Stroke: Vascular and Interventional Neurology

ORIGINAL RESEARCH

Association of the 24-Hour National Institutes of Health Stroke Scale After Mechanical Thrombectomy With Early and Long-Term Survival

Christoph C. Kurmann, MD; Morin Beyeler, MD; Lorenz Grunder, MD; Matthias F. Lang, MD; Eike I. Piechowiak, MD; Thomas R. Meinel, MD; Simon Jung, MD; Angelika Hoffmann, MD; David J. Seiffge, MD; Mirjam R. Heldner, MD; Tomas Dobrocky, MD; Pasquale Mordasini, MD; Marcel Arnold, MD; Jan Gralla, MD; Urs Fischer, MD; Johannes Kaesmacher, MD

BACKGROUND: The National Institutes of Health Stroke Scale (NIHSS) obtained 24 hours after ischemic stroke is a good indicator for functional outcome and early mortality, but the correlation with long-term survival is less clear. We analyzed the correlation of the NIHSS after 24 hours (24h NIHSS) and early clinical neurological development after mechanical thrombectomy with early and long-term survival as well as its predictive power on survival.

METHODS: We reviewed a prospective observational registry for all patients undergoing mechanical thrombectomy between January 2010 and December 2018. Vital status was extracted from the Swiss Population Registry. Adjusted hazard ratio (aHR) and crude hazard ratios were calculated using Cox regression. To assess predictive power of the 24h NIHSS, different Random Survival Forest models were evaluated.

RESULTS: We included 957 patients (median follow-up 1376 days). Patients with lower 24h NIHSS and major early neurological improvement had substantially better survival rates. We observed significantly higher aHR for death in patients with 24h NIHSS 12 to 15 (aHR, 1.78; 95% CI, 1.1–2.89), with 24h NIHSS 16 to 21 (aHR, 2.54, 95% CI, 1.59–4.06), and with 24h NIHSS >21 (aHR, 5.74; 95% CI, 3.47–9.5). The 24h NIHSS showed the best performance predicting mortality (receiver operating characteristic area under the curve at 3 months [0.85±0.034], at 1 year [0.82±0.029], at 2 years [0.82±0.031], and at 5 years [0.83±0.035]), followed by NIHSS change.

CONCLUSIONS: Patients with acute ischemic stroke achieving a low 24h NIHSS or major early neurological improvement after mechanical thrombectomy had markedly lower long-term mortality. Furthermore, 24h NIHSS had the best predictive power for early and long-term survival in our machine learning–based prediction.

In acute ischemic stroke, the clinical presentation may vary over time after initial presentation and especially after acute treatment with intravenous thrombolysis or mechanical thrombectomy (MT).[1–4] Baseline evaluation of the National Institutes of Health Stroke Scale (NIHSS) and an early follow-up after

Correspondence to: Johannes Kaesmacher MD, University Institute of Diagnostic and Interventional Neuroradiology, University Hospital Bern, Inselspital, University of Bern, Bern 3010, Switzerland.
E-mail: Johannes.kaesmacher@insel.ch

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/SVIN.121.000244

Christoph C. Kurmann, Morin Beyeler, Urs Fischer, and Johannes Kaesmacher contributed equally to this work.

Stroke: Vascular and Interventional Neurology is available at: www.ahajournals.org/journal/svin

24 hours (24h NIHSS) are readily available and quantify the severity of neurological deficits and their dynamic evolution. Additionally, the 24h NIHSS is a good indicator for functional outcome[1,5–8] and mortality after 3 months[9] and has been proposed as early surrogate study end point.[5,6,10] However, the correlation with long-term survival is less clear.

Successful recanalization of occluded vessels is the goal of acute ischemic stroke treatment and is usually associated with early neurological improvement (ENI)[4,11,12] and reduced 3-month mortality.[13–19] Because recent results have also shown an association between successful reperfusion and reduced long-term mortality,[20] early neurological deficit severity (represented as the 24h NIHSS) may be considered as an indicator of long-term survival.

We analyzed the correlation of the 24h NIHSS and the change of the NIHSS within 24 hours after MT in acute ischemic stroke with early and long-term survival as well as with the final degree of reperfusion. Furthermore, we evaluated their predictive power on survival at different time points.

Clinical Perspective

- In patients undergoing mechanical thrombectomy, there is a strong correlation between day 1 neurological deficit and long-term mortality.
- National Institutes of Health Stroke Scale after 24 hours was the most precise predictor of long-term mortality when compared with other measures of the early neurological clinical course.
- Random Survival Forests resulted in good accuracy of long-term mortality prediction, which may be used for clinical prediction or for predicted treatment effect estimators in clinical trials.

Nonstandard Abbreviations and Acronyms

aHR	adjusted hazard ratio
cHR	crude hazard ratio
END	early neurological deterioration
ENI	early neurological improvement
ENS	early neurological stability
eTICI	Expanded Thrombolysis in Cerebral Infarction
mENI	major early neurological improvement
MT	mechanical thrombectomy
NIHSS	National Institutes of Health Stroke Scale
RSF	Random Survival Forest
ASPECTS	Alberta Stroke Programme Early CT Score

METHODS

Population

We reviewed all consecutive patients with acute ischemic stroke treated with MT from January 2010 to December 2018 who met the following inclusion criteria:

- Complete records for NIHSS on admission, 24h NIHSS, and other clinically relevant covariables (see below)
- Available long-term vital status follow-up
- Available anterior-posterior and lateral digital subtraction angiography projections post-MT without severe imaging/motion artifacts

The vital status was extracted from the Swiss Population Registry between September 2019 and May 2020. Follow-up time was defined as time from the index stroke to the last update of the Swiss Population Registry or the date of death. The local ethics committee agreed to use assessment of long-term mortality for patients who had not actively opposed to the use of their biological data (reference ID 2019-00547, Kantonale Ethikkomission Bern). The data that support the findings of this study are available from the corresponding author upon reasonable request.

The extent of reperfusion after MT was core lab adjudicated by 3 neuroradiologists (J.K., C.C.K., E.I.P.) using the Expanded Thrombolysis in Cerebral Infarction (eTICI) score, which makes the following distinctions: eTICI 0 (no reperfusion), eTICI 1 (thrombus reduction without any reperfusion of distal arteries), eTICI 2a (<50% reperfusion), eTICI 2b50 (50%–66% reperfusion), eTICI 2b67 (67%–89% reperfusion), eTICI 2c (near-complete reperfusion, 90%–99%), and eTICI 3 (100% reperfusion).[21]

We excluded patients who died within 24 hours after MT from all analyses. Missing values were not imputed.

Statistical Analysis

Normality of all baseline variables was tested using the Shapiro-Wilk test and visual inspection of density plots. Data are presented as n (%) or median (interquartile range) if not otherwise specified. Baseline

characteristics for included and excluded patients were compared using Mann-Whitney *U* and Fisher exact tests for continuous and categorical variables, respectively.

The following variables were defined for analysis: 24h NIHSS, NIHSSΔ (24h NIHSS – NIHSS on admission), and NIHSS% ($\frac{\text{NIHSS}\Delta}{\text{NIHSS on admission}} * 100$). Major early neurological improvement (mENI) was defined as reduction in NIHSS score of at least 8 points or reaching 24h NIHSS of 0 to 1,[22,23] ENI was defined as NIHSS improvement of 4–7 points,[2] early neurological stability (ENS) as change of the NIHSS of −3 to +3,[24] and early neurological deterioration (END) as NIHSS deterioration of ≥4.[25]

Patients were assigned to different subgroups on the basis of their respective octiles for 24h NIHSS, NIHSSΔ, and NIHSS%.

Right censored data over a period of 2500 days (6.8 years) were analyzed. We truncated at 2500 days, as the population at risk dropped to <10 patients in individual subgroups at this time point.

Kaplan-Meier curves were plotted stratified by subgroups for 24h NIHSS, NIHSSΔ, and NIHSS%.

Semiparametric univariable and multivariable Cox regression were used to calculate crude and adjusted hazard ratios (cHRs, aHRs) and corresponding 95% CIs.

Covariables were selected a priori on the basis of clinical reasoning and known associations and included age, sex, Alberta Stroke Programme Early CT Score (ASPECTS), site of intracranial occlusion, general anesthesia, time from onset to puncture, number of retrieval attempts, eTICI, prestroke independence (modified Rankin scale≤2), risk factors (diabetes, hypertension, dyslipidemia, smoking, previous stroke, and coronary heart disease), glucose on admission, and bridging IV thrombolysis.

Interrater reliability of core-lab adjudicated eTICI scores was tested using Krippendorff's alpha.

Statistical analyses were performed using R (version 4.0.2).[26] A 2-tailed *P* value of <0.05 was considered statistically significant.

Machine Learning Model

Applying Random Survival Forests (RSF) to right censored survival data is of great value. In contrast to relatively rigid methods as proportional hazards, it automatically handles the evaluation of nonlinear/interaction effects of variables.[27] For our RSF models, the same clinical covariates as mentioned above were used including NIHSS on admission, 24h NIHSS, NIHSSΔ, or NIHSS% for model development.

Concordance index and area under the curve values of cumulative dynamic receiver operating characteristic curves for 3 months, 1 year, 2 years, and 5 years were used as metrics. We trained the model on training data (n=765, 80%) and repeated evaluation on withheld test data (n=192, 20%) 20 times for each model using a different random seed for initialization. Results are reported as mean ± SD or with 95% CI. Permutation-based feature importance calculated the predictive performance of the different features.

RSF was implemented using Python (3.8.8) with scikit-learn (0.23.1),[28] scikit-survival (0.15.1),[29] and eli5 (0.10.1) modules.

RESULTS

Study Population

Of 1316 patients screened, 37 were lost to follow-up (28 not in the Swiss Population Registry [eg, moved abroad], 9 due to unknown date of death), and 292 patients were excluded because of incomplete clinical or imaging data (186 patients with missing 24h NIHSS) (Figure SI). Of the remaining 987 patients, 30 patients died within 24 hours, resulting in a final cohort of 957 patients (see Table 1 for baseline characteristics). mENI occurred in 406 (42.4%) patients (153 patients with NIHSS 0–1), ENI in 160 (16.7%), ENS in 289 (30.2%) patients, and END in 102 (10.7%) patients. Median follow-up time was 1376 days (interquartile range, 939–2269 days), with a total follow-up time of 2947 patient-years.

Excluded patients had higher ASPECTS on admission, higher NIHSS on admission, and higher blood glucose on admission. They also had longer times from onset or last seen well to groin puncture and more occlusions of the posterior circulation. On follow-up, they had higher 24h NIHSS and higher 3-month modified Rankin scale (Table SI).

Correlation of NIHSS and Long-Term Survival

Twenty-Four Hour NIHSS

Patients with higher 24h NIHSS scores generally showed poorer survival curves (Figure 1) and survival rates (Table SII), which diverged most in the first days after the index stroke. In Cox regression analysis, patients with higher 24h NIHSS also showed higher cHRs and aHRs for death (Figure 2). Compared with patients with 24h NIHSS of 0 to 1, cHR for death was significantly higher for patients with 24h NIHSS >8, and aHR for death was significantly higher for patients with 24h NIHSS >12, respectively. This trend was also present in landmark analyses truncated at 1 year (log

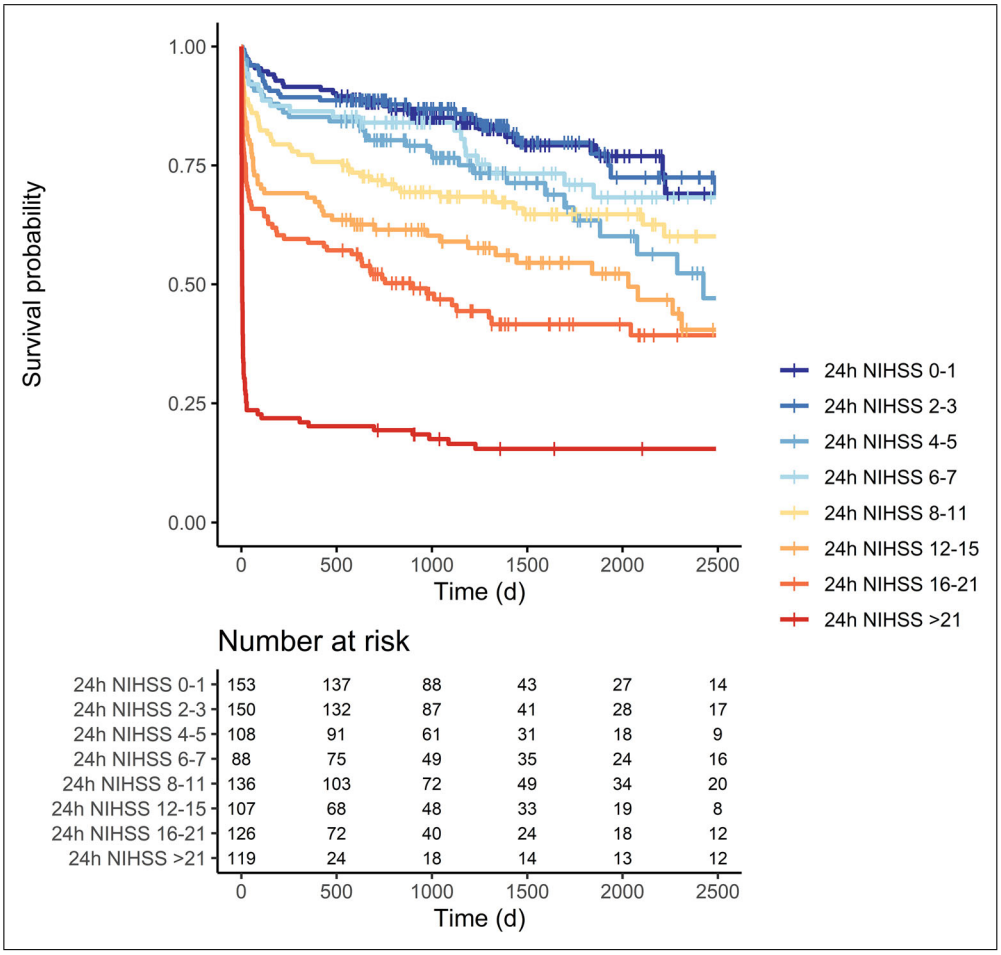

Figure 1. Kaplan–Meier curves with strata of 24-hour National Institutes of Health Stroke Scale (NIHSS) octiles. Overall, patients with lower 24-hours NIHSS had higher survival rates.

rank test, *P*=0.067) (Figure SII). In Kaplan-Meier curves stratified to admission NIHSS quartiles (0–9, 10–14, 15–19, 20–41), the results overall remained constant, with better survival curves for patients with lower 24h NIHSS (Figure SIII).

Development of the NIHSS Within 24 Hours

Patients with mENI showed the best survival curves and, consequently, patients with END showed the worst survival curves (Figure 3). The survival curve of patients with ENI was intermediate between that of patients with mENI and ENS in the first years after the index stroke, but converged to the survival curve of patients with ENS in the long term. These results also reflect in increased cHR and aHR for death for patients with stable or increasing NIHSSΔ (Figure 2). Evolution of the NIHSS measured as change in percentage provided similar results: increasing NIHSS correlated with increasing cHR and aHR for death (Figure 2).

Correlation of Degree of Reperfusion and NIHSS After 24 Hours

Interrater agreement among the 3 raters for eTICI ratings of 142 randomly selected patients reached reliable agreement (Krippendorff's alpha=0.87; 95% CI, 0.83–0.91).

Patients with better reperfusion results generally had a more favorable distribution of 24h NIHSS scores (Figure SIV). No patient achieved a 24h NIHSS of 0 to 1 with a final eTICI of ≤2a; furthermore, 58.2% of all patients with eTICI 0 had a 24h NIHSS of ≥16. Conversely, almost half of all patients with eTICI 3 had a 24h NIHSS of 0 to 3 and only 12.7% a 24h NIHSS of ≥16.

Correspondingly, patients with better reperfusion results also generally presented more often with mENI and less often with END (Figure SV). The occurrence of mENI was 58.7% in patients with eTICI 3 and decreased thereafter with lower eTICI scores (7% in eTICI 0). On the other hand, the frequency of END was highest in patients with eTICI 0 (39.5%) and decreased with higher eTICI scores (3.1% in eTICI 3).

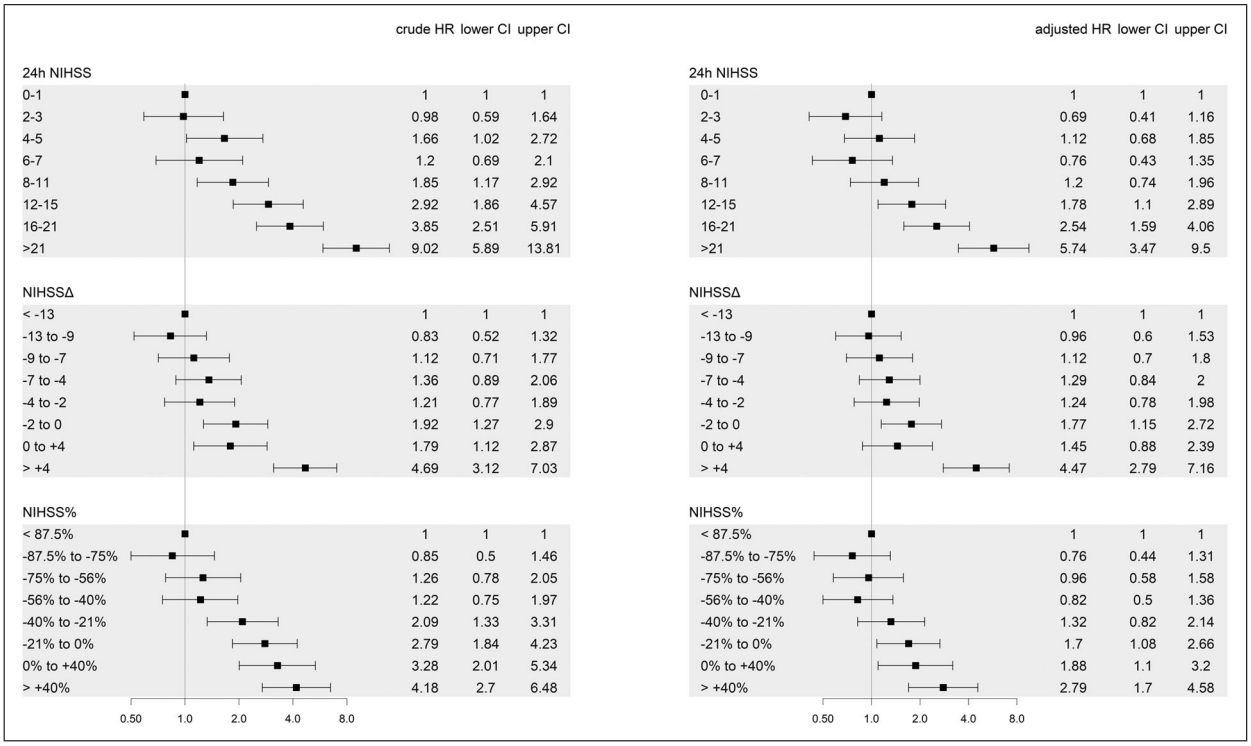

Figure 2. Crude (left) and adjusted (right) HRs with 95% CI for 24-hour NIHSS, NIHSSΔ, and NIHSS% octiles. Patients with higher 24-hour NIHSS and patients with increasing NIHSS showed higher HRs for death.
HR, indicates hazard ratio; and NIHSS, National Institutes of Health Stroke Scale.

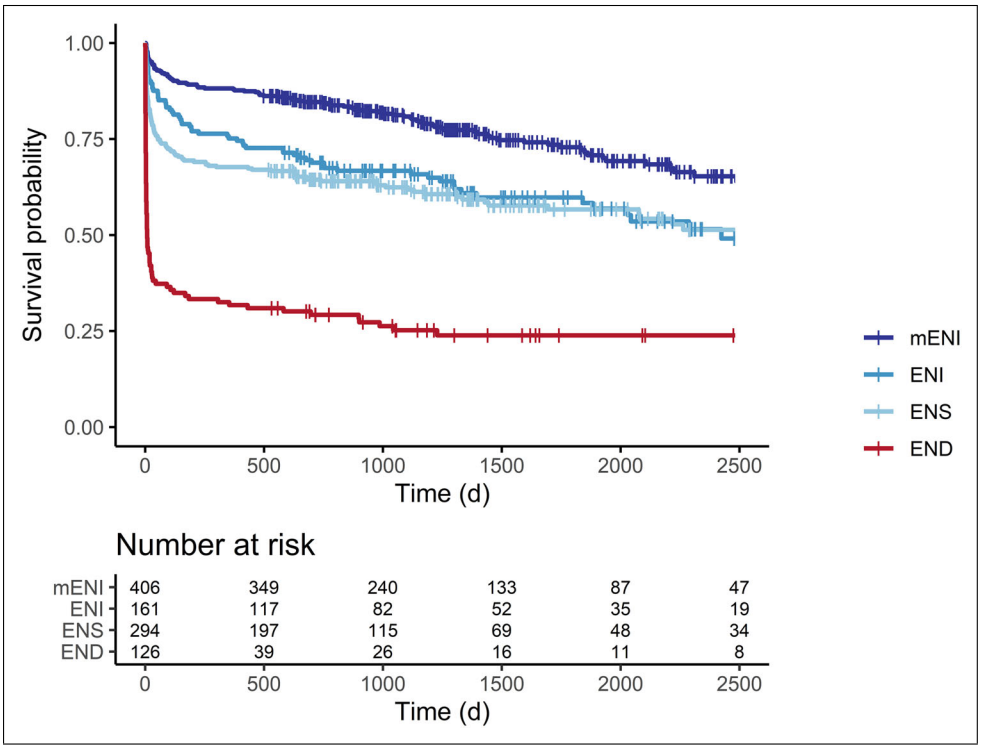

Figure 3. Kaplan-Meier curves stratified by early neurological development. Patients with mENI had the best survival rates, followed by patients with ENI and ENS (which converged with increasing time). Patients with END had the worst survival rates.
END indicates early neurological deterioration; ENI, early neurological improvement; ENS, early neurological stability; and mENI, major early neurological improvement.

Table 1. Baseline Characteristics

	Overall
n	957
Age on admission	73.81 (61.97–81.75)
Sex, female	470 (49.1)
Prestroke modified Rankin scale ≤2	855 (89.3)
NIHSS on admission	14 (9–19)
24h NIHSS	7 (3–15)
IV thrombolysis bridging	382 (39.9)
eTICI	
0	43 (4.5)
1	15 (1.6)
2a	60 (6.3)
2b50	94 (9.8)
2b67	249 (26.0)
2c	237 (24.8)
3	259 (27.1)
3-mo modified Rankin scale	
0	111 (12.2)
1	178 (19.5)
2	148 (16.2)
3	137 (15.0)
4	109 (12.0)
5	29 (3.2)
6	199 (21.8)
Emboli to new territory	36 (3.8)
Time from symptom onset or last seen well until groin puncture, min	233 (166–363)
Admission imaging modality, MRI	528 (55.2)
Site of intracranial occlusion	
Intracranial carotid artery	218 (22.8)
M1 segment of middle cerebral artery	504 (52.7)
M2 segment of middle cerebral artery	160 (16.7)
Posterior circulation	64 (6.7)
Other occlusion	11 (1.1)
Retrieval attempts	
1	546 (57.1)
2	223 (23.3)
≥3	188 (19.6)
Admission glucose (mmol/L)	6.60 (5.70–7.80)
ASPECTS	8 (6–9)
Risk factors	
Diabetes	156 (16.3)
Arterial hypertension	671 (70.1)
Dyslipidemia	534 (55.8)
Smoking history	234 (24.5)
Previous stroke	112 (11.7)
Coronary heart disease	192 (20.1)
TOAST	
Atherosclerotic	109 (11.4)
Cardioembolic	426 (44.5)
Other determined cause	64 (6.7)
Undetermined cause	358 (37.4)

Data are displayed as median (IQR) and n (%).

ASPECTS indicates Alberta stroke programme early CT score; eTICI, Expanded Thrombolysis in Cerebral Infarction; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; and TOAST, Trial of Org 10172 in Acute Stroke Treatment.

Machine Learning-Based Prediction of Survival

Table 2 and Figure SVI show the performance of different RSF models for the prediction of long-term survival including all covariables (see Methods section). The model including 24h NIHSS had the best concordance index (0.74) as well as mean receiver operating characteristic area under the curve for survival at 3 months, 1 year, and 2 years. When these time points were compared, performance was best for predicting survival at 3 months (0.85±0.034) and decreased thereafter. The receiver operating characteristic area under the curve of the different models converged at later time points and were almost the same after 5 years. The top predictive features besides NIHSS scores were age, Alberta Stroke Programme Early CT Score, admission glucose, and final eTICI score.

Univariable RSF models predicted worse than multivariable RSF models (Figure 4). Furthermore, the performance declined steadily with increasing time points. However, 24h NIHSS again had the best predictive power (receiver operating characteristic area under the curve at 3 months [0.79±0.038], at 1 year [0.74±0.034], at 2 years [0.73±0.025], and at 5 years [0.65±0.036]) and was significantly better than NIHSS on admission and better than early neurological development, representing grouped categories.

DISCUSSION

This study has the following main findings: (1) There is a close association between 24h NIHSS and long-term survival rates, (2) patients with mENI have markedly lower early and long-term mortality, and (3) the 24h NIHSS significantly improves the prediction of long-term mortality among various parameters evaluating clinical evolution after an ischemic stroke, including baseline NIHSS.

Survival Benefits of Low 24h NIHSS and Early Clinical Improvement

We found an association between lower 24h NIHSS and improved early and long-term survival rates in patients with stroke with vessel occlusions of the anterior and posterior circulation. Several previous studies have shown the association of lower 24h NIHSS with good functional outcome in the early follow-up[1,5–8] and with lower 3-month mortality,[9] and our results corroborate these findings also in the long-term outcome. The association of successful reperfusion with improved 24h NIHSS is another finding of our study that has been previously reported.[4,11,12]

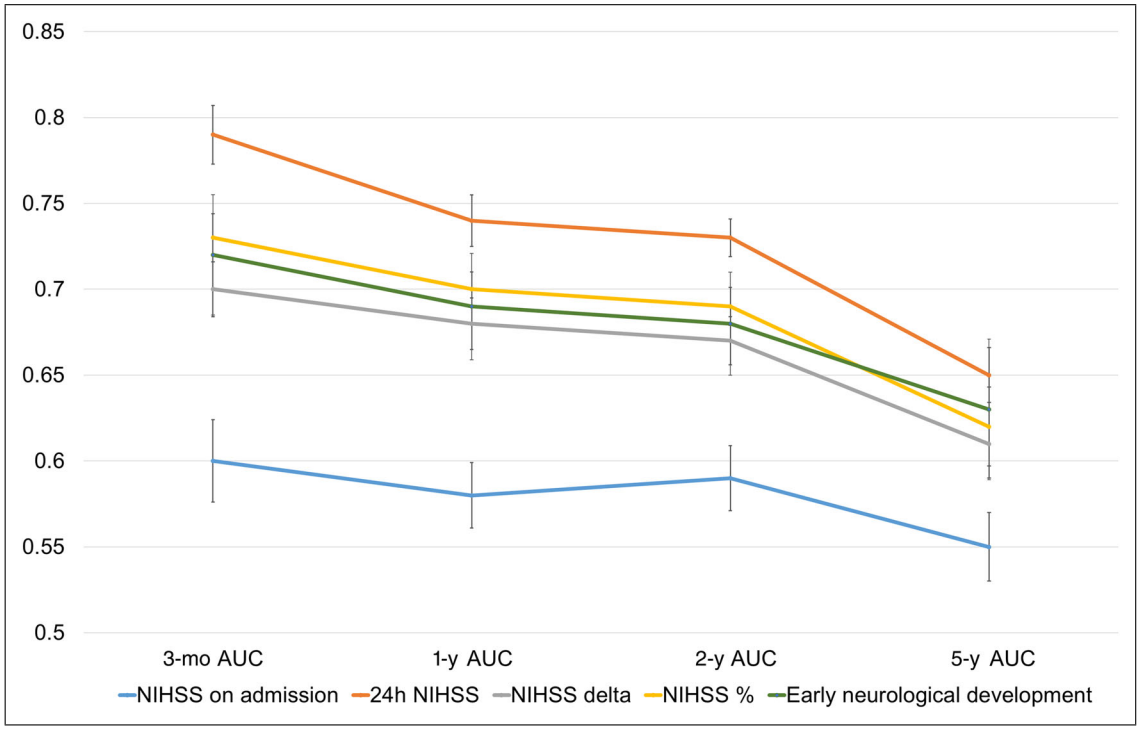

Figure 4. ROC-AUC at 3 months, 1 year, 2 years, and 5 years with corresponding 95% CIs for RSF models including only NIHSS on admission, 24-hour NIHSS, NIHSSΔ, NIHSS%, or early neurological development.
NIHSS indicates National Institutes of Health Stroke Scale; ROC-AUC, receiver operating characteristic area under the curve; and RSF, random survival forest.

Table 2. C-Index and ROC-AUC±SD for Random Survival Forest Models at Different Time Points Including Potential Confounders and Baseline NIHSS, 24h NIHSS, NIHSSΔ, NIHSS%, or Categorized Early Neurological Development (END, ENS, ENI, mENI)

	C-index	ROC-AUC at 3 mo	ROC-AUC at 1 y	ROC-AUC at 2 y	ROC-AUC at 5 y
Baseline NIHSS	0.71	0.77±0.032	0.76±0.026	0.78±0.032	0.82±0.032
24h NIHSS	**0.74**	**0.85±0.034**	**0.82±0.029**	**0.82±0.031**	0.83±0.035
NIHSSΔ	0.69	0.79±0.038	0.77±0.028	0.79±0.034	0.83±0.032
NIHSS%	0.71	0.80±0.039	0.79±0.028	0.80±0.034	0.83±0.036
ENS, END, ENI, mENI	0.72	0.80±0.039	0.79±0.027	0.80±0.033	0.84±0.033

C-index indicates concordance index; END early neurological deterioration; ENI, early neurological improvement; ENS, early neurological stability; mENI, major early neurological improvement; NIHSS, National Institutes of Health Stroke Scale; and ROC-AUC, receiver operating characteristic area under the curve.

The assessment of the NIHSS at 24 hours seems to be appropriate to depict the dynamic process of ischemic stroke as well as the effect of applied therapies, and thus be more informative than the NIHSS at baseline or at 2 hours.[4] In addition, it can be interpreted in correlation with 24-hour follow-up imaging and clinical data collected in the meantime.

Another argument to obtain the NIHSS after 24 hours is the finding that improvement of the NIHSS or complete regression of the neurologic impairment (mENI) within the first 24 hours correlates with improved survival, consistent with previous results that found associations of mENI and good functional outcome.[4,23] Further, Rudilosso et al[3] demonstrated the importance of a short delay between the index stroke to clinical improvement, as it was strongly related to better chances of a good long-term outcome. However, it is important to notice that the population of this study presented with a rather high rate of good functional outcome (79% with modified Rankin scale 0–2 at 90 days).

Patients with ENI showed significantly inferior survival rates compared with patients with mENI. This could be attributable to the inclusion of patients with a 24h NIHSS of 0 to 1 in the latter group, which are likely to have the most favorable survival rates. Second, the ENI group is heterogeneous and a patient improving 4 points from a relatively high baseline NIHSS (eg, from baseline NIHSS 18 to 24h NIHSS 14) will most likely have a different prognosis than a patient with a rather low baseline NIHSS (eg, from baseline NIHSS 6 to 24h NIHSS 2).

The survival rates of patients with ENI were superior to patients with ENS only in the first years after the index stroke. Stable NIHSS after 24 hours has been shown to be a predictor for poor short-term outcome after acute ischemic stroke,[24] but patients with ENI and ENS showed similar survival rates in the long term.

Twenty-Four Hour NIHSS and Early Clinical Improvement as Predictors of Survival

In our machine learning–based model, the 24h NIHSS was the best predictor for survival, followed by NIHSSΔ, NIHSS%, and early neurological development. In line with previous results, the baseline NIHSS had the poorest predictive power.[30] The 24h NIHSS is likely to be a better predictor than baseline NIHSS because it is influenced by final ischemic core size, the effectiveness of collaterals, and adverse events such as hemorrhagic transformation or peri-interventional complications (eg, emboli in a new territory, emboli in an initially nonhypoperfused territory[31]). As a consequence, it may provide a valuable tool to predict long-term outcomes.

Second, models including multiple variables performed substantially better than models including only individual NIHSS variables, especially in the long term. Other important factors that influenced our machine learning–based prediction of survival have been described as modifying factors of outcome after stroke elsewhere before and included age,[32] Alberta Stroke Programme Early CT Score,[33] admission glucose,[34] and final eTICI score.[20]

The results of our machine learning–based predictions indicate that 24h NIHSS has good predictive power for survival, especially in the early phase after the index stroke. The small drop in performance of long-term survival prediction could be attributed to low influence of the 24h NIHSS on long-term survival or to the relatively smaller sample size of patients who were followed up to 5 years. Additionally, withdrawal of care in patients with poor 24h NIHSS likely influences short-term mortality but not long-term mortality. Further studies to answer this question are warranted.

Clinical Implications

Our results highlight the clinical relevance of the NIHSS at 24 hours and early clinical improvement as correlates of successful therapy and as useful adjuncts to other clinical diagnostics and radiologic imaging. Additionally, the use of the 24h NIHSS could refine and improve (machine learning–based) models predicting outcome after ischemic stroke and help involved physicians in decision making regarding further therapy options. Finally, the 24h NIHSS may be a useful clinical surrogate end point in future ischemic stroke therapy trials since few patients would be lost to follow-up, costs associated with clinical stroke trials could be reduced, and, most importantly, the 24h NIHSS is less influenced by comorbidities but still correlates well with long-term survival.

Limitations

Our study is limited by its retrospective and observational nature and the lack of a control group of patients not submitted to MT. Second, we included only patients from 1 center, which could affect generalizability of our results and models on external data. Third, we did not specifically analyze the effect of delayed neurological improvement (modified Rankin scale≤2 at 90 days after stroke despite absence of ENI).[35] Finally, we did not include the influence of subsequent therapy decisions and other comorbidities into our multivariate analysis, which may influence survival after the index stroke.

CONCLUSIONS

Patients achieving a low 24h NIHSS or mENI after MT for an acute ischemic stroke have the best early and long-term survival rates. Furthermore, 24h NIHSS has the best predictive power on early and long-term survival in our machine learning–based prediction, followed by ENI. Twenty-four hour NIHSS is readily available, is a useful adjunct to other clinical and imaging data, and could help to improve models predicting early and long-term outcome after ischemic stroke.

ARTICLE INFORMATION

Received November 8, 2021; Accepted January 13, 2022

Affiliations

University Institute of Diagnostic and Interventional Neuroradiology, University Hospital Bern, Inselspital, University of Bern, Bern, Switzerland (C.C.K., M.F.L., E.I.P., A.H., T.D., P.M., J.G., J.K.); Department of Neurology, University Hospital Bern, Inselspital, University of Bern, Bern, Switzerland (M.B., T.R.M., S.J., D.J.S., M.R.H., M.A., U.F.); University Institute of Diagnostic and Interventional and Pediatric Radiology, University Hospital Bern, Inselspital, University of Bern, Bern, Switzerland (L.G., J.K.); Department of Neurology, University Hospital Basel, University of Basel, Basel, Switzerland (U.F.)

Acknowledgment

None.

Funding

This work was supported by the Swiss Academy of Medical Sciences within the framework of the Young Talents in Clinical Research Program (grant number YTCR 03/19) and grants provided by the Clinical Trials Unit Bern, University of Bern (grant number 84801869).

Disclosures

Urs Fischer reports grants during the conduct of the study from Medtronic, Stryker, and CSL Behring, unrelated to the submitted work. Jan Gralla is a global

principal investigator of STAR (Solitaire FR Thrombectomy for Acute Revascularisation), Clinical Event Committee member of the PROMISE study (Prospective, Multicenter, Observational, Single-Arm European Registry on the ACE Reperfusion Catheters, and the Penumbra System in the Treatment of Acute Ischemic Stroke; Penumbra), a principal investigator and consultant for the SWIFT DIRECT study (Solitaire With the Intention for Thrombectomy Plus Intravenous tPA Versus DIRECT Solitaire Stent-Retriever Thrombectomy in Acute Anterior Circulation Stroke; Medtronic), and receives Swiss National Science Foundation grants for magnetic resonance imaging in stroke. Johannes Kaesmacher reports grants from the Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss Stroke Society, and Clinical Trials Unit Bern during the conduct of the study. Marcel Arnold reports personal fees from Bayer, Bristol-Myers Squibb, Medtronic, Amgen, Daiichi Sankyo, Nestlé Health Sciences, Boehringer Ingelheim, and Covidien during the conduct of the study. Thomas R. Meinel reports research support from the Bangerter Rhyner Foundation, Swiss National Foundation, and the Swiss Heart Foundation. Mirjam R. Heldner reports research support from the Bangerter Foundation, scientific advisory board honoraria from Amgen, and personal fees from Bayer. Pasquale Mordasini reports receipt of research support from Siemens, Cerenovus, Medtronic, Stryker, the Swiss Heart Foundation, and the Swiss National Foundation, receipt of consultant fees from Medtronic, Cerenovus, Phenox, and Microvention, unrelated to the submitted work. All other authors do not report any disclosures.

Supplemental Materials

Supplementary Tables I–II

Supplementary Figures I–VI

TRIPOD Checklist: Prediction Model Development and Validation

STROBE Statement—checklist of items that should be included in reports of observational studies

REFERENCES

1. Heit JJ, Mlynash M, Kemp SM, Lansberg MG, Christensen S, Marks MP, Ortega-Gutierrez S, Albers GW. Rapid neurologic improvement predicts favorable outcome 90 days after thrombectomy in the DEFUSE 3 study. *Stroke*. 2019;50:1172–1177.
2. Agarwal S, Scher E, Lord A, Frontera J, Ishida K, Torres J, Rostanski S, Mistry E, Mac Grory B, Cutting S, et al. redefined measure of early neurological improvement shows treatment benefit of alteplase over placebo. *Stroke*. 2020;1226–1230.
3. Rudilosso S, Urra X, Amaro S, Llull L, Renú A, Laredo C, Obach V, Chamorro Á. Timing and relevance of clinical improvement after mechanical thrombectomy in patients with acute ischemic stroke. *Stroke*. 2019;50:1467–1472.
4. Kharitonova T, Mikulik R, Roine RO, Soinne L, Ahmed N, Wahlgren N. Association of early national institutes of health stroke scale improvement with vessel recanalization and functional outcome after intravenous thrombolysis in ischemic stroke. *Stroke*. 2011;42:1638–1643.
5. Mistry EA, Yeatts S, de Havenon A, Mehta T, Arora N, De Los Rios La Rosa F, Starosciak AK, Siegler JE 3rd, Mistry AM, Yaghi S, et al. Predicting 90-day outcome after thrombectomy: baseline-adjusted 24-hour NIHSS is more powerful than NIHSS score change. *Stroke*. 2021;52:2547–2553.
6. Meyer L, Broocks G, Bechstein M, Flottmann F, Leischner H, Brekenfeld C, Schön G, Deb-Chatterji M, Alegiani A, Thomalla G, et al. Early clinical surrogates for outcome prediction after stroke thrombectomy in daily clinical practice. *J Neurol Neurosurg Psychiatry.* 2020;91:1055–1059.
7. Dávalos A, Cobo E, Molina CA, Chamorro A, de Miquel MA, Román LS, Serena J, López-Cancio E, Ribó M, Millán M, et al. Safety and efficacy of thrombectomy in acute ischaemic stroke (REVASCAT): 1-year follow-up of a randomised open-label trial. *Lancet Neurol*. 2017;16:369–376.
8. Hendrix P, Melamed I, Collins M, Lieberman N, Sharma V, Goren O, Zand R, Schirmer C M., Griessenauer CJ. NIHSS 24 h After Mechanical Thrombectomy Predicts 90-Day Functional Outcome. *Clin Neuroradiol*. 2021. https://doi.org/10.1007/s00062-021-01068-4
9. Abdul-Rahim AH, Fulton RL, Sucharew H, Kleindorfer D, Khatri P, Broderick JP, Lees KR. National institutes of health stroke scale item profiles as predictor of patient outcome: external validation on safe implementation of thrombolysis in stroke-monitoring study data. *Stroke*. 2015;46:2779–2785.
10. Rangaraju S, Frankel M, Jovin TG. Prognostic value of the 24-hour neurological examination in anterior circulation ischemic stroke: a post hoc analysis of two randomized controlled stroke trials. *Interv Neurol.* 2015;4:120–129.
11. Askevold ET, Naess H. Predictors for recanalization after intravenous thrombolysis in acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2007;16:21–24.
12. Mikulik R, Ribo M, Hill MD, Grotta JC, Malkoff M, Molina C, Rubiera M, Delgado-mederos R, Alvarez-sabin J, Alexandrov AV, et al. Accuracy of serial national institutes of health stroke scale scores to identify artery status in acute ischemic stroke. *Circulation*. 2007;115:2660–2665.
13. Berkhemer O, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJH, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med.* 2015;372:11–20.
14. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, Roy D, Jovin TG, Willinsky RA, Sapkota BL, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med.* 2015;372:1019–1030.
15. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, Yan B, Dowling RJ, Parsons MW, Oxley TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med.* 2015;372:1009–1018.
16. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM, Albers GW, Cognard C, Cohen DJ, Hacke W, et al. Solitaire™ With the Intention for Thrombectomy as Primary Endovascular Treatment for Acute Ischemic Stroke (SWIFT PRIME) trial: protocol for a randomized, controlled, multicenter study comparing the Solitaire revascularization device with IV tPA with IV. *Int J Stroke.* 2015;10:439–448.
17. Molina CA, Chamorro A, Rovira À, de Miquel A, Serena J, Roman LS, Jovin TG, Davalos A, Cobo E. REVASCAT: a randomized trial of revascularization with SOLITAIRE FR® device vs. best medical therapy in the treatment of acute stroke due to anterior circulation large vessel occlusion presenting within eight-hours of symptom onset. *Int J Stroke.* 2015;10:619–626.
18. Katsanos AH, Malhotra K, Goyal N, Palaiodimou L, Schellinger PD, Caso V, Cordonnier C, Turc G, Magoufis G, Arthur A, et al. Mortality risk in acute ischemic stroke patients with large vessel occlusion treated with mechanical thrombectomy. *J Am Heart Assoc.* 2019;8:e014425.
19. Lin Y, Schulze V, Brockmeyer M, Parco C, Karathanos A, Heinen Y, Gliem M, Hartung H. Endovascular thrombectomy as a means to improve survival in acute ischemic stroke a meta-analysis. 2020;76:850–854.
20. Beyeler M, Weber L, Kurmann CC, Piechowiak EII, Mosimann PJ, Zibold F, Meinel TR, Branca M, Grunder L, Arnold M, et al. Association of reperfusion success and emboli in new territories with long term mortality after mechanical thrombectomy. *J Neurointerv Surg.* 2021;1–7. https://doi.org/10.1136/neurintsurg-2021-017422
21. Liebeskind DS, Bracard S, Guillemin F, Jahan R, Jovin TG, Majoie CBLM, Mitchell PJ, Van Der Lugt A, Menon BK, San Román L, et al. ETICI reperfusion: defining success in endovascular stroke therapy. *J Neurointerv Surg.* 2019;11:433–438.
22. Goyal M, Menon BK, Van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CBLM, Van Der Lugt A, De Miquel MA, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731.
23. Saposnik G, Di Legge S, Webster F, Hachinski V, Saposnik G., Di Legge S., Webster F. & Hachinski V. Predictors of major neurologic improvement after thrombolysis in acute stroke. *Neurology*. 2005;65(8):1169–1174.
24. Irvine HJ, Battey TWK, Ostwaldt A-C, Campbell BCV, Davis SM, Donnan GA, Sheth KN, Kimberly WT. Early neurological stability predicts adverse outcome after acute ischemic stroke. *Int J Stroke*. 2016;11:882–889.
25. Arenillas JF, Rovira Á, Molina CA, Grivé E, Montaner J, Álvarez-Sabín J. Prediction of early neurological deterioration using diffusion- and perfusion-weighted imaging in hyperacute middle cerebral artery ischemic stroke. *Stroke*. 2002;33:2197–2203.
26. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.
27. Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. *Ann Appl Stat.* 2008;2:841–860.

28. Pedregosa F, Varoquaux G, Gramfort A, Michel V, Thirion B, Grisel O, Blondel M, Prettenhofer P, Weiss R, Dubourg V, et al. Scikit-learn: machine learning in python. *J Mach Learn Res.* 2011;12.
29. Pölsterl S. Scikit-survival: a library for time-to-event analysis built on top of scikit-learn. *J Mach Learn Res.* 2020;21:1–6.
30. Saver JL, Altman H. Relationship between neurologic deficit severity and final functional outcome shifts and strengthens during first hours after onset. *Stroke*. 2012;43:1537–1541.
31. Kaesmacher J, Kurmann C, Jungi N, Breiding P, Lang MF, Meier R, Dobrocky T, Piechowiak E, Zibold F, Bellwald S, et al. Infarct in new territory after endovascular stroke treatment: a diffusion-weighted imaging study. *Sci Rep.* 2020;10:1–10.
32. Castonguay AC, Zaidat OO, Novakovic R, Nguyen TN, Gupta R, Sun C-HJ, Martin C, Holloway WE, Mueller-Kronast N. Influence of age on clinical and revascularization outcomes in the North American Solitaire Stent-Retriever Acute Stroke Registry. In: Stroke*. Lippincott Williams and Wilkins*; 2014: 3631–3636.
33. Goyal M, Menon BK, Coutts SB, Hill MD, Demchuk AM. Effect of baseline CT scan appearance and time to recanalization on clinical outcomes in endovascular thrombectomy of acute ischemic strokes. *Stroke*. 2011;42:93–97.
34. Rinkel LA, Nguyen TTM, Guglielmi V, Groot AE, Posthuma L, Roos YBWEM, Majoie CBLM, Lycklama À Nijeholt GJ, Emmer BJ, Van Der Worp HB, et al. High admission glucose is associated with poor outcome after endovascular treatment for ischemic stroke. *Stroke*. 2020;3215–3223.
35. Talavera B, Gómez-Vicente B, Martínez-Galdámez M, López-Cancio E, García-Cabo C, Castellanos M, Roel A, Tejada-Meza H, Marta-Moreno J, Pérez-Lázaro C, et al. Delayed neurological improvement after full endovascular reperfusion in acute anterior circulation ischemic stroke. *Stroke*. 2021;2210–2217.