scientific reports

Check for updates

OPEN

NIHSS mismatch as a predictor of early neurological improvement after mechanical thrombectomy

Laura Amaya-Pascasio[1,6], Miriam Fernández-Gómez[2,6], María del Mar Martínez-Salmerón[1,6], Eva Guevara-Sánchez[1], Marisa Luisa Ruiz-Franco[1], Carlos Hidalgo-Barranco[2], Cristina del Toro-Pérez[1], Diana Vidal de Francisco[1], Antonio José Rodríguez-Sánchez[1,3], José García-Pinteño[1,3], Antonio Arjona-Padillo[1] & Patricia Martínez-Sánchez[1,4,5]✉

The selection of acute ischemic stroke (AIS) patients for mechanical thrombectomy (MT) is based on the clinical-radiological mismatch, where the NIHSS is higher than expected based on the ASPECT score. Our objective was to estimate the mismatch ($NIHSS_{mismatch\%}$) between the expected NIHSS ($NIHSS_{expected}$) and the actual NIHSS ($NIHSS_{actual}$) on admission, and to study its prognostic value for early neurological improvement (ENI, defined as a reduction of NIHSS of ≥ 8 points or reaching 0/1 at 24 h) in AIS patients with large vessel occlusion (LVO) of the anterior circulation treated with MT. A cross-sectional study was conducted on AIS related to anterior territory LVO (2017–2022) at a Stroke Center. Using multivariate linear regression models in the derivation cohort, a formula for calculating the $NIHSS_{expected}$ on admission was developed, and the $NIHSS_{mismatch\%}$ between $NIHSS_{actual}$ and $NIHSS_{expected}$ was measured. Multivariate analyses were performed to identify if $NIHSS_{mismatch\%}$ levels predicted ENI. In the derivation cohort ($n = 123$), the following formula was developed: $NIHSS_{expected} = 10.8 + 0.05 \times Age + 2.5 \times DM + 2.6 \times Hemisphere - 1.5 \times ASPECTS_{admission}$. In the validation cohort ($n = 185$), 64 (34.6%) patients experienced ENI. The ROC curve identified 75% of $NIHSS_{mismatch\%}$ as the optimal cutoff for predicting ENI (80% sensitivity and 58% specificity). Multivariate analyses showed that both $NIHSS_{mismatch\%}$ and $NIHSS_{mismatch\%}$ >75 were predictors of ENI (OR 1.062; 95% CI 1.033–1.092 and OR 5.687; 95% CI 2.562–12.623, respectively), adjusted for potential confounders. $NIHSS_{mismatch\%}$ could be a predictor of ENI in AIS patients treated with MT.

Abbreviations

AIS	Acute ischemic stroke
ASPECTS	Alberta Stroke Program Early Computed Tomography Score
CED	Cerebral edema
CTA-SI	Computed Tomography-Angiography source images
CTP	Computed tomography perfusion
DW-MRI	Diffusion-weighted magnetic resonance imaging
ENI	Early neurological improvement
LVO	Large vessel occlusion
MT	Mechanical thrombectomy
NIHSS	National Institutes of Health Stroke Scale
NCCT	Non-contrast computed tomography

Mechanical thrombectomy (MT) is the standard of care for patients with large vessel occlusions (LVO) of the proximal anterior circulation[1]. An essential criterion for this treatment is that cerebral infarction is not established, and that salvageable brain tissue (so called penumbra), remains, to produce neurological improvement and

[1]Stroke Centre, Department of Neurology, Torrecárdenas University Hospital, Almería, Spain. [2]Division of Interventional Neuroradiology, Torrecárdenas University Hospital, Almería, Spain. [3]Foundation for Biosanitary Research of Eastern Andalusia, Torrecárdenas University Hospital, Almería, Spain. [4]Faculty of Health Sciences, CEINSA Health Research Centre, University of Almeria,, Almería, Spain. [5]Department of Neurology and Stroke Center, Torrecárdenas University Hospital, University of Almería, Hermandad de Donantes de Sangre S/N Street, Almería PC: 04009, Andalusia, Spain. [6]These authors contributed equally to this work: Laura Amaya-Pascasio, Miriam Fernández-Gómez and María del Mar Martínez-Salmerón. ✉email: patrinda@ual.es; patrindalo@hotmail.com

avoid post-reperfusion neurological complications (hemorrhagic transformation/malignant cerebral edema)[2]. To this end, many clinical trials with different time windows have been conducted in recent years[3,4].

To indicate MT within the first 6 h of an acute ischemic stroke (AIS) with a LVO in the anterior circulation is sufficient to estimate the salvageable brain tissue through a clinical-radiological mismatch, that is, an NIHSS (National Institutes of Health Stroke Scale) score >6 and an ASPECTS (Alberta Stroke Program Early Computed Tomography Score) score ≥ 6 on non-contrast computed tomography (NCCT)[1]. For time windows between 6 and 24 h, the "neuroimaging" criterion predominates, requiring advanced neuroimaging techniques, such as CT perfusion (CTP) and Diffusion-weighted magnetic resonance imaging (DW-MRI), with or without MRI perfusion[1]. However, the access and utilization of these modalities face several limitations such as heterogeneity in acquisition and postprocessing parameters, potentially hindering comparisons between studies[6], as well as geographical variations in imaging protocols and resources[7]. A recent clinical trials and observational studies also supports the benefit of mechanical thrombectomy in patients with large core infarcts, showing improved functional outcomes and reduced mortality, even in expanded populations beyond traditional imaging-based criteria[8].

It would be of interest to have estimates of salvageable brain tissue based on clinical parameters and simple neuroimaging[9–12], which would also help to estimate which patients are most likely to haver early neurological improvement (ENI), independently of the time window and the procedural factors associated to MT[13]. Recent studies show that the key to patient selection may lie in the clinical-radiological mismatch, thus is, a NIHSS score on admission higher than expected based on the ASPECT score[14,15]. Indeed, after 24 h, when brain infarction is fully established, there is a strong negative lineal correlation between NIHSS and ASPECTS and, on average, an increase of 10 points on NIHSS corresponds to a decrease of ≈ 3 points on ASPECTS[16]. However, no studies are available that measure the discordance between the NIHSS on admission and the theoretical NIHSS that would be expected based on clinical and neuroimaging parameters.

The hypothesis of the present study is that it is feasible to develop a predictive model that measures the discrepancy between the "real" and "expected" NIHSS score on admission (referred to as $NIHSS_{mismatch\%}$) in patients with AIS caused by a LVO in the anterior circulation, based on clinical data and the ASPECTS score on NCCT; and this $NIHSS_{mismatch\%}$ has a short-term prognostic value in patients undergoing MT. Thus, the objectives were: (1) To develop a model to estimate the "expected" NIHSS of a patient, considering the extension of the stroke, measured by the ASPECTS score on the concurrent cranial CT, as well as clinical parameters; (2) To calculate the $NIHSS_{mismatch\%}$ as the percentage discrepancy between the "expected" NIHSS and the "real" NIHSS, and (3) to perform an internal validation of the predictive capacity of the $NIHSS_{mismatch\%}$ for ENI in patients undergoing successful reperfusion.

Methods

Study design

A retrospective cross-sectional modeling study was conducted using a prospective database including patients aged ≥ 18 years with acute ischemic stroke (AIS) and large vessel occlusion (LVO) who were evaluated at Torrecárdenas University Hospital (TUH) in Almería, Spain, between 2017 and 2022. This hospital serves as the reference Stroke Center for a population of ≈ 700,000 inhabitants. Modeling was performed to estimate the "expected" $NIHSS_{expected}$ of a patient on admission, followed by modeling to establish the value of $NIHSS_{mismatch\%}$ that best predicts the development of ENI at 24 h.

The TRIPOD guidelines (Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis) were followed for study execution and reporting[17].

Patient inclusion/exclusion criteria

The inclusion criteria were patients with ischemic stroke aged ≥ 18 years who were hospitalized in the Stroke Unit between 2017 and 2022, with a symptom duration window of < 24 h, and who had a LVO detected by CT angiography upon admission in the anterior territory (internal carotid artery and/or middle cerebral artery), and who underwent MT. The exclusion criteria were to present a transient ischemic attack or cerebral hemorrhage, patients with incomplete data, patients with single anterior cerebral artery occlusion, and patients with LVO in the posterior territory.

All patients were managed and treated according to the international guidelines[1] and received general anesthesia with endotracheal intubation during the endovascular procedure.

Variables

Demographic data, comorbidities, vascular risk factors, neurological status (NIHSS score on admission and at 24 h), neuroimaging data on admission (NCCT plus multiphase CT angiography) and at 24 h (NCCT) including ASPECTS[18], the most proximal location of arterial occlusion (M1, M2 or internal carotid artery), the affected hemisphere (right/left) and the presence of collaterals grade on CT-Angiography source images (CTA-SI) according to DAWN trial[19] were collect. A single reader (M. F.-G.) determined the ASPECTS and collaterals grade on neuroimaging.

A NCCT were performed at 24+/−2 h hours according to our MT protocol and the presence of relevant neurological complications were recorded, such as parenchymal hemorrhage (PH1: hematoma within infarcted tissue, occupying < 30%, no substantive mass effect; PH2: hematoma occupying 30% or more of the infarcted tissue, with obvious mass effect)[20] and severe cerebral edema (CED) (characterized by focal brain swelling with visible midline shift [grade 3]) according to SITS-MOST criteria[21].

Early neurological improvement was defined as a reduction in the NIHSS score by ≥ 8 points or achieving an NIHSS score of 0/1 at 24 h, in patients undergoing MT[22].

Sample size

It was a pilot study in which the $NIHSS_{mismatch\%}$ was to be calculated for the first time, so there was no accurate estimate of the magnitude of the effect this parameter would have on ENI of patients with AIS undergoing MT. However, it was estimated that a sensitivity of at least 60% could be expected, with a 95% confidence interval and a lower limit of 50%, so at least 119 patients would be required[23]. To increase the study's power, all available patients during the study period were included.

Statistical analysis

All statistical analyses were conducted with SPSS (IBM SPSS Statistics 28.0, SPSS Inc. Chicago, IL) and Python (version 3.11). Missing data were minimal (< 2%) across variables included in the main analyses. These missing values were assumed to be missing completely at random (MCAR) based on the clinical context and absence of systematic patterns. Therefore, no imputation was performed, and analyses were conducted using complete-case data. An exception was made for covariates in multivariable modeling, where appropriate imputation was applied to preserve sample size and avoid unnecessary bias. Comparisons between groups were analyzed with the χ 2 or Fisher's exact test for dichotomous variables. Continuous variables were expressed as mean ± SD or median (interquartile range [IQR],) and compared with Student's t test or the Mann-Whitney test, as appropriate. Comparison between two dependent continuous variables were performed with the Wilcoxon rank-sum test. The correlations between two quantitative variables or between two ordinal variables were performed with Spearman's rho. Discrimination was assessed by calculating the area under the receiver operating characteristic (ROC) curve. Calibration was assessed by performing the R^2 and the Hosmer–Lemeshow goodness-of-fit test.

Patients included in the analysis were divided into two cohorts: the derivation and the validation cohort. The derivation cohort comprised first 40% of patients treated with MT. The validation cohort included the remaining 60% of patients treated with MT (Fig. 1).

Calculation of $NIHSS_{expected}$ and $NIHS_{mismatch\%}$ on admission

This calculation was developed in the derivation cohort. Multivariate generalized linear models were performed to identify independent factors explaining the NIHSS at 24 h, when the cerebral infarction was assumed to be established, adjusted based on the ASPECT score from the 24 h-NCCT scan, as well potential confounders (age, sex and variables with a p-value < 0.2 in the bivariate analysis). With the β-coefficients and the intercept from this linear correlation, the regression line equation was obtained. Then, the formula was used to calculate

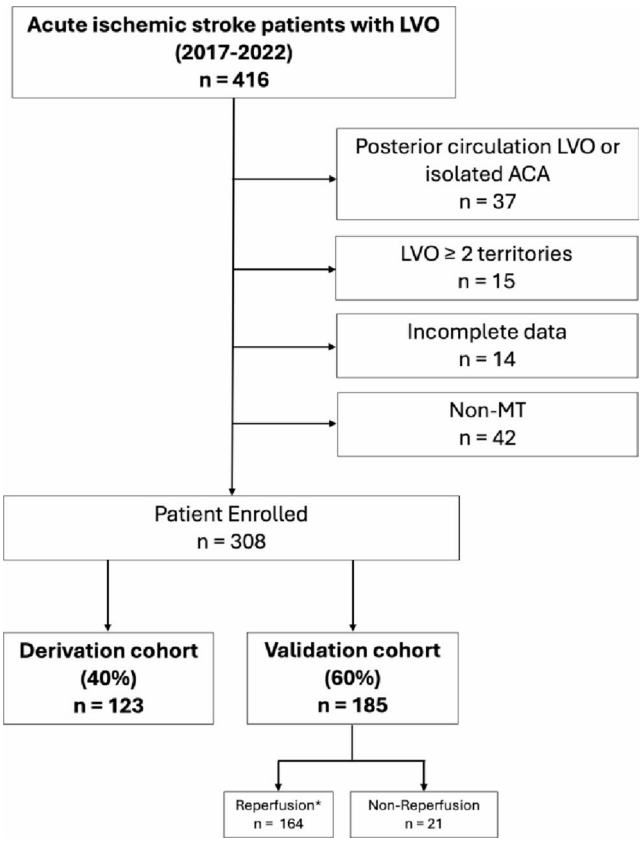


Fig. 1. Flowchart. Between January 2017 and December 2022, 416 patients were attended for large vessel occlusion-related ischemic stroke. Reasons for non-inclusion and patients included in the derivation and validations cohort are listed in the figure. ACA, anterior cerebral artery; LVO, large vessel occlusion; MT, mechanical thrombectomy. * mTICI 2bc3.

the "expected" NIHSS upon the patient's arrival at the Emergency Department, using neuroimaging data at admission (instead of at 24 h). After that, the following calculation was performed to determine the percentage discrepancy, or mismatch, between the "real" admission NIHSS ($NIHSS_{actual}$) and the "expected" admission NIHSS ($NIHSS_{expected}$):

$NIHSS_{mismatch\%} = (NIHSS_{actual} - NIHSS_{expectedl})/NIHSS_{actuall} \times 100$.

Internal validation

To assess the discriminative performance of NIHSS mismatch% for predicting ENI, we performed receiver operating characteristic (ROC) curve analysis in both the derivation and validation cohorts. The area under the curve (AUC) was calculated for each cohort, and 95% confidence intervals were estimated using 1000 bootstrap iterations to account for sampling variability. To formally test whether the AUCs differed significantly between cohorts, we applied a z-test for independent AUCs, which evaluates whether the observed difference between AUCs exceeds what would be expected by chance, given their respective standard errors.

On the other hand, the relationship between $NIHSS_{mismatch\%}$, and the development of ENI was analyzed in the group of patients with successful MT (eTICI grades 2b, 2c or 3)[24] in the validation cohort in two steps. First, another receiver ROC curve analysis was conducted determining the AUC as well as a cutoff point for $NIHSS_{mismatch\%}$. We considered the point at which the sum of the specificity and sensitivity was highest, giving the same weight to false-positives and false-negatives. Second, the relationship between this $NIHSS_{mismatch\%}$ cutoff point and the developments of ENI in the validation cohort was assessed using multivariate logistic regression models. Variables with a value of $P \leq 0.2$ in the bivariate testing were included. A forward stepwise logistic regression analysis was followed as the modelling strategy, using the log-likelihood ratio test to assess the correctness of fit and compare nested models. Two versions of the regression model were performed, one introducing $NIHSS_{mismatch\%}$ as continuous variable and the other with it dichotomized according to the results of the ROC curve. Models were validated by a ROC curve analysis. 95% confidence intervals (CI) are presented. All tests were two-sided and *P*-values ≤ 0.05 were considered statistically significant.

Ethical considerations

All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were approved by the Ethics Committee of the Torrecárdenas University Hospital. An informed consent was obtained from all subjects and/or their legal guardians.

Results

A total of 416 AIS patients with LVO were attended during the study period, of them 308 patients met de inclusion criteria, 123 in the derivation cohort and 185 in the validation cohort (Fig. 1).

Calculation of expected NIHSS ($NIHSS_{expected}$) on admission

In the derivation cohort, the mean (SD) age was 68.3 (14.9) and 58.5% were male. Median (IQR) of NIHSS on admission was 17[9] and at 24 h was 7[15]. The medina (IQR) of NCCT-ASPECTS was 8[2] on admission and 7[4] at 24 h. Furthermore, at 24 h the NCCT showed parenchymal hemorrhagic transformation (PH1/PH2) in 11.4% whereas grade 3 CED was present in 16.3% of patients. Basal data of the derivation cohort are showed in Table S1.

Table 1 summarizes NIHSS scores at 24 h according to baseline characteristics in the derivation cohort ($n = 123$). Patients with diabetes mellitus had higher NIHSS scores compared with those without diabetes (13.5 [IQR 14] vs. 5 [IQR 14]; $P = 0.009$). Smokers showed a tendency toward lower NIHSS compared with non-smokers (3.5 [IQR 11] vs. 8 [IQR 18]; $P = 0.091$). Scores differed significantly by baseline NCCT-ASPECTS: 1 [IQR 4] for 9–10, 5 [IQR 11] for 6–8, and 19 [IQR 10] for 0–5 ($P < 0.001$). Thrombus location showed a statistical trend, with higher NIHSS in ICA occlusions (13 [IQR 15]) compared with M1 (6 [IQR 14]) and M2 (5 [IQR 11]) occlusions ($P = 0.062$). Left-sided occlusions were associated with higher scores than right-sided (11 [IQR 16] vs. 5 [IQR 10]; $P = 0.012$). Finally, parenchymal hemorrhagic transformation (PH1/PH2) and severe cerebral edema (grade 3 CED) were strongly associated with higher NIHSS scores (19 [IQR 6] and 21 [IQR 5], respectively) compared with those without these complications (5 [IQR 13] and 5 [IQR 12]; both $P < 0.001$).

Multivariate generalized linear models were performed to identify independent factors explaining the NIHSS at 24 h based on age, sex, NCCT-ASPECTS at 24 h and other potential confounders showed in Table S2. With the approximated coefficients of this linear correlation, the following equation of the regression line was obtained:

$NIHSS_{24\_h} = 10.8 + 0.05xAge + 2.5xDM + 2.6xHemisphere + 4.1xHemorrhagic\ \ transformation + 6.5xEdema - 1.5x\ ASPECTS_{24h}$.

Where age was a quantitative variable (years), DM was a dichotomous variable (1 = yes, 0 = no), hemisphere was a dichotomous variable (0 = right, 1 = left), Hemorrhagic transformation (PH1/PH2) was a dichotomous variable (1 = yes, 0 = no), edema (grade 3 CED) was a dichotomous variable (1 = yes, 0 = no), and $ASPECTS_{24h}$ (NCCT-ASPECTS at 24 h) was a quantitative variable (with scores ranging from 0 to 10).

That formula was then used to calculate the theoretical NIHSS that a patient should have on admission, based on the ASPECT score on the first NCCT performed on arrival to the Emergency Department. As patients eligible for MT should not present with hemorrhagic transformation or grade 3 CED prior to treatment, the formula was simplified as follow:

$NIHSS_{expected} = 10.8 + 0.05xAge + 2.5xDM + 2.6xHemisphere - 1.5x\ ASPECTS_{admission}$.

Then, the $NIHSS_{mismatch\%}$ was calculated, showing a median (IQR) of 72.5[28]. Those cases with negative NIHSS ($n = 7$) were considered as having a value of 0.

Variables		NIHSS scale at 24 h Median (IQR)	*P*
Demographic data and comorbidities			
Age >65	Yes	8 (16)	0.072
	No	4 (14)	
Male sex, n (%)	Yes	6 (14)	0.849
	No	7 (17)	
Previous mRS < 2, n (%)	Yes	6 (15)	0.168
	No	13.5 (15)	
Arterial hypertension, n (%)	Yes	9 (14)	0.108
	No	5 (15)	
Dyslipidemia, n (%)	Yes	8 (16)	0.308
	No	6 (14)	
Diabetes mellitus, n (%)	Yes	13.5 (14)	0.009
	No	5 (14)	
Smoking, n (%)	Yes	3.5 (11)	0.091
	No	8 (18)	
Alcohol abuse, n (%)	Yes	6.5 (17)	0.313
	No	7 (15)	
Atrial fibrillation, n (%)	Yes	5.5 (14)	0.492
	No	8 (16)	
Coronary heart disease, n (%)	Yes	6 (20)	0.977
	No	7 (15)	
Previous stroke, n (%)	Yes	4 (6)	0.181
	No	8 (17)	
Prior treatments			
Antiplatelet Agents, n (%)	Yes	8.5 (16)	0.334
	No	5 (11)	
Anticoagulants, n (%)	Yes	4 (19)	0.313
	No	5 (11)	
Statins, n (%)	Yes	5 (18)	0.587
	No	6.5 (14)	
Neuroimaging			
NCCT-ASPECTS at 24 h	9–10	1 (4)	< 0.001
	6–8	5 (11)	
	0–5	19 (10)	
Proximal thrombus location on admission	ICA	13 (15)	0.062
	M1	6 (14)	
	M2	5 (11)	
Lateralization of the occlusion	Left	11 (16)	0.012
	Right	5 (10)	
Collaterals on CTA on admission*	Good	13 (18)	0.331
	Fair	6 (13)	
	Poor	5 (15)	
Parenchymal hemorrhagic transformation (PH1/PH2) at 24 h**	Yes	19 (6)	< 0.001
	No	5 (13)	
Cerebral edema with midline shift (grade 3) at 24 h, n (%)†	Yes	21 (5)	< 0.001
	No	5 (12)	

Table 1. NIHSS scale score distribution at 24 h, according to baseline data, in the derivation cohort ($n = 123$). * Dawn trial criteria[18]; **Heidelberg bleeding classification[19]; †SITS-MOST criteria[20].

Internal validation

The validation cohort comprised 185 patients (Fig. 1), being 56,8% males. The mean age (SD) was 71.4 (13.1) years (Table 2).

On admission, the median (IQR) of $NIHSS_{expected}$ was lower than $NIHSS_{actual}$ (4 [4] vs. 17 [7], $P < 0.001$). There was a weak and negative correlation between the $NIHSS_{actual}$ and the NCCT-ASPECTS on admission

	All (n = 185)	Early neurological improvement		
		Yes (n = 64)	No (n = 121)	P
Demographic data and comorbidities				
Male sex, n (%)	105 (56.8)	34 (53.1)	71 (58.7)	0.468
Age, mean (SD), years	71.4 (13.1)	68.6 (14.6)	72.7 (12.2)	0.174
Previous mRS < 2, n (%)	120 (64.9)	44 (68.8)	76 (62.8)	0.421
Arterial hypertension, n (%)	166 (89.7)	55 (85.9)	111 (91.7)	0.217
Dyslipidemia, n (%)	85 (45.9)	32 (50)	53 (43.8)	0.421
Diabetes mellitus, n (%)	61 (33)	17 (26.6)	44 (36.4)	0.177
Smoking, n (%)	37 (20)	12 (18.8)	25 (20.7)	0.757
Alcohol abuse, n (%)	15 (8.1)	4 (6.3)	11 (9.1)	0.501
Atrial fibrillation, n (%)	96 (51.9)	34 (53.1)	62 (51.2)	0.807
Coronary heart disease, n (%)	32 (17.3)	6 (9.4)	26 (21.5)	0.038
Previous stroke, n (%)	15 (8.1)	8 (12.5)	7 (5.8)	0.111
Prior treatments				
Antiplatelet Agents, n (%)	74 (40)	23 (35.9)	51 (42.1)	0.412
Anticoagulants, n (%)	25 (13.5)	10 (15.6)	15 (12.4)	0.541
Statins, n (%)	99 (53.5)	32 (50)	67 (55.4)	0.486
Stroke severity				
NIHSS on admission, median (IQR)	17 (7)	18 (8)	16 (6)	0.022
$NIHSS_{expected}$, median (IQR)	4 (4)	3 (4)	4 (4)	0.004
$NIHSS_{mismatch\%}$, median (IQR), %	77.4 (22.3)	83.1 (17.6)	72 (21.3)	< 0.001
$NIHSS_{mismatch\%}$ >72, n (%)	85 (45.9)	45 (70.3)	40 (33.1)	< 0.001
Extended time window (6–24 h), n (%)	53 (28.6)	18 (28.1)	35 (28.9)	0.909
Neuroimaging on admission				
NCCT-ASPECTS, median (IQR)	9 (2)	9 (2)	8 (3)	< 0.001
Proximal thrombus location M2 M1 ICA	19 (10.3) 126 (68.1) 40 (21.6)	4 (6.3) 46 (71.9) 14 (21.9)	15 (12.4) 80 (66.1) 26 (21.5)	0.418
Side of the occlusion: Left, n (%)	103 (55.7)	38 (59.4)	65 (53.7)	0.461
Collaterals grade on CTA-SI* on admission Good, n (%) Fair, n (%) Poor, n (%)	38 (20.5) 121 (65.4) 26 (14.1)	17 (26.6) 39 (60.9) 8 (12.5)	21 (17.4) 82 (67.8) 18 (14.9)	0.334
Thrombolysis, n (%)	120 (64.9)	44 (68.8)	76 (62.8)	0.421
Mechanical thrombectomy data				
Onset-to-groin puncture time, median (IQR), min	265 (264)	210 (168)	298.5 (311)	0.004
Door-to-groin puncture time, median (IQR), min	90 (47)	86 (35)	95 (63.5)	0.132
Number of passes, median (IQR)	3 (3)	3 (4)	3 (3)	0.082
Reperfusion-mTICI 2bc3, n (%)	164 (88.6)	60 (93.8)	104 (86)	0.112
Stroke aetiology (TOAST), n (%)				0.456
Large-vessel occlusive	43 (23.2)	15 (23.4)	28 (23.1)	
Cardioembolic	111 (60)	40 (62.5)	71 (58.7)	
Other	3 (1.6)	2 (3.1)	1 (0.8)	
Unknown	28 (15.1)	7 (10.9)	21 (17.4)	
Blood pressure on admission				
Systolic, mean (SD), mmHg	151.3 (28.9)	148.3 (25.3)	152.8 (30.5)	0.383
Diastolic, mean (SD), mmHg	81 (17.5)	80 (17)	81 (17.8)	0.674
Glycaemia on admission, mean (IQR) mg/dL	141.2 (53.6)	133.4 (42.5)	145 (58.2)	0.095

Table 2. Basal data of the validation cohort (n = 185) according with early neurological improvement (ENI). * Dawn trial criteria[18]. NIHSS, National Institutes of Health Stroke Scale; NCCT; *Non-contrast* computed tomography; ASPECTS, *Alberta* stroke program early CT score; CTA-SI, Computer Tomography Angiography source images; mTICI, modified Thrombolysis in cerebral infarction scale.

(Figure S1). However, the correlation between the $NIHSS_{expected}$ and the NCCT-ASPECTS on admission was as strong as that one between NIHSS and NCCT-ASPECTS at 24 h (Figure S1).

The $NIHSS_{mismatch\%}$ showed a median (IQR) of 77.4 (22.3). Those cases with negative $NIHSS_{mismatch\%}$ ($n = 1$) were considered as having a value of 0.

Table 2 shows the basal data of the validation cohort according with ENI. Sixty-four experienced ENI (34.6%). There was a higher prevalence of coronary heart disease in patients without ENI (21.5% vs. 9.4%, $p = 0.038$) as well as a higher median NIHSS on admission (18 vs. 16, $p = 0.022$). The median (IQR) of $NIHSS_{mismatch\%}$ was a greater in the ENI group (83.1 [17.6] vs. 72 [21.3], $P < 0.001$). Additionally, the median (IQR) of NCCT-ASPECTS on admission was higher in the ENI group (9 [2] vs. 8 [3], $P < 0.001$), whereas the median (IQR) onset-to-groin puncture time was shorter in the ENI (210 [168] min vs. 298.5 [311] min, $P = 0.004$).

Figure 2 shows the boxplots of the $NIHSS_{mismatch\%}$ distribution according to ENI in the derivation ($n = 123$) and the validation cohort, both in the whole cohort ($n = 185$) and in the cohort in which thrombectomy was successful ($n = 164$). Patients with ENI showed significantly greater $NIHSS_{mismatch\%}$ scores than patients without it, with minimal overlap in their distribution ($P < 0.001$).

In the derivation cohort, the ROC analysis for NIHSS mismatch% yielded an AUC of 0.754 with a 95% confidence interval of 0.659 to 0.838. In the validation cohort, the AUC was 0.689 (95% CI: 0.610 to 0.767) (Figure S2). Although there was a slight difference in point estimates, the overlap in confidence intervals and a non-significant z-test ($z = 1.07$, $p = 0.28$) indicate no meaningful difference in discriminative performance between the two cohorts.

The ROC curve for NIHSS mismatch% in the subgroup of patients with successful recanalization in the validation cohort ($n = 164$) is shown in Fig. 3. The analysis identified 75% as the optimal NIHSS mismatch% cutoff for predicting ENI, yielding a sensitivity of 80% and specificity of 58%.

The multivariate analyses (Table 3) showed that $NIHSS_{mismatch\%}$ and $NIHSS_{mismatch\%}$ >75 were predictors of ENI (OR 1.062; 95% CI 1.033–1.092 and OR 5.687; 95% CI 2.562–12.623, respectively), adjusted for potential confounders. Both models showed a good discriminatory ability assessed by the c-statistic (AUC = 0.777; 95% CI 0.705–0.848 and AUC = 0.791; 95% CI 0.722–0.859, respectively) (Fig. 3) as well as a good calibration (Cox and Snell R2 = 0.212 and 0.231, respectively) (Table 3). Furthermore, the discriminatory ability of $NIHSS_{mismatch\%}$ and models was superior to that of the ASPECTS (Fig. 3).

The subgroups analyses showed that the prognostic value of $NIHSS_{mismatch\%}$ remained constant in most cases (Figure S3).

Representative examples of patients with similar baseline NIHSS scores and M1 occlusions but differing NIHSS mismatch% are shown in Fig. 4. Patient 1, with a mismatch of 88%, experienced early neurological improvement at 24 h, while Patient 2, with a mismatch of 33%, did not.

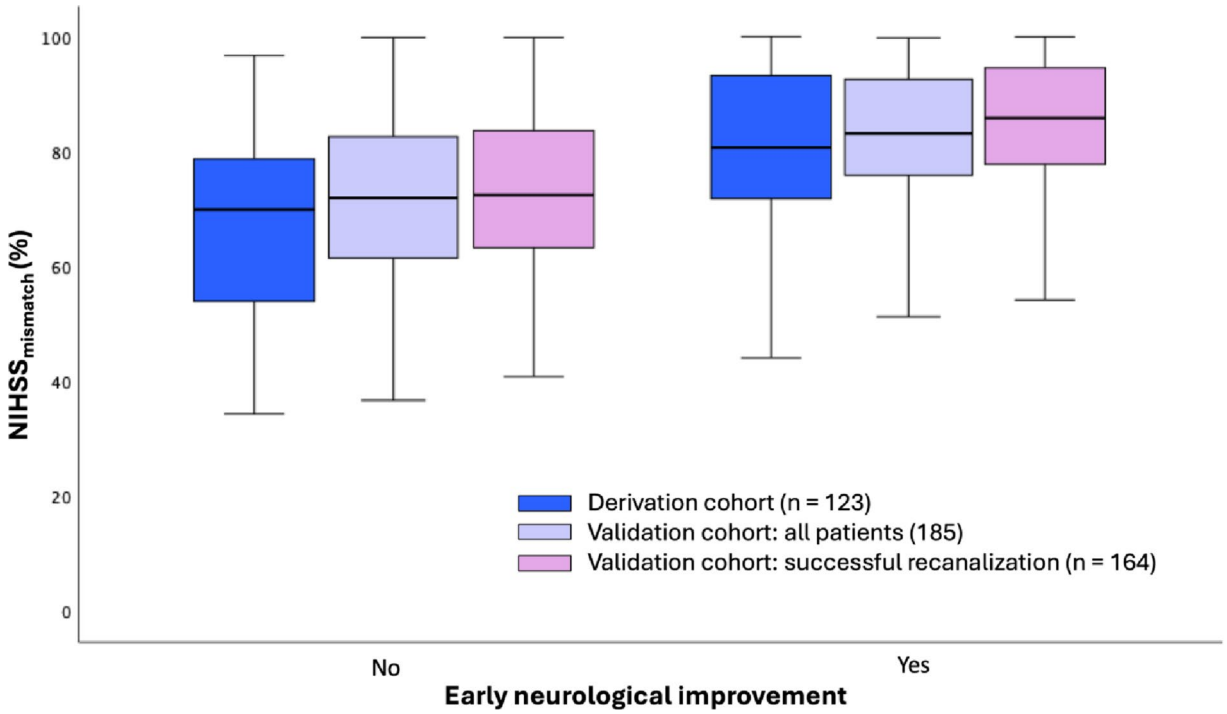


Fig. 2. $NIHSS_{mismatch\%}$ distribution according to early neurological improvement in the derivation and the validation cohort. $P < 0.001$ for comparisons between early neurological improvement (ENI) and non-ENI patients in all groups.

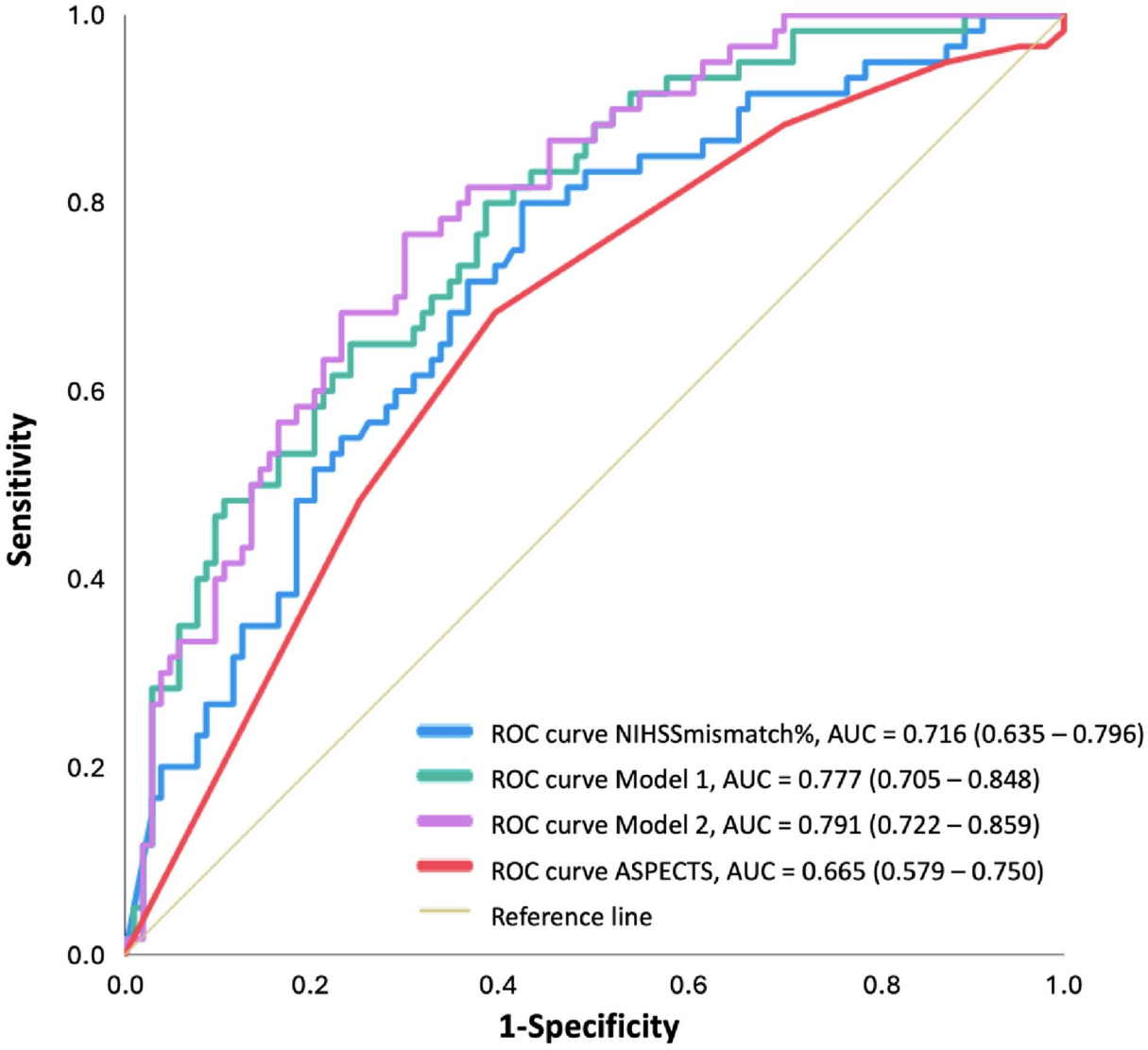


Fig. 3. ROC curve for early neurological improvement in patient with successful recanalization (validation cohort, $n = 164$). ROC curves for early neurological improvement based on $NIHSS_{mismatch\%}$ (blue curve) as well as on the logistic regression Model 1 (green curve) which include $NIHSS_{mismatch\%}$, the Model 2 (mauve curve) which include $NIHSS_{mismatch\%}$ >75 and on the ASPECTS on admission (red curve). Models 1 and 2 are detailed in Table 3.

Discussion

To the best of our knowledge, this is the first study that analyses the discordance or mismatch between the "real" NIHSS and the "expected" NIHSS ($NIHSS_{mismatch\%}$), as well as its influence on the short-term prognosis in patients with LVO in the anterior circulation reaching successful reperfusion. The results show that patients with an $NIHSS_{mismatch\%}$ >75 had five times more the probability of experiencing ENI compared to those with a lower mismatch, adjusted for potential confounders.

In this study, it was observed that the factors related to the NIHSS score on admission included the ASPECTS score, the affected hemisphere, the thrombus location, age, DM and acute neurological complications (hemorrhage/edema). Previous studies have shown that these factors affect stroke severity, as measured by the NIHSS[25–28]. For example, several studies have demonstrated an inverse relationship between the NIHSS, and the ASPECTS score at stroke onset[25–28], and it has been estimated that each 10-point increase in the initial NIHSS is associated with a 3-point decrease in the ASPECTS score[16] as previously said, while an ASPECTS score of 6–10 points is associated with a higher likelihood of a favorable outcome[29]. Additionally, the NIHSS depends on the affected hemisphere, being greater if left one[30], as well as the thrombus location, the age and the vascular risk factors[28].

In recent decades, several studies have analyzed clinical-radiological mismatch in patients undergoing reperfusion treatments, especially those receiving intravenous thrombolysis (IVT) with alteplase, with conflicting results[14,16]. Kent et al. concluded that clinical-radiological mismatch between the NIHSS and the ASPECTS score

Variable	Un-adjusted		Model 1*		Model 2**	
	OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Demographic data and comorbidities						
Age, years	0.975 (0.951–0.999)	0.043	-	-	-	-
Male sex	0.677 (0.357–1.285)	0.233				
Diabetes mellitus	0.604 (0.297–1.226)	0.163	-	-	-	-
Coronary heart disease	0.287 (0.104–0.797)	0.017	-	-	-	-
Previous stroke	1.961 (0.840–4.581)	0.120	-	-	-	-
Stroke severity			-	-	-	-
NIHSS on admission	1.075 (1.012–1.142)	0.020	1.092 (1.018–1.172)	0.014	1.085 (1.012–1.163)	0.021
$NIHSS_{mismatch}$%	1.056 (1.030–1.082)	<0.001	1.062 (1.033–1.092)	<0.001		
$NIHSS_{mismatch\%}$>75	5.455 (2.596–11.462)	<0.001			5.687 (2.562–12.623)	0.007
NCCT-ASPECT on admission	1.445 (1.128–1.850)	0.004	-	-	-	-
Mechanical thrombectomy data			-	-	-	-
Onset-to-door time, min	0.998 (0.997–0.999)	0.058	-	-	0.998 (0.996–0.999)	0.048
Door-to-groin puncture time, min	0.996 (0.991–1.001)	0.085	0.995 (0.990–0.999)	0.038	0.994 (0.9889–0.999)	0.022
Number of passes	0.830 (0.701–0.983)	0.028	0.773 (0.637–0.938)	0.009	0.759 (0.623–0.926)	0.007
Glycaemia on admission mg/dL	0.994 (0.987–1.001)	0.076	-	-	-	-

Table 3. Multivariate analysis of factors associated with early major neurological improvement in patient with successful recanalization (validation cohort, $n = 164$). *Model 1: Forward Stepwise Logistic regression analysis adjusted for the variables listed except for $NIHSS_{mismatch\%}$ >75. Cox and Snell R2 = 0.212. **Model 2: Forward Stepwise Logistic regression analysis adjusted for the variables listed except for $NIHSS_{mismatch}$%. Cox and Snell R2 = 0.231. NIHSS, National Institutes of Health Stroke Scale; NCCT, non-contrast computed tomography.

did not reliably identify patients with higher or lower likelihoods of benefiting from IVT[16]. In contrast, Deng et al. showed that patients with a positive NIHSS-ASPECTS mismatch, defined as NIHSS ≥ 8 and ASPECTS ≥ 8, had a higher probability of favorable evolution, with better risk profiles for intracranial hemorrhage and mortality, after IVT[14]. A "clinical-radiological mismatch" means that the patient's clinical symptoms may be milder or less pronounced than expected based on visible changes in brain imaging. This may be due to the presence of "ischemic penumbra", an area of brain tissue where cerebral blood flow is insufficient, but cell death has not yet occurred[31]. The DAWN clinical trial was the first to demonstrate that patients eligible for MT could be selected based on a large penumbra area, considering the clinical-radiological mismatch from a high NIHSS score and the presence of a small infarct on advanced neuroimaging (DW-MRI or CTP)[32].

On the other hand, ENI following MT for AIS is a strong predictor of favorable long-term outcomes. ENI, typically defined as a significant reduction in the NIHSS score within 24 h post-treatment, is associated with higher rates of good functional outcomes at 90 days, lower mortality, and reduced symptomatic intracranial hemorrhage[33]. Previous studies have shown that factors predicting ENI include younger age, lower baseline NIHSS score, absence of early CT hypodensity, arterial patency, and presence of collateral blood supply[13,34]. Additionally, shorter time from onset to admission and from groin-puncture to reperfusion, as well as higher baseline CT perfusion ASPECTS, are associated with ENI[13]. It has recently been reported that ischemic penumbra, estimated by perfusion CT, is present in at least 80% of patients with large vessel occlusion undergoing TM and that reperfusion is associated with higher rates of good functional outcomes at 3 months in those patients with more favorable mismatch patterns[5]. However, the effect of ischemic penumbra on ENI in these patients is unknown.

In the present study, the mismatch between the "real" and "expected" NIHSS was estimated using a model that included the ASPECTS and other clinical and neuroimaging data. The presence of a mismatch > 75% between the "real" and "expected" NIHSS on admission was associated with a higher probability of experiencing an ENI after MT. This simple method for estimating the penumbra area, using only clinical and basic neuroimaging data, has not been described in the scientific literature to date, opening a novel line of research that will need to be developed in multicentric studies.

This study has several limitations. First, it was conducted at a single center and is based on retrospective data, which may introduce selection bias and limits generalizability. Although the sample size is relatively large for a pilot study and exceeded the a priori estimation based on the expected effect size, the findings should be confirmed in larger, multicenter prospective cohorts. Second, our approach derives $NIHSS_{expected}$ at admission from a multivariable model of NIHSS at 24 h; this operational choice assumes that determinants of NIHSS at 24 h approximate those at baseline. We recognize that acute ischemic stroke evolves non-linearly and that treatments administered between admission and 24 h (including MT) may shift NIHSS independently of baseline infarct burden, potentially biasing estimates of NIHSSexpected. Third, while site of occlusion and collateral grade were included among the candidate predictors and tested in the modelling process, they were not retained in the final parsimonious model after collinearity checks and stepwise selection. Moreover, other relevant covariates—particularly perfusion-based imaging parameters —were not consistently available in our dataset and therefore could not be incorporated. Finally, NIHSS provides a quantitative clinical measure of deficit, whereas ASPECTS

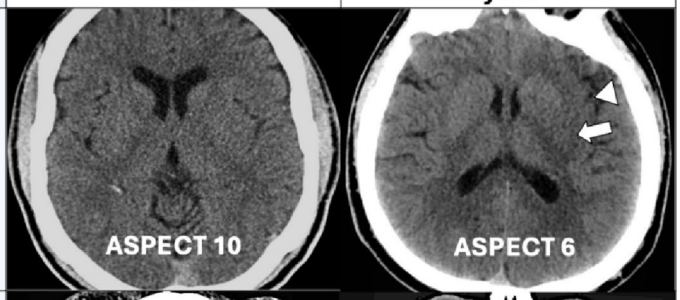
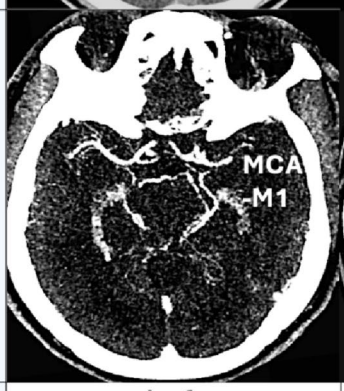
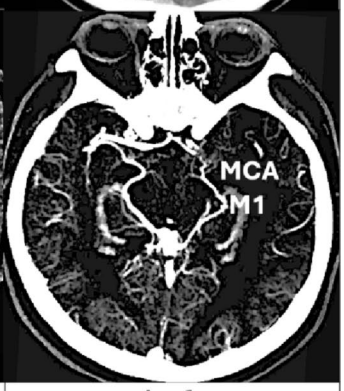
	Patient 1 (High NIHSSmismatch)	Patient 2 (Low NIHSSmismatch)
Sex	Male	Male
Age, years	49	52
Diabetes mellitus	No	yes
NCCT-ASPECT on admission		
Oclusion location on CTA on admission		
Affected hemisphere	Left	Left
NIHSSactual	15	15
NIHSSexpected*	1	10
NIHSSmismatch**	94%	37%
NIHSS at 24h	1	18
Early neurological improvement	**Yes**	**No**

Fig. 4. Representative cases of high and low $NIHSS_{mismatch\%}$ illustrating its prognostic value for early neurological improvement. Comparative clinical and imaging data from two patients with left M1 middle cerebral artery occlusion and similar baseline NIHSS scores[15]. Patient 1 had a higher NCCT-ASPECTS score on admission (ASPECTS 10), resulting in a lower predicted NIHSS ($NIHSS_{expected}$ = 2) and a higher $NIHSS_{mismatch\%}$ (94%), and experienced early neurological improvement (NIHSS at 24 h = 1). Patient 2 had a lower ASPECTS score (ASPECTS 6, arrow and arrowhead), a higher predicted NIHSS ($NIHSS_{expected}$ = 10), and lower $NIHSS_{mismatch\%}$ (33%), and did not show early neurological improvement (NIHSS at 24 h = 18). This figure illustrates how $NIHSS_{mismatch\%}$ reflects the discordance between clinical severity and infarct extent, and its potential value as a marker of salvageable tissue. NIHSS, National Institutes of Health Stroke Scale; $NIHSS_{actual}$, NIHSS on admission; NCCT; *Non-contrast* computed tomography; ASPECTS, *Alberta* stroke program early CT score; CTA-SI, Computer Tomography Angiography source images. *$NIHSS_{expected}$ = 10.8 + 0.05xAge + 2.5xDM + 2.6xHemisphere – 1.5x $ASPECTS_{admission}$. **$NIHSS_{mismatch\%}$ = ($NIHSS_{actual}$ – $NIHSS_{expectedl}$)/$NIHSS_{actuall}$ x 100.

is a semi-quantitative measure of infarct extent that does not encode eloquence or lateralization; this conceptual difference may limit the precision of NIHSSmismatch% and motivates further refinement of the model. Despite these limitations, the study provides proof-of-concept evidence that $NIHSS_{mismatch\%}$ is a promising predictor of ENI after MT.

Conclusions

The "expected" NIHSS score at the emergency admission of a stroke patient can be calculated using a model based on clinical and conventional neuroimaging variables. The discordance between the "expected" and the "real" NIHSS, or $NIHSS_{mismatch\%}$, can be quantified. The ROC curve identifies a $NIHSS_{mismatch\%}$ of 75% as the optimal cutoff for predicting ENI (80% sensitivity and 58% specificity). $NIHSS_{mismatch\%}$ is a factor associated with ENI after MT, defined as a reduction in the NIHSS of ≥ 8 points or achieving a NIHSS score of 0/1 at 24 h. Moreover, the $NIHSS_{mismatch\%}$, could be an estimator of ischemic penumbra in patients with AIS, although this needs to be confirmed in specific studies.

In conclusion, the $NIHSS_{mismatch\%}$ is a predictor of ENI after successful MT. Its value needs to be tested in large multi-center studies.

Data availability

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

Received: 21 October 2024; Accepted: 10 November 2025
Published online: 24 December 2025

References

1. Powers, W. J. et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the. *Stroke*. **50**(12), e344-e418. (2019). https://doi.org/10.1161/STR.0000000000000211. Epub 2019 Oct 30. Erratum in: Stroke. **50**(12):e440-e441 (2019).
2. Ng, F. C. et al. HERMES Collaborators. Cerebral edema in patients with large hemispheric infarct undergoing reperfusion treatment: A HERMES Meta-Analysis. *Stroke* **52** (11), 3450–3458. https://doi.org/10.1161/STROKEAHA.120.033246 (2021).
3. Goyal, M. et al. HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* **387** (10029), 1723–1731. https://doi.org/10.1016/S0140-6736(16)00163-X (2016).
4. Jovin, T. G. et al. Thrombectomy for anterior circulation stroke beyond 6 h from time last known well (AURORA): a systematic review and individual patient data meta-analysis. *Lancet* **399** (10321), 249–258. https://doi.org/10.1016/S0140-6736(21)01341-6 (2022).
5. Olivot, J. M. et al. FRAME Investigators*. Mismatch profile influences outcome after mechanical thrombectomy. *Stroke* **52** (1), 232–240. https://doi.org/10.1161/STROKEAHA.120.031929 (2021).
6. Dani, K. A. et al. Systematic review of perfusion imaging with computed tomography and magnetic resonance in acute ischemic stroke: heterogeneity of acquisition and postprocessing parameters: a translational medicine research collaboration multicentre acute stroke imaging study. *Stroke* **43** (2), 563–566. https://doi.org/10.1161/STROKEAHA.111.629923 (2012).
7. Nguyen, T. N. et al. Late window imaging selection for endovascular therapy of large vessel occlusion stroke: an international survey. *Stroke Vasc Interv Neurol.* **3** (1), e000595. https://doi.org/10.1161/svin.122.000595 (2023).
8. Hukamdad, M., Biller, J., Testai, F. D. & Trifan, G. Endovascular thrombectomy for large core volume acute ischemic stroke. Updated systematic review and meta-analysis: thrombectomy for large core acute ischemic strokes. *J. Stroke Cerebrovasc. Dis.* **34**, 108135. https://doi.org/10.1016/j.jstrokecerebrovasdis.2024.108135 (2025).
9. Hendrix, P. et al. Outcomes of mechanical thrombectomy in the early (< 6-hour) and extended (≥ 6-hour) time window based solely on Noncontrast CT and CT angiography: A propensity Score-Matched cohort study. *AJNR Am. J. Neuroradiol.* **42** (11), 1979–1985. https://doi.org/10.3174/ajnr.A7271 (2021).
10. Nguyen, T. N. et al. Noncontrast computed tomography vs computed tomography perfusion or magnetic resonance imaging selection in late presentation of stroke with Large-Vessel occlusion. *JAMA Neurol.* **79** (1), 22–31. https://doi.org/10.1001/jamaneurol.2021.4082 (2022).
11. Porto, G. B. F. et al. Stroke thrombectomy and aneurysm registry (STAR) Collaborators. Association of Noncontrast computed tomography and perfusion modalities with outcomes in patients undergoing Late-Window stroke thrombectomy. *JAMA Netw. Open.* **5** (11), e2241291. https://doi.org/10.1001/jamanetworkopen.2022.41291 (2022).
12. Kim, M. S. & Kim, G. S. Single centre experience on decision making for mechanical thrombectomy based on Single-Phase CT angiography by including NCCT and maximum intensity projection Images - A comparison with magnetic resonance imaging after Non-Contrast CT. *J. Korean Neurosurg. Soc.* **63** (2), 188–201. https://doi.org/10.3340/jkns.2019.0131 (2020).
13. Weyland, C. S. et al. Predictors for Failure of Early Neurological Improvement After Successful Thrombectomy in the Anterior Circulation. *Stroke*. **52**(4), 1291–1298. (2021). https://doi.org/10.1161/STROKEAHA.120.030519. Epub 2021 Feb 25. Erratum in: Stroke. **52**(5), e211 (2021). doi: 10.1161/STR.0000000000000372.
14. Deng, P. P. et al. NIHSS-the Alberta stroke program early CT score mismatch in guiding thrombolysis in patients with acute ischemic stroke. *J. Neurol.* **269** (3), 1515–1521. https://doi.org/10.1007/s00415-021-10704-5 (2022).
15. Nagaraja, N. Diffusion weighted imaging in acute ischemic stroke: A review of its interpretation pitfalls and advanced diffusion imaging application. *J. Neurol. Sci.* **425**, 117435. https://doi.org/10.1016/j.jns.2021.117435 (2021).
16. Kent, D. M. et al. Clinical-CT mismatch and the response to systemic thrombolytic therapy in acute ischemic stroke. *Stroke* **36** (8), 1695–1699. https://doi.org/10.1161/01.STR.0000173397.31469.4b (2005).
17. Collins, G. S., Reitsma, J. B., Altman, D. G. & Moons, K. G. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *BMJ* **350**, g7594. https://doi.org/10.1136/bmj.g7594 (2015).
18. Pexman, J. H. et al. Use of the Alberta stroke program early CT score (ASPECTS) for assessing CT scans in patients with acute stroke. *AJNR Am. J. Neuroradiol.* **22** (8), 1534–1542 (2001).
19. Liebeskind, D. S. et al. DAWN Investigators. Collateral circulation in thrombectomy for stroke after 6 to 24 hours in the DAWN trial. *Stroke* **53** (3), 742–748. https://doi.org/10.1161/STROKEAHA.121.034471 (2022).
20. von Kummer, R. et al. The Heidelberg bleeding classification: classification of bleeding events after ischemic stroke and reperfusion therapy. *Stroke* **46**, 2981–2986. https://doi.org/10.1161/STROKEAHA.115.010049 (2015).
21. Thorén, M. et al. Predictors for cerebral edema in acute ischemic stroke treated with intravenous thrombolysis. *Stroke* **48**, 2464–2471. https://doi.org/10.1161/STROKEAHA.117.018223 (2017).
22. Faizy, T. D. et al. Favourable arterial, tissue-level and venous collaterals correlate with early neurological improvement after successful thrombectomy treatment of acute ischaemic stroke. *J. Neurol. Neurosurg. Psychiatry*. **16**, jnnp–2021. https://doi.org/10.1136/jnnp-2021-328041 (2022 May).
23. Flahault, A., Cadilhac, M. & Thomas, G. Sample size calculation should be performed for design accuracy in diagnostic test studies. *J. Clin. Epidemiol.* **58** (8), 859–862. https://doi.org/10.1016/j.jclinepi.2004.12.009 (2005).
24. Liebeskind, D. S. et al. HERMES Collaborators. eTICI reperfusion: defining success in endovascular stroke therapy. *J. Neurointerv Surg.* **11** (5), 433–438. https://doi.org/10.1136/neurintsurg-2018-014127 (2019). Epub 2018 Sep 7. PMID: 30194109.

25. Esmael, A., Elsherief, M. & Eltoukhy, K. Predictive value of the Alberta stroke program early CT score (ASPECTS) in the outcome of the acute ischemic stroke and its correlation with stroke Subtypes, NIHSS, and cognitive impairment. *Stroke Res. Treat.* **2021**, 5935170. https://doi.org/10.1155/2021/5935170 (2021).
26. Amalia, L. et al. Clinical significance Alberta stroke program early computed tomography score (ASPECTS) and National Institute of health stroke score (NIHSS) on first ever acute ischemic stroke patients. *Internet J. Neurol.* **21** (1), 2019 (2019).
27. Hill, M. D. & Buchan, A. M. Canadian Alteplase for stroke effectiveness study (CASES) Investigators. Thrombolysis for acute ischemic stroke: results of the Canadian Alteplase for stroke effectiveness study. *CMAJ* **172** (10), 1307–1312. https://doi.org/10.1503/cmaj.1041561 (2005).
28. Montaner, J. & Alvarez-Sabín, J. La Escala de ictus Del National Institute of health (NIHSS) y Su adaptación al español [NIH stroke scale and its adaptation to Spanish]. *Neurologia* **21** (4), 192–202 (2006). Spanish.
29. Yang, S. H. & Liu, R. Four decades of ischemic penumbra and its implication for ischemic stroke. *Transl Stroke Res.* **12** (6), 937–945. https://doi.org/10.1007/s12975-021-00916-2 (2021).
30. Vitti, E., Kim, G., Stockbridge, M. D., Hillis, A. E. & Faria, A. V. Left hemisphere bias of NIH stroke scale is most severe for middle cerebral artery strokes. *Front. Neurol.* **13**, 912782. https://doi.org/10.3389/fneur.2022.912782 (2022).
31. Ermine, C. M., Bivard, A., Parsons, M. W. & Baron, J. C. The ischemic penumbra: from concept to reality. *Int. J. Stroke.* **16** (5), 497–509. https://doi.org/10.1177/1747493020975229 (2021).
32. Nogueira, R. G. et al. DAWN trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl. J. Med.* **378** (1), 11–21. https://doi.org/10.1056/NEJMoa1706442 (2018).
33. Kobeissi, H., Ghozy, S., Bilgin, C., Kadirvel, R. & Kallmes, D. F. Early neurological improvement as a predictor of outcomes after endovascular thrombectomy for stroke: a systematic review and meta-analysis. *J. Neurointerv Surg.* **15** (6), 547–551. https://doi.org/10.1136/neurintsurg-2022-019008 (2023). Epub 2022 May 30. PMID: 35636948.
34. Li, Y. et al. Predictors of early neurological improvement in patients with anterior large vessel occlusion and successful reperfusion following endovascular Thrombectomy-Does CT perfusion imaging matter? *Clin. Neuroradiol.* **32** (3), 839–847. https://doi.org/10.1007/s00062-022-01147-0 (2022).

Author contributions

L A-P and P M-S designed the study and wrote the first draft of the manuscript. M F-G and C H-B undertook analyses and interpretation of study findings. E G-S, ML R-F, MM M-S, C T-P, D V-F and A A-P contributed to the interpretation of study findings, reviews, and revision ofthe manuscript. AJ R-S, J G-P contributed to the findings review and revision of the manuscript. All the authors critically reviewed the various versions of the full paper and approved the final manuscript.

Funding

This work is part of the Spanish Health Outcomes-Oriented Cooperative Research Networks (RICORS-ICTUS), Instituto de Salud Carlos III (Carlos III Health Institute), Ministerio de Ciencia e Innovación (Ministry of Science and Innovation), RD241/0009/0030 (Torrecardenas University Hospital). Funded by the European Union – NextGenerationEU. Recovery, Transformation, and Resilience Plan.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Torrecárdenas University Hospital.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-28303-z.

Correspondence and requests for materials should be addressed to P.M.-S.