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RESEARCH ARTICLE

Prediction of epilepsy after stroke: Proposal of a modified SeLECT 2.0 score based on posttreatment stroke outcome

Stefano Meletti[1,2] | **Claudia Cuccurullo**[3] | **Niccolò Orlandi**[1,2] | **Giuseppe Borzì**[1,4] | **Guido Bigliardi**[1,4] | **Stefania Maffei**[1,4] | **Cinzia Del Giovane**[5] | **Riccardo Cuoghi Costantini**[5] | **Giada Giovannini**[1] | **Simona Lattanzi**[6]

[1]Neurology Unit, OCB Hospital, AOU Modena, Modena, Italy

[2]Department of Biomedical, Metabolic, and Neural Science, Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy

[3]Neurology and Stroke Unit, Ospedale del Mare Hospital, ASL Napoli 1, Naples, Italy

[4]Stroke Unit, OCB Hospital, AOU Modena, Modena, Italy

[5]Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy

[6]Neurological Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, Ancona, Italy

Correspondence
Simona Lattanzi, Neurological Clinic, Department of Experimental and Clinical Medicine, Marche Polytechnic University, Via Conca 71, Ancona 60020, Italy.
Email: alfierelattanzisimona@gmail.com

Stefano Meletti, Department of Biomedical, Metabolic, and Neural Science, Center for Neuroscience and Neurotechnology, University of Modena and Reggio Emilia, Modena, Italy.
Email: stefano.meletti@unimore.it

Abstract

Objective: The SeLECT 2.0 score is a prognostic model of epilepsy after ischemic stroke. We explored whether replacing the severity of stroke at admission with the severity of stroke after treatment at 72 h from onset could improve the predictive accuracy of the score.

Methods: We retrospectively identified consecutive adults with acute first-ever neuroimaging-confirmed ischemic stroke who were admitted to the Stroke Unit of the Ospedale Civile Baggiovara (Modena, Italy) and treated with intravenous thrombolysis and/or endovascular treatment. Study outcome was the occurrence of at least one unprovoked seizure presenting >7 days after stroke.

Results: Participants included in the analysis numbered 1094. The median age of the subjects was 74 (interquartile range [IQR] = 64–81) years, and 595 (54.4%) were males. Sixty-five (5.9%) subjects developed unprovoked seizures a median of 10 (IQR = 6–27) months after stroke. The median values of the original and modified SeLECT2.0 scores were 3 (IQR = 2–4) and 2 (IQR = 1–3). The modified SeLECT 2.0 score showed better discrimination for the prediction of poststroke epilepsy at 36, 48, and 60 months after stroke compared to the original score according to the area under time-dependent receiver operating characteristic curves. The modified SeLECT 2.0 score had higher values of Harrell C and Somers D parameters and lower values of Akaike and Bayesian information criteria than the original score. The modified SeLECT 2.0 score produced more accurate risk predictions compared to the SeLECT 2.0 score at all evaluated time points from 12 to 60 months after stroke according to the Net Reclassification Index.

Significance: Replacing baseline with posttreatment stroke severity may improve the ability of the SeLECT 2.0 score to predict poststroke epilepsy.

KEYWORDS

epilepsy, seizures, stroke

1 | INTRODUCTION

Stroke represents the major cause of acquired epilepsy in the elderly.[1] Typically, epileptogenic processes occur during the latent period of several weeks to years between the onset of stroke and the first unprovoked seizure.[2]

SeLECT is a scoring system developed to predict epilepsy after ischemic stroke,[3] and it has been recently updated, taking into consideration the type of acute symptomatic seizures to produce a new version with enhanced accuracy, the SeLECT 2.0 score.[4] Both models include stroke severity at baseline as a covariate and do not consider the impact that stroke treatment may have. Revascularization interventions including intravenous fibrinolysis and endovascular treatment (EVT) can save hypoperfused brain areas that are only reversibly damaged, improving the functional outcome of people with ischemic stroke.[5] Stroke severity after treatment may, hence, be a more reliable indicator of the actual brain damage, which acts as substrate for the development of poststroke epilepsy (PSE).[6]

In this study, we aimed to evaluate whether the residual severity of stroke after revascularization treatment can predict the risk of PSE and outweigh the prognostic ability of baseline stroke severity. We also explored whether replacing the severity of stroke at admission with the severity of stroke after treatment could improve the predictive accuracy of the SeLECT 2.0 score.

Key points

- The SeLECT 2.0 score is a prognostic model of epilepsy after ischemic stroke.
- We modified the SeLECT 2.0 score by replacing baseline with posttreatment stroke severity.
- The modified SeLECT 2.0 score showed better discrimination for the prediction of epilepsy at 36, 48, and 60 months after stroke.
- The modified SeLECT 2.0 score had higher values of Harrell C and Somers D parameters and lower values of Akaike and Bayesian information criteria.
- The modified SeLECT 2.0 score produced more accurate risk predictions compared to the SeLECT 2.0 score.

2 | MATERIALS AND METHODS

2.1 | Participants and procedures

Consecutive adults with acute first-ever neuroimaging-confirmed ischemic stroke who were admitted at the Stroke Unit of the Ospedale Civile Baggiovara (Modena, Italy) from January 1, 2014 to December 31, 2021 and treated with intravenous thrombolysis (IVT) and/or EVT were reviewed.

Subjects with transient ischemic attack, previous history of stroke, previous history of seizures, recurrent stroke during follow-up were excluded. Transient ischemic attack was defined as a transient episode of neurological dysfunction caused by focal brain ischemia, without evidence of acute infarction.[7] We also excluded patients with comorbidities known to confer a significant risk of developing seizures ("epileptogenic comorbidities"), for example, alcohol or drug abuse, previous brain lesions such as intracranial tumors, cerebral venous thrombosis, cerebral bleeding, severe traumatic brain injury, supratentorial brain surgery, and cerebral arteriovenous malformations. Finally, subjects who were lost to follow-up were excluded; data were not available for subjects who died within 30 days after the index stroke.

All subjects were treated following the guidelines for stroke management in place at the time of the index event.[8–10] IVT consisted of the administration of recombinant tissue plasminogen activator at the dose of .9 mg/kg (maximum 90 mg; 10% bolus followed by a 60-min infusion). EVT consisted of mechanical thrombectomy with aspiration catheters alone, stent-retrievers alone, or both, depending on occlusion type/location and the neurointerventionist's choice.

Stroke etiology was categorized according to the Trial of Org 10172 in Acute Stroke Treatment classification.[11] Stroke severity was measured with the National Institutes of Health Stroke Scale (NIHSS) at admission and after treatment at 72 h from onset. The NIHSS was stratified into mild (≤3), moderate (4–10), and severe (≥11).[12,13] The vascular territory involved was classified according to a published atlas.[14]

2.2 | Outcome measure

Seizures that occurred within 7 days of stroke onset were considered to be acute symptomatic seizures and those that occurred after 7 days were considered to be unprovoked seizures.[15] Poststroke epilepsy was diagnosed as the occurrence of one or more unprovoked seizures (i.e., seizures occurring beyond 7 days of stroke onset) during the follow-up[6] according to the current operational definition of epilepsy.[16]

By internal protocol, patients treated by reperfusion therapy undergo outpatient follow-up at 3 at 12 months; subsequent telephone interviews are performed at 24 and

36 months. Of note, in the province of Modena there is a single hub for 24-h neurological emergencies, and all patients with acute neurological symptoms (including seizures) are registered in the same hospital information system. Therefore, follow-up data were acquired by the computerized hospital chart review, outpatient visits, and telephone interviews, and were updated to December 31, 2023. The diagnosis of PSE was assessed and confirmed by epileptologists of the Modena comprehensive epilepsy center, who could acquire information about the medical history for all the patients.

2.3 | Statistical analysis

Values were presented as median (interquartile range [IQR]) for continuous variables and as *n* (%) of subjects for categorical variables. Comparisons were made through the Mann–Whitney test, Wilcoxon matched-pairs signed-rank test, chi-squared test, and Cochran *Q* test. Kaplan–Meier survival curves analysis was used to analyze the time to the occurrence of unprovoked seizures during the follow-up. The association of baseline and posttreatment stroke severity with the study outcome was evaluated. Two SeLECT 2.0 scores were then considered. The original SeLECT 2.0 score included the following variables: (1) NIHSS at admission (NIHSS ≤3: 0 points, NIHSS = 4–10: 1 point, NIHSS ≥11: 2 points), (2) large-artery atherosclerosis (no: 0 point, yes: 1 point), (3) short acute symptomatic seizure (no: 0 point, yes: 3 points), (4) acute symptomatic status epilepticus (no: 0 point, yes: 7 points), (5) cortical involvement (no: 0 point, yes: 2 points), and (6) territory of middle cerebral artery involvement (no: 0 point, yes: 1 point).[4] In the modified SeLECT 2.0 score, we replaced the NIHSS at admission with the NIHSS at 72 h after stroke onset. The variables included in the modified SeLECT, hence, were (1) NIHSS at 72 h after stroke onset (NIHSS ≤3: 0 points; NIHSS 4–10: 1 point, NIHSS ≥11: 2 points), (2) large-artery atherosclerosis (no: 0 point, yes: 1 point), (3) short acute symptomatic seizure (no: 0 point, yes: 3 points), (4) acute symptomatic status epilepticus (no: 0 point, yes: 7 points), (5) cortical involvement (no: 0 point, yes: 2 points), and (6) territory of middle cerebral artery involvement (no: 0 point, yes: 1 point). Cox proportional hazards models were adopted to estimate hazard ratios (HRs) with the 95% confidence intervals (CIs); the prescription of antiseizure medications (ASMs) at discharge was considered as a potential confounder in secondary analysis. A competing-risk regression model was performed as a sensitivity analysis to assess the impact of mortality as a competing event with the occurrence of seizures during the follow-up. The cumulative incidence function was used to estimate the risk of seizures over time considering mortality as a competing risk event. People who died were censored at the time of death unless they had previously experienced one unprovoked seizure.

The performance of the models in predicting PSE was evaluated using multiple indicators. First, the predictive accuracy of the original and modified SeLECT 2.0 score was assessed by discrimination and calibration. Discrimination (i.e., the ability of a model to differentiate between individuals who developed or did not develop PSE) was measured using time-dependent receiver operating characteristic (ROC) curves. The areas under time-dependent ROC curves (AUCs) at 12, 24, 36, 48, and 60 months were calculated and compared using the procedure proposed by Blanch et al.[17] and implemented in the R package "TimeROC." Calibration (i.e., the agreement between the predicted and observed risk of PSE) was assessed with calibration plots. Perfect calibration is implied by a 45° diagonal line; relevant deviations above or below it reflect underprediction or overprediction. Second, the performance of the models in predicting PSE was compared using the Harrell C and Somers D rank parameters and the Akaike and Bayesian information criteria. A superior model is the model with the highest value of Harrell C and Somers D parameters and the lowest value of information criteria. Third, the reclassification produced by the modified SeLECT 2.0 score with respect to the original version was quantified using the continuous Net Reclassification Index (NRI). Results were considered significant for *p*-values $< .05$ (two-sided). Data analysis was performed using Stata/IC 13.1 statistical package (StataCorp) and R version 4.3.2 statistical software (R Foundation for Statistical Computing). The study was reported according to the recommendations of STROBE (Strengthening the Reporting of Observational Studies in Epidemiology).[18]

2.4 | Standard protocol approvals, registrations, and patient consent

The scientific advisory board of our institution approved the research protocol according to local regulations and the retrospective analysis of patients' data. The Safe Implementation of Treatments in Stroke–International Stroke Thrombolysis Register dataset was approved by the local ethics committee. Informed consent was obtained from all individual participants included in the registry.

3 | RESULTS

A total of 1644 subjects with ischemic stroke who underwent treatment with IVT and/or EVT were initially

identified. After the exclusion of 550 subjects due to exclusion criteria, 1094 participants were included in the analysis (Figure 1). The median duration of poststroke observation was 47.5 (IQR = 27.0–75.7) months, with a total of 56 000 person-months.

The median age of the subjects was 74 (IQR = 64–81) years, and 595 (54.4%) were males. A total of 665 (60.8%) subjects were treated with IVT alone, 169 (15.4%) with EVT alone, and 260 (23.8%) with IVT plus EVT; hemicraniectomy was performed in 14 of 1094 (1.3%) subjects.

Sixty-five (5.9%) subjects developed unprovoked seizures a median of 10 (IQR = 6–27) months after stroke. Data about the diagnosis of PSE were most commonly obtained through outpatient visits (57/65, 87.7%) and less commonly acquired by means of hospital chart review and telephone interviews (8/65, 12.3%); in these latter cases, face-to-face evaluation outpatient visits were further performed for confirmation. People who experienced unprovoked seizures during the follow-up had more severe strokes, more commonly due to large-artery atherosclerosis, and with more frequent involvement of cortex and middle cerebral artery territory compared to people who did not experience seizures. People who developed PSE also more commonly presented acute symptomatic seizures and acute symptomatic status epilepticus than people who did not develop PSE. The characteristics of participants according to the occurrence of unprovoked poststroke seizures are shown in Table 1.

The estimated seizure occurrence rate was 3.3% (95% CI = 2.4–4.6) in the first year, 4.3% (95% CI = 3.3–5.7) in the second year, 5.6% (95% CI = 4.3–7.2) in the third year, 6.0% (95% CI = 4.7–7.8) in the fourth year, and 6.2% (95% CI = 4.8–8.0) at 5 years. In 46 of 65 (70.8%) subjects, seizures occurred within the first 2 years from stroke onset, and in 56 of 65 (86.2%) subjects within the first 3 years. The Kaplan–Meier curve of seizure occurrence in the study cohort is shown in Figure 2A. The overall cumulative incidence function for competing events is shown in Figure S1.

3.1 | Pre- and posttreatment stroke severity as predictors of unprovoked seizure occurrence

The median NIHSS at baseline and after treatment was 8 (IQR = 5–14) and 1 (IQR = 0–4; $p < .001$), respectively. At admission, the NIHSS was <4 in 165 (15.1%), 4–10 in 502 (45.9%), and ≥11 in 427 (39.0%) subjects; after treatment, the NIHSS was <4 in 770 (70.4%), 4–10 in 215 (19.6%), and ≥11 in 109 (10.0%) participants ($p < .001$).

The time to the occurrence of unprovoked seizures during the follow-up according to the baseline and posttreatment stroke severity is shown in Figure 2B and Figure 2C. The baseline (HR = 1.08, 95% CI = 1.05–1.11 for unitary NIHSS increase; $p < .001$) and posttreatment (HR = 1.13, 95% CI = 1.10–1.16 for unitary NIHSS increase; $p < .001$) stroke severity were significant predictors of PSE (Table S1). The cumulative incidence functions for competing events according to

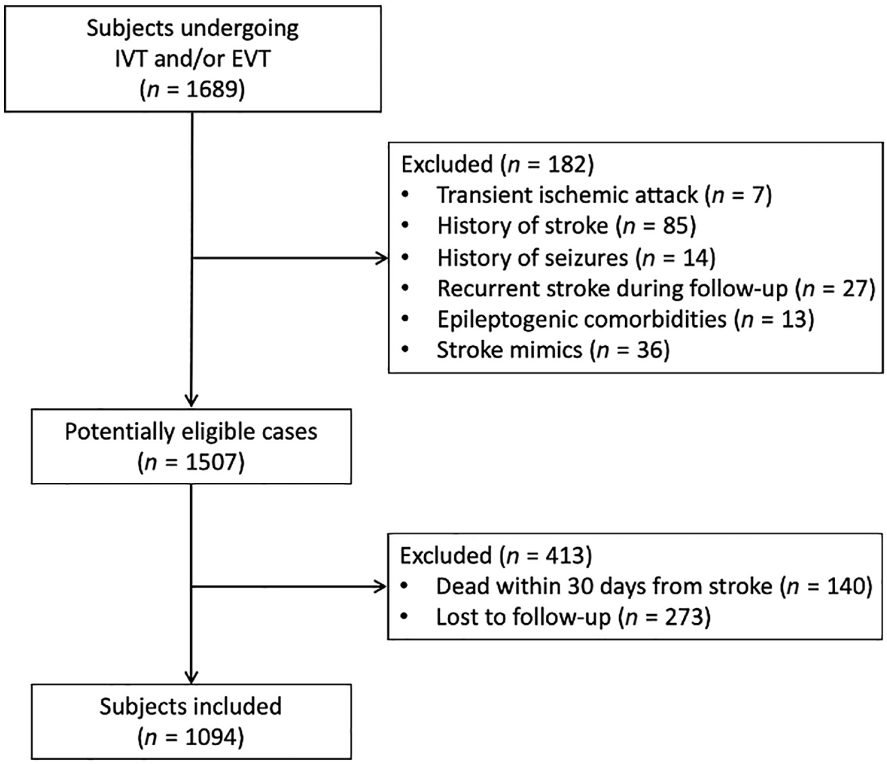

FIGURE 1 Study flow participants. EVT, endovascular treatment; IVT, intravenous thrombolysis.

TABLE 1 Characteristics of study participants and comparison according to the occurrence of unprovoked seizures during follow-up.

Characteristic	Study participants, $n = 1094$	Unprovoked seizures during follow-up		p
		No, $n = 1029$	Yes, $n = 65$	
Sex				
Male	595 (54.4)	562 (54.6)	33 (50.8)	.54
Female	499 (45.6)	467 (45.4)	32 (49.2)	
Age, years	74 [64–81]	74 [64–81]	73 [60–80]	.28
Stroke risk factors				
Hypertension	808 (73.9)	756 (73.5)	52 (80.0)	.24
Diabetes mellitus	171 (15.6)	159 (15.5)	12 (18.5)	.51
Dyslipidemia	548 (50.1)	518 (50.3)	30 (46.2)	.51
Smoking	279 (25.5)	265 (25.8)	14 (21.5)	.45
Acute reperfusion therapy				
IVT alone	665 (60.8)	640 (62.2)	25 (38.5)	<.001
EVT alone	169 (15.4)	151 (14.7)	18 (27.7)	
Both IVT and EVT	260 (23.8)	238 (23.1)	22 (33.8)	
NIHSS at admission				
≤3	165 (15.1)	161 (15.7)	4 (6.2)	<.001
4–10	502 (45.9)	486 (47.2)	16 (24.6)	
≥11	427 (39.0)	382 (37.1)	45 (69.2)	
Stroke etiology				
Large-artery atherosclerosis	174 (15.9)	159 (15.4)	15 (23.1)	.025
Cardioembolism	384 (35.1)	361 (35.1)	23 (35.4)	
Small-vessel occlusion	134 (12.2)	134 (13.0)	—	
Other determined cause	48 (4.4)	45 (4.4)	3 (4.6)	
Undetermined cause	354 (32.4)	330 (32.1)	24 (36.9)	
Cortical involvement	499 (45.6)	436 (42.4)	63 (96.9)	<.001
Stroke vascular territory				
Internal carotid artery	127 (11.6)	111 (10.8)	16 (24.6)	<.001
Middle cerebral artery	644 (58.9)	599 (58.2)	45 (69.2)	
Anterior cerebral artery	43 (3.9)	41 (4.0)	2 (3.1)	
Posterior cerebral artery	35 (3.2)	34 (3.3)	1 (1.5)	
Posttreatment NIHSS				
≤3	770 (70.4)	754 (73.3)	16 (24.6)	<.001
4–10	215 (19.6)	193 (18.7)	22 (33.9)	
≥11	109 (10.0)	82 (8.0)	27 (41.5)	
Short acute symptomatic seizures	21 (1.9)	17 (1.7)	4 (6.2)	.010
Acute symptomatic status epilepticus	7 (.6)	5 (.5)	2 (3.1)	.011
SeLECT 2.0 score	3 [2–4]	3 [2–4]	5 [4–6]	<.001
Modified SeLECT 2.0 score	2 [1–3]	2 [1–3]	5 [4–5]	<.001
ASMs at discharge	26 (2.4)	20 (1.9)	6 (9.2)	<.001

Note: Data are presented as median [interquartile range] for continuous variables and *n* (%) for categorical variables.

Abbreviations: ASM, antiseizure medication; EVT, endovascular treatment; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale.

baseline and posttreatment stroke severity are shown in Figure S1B,C. The results of the analyses adjusted for the prescription of ASMs at discharge (Table S2) and mortality as a competing outcome during follow-up (Table S3) were consistent with the results obtained in the analyses of the full cohort.

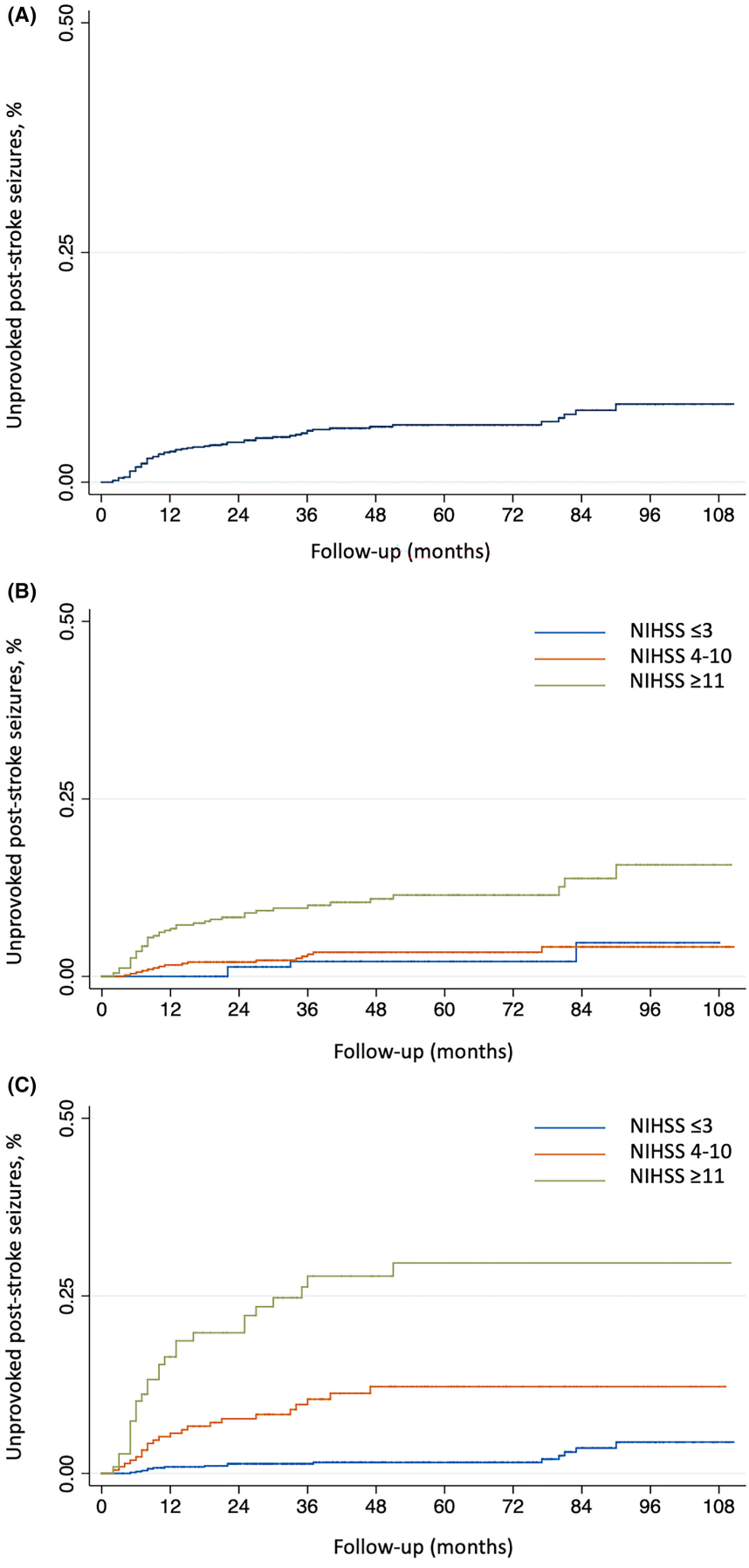

FIGURE 2 Time to occurrence of unprovoked poststroke seizures. (A) Total cohort. (B) Stratified by National Institutes of Health Stroke Scale (NIHSS) on admission. (C) Stratified by posttreatment NIHSS. Kaplan–Meier estimates are given for the time to the occurrence of unprovoked poststroke seizures during the follow-up in the whole study cohort (A) and according to stroke severity at admission (B) and after treatment (C).

3.2 | Predictive performance of statistical models

The median values of the original and modified SeLECT 2.0 scores were 3 (IQR = 2–4) and 2 (IQR = 1–3), respectively. Both the original (HR = 1.58, 95% CI = 1.45–1.72 for unitary increase; $p < .001$) and modified (HR = 1.57, 95% CI = 1.45–1.69 for unitary increase; $p < .001$) SeLECT 2.0 scores were associated with the risk of PSE. The equations for the prediction of PSE at 12 months for the original and modified SeLECT 2.0 score were $HR_{poststroke\ epilepsy(12)} = .0053 * exp^{[.455*SeLECT\ 2.0\ score]}$ and $HR_{poststroke\ epilepsy(12)} = .0075 * exp^{[.450*modified\ SeLECT\ 2.0\ score]}$.

The AUC values of the ROC curves for the original and modified SeLECT 2.0 score are shown in Table 2. No significant differences in discrimination were observed at 12 and 24 months after stroke, whereas the modified SeLECT 2.0 score showed better discrimination for the prediction of PSE at 36, 48, and 60 months after stroke. Calibration plots suggested that both the original and modified SeLECT 2.0 score models underestimate the probability of unprovoked seizures for predicted probabilities of <80% (Figure S2).

The goodness of fit statistic metrics for the original and modified SeLECT scores are summarized in Table 3 and indicated a better predictive performance for the model with posttreatment NIHSS. According to continuous NRI, the modified SeLECT score produced more accurate risk predictions compared to the SeLECT 2.0 at all evaluated time points from 12 to 60 months (Table 4). The classification obtained with the original and modified SeLECT 2.0 score is shown in Table S4.

4 | DISCUSSION

The current study suggested that posttreatment stroke severity in subjects with cerebral infarct undergoing IVT and/or EVT can be a more reliable predictor of PSE compared to stroke severity at admission. In addition, the SeLECT 2.0 score could more adequately predict the risk of PSE when the baseline stroke severity is replaced with the severity of the neurological deficit persisting after the reperfusion treatments. These findings can indirectly support the current understanding of PSE pathophysiology, in which stroke size is one contributor for epileptogenesis.[6]

Recent advances in acute stroke treatment have been only marginally investigated in the development of the SeLECT and SeLECT 2.0 scores. In the development of the SeLECT score, 139 subjects of the derivation cohort corresponding to only 12% of the total were treated with IVT, and only 186 subjects received this treatment across the Austrian, German, and Italian cohorts, corresponding to 15.9% of the population used to validate the model.[3] Model discrimination remained consistent in the subset of people receiving IVT in the validation cohorts. In addition, data for EVT were available for only 28 cases from the Austrian nested case–control validation study.[3] In the development of the SeLECT 2.0 score, 1286 subjects of the derivation cohort corresponding to 28% of the included population and only 13 subjects corresponding to 33% of the replication cohort underwent acute reperfusion treatment.[4] Acute reperfusion treatment was not associated with the time to first remote symptomatic seizure in stroke survivors in a subcohort with data acquired after 2014, and neither IVT nor mechanical thrombectomy were associated with remote symptomatic seizures in subjects with acute symptomatic status epilepticus included in the replication cohort.[4] Although these analyses may suggest the validity of the scores irrespective of the acute stroke treatment, they did not consider the effect of poststroke treatment in the development of models and did not adequately explore any potential benefit deriving from the reperfusion therapies regarding the risk of PSE.

The relationship between revascularization treatment and the risk of PSE has been the subject of much debate in recent years. Small studies have found a high risk of PSE after EVT and IVT,[19–21] but the high risk of inclusion bias precluded a definite answer. Recently, a Swedish nationwide study based on several registers included a total of 2120 individuals treated with EVT, who were matched by age, sex, NIHSS score at admission, and time of stroke with 1535 controls treated with IVT and 1545 controls receiving no acute treatment.[22]

TABLE 2 Time-dependent receiver operating characteristic curves.

	SeLECT 2.0 score			Modified SeLECT 2.0 score			
Time	**AUC**	**95% CI**		**AUC**	**95% CI**		***p***
12 months	84%	79%	90%	86%	81%	92%	.100
24 months	84%	79%	89%	86%	81%	91%	.090
36 months	84%	79%	88%	88%	84%	92%	.002
48 months	84%	80%	88%	88%	84%	91%	.006
60 months	84%	80%	89%	88%	84%	92%	.003

Abbreviations: AUC, area under the curve, CI, confidence interval.

TABLE 3 Goodness of fit statistic metrics.

	Harrell C parameter	Somers D parameter	Akaike information criterion	Bayesian information criterion
SeLECT 2.0 score	.83	.66	802.30	807.30
Modified SeLECT 2.0 score	.86	.72	788.05	793.05

TABLE 4 Net Reclassification Index.

Time	NRI	95% confidence interval		*p*
12 months	.222	.012	.420	.040
24 months	.220	.030	.392	.040
36 months	.304	.085	.426	.007
48 months	.278	.014	.398	.033
60 months	.302	.124	.013	.040

Note: Continuous NRI of the modified SeLECT 2.0 score over the SeLECT 2.0 score for different time points after stroke is shown. The continuous NRI is a measure for evaluating the improvement in prediction performance gained by one model over another.

Abbreviation: NRI, Net Reclassification Index.

After a median follow-up time of 19 months, the overall incidence of PSE was 7.9%. The lowest incidence of PSE was seen after EVT followed by IVT, whereas the highest incidence occurred after no treatment. Higher posttreatment NIHSS was an independent predictor of PSE, whereas IVT given before EVT was protective and associated with a reduced risk of PSE development likely due to improved or faster reperfusion.[22] In a systematic review and meta-analysis of 25 studies including 13 753 patients, the pooled incidence of poststroke seizures was 5.9% among patients who received any form of reperfusion therapy. The incidence of late poststroke seizures was more than twofold higher than the incidence of early poststroke seizures (6.7% vs. 3.2%), but the difference did not reach statistical significance. There was no difference in the overall incidence of poststroke seizures between patients who were treated with IVT, mechanical thrombectomy, or combined IVT and mechanical thrombectomy, but no subgroup analyses were performed for early and late poststroke seizures separately.[23]

Identifying people at high risk of unprovoked seizures after stroke may have many practical applications. It may optimize the enrollment strategy of participants for treatment trials of antiepileptogenesis, aid group comparisons in nonrandomized studies, and personalize medical management of stroke survivors, including potentially prophylactic treatment with ASMs even before a first late seizure. This study built upon current predictive models of epilepsy after ischemic stroke and proposed a modified SeLECT 2.0 score that may refine the predictive accuracy of the original version. Of note, results were obtained from a large cohort of participants with long-term follow-up. The sensitivity analysis based on the competing-risk regression model contributed to give robustness to the results. Some shortcomings need, however, to be acknowledged. The retrospective collection of data at a single center may have introduced potential sources of bias, data were not available for subjects who died within 30 days after the index stroke, and there was not a group receiving no acute treatment; although the posttreatment NIHSS scores were consistent with those observed in historical cohorts from clinical trials,[24–26] indirect comparisons are difficult to perform, considering the differences in setting and populations of the studies. The lack of an external validation cohort, hence, hampered the generalizability of the results. Future, ideally prospective, studies are warranted to confirm the findings in independent populations and identify the optimal timing of the NIHSS assessment. In this regard, the inclusion of both treated and untreated stroke patients undergoing a standardized assessment of stroke severity during the admission period would explore the global usefulness of a new scale. Compared to the original SeLECT 2.0 score, the modified version showed better discrimination from 36 months and produced overall more accurate risk predictions according to the NRI from 12 months after stroke. Further analyses in different cohorts would be useful to better delineate the actual gain of the modified SeLECT 2.0 score in the accuracy of predicting PSE. The similar accuracy of the two models during the first few years after stroke may suggest that some factors, irrespective of the size of the ischemic lesion, have a prominent role in predicting the risk of unprovoked seizures within this time frame, and other variables such as the volume of brain damage may act as stronger predictors of seizures over the longer term. Analyses including information about the success of reperfusion after treatment may also provide additional insights regarding the risk of epilepsy after stroke.[27]

5 | CONCLUSIONS

Defining a prognostic model of unprovoked seizures after stroke is a crucial goal to advance clinical research and

practice. The current models do not fully consider the potential predictors, and a novel scoring systems may result in enhanced accuracy. Stroke severity after revascularization treatment may account for the beneficial effects of these interventions and refine the performance of the SeLECT 2.0 score. Future research is warranted to explore whether and to what extent other covariates, including lesion size and location (information at the sublobar level and according to functional networks),[28] electroencephalographic findings (e.g., epileptiform abnormalities),[29] serum biomarkers of inflammation and brain damage,[30,31] advanced imaging (informing about the extent of brain hypoperfusion and structural/functional brain connectivity alterations),[32] and genetic data investigating polygenic risk factors,[33] might further improve the prediction of PSE among stroke survivors.

AUTHOR CONTRIBUTIONS

Stefano Meletti planned and designed the study, interpreted the data, and revised the manuscript. Claudia Cuccurullo, Giuseppe Borzì, Guido Bigliardi, and Stefania Maffei acquired and interpreted the data, and revised the manuscript. Niccolò Orlandi and Giada Giovannini revised the manuscript. Riccardo Cuoghi Costantini and Cinzia Del Giovane performed the statistical analyses and revised the manuscript. Simona Lattanzi planned and designed the study, performed the statistical analyses, interpreted the data, and drafted and revised the manuscript. All authors approved the final submitted version.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Anonymized data will be shared upon reasonable request of any qualified investigator.

ORCID

Stefano Meletti https://orcid.org/0000-0003-0334-539X
Claudia Cuccurullo https://orcid.org/0000-0001-5118-5103
Niccolò Orlandi https://orcid.org/0000-0002-5717-7363
Giada Giovannini https://orcid.org/0000-0002-3585-5872
Simona Lattanzi https://orcid.org/0000-0001-8748-0083

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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