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Endovascular Recanalization for Acute Internal Carotid Artery Terminus Occlusion: A Subgroup Analysis From the Direct-MT Trial

BACKGROUND: The efficacy of endovascular recanalization for internal carotid artery (ICA) terminus occlusion has not been completely evaluated.

OBJECTIVE: To investigate the efficacy of endovascular recanalization for ICA terminus occlusion.

METHODS: Data from Direct-MT, a randomized controlled trial, were applied. ICA terminus occlusions were diagnosed with preprocedure computed tomography angiography by the core laboratory. We dichotomized the ICA terminus occlusions into 2 groups (non-T and T) and analyzed the differences between them. Single-factor analysis and multiple logistic regression were applied to detect independent factors for clinical outcomes and futile recanalization.

RESULTS: The rates of first-pass effect, successful recanalization, good clinical outcome, mortality, and futile recanalization were 22.3% (50 of 224), 83.0% (181 of 224), 24.6% (55 of 224), 26.7% (60 of 224), and 69.6% (126 of 181), respectively. Baseline National Institutes of Health Stroke Scale (negative factor; odds ratio [OR] 0.89; 95% CI 0.84-0.95; $P < .001$), hypertension (negative factor; OR 0.38; 95% CI 0.18-0.80; $P = .010$), Alberta Stroke Program Early CT Score ≥ 6 (OR 3.68; 95% CI 1.29-10.5; $P = .014$), tirofiban use (OR 2.46; 95% CI 1.16-5.19; $P = .018$), first-pass effect (OR 2.87; 95% CI 1.28-6.41; $P = .010$), and final extended thrombolysis in cerebral infarction ≥ 2b (OR, 3.50; 95% CI 1.17-10.4; $P = .024$) were independent factors for good clinical outcome. Baseline National Institutes of Health Stroke Scale (OR 1.12; 95% CI 1.05-1.20; $P = .004$), Alberta Stroke Program Early CT Score < 6 (OR 4.68; 95% CI 1.51-14.5; $P = .007$), tirofiban use (negative factor; OR 0.39; 95% CI 0.18-0.86; $P = .020$), and first-pass effect (negative factor; OR 0.44; 95% CI 0.19-0.99; $P = .047$) were independent factors for futile recanalization.

CONCLUSION: More efforts in modifiable factors should be made to improve the efficacy of endovascular recanalization for better clinical outcomes and less futile recanalization in ICA terminus occlusions.

KEY WORDS: Endovascular, Internal carotid artery, Terminus, Stroke, Thrombectomy

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Acute internal carotid artery (ICA) terminus occlusion refers to vessel occlusion at the ICA terminal segment, with or without downstream flow disruption. ICA terminus occlusion has a poorer outcome as compared with occlusions of more distal vessels for its large clot burden and impairment in collaterals.[1,2] Meanwhile, patients with ICA terminus occlusion were less likely to have favorable outcomes as compared with tandem occlusion and with ICA plus cerebral branch occlusions.[3,4] However, the endovascular recanalization for ICA terminus occlusions have been reported by a few studies with only limited quantities.[1,5-8]

In recent years, several randomized controlled trials have verified the endovascular recanalization as a standard therapy for large vessel occlusions

ABBREVIATIONS: AIS, acute ischemic stroke; **ASPECTS,** Alberta Stroke Program Early CT Score; **eTICI,** extended thrombolysis in cerebral infarction; **FPE,** first-pass effect; **LVO,** large vessel occlusion; **NIHSS,** National Institutes of Health Stroke Scale.

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(LVOs).[9] Successful recanalization (extended thrombolysis in cerebral infarction [eTICI] ≥ 2b) rates for LVOs have achieved great progress, but the 90-day clinical outcomes have not improved in keeping with the excellent reperfusion results. The concept of futile recanalization (unfavorable clinical outcome despite successful recanalization) is getting increased attention in the recent years, notwithstanding the paucity of data for acute ICA terminus occlusion.[10]

Direct-MT was the first randomized controlled trial to prove the noninferiority of thrombectomy alone to thrombectomy with preceding intravenous thrombolysis for LVOs and included more than 200 ICA terminus occlusions.[11] In this study, we conducted a subgroup analysis focusing on ICA terminus occlusions based on data from the Direct-MT trial. We described the characteristics of different occlusion morphologies and evaluated the independent factors for good clinical outcome, mortality, and futile recanalization to provide a reference to the efficacy of endovascular recanalization for acute ICA terminus occlusions.

METHODS

Patient Sample

The data of this study are available from the corresponding author upon reasonable request. Data from the Direct-MT trial were applied for this subgroup analysis. Patient eligibility and protocol of the Direct-MT trial (NCT03469206) have been reported previously.[12] In this subgroup analysis, we only focused on patients with ICA terminus occlusion from the Direct-MT trial based on preprocedure computed tomography angiography (CTA), according to the core laboratory analysis. As for occlusion type, ICA terminus occlusions were dichotomized into 2 types: type non-T occlusion was defined as the occlusion involving (1) the terminal ICA alone or (2) either middle cerebral artery (MCA) or anterior cerebral artery (ACA) combined with the terminal ICA; type T occlusion was defined as occlusion involving the MCA, ACA, and terminal ICA simultaneously. This study was approved by all relevant local ethics committees and research boards. Written informed consent was obtained from all the patients or their legal representatives.

Qualitative and Quantitative Assessment

The collateral grading system was scored on a 4-point scale of 0 to 3. A score of 0 indicated no collateral. A score of 1 indicated collaterals filling ≤50% but >0% of the occluded territory. A score of 2 indicated collaterals filling >50% but <100% of the occluded territory. A score of 3 indicated collaterals filling 100% of the occluded territory.[13] The extent of thrombus was quantified using the clot burden score.[14] Successful reperfusion was defined as final eTICI 2b, 2c, or 3.[15] The first-pass effect (FPE) was defined as achieving complete recanalization (eTICI3) with a single thrombectomy device pass.[16] Symptomatic intracranial hemorrhage was defined according to the Heidelberg criteria.[17] Perioperative complications included symptomatic intracranial hemorrhage and

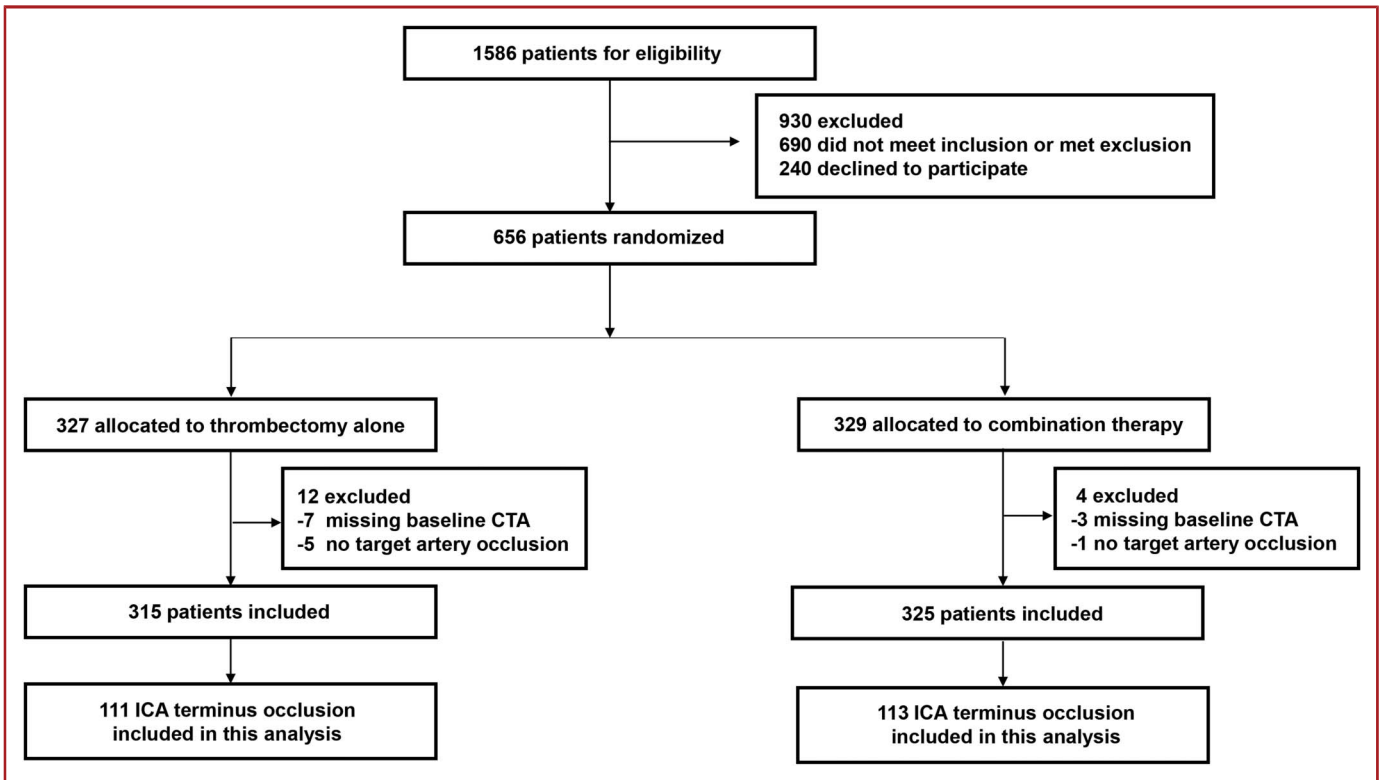

FIGURE. *Flow diagram of patient selection. CTA, computed tomography angiography; ICA, internal carotid artery.*

asymptomatic intracranial hemorrhage, embolization into a new territory,[18] infarction in new territory at 5 to 7 days, large or malignant MCA infarction, and any other procedural complications. The outcome lesion volume was assessed on follow-up CT on days 5 to 7 using an automated algorithm.[19] Tirofiban use was defined as periprocedural transarterial and/or transvenous use of tirofiban, a nonpeptide selective glycoprotein IIb/IIIa receptor inhibitor, by operators based on their experience to eliminate clot growing or to achieve unavoidable emergent stent angioplasty.

Outcomes of Interest

A good clinical outcome was defined as modified Rankin Scale (mRS) 0 to 2 at 90 days. Mortality was defined as an mRS score of 6 at 90 days. Futile recanalization was defined as 90-day mRS > 2 despite a final eTICI ≥ 2b.[20,21]

Statistical Analysis

Categorical variables were expressed as frequencies and percentages, continuous as mean (SD) for normal distribution or median (IQR) for non-normal distribution. Missing data were imputed with the use of multiple imputation by fully conditional specification regression for continuous variables or by fully conditional specification logistic regression for binary and ordinal variables. Categorical variables were tested using the χ^2 test. Continuous variables with normal distribution were tested using the *t* test. Continuous variables with non-normal distribution were tested using the rank sum test. Nonparametric testing of categorical variables was tested using the Fisher exact test. Statistical testing was conducted at a 2-tailed α level of 0.05. Multiple logistic regression was conducted when variables related to good clinical outcome, mortality, and futile recanalization significantly in the single-factor analysis, $P < .05$. All the analyses were performed using the SAS software, version 9.2 (SAS Institute).

RESULTS

Baseline Data and General Description of ICA Terminus Occlusions in the Direct-MT Trial

There were 1586 patients screened for eligibility and 656 patients randomized. Of 656 patients, 327 patients allocated to the thrombectomy alone group and 329 patients to the combination therapy group. Then, 12 patients were excluded from thrombectomy alone group because of missing baseline CTA in 7 and absence of target artery occlusion in 5. Four patients were excluded from the combination therapy group because of missing baseline CTA in 3 and absence of target artery occlusion in 1. Finally, 224 patients met the criteria of ICA terminus occlusion based on core laboratory diagnosis, with 111 in the thrombectomy alone group and 113 in the combination therapy group. The flow diagram of patient selection is presented in Figure. The rates of first-pass effect, successful recanalization, good clinical outcome, mortality, and futile recanalization were 22.3% (50 of 224), 83.0% (181 of 224), 24.6% (55 of 224), 26.7% (60 of 224), and 69.6% (126 of 181), respectively. Relevant data are presented in Table 1. There was no difference between the thrombectomy alone group and combination therapy group in final eTICI ≥ 2b and 90-day mRS 0 to 2 (see **Table S1 in Supplemental Digital Content**, http://links.lww.com/NEU/D243).

TABLE 1. Baseline Data and General Description for Acute ICA Terminus Occlusion

Variable	ICA terminus occlusion
Overall, No.	224
Male	125 (55.80%)
Age, y; median (IQR)	70 (62.76)
BMI, median (IQR)[a]	22.86 (21.45, 25.47)
Medical history	
Atrial fibrillation	109 (48.66%)
Hypertension	135 (60.27%)
Diabetes mellitus	42 (18.75%)
Hypercholesterolemia	8 (3.57%)
Chronic heart failure	16 (7.14%)
Smoking	42 (18.75%)
Cause of stroke	
Cardioembolic	105 (46.88%)
Intracranial atherosclerosis	4 (1.79%)
Ipsilateral extracranial stenosis	30 (13.39%)
Undetermined	85 (37.95%)
Baseline NIHSS, median (IQR)	19 (15, 23)
Baseline SBP, mmHg; median (IQR)	145 (131, 160.5)
Baseline DBP, mmHg; median (IQR)	84.5 (76, 93)
Thrombectomy alone	111 (49.55%)
First-pass effect	50 (22.3%)
Final eTICI[b]	
≥2b	181 (83.03%)
3	71 (31.70%)
90-d mRS 0-2	55 (24.66%)
Mortality	60 (26.79%)
Futile recanalization[c]	126 (69.6%)

BMI, body mass index; DBP, diastolic blood pressure; eTICI, extended thrombolysis in cerebral ischemia; ICA, internal carotid artery; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure.
[a]3 missing BMI (n = 3 in the thrombectomy group).
[b]6 missing final eTICI (n = 3 in the thrombectomy group).
[c]Futile recanalization indicates 90-day mRS > 2 despite eTICI ≥ 2b.
Data are presented as No./total No. (%) unless otherwise stated. Mortality indicates 90-day mRS = 6.

Analysis for ICA Terminus Occlusion Based on Occlusion Types

We dichotomized the acute ICA terminus occlusions into 2 types (non-T and T) and analyzed the differences between them. There were 39 ICA terminus occlusions for type non-T and 185 for type T. For the cause of stroke, the proportions of intracranial atherosclerosis and ipsilateral extracranial stenosis were higher in type non-T than in type T ($P < .001$). Clot burden score was 4 (2, 6) for type non-T vs 1 (1, 2) for type T ($P < .001$). Collateral score 0 to 1 was found in 90.2% for type T and 61.5% for type non-T ($P < .001$). The patency of anterior communicating artery was of no difference between 2 types ($P = .42$). The 24 to 72 h ASPECTS

TABLE 2. Analysis for ICA Terminus Occlusion Based on Occlusion Types

Variable	Type non-T	Type T	*P*
Overall; No.	39	185	
Cause of stroke			<.001
Cardioembolism	15 (38.46%)	90 (48.65%)	
Intracranial atherosclerosis	4 (10.26%)	0 (0%)	
Ipsilateral extracranial stenosis	10 (25.64%)	20 (10.81%)	
Undetermined	10 (25.64%)	75 (40.54%)	
Baseline NIHSS; median (IQR)	18 (14, 22)	20 (15, 24)	.06
Baseline ASPECTS; median (IQR)	8 (6, 9)	8 (6, 10)	.72
ASPECTS ≥ 6	31 (79.49%)	139 (75.14%)	.56
Clot burden score; median (IQR)	4 (2, 6)	1 (1, 2)	<.001
Collateral score 0-1	24 (61.54%)	167 (90.27%)	<.0001
Patency of ACoA	38 (97.44%)	175 (94.59%)	.42
Treatment with iv alteplase	20 (51.28%)	91 (49.19%)	.81
General anesthesia[a]	13 (34.21%)	53 (28.80%)	.51
Stroke onset time to recanalization time, min; median (IQR)[b]	268 (214.5, 342)	286.5 (229, 332)	.60
Stent retriever first	34 (87.18%)	170 (91.89%)	.53
No. of attempts; median (IQR)[c]	2 (1, 3)	2 (1, 3)	.28
Tirofiban use[d]	16 (42.11%)	48 (26.09%)	.05
First-pass effect[e]	9 (23.68%)	41 (22.28%)	.85
Final eTICI[f]			
≥2b	32 (91.43%)	146 (83.43%)	.23
3	14 (40.00%)	57 (32.57%)	.40
24-72 h ASPECTS; median (IQR)[f]	5 (3, 8)	3 (1, 6)	.012
Outcome lesion volume on CT, mL; median (IQR)[g]	24.90 (7.75, 67.11)	75.85 (21.94, 149.04)	.018
mRS at 90 days; median (IQR)	3 (2, 5)	4 (3, 6)	.12
mRS 0-2 at 90 days[h]	14 (35.90%)	41 (22.28%)	.07
Mortality	8 (20.51%)	52 (28.11%)	.33
Symptomatic intracranial hemorrhage	3 (7.69%)	12 (6.49%)	1.00
Asymptomatic intracranial hemorrhage	15 (38.46%)	78 (42.16%)	.67
Embolization into a new territory	4 (10.26%)	37 (20.00%)	.15
Infarction in new territory at 5-7 days	0 (0%)	6 (3.24%)	.55
Large or malignant MCA infarction	5 (12.82%)	51 (27.57%)	.05
Any other procedural complications	7 (17.95%)	45 (24.32%)	.39

ACoA, anterior communicating artery; ASPECTS, Alberta Stroke Program Early Computed Tomography score; CT, computed tomography; eTICI, extended thrombolysis in cerebral ischemia; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale. Mortality indicates 90-day mRS = 6.
[a]2 missing general anesthesia (n = 1 in the non-T group).
[b]14 missing stroke onset time to recanalization time (n = 3 in the non-T group).
[c]8 missing number of attempts (n = 3 in the non-T group).
[d]2 missing tirofiban use (n = 1 in non-T group).
[e]2 missing first attempt eTICI (n = 1 in the non-T group).
[f]14 missing final eTICI (n = 4 in the non-T group).
[g]5 missing 24-72 ASPECTS (n = 2 in the non-T group).
[g]68 missing outcome lesion volume on CT (n = 10 in the non-T group).
[h]1 missing mRS at 90 days (n = 1 in the T group).
Data are presented as No./total No. (%), unless otherwise stated.

was 5 (3, 8) for type non-T and 3 (1, 6) for type T (P = .010). Outcome lesion volume was larger in type T than in type non-T (75.8 (21.9, 149.0) mL vs 24.9 (7.75, 67.1) mL, P = .018). The FPE%, rates of final eTICI ≥ 2b, good clinical outcome, and mortality were of no difference between type T and type non-T occlusion (Table 2). There was no difference in rates of final eTICI ≥ 2b, final eTICI3, first-pass effect, good clinical outcome, mortality, and symptomatic intracranial hemorrhage between 2 arms (mechanical thrombectomy vs intravenous thrombolysis plus mechanical thrombectomy) in either occlusion type (see **Table S2 in Supplemental Digital Content**, http://links.lww.com/NEU/D244).

Factors for Clinical Outcomes of ICA Terminus Occlusions in the Direct-MT Trial

According to multiple logistic regression, baseline National Institutes of Health Stroke Scale (NIHSS; negative factor; OR 0.89; 95% CI 0.84-0.95; P < .001), hypertension (negative factor;

TABLE 3. Factors Analysis for 90-Day mRS 0-2

	Single-factor analysis		Multiple logistic regression	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Baseline NIHSS[a]	0.888 (0.838, 0.940)	<.001	0.896 (0.843, 0.952)	.0004
Male	2.131 (1.116, 4.070)	.0204		
Hypertension	0.498 (0.269, 0.922)	.0253	0.382 (0.183, 0.800)	.0108
Diabetes mellitus	0.354 (0.132, 0.952)	.0332		
Smoking	2.241 (1.094, 4.587)	.0250		
Cardioembolism	0.453 (0.239, 0.858)	.0140		
ASPECTS ≥ 6	5.147 (1.763, 15.026)	.0011	3.686 (1.294, 10.500)	.0146
Collateral score 2-3	2.290 (1.052, 4.986)	.0334		
Tirofiban use	2.264 (1.190, 4.307)	.0116	2.461 (1.166, 5.192)	.0181
First-pass effect, %	2.629 (1.336, 5.171)	.0051	2.871 (1.285, 6.414)	.0101
Final eTICI ≥ 2b	3.806 (1.109, 13.058)	.0239	3.500 (1.174, 10.437)	.0246

ASPECTS, Alberta Stroke Program Early Computed Tomography score; eTICI, extended thrombolysis in cerebral ischemia; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.
[a]Baseline NIHSS (median [IQR]) referred to 16 (12, 20) for patients with 90-day mRS 0-2 vs 20 (16, 24) for patients with 90-day mRS > 2.

OR 0.38; 95% CI 0.18-0.80; *P* = .010), ASPECTS ≥ 6 (OR 3.68; 95% CI 1.29-10.5; *P* = .014), tirofiban use (OR 2.46; 95% CI 1.16-5.19; *P* = .018), FPE (OR 2.87; 95% CI 1.28-6.41; *P* = .010), and final eTICI ≥ 2b (OR 3.50; 95% CI 1.17-10.4; *P* = .024) were independent factors for good clinical outcome. Meanwhile, baseline NIHSS (OR 1.05; 95% CI 1.01-1.11; *P* = .018), diabetes mellitus (negative factor; OR 0.32; 95% CI 0.15-0.69; *P* = .003), and collateral score 0 to 1 (OR 5.73; 95% CI 1.24-26.3; *P* = .024) were independent factors for mortality (Tables 3 and 4).

The futile recanalization rate for acute ICA terminus occlusion was 69.6% (126 of 181). Ninety-day mRS > 2 was observed in 67.6% (48 of 71) of patients despite final eTICI3. Baseline NIHSS (OR 1.12; 95% CI 1.05-1.20; *P* = .004), ASPECTS < 6 (OR 4.68; 95% CI 1.51-14.5; *P* = .007), tirofiban use (negative factor; OR 0.39; 95% CI 0.18-0.86; *P* = .020), and FPE (negative factor; OR 0.44; 95% CI 0.19-0.99; *P* = .047) were independent factors for futile recanalization. However, the collateral score 0 to 1 was not associated with futile recanalization (Table 5).

DISCUSSION

The main results of this subgroup analysis from the Direct-MT trial include that, for acute ICA terminus occlusions, (1) the futile recanalization rate reached 69.6%, (2) the first-pass effect, as an independent protective factor for good clinical outcome and futile recanalization elimination, was achieved in only 22.3% patients and warrants improvement, (3) and tirofiban use might be protective. These results provide insights into endovascular recanalization for acute ICA terminus occlusions.

Collateral flow can modify endovascular treatment efficacy by facilitating thrombus retrieval and lowering the number of device passes.[22] In addition, under different collateral flows, even the association between the clot burden score and functional outcome

TABLE 4. Factors Analysis for 90-Day mRS 6

	Single-factor analysis		Multiple logistic regression	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Baseline NIHSS[a]	1.060 (1.017, 1.106)	.0059	1.057 (1.009, 1.106)	.0183
Diabetes mellitus	0.352 (0.175, 0.709)	.0027	0.323 (0.151, 0.694)	.0038
Collateral score 0-1	6.759 (1.565, 29.185)	.0036	5.731 (1.246, 26.364)	.0249
Stent retriever first	0.259 (0.101, 0.661)	.0028		
Final eTICI < 2b	2.439 (1.107, 5.372)	.0239		
Symptomatic intracranial hemorrhage	6.359 (2.076, 19.482)	.0009		
Hemicraniectomy	2.754 (1.059, 7.160)	.0319		
Large or malignant MCA infarction	10.799 (5.380, 21.677)	<.0001		

eTICI, extended thrombolysis in cerebral ischemia; MCA, middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.
[a]Baseline NIHSS (median [IQR]) referred to 22 (17, 25) for patients with 90-day mRS = 6 vs 18 (14, 22) for patients with 90-day mRS < 6.

TABLE 5. Factors Analysis for Futile Recanalization[a]

	Single-factor analysis		Multiple logistic regression	
Variable	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Baseline NIHSS[b]	1.139 (1.068, 1.214)	<.001	1.126 (1.054, 1.202)	.004
Diabetes mellitus	2.663 (0.967, 7.331)	.0455		
Cardioembolism	2.168 (1.097, 4.283)	.0189		
ASPECTS < 6	5.682 (1.917, 16.842)	.0005	4.687 (1.515, 14.502)	.0074
Collateral score 0-1	2.474 (1.025, 5.973)	.0453		
Tirofiban use	0.355 (0.175, 0.722)	.0021	0.395 (0.180, 0.867)	.0206
First-pass effect%	0.441 (0.216, 0.898)	.0240	0.442 (0.197, 0.992)	.0478

ASPECTS, Alberta Stroke Program Early Computed Tomography score; eTICI, extended thrombolysis in cerebral ischemia; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

[a]Futile recanalization indicates 90-day mRS > 2 despite eTICI ≥ 2b.

[b]Baseline NIHSS (median [IQR]) referred to 20 (16, 25) for patients with final eTICI ≥ 2b and 90-day mRS > 2 vs 16 (12, 20) for patients with final eTICI ≥ 2b and 90-day mRS 0-2.

varies.[23] It is rational to speculate that, especially for ICA terminus occlusion, heavy clot burdens and concurrent insufficient collateral flow are associated with poor clinical outcome. However, there was no difference in clinical outcome despite significant differences in the collateral status between the 2 occlusion types. The reason might be the comparable rates of the first-pass effect between 2 occlusion types.

The first-pass effect was first introduced to evaluate thrombectomy devices as a new metric in 354 patients from the North American Solitaire Acute Stroke Registry database.[16] In Systematic Evaluation of Patients Treated with Stroke Devices for Acute Ischemic Stroke registry, FPE was demonstrated as a surrogate for superior clinical outcome.[24] The FPE group in each registry had only 10.1% and 13.5% ICA terminus occlusions, less than the non-FPE group significantly. Moreover, the ICA terminus clot was considered a negative predictor of FPE. According to our data, although it was only achieved in 22.3% ICA terminus occlusions, FPE remained an independent factor for good clinical outcome and provided protection from futile recanalization. Recently, a large manually expandable stent retriever achieved 34.8% (8 of 23) of FPE in ICA terminus occlusion with successful recanalization in 95.7% (22 of 23) and mRS 0 to 2 in 26.1% (6 of 23) of patients.[25] FPE, as a modifiable factor, warrants further improvements to achieve better clinical outcomes in thrombectomy for ICA terminus occlusions.

Futile recanalization refers to the absence of clinical improvement after successful endovascular recanalization.[10,26] In one multicenter study, advanced age, higher baseline NIHSS score, delayed puncture to reperfusion, and use of general anesthesia were associated with a futile recanalization rate of 49.6%.[27] In a prospective single-center registry, greater age, higher admission NIHSS score, and lower ASPECTS were predictors for 90-day mRS 3 to 6 despite final TICI3, which was observed in 54.5% of patients.[28] In this subanalysis, higher baseline NIHSS and ASPECTS < 6 were independent risk factors for a futile recanalization rate of 69.6%. Recently, complete TICI 3 reperfusion was found to have greater functional outcomes than incomplete TICI 2b reperfusion in several studies.[29,30] However, no substantial difference in the futile recanalization rate was detected between the final eTICI ≥ 2b group and final eTICI3 group according to our data (69.6% for the final eTICI ≥ 2b group vs 67.6% for the final eTICI3 group).

Tirofiban has been evaluated for its safety and efficacy in mechanical thrombectomy for LVOs, even in intravenous thrombolysis bridging.[31] By local infusion alone or with subsequent intravenous infusion, rescue tirofiban use improved 90-day clinical outcome even at low dose.[32,33] Given that tirofiban use might be protective in achieving good clinical outcome and eliminating futile recanalization, its in-depth value should be explored in the near future. However, no guideline or consensus is yet available to determine the occasion or accurate dosage for tirofiban use during thrombectomy.

Limitations

This subgroup analysis had limitations. First, in line with the Direct-MT trial design, all conclusions should be applied to acute ICA terminus occlusions treated within 4.5 hours after stroke onset and are not generalized to others later than the time window. Second, according to the protocol of the Direct-MT trial, the evaluation of vessel anatomy was based on preprocedure CTA. No further evaluation by contralateral injection was mandatory, considering the risk of reperfusion delay. Actually, we are unable to exclude the situation that the deficiency of ipsilateral A1 segment as the consequence of the anatomic absence rather than the pathologic occlusion, which might overestimate the T occlusion in this analysis. However, we further evaluated the patency of anterior communicating artery on preprocedure CTA in all patients and found no difference between 2 occlusion groups. It might provide indirect support that the differences detected in variables in this analysis reflected, to some extent, the inherent discrepancy between 2 occlusion morphologies. Third, although tirofiban use might be protective, it was given based on operator experience instead of guidelines or consensus instructions. Further studies should be designed to explore the standard use of tirofiban in ICA terminus clot thrombectomy. Fourth, the number of patients of each preferred first strategy (with stent retriever vs with

aspiration) differed widely. Thus, the efficacy of each strategy in the first attempt to complete recanalization is not comparable. Fifth, given the nature of this subgroup analysis, the independent factors provided may not have the power to predict clinical outcomes. More specifically designed studies should be conducted to address these issues.

CONCLUSION

For acute ICA terminus occlusion, the successful recanalization is unable to ensure compatible good clinical outcomes, and the issues of futile recanalization remain unresolved. More efforts, especially in the modifiable factors, should be made to improve the efficacy of endovascular recanalization for the purpose of better clinical outcomes and less futile recanalization.

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Supplemental Digital Content 1. Table S1. Comparison between the thrombectomy alone group and combination therapy group in baseline data and clinical outcomes.

Supplemental Digital Content 2. Table S2. Comparison between the 2 arms (mechanical thrombectomy vs intravenous thrombolysis plus mechanical thrombectomy) of either occlusion type.

COMMENT

The authors have submitted a manuscript exploring endovascular treatment of acute ICA terminus occlusions from a subset of the previously performed Direct-MT trial. The authors examined the 224 patients with an acute ICA terminus occlusion in this study and dichotomized them to 2 types (occlusions involving the terminal ICA alone or a combination of the ICA terminus and ACA or MCA). The results of this analysis demonstrated that ICA occlusions suffer from poor clinical outcomes despite a high percentage of successful recanalization (83%) observed. The authors mention this in the context of known low first pass effect when performing thrombectomy for ICA terminus occlusions. The results from this current analysis demonstrating the difficult nature of thrombectomy for ICA terminus occlusions serve as a view of where we can continue to advance the field of endovascular neurosurgery. New device development and the advent of novel techniques or protocols offer promise in addressing these challenges. The Direct-MT trial was performed with stent retrievers used as the primary option for thrombectomy based on 2015 AHA/ASA guidelines, with aspiration devices as a secondary option. Recent evidence from the Compass Trial[1a] demonstrates non-inferiority of direct aspiration as a first pass thrombectomy technique, however the current study only utilized aspiration first in 7 patients. As we continue to expand our ability to treat large-vessel occlusions and address increasingly complex challenges, studies such as this current one are necessary to highlight where we as a field should direct our focus.

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