Operator Versus Core Lab Adjudication of Reperfusion After Endovascular Treatment of Acute Ischemic Stroke

Operator Versus Core Lab Adjudication of Reperfusion After Endovascular Treatment of Acute Ischemic Stroke

Guang Zhang, MD; Kilian M. Treurniet, MD, MSc; Ivo G.H. Jansen, MD; Bart J. Emmer, MD, PhD; Rene van den Berg, MD, PhD; Henk A. Marquering, PhD; Maarten Uyttenboogaart, MD, PhD; Sjoerd F.M. Jenniskens, MD; Yvo B.W.E.M. Roos, MD, PhD; Pieter Jan van Doormaal, MD; Adriaan C.G.M. van Es, MD, PhD; Aad van der Lugt, MD, PhD; Jan-Albert Vos, MD, PhD; Geert J. Lycklama à Nijeholt, MD, PhD; Wim H. van Zwam, MD, PhD; Huaizhang Shi, MD, PhD; Albert J. Yoo, MD, PhD; Diederik W.J. Dippel, MD, PhD; Charles B.L.M. Majoie, MD, PhD; for the MR CLEAN Registry Investigators*

***Background and Purpose*—**The modified Treatment In Cerebral Ischemia (mTICI) score is the standard method to quantify the degree of reperfusion after endovascular treatment in acute ischemic stroke. In clinical practice, it is commonly assessed by local operators after the procedure. In clinical trials and registries, mTICI is evaluated by an imaging core lab. The aim of this study was to compare operator mTICI with core lab mTICI scores in patients included in the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) Registry.

***Methods*—**All patients with an intracranial carotid or middle cerebral artery occlusion with anteroposterior and lateral digital subtraction angiography runs were included. Operators determined the mTICI score immediately after endovascular treatment. Core lab neuroradiologists were blinded to clinical characteristics and assessed mTICI scores based on pre- and postintervention digital subtraction angiography. The agreement between operator and core lab mTICI scores and their value in the prediction of outcome (score on modified Rankin Scale at 90 days) was determined.

***Results*—**In total, 1130 patients were included. The proportion of agreement between operator and core lab mTICI score was 56% (95% CI, 54%–59%). In 33% (95% CI, 31%–36%), mTICI was overestimated by operators. Operators reported a higher rate of successful reperfusion than the core lab (77% versus 67%; difference 10% [95% CI, 6%–14%]; *P*<0.001). In 252 (33%) of 763 patients scored as incomplete reperfusion by the core lab (mTICI <3), the local read was mTICI 3. Multivariable logistic regression models containing either core lab scored or operator scored successful reperfusion predicted outcome on the full (C statistic of both models: 0.76) or dichotomized modified Rankin Scale (modified Rankin Scale, 0–2; C statistic of both models: 0.83) equally well.

***Conclusions*—**Operators tend to overestimate the degree of reperfusion compared with the core lab although this does not affect the accuracy of outcome prediction. **(*Stroke*. 2018;49:2376-2382. DOI: 10.1161/STROKEAHA.118.022031.)**

Key Words: infarction, middle cerebral artery ■ logistic models ■ reperfusion ■ stroke ■ thrombectomy

Endovascular thrombectomy (EVT) has become standard care for patients with acute ischemic stroke caused by large vessel occlusion in the anterior circulation.[1–5] Estimation of reperfusion in patients who undergo EVT is a means to evaluate the immediate effect of therapy and is strongly associated with outcome. To quantify the degree of reperfusion, the modified Treatment in Cerebral Ischemia (mTICI) score is widely applied.[6] Its categories span from no reperfusion (grade 0) to complete reperfusion (grade 3), and mTICI 2b to 3 is considered successful reperfusion after EVT in acute ischemic stroke trials.[7]

It has been shown that mTICI 2b to 3 is an accurate predictor of functional independence and also a pivotal biomarker for comparing the efficacy of different techniques

Received May 1, 2018; final revision received July 2, 2018; accepted July 27, 2018.

From the Department of Neurosurgery, the First Affiliated Hospital of Harbin Medical University, China (G.Z., H.S.); Departments of Radiology and Nuclear Medicine (G.Z., K.M.T., I.G.H.J., B.J.E., R.v.d.B., C.B.L.M.M.), Biomedical Engineering and Physics (H.A.M.), and Neurology (Y.B.W.E.M.R.), Academic Medical Center, Amsterdam, the Netherlands; Department of Neurology, University Medical Center Groningen, the Netherlands (M.U.); Department of Radiology, Radboud University Medical Center, Nijmegen, the Netherlands (S.F.M.J.); Departments of Radiology (P.J.v.D.) and Neurology (D.W.J.D.), Erasmus MC University Medical Center, Rotterdam, the Netherlands; Department of Radiology, Sint Antonius Hospital, Nieuwegein, the Netherlands (J.-A.V.); Department of Radiology, MC Haaglanden, the Hague, the Netherlands (G.J.L.à.N.); Department of Radiology, Maastricht University Medical Center, the Netherlands (W.H.v.Z.); and Division of Neurointervention, Texas Stroke Institute, Plano (A.J.Y.).

*A list of all MR CLEAN Registry Investigators is given in the Appendix.

Guest Editor for this article was Donna M. Ferriero, MD, MS.

The online-only Data Supplement is available with this article at https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.118.022031.

Correspondence to Guang Zhang, MD, Department of Radiology and Nuclear Medicine, Academic Medical Center, PO Box 22660, 1100 DD, Amsterdam, the Netherlands. Email g.zhang@amc.uva.nl

***Stroke* is available at https://www.ahajournals.org/journal/str** **DOI: 10.1161/STROKEAHA.118.022031**

or devices.[7,8] In clinical practice, mTICI score is commonly assessed by operators after EVT. In major clinical trials and some registries, mTICI score assessment is also performed by imaging core laboratories.[9] Core lab assessment is considered as gold standard because of its rigor. It remains unclear to what degree operator bias exists in the estimation of mTICI. In particular, operators may tend to overestimate mTICI score because they evaluate their own work. Such an overestimation could lead to unreliable results in studies without core lab adjudication of reperfusion.

The aim of this study was to compare operator mTICI with core lab mTICI scores to gain an insight into the agreement between the operator and core lab mTICI score assessment.

Methods

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

All patients undergoing EVT (defined as entry into the angiography suite and undergoing arterial puncture) for acute ischemic stroke from March 16, 2014, to June 15, 2016, in the 16 MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) centers in the Netherlands have been registered in the MR CLEAN Registry. The MR CLEAN Registry is a prospective national multicenter registry of all patients with acute ischemic stroke who underwent EVT (defined as entry into the angiography suite and undergoing arterial puncture) after the MR CLEAN, with core lab evaluation of all imaging data.[10] The MR CLEAN Registry was approved by the ethics committee of the Erasmus University Medical Center, Rotterdam, the Netherlands (MEC-2014–235) and therefore by the research board of each participating center. At the University Medical Center Utrecht, approval to participate in the study was obtained from their own research board and ethics committee.

Only patients with an intracranial carotid artery or middle cerebral artery (M1, M2, M3) occlusion demonstrated by computed tomographic angiography with both anteroposterior and lateral digital subtraction angiography (DSA) runs were included in this post hoc analysis.

mTICI Score Assessment

The mTICI was scored as follows[11]: grade 0, no perfusion; grade 1, antegrade reperfusion past the initial occlusion, but limited distal branch filling with little or slow distal reperfusion; grade 2a, antegrade reperfusion of less than half of the downstream vascular territory; grade 2b, antegrade reperfusion of half or more (but less than complete) of the downstream vascular territory; grade 3, complete antegrade reperfusion of the downstream vascular territory, with absence of visualized occlusion in all distal branches. Successful reperfusion was defined as mTICI 2b to 3.

Local operators from the 16 intervention centers determined the mTICI score using a standard case report form directly after the procedure. The core lab (consisting of 8 experienced neuroradiologists who were blinded to clinical characteristics) assessed pre- and postintervention DSA mTICI scores using a similar case report form.

Outcome Measures

Functional outcome was determined at ≈90 days after treatment with the modified Rankin Scale (mRS), which ranges from 0 no symptoms to 6 death. Functional independence was defined as an mRS score of 0 to 2.

Statistical Analysis

To assess agreement, the proportion of agreement between operator and core lab mTICI with its 95% CI determined with Wilson score method was assessed.[12]

The association of both operator and core lab mTICI with functional outcome was assessed with multivariable ordinal logistic regression (shift analysis) adjusted for age, sex, baseline National Institutes of Health Stroke Scale, prestroke mRS, Alberta Stroke Program Early CT Score, collateral status, use of intravenous thrombolysis, and the time from onset to reperfusion and expressed as an adjusted common odds ratio (OR) for a shift on the mRS toward good outcome. Multivariable binary logistic regression (with adjustment for the same variables) was used to determine the association between successful reperfusion and functional independence. The association was expressed with an adjusted OR. To estimate the difference between operator and core lab adjudication of successful reperfusion, the χ^2 test was used to estimate the difference between operator and core lab adjudication of successful reperfusion. The C statistic was estimated to compare the discriminatory power of core lab and operator scored successful reperfusion for full-scale outcome and functional independence. All analyses were performed using Empower (R) (http://www.empowerstats.com, X & Y Solutions Inc, Boston, MA) and R (R version 3.4.4, The R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org).

Missing Data

For more precise effect estimation with logistic regression, multiple imputation for missing data was performed with the Hmisc package in R (v4.1-1). The following variables were used for imputation: operator and core lab mTICI score, mRS, age, sex, baseline National Institutes of Health Stroke Scale score, glucose level, collateral status, diabetes mellitus, hypertension, previous myocardial infarction, previous stroke, pre-mRS, hypercholesterolemia, atrial fibrillation, peripheral arterial disease, smoking, medication use (antiplatelets, statins, anticoagulants, and antihypertensives), use of intravenous thrombolysis, if transferred from other hospital, blood pressure, baseline Alberta Stroke Program Early CT Score, occlusion location, thrombocyte, type of anesthesia, international normalized ratio, time from symptom onset to start of EVT, time from onset to computed tomographic scan, time from symptom onset to successful reperfusion or last contrast bolus, and National Institutes of Health Stroke Scale score after 24 to 48 hours. Data after imputation were only used for the regression analyses and not for the descriptive analyses.

Results

In the MR CLEAN Registry, 1628 patients were registered between the March 16, 2014, and the June 15, 2016. For the current analysis, 328 patients were excluded because of an occlusion of the posterior circulation, M4 or anterior cerebral artery occlusion or missing lateral DSA images (see Figure I in the online-only Data Supplement). A total of 1300 patient with complete lateral and anteroposterior DSA runs after EVT were included. Of these 1300 patients, the mean age was 68.6±14.5 years and 598 (46.0%) were women. In 695 (53.5%) patients, occlusions were located in the left hemisphere. Occlusions on initial vessel imaging involved intracranial carotid artery in 252 (21.0%) patients, M1 in 660 (54.9%) patients, M2 in 224 (18.6%), and M3 in 31(2.6%) patients. Thirty-five patients with occlusions demonstrated by computed tomographic angiography but without occlusion on DSA imaging were also included. The median admission National Institutes of Health Stroke Scale score was 16 (interquartile range, 11–20). Nine hundred ninety-nine (76.8%) patients received intravenous alteplase therapy before EVT. The mean time from stroke onset to groin puncture was 222±87 minutes. Further baseline characteristics of all included patients are presented in

Table 1. Patient Characteristics

Variable	n=1300
Age, mean (SD), y	68.6 (14.5)
Female, n (%)	598 (46.0%)
Diabetes mellitus, n (%)	230 (17.8%)
Hypertension, n (%)	647 (50.5%)
Atrial fibrillation, n (%)	279 (21.8%)
Intracranial arterial occlusion, n (%)	
Intracranial ICA	252 (21.0%)
M1 middle cerebral artery segment	660 (54.9%)
M2 middle cerebral artery segment	224 (18.6%)
M3 middle cerebral artery segment	31 (2.6%)
None*	35 (2.9%)
Collaterals grade, n (%)	
0	84 (7.0%)
1	390 (32.3%)
2	466 (38.6%)
3	268 (22.2%)
NIHSS score, median (interquartile range)	16 (11–20)
ASPECTS score, median (interquartile range)	9 (7–10)
Previous use of intravenous thrombolysis	999 (76.8%)
Mean time from onset to groin puncture (SD), min	222 (87)
Mean time from onset to reperfusion (SD), min	280 (93)

ASPECTS indicates Alberta Stroke Program Early CT Score; CTA, computed tomographic angiography; DSA, digital subtraction angiography; ICA, intracranial carotid artery; and NIHSS, National Institute Health Stroke Scale.

*Patients with occlusions demonstrated by CTA before intervention but occlusions were not found in DSA imaging were also included.

Table 1. In 118 of 1300 (9%) of patients, either an operator or core lab mTICI score was missing. Functional outcome was missing for 8.2% of patients. The mean percentage of missing variables for the baseline characteristics ranged from 0% to 32.8% (mean, 4.2%).

Distribution of mTICI in MR CLEAN Registry

In 1182 patients, mTICI scores assessed by both operator and core lab were available (Figure I in the online-only Data Supplement). The distribution of operator and core lab mTICI score is shown in Figure 1. According to the operator assessment, a total of 916 of 1182 (77%) patients were scored as successful reperfusion; 46.3% of these patients achieved functional independence at 90 days. Core lab adjudication revealed that successful reperfusion was scored in 796 of 1182 (67%) patients; 48.1% of these patients achieved functional independence. Operators reported a higher rate of successful reperfusion than the core lab (77% versus 67%; difference 10% [95% CI, 6%–14%]; P<0.001).

Disagreement Between Operator and Core Lab mTICI

The overall proportion of agreement between operator and core lab mTICI scores was 56% (95% CI, 54%–59%). In 33% (95% CI, 31%–36%), the mTICI score was overestimated by operators compared with core lab assessment and in 10% (95% CI, 9%–12%) underestimated. Of the 386 patients with core lab scores 0 to 2a, 158 (41%) were overestimated to 2b to 3 by the local operator. Furthermore, in 252 (33%) of the 763 patients where the core lab scored incomplete reperfusion (mTICI <3), the local score was mTICI 3. The percentage of operator's overestimation was 28% (40 of 143) for score 0, 65% (22 of 34) for 1, 64% (134 of 209) for 2a, and 52% (198 of 377) for 2b (Figure 2). Overestimation was more common in patients with M2 and M3 occlusions (40% and 43%, respectively, compared with 31% and 34% for intracranial carotid artery and M1).

Prediction of Clinical Outcome: Operator Versus Core Lab mTICI

The distribution of mRS for each mTICI grade was shown in Figure 3. The proportion of functional independence was similar in patients with operator and core lab successful reperfusion scores (46.3% versus 48.1%; P=0.482). In patients with successful reperfusion scored by the local operator but a core lab mTICI score of 0 to 2a, the proportion of functional independence was 34% (51 of 151). However, this proportion in patients with both operator and core lab mTICI 2b to 3 was 49% (334 of 680).

Successful reperfusion assessed by the operator was associated with outcome both on full-scale mRS (adjusted common OR, 3.40 [95% CI, 2.58–4.48]) and functional independence (adjusted OR, 4.33 [95% CI, 2.94–6.39]). Similar associations were found for core lab scored mTICI; patients with successful reperfusion had a lower mRS at 90 days compared with those with unsuccessful reperfusion (adjusted common OR, 2.89 [95% CI, 2.28–3.68]) and a higher likelihood to

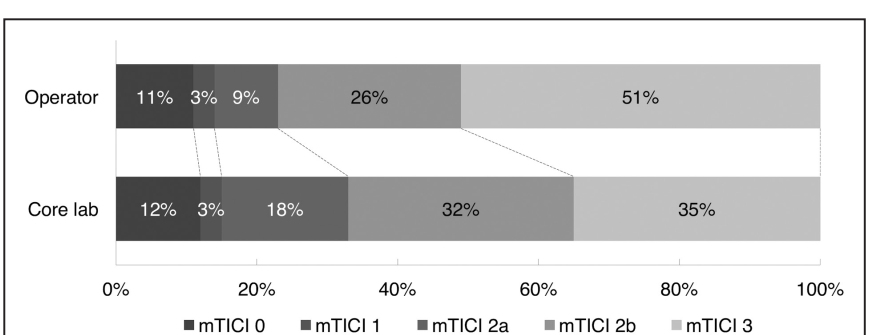

Figure 1. Distribution of modified Treatment In Cerebral Ischemia (mTICI) score assessed by operator and core lab. Operators reported a higher rate of successful reperfusion (mTICI, 2b–3) than the core lab (77% vs 67%; difference 10% [95% CI, 6%–14%]; P<0.001).

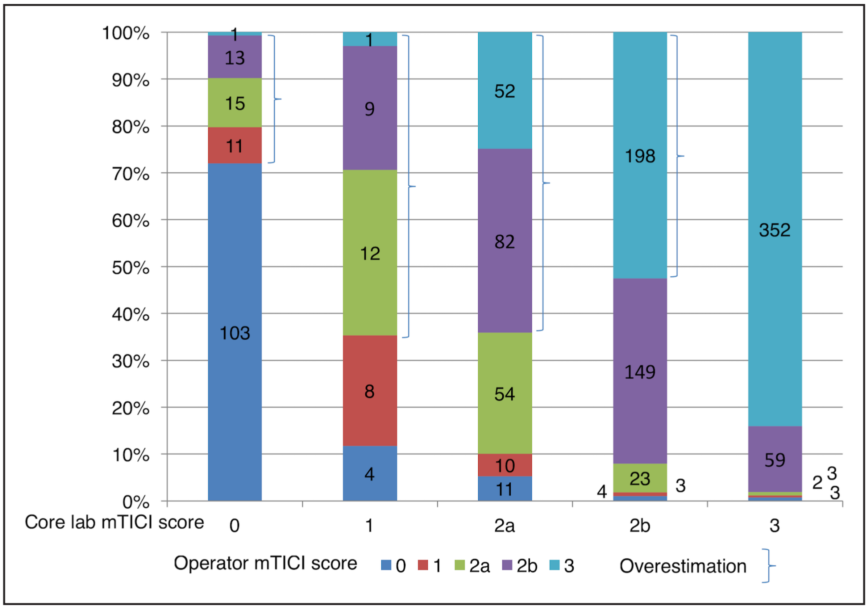

Figure 2. Disagreement between operator modified Treatment In Cerebral Ischemia (mTICI) and core lab mTICI score. The percentage of operator's overestimation was 28% (40 of 143) in core lab mTICI grade 0, 65% (22 of 34) in 1, 64% (134 of 209) in 2a, and 52% (198 of 254) in 2b. In 41% (158 of 386) of the patients with core lab scores 0 to 2a were overestimated to 2b to 3 by the operator; in 33% (252 of 763) of the patients where the core lab scored incomplete reperfusion (mTICI <3), the operator score was mTICI 3.

achieve functional independence (adjusted OR, 3.54 [95% CI, 2.58–4.86]). Multivariable logistic regression models containing either core lab scored successful reperfusion or operator scored successful reperfusion predicted outcome (C statistic of both models: 0.76) and functional independence (C statistic of both models: 0.83) equally well (Table 2).

Discussion

This study shows that substantial disagreement exists between the assessment of the degree of reperfusion by local operators and the independent core lab of the MR CLEAN Registry. In general, the operator scores were higher than core lab scores. In addition, mTICI scores were more likely to be

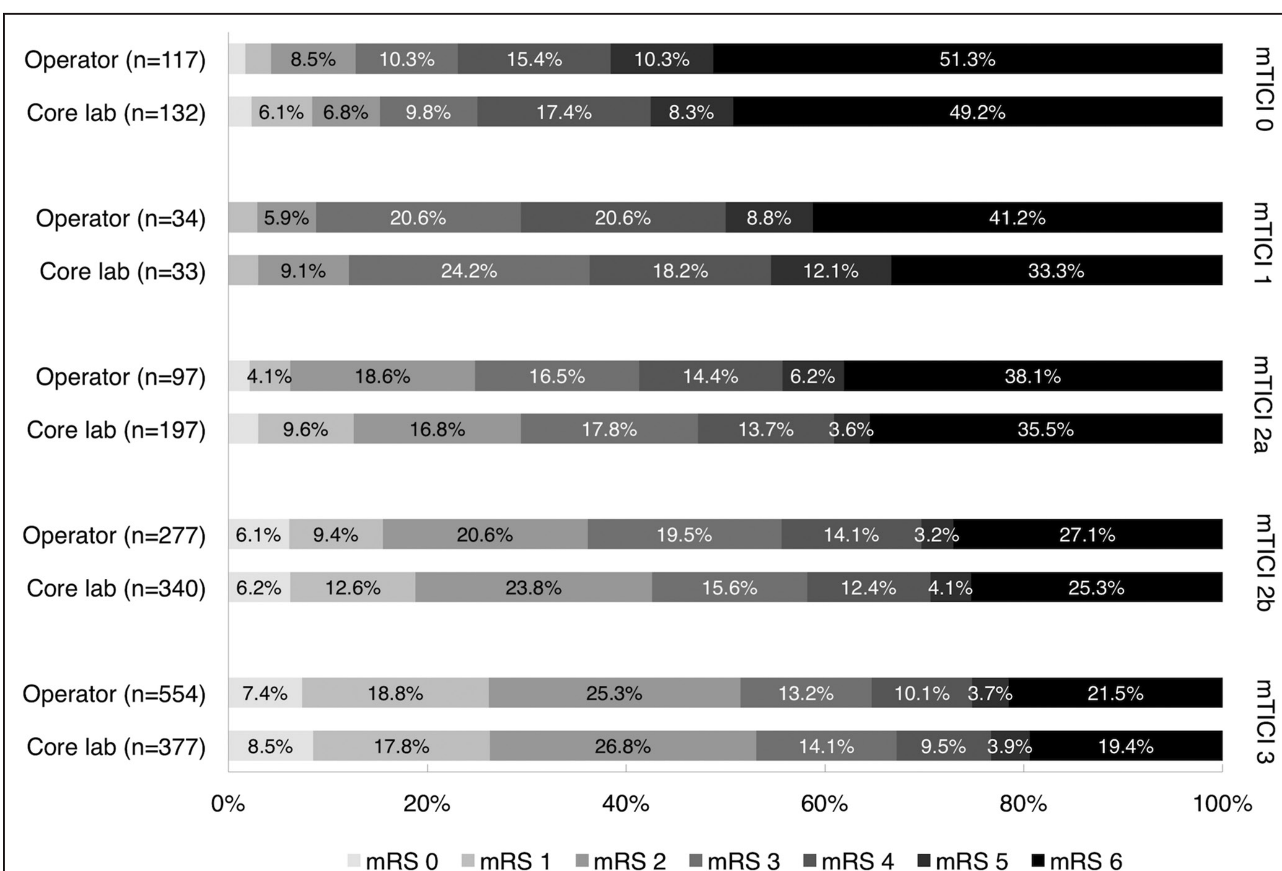

Figure 3. Distribution of scores on the modified Rankin Scale (mRS) per modified Treatment In Cerebral Ischemia (mTICI) grade assessed for both operator and core lab.

Table 2. Association With Clinical Outcome (After Imputation): Operator mTICI Versus Core Lab mTICI

		Operator mTICI (2b–3)		Core Lab mTICI (2b–3)	
Outcome	Effect Parameter	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Full-scale mRS	cOR (95% CI)	3.32 (2.62, 4.21)	3.40 (2.58, 4.48)	2.71(2.19, 3.35)	2.89 (2.28, 3.68)
	C statistic	0.58	0.76	0.58	0.76
mRS 0–2	OR (95% CI)	4.24 (3.01, 5.97)	4.33 (2.94, 6.39)	3.16 (2.43, 4.12)	3.54 (2.58, 4.86)
	C statistic	0.61	0.83	0.62	0.83

ASPECTS indicates Alberta Stroke Program Early CT Score; cOR, common odds ratio; mRS, modified Rankin Scale; mTICI score, modified Treatment In Cerebral Ischemia score; NIHSS, National Institutes of Health Stroke Scale; and OR, odds ratio.

*Values were adjusted for age, sex, baseline NIHSS, prestroke mRS, use of intravenous thrombolysis, ASPECTS, collateral status, and the time from onset to reperfusion.

overestimated by the operator in patients with distal artery occlusions.

There is some disagreement within the literature on the reliability of angiographic reperfusion grading. Previous studies have shown good inter- and intrarater agreement for the mTICI score.[13,14] However, this study confirms the findings reported in the SWIFT trial (SOLITAIRE With the Intention for Thrombectomy), where substantial reperfusion was scored more often by the study site compared with the core lab in both the Solitaire arm and the Merci arm.[15]

Our results are also in line with studies from other disciplines. Alhadramy et al[16] found a significant discrepancy between the operator and core lab assessments of the Thrombolysis in Myocardial Infarction scale, used to determine reperfusion after coronary angioplasty. The disagreement between operator and core lab was also observed in the evaluation of endovascular treatment outcomes of intracranial aneurysms.[17]

In our study, the proportion of successful reperfusion scored by the operator exceeded the core lab assessment by 10%. This overestimation of mTICI could be of clinical relevance because it may cause procedures to be terminated prematurely. Operators may terminate the procedure without additional effort to optimize recanalization after they overestimate reperfusion. Furthermore, in recent studies without core lab evaluation, reported proportion of successful reperfusion may be too high because of the bias of local operator mTICI estimation.[18]

As previous studies have shown, the rate of functional independence is different for each mTICI score.[19,20] In previous studies, in the mTICI 3 group, 60% to 70% of patients reached functional independence while these rates were 45% to 55% and 15% to 35% for mTICI 2b and 2a, respectively.[21,22] This suggests that an overestimation of the reperfusion rate may lead to overestimation of the probability of functional independence. In our population, functional independence rates for core lab mTICI 3, 2b, and 2a were 53%, 43%, and 29%, respectively. These lower rates compared with previous studies could reflect the broader inclusion criteria of the MR CLEAN Registry.[10] Rates of functional independence in operator assessment were only slightly lower (2%–6%) for each operator mTICI grade compared with the core lab. Furthermore, clinical outcome prediction of the 2b to 3 score of the operators was also similar to that of the core lab. Therefore, one could conclude that the value of the core lab in registries might be limited. Last, in clinical trials investigating the relative superiority of a device or technique with technical success as primary outcome, blinded assessment is mandatory to achieve reliable results.

Although the majority of the occlusions are located in intracranial carotid artery and M1 in this study, we found that mTICI in patients with an M2 or M3 occlusion were more likely to be overestimated by operators. The increased operator overestimation of reperfusion in distal occlusions may be because of the greater difficulty of assessing the territory at risk because of overprojection of other branches. Operators should be more cautious when estimating mTICI score in M2 and M3 occlusions.

The strengths of our study are the use of large consecutive and prospectively collected patient cohort with acute ischemic stroke because of large vessel occlusion, treated with EVT and the use of standard case report form to assess the reperfusion by local operators and core lab members.

This study is limited by the lack of interrater variability assessments of mTICI scores by members of the core lab. However, we thought the good interrater agreement within core lab members[13,14] found in previous studies justified the adjudication of 1 mTICI score per patient by 1 experienced neuroradiologist. The study may also be limited by the small sample of unsuccessful reperfusion (only 33% in the core lab adjudication). In addition, mTICI score with 2c category is widely used in recent studies. However, we did not use it in this study.[23] First, because we started the registry in 2014, mTICI 2C was not common at that time. Second, previous studies showed mTICI 2C category may not have sufficient interrater reliability for use in clinical practice.[19,24] In our opinion, the original mTICI score may, therefore, be more rational for operator assessment.

Conclusions

Our findings show that operators tend to overestimate achieved reperfusion after endovascular treatment compared with assessment by a core lab although this overestimation does not affect the association with outcome.

Appendix

A list of all MR CLEAN Registry Investigators are as follows: Executive committee: Diederik W.J. Dippel,[1] Aad van der Lugt,[2] Charles B.L.M. Majoie,[3] Yvo B.W.E.M. Roos,[4] Robert J. van Oostenbrugge,[5] Wim H. van Zwam,[6] Jelis Boiten,[14] Jan Albert Vos.[8] Study coordinators: Ivo G.H. Jansen,[3] Maxim J.H.L. Mulder,[1,2] Robert-Jan B. Goldhoorn.[5,6] Local principal investigators: Wouter J. Schonewille,[7] Jan Albert

Vos,[8] Charles B.L.M. Majoie,[3] Jonathan M. Coutinho,[4] Marieke J.H. Wermer,[9] Marianne A.A. van Walderveen,[10] Julie Staals,[5] Wim H. van Zwam,[6] Jeannette Hofmeijer,[11] Jasper M. Martens,[12] Geert J. Lycklama à Nijeholt,[13] Jelis Boiten,[14] Bob Roozenbeek,[1] Bart J. Emmer,[2] Sebastiaan F. de Bruijn,[15] Lukas C. van Dijk,[16] H. Bart van der Worp,[17] Rob H. Lo,[18] Ewoud J. van Dijk,[19] Hieronymus D. Boogaarts,[20] Paul L.M. de Kort,[21] Jo J.P. Peluso,[26] Jan S.P. van den Berg,[22] Boudewijn A.A.M. van Hasselt,[23] Leo A.M. Aerden,[24] René J. Dallinga,[25] Maarten Uyttenboogaart,[28] Omid Eshghi,[29] Tobien H.C.M.L. Schreuder,[30] Roel J.J. Heijboer,[31] Koos Keizer,[32] Lonneke S.F. Yo,[33] Heleen M. den Hertog,[34] Emiel J.C. Sturm.[35] Imaging assessment committee: Charles B.L.M. Majoie (chair),[3] Wim H. van Zwam,[6] Aad van der Lugt,[2] Geert J. Lycklama à Nijeholt,[13] Marianne A.A. van Walderveen,[10] Marieke E.S. Sprengers,[3] Sjoerd F.M. Jenniskens,[27] René van den Berg,[3] Albert J. Yoo,[37] Ludo F.M. Beenen,[3] Alida A. Postma,[6] Stefan D. Roosendaal,[3] Bas F.W. van der Kallen,[13] Ido R. van den Wijngaard,[13] Adriaan C.G.M. van Es,[2] Bart J. Emmer,[2,3] Jasper M. Martens,[12] Lonneke S.F. Yo,[33] Jan Albert Vos,[8] Joost Bot,[36] Pieter-Jan van Doormaal.[2] Writing committee: Diederik W.J. Dippel (chair),[1] Aad van der Lugt,[2] Charles B.L.M. Majoie,[3] Yvo B.W.E.M. Roos,[4] Robert J. van Oostenbrugge,[5] Wim H. van Zwam,[6] Geert J. Lycklama à Nijeholt,[13] Jelis Boiten,[14] Jan Albert Vos,[8] Wouter J. Schonewille,[7] Jeannette Hofmeijer,[11] Jasper M. Martens,[12] H. Bart van der Worp,[17] Rob H. Lo.[18] Adverse event committee: Robert J. van Oostenbrugge (chair),[5] Jeannette Hofmeijer,[11] H. Zwenneke Flach.[23] Trial methodologist: Hester F. Lingsma.[38] Research nurses/local trial coordinators: Naziha el Ghannouti,[1] Martin Sterrenberg,[1] Corina Puppels,[7] Wilma Pellikaan,[7] Rita Sprengers,[4] Marjan Elfrink,[11] Joke de Meris,[14] Tamara Vermeulen,[14] Annet Geerlings,[19] Gina van Vemde,[22] Tiny Simons,[30] Cathelijn van Rijswijk,[21] Gert Messchendorp,[28] Hester Bongenaar,[32] Karin Bodde,[24] Sandra Kleijn,[34] Jasmijn Lodico,[34] Hanneke Droste,[34] M. Wollaert,[5] D. Jeurrissen,[5] Ernas Bos,[9] Yvonne Drabbe,[15] Marjan Elfrink,[11] Berber Zweedijk,[17] Mostafa Khalilzada.[15] PhD/Medical students: Esmee Venema,[38] Vicky Chalos,[1,38] Kars C.J. Compagne,[2] Ralph R. Geuskens,[3] Tim van Straaten,[19] Saliha Ergezen,[1] Roger R.M. Harmsma,[1] Daan Muijres,[1] Anouk de Jong,[1] Wouter Hinseveld,[7] Olvert A. Berkhemer,[1,3,6] Anna M.M. Boers,[3,39] J. Huguet,[3] P.F.C. Groot,[3] Marieke A. Mens,[3] Katinka R. van Kranendonk,[3] Kilian M. Treurniet,[3] Manon Kappelhof,[3] Manon L. Tolhuijsen,[3] Heitor Alves.[3]

List of affiliations: Department of [1]Neurology, [2]Radiology, [38]Public Health, Erasmus MC University Medical Center; [3]Department of Radiology, [4]Neurology, [39]Biomedical Engineering & Physics, Academic Medical Center, Amsterdam; Department of [5]Neurology, [6]Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM); Department of [7]Neurology, [8]Radiology, Sint Antonius Hospital, Nieuwegein; Department of [9]Neurology, [10]Radiology, Leiden University Medical Center; Department of [11]Neurology, [12]Radiology, Rijnstate Hospital, Arnhem; Department of [13]Radiology, [14]Neurology, MC Haaglanden, the Hague; Department of [15]Neurology, [16]Radiology, HAGA Hospital, the Hague; Department of [17]Neurology, [18]Radiology, University Medical Center Utrecht; [19]Department of Neurology, [20]Neurosurgery, [27]Radiology, Radboud University Medical Center, Nijmegen; Department of [21]Neurology, [26]Radiology, Sint Elisabeth Hospital, Tilburg; Department of [22]Neurology, [23]Radiology, Isala Klinieken, Zwolle; Department of [24]Neurology, [25]Radiology, Reinier de Graaf Gasthuis, Delft; Department of [28]Neurology, [29]Radiology, University Medical Center Groningen; Department of [30]Neurology, [31]Radiology, Atrium Medical Center, Heerlen; Department of [32]Neurology, [33]Radiology, Catharina Hospital, Eindhoven; Department of [34]Neurology, [35]Radiology, Medical Spectrum Twente, Enschede; Department of [36]Radiology, VUMC, Amsterdam; Department of [37]Radiology, Texas Stroke Institute, Texas, United States of America.

Sources of Funding

This study was funded and performed by the Erasmus University Medical Center, the Academic Medical Center Amsterdam, and the Maastricht University Medical Center. The study was additionally funded by the Applied Scientific Institute for Neuromodulation (Toegepast Wetenschappelijk Instituut voor Neuromodulatie), which played no role in trial design and patient enrolment, nor in data collection, analysis, or writing of the manuscript.

Disclosures

Erasmus University Medical Center received funds from Stryker for consultations by Drs Dippel and van der Lugt and from Bracco Imaging for consultations by Dr Dippel. Academic Medical Center Amsterdam received funds from Stryker for consultations by Drs Majoie and Roos. Maastricht University Medical Center received funds from Stryker and Codman for consultations by Dr van Zwam. Dr Marquering is cofounder and shareholder of Nico-lab. Drs Jansen, Roos, and Majoie own stock in Nico-lab. The other authors report no conflicts.

References

1. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11–20. doi/10.1056/NEJMoa1411587
2. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2015;372:1019–1030. doi/10.1056/NEJMoa1414905
3. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, et al; SWIFT PRIME Investigators. 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
4. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009–1018. doi/10.1056/NEJMoa1414792
5. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296–2306. doi: 10.1056/NEJMoa1503780
6. Manning NW, Chapot R, Meyers PM. Endovascular stroke management: key elements of success. *Cerebrovasc Dis*. 2016;42:170–177. doi: 10.1159/000445449
7. Fugate JE, Klunder AM, Kallmes DF. What is meant by "TICI"? *AJNR Am J Neuroradiol*. 2013;34:1792–1797. doi: 10.3174/ajnr.A3496
8. Lapergue B, Blanc R, Gory B, Labreuche J, Duhamel A, Marnat G, et al; ASTER Trial Investigators. Effect of endovascular contact aspiration vs stent retriever on revascularization in patients with acute ischemic stroke and large vessel occlusion: the ASTER randomized clinical trial. *JAMA*. 2017;318:443–452. doi: 10.1001/jama.2017.9644
9. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X
10. Jansen IGH, Mulder MJHL, Goldhoorn RB; MR CLEAN Registry Investigators. Endovascular treatment for acute ischaemic stroke in routine clinical practice: prospective, observational cohort study (MR CLEAN Registry). *BMJ*. 2018;360:k949. doi: 10.1136/bmj.k949
11. Zaidat OO, Yoo AJ, Khatri P, Tomsick TA, von Kummer R, Saver JL, 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;44:2650–2663. doi: 10.1161/STROKEAHA.113.001972
12. Bender R. Calculating confidence intervals for the number needed to treat. *Control Clin Trials*. 2001;22:102–110.
13. Arnold M, Nedeltchev K, Remonda L, Fischer U, Brekenfeld C, Keserue B, et al. Recanalisation of middle cerebral artery occlusion after intra-arterial thrombolysis: different recanalisation grading systems and clinical functional outcome. *J Neurol Neurosurg Psychiatry*. 2005;76:1373–1376. doi: 10.1136/jnnp.2004.055160
14. Suh SH, Cloft HJ, Fugate JE, Rabinstein AA, Liebeskind DS, Kallmes DF. Clarifying differences among thrombolysis in cerebral infarction scale variants: is the artery half open or half closed? *Stroke*. 2013;44:1166–1168. doi: 10.1161/STROKEAHA.111.000399
15. Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, et al; SWIFT Trialists. Solitaire flow restoration device versus the Merci

Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet*. 2012;380:1241–1249. doi: 10.1016/S0140-6736(12)61384-1

16. Alhadramy O, Westerhout CM, Brener SJ, Granger CB, Armstrong PW; APEX AMI Investigators. Is visual interpretation of coronary epicardial flow reliable in patients with ST-elevation myocardial infarction undergoing primary angioplasty? Insights from the angiographic substudy of the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial. *Am Heart J*. 2010;159:899–904. doi: 10.1016/j.ahj.2010.02.028
17. Rezek I, Lingineni RK, Sneade M, Molyneux AJ, Fox AJ, Kallmes DF. Differences in the angiographic evaluation of coiled cerebral aneurysms between a core laboratory reader and operators: results of the Cerecyte Coil Trial. *AJNR Am J Neuroradiol*. 2014;35:124–127. doi: 10.3174/ajnr.A3623
18. Kammerer S, du Mesnil de Rochemont R, Wagner M, You S-, Tritt S, Mueller-Eschner M, et al. Efficacy of mechanical thrombectomy using stent retriever and balloon-guiding catheter. *Cardiovasc Intervent Radiol*. 2018;41:699–705. doi: 10.1007/s00270-018-1901-8
19. Kallmes DF, Rabinstein AA, Gounis MJ. To be or not 2b? To see or not 2c? Alas, the clock is ticking on TICI. *J Neurointerv Surg*. 2018;10:323–324. doi: 10.1136/neurintsurg-2017-013521
20. Dargazanli C, Fahed R, Blanc R, Gory B, Labreuche J, Duhamel A, et al; ASTER Trial Investigators. Modified thrombolysis in cerebral infarction 2C/thrombolysis in cerebral infarction 3 reperfusion should be the aim of mechanical thrombectomy: insights from the ASTER trial (Contact Aspiration Versus Stent Retriever for Successful Revascularization). *Stroke*. 2018;49:1189–1196. doi: 10.1161/STROKEAHA.118.020700
21. Yoo AJ, Simonsen CZ, Prabhakaran S, Chaudhry ZA, Issa MA, Fugate JE, et al; Cerebral Angiographic Revascularization Grading Collaborators. Refining angiographic biomarkers of revascularization: improving outcome prediction after intra-arterial therapy. *Stroke*. 2013;44:2509–2512. doi: 10.1161/STROKEAHA.113.001990
22. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med*. 2013;368:893–903. doi: 10.1056/NEJMoa1214300
23. Kaesmacher J, Maegerlein C, Zibold F, Wunderlich S, Zimmer C, Friedrich B. Improving mTICI2b reperfusion to mTICI2c/3 reperfusions: a retrospective observational study assessing technical feasibility, safety and clinical efficacy. *Eur Radiol*. 2018;28:274–282. doi: 10.1007/s00330-017-4928-3
24. Volny O, Cimflova P, Szeder V. Inter-rater reliability for thrombolysis in cerebral infarction with TICI 2c category. *J Stroke Cerebrovasc Dis*. 2017;26:992–994. doi: 10.1016/j.jstrokecerebrovasdis.2016.11.008