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ABSTRACT

BACKGROUND AND PURPOSE: The TICI score is widely used to evaluate cerebral perfusion before and after the endovascular treatment of stroke. Recent studies showing the effectiveness and safety of mechanical thrombectomy combine modified TICI 2b and modified TICI 3 to assess the technical success of endovascular treatment. The purpose of this study was to determine how much clinical outcomes differ between patients achieving modified TICI 2b and modified TICI 3 reperfusion.

MATERIALS AND METHODS: We analyzed 222 consecutive patients with acute large intracranial artery occlusion of the anterior circulation having achieved modified TICI 2b or modified TICI 3 reperfusion after thrombectomy. The primary end point was the rate of favorable outcome defined as the achievement of a modified Rankin Scale score of 0-2 at 3 months.

RESULTS: Patients with modified TICI 3 more often had favorable collateral circulation and atherosclerosis etiology, with a shorter time from onset to reperfusion than patients with modified TICI 2b (all P < .05). The number of total passes to achieve reperfusion was higher in the modified TICI 2b group (median, 2; interquartile range, 1–3, 1–9) versus (median, 1; interquartile range, 1–2, 1–8) in the modified TICI 3 group (P = .0002). Favorable outcome was reached more often for patients with modified TICI 3 than for those with modified TICI 2b (71.7% versus 50.5%, P = .001), with a similar difference when considering excellent outcome. In addition, patients with modified TICI 3 had a lower intracerebral hemorrhage rate (23.0% versus 45.0%, P < .001).

CONCLUSIONS: Patients with modified TICI 3 reperfusion have better functional outcomes than those with modified TICI 2b. Given the improving reperfusion rates obtained with thrombectomy devices, future thrombectomy trials should consider modified TICI 2b and modified TICI 3 status separately.

ABBREVIATIONS: ADAPT = A Direct Aspiration First-Pass Technique; ICH = intracranial hemorrhage; IQR = interquartile range; mTICI = modified TICI

Thrombectomy is now recommended as the standard of care for acute ischemic stroke with proximal large-vessel occlusion in the anterior circulation,¹ and successful revascularization is a major predictor of good outcome following endovascular therapy for acute large-vessel occlusions.² The Thrombolysis in Cerebral Infarction score is currently used to assess cerebral perfusion be-

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fore and after endovascular stroke treatment.³ Recent studies demonstrating the effectiveness of intracranial large-vessel reperfusion by using mechanical thrombectomy considered modified TICI (mTICI) 2b and mTICI 3 (complete reperfusion) to represent technical success,⁴ though some researchers have suggested that patients with mTICI 2b reperfusion have a poorer outcome than patients with complete reperfusion.⁵⁻⁷ Thus, the aim of our study was to determine how much functional outcome differed between patients achieving mTICI 2b and those with mTICI 3 reperfusion after thrombectomy for acute stroke in the anterior circulation.

MATERIALS AND METHODS

Inclusion Criteria

In this retrospective study, data were extracted from a bicentric prospective clinical registry (EFFECTS registry, Endovascular Treatment at Foch Hospital–Rothschild Foundation for Ischemic Stroke) of consecutive patients treated by mechanical thrombectomy for acute cerebral infarct between January 2012 and Novem-

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ber 2015. The local ethics committees approved the use of patient data for this retrospective analysis.

All patients referred for endovascular treatment of acute intracranial large-vessel occlusion involving the anterior circulation, with the exception of tandem and multifocal occlusions, were potentially included. Inclusion criteria were the following: 1) middle cerebral artery M1 or M2 segment and/or intracranial internal carotid artery occlusion; 2) intracranial artery occlusion and acute stroke confirmed on cerebral MRA and DWI, respectively; and 3) achievement of mTICI 2b or mTICI 3 reperfusion status after endovascular treatment by mechanical thrombectomy. Exclusion criteria were the following: 1) patients without baseline functional independence (modified Rankin Scale score of >2), and 2) patients with tandem occlusions, with >1 cerebral territory involved or a large ischemic score (DWI-ASPECTS < 6).

Patient Characteristics

Patient demographics, vascular risk factors, imaging findings, vital signs before treatment, severity of ischemic stroke, and clinical outcomes were collected prospectively with a structured questionnaire. Data on age, sex, cardiovascular risk factors (hypertension, dyslipidemia, diabetes, and smoking habits), time of symptom onset, National Institutes of Health Stroke Scale score at baseline and day 1, use of IV thrombolytics, and time of IV thrombolysis were collected. The Alberta Stroke Program Early CT Score on diffusion-weighted MR imaging was calculated by a neuroradiologist blinded to the results of the endovascular procedure. For each patient, the final mTICI score was retrospectively assessed by a neurointerventionalist (C.D.) blinded to both the first reader's scoring and the clinical outcome. A consensus was reached with an additional reader (M.P.) for cases with discrepant judgments. After an in-hospital work-up, stroke etiology was defined, according to the Trial of ORG 10172 in Acute Stroke Treatment classification.8

Endovascular Procedure

All patients were treated in a dedicated neuroangiography suite under general anesthesia or conscious sedation, after evaluation by a dedicated anesthesiology team. The thrombectomy device was chosen at the interventionalist's discretion, by using a stent retriever or A Direct Aspiration First-Pass Technique (ADAPT) in the first instance. Arterial occlusion site, time from symptom onset to groin puncture, procedure time, and time to reperfusion were recorded. Reperfusion results were reported by using the mTICI score and were defined as ranging from no reperfusion (mTICI 0) to complete reperfusion (mTICI 3), including partial reperfusion (mTICI 2). Partial perfusion occurs when the iodine contrast medium passes beyond the obstruction, opacifying the distal arterial bed but with a rate of entry of contrast material and/or its rate of clearance from the vascular bed slower than that in comparable areas not perfused by the previously occluded vessel. The contralateral cerebral angiography, often available for T-carotid occlusions, was used for comparison. In other cases, the arterial bed proximal to the occlusion could be used for comparisons. mTICI 2 was further divided into 2a and 2b as less than and greater than 50%, respectively.9 This definition is

different from the original TICI score in which 2a was defined as less than two-thirds perfusion of the distal territory, and 2b, as greater than two-thirds perfusion.¹⁰ Collateral arterial supply was assessed by using the capillary index score,¹¹ and patients were dichotomized into favorable and unfavorable collateral flow groups (capillary index score 2 or 3 and capillary index score 0–1, respectively). Periprocedural complications (embolization in a new territory, defined as an angiographic occlusion in a previously unaffected vascular territory observed on the angiogram after clot removal; arterial dissection or perforation; vasospasm; and subarachnoid hemorrhage) were also noted.

A Direct Aspiration First-Pass Technique Group

Patients in this treatment arm received aspiration thrombectomy by ADAPT by using the 5MAX ACE Reperfusion Catheter (Penumbra, Alameda, California) as frontline therapy. The detailed technical procedure has been published previously.¹² In brief, access was achieved through the femoral artery in compliance with the standard of care. A large-bore catheter was placed distally into the internal carotid artery to provide access for the 5MAX ACE aspiration catheter. Adhering to the instructions for use, we then performed aspiration by using the Penumbra Aspiration Pump (Penumbra, Alameda, California) in all cases. Angiography was performed following recovery to evaluate the flow rate. Steps were repeated if necessary until successful reperfusion to mTICI 2b-3 was achieved. The interventional neuroradiologist could, in case of reperfusion failure (mTICI < 2b) with ADAPT, use another thrombectomy device of the operator's choice (rescue therapy).

Stent-Retriever Group

Procedures were performed by using the Solitaire FR (Covidien, Irvine, California) or the Trevo device (Stryker, Kalamazoo, Michigan) via the femoral artery approach. Following the instructions for use of the stent retriever, we positioned a balloon catheter within the internal carotid artery to allow flow arrest during thrombus retrieval. The stent retriever was delivered through a microcatheter and deployed inside the thrombus. A control angiogram was performed to determine the immediate reperfusion status, and the device was left deployed for a minimum of 3 minutes. Subsequently, the device and microcatheter were slowly retrieved. A control angiogram was obtained to assess recanalization and reperfusion.^{13,14} This sequence was repeated until mTICI 2b or 3 flow (defined as successful reperfusion) was established. The interventional neuroradiologist could, in the case of reperfusion failure (mTICI < 2b) with the stent retriever, use another thrombectomy device of the operator's choice (rescue therapy).

Adjunctive Therapies

Use of complementary mechanical (intracranial angioplasty or stent placement) and/or pharmacologic treatment was recorded. Complementary pharmacologic treatments used were intra-arterial fibrinolysis (alteplase) or intravenous administration of abciximab (Reopro).

Table 1: Baseline characteristics, procedure details, and complications according to	0
reperfusion status ^a	

	Successful Rep		
	(mTICI 2b)	Complete (mTICI 3)	<i>P</i> Value
No. of patients	109	113	
Age (mean) (yr)	69.0 ± 15.9	68.9 ± 14.7	.95
Men	41 (37.6)	55 (48.7)	.096
Medical history			
Hypertension	63 (57.8)	70 (62.0)	.53
Diabetes	18 (16.5)	21 (18.6)	.69
Dyslipidemia	32 (29.4)	37 (32.7)	.59
Current smoking ^b	20 (20.0)	22 (20.4)	.95
NIHSS score (mean)	14.6 ± 6.3	13.7 ± 6.7	.30
Prestroke mRS \geq 1	11 (10.1)	12 (10.6)	.90
ASPECTS (median) (IQR)	8 (7–8)	8 (7–9)	.32
Occlusion site			
ICA	27 (24.8)	18 (15.9)	.18
MCA-M1	66 (60.5)	81 (71.7)	
MCA-M2	16 (14.7)	14 (12.4)	
TICI initial (1 vs 0)	10 (9.2)	9 (8.0)	.75
Favorable collateral flow ^c	79 (77.5)	97 (91.5)	.005
Etiology			
Cardioembolism	73 (67.0)	64 (56.7)	.020
Large-artery atherosclerosis	5 (4.6)	18 (15.9)	
Other or undetermined	31 (28.4)	31 (27.4)	
Previous use of IV thrombolysis	77 (70.6)	73 (64.6)	.34
General anesthesia	36 (33.0)	34 (30.1)	.64
Onset to reperfusion time (median) (IQR) (min)	310 (260–361)	285 (225–340)	.021
Onset-to-groin puncture	251 (208–300)	237 (191–292)	.11
Groin puncture to reperfusion (median) (IQR) (min)	50 (31–68)	40 (24–58)	.018
Total number of passes (median) (IQR)	2 (1–3)	1 (1–2)	.0002
Periprocedural complication	13 (11.9)	9 (8.0)	.32
Adjunctive treatment	7 (6.4)	3 (2.7)	.21

^a Values expressed as number (percentage) unless otherwise indicated.

^b Fourteen missing data (9 in mTICI 2b and 5 in mTICI 3).

^c Fourteen missing data (7 in mTICI 2b and 7 in mTICI 3).

Follow-Up and Outcome

All patients underwent cross-sectional imaging (CT or MR imaging) within 18–24 hours after the procedure. Intracranial hemorrhage (ICH) was classified according to the European Cooperative Acute Stroke Study (ECASS) criteria.¹⁵ Patients were evaluated 24 hours after the procedure by using the NIHSS, and "symptomatic intracranial hemorrhage" was defined as any intracerebral hemorrhage with an increase of at least 4 NIHSS points within 24 hours, or resulting in death. The mRS at 90 days was assessed by trained research nurses unaware of the study group assignments during face-to-face interviews or via telephone conversations with the patients, their relatives, or their general practitioners.

The primary study outcome was the achievement of an mRS score of 0-2 at 3 months (favorable outcome). Secondary outcomes included excellent outcome (defined as an mRS score of 0-1), any ICH, all-cause mortality at 90 days, and procedural complications. Furthermore, attention was given to the type of endovascular procedure performed for all patients.

Statistical Analysis

Quantitative variables are expressed as means \pm SD or medians (interquartile range [IQR]), and categoric variables are expressed as numbers (percentages). Normality of distributions was assessed by using histograms and the Shapiro-Wilk test. Bivariate

comparisons between complete and mTICI 2b reperfusion groups were made by using the χ^2 test or Fisher exact test for categoric variables, the Cochran-Armitage Trend test for ordinal variables, and the Student t test or Mann-Whitney U test for quantitative variables as appropriate. We assessed the heterogeneity in the relationship between successful reperfusion status and each outcome (excellent outcome, favorable outcome, 90-day mortality, and any ICH) across the 2 centers by using the Breslow-Day test. Comparisons in outcomes between the 2 successful reperfusion groups were further adjusted for the center and prespecified confounders regarding prior evidence of an association with clinical outcome (namely age, diabetes, admission NIHSS score, site of occlusion, collateral flow, etiology, previous IV thrombolysis, and onset to reperfusion time) by using logistic regression models.7 An additional adjustment for ICH occurrence was performed for comparison in functional outcomes (excellent and favorable). To avoid case deletion in multivariable analyses due to missing data on the collateral favorable covariate (missing in 14 patients), we imputed missing data under a missing-at-random assumption by using a regression-switching approach

(chained equation with m = 10 imputations obtained by using the R statistical software, Version 3.03; http://www.r-project. org/).^{16,17} Imputation procedures were performed by using all variables listed in Table 1 and each study outcome. Multiple imputed datasets were combined by using the Rubin rules.¹⁸ Unadjusted and adjusted odds ratios for reaching each outcome were calculated by using mTICI 2b as the reference group. Statistical testing was performed at the 2-tailed α level of .05. Data were analyzed by using SAS software, Version 9.3 (SAS Institute, Cary, North Carolina).

RESULTS

A total of 593 consecutive patients with an acute internal carotid artery or middle cerebral artery occlusion were treated by endovascular therapy at 2 comprehensive stroke centers (Fig 1). Of these, 92 with no baseline MR imaging, 153 with DWI-ASPECTS of <6, 95 with substantial perfusion on the baseline angiogram (mTICI \geq 2), and 20 with failure of endovascular treatment (final mTICI<2b) were excluded. Overall, 233 patients achieved successful reperfusion (mTICI \geq 2b) and were included in the study. Two initially included patients with intracranial stenosis and early arterial reocclusion were excluded, and 9 patients were lost to follow-up, resulting in a final study sample size of 222 patients. Among them, 113 (50.9%) achieved mTICI 3 reperfusion and 109

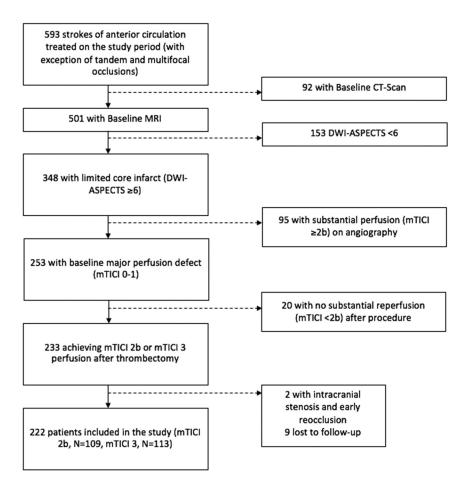


FIG 1. Flow chart of the study.

(49.1%) achieved mTICI 2b reperfusion. The median time of successful reperfusion from symptom onset was 291 minutes (IQR, 240–355).

Baseline characteristics, including time from onset to reperfusion, number of passes to achieve reperfusion, and periprocedural complications are shown in Table 1, according to successful reperfusion status. There was no significant difference in age, vascular risk factors, admission NIHSS score, ASPECTS, or fibrinolysis administration between the 2 reperfusion groups. However, patients with complete reperfusion (mTICI 3) more often had favorable collateral flow and large-artery atherosclerosis etiology, together with a lower onset-to-reperfusion time than patients with mTICI 2b reperfusion (all P < .05). The number of total passes to achieve reperfusion was higher in the mTICI 2b group (median, 2; interquartile range, 1-3, 1-9) versus (median, 1; interquartile range, 1-2, 1-8) in the mTICI 3 group (P = .0002). Procedural complications (emboli into new territories, procedure-related arterial dissection or perforation, subarachnoid hemorrhage, and vasospasm) occurred in 9 (8%) patients with complete reperfusion and in 13 (11.9%) patients with mTICI 2b reperfusion (P = .32).

ADAPT was used in the first instance in 110 patients (49.5%), among whom switching to the stent-retriever technique occurred in 12 patients (11%). The stent-retriever technique was used in the first instance in 112 patients (50.5%), and switching to ADAPT occurred in 3 (11.9%) of these. No difference was found regarding the use of adjunctive treatment.

The distribution of 90-day mRS according to successful reperfusion status is shown in Fig 2. Favorable outcome $(mRS \le 2)$ was achieved more often in patients with complete reperfusion than in those with mTICI 2b reperfusion (71.7% versus 50.5%, P = .001). A similar difference was found when considering excellent outcome (mRS < 2, Table 2). In addition, patients with complete reperfusion had a nonsignificantly lower mortality rate (8.9% versus 16.5%, P = .086) and a lower ICH rate (23.0% versus 45.0%, P < .001) compared with those with mTICI 2b reperfusion. Regarding the ECASS classification, HI1, HI2, PH1, and PH2 types occurred respectively in 20, 4, 1, and 1 patients with complete reperfusion and 22, 17, 4, and 6 patients with mTICI 2b reperfusion. Symptomatic ICH occurred in only 1 patient (0.9%) with complete reperfusion and in 4 patients (3.7%) with mTICI 2b reperfusion.

We found no significant heterogeneity in the impact of successful reperfusion status on outcomes across the 2 centers (All *P* values for heterogeneity, >.26). After we adjusted for center and baseline between-group differences, mTICI

3 status remained significantly associated with an increased probability of excellent and favorable outcomes and a decreased probability of any ICH (Table 2). When comparison in functional outcomes was further adjusted for ICH, the differences were not modified; the adjusted ORs of excellent and favorable outcomes for complete relative to mTICI 2b reperfusion groups were, respectively, 2.55 (95% CI, 1.23–5.26) and 2.78 (95% CI, 1.28–6.08).

DISCUSSION

Our study shows that patients with complete reperfusion after endovascular treatment by using new-generation mechanical thrombectomy devices have a better outcome than those who achieve a mTICI 2b reperfusion. To our knowledge, this is the first study to specifically compare the impact of mTICI 2b versus mTICI 3 on functional outcome at 3 months, though it has already been shown that patients with TICI 3 have a lower NIHSS score at discharge than those with TICI 2b (the original TICI definition was used in this article).⁶ One recent study also suggested that patients with mTICI 3 had better functional outcomes than those with mTICI 2b, though significance was only achieved in univariate analysis.⁷

Recent controlled trials demonstrating the efficiency and safety of mechanical thrombectomy⁴ consider that technical success of the endovascular procedure is achieved when mTICI 2b or 3 reperfusion is obtained. According to a recent meta-analysis of individual data about endovascular therapy, this threshold is

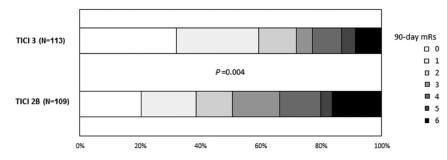


FIG 2. Distribution of modified Rankin Scale scores at 90 days according to successful reperfusion status.

Table 2: Outcomes according to successful reperfusion status ^a										
		Complete								
	mTICI 2b	(mTICI 3)			h	L				
	(n = 109)	(n = 113)	OR (95% CI)	Р	OR (95% CI) ⁶	Р ^ь				
Excellent outcome	42 (38.5)	67 (59.3)	2.32 (1.35–3.98)	.002	2.98 (1.46–6.06)	.0037				
Favorable outcome	55 (50.5)	81 (71.7)	2.49 (1.42–4.33)	.001	3.34 (1.56–7.11)	.002				
90-Day mortality	18 (16.5)	10 (8.9)	0.49 (0.21–1.12)	.086	NR	NR				
Any ICH	49 (45.0)	26 (23.0)	0.37 (0.20–0.65)	<.001	0.33 (0.16–0.64)	.001				
HII	22 (20.2)	20 (17.7)	-	-	-	-				
HI2	17 (15.6)	4 (3.5)	-	-	-	-				
PH1	4 (3.7)	1 (0.9)	-	-	-	_				
PH2	6 (5.5)	1 (0.9)	-	-	-	-				

Note:----NR indicates not reportable regarding the small number of events; OR, odds ratio.

^a Excellent outcome was defined as 90-day mRS \leq 1, and favorable outcome, as 90-day mRS \leq 2. ORs were calculated using mTICI 2b reperfusion as a reference.

^b Adjusted on center, age, diabetes, admission NIHSS score, prior use of IV thrombolysis, site of occlusion, favorable collateral flow, etiology, and onset to reperfusion time using multivariable logistic regression models (after a mean of 10 imputations to handle missing data on favorable collateral flow).

reached in 71% of cases in the trials mentioned above.⁴ After a clinical study showing a trend to more favorable outcomes for patients with mTICI 3 compared with mTICI 2b but with no statistically significant difference,13 a consensus statement defined the mTICI 2b threshold as the target angiographic end point for technical success of mechanical thrombectomy.¹⁴ Since the MERCI trials era, it is well-accepted that greater degrees of recanalization are associated with an increased rate of favorable functional outcome.¹⁹ In the Interventional Management of Stroke (IMS) III study,⁵ though performed during the pre-stentretriever period, the authors reported that the proportions of patients with mRS \leq 2 at 90 days (primary outcome) increased with greater reperfusion. However, these studies had a lack of distinction between the various degrees of partial recanalization and the use of the Thrombolysis in Myocardial Infarction score. Currently, the mTICI score is widely used in the literature to assess cerebral reperfusion following stroke therapy.³ Indeed, it has been demonstrated to better correlate with clinical outcome than the Thrombolysis in Myocardial Infarction score.¹⁹ The current definition of the TICI 2b score (the modified TICI 2b) is the version introduced by the IMS investigators,²⁰ which is simpler and shows better interrater agreement than the original definition.

Etiologies

We observed in our retrospective cohort that patients with a stroke of atherothrombotic origin achieved complete reperfusion with a higher frequency than those with a stroke from other causes (mainly cardioembolism). In the literature or in recent trials demonstrating the efficiency of thrombectomy, limited data are available about recanalization or reperfusion rates according to stroke etiologic sub-

Rate of Hemorrhage

In our cohort, ICH was less frequent in patients with mTICI 3 than in those with mTICI 2b (23.0% versus 45.0%, P < .001). Both the time from symptom onset to reperfusion (median, 310 versus 285 minutes; P = .021) and the procedure time (median, 50 versus 40 minutes; P = .018) were longer in the mTICI 2b group. Delayed reperfusion and longer procedural times are independently associated with occurrence of intracranial hemorrhage in patients with large-vessel occlusion undergoing endovascular reperfusion therapy of stroke.²² These data are supported by experimental evidence.²³ Mechanisms involved are multiple, mainly involving blood-brain barrier disruption.²⁴ However, our results may be affected by the low frequency of symptomatic ICH in our study, which can be explained by our inclusion criteria, excluding patients with large-core infarcts, known to have a higher risk of ICH.

Baseline Collateral Status and Reperfusion Rate

Baseline collateral status varies in patients with acute ischemic stroke. Most patients in this study had good collateral flow. This is related to the selection of patients with proximal occlusion and both a limited clinical deficit and limited infarct core who likely have good collateral circulation.²⁵ Nevertheless, we observed that patients achieving complete reperfusion had better collateral flow on baseline angiograms than those who did not. This finding is consistent with the literature, and a recent meta-analysis showed that good pretreatment collateral status may enhance the rate of both recanalization and reperfusion in patients with stroke receiving mechanical revascularization therapy.²⁶ However, mecha-

type.² Further studies may explore this concern, and clot composition and mechanical characteristics may be a clue to explain this difference.²¹

Time from Symptom Onset and Procedure Time

Patients achieving mTICI 2b reperfusion had longer times from symptom onset to reperfusion than those achieving mTICI 3 reperfusion. Indeed, the procedure time was longer and the total number of passes to achieve reperfusion was higher in the mTICI 2b group than in the mTICI 3 group. This higher number of passes was not associated with a higher rate of periprocedural complications or adjunctive therapies in this study. After adjustment for differences in time to reperfusion, mTICI 3 remained a predictor of better clinical outcome than mTICI 2b reperfusion. The onset-to-reperfusion time in our study (297.5 minutes) is in accordance with those reported in recent trials evaluating thrombectomy, calculated as 285 minutes in a recent meta-analysis.4

nisms of the effects of good collateral flow on successful revascularization remain poorly understood. One explanation may be that retrograde filling would allow neuroprotective agents (intrinsic or extrinsic) to access the clot.²⁷ A mechanical effect of collateral flow facilitating clot removal may also provide an explanation.

Limitations

Our study has the limitations inherent in its retrospective design, with a relatively small sample size extracted from 2 centers. Bias related to missing data on collateral flow (n = 14) cannot be completely ruled out because multiple imputation procedures replacing missing values with a set of plausible values were performed under a missing-at-random assumption. No core laboratory has adjudicated MR imaging/MRA and angiographic findings, though mTICI, DWI-ASPECTS, and clinical outcomes were all assessed in a blinded manner.

Among baseline characteristics, we observed more terminal carotid occlusion in the mTICI 2b group, though the difference was not significant. Intuitively, thrombus burden may be higher in this group, resulting in a lower complete reperfusion rate. Moreover, mTICI 2b reperfusion occurred in a heterogeneous group of patients with various parenchymal defects regardless of their clinical significance. Indeed, a patient presenting with a defect in the right prefrontal area will be categorized as mTICI 2b, as will be a patient with a defect in the right central area. However, their respective clinical outcomes may not be the same. Similarly, a parenchymal defect in the same area but located in the left or right hemisphere may have a distinct clinical outcome. Further research should be performed to analyze this heterogeneous subgroup of mTICI 2b, regarding the complex anatomy of the MCA and its territories of supply, and to take into account the lateralization of the defect as well.

Second, we did not consider here the TICI 2c subcategory,²⁸ defined by near-complete perfusion except for slow flow or distal emboli in a few distal cortical vessels. However, Alme-khlafi et al²⁸ reported similar clinical outcomes between TICI 2c and TICI 3.

CONCLUSIONS

We found that patients with mTICI 3 reperfusion achieve better clinical outcomes and less hemorrhagic transformation than patients achieving mTICI 2b reperfusion. Therefore, mTICI 3 may be considered as representing the optimal technical success in reperfusion and a target end point for the neurointerventionalist. Future thrombectomy devices or techniques should focus on achieving mTICI 3 reperfusion. Our results, though requiring confirmation in further studies, suggest considering patients with mTICI 2b and mTICI 3 separately in future prospective studies evaluating the effectiveness of mechanical thrombectomy. Moreover, other potential areas for future research could include a subgroup analysis of the recent major stroke trials or an analysis of one of the major stroke data bases (such as Get With The Guidelines Stroke Registry of the American Heart Association), with comparison of mRS outcomes between patients with mTICI 2b versus mTICI 3 reperfusion.

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REFERENCES

- Powers WJ, Derdeyn CP, Biller J, et al; American Heart Association Stroke Council. 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;46:3020-35 CrossRef Medline
- 2. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. *Stroke* 2007;38:967–73 CrossRef Medline
- Fugate JE, Klunder AM, Kallmes DF. What Is meant by "TICI"? AJNR Am J Neuroradiol 2013;34:1792–97 CrossRef Medline
- Goyal M, Menon BK, van Zwam WH, et al; HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387:1723–31 CrossRef Medline
- Broderick JP, Palesch YY, Demchuk AM, et al; Interventional Management of Stroke (IMS) III Investigators. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. N Engl J Med 2013;368:893–903 CrossRef Medline
- Kleine JF, Wunderlich S, Zimmer C, et al. Time to redefine success? TICI 3 versus TICI 2b recanalization in middle cerebral artery occlusion treated with thrombectomy. *J NeuroInterventional Surg* 2016 Feb 17. [Epub ahead of print] CrossRef Medline
- Linfante I, Starosciak AK, Walker GR, et al. Predictors of poor outcome despite recanalization: a multiple regression analysis of the NASA registry. J Neurointerv Surg 2016;8:224–29 CrossRef Medline
- Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke: definitions for use in a multicenter clinical trial—TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35–41 CrossRef Medline
- Tomsick T, Broderick J, Carrozella J, et al; Interventional Management of Stroke II Investigators. Revascularization results in Interventional Management of Stroke II Trial. AJNR Am J Neuroradiol 2008;29:582–87 CrossRef Medline
- Higashida RT, Furlan AJ, Roberts H, et al; Technology Assessment Committee of the American Society of Interventional and Therapeutic Neuroradiology; Technology Assessment Committee of the Society of Interventional Radiology. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke 2003;34:e109–37 CrossRef Medline
- Al-Ali F, Jefferson A, Barrow T, et al. The capillary index score: rethinking the acute ischemic stroke treatment algorithm—results from the Borgess Medical Center Acute Ischemic Stroke Registry. *J Neurointerv Surg* 2013;5:139–43 CrossRef Medline
- Turk AS, Frei D, Fiorella D, et al. ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy. J Neurointerv Surg 2014;6:260-64 CrossRef Medline
- Yoo AJ, Simonsen CZ, Prabhakaran S, et al; Cerebral Angiographic Revascularization Grading Collaborators. Refining angiographic biomarkers of revascularization: improving outcome prediction after intra-arterial therapy. *Stroke* 2013;44:2509–12 CrossRef Medline
- 14. Zaidat OO, Yoo AJ, Khatri P, et al; Cerebral Angiographic Revascularization Grading (CARG) Collaborators, STIR Revascularization

working group, STIR Thrombolysis in Cerebral Infarction (TICI) Task Force. **Recommendations on angiographic revascularization** grading standards for acute ischemic stroke: a consensus statement. *Stroke* 2013;44:2650–63 CrossRef Medline

- Hacke W, Kaste M, Fieschi C, et al. Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke: the European Cooperative Acute Stroke Study (ECASS). *JAMA* 1995;274:1017–25 CrossRef Medline
- Buuren S, Groothuis-Oudshoorn K. Mice: multivariate imputation by chained equations in R. J Stat Softw 2011;45:1–67
- 17. R Core Team. R Language and Environment for Statistical Computing. R Foundation for Statistical Computing:Vienna, Austria, 2013. http://www.R-project.org
- Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: Wiley; 1987
- Fields JD, Lutsep HL, Smith WS, et al; MERCI Multi MERCI Investigators. Higher degrees of recanalization after mechanical thrombectomy for acute stroke are associated with improved outcome and decreased mortality: pooled analysis of the MERCI and Multi MERCI trials. *AJNR Am J Neuroradiol* 2011;32:2170–74 CrossRef Medline
- Khatri P, Hill MD, Palesch YY, et al; Interventional Management of Stroke III Investigators. Methodology of the Interventional Management of Stroke (IMS) III Trial. Int J Stroke 2008;3:130–37 CrossRef Medline
- 21. Dargazanli C, Rigau V, Eker O, et al. **High CD3+ cells in intracranial thrombi represent a biomarker of atherothrombotic stroke.** *PLoS One* 2016;11:e0154945 CrossRef Medline

- 22. Kass-Hout T, Kass-Hout O, Sun CH, et al. Longer procedural times are independently associated with symptomatic intracranial hemorrhage in patients with large vessel occlusion stroke undergoing thrombectomy. *J Neurointerv Surg* 2016 Feb 1. [Epub ahead of print] CrossRef Medline
- 23. Jickling GC, Liu D, Stamova B, et al. Hemorrhagic transformation after ischemic stroke in animals and humans. J Cereb Blood Flow Metab 2014;34:185–99 CrossRef Medline
- 24. Mokin M, Kan P, Kass-Hout T, et al. Intracerebral hemorrhage secondary to intravenous and endovascular intraarterial revascularization therapies in acute ischemic stroke: an update on risk factors, predictors, and management. *Neurosurg Focus* 2012;32:E2 CrossRef Medline
- 25. Hakimelahi R, Vachha BA, Copen WA, et al. Time and diffusion lesion size in major anterior circulation ischemic strokes. *Stroke* 2014;45:2936-41 CrossRef Medline
- 26. Leng X, Fang H, Leung TWH, et al. Impact of collateral status on successful revascularization in endovascular treatment: a systematic review and meta-analysis. *Cerebrovasc Dis* 2016;41:27–34 CrossRef Medline
- 27. Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. Arch Neurol 1998;55:1475–82 CrossRef Medline
- Almekhlafi MA, Mishra S, Desai JA, et al. Not all "successful" angiographic reperfusion patients are an equal validation of a modified TICI scoring system. *Interv Neuroradiol* 2014;20:21–27 CrossRef Medline