Original research

Predictors of poor outcome despite successful endovascular treatment for ischemic stroke: results from the MR CLEAN Registry

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ABSTRACT

Background Approximately one-third of patients with ischemic stroke treated with endovascular treatment do not recover to functional independence despite rapid and successful recanalization. We aimed to quantify the importance of predictors of poor functional outcome despite successful reperfusion.

Methods We analyzed patients from the MR CLEAN Registry between March 2014 and November 2017 with successful reperfusion (extended Thrombolysis In Cerebral Infarction ≥2B). First, predictors were selected based on expert opinion and were clustered according to acquisition over time (ie, baseline patient factors, imaging factors, treatment factors, and postprocedural factors). Second, several models were constructed to predict 90-day functional outcome (modified Rankin Scale (mRS)). The relative importance of individual predictors in the most extensive model was expressed by the proportion of unique added χ^2 to the model of that individual predictor.

Results Of 3180 patients, 1913 (60%) had successful reperfusion. Of these 1913 patients, 1046 (55%) were functionally dependent at 90 days (mRS >2). The most important predictors for mRS were baseline patient factors (ie, pre-stroke mRS, added χ^2 0.16; National Institutes of Health Stroke Scale score at baseline, added χ^2 0.12; age, added χ^2 0.10), and postprocedural factors (ie, symptomatic intracranial hemorrhage (sICH), added χ^2 0.12; pneumonia, added χ^2 0.09). The probability of functional independence for a typical stroke patient with sICH was 54% (95% CI 36% to 72%) lower compared with no sICH, and 21% (95% CI 4% to 38%) for pneumonia compared with no pneumonia.

Conclusion Baseline patient factors and postprocedural adverse events are important predictors of poor functional outcome in successfully reperfused patients with ischemic stroke. This implies that prevention of postprocedural adverse events has the greatest potential to further improve outcomes in these patients.

INTRODUCTION

Approximately 50% of patients with ischemic stroke caused by a proximal large vessel occlusion in the anterior circulation do not recover to functional independence, even when successful reperfusion is achieved by endovascular treatment (EVT).[1] Factors such as age, National Institutes of Health Stroke Scale (NIHSS) score at baseline, and Alberta Stroke Program Early CT Score (ASPECTS) are associated with poor outcome after successful reperfusion.[2–5] A better understanding of the key determinants of poor recovery despite successful reperfusion after EVT could guide researchers and physicians in the development of new treatments to further improve outcomes. Therefore, we aimed to quantify the importance of predictors of poor functional outcome despite successful reperfusion.

METHODS

Study design

We used data from the MR CLEAN Registry, which is a national, prospective, open, multicenter, observational monitoring study for stroke intervention centers that perform EVT in the Netherlands. The complete methods and description of variables of the MR CLEAN Registry have been described elsewhere.[6] For the present study, we selected patients who were registered between March 2014 and November 2017 and complied with the following criteria: age ≥18 years; presence of a proximal intracranial occlusion in the anterior circulation confirmed on CT angiography (intracranial carotid artery (ICA/ICA-T), middle cerebral artery (M1/M2), anterior cerebral artery (A1/A2)); groin puncture within 6.5 hours after symptom onset; treatment in a center that participated in the MR CLEAN trial; and successful postinterventional macrovascular reperfusion status (extended Thrombolysis In Cerebral Infarction (eTICI) ≥2B) assessed by an independent core laboratory. The current observational study was guided by the STROBE statement.[7]

Measures and outcomes

We constructed multivariable ordinal regression models to predict functional outcome measured with the modified Rankin Scale (mRS) at 90 days. We selected candidate predictors based on expert opinion and availability.[2–5 8] In the selection, priority was given to causal and modifiable factors. The predictors were clustered in four groups according to the time of acquisition: baseline patient factors, imaging factors, treatment factors, and postprocedural factors (ie, adverse events). We successively added each group of predictors to a basic model only including baseline patient factors. This resulted in four multivariable ordinal regression models of increasing extensiveness. The most extensive model was used to quantify the relative importance of the individual predictors. Finally, we evaluated the overall explained variance of the most extensive model.

Subsequently, we repeated these analyses (1) for the subgroup with excellent reperfusion (eTICI ≥2C) and (2) using a modified NIHSS score at 24–48 hours as the outcome. A modification of the NIHSS score at 24–48 hours was necessary to also include patients who died within 48 hours, by assigning them the maximum NIHSS score of 42. This early modified NIHSS score may be a better representation of direct stroke-related factors associated with outcome after EVT as opposed to the mRS and less inflicted by patients who died early.[9]

Statistical methods

Any mRS score assessed within 30 days of symptom onset was considered invalid and treated as missing. For the purpose of unbiased estimation of associations of outcome with baseline characteristics, we replaced missing outcome and predictor values by values derived from multiple imputation by chained equations with five imputations.[10 11] After constructing ordinal logistic or linear regression models as appropriate, quantification measures were derived. Nagelkerke's pseudo-R^2 for the mRS (ordinal outcome) and R^2 for the modified NIHSS at 24–48 hours (continuous outcome) were applied to quantify the explained variance in outcome by the models. This derived (pseudo-)R^2 reflects the explained variance in outcome of the models by the included predictors, ideally aiming to achieve a highest possible score of 1 representing complete variance explanation. Subsequently, the strength of relationship between an individual predictor in the model and the outcome was quantified by the proportion of unique added value in that particular model using the Wald χ^2 test, with penalization for df. Further explanation on this approach is provided in online supplemental material 1. For the most important modifiable predictors associated with functional outcome, we calculated the absolute difference in predicted probability for good functional outcome (mRS ≤2) for a typical stroke patient.

To account for non-linearity of the associations between continuous parameters and outcome, the variables age and systolic blood pressure were handled using restricted cubic splines with three knots based on prior knowledge.[8 12] The modified NIHSS at 24–48 hours was log transformed, after adding one point to all NIHSS scores, to best satisfy the linear model (normal distribution of residuals and homoscedasticity).[9]

Confidence intervals for individual predictor importance were calculated using bootstrapping with 10 000 iterations. All statistical analyses were performed with R version 3.5.0 (R foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study population

In total, 3180 patients were analyzed. Successful reperfusion was achieved in 1913/3180 (60%) and excellent reperfusion in 1218/3180 (38%) patients (figure 1). The characteristics of patients with successful and excellent reperfusion, together with clustering of predictors according to the four predefined groups, are shown in table 1 (and per reperfusion grade in online supplemental table).

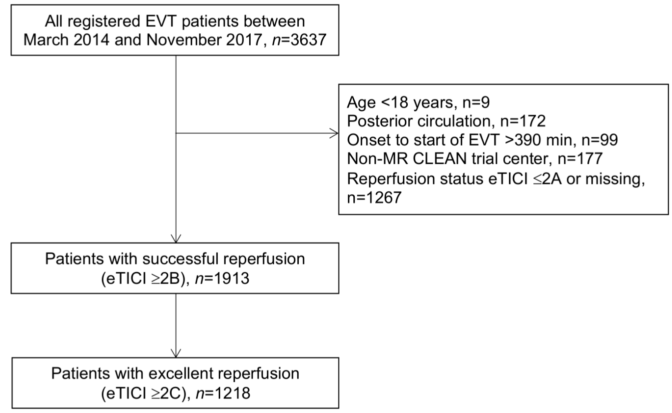

Figure 1 Flowchart.

Within 90 days following EVT, 900/1913 (51%) patients in whom successful reperfusion was achieved remained functionally dependent (mRS >2) or died. This was similar for patients in whom excellent reperfusion was achieved, with 554/1218 (49%) being dependent or died at 90 days. Of the 1913 patients with successful reperfusion, 78 (4%) died within 48 hours and, of the 1218 patients in whom excellent reperfusion was achieved, 46 (4%) died within 48 hours. The median modified NIHSS score at 24–48 hours was 8 (IQR 3, 15) for successful reperfusion and 7 (IQR 3, 14) for excellent reperfusion.

Variable importance

The basic model including patient factors already explained the largest proportion in variance (figure 2). Successive addition of the other grouped factors based on clustering on acquisition over time (ie, imaging factors, treatment factors, and postprocedural factors) increased the explained variance by the models, but these were relatively less important than the contribution of patient factors. The four most extensive models, including all independent variables, explained between 42% and 47% of the variation in outcome prediction among patients with reperfusion after EVT. In patients with successful reperfusion (eTICI ≥2B), the five most important individual predictors of functional outcome at 90 days were pre-stroke mRS (added χ^2: 0.16), NIHSS at baseline (added χ^2: 0.12), symptomatic intracranial hemorrhage (sICH) (added χ^2: 0.12), age (added χ^2: 0.10), and pneumonia (added χ^2: 0.09; figure 3A). The five individual predictors with the highest added χ^2 were similar in patients with excellent reperfusion (eTICI ≥2C), although the order of importance and the quantity of added χ^2 differed: pre-stroke mRS (added χ^2: 0.19), pneumonia (added χ^2: 0.12), sICH (added χ^2: 0.11), NIHSS at baseline (added χ^2: 0.10), and age (added χ^2: 0.09; figure 3C). The most important predictors of the modified NIHSS at 24–48 hours as outcome were NIHSS on admission (added χ^2: 0.26), sICH that occurred within 24 hours (added χ^2: 0.07), collaterals (added χ^2: 0.06), duration of the procedure (added χ^2: 0.03), and ASPECTS on admission (added χ^2: 0.02; figure 3B). In patients with excellent reperfusion, the order of importance of added χ^2 of the four most important predictors was similar to those with successful reperfusion, only the fifth most important predictor differed: NIHSS at baseline (added χ^2: 0.28), sICH that occurred within 24 hours (added χ^2: 0.08), collaterals (added χ^2: 0.05), duration of the procedure (added χ^2: 0.02), and glucose (added χ^2: 0.02; figure 3D).

Table 1 Cohort characteristics and predictor clustering

	eTICI ≥2B (n=1913)	Missing	eTICI ≥2C (n=1218)	Missing
Patient factors				
Age	69 (14)	0	70 (14)	0
Male sex	1010 (53)	0	651 (53)	0
NIHSS on admission	16 (11, 19)	1.5	16 (11, 20)	1.6
Ischemia in left hemisphere	1019 (54)	0.6	637 (53)	0.5
Systolic blood pressure on admission	148.7 (24)	3.2	149 (24)	2.9
INR on admission	1.2 (0.4)	19	1.2 (0.4)	18
Glucose level on admission	7.4 (2.6)	11	7.4 (2.5)	11
Previous stroke	309 (16)	0.8	197 (16)	0.7
Atrial fibrillation	427 (23)	1.3	286 (24)	1.3
Hypertension	967 (52)	2.2	626 (52)	1.7
Diabetes mellitus	310 (16)	0.7	209 (17)	0.5
Pre-stroke mRS (%)		2.3		2.1
0: No symptoms	1280 (69)		823 (69)	
1: Minor symptoms, no limitations	247 (13)		161 (14)	
2: Slight disability, no help needed	135 (7.2)		90 (7.5)	
>2	207 (11)		119 (10)	
Prior antiplatelet therapy	601 (32)	1.4	397 (33)	1.0
Time from symptom onset to admission to ER (intervention center)	133 (65, 185)	4.9	133 (65, 183)	4.3
Imaging factors				
Occluded segment		3.8		3.4
Intracranial ICA	81 (4.4)		51 (4.3)	
ICA-T	366 (20)		239 (20)	
M1	1118 (61)		730 (62)	
M2	262 (14)		149 (13)	
Other (eg, M3, ACA)	14 (0.8)		8 (0.7)	
ASPECTS	9(8, 10)	2.9	9(8, 10)	2.2
Collaterals		6.1		5.9
Grade 0: Absent collaterals	101 (5.6)		63 (5.5)	
Grade 1: Occluded area filling <50%	649 (36)		408 (36)	
Grade 2: Occluded area filling >50% but <100%	708 (39)		452 (39)	
Grade 3: Occluded area filling 100%	338 (19)		223 (20)	
Treatment factors				
Treatment with intravenous alteplase	1472 (77)	0.4	925 (76)	0.4
Time from admission to ER (intervention center) to groin puncture	58 (35, 87)	8.9	58 (35, 84)	8.2
Duration procedure	50 (35, 73)	7.4	50 (35, 70)	5.5
General anesthetic management	528 (29)	5.1	363 (31)	4.0
Periprocedural heparin use	548 (29)	0	373 (31)	0
Reperfusion grade after intervention or spontaneous		0		0
eTICI 2B	695 (36)		NA	NA
eTICI 2C	332 (17)		332 (27)	0
eTICI 3	886 (46)		886 (73)	0
First pass success	719 (47)	20	539 (51)	13
*Postprocedural factors**				
New ischemic stroke	30 (1.6)	0	17 (1.4)	0
sICH	88 (4.6)	0	54 (4.4)	0
Pneumonia	177 (9.3)	0	108 (8.9)	0

Cohort characteristics of patients with successful (eTICI ≥2B) and with excellent reperfusion (eTICI ≥2C). Continuous data are presented as mean (SD) for normal distributed data or as median (IQR) for skewed data. Categorical data are presented as numbers (%).
*For the model with the modified NIHSS at 24–48 hours as outcome, postprocedural factors in the model were restricted to occurrence within 24 hours, which was only recorded for sICH (so new ischemic stroke and pneumonia were excluded).
ACA, anterior cerebral artery; APT, antiplatelet therapy; ASPECTS, Alberta Stroke Program Early CT Score; DOAC, direct oral anticoagulant; ER, emergency room; eTICI, extended Thrombolysis In Cerebral Infarction including a 2C grade; ICA (T), internal carotid artery (terminus); INR, international normalized ratio; mRS, modified Rankin Scale; M(segment), middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Probability of good functional outcome (mRS ≤2) for a typical stroke patient with sICH was 54% (95% CI 36% to 72%) lower compared with a patient without sICH, and 21% (95% CI 4% to 38%) for pneumonia compared with no pneumonia.

DISCUSSION

In this study, in which we evaluated the importance of predictors according to their acquisition over time, we found that baseline patient factors and postprocedural adverse events are the most important predictors of poor functional outcome in patients with ischemic stroke with successful reperfusion after EVT. It is conceivable that prevention of postprocedural adverse events (ie, sICH, pneumonia) has the greatest potential to further improve outcomes.

Strategies currently investigated that could be of benefit in the prevention of postprocedural adverse events are (1) direct EVT without preceding intravenous alteplase to reduce sICH (MR CLEAN-NO IV (ISRCTN80619088), DIRECT MT (NCT03469206), SKIP (UMIN000021488), SWIFT-DIRECT (NCT03192332), DIRECT-SAFE (NCT03494920), DEVT (ChiCTR-IOR-17013568)), (2) strict blood pressure control to reduce the risk of intracranial hemorrhage (BP TARGET (NCT03160677)), and (3) pharmacological strategies reducing complications like pneumonia (PRECIOUS (ISRCTN82217627)).

Comparing the most important predictors for the group with successful reperfusion and those with excellent reperfusion, this resulted only in minor differences, assuming that predictor importance seems relatively constant with regard to the level of reperfusion. The results of this study should not be used to determine for which reperfusion grade one should strive as this was not our aim. The observation that pre-stroke mRS was a strong predictor in explaining outcomes after 90 days confirms the hypothesis that most patients with poor outcomes at 90 days already have poor outcomes at baseline and vice versa. Yet, as no perfect prediction was observed, other factors contribute to the prediction of outcomes at 90 days. We observed that the time from stroke onset to admission to the emergency room of the intervention hospital and time from admission to the emergency room of the intervention hospital to groin puncture were relatively less important than the duration of the procedure. It is possible that the importance of preinterventional time intervals was negated by the achievement of successful reperfusion as our analyses were inherent to this selection criterion. The relative importance of duration of the procedure could reflect the difficulty of the procedure caused, for example, by agitation of the patient, tortuosity of the vessels, or performance of multiple attempts, which is associated with poor functional outcomes.[13]

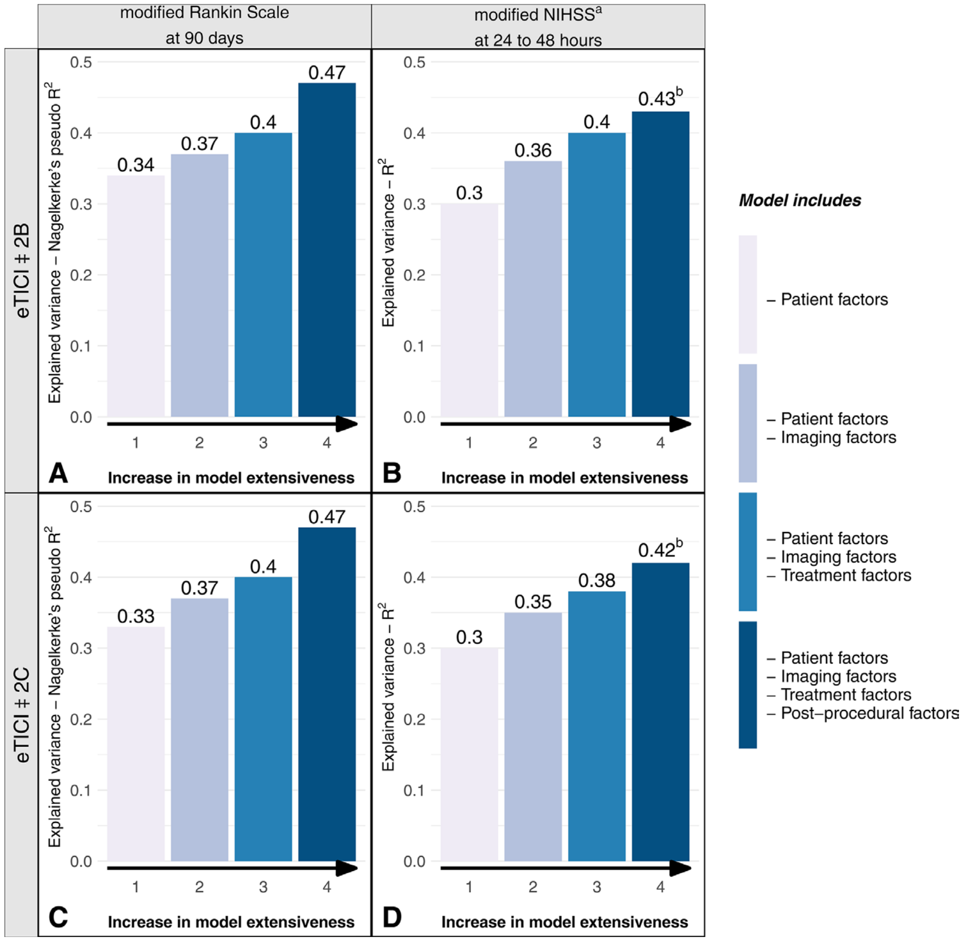

Figure 2 Performance of models with increasing extensiveness in patients with successful reperfusion defined as eTICI ≥2B (A, B) and excellent reperfusion defined as eTICI ≥2C (C, D), predicting mRS at 90 days (A, C), and modified NIHSS at 24–48 hours (B, D). [a]Death within 48 hours was assigned the maximum score of 42. [b]For the model with the modified NIHSS at 24–48 hours as outcome, postprocedural factors in the model were restricted to occurrence within 24 hours, which was only recorded for symptomatic intracranial hemorrhage (resulting in exclusion of new ischemic stroke and pneumonia for these analyses). eTICI, extended Thrombolysis In Cerebral Infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

Six earlier studies also found that the non-modifiable patient factor baseline NIHSS score was a very important predictor of poor functional outcome despite reperfusion.[3–5 14–16] In five of these studies, age was found to be an important predictor of poor functional outcome.[3–5 15 16] Two studies found that EVT without prior IV alteplase administration was associated with a poor outcome.[4 14] Lower diffusion weighted imaging (DWI) ASPECTS on admission was found to be related to a poor outcome in two studies.[5 16] Factors such as collateral status, blood glucose, occlusion location, diabetes mellitus, neutrophil-to-lymphocyte ratio, delayed EVT, mTICI 2B (vs mTICI 3), procedural complications, and higher number of passes (≥3) were mentioned in only one study to be associated with poor functional outcome.[4 5 14 15] Our results confirm the suggestion of an opinion review that unfavorable non-modifiable patient factors (reflecting limited 'brain reserve') are the most notable factors explaining why patients do not recover despite reperfusion.[17] Remarkably, none of these studies evaluated the influence of postprocedural factors such as sICH, pneumonia, and new ischemic stroke (ie, imaging of new brain infarction with corresponding clinical neurologic deficit within 90 days) which, based on our results, are very important in explaining why some patients with successful reperfusion recover well and others do not. It should be kept in mind that the identified factor is not necessarily causal in explaining the detrimental outcomes. For example, it is possible that the occurrence of pneumonia is associated with other conditions like heart failure and sepsis followed by hemodynamic instability and hypoperfusion requiring ICU admission, which actually explains why these patients do worse.

The variance in outcome explained by the models varied between 42% and 47% so a substantial part of the variability in outcome after successful reperfusion is still unexplained. Therefore, we advocate incentivizing the identification of new predictors as well as optimizing the determination of current predictors. Considering the identification of new predictors, additional information on quantification of perfusion at the microvascular level—preferably at an early stage—could be a useful new approach to improve outcome prediction. Current visual scoring techniques are unable to evaluate vessels <90 μm in diameter,[18] yet it is believed that microvascular dysfunction (vasculature <90 μm in diameter) following reperfusion could contribute to poor functional outcomes despite macrovascular reperfusion.[19]

Regarding optimization of predictor determination, our current models could be optimized even more by improving both preinterventional and postinterventional quantification of brain tissue status with more advanced neuroimaging techniques such as MRI or CT perfusion instead of CT.

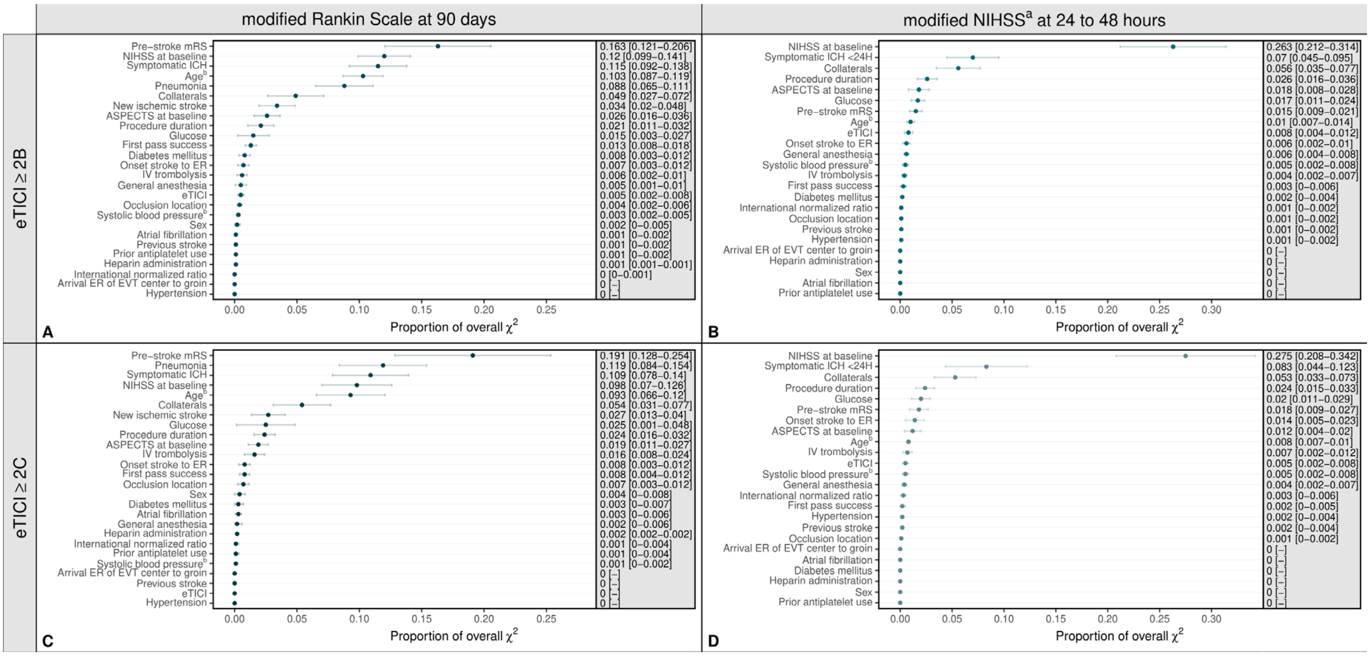

Figure 3 Individual penalized variable importance within the most extensive models in patients with successful reperfusion defined as eTICI ≥2B (A, B) and excellent reperfusion defined as eTICI ≥2C (C, D), predicting mRS at 90 days (A, C) and modified NIHSS at 24–48 hours (B, D). Confidence intervals for individual predictor importance were calculated using bootstrapping with 10 000 iterations. [a]Death within 48 hours was assigned the maximum score of 42. [b]Handled using three restricted cubic spines. ASPECTS, Alberta Stroke Program Early CT Score; ER, emergency room; eTICI, extended Thrombolysis In Cerebral Infarction; EVT, endovascular treatment; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

As no baseline MRI-DWI or CT perfusion data (eg, information on preinterventional perfusion status such as cerebral blood flow and core volume) were available in this observational registry, our analyses were limited to ASPECTS evaluation, which is probably a less accurate measure of the infarct core. Also, in-depth information on, for example, the periprocedural device technique used (eg, use of balloon protection, assisted aspiration), periprocedural blood pressure course, and malignant brain edema could be of additional value to further improve outcome explanation. Furthermore, addition of the follow-up infarct volume might have improved the model's performance further.[20–22] However, this assessment was not available in our dataset. Besides, as we only documented the occurrence of pneumonia, not the occurrence of other infections, this could have limited our study. Nevertheless, pneumonia accounts for at least half of all stroke-related infections and is by far the strongest prognostic factor among the stroke-associated infections.[23 24] Another limitation is the possibility of information bias as factors were selected for the model based on prior knowledge. Furthermore, it should be considered that the chosen outcome of the modified NIHSS (including death) should be interpreted with caution as it is not known whether assigning the maximum NIHSS score of 42 to patients who died before 24–48 hours NIHSS assessment is the most optimal strategy for the evaluation of early stroke-related outcome after EVT. However, this outcome is a strong mediator of the mRS at 90 days and might be seen as a more essential evaluation of neurological deficit and directly stroke-related outcome measure, which is less inflicted by early death.[9] Finally, although we did not detect a large influence of the included modifiable factors—that is, use of antithrombotic medication (eg, antiplatelets, heparin) or anesthesia type—on poor functional outcome despite reperfusion, it should be kept in mind that these treatments were not assigned systematically and confounding by indication may have occurred. To improve outcomes further, we suggest evaluating the effect of modifiable factors in randomized studies as well as incentivizing the identification of additional modifiable predictors. As these treatments are modifiable, this warrants a further randomized study.

CONCLUSIONS

Both patient and postprocedural factors are important predictors of outcome in successfully reperfused patients with ischemic stroke. This implies that prevention of postprocedural adverse events has the greatest potential to further improve clinical outcomes in these patients.

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SUPPLEMENTAL MATERIAL

PREDICTORS OF POOR OUTCOME DESPITE SUCCESSFUL ENDOVASCULAR THROMBECTOMY FOR ISCHEMIC STROKE: RESULTS FROM THE MR CLEAN REGISTRY

Supplemental methods

In the evaluation of the added Chi^2 of the individual parameters, the sum of all individual Chi^2 proportions can be below or above 1 and quantification measures should be interpreted in context of the model. For example, if all independent variables are perfectly identical (collinear), the model can have good performance, but proportion Chi^2 for all independent variables will be zero, because any single predictor has zero additional explanatory value. On the other hand, if all independent variables together explain the dependent variable perfectly, proportion Chi^2 for each predictor will be 1, because whatever is unexplained by all other predictors can perfectly be explained by the remaining variable.

Table 1. Cohort characteristics and predictor clustering

	eTICI 2B, n=695	eTICI 2C, n=332	eTICI 3, n=886	Missing
Patient factors				
Age	69 (15)	69 (14)	70 (14)	0
Male sex	359 (52)	184 (55)	467 (53)	0
NIHSS on admission	15 [10, 19]	16 [11, 20]	16 [11, 20]	1.5
Ischemia in left hemisphere	382 (55)	177 (53)	460 (52)	0.6
Systolic blood pressure on admission	149 (25)	151 (25)	148 (24)	3.2
INR on admission	1.1 (0.4)	1.2 (0.4)	1.2 (0.4)	18
Glucose level on admission	7.4 (2.7)	7.4 (2.4)	7.4 (2.6)	11
Previous stroke	112 (16)	58 (18)	139 (16)	0.8
Atrial fibrillation	141 (21)	87 (26)	199 (23)	1.3
Hypertension	341 (51)	171 (52)	455 (52)	2.2
Diabetes mellitus	101 (15)	63 (19)	146 (17)	0.7
Pre-stroke mRS (%)				2.3
0 - No symptoms	457 (68)	229 (71)	594 (68)	
1 - Minor symptoms, no limitations	86 (13)	39 (12)	122 (14)	
2 - Slight disability, no help needed	45 (6.7)	30 (9.2)	60 (6.9)	
>2	88 (13)	27 (8.3)	92 (11)	
Prior antiplatelet therapy	204 (30)	112 (34)	285 (33)	1.4
Time from symptom onset to admission ER (intervention center)	133 [65, 186]	135 [60, 189]	130 [68, 181]	4.9
Imaging factors				
Occluded segment				3.8
Intracranial ICA	30 (4.5)	15 (4.7)	36 (4.2)	
ICA-T	127 (19)	73 (23)	166 (19)	
M1	388 (58)	194 (61)	536 (63)	
M2	113 (17)	37 (12)	112 (13)	
Other (e.g., M3, ACA)	6 (0.9)	0 (0)	8 (0.9)	
ASPECTS	9 [7, 10]	9 [8, 10]	9 [8, 10]	2.9
Collaterals				6.1
Grade 0 - Absent collaterals	38 (5.8)	21 (6.7)	42 (5)	
Grade 1 - Occluded area filling <50%	241 (37)	115 (37)	293 (35)	
Grade 2 - Occluded area filling >50% but <100%	256 (39)	129 (41)	323 (39)	
Grade 3 - Occluded area filling 100%	115 (18)	47 (15)	176 (21)	
Treatment factors				
Treatment with intravenous alteplase	547 (78.9)	243 (73)	682 (77)	0.4
Time from admission ER (intervention center) to groin puncture	58 [35, 93]	60 [38, 86]	57 [35, 83]	8.9
Duration procedure	53 [35, 75]	56 [40, 79]	46 [32, 70]	7.4
General anesthetic management	165 (26)	115 (37)	248 (29)	5
Periprocedural heparin use	175 (25)	115 (35)	258 (29)	0
First pass success	180 (39)	128 (45)	411 (53)	20
*Post-procedural factors**				
New ischemic stroke	13 (1.9)	3 (0.9)	14 (1.6)	0
Symptomatic intracranial hemorrhage	34 (4.9)	16 (4.8)	38 (4.3)	0
Pneumonia	69 (9.9)	32 (9.6)	76 (8.6)	0

Summary: Cohort characteristics of patients with successful (eTICI≥2B) and with excellent reperfusion (eTICI≥2C). Continuous data are presented as mean (SD) for normal distributed data or as median [IQR] for skewed data. Categorical data are presented as numbers (%).
Abbreviations: ACA, anterior cerebral artery; APT, antiplatelet therapy; ASPECTS, Alberta stroke program early computed tomography score; DOAC, direct oral anticoagulant; ER, emergency room; eTICI, extended thrombolysis in cerebral infarction including a 2C grade; ICA (T), internal carotid artery (terminus); INR, international normalized ratio; M(*segment*), middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale
**For the model with the modified NIHSS at 24-48 hour as outcome, post-procedural factors in the model were restricted to occurrence within 24 hours, which was only recorded for sICH (so new ischemic stroke and pneumonia were excluded).*

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