in 29 provinces in China. In summary, high recanalization rates and low

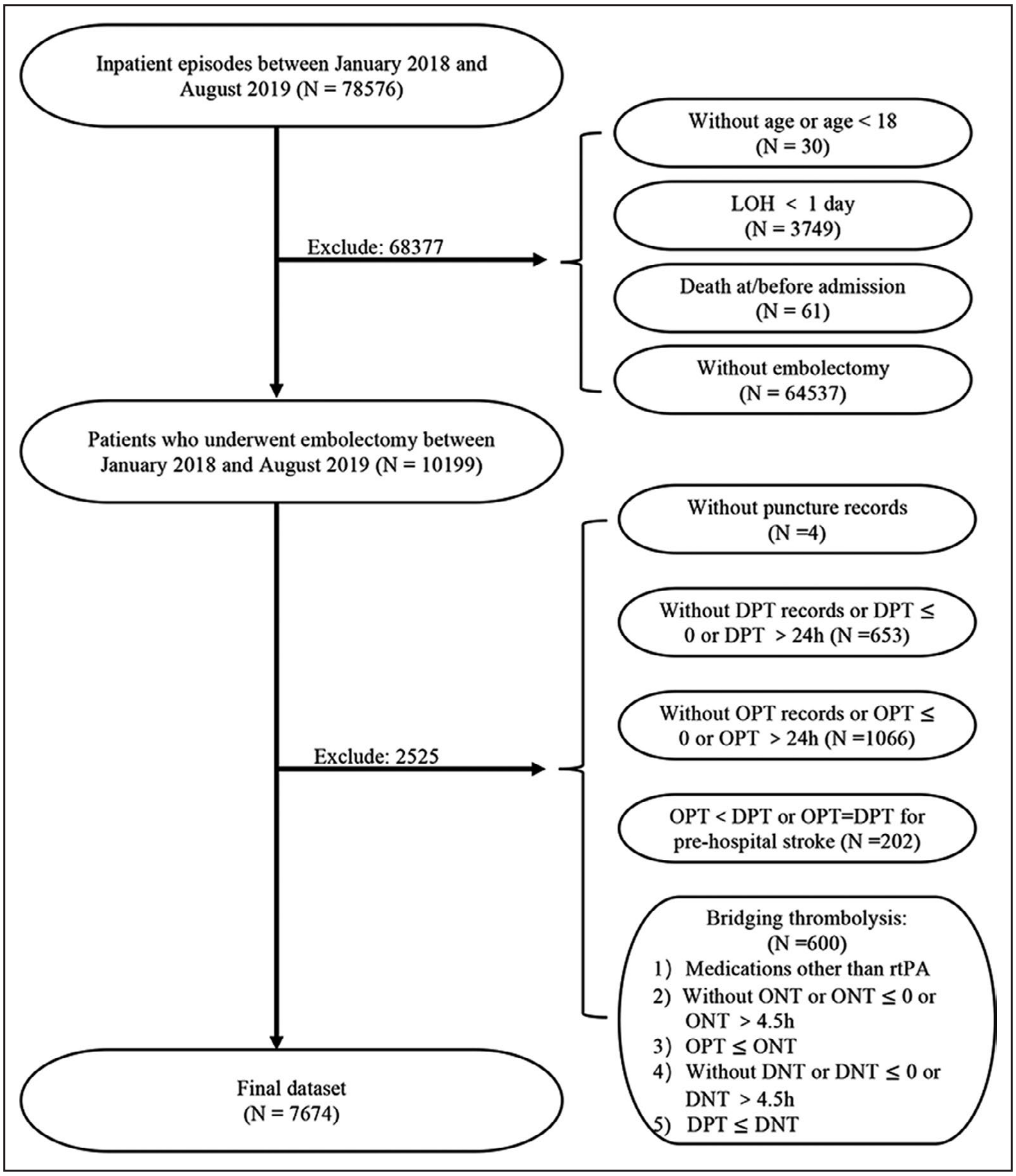

Figure 1. Inclusion criteria of the final data set.
DNT indicates door-to-needle time; DPT, door-to-puncture time; LOH, length of hospitalization; ONT, onset-to-needle time; OPT, onset-to-puncture time; and rtPA, recombinant tissue-type plasminogen activator.

in-hospital mortality were achieved and suggest good management of ET in Chinese stroke units. However, the median OPT and DPT found in our study were longer than those reported in other countries and clinical trials.[5–9,31,32] The relatively long procedural time revealed by our study showed that the prehospital and emergency response to stroke in China still requires optimization. A more efficient workflow in stroke units will lead to improvements in the functional outcomes of patients[33,34] and should be one of the crucial goals in everyday clinical practice.

Of all patients treated with ET, 27.0% of patients had received IVT before thrombectomy, which was similar to the percentage reported in the United States (30.0%),[35] but lower than that of Germany (55.8%),[31] Czech Republic (76%),[32] and Korea (80%).[36] The main reason for patients not receiving IVT in our study was attributable to patients surpassing the time window (44.3%), which was higher than that of a previous study.[14,17] This was not surprising considering the relatively long OPT and onset-to-door time of the included patients. Oral anticoagulation agents or international normalized ratio >1.7 was another important contraindication for IVT,[14,17] yet we did not specify this information in our database, which was a limitation of our study. The relatively longer delay in DPT (35 minutes)

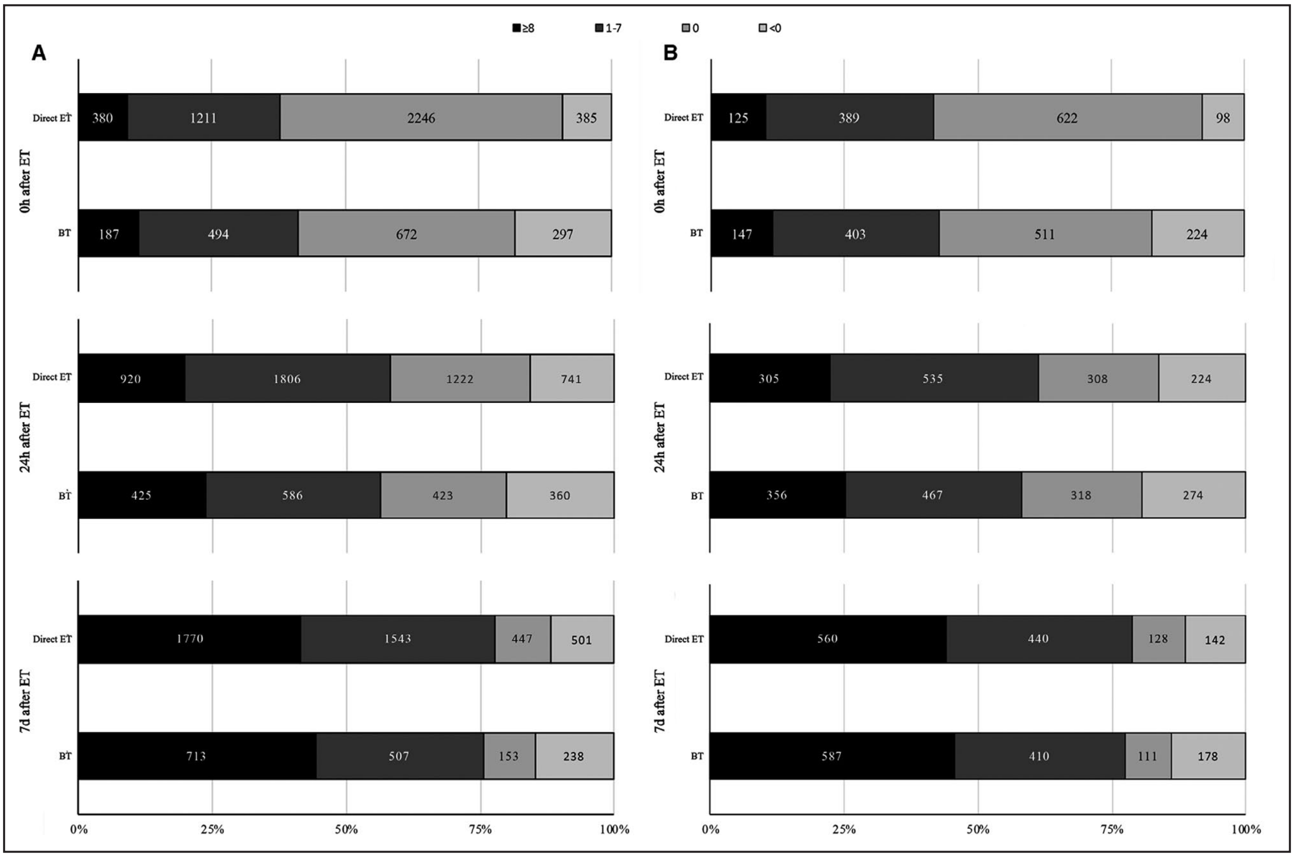

Figure 2. Distribution of change of National Institutes of Health Stroke Scale (NIHSS) scores at 0 h, 24 h, and 7 days in patients receiving bridging thrombolysis (BT) and endovascular thrombectomy (ET), before (A) and after (B) propensity-score matching.
Change of NIHSS scores was divided into 4 groups: scores of ≥8, 1–7, 0, and <0 at 0 h, 24 h, and 7 days.

in the BT group was reported in our clinical practice, which was not observed in highly controlled clinical trials[7,17,20,23] and was longer than the delay reported in a previous observational study.[37] The delay may have occurred as a result of informed consent being required before administration of IVT in China, which results in a relatively long counseling time with patients and their relatives.

Changes in the NIHSS scores at 0 hours, 24 hours, and 7 days showed consecutive functional

Table 3. Multivariate Analyses and Propensity-Matched Analyses About Outcomes Associated With BT and ET

	Multivariate Analyses			Propensity-Matched Analyses†	
Outcome Variables*	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
RNI (reference: direct ET)	0.78 (0.69–0.98)	0.84 (0.72–0.98)‡	0.01	0.83 (0.70–0.98)	0.03
ICH (reference: direct ET)	1.24 (1.05–1.46)	1.45 (1.18–1.79)§	<0.001	1.60 (1.24–2.06)	<0.001
In-hospital mortality (reference: direct ET)	1.18 (0.94–1.49)	0.99 (0.73–1.34)‡	0.99	0.89 (0.64–1.24)	0.50

BT indicates bridging thrombolysis; ET, endovascular thrombectomy; ICH, intracranial hemorrhage; OR, odds ratio; and RNI, rapid neurological improvement.
*Value assignment: "1" for "no RNI," "ICH," and "in-hospital mortality," respectively.
†Matched on a propensity score with age, sex, systolic blood pressure, body mass index, pulse, hospital level, way to hospital, region, Trial of Org 10172 in Acute Stroke Treatment, National Institutes of Health Stroke Scale score at admission, thrombectomy, onset-to-puncture time, thrombolysis in cerebral infarction grade, and length of hospitalization.
‡Adjusted for age, sex, ethnicity, systolic blood pressure, pulse, body mass index, hospital level, way to hospital, region, Trial of Org 10172 in Acute Stroke Treatment, National Institutes of Health Stroke Scale score at admission, thrombectomy, onset-to-puncture time, thrombolysis in cerebral infarction grade, length of hospitalization, and ICH.
§Adjusted for age, sex, ethnicity, systolic blood pressure, pulse, body mass index, hospital level, way to hospital, region, Trial of Org 10172 in Acute Stroke Treatment, National Institutes of Health Stroke Scale score at admission, thrombectomy, onset-to-puncture time, thrombolysis in cerebral infarction grade, and length of hospitalization.

improvement in patients who received ET. Patients treated with BT were more likely to have improvements based on our results, but no significant results were found in PSM analyses. In addition, the RNI, which reflects early and dramatic neurological improvement, has been shown to be a marker of excellent long-term functional outcomes (ie, modified Rankin Scale score of 0–2 at 90 days) in patients treated with IVT or ET.[28,29] In multivariate logistic models, significantly higher rates of RNI were associated with the administration of IVT before ET in clinical practice in China, which supports similar results in previous matched studies and meta-analyses[10,14,16] and is consistent with current guidelines.[11,12,26] Furthermore, because the treatment assignment was nonrandom in our study and OPT was significantly longer in direct ET group, we conducted PSM analyses to help decrease the confounding effects of covariates. The results in PSM analyses further supported the potential benefit of IVT before ET with regard to short-term outcomes.

In addition, although the application of IVT before ET would not significantly increase in-hospital mortality, it is associated with a higher risk of ICH in all patients and in patients after PSM. A previous study also found higher rates of asymptomatic ICH in patients receiving BT.[18] Besides, the prior use of IVT before ET may also result in longer length of hospitalization (ie, more medical costs and lower quality of life). Therefore, balancing the potential benefits and risks of prior use of IVT is vital when making real-world clinical decisions.

Our study had several limitations. First, because our study used an internet-based national registry, the results of this study should be evaluated critically compared with prospective clinical controlled trials. The assignment of treatment in our study was nonrandom, and OPT was statistically longer in direct ET group than BT group, serving as confounding factors. However, we have performed PSM analyses to minimize the effects of confounding covariates, including OPT time, and thus to ensure the reliability of these results. In addition, the risk profiles of stroke, medical histories, and intracranial occlusion locations were not collected in BOSC, and thus could not be analyzed in our study. Therefore, the relationship between those factors and clinical outcomes was lacking in our study. The exact time of ICH occurrence was not included. Moreover, the included patients were only followed up for 7 days after the operation; thus, we could not assess the modified Rankin Scale scores and mortality at 90 days, and only evaluated the short-term functional outcomes in the study.

The latest published DIRECT-MT (Direct Intraarterial Thrombectomy in Order to Revascularize Acute Ischemic Stroke Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: a Multicenter Randomized Clinical Trial) (ClinicalTrials.gov No. NCT03469206)[20] showed that direct ET alone was noninferior to BT (ET combined with alteplase) with regard to modified Rankin Scale scores at 90 days in Chinese patients eligible for both ET and IVT. Yet, randomized controlled trials may have sufficient external validity.[38] For example, the administration of IVT resulted in a 35-minute delay in real-world clinical practice before puncture compared with just 5 minutes in a DIRECT-MT trial, which indicated more alteplase infused in real-world practice. Still, more clinical trials and real-world studies are warranted.

CONCLUSIONS

In conclusion, this study reflects the current situation of ET in clinical practice in China. Because of the relatively longer delay in prehospital management, most patients received direct ET rather than BT, highlighting the need for more efficient workflows in everyday clinical practice. Our study suggested that short-term favorable outcomes in BT-treated patients could be achieved compared with direct ET, although a higher risk of ICH was observed in the BT group. Therefore, further randomized control studies in multiple populations are warranted.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S6
Figures S1–S2

REFERENCES

1. Dhamoon MS, Moon YP, Paik MC, Sacco RL, Elkind MS. Trajectory of functional decline before and after ischemic stroke: the northern Manhattan study. *Stroke*. 2012;43:2180–2184. DOI: 10.1161/STROKEAHA.112.658922.
2. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C, et al. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. *Circulation*. 2017;135:e146–e603.
3. Wang W, Jiang B, Sun H, Ru X, Sun D, Wang L, Wang L, Jiang Y, Li Y, Wang Y, et al. Prevalence, incidence, and mortality of stroke in China. *Circulation*. 2017;135:759–771. DOI: 10.1161/CIRCULATIONAHA.116.025250.
4. Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, Sandercock P, Wang Y, Huang Y, Cui L, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol*. 2019;18:394–405.
5. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. DOI: 10.1056/NEJMoa1411587.
6. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, Yan B, Dowling RJ, Parsons MW, Oxley TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. DOI: 10.1056/NEJMoa1414792.
7. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, Roy D, Jovin TG, Willinsky RA, Sapkota BL, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019–1030. DOI: 10.1056/NEJMoa1414905.
8. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, San Roman L, Serena J, Abilleira S, Ribo M, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. DOI: 10.1056/NEJMoa1503780.
9. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, Albers GW, Cognard C, Cohen DJ, Hacke W, et al. Stent-retriever thrombectomy after intravenous t-pa vs. T-pa alone in stroke. *N Engl J Med*. 2015;372:2285–2295. DOI: 10.1056/NEJMoa1415061.
10. Mistry EA, Mistry AM, Nakawah MO, Chitale RV, James RF, Volpi JJ, Fusco MR. Mechanical thrombectomy outcomes with and without intravenous thrombolysis in stroke patients: a meta-analysis. *Stroke*. 2017;48:2450–2456. DOI: 10.1161/STROKEAHA.117.017320.
11. Fiehler J, Cognard C, Gallitelli M, Jansen O, Kobayashi A, Mattle HP, Muir KW, Mazighi M, Schaller K, Schellinger PD. European recommendations on organisation of interventional care in acute stroke (EROICAS). *Eur Stroke J*. 2016;1:155–170. DOI: 10.1177/2396987316659033.
12. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, Johnston KC, Johnston SC, Khalessi AA, Kidwell CS, et al. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2015;46:3020–3035. DOI: 10.1161/STR.0000000000000074.
13. Peng B, Wu B. Chinese guidelines for diagnosis and treatment for acute ischemic stroke 2018 (in Chinese). *Chin J Neurol*. 2018;51:666–682.
14. Gamba M, Gilberti N, Premi E, Costa A, Frigerio M, Mardighian D, Vergani V, Spezi R, Delrio I, Morotti A, et al. Intravenous fibrinolysis plus endovascular thrombectomy versus direct endovascular thrombectomy for anterior circulation acute ischemic stroke: clinical and infarct volume results. *BMC Neurol*. 2019;19:103. DOI: 10.1186/s12883-019-1341-3.
15. Fan L, Zang L, Liu X, Wang J, Qiu J, Wang Y. Outcomes of mechanical thrombectomy with pre-intravenous thrombolysis: a systematic review and meta-analysis. *J Neurol*. 2020. DOI: 10.1007/s00415-020-09778-4.
16. Katsanos AH, Malhotra K, Goyal N, Arthur A, Schellinger PD, Kohrmann M, Krogias C, Turc G, Magoufis G, Leys D, et al. Intravenous thrombolysis prior to mechanical thrombectomy in large vessel occlusions. *Ann Neurol*. 2019;86:395–406. DOI: 10.1002/ana.25544.
17. Coutinho JM, Liebeskind DS, Slater LA, Nogueira RG, Clark W, Davalos A, Bonafe A, Jahan R, Fischer U, Gralla J, et al. Combined intravenous thrombolysis and thrombectomy vs thrombectomy alone for acute ischemic stroke: a pooled analysis of the swift and star studies. *JAMA Neurol*. 2017;74:268–274. DOI: 10.1001/jamaneurol.2016.5374.
18. Broeg-Morvay A, Mordasini P, Bernasconi C, Buhlmann M, Pult F, Arnold M, Schroth G, Jung S, Mattle HP, Gralla J, et al. Direct mechanical intervention versus combined intravenous and mechanical intervention in large artery anterior circulation stroke: a matched-pairs analysis. *Stroke*. 2016;47:1037–1044. DOI: 10.1161/STROKEAHA.115.011134.
19. Bellwald S, Weber R, Dobrocky T, Nordmeyer H, Jung S, Hadisurya J, Mordasini P, Mono ML, Stracke CP, Sarikaya H, et al. Direct mechanical intervention versus bridging therapy in stroke patients eligible for intravenous thrombolysis: a pooled analysis of 2 registries. *Stroke*. 2017;48:3282–3288. DOI: 10.1161/STROKEAHA.117.018459.
20. Yang P, Zhang Y, Zhang L, Zhang Y, Treurniet KM, Chen W, Peng Y, Han H, Wang J, Wang S, et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. *N Engl J Med*. 2020;382:1981–1993. DOI: 10.1056/NEJMoa2001123.
21. Desilles JP, Loyau S, Syvannarath V, Gonzalez-Valcarcel J, Cantier M, Louedec L, Lapergue B, Amarenco P, Ajzenberg N, Jandrot-Perrus M, et al. Alteplase reduces downstream microvascular thrombosis and improves the benefit of large artery recanalization in stroke. *Stroke*. 2015;46:3241–3248. DOI: 10.1161/STROKEAHA.115.010721.
22. Menon BK, Almekhlafi MA, Pereira VM, Gralla J, Bonafe A, Davalos A, Chapot R, Goyal M. Optimal workflow and process-based performance measures for endovascular therapy in acute ischemic stroke: analysis of the solitaire FR thrombectomy for acute revascularization study. *Stroke*. 2014;45:2024–2029. DOI: 10.1161/STROKEAHA.114.005050.
23. Leker RR, Pikis S, Gomori JM, Cohen JE. Is bridging necessary? A pilot study of bridging versus primary stentriever-based endovascular reperfusion in large anterior circulation strokes. *J Stroke Cerebrovasc Dis*. 2015;24:1163–1167. DOI: 10.1016/j.jstrokecerebrovasdis.2015.01.008.
24. Shen Y, Chao BH, Cao L, Tu WJ, Wang LD. Stroke center care and outcome: results from the csppc stroke program. *Transl Stroke Res*. 2019;11:377–386. DOI: 10.1007/s12975-019-00727-6.
25. Chao BH, Yan F, Hua Y, Liu JM, Yang Y, Ji XM, Peng B, Zhao GG, Wang YJ, Kang DZ, et al. Stroke prevention and control system in China: CSPPC-stroke program. *Int J Stroke*. 2020;1747493020913557. DOI: 10.1177/1747493020913557.
26. Wang G, Fang B, Yu X, Li Z. Interpretation of 2018 guidelines for the early management of patients with acute ischemic stroke. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2018;30:289–295.
27. Brown DL, Johnston KC, Wagner DP, Haley EC Jr. Predicting major neurological improvement with intravenous recombinant tissue plasminogen activator treatment of stroke. *Stroke*. 2004;35:147–150. DOI: 10.1161/01.STR.0000105396.93273.72.
28. Heit JJ, Mlynash M, Kemp SM, Lansberg MG, Christensen S, Marks MP, Ortega-Gutierrez S, Albers GW. Rapid neurologic improvement predicts favorable outcome 90 days after thrombectomy in the defuse 3 study. *Stroke*. 2019;50:1172–1177. DOI: 10.1161/STROKEAHA.119.024928.
29. Saposnik G, Di Legge S, Webster F, Hachinski V. Predictors of major neurologic improvement after thrombolysis in acute stroke. *Neurology*. 2005;65:1169–1174. DOI: 10.1212/01.wnl.0000180687.75907.4b.
30. Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. *J Thorac Cardiovasc Surg*. 2007;134:1128–1135. DOI: 10.1016/j.jtcvs.2007.07.021.
31. Wollenweber FA, Tiedt S, Alegiani A, Alber B, Bangard C, Berrouschot J, Bode FJ, Boeckh-Behrens T, Bohner G, Bormann A, et al. Functional outcome following stroke thrombectomy in clinical practice. *Stroke*. 2019;50:2500–2506. DOI: 10.1161/STROKEAHA.119.026005.
32. Volny O, Krajina A, Belaskova S, Bar M, Cimflova P, Herzig R, Sanak D, Tomek A, Köcher M, Rocek M, et al. Mechanical thrombectomy performs similarly in real world practice: a 2016 nationwide study from the Czech Republic. *J NeuroIntervent Surg*. 2018;10:741–745. DOI: 10.1136/neurintsurg-2017-013534.
33. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, Campbell BC, Nogueira RG, Demchuk AM, Tomasello A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288. DOI: 10.1001/jama.2016.13647.
34. Ribo M, Molina CA, Cobo E, Cerda N, Tomasello A, Quesada H, De Miquel MA, Millan M, Castano C, Urra X, et al. Association between time to reperfusion and outcome is primarily driven by the time from

imaging to reperfusion. *Stroke*. 2016;47:999–1004. DOI: 10.1161/STROKEAHA.115.011721.
35. Stein LK, Tuhrim S, Fifi J, Mocco J, Dhamoon MS. Interhospital transfers for endovascular therapy for acute ischemic stroke. *Stroke*. 2019;50:1789–1796. DOI: 10.1161/STROKEAHA.119.024869.
36. Seo KD, Suh SH. Endovascular treatment in acute ischemic stroke: a nationwide survey in Korea. *Neurointervention*. 2018;13:84–89. DOI: 10.5469/neuroint.2018.01053.
37. Chalos V, LeCouffe NE, Uyttenboogaart M, Lingsma HF, Mulder M, Venema E, Treurniet KM, Eshghi O, van der Worp HB, van der Lugt A, et al. Endovascular treatment with or without prior intravenous alteplase for acute ischemic stroke. *J Am Heart Assoc*. 2019;8:e011592. DOI: 10.1161/JAHA.118.011592.
38. Rothwell PM. External validity of randomised controlled trials: "To whom do the results of this trial apply?" *Lancet*. 2005;365:82–93. DOI: 10.1016/S0140-6736(04)17670-8.

Supplemental Material

Table S1. Characteristics about IVT procedures.

Characteristics	BT N = 2069	Direct ET N = 5605
Time, median (IQR), min		
ONT	142 (100-190), n = 2069	/
DNT	40 (30-59), n = 2069	/
Reasons for not receiving IVT		
Beyond time-window	/	44.3 (2481/5605)
Contraindications	/	11.2 (630/5605)
Refusion by patients	/	10.5 (590/5605)
Others	/	31.6 (1769/5605)
Places for patients receiving IVT		
Ambulance	2.5 (52/2069)	/
Emergency room	48.2 (998/2069)	/
CT room	8.6 (177/2069)	/
Wards	39.9 (825/2069)	/
Other hospitals	0.8 (17/2069)	/

BT, bridging thrombolysis; ET, endovascular thrombectomy; ONT, onset to needle time; DNT, door to needle time

Table S2. Change of NIHSS scores at 0h, 24h and 7d after ET of patients receiving bridging thrombolysis and endovascular thrombectomy, before and after propensity-score matching.

	Unmatched patients			**Matched patients**		
Change of NIHSS	**BT N = 2069**	**Direct ET N = 5605**	**P value**	**BT N = 1539**	**Direct ET N=1539**	**P value**
0h						
Median (IQR)	0 (0-3), n = 1650	0 (0-3), n = 4222	0.24‡	0 (0-4), n =1285	0 (0-3), n = 1234	0.05‡
Different groups			**< 0.001†**			**< 0.001†**
≥8	11.3 (187/1650)	9.0 (380/4222)	**0.01†**	11.4 (147/1285)	10.1 (125/1234)	0.32†
1-7	29.9 (494/1650)	28.7 (1211/ 4222)		31.4 (403/1285)	31.5 (389/1234)	
0	40.7 (672/1650)	53.2 (2246/4222)		39.8 (511/1285)	50.4 (622/1234)	
<0	18.0 (297/1650)	9.1 (385/ 4222)		17.4 (224/1285)	7.9 (98/1234)	
24h						
Median (IQR)	2 (0-7), n = 1794	2 (0-6), n = 4689	0.67‡	2 (0-8), n = 1415	2 (0-7), n = 1372	0.37‡
Different groups			**< 0.001†**			**0.004†**
≥8	23.7 (425/1794)	19.6 (920/4689)	**< 0.001†**	25.2 (356/1415)	22.2 (305/1372)	0.07†
1-7	32.7 (586/1796)	38.5 (1806/4689)		33.0 (467/1415)	39.0 (535/1372)	
0	23.6 (423/1796)	26.1 (1222/4689)		22.5 (318/1415)	22.4 (308/1372)	
<0	20.1 (360/1796)	15.8 (741/4689)		19.4 (274/1415)	16.3 (224/1372)	
7d						
Median (IQR)	6 (1-12), n = 1611	6 (1-10), n = 4261	0.27‡	7 (1-12), n = 1286	6 (2-11), n = 1270	0.41‡
Different groups			**< 0.001†**			0.08†
≥8	44.3 (713/1611)	41.5 (1770/4261)	**0.04†**	45.6 (587/1286)	44.1 (560/1270)	0.47†
1-7	31.5 (507/1611)	36.2 (1543/4261)		31.9 (410/1286)	34.6 (440/1270)	
0	9.5 (153/1611)	10.5 (447/4261)		8.6 (111/1286)	10.1 (128/1270)	
<0	14.8 (238/1611)	11.8 (501/4261)		13.8 (178/1286)	11.2 (142/1270)	

*Change of NIHSS were calculated as (NIHSS scores at admission) – (NIHSS scores at 0h, 24h and 7d)

† p value was calculated by Pearson χ^2 tests

‡ p value was calculated by Mann-Whitney tests

BT, bridging thrombolysis; ET, endovascular thrombectomy; IQR, interquartile range

Table S3. Multivariate logistic analyses about factors associated with RNI.

	Adjusted OR	Lower limit	Upper limit	p value
Age (ref: ≤45)				**< 0.001**
46-65	1.543	1.173	2.030	**0.002**
65-85	1.816	1.378	2.391	**< 0.001**
≥86	2.104	1.348	3.283	**0.001**
Sex (ref: female)	1.102	0.958	1.267	0.174
Ethnicity (Ref: Han)	0.869	0.386	1.553	0.635
SBP (ref: 90-140)				**< 0.001**
≤89	4.610	0.583	36.461	0.148
141-180	1.304	1.137	1.496	**< 0.001**
≥181	1.857	1.384	2.492	**< 0.001**
Pulse (ref: 60-100)				0.069
≤59	1.044	0.781	1.394	0.772
≥101	1.314	1.042	1.658	**0.021**
BMI (ref: 18.5)				0.176
⩽18.4	0.814	0.580	1.142	0.234
24-27.9	1.124	0.972	1.299	0.115
⩾28	0.969	0.756	1.242	0.803
Hospital level (ref: tertiary hospital)	0.498	0.327	0.758	**0.001**
Way to hospital (ref: EMS)				**< 0.001**
Interhospital transfer	1.515	1.226	1.873	**< 0.001**
Personal transport	1.144	0.981	1.335	0.087
Region (ref: Northeast)				**0.001**
North	1.255	0.908	1.734	0.169
East	1.091	0.850	1.400	0.494
Central	1.553	1.151	2.096	**0.004**
South	1.703	1.228	2.344	**0.001**
Southwest	1.135	0.841	1.532	0.407
Northwest	1.530	0.989	2.366	0.056
TOAST (ref: large artery atherosclerosis)				0.003
Cardio-embolism	0.762	0.660	0.879	**< 0.001**
Small artery occlusion	0.748	0.389	1.437	0.383
Stroke of other determined cause	0.619	0.371	1.032	0.066
Stroke of undetermined cause	0.807	0.575	1.132	0.214
NIHSS at admission (ref: 0-4)				**< 0.001**
5-15	2.472	1.718	3.559	**< 0.001**
16-20	1.721	1.187	2.494	**0.004**
21-42	1.278	0.881	1.852	0.196
Bridging thrombolysis (ref: ET)	0.840	0.721	0.978	**0.025**
Thrombectomy (ref: MT)				**0.001**
AT	0.892	0.690	1.155	0.386

MT+AT	1.336	1.131	1.577	**0.001**
OPT (ref: ≤6h)	1.586	1.346	1.869	**< 0.001**
TICI grade (ref: 2b/3)	2.831	2.248	3.566	**< 0.001**
LOH (ref: ≤11d)	1.254	1.098	1.432	**0.001**
ICH (ref: no ICH)	4.183	2.944	5.944	**< 0.001**

RNI, rapid neurological improvement; SBP, systolic blood pressure; BMI, body mass index; EMS, emergency medical services; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institutes of Health Stroke Scale; ET, endovascular thrombectomy; MT, mechanical thrombectomy; AT, Aspiration thrombectomy; OPT, onset to puncture; TICI, thrombolysis in Cerebral Infarction; LOH, length of hospitalization; ICH, intracranial hemorrhage; ref, reference

Table S4. Multivariate logistic analyses about factors associated with ICH.

	Adjusted OR	Lower limit	Upper limit	p value
Age (ref: ≤45)				0.640
46-65	0.953	0.625	1.453	0.823
65-85	1.087	0.715	1.653	0.697
⩾86	1.114	0.607	2.046	0.728
Sex (ref: female)	1.111	0.920	1.341	0.276
Ethnicity (Ref: Han)	0.579	0.250	1.470	0.250
SBP (ref: 90-140)				0.842
⩽89	0.827	0.107	6.414	0.856
141-180	1.041	0.859	1.261	0.684
⩾181	1.164	0.829	1.635	0.380
BMI (ref: 18.5-23.9)				0.169
⩽18.4	0.562	0.319	0.989	**0.046**
24-27.9	0.940	0.770	1.147	0.540
⩾28	1.115	0.807	1.541	0.51
Pulse (ref: 60-100)				0.055
⩽59	1.519	1.076	2.146	**0.018**
⩾101	1.096	0.824	1.457	0.528
Hospital level (ref: tertiary hospital)	1.228	0.659	2.288	0.518
Way to hospital (ref: EMS)				0.267
Interhospital transfer	1.125	0.867	1.461	0.375
Personal transport	0.884	0.711	1.099	0.267
Region (ref: Northeast)				**0.001**
North	0.745	0.481	1.154	0.188
East	0.661	0.474	0.920	**0.014**
Central	0.729	0.494	1.074	0.110
South	0.921	0.618	1.371	0.684
Southwest	0.672	0.448	1.010	0.056
Northwest	1.474	0.924	2.352	0.103
TOAST (ref: large artery atherosclerosis)				**0.011**
Cardio-embolism	1.358	1.116	1.653	**0.002**
Small artery occlusion	0.494	0.152	1.606	0.241
Stroke of other determined cause	0.993	0.421	2.343	0.987
Stroke of undetermined cause	1.526	0.977	2.369	0.063
NIHSS at admission (ref: 0-4)				**< 0.001**
5-15	2.043	0.886	4.712	0.094
16-20	3.295	1.425	7.619	**0.005**
21-42	2.824	1.217	6.5555	**0.016**
Bridging thrombolysis (ref: ET)	1.452	1.178	1.791	**< 0.001**
Thrombectomy (ref: MT)				0.468

AT	0.907	0.629	1.306	0.598
MT+AT	0.871	0.693	1.096	0.239
OPT (ref: ≤6h)	1.186	0.960	1.465	0.113
TICI grade (ref: 2b/3)	1.497	1.200	1.867	< **0.001**
LOH (ref:≤11d)	0.721	0.599	0.866	< **0.001**

ICH, intracranial hemorrhage; SBP, systolic blood pressure; BMI, body mass index; EMS, emergency medical services; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institutes of Health Stroke Scale; ET, endovascular thrombectomy; MT, mechanical thrombectomy; AT, Aspiration thrombectomy; OPT, onset to puncture; TICI, thrombolysis in Cerebral Infarction; LOH, length of hospitalization; ref, reference

Table S5. Multivariate logistic analyses about factors associated with in-hospital mortality.

	Adjusted OR	Lower limit	Upper limit	p value
Age (ref: ≤45)				0.085
46-65	1.100	0.549	2.205	0.788
65-85	1.512	0.763	2.999	0.236
⩾86	1.957	0.822	4.662	0.129
Sex (ref: female)	0.930	0.712	1.215	0.594
Ethnicity (Ref: Han)	0.293	0.2040	2.163	0.229
SBP (ref: 90-140)				0.510
⩽89	2.451	0.284	21.177	0.415
141-180	1.196	0.909	1.574	0.200
⩾181	1.212	0.765	1.921	0.413
BMI (ref: 18.5-23.9)				0.194
⩽18.4	1.089	0.577	2.055	0.793
24-27.9	0.921	0.692	1.224	0.570
⩾28	1.472	0.965	2.246	0.073
Pulse (ref: 60-100)				0.416
⩽59	0.991	0.559	1.757	0.974
⩾101	1.281	0.886	1.851	0.188
Hospital level (ref: tertiary hospital)	0.186	0.025	1.359	0.097
Way to hospital (ref: EMS)				0.405
Interhospital transfer	0.802	0.538	1.196	0.279
Personal transport	0.856	0.633	1.158	0.313
Region (ref: Northeast)				**< 0.001**
North	0.651	0.385	1.099	0.108
East	0.294	0.196	0.443	**< 0.001**
Central	0.447	0.273	0.732	**0.001**
South	0.611	0.371	1.007	0.053
Southwest	0.561	0.347	0.907	**0.018**
Northwest	0.768	0.417	1.415	0.397
TOAST (ref: large artery atherosclerosis)				0.618
Cardio-embolism	1.199	0.912	1.575	0.193
Small artery occlusion	0.664	0.156	2.829	0.580
Stroke of other determined cause	0.774	0.182	3.298	0.729
Stroke of undetermined cause	0.858	0.401	1.835	0.693
NIHSS at admission (ref: 0-4)				**< 0.001**
5-15	1.210	0.370	3.956	0.753
16-20	2.673	0.821	8.708	0.103
21-42	3.460	1.064	11.252	**0.039**
Bridging thrombolysis (ref: ET)	0.993	0.733	1.344	0.962
Thrombectomy (ref: MT)				0.887
AT	0.981	0.593	1.622	0.940

MT+AT	1.076	0.792	1.461	0.641
OPT (ref: ≤6h)	0.912	0.674	1.234	0.549
TICI grade (ref: 2b/3)	1.513	1.119	2.045	**0.007**
LOH (ref:≤11d)	0.266	0.194	0.363	**< 0.001**
ICH (ref: no ICH)	1.826	1.303	2.559	**< 0.001**

BMI, body mass index; SBP, systolic blood pressure; EMS, emergency medical services; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institutes of Health Stroke Scale; ET, endovascular thrombectomy; MT, mechanical thrombectomy; AT, Aspiration thrombectomy; OPT, onset to puncture; TICI, thrombolysis in Cerebral Infarction; LOH, length of hospitalization; ICH, intracranial hemorrhage; ref, reference

Table S6. Multivariate analyses in a model with continuous variables not transformed into categorical variables.

Outcome variables*	Adjusted OR (95%CI)	P value
RNI (reference: direct ET)	0.83 (0.71-0.96)†	**0.02**
ICH (reference: direct ET)	1.45 (1.18-1.78)‡	**< 0.001**
In-hospital mortality (reference: direct ET)	1.03 (0.76-1.40)†	0.84

* Value assignment: '1' for 'no RNI', 'ICH' and 'in-hospital mortality', respectively

† Adjusted for age, sex, ethnicity, SBP, pulse, BMI, hospital level, way to hospital, region, TOAST, NIHSS at admission, thrombectomy, OPT, TICI grade, LOH and ICH

‡ Adjusted for age, sex, ethnicity, SBP, pulse, BMI, hospital level, way to hospital, region, TOAST, NIHSS at admission, thrombectomy, OPT, TICI grade and LOH

BT, bridging thrombolysis; ET, endovascular thrombectomy; RNI, rapid neurological improvement; ICH, intracranial hemorrhage; OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure; TOAST, Trial of Org 10172 in Acute Stroke Treatment; NIHSS, National Institutes of Health Stroke Scale; OPT, onset to puncture; TICI, thrombolysis in Cerebral Infarction; LOH, length of hospitalization

Figure S1. The distribution of propensity scores in unmatched and matched patients.

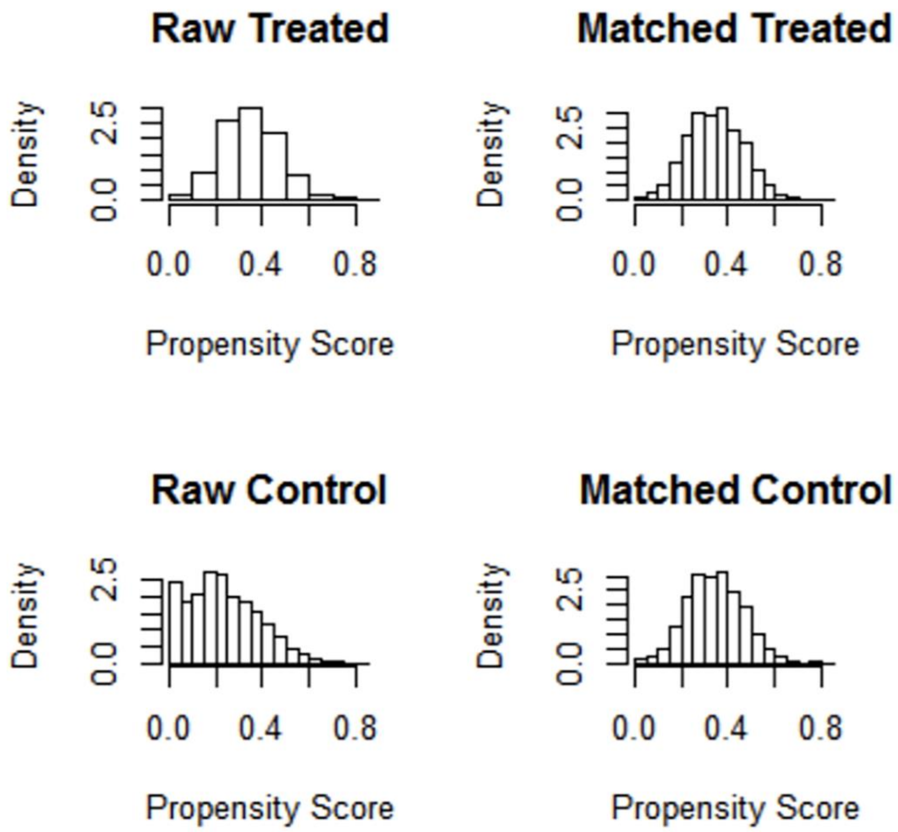
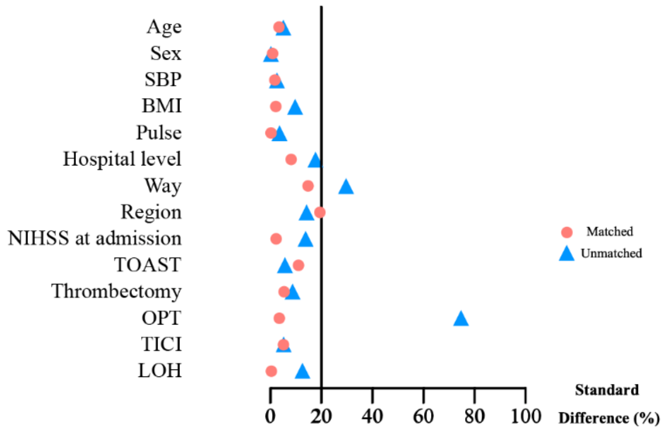


Figure S2. Standard differences of unmatched and matched patients.



Standard differences of all variates all below 20% in matched patients (indicated in red circle).