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Carotid I's, L's and T's: collaterals shape the outcome of intracranial carotid occlusion in acute ischemic stroke

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Abstract

Background—Collaterals may affect revascularization, ischemic severity, and clinical outcomes in acute stroke owing to internal carotid artery (ICA) occlusion.

Objective—To examine the hypothesis that morphology of occlusive thrombus and collateral flow patterns may influence the outcome of ICA occlusions after mechanical thrombectomy.

Methods—Pooled analyses of ICA occlusions in the MERCI and Multi-MERCI trials employed central angiography review readings to categorize lesions as I, L, or T clots and functional lesions based on collateral flow patterns. Demographic variables, procedural details, and clinical outcomes were compared across ICA lesion types.

Results—A total of 72 subjects (mean age 67 years (SD 16), 51% female, median National Institutes of Health Stroke Scale 20 (range 8–35)) were included, with 90-day modified Rankin score ≤2 in 28% and 51% mortality. Clots were categorized as an I lesion in 9/72 (12.5%), L lesion in 12/72 (16.7%), and T lesion in 51/72 (70.8%). Based on collateral flow patterns, cases were categorized as having a functional I lesion in 7/72 (9.7%), functional L in 38/72 (52.8%), and

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Collaborators for the MERCI and Multi-MERCI Investigators.

Competing interests DSL, WSS, and GRD were employed by the University of California, which holds a patent on retriever devices for stroke, at the time of this work. DSL: consultant/advisory board; Modest, Stryker, and Covidien. RGN: consultant/advisory board; Modest, Stryker/Concentric Medical, Inc, Covidien/ev3 Neurovascular, Inc, Co-Axia, Inc, Penumbra, Inc, Rapid Medical, Inc, Reverse Medical, Inc, and Neurointervention, Inc.

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functional T in only 27/72 (37.5%). Multivariate analyses showed that a functional T lesion, with insufficient collateral flow to ipsilateral anterior cerebral arteries via the contralateral ICA, was a strong predictor of both revascularization success and subsequent clinical outcomes.

Conclusions—Collateral flow patterns distinguish the nature and impact of ICA occlusions on expected revascularization and subsequent clinical outcomes in acute ischemic stroke. The nomenclature of terminal ICA occlusions introduced here (carotid I's, L's, and T's) may enhance future endovascular trials targeting such proximal occlusions.

INTRODUCTION

Acute ischemic stroke caused by occlusion of the intracranial carotid artery is associated with poor outcomes.[1] However, the clinical course is also quite variable, as intracranial internal carotid artery (ICA) occlusion may even be asymptomatic when robust collateral circulation compensates for down-stream hypoperfusion. In acute ischemic stroke, ICA occlusions are routinely designated as terminal or carotid T lesions, despite variable anatomic and functional effects of such occlusions at the origins of the anterior and middle cerebral arteries (ACAs and MCAs). Collaterals, via pial or Willisian routes, are infrequently characterized before endovascular therapy.[23] Arterial segments at the circle of Willis, however, may easily shunt flow across such ICA occlusions or into adjacent territories. Contralateral ICA injections at angiography may easily reveal patency and flow characteristics in the contralateral proximal ACA (A1), anterior communicating artery, ipsilateral A1 and M1 arterial segments downstream from the occluded carotid. As such collateral flow patterns and the resultant functional nature of an ICA occlusion may affect potential revascularization, severity of ischemic injury, and associated clinical outcomes, it is imperative to distinguish these heterogeneous lesions.[45]

We hypothesized that the morphology of the occlusive thrombus and collateral flow patterns might influence the outcome of terminal carotid occlusions treated with mechanical thrombectomy. Using angiography to discern differences in clot morphology and functional impact balanced by collaterals, we categorized ICA occlusions in MERCI and Multi-MERCI studies as carotid I's, L's, or T's to disclose the potential impact on acute stroke treatment benchmarks.[67]

METHODS

The MERCI study and subsequent Multi-MERCI studies tested the use of the Merci Retrieval System for mechanical thrombectomy in acute ischemic stroke. Detailed methods and results of these studies have been previously published.[67] In the multicenter MERCI study, patients were treated within 8 h of symptom onset without intravenous tissue plasminogen activator (IV tPA) use. In the multicenter Multi-MERCI studies, IV tPA-ineligible patients and those patients with persistent occlusion at angiography after IV tPA were enrolled. The definitions and measurement of baseline clinical variables and subsequent outcomes were similar in MERCI and Multi-MERCI trials, as previously described.[67]

This pooled analysis of intracranial carotid occlusions used the source angiography datasets from these trials to verify the exact site of arterial occlusion on baseline angiography before mechanical thrombectomy. Central review of the archived, digital angiography dataset was conducted by the core laboratory with extensive experience in adjudication of imaging and angiographic measures in endovascular stroke trials, using a DICOM (digital imaging and communications in medicine) reader for image display. Inclusion criteria for this pooled analysis were the presence of an intracranial ICA occlusion with availability of angiography detailing potential collateral circulation.

A total of 72 intracranial ICA occlusions were identified, including 29 from MERCI and 43 from the Multi-MERCI trials. Angiographic data on potential collateral flow routes were not available in 18/47 (38%) ICA occlusions in MERCI and 9/52 (17%) in the Multi-MERCI trial. Angiographic patency of the contralateral proximal ACA or A1, anterior communicating artery, and ipsilateral A1, posterior communicating artery and M1 segments were documented. Partial or complete patency of the ipsilateral A1 was also delineated to enable analysis of clot morphology and the functional impact of collaterals. The morphology of ICA occlusions was categorized as an I, L, or T lesion (figure 1), depending on involvement of the proximal ACA and MCA, considering perfusion of distal arterial territories. Clot shape was categorized as I, L, or T based on the presence of any occlusive lesion in each of the ipsilateral A1, ICA, and M1 segments. In addition, functional I, L, or T lesions of the ICA were designated in each case based on perfusion of the downstream territory. For example, a T clot ICA may demonstrate occlusion of the A1, ICA, and M1 segments, whereas filling of the ipsilateral ACA territory from the contralateral ICA would define this occlusion as a functional L lesion. Complete and equivalent timing of filling compared with the normal adjacent territory of the ipsilateral ACA territory via collaterals was required to define the presence of a functional L occlusion. Demographic variables, procedural details, and clinical outcomes were compared across ICA lesion types.

Statistical analyses were conducted using clinical variables obtained from the main datasets, with angiographic variables extracted as described above. Descriptive statistics were used to summarize clinical, procedural, and angiographic variables. Clinical outcomes considered were functional independence at 90 days (modified Rankin Scale of 0, 1, or 2) and 90-day mortality. Postprocedure successful revascularization was defined as Thrombolysis in Myocardial Infarction (TIMI) 2 or 3 flow after mechanical thrombectomy and any adjunctive treatments. Detailed analyses comparing ICA occlusions and the impact of collateral flow were based on classification of I-, L-, or T-shaped clots and functional lesions. Angiographic lesion type was treated as a categorical variable.

A separate analysis was conducted to discern whether the presence of any flow or patency of the ipsilateral A1 affected revascularization or clinical outcomes. Univariate associations were established using Fisher's exact test or Fisher–Freeman–Halton test for categorical variables, or Wilcoxon rank-sum test or Kruskal–Wallis test for multiple categories in ordinal order and the t test or F test for continuous variables. Logistic regression was used to model revascularization success and good clinical outcome, using covariates selected by stepwise selection methodology. Baseline variables potentially associated with outcomes at the 0.20 significance level were considered for inclusion in the multivariable model and removed at the 0.10 level (Wald χ^2 statistics). A significance level of $p<0.05$ was used to identify significant predictors of revascularization and clinical outcomes. All statistical analyses were performed using SAS, V.9.2.

RESULTS

The MERCI and Multi-MERCI studies included a total of 305 patients; detailed methods and results have been described previously.[67] These studies contained 99 subjects who underwent endovascular therapy for recanalization of intracranial ICA occlusion causing acute ischemic stroke.[1] Angiography data from the carotid injection contralateral to the occluded ICA, detailing extent of thrombus and the degree of collateral flow to the anterior cerebral artery beyond the occlusion, were available for review in 29 MERCI subjects and 43 Multi-MERCI subjects. A total of 72 subjects (mean age 67 years (SD 16), 51% female, median National Institutes of Health Stroke Scale (NIHSS) 20 (range 8–35)) were included in our analyses. The demographics, baseline characteristics, procedural details, and clinical outcomes are detailed in table 1, delineated by clinical study and summarized for our pooled dataset. Overall, subjects were treated with IV tPA in 14/43 (32.6%) and received endovascular stroke treatment at a mean of 4.2 h (SD 1.5) from symptom onset to arterial puncture, resulting in 28% with good clinical outcome of the modified Rankin score (mRS) ≤2 and 51% mortality at day 90, respectively.

Angiographic analyses of the contralateral carotid injections showed the presence of any flow into the A1 ACA segment in 50/72 (69.4%) subjects. Based on these angiographic injections and the presence of opacification distal to the occlusion, clots were categorized as an I lesion in 9/72 (12.5%), L lesion in 12/72 (16.7%), and T lesion in 51/72 (70.8%). Once the degree of collateral perfusion to the ACA territory downstream from the occlusion is considered, these cases were categorized as a functional I lesion in 7/72 (9.7%), functional L in 38/72 (52.8%), and functional T in only 27/72 (37.5%).

Thrombus extent or categorization of clots as an I, L, or T shape did not differ based on age, sex, height, weight, body mass index, baseline blood pressure, NIHSS, or comorbidities. Subjects with an I clot, however, had a lower frequency of those with baseline mRS≤2 (55.6% vs 83.3% (L) and 90.2% (T); p=0.035). Similarly, procedural details did not differ based on clot category, except that I lesions had a smaller average number of attempts to remove a clot with the device (1.4±0.7 vs 2.5 ±1.7 (L) and 3.2±1.6 (T); p=0.01). Interestingly, clot shape was unrelated to successful revascularization, 90-day mRS, or 90-day mortality (table 2).

Classification of lesions based on the functional nature of the ICA occlusion, considering collateral perfusion of the ACA territory, showed several distinctions not noticed in analyses based on clot shape. Functional I or L lesions were more common in younger subjects (I, mean ± SD age 64.9±13.1 years; L, 63.0 ±16.5; T, 73.7±12.9; p=0.019). A history of hypertension was also more uncommon in functional I lesions (42.9% vs 63.2% (L) and 88.9% (T); p=0.026). Other baseline variables and procedural details did not differ except for the number of device attempts (1.4±0.8 (I) vs 2.7±1.6 (L) and 3.4±1.7 (T); p=0.014). When only functional L and T lesions were compared (figure 2), it was noted that subjects with functional T lesions were older (L, mean age 63.0±16.5 years; T, 73.7 ±12.9; p=0.006), had higher systolic blood pressure at baseline (L, mean 138.6±24.5 mm Hg; T, 150.4±24.1; p=0.057), and more severe neurological deficits (L, median NIHSS 19.5 (8–26); T, 21.0 (12–35); p=0.021). Unlike clot shape, the functional nature of the ICA occlusion was strongly associated (table 3) with successful revascularization, good clinical outcome (90-day mRS≤2) and 90-day mortality.

Multivariate analyses confirmed that presence of a functional T lesion, or ICA occlusion with insufficient collateral flow to the ipsilateral ACA territory from the contralateral ICA, was a strong predictor of both revascularization success and subsequent clinical outcomes (table 4). When the number of device passes was forced into the model, we noted that the effect of a functional T lesion on outcome was independent of the number of device passes. The presence of any flow in the ipsilateral A1 segment or clot shape alone predicted neither angiographic nor clinical outcomes.

DISCUSSION

Characterization of intracranial ICA occlusions based on clot extent and functional nature considering collateral flow patterns on angiography discloses marked heterogeneity in both revascularization and the clinical outcomes after endovascular therapy. Terminal ICA occlusions may be readily classified as an I, L or T lesion with respect to clot extent and separately, as functional lesions. This systematic approach developed for these pooled analyses of the MERCI and Multi-MERCI trials suggests that ICA occlusions should be differentiated before mechanical thrombectomy, owing to the dramatic impact of functional T lesions. Clot burden and even partial extension of thrombus into the ipsilateral A1 segment was not as influential as functional lesion type, challenging the suggestion that flow information is critical.[89] This finding is further evidence that collateral status–distal perfusion is more important than anatomic segmental occlusion analysis. The nomenclature of intracranial ICA occlusions should reserve ‘carotid-T’ for functional T lesions as we describe, rather than assume that all ‘terminal’ ICA occlusions are the same.

Such detailed analyses of ICA occlusions have not been conducted in previous studies and the availability of adequate angiographic data has been limited to date.[3] This retrospective analysis showed that 73% of cases in MERCI and Multi-MERCI had such information based on routine acquisitions. Recent endovascular studies have reported limited numbers of ICA occlusions with minimal characterization of both anatomic and functional impact on downstream flow.[10-15] Many interventionalists may intentionally avoid injection of the contralateral ICA or other collateral routes citing the need for speed in revascularization, yet such lesions may ultimately yield minimal reperfusion and the prognosis may be dramatically influenced by knowledge of such information.

Our analyses showed that functional L and functional T lesions are relatively common and that most T-shaped clots are actually functional L lesions due to sparing of the ACA territory by collateral perfusion. In fact, only 27/51 (53%) T-shaped clots were functional T lesions. Relatively poor collateral status and resultant stasis may be a determinant of thrombus shape. Thrombus shape or clot burden was unrelated to clinical variables and procedural factors, including revascularization, although more extensive clot burden was associated with increased device attempts. Subjects with functional T lesions were older, more hypertensive, had a higher NIHSS, culminating in worse revascularization rates, more disability, and higher mortality. Multivariable analyses confirmed, however, that the presence of a functional T lesion itself, beyond age and NIHSS, was a strong predictor of both revascularization and clinical outcomes.

Evaluation of clot location, patency of adjacent arterial segments, and collateral flow to the ischemic territory at angiography may provide subtle, yet critical, differences among ICA occlusions. More robust collateral perfusion of functional L lesions may facilitate recanalization and portend good clinical outcome and reduced mortality, whereas functional T lesions harbor more ominous prognoses. Characterization of terminal ICA occlusions based on functional I, L, or T lesion type may be used in future endovascular trials as selection criteria and for prognostication in acute ischemic stroke.[16] These proximal lesions are increasingly the focus of current endovascular trials, due to the potential relatively large therapeutic benefit, but further characterization of ICA lesions based on flow and collaterals may be key. Such information about subject-specific pathophysiology at baseline may rival the impact of a specific device or treatment strategy. Functional lesion characterization may also be important for adjudication of emboli in the ACA or previously unaffected territories and for measurement of reperfusion scores.[17] Future classification schemes may use non-invasive imaging such as 4D CT angiography. However, our analyses suggest that perfusion data of the ACA territory may be essential.[9]

Limitations of these retrospective analyses include incomplete angiographic data for characterization of ICA lesions, especially in the MERCI trial. Validation of this new classification algorithm is also warranted. Prospective acquisition of such angiographic data must also be balanced by the need for rapid treatment.

CONCLUSIONS

Collateral flow patterns distinguish the nature and impact of ICA occlusions on expected revascularization and subsequent clinical outcomes in acute ischemic stroke. The nomenclature of terminal ICA occlusions based on characterization of carotid I's, L's, and T's may enhance future endovascular trials targeting such proximal occlusions.

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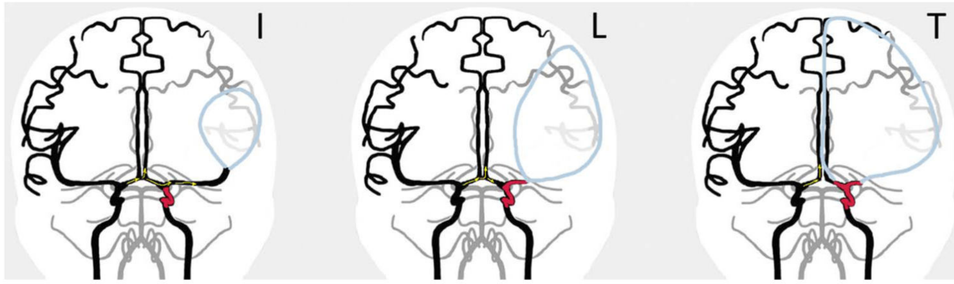

Figure 1.
Schematic diagram of terminal internal carotid artery occlusions with I (left), L (center), or T (right) morphology, indicating occlusive thrombus (red), collateral flow (yellow) and ischemic territory (blue). Other configurations exist such as an L-shaped clot that may function as a T occlusion owing to absent contralateral flow, or alternatively, a T-shaped clot that may function as an L occlusion owing to robust collateral flow across the circle of Willis.

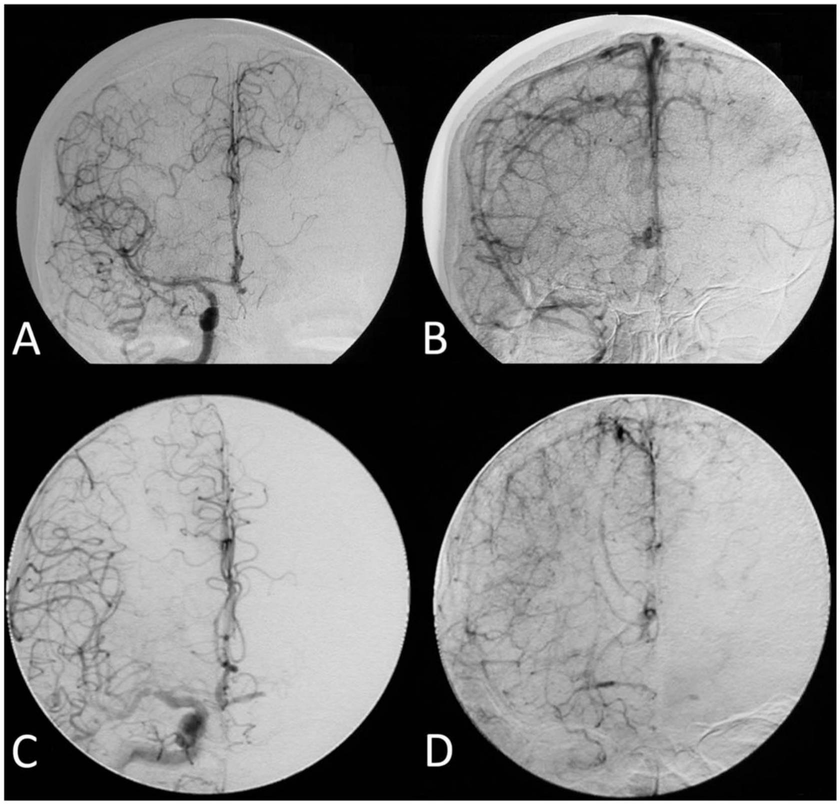

Figure 2.

'Characterization of terminal internal carotid artery (ICA) occlusions as functional L or functional T lesions based on perfusion of the ipsilateral anterior cerebral arteries territory from the contralateral ICA injection at DSA showed dramatically superior revascularization and clinical outcomes with functional L compared with functional T lesions. DSA reveals a T-shaped clot with a functional L lesion pattern on arterial (A) and venous (B) phase images with robust collateral flow. In another case, an L-shaped clot with patency of the ipsilateral A1 segment demonstrates a functional T lesion pattern with marginal collateral perfusion in the arterial (C) and venous (D) phase images.

Table 1

Demographics, baseline characteristics, procedural details, and clinical outcomes, delineated by clinical study and summarized for the pooled dataset

Clinical or procedural variable	MERCI (n=29)	Multi-MERCI (n=43)	Pooled (n=72)
Age (years), median (min-max)	74.0 (32.0–93.0)	67.0 (28.0–93.0)	69.5 (28.0–93.0)
Sex, n (%)			
Female	13 (44.8)	24 (55.8)	37 (51.4)
Male	16 (55.2)	19 (44.2)	35 (48.6)
History of atrial fibrillation, n (%)	12 (41.4)	19 (44.2)	31 (43.1)
History of congestive heart failure, n (%)	5 (17.2)	6 (14.0)	11 (15.3)
History of coronary artery disease, n (%)	10 (34.5)	20 (46.5)	30 (41.7)
History of diabetes, n (%)	3 (10.3)	7 (16.3)	10 (13.9)
History of hypertension, n (%)	18 (62.1)	33 (76.7)	51 (70.8)
Systolic blood pressure (mm Hg), mean (SD)	147.4±21.2	142.8±27.1	144.7±24.8
Diastolic blood pressure (mm Hg), mean (SD)	73.9±12.8	72.3±18.8	72.9±16.6
Baseline NIHSS, n (%)			
<8	0 (0)	0 (0)	0 (0)
8–10	0 (0)	4 (9.3)	4 (5.6)
11–20	18 (62.1)	15 (34.9)	33 (45.8)
21–30	10 (34.5)	22 (51.2)	32 (44.4)
>30	1 (3.4)	2 (4.7)	3 (4.2)
Baseline modified Rankin score ≤2, n (%)	23 (79.3)	38 (88.4)	61 (84.7)
Time from symptom onset to arterial puncture (h), mean (SD)	4.4±1.5	4.0±1.4	4.2±1.5
Time from arterial puncture to final angiogram (h), mean (SD)	2.1±1.0	1.9±0.8	2.0±0.9
Time from symptom onset to procedure end (h), mean (SD)	6.6±1.7	5.8±1.6	6.1±1.7
Number of attempts to remove clot with retriever, mean (SD)	2.8±1.4	2.9±1.8	2.8±1.6
Treatment with IV tPA, n (%)	NA	14 (32.6)	14 (32.6)
Treatment with IA tPA, n (%)	6 (20.7)	17 (39.5)	23 (31.9)
Treatment with other endovascular device, n (%)	4 (13.8)	2 (4.7)	6 (8.3)
Postprocedure revascularization success (TIMI 2/3), n (%)	18 (62.1)	26 (60.5)	44 (61.1)
90-Day good outcome (modified Rankin Score 0–2), n (%)	6 (21.4)	14 (32.6)	20 (28.2)
90-Day mortality, n (%)	16 (55.2)	21 (48.8)	37 (51.4)

IA tPA, intra-arterial tissue plasminogen activator; IV tPA, intravenous tissue plasminogen activator; TIMI, Thrombolysis in Myocardial Infarction.

Table 2

Revascularization and clinical outcomes based on shape of clot (I, L, or T types of terminal carotid occlusions)

	Clot I (n=9)	Clot L (n=12)	Clot T (n=51)	p Value
Post-procedure revascularization success (TIMI 2/3), n (%)	7 (77.8)	10 (83.3)	27 (52.9)	0.087
90-Day modified Rankin score, n (%)				0.555
0	2 (25.0)	3 (25.0)	0(0)	
1	0 (0)	0 (0)	7 (13.7)	
2	1 (12.5)	2 (16.7)	5 (9.8)	
3	1 (12.5)	0 (0)	5 (9.8)	
4	0 (0)	0 (0)	6 (11.8)	
5	1 (12.5)	0 (0)	1 (2.0)	
6	3 (37.5)	7 (58.3)	27 (52.9)	
90-Day good outcome (modified Rankin score 0–2), n (%)	3 (37.5)	5 (41.7)	12 (23.5)	0.331
90-Day mortality, n (%)	3 (37.5)	7 (58.3)	27 (52.9)	0.538

TIMI, Thrombolysis in Myocardial Infarction.

Table 3

Revascularization and clinical outcomes based on functional classification of I, L, or T types of terminal carotid occlusions, considering collateral flow patterns

	Functional I (n=7)	Functional L (n=38)	Functional T (n=27)	p Value
Post-procedure revascularization success (TIMI 2/3), n (%)	5 (71.4)	28 (73.7)	11 (40.7)	0.023
90-Day modified Rankin score, n (%)				<0.001
0	1 (16.7)	4 (10.5)	0 (0)	
1	0 (0)	6 (15.8)	1 (3.7)	
2	1 (16.7)	7 (18.4)	0(0)	
3	1 (16.7)	5 (13.2)	0 (0)	
4	0 (0)	4 (10.5)	2 (7.4)	
5	1 (16.7)	0 (0)	1 (3.7)	
6	2 (33.3)	12 (31.6)	23 (85.2)	
90-Day good outcome (modified Rankin score 0–2), n (%)	2 (33.3)	17 (44.7)	1 (3.7)	<0.001
90-Day mortality, n (%)	2 (33.3)	12 (31.6)	23 (85.2)	<0.001

TIMI, Thrombolysis in Myocardial Infarction.

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Table 4

Multivariate logistic regression modeling for prediction of revascularization success and 90-day good outcome (modified Rankin score 0–2)

Variable	Coefficient (SE)	OR (95% CI)	p Value
Revascularization success (TIMI 2/3)			
Intercept	1.012		
Functional T	−1.386 (0.517)	0.25 (0.09 to 0.69)	0.007
90-Day good outcome (modified Rankin score 0–2)			
Intercept	5.491		
Functional T	−2.527 (1.100)	0.08 (0.01 to 0.69)	0.021
Baseline NIHSS	−0.180 (0.074)	0.84 (0.72 to 0.97)	0.015
Age (years)	−0.037 (0.022)	0.96 (0.92 to 1.01)	0.096

NIHSS, National Institutes of Health Stroke Scale; TIMI, Thrombolysis in Myocardial Infarction.