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Original research

Implications for driving based on the risk of seizures after ischaemic stroke

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ABSTRACT

Background In addition to other stroke-related deficits, the risk of seizures may impact driving ability after stroke.

Methods We analysed data from a multicentre international cohort, including 4452 adults with acute ischaemic stroke and no prior seizures. We calculated the Chance of Occurrence of Seizure in the next Year (COSY) according to the SeLECT$_{2.0}$ prognostic model. We considered COSY<20% safe for private and <2% for professional driving, aligning with commonly used cut-offs.

Results Seizure risks in the next year were mainly influenced by the baseline risk-stratified according to the SeLECT$_{2.0}$ score and, to a lesser extent, by the poststroke seizure-free interval (SFI). Those without acute symptomatic seizures (SeLECT$_{2.0}$ 0–6 points) had low COSY (0.7%–11%) immediately after stroke, not requiring an SFI. In stroke survivors with acute symptomatic seizures (SeLECT$_{2.0}$ 3–13 points), COSY after a 3-month SFI ranged from 2% to 92%, showing substantial interindividual variability. Stroke survivors with acute symptomatic status epilepticus (SeLECT$_{2.0}$ 7–13 points) had the highest risk (14%–92%).

Conclusions Personalised prognostic models, such as SeLECT$_{2.0}$, may offer better guidance for poststroke driving decisions than generic SFIs. Our findings provide practical tools, including a smartphone-based or web-based application, to assess seizure risks and determine appropriate SFIs for safe driving.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Current restrictions on driving for people with epilepsy and those at risk of unprovoked seizures primarily rely on seizure-free intervals, often overlooking the underlying causes and individual characteristics.

WHAT THIS STUDY ADDS

⇒ In addition to other stroke-related deficits, the risk of unprovoked seizures following ischaemic stroke may impact the ability to drive. A novel predictive model (SeLECT$_{2.0}$) allows the prediction of unprovoked seizures and could support decisions on driving eligibility.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Clinicians, particularly those specialising in stroke and epilepsy care, will find this information valuable to make critical decisions regarding an individual's ability to drive or perform specific jobs and activities. Regulators will use the data to devise evidence-based guidelines for driving after stroke. This could lead to a paradigm change in assessing the ability to drive after a stroke.

INTRODUCTION

Driving is often considered an integral part of life. Restrictions on driving may affect an individual's independence, employment and quality of life.[1–4] People with epilepsy and those at risk of unprovoked seizures may be subject to driving restrictions. In people with stroke, apart from stroke-related deficits, the risk of seizures may also impact the ability to drive.

Many regulators consider a chance of an occurrence of a seizure in the next year (COSY) below 20%–40% acceptable for private driving and below 2% for professional driving.[5–7] Several countries require a seizure-free interval (SFI) following a provoked or unprovoked seizure to achieve a sufficiently low COSY for driving.[5 7] Not all recommendations for SFIs may be based on robust data.[6 8] In the USA and many other countries, there is a wide

Table 1 SeLECT$_{2.0}$ scoring system

Select-Score$_{2.0}$	No. of points
NIHSS 4–10	1
NIHSS≥11	2
Large-artery atherosclerosis	1
Short acute symptomatic seizure	3
Acute symptomatic status epilepticus	7
Cortical involvement	2
Territory of MCA involvement	1
Maximum points	13

The SeLECT scoring system is designed to predict the risk of seizures following a stroke by evaluating a comprehensive set of clinical and diagnostic criteria. It involves five parameters: severity of stroke, large-artery atherosclerotic aetiology, early (ie, acute symptomatic) seizures, cortical involvement and territory of middle cerebral artery involvement (MCA).
MCA, Middle cerebral artery ; NIHSS, National Institutes of Healthy Stroke Scale.

range of recommendations for granting driving privileges following seizures.[9]

We developed and validated a predictive model (SeLECT$_{2.0}$) that accurately quantifies the risk of unprovoked seizures following ischaemic stroke.[10] We hypothesised that an acceptable risk of seizures for driving is influenced by the SFI but also by personalised factors that regulators have not considered. Here, we used the SeLECT$_{2.0}$ model to provide quantifiable COSY's and propose SFIs for safe driving based on a stroke survivor's characteristics.

METHODS

Participants

We analysed data from a multicentre registry of poststroke seizures incepted as part of the SeLECT study.[10] The cohort comprises nine international subcohorts and includes adults with neuroimaging-confirmed acute ischaemic stroke. Excluded were people with a transient ischaemic attack, history of seizures or epilepsy, primary haemorrhagic stroke, reinfarction during follow-up or potentially epileptogenic comorbidities (ie, intracranial tumours, cerebral venous thrombosis, history of severe traumatic brain injury, history of brain surgery) and those initially receiving palliative care. The individual cohorts are described in online supplemental file 1.

Statistical analysis

We estimated the SeLECT$_{2.0}$ score for each participant, as described previously (table 1).[11] We modelled the risk of unprovoked seizures following a stroke in the whole cohort using Cox proportional hazards regression. The proportional hazards assumption was met. We estimated the predicted risk of unprovoked seizures for each SeLECT$_{2.0}$ score (range 0–13 points).

COSY was defined as the probability of having unprovoked seizures in the next year, given that the individual remained seizure-free for several months (SFI). For example, COSY at 3 months was the conditional probability of having a seizure during the next 12 months (ie, 15 months since stroke) given that the individual had no unprovoked seizures during the first 3 months poststroke. According to the ILAE recommendation,[12] acute symptomatic seizures during the first 7 days poststroke were not counted as unprovoked seizures.

COSY was estimated according to the standard statistical definition of conditional risks.[13] We considered a COSY below 20% safe for private driving and below 2% for professional driving. These are widely used empirical cut-offs.[5–7]

To account for other stroke-related deficits that may influence driving ability, we analysed the distribution of modified Rankin Scale (mRS) scores 3 months after the incident event in a cohort where the data were available.

We used SPSS V.26 (IBM) for the analyses.

Table 2 Baseline characteristics of derivation cohorts (n=4552)

Variable	N (%) or median (IQR)
Cohort	
Austria	459 (10)
Colombia	322 (7)
Germany (1)	182 (4)
Germany (2)	311 (7)
Italy	399 (9)
Portugal	151 (3)
Spain	512 (11)
Switzerland (1)	1200 (26)
Switzerland (2)	1016 (22)
Age (years)	73 (62–81)
Sex	
Male	2547 (56)
Female	2005 (44)
NIHSS at admission	
≤3	1932 (42)
4–10	1545 (34)
≥11	1075 (24)
Stroke location	
Middle cerebral artery territory involvement	3120 (69)
Cortical involvement	2332 (51)
Stroke cause	
Small-vessel occlusion	893 (20)
Large-artery atherosclerosis	831 (18)
Cardioembolism	1374 (30)
Other or undetermined	1454 (32)
Treatment	
Acute reperfusion treatment	1286 (28)
ASM treatment after acute symptomatic seizure	189 (4)
Acute symptomatic seizure	
Focal aware, short seizure	58 (1.3)
Focal with impaired awareness, short seizure	36 (0.8)
Focal to bilateral tonic clonic, short seizure	88 (1.9)
Status epilepticus	8 (0.2)
Undetermined	36 (0.8)
Duration of follow-up (months)	28 (13–61)

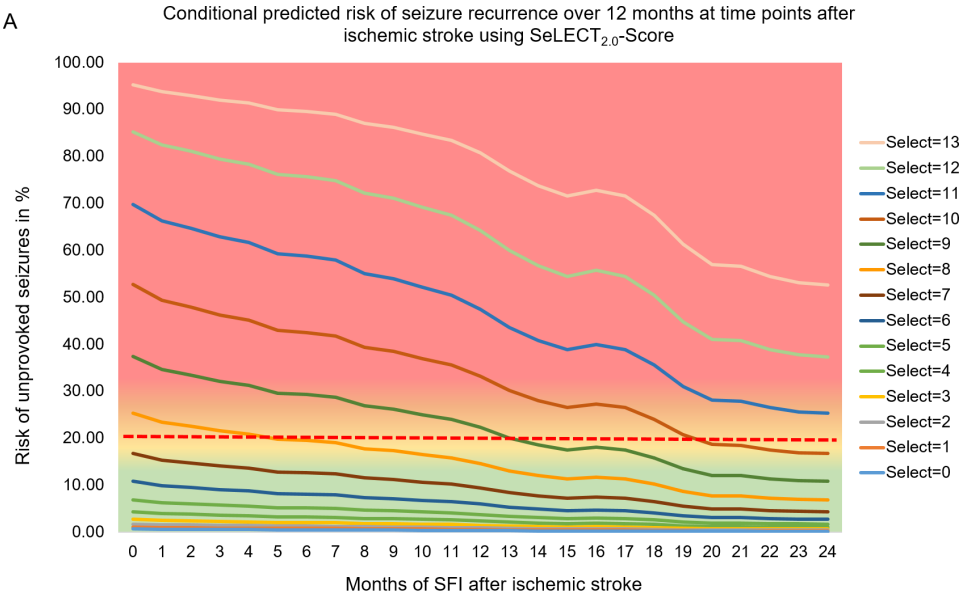
ASM, antiseizure medication; NIHSS, National Institutes of Healthy Stroke Scale.

RESULTS

The cohort included 4552 individuals from 9 centres. Baseline characteristics are displayed in table 2.

We estimated COSYs according to each SeLECT$_{2.0}$ score value and a range of SFIs (between 0 and 24 months) and presented the results as a plot and risk table (figure 1). We colour-coded the results according to the acceptable COSY for private driving (<20%): green, low risk; yellow/orange, borderline; red, high risk. Online supplemental figure 1 shows colour coding for a COSY acceptable for professional driving (<2%).

A



B

SeLECT 2.0	Risk of unprovoked seizures in % for time points after SFI after ischemic stroke (95% CI) in months								
	0	1	2	3	6	9	12	18	24
13	95 (81-99)	94 (79-99)	93 (77-98)	92 (76-98)	90 (71-97)	86 (66-95)	81 (59-92)	68 (45-81)	53 (33-69)
12	85 (68-95)	82 (65-92)	81 (64-91)	79 (62-90)	76 (57-88)	71 (52-84)	64 (45-79)	51 (34-63)	37 (24-50)
11	70 (53-83)	66 (51-79)	65 (50-76)	63 (48-75)	59 (44-72)	54 (40-67)	47 (34-61)	36 (24-45)	25 (17-34)
10	53 (40-66)	49 (38-61)	48 (37-58)	46 (36-57)	43 (32-54)	38 (29-48)	33 (24-43)	24 (17-30)	17 (12-22)
9	37 (29-48)	35 (28-43)	33 (27-41)	32 (25-40)	29 (23-37)	26 (20-33)	22 (17-29)	16 (12-20)	11 (8-14)
8	25 (20-33)	23 (19-29)	23 (19-27)	22 (18-26)	20 (16-24)	17 (14-21)	15 (12-18)	10 (8-12)	7 (5-9)
7	17 (14-21)	15 (13-19)	15 (13-17)	14 (12--17)	13 (11-16)	11 (10-13)	9 (8-12)	7 (5-8)	4 (4-5)
6	11 (9-14)	10 (9-12)	10 (8-11)	9 (8-11)	8 (7-10)	7 (6-8)	6 (5-7)	4 (4-5)	3 (2-3)
5	7 (6-9)	6 (6-7)	6 (5-7)	6 (5-7)	5 (5-6)	5 (4-5)	4 (3-4)	3 (2-3)	2 (2-2)
4	4 (4-6)	4 (4-5)	4 (3-4)	4 (3-4)	3 (3-4)	3 (3-3)	2 (2-3)	2 (1-2)	1 (1-1)
3	3 (2-4)	3 (2-3)	2 (2-3)	2 (2-3)	2 (2-2)	2 (2-2)	2 (1-2)	1 (1-1)	1 (1-1)
2	2 (1-2)	2 (1-2)	2 (1-2)	1 (1-2)	1 (1-2)	1 (1-1)	1 (1-1)	1 (1-1)	0 (0-1)
1	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (1-1)	1 (0-1)	0 (0-0)	0 (0-0)
0	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	1 (0-1)	0 (0-1)	0 (0-0)	0 (0-0)	0 (0-0)

Figure 1 Private driving: impact of different SeLECT2.0 score values and seizure-free intervals (SFI) on the chance of an occurrence of a seizure in the next year: (A) The impact of different SFI on the chance of an occurrence of a seizure in the next year (COSY) following ischaemic stroke. The lines represent different SeLECT2.0 scores. (B) The numerical estimates of COSY stratified by different SFIs and SeLECT2.0 values including the 95% CIs. Colours suggested by different approaches by Bonnett *et al* and Marson[5 16] (acceptable range of risk for private driving for COSY of 20%–40% suggested by Schmedding *et al*[6]): risk estimates ≥20% (and lower CI≥20%) in red (='permissive approach'); risk estimates <20% (and higher CI<20%) in green (='conservative approach') in orange and yellow: orange when risk estimate ≥20% but lower CI<20% (='liberal approach'); yellow when risk estimate <20% but upper CI>20% (='intermediate approach').

COSY was influenced by the $SeLECT_{2.0}$ score at baseline (figure 1). COSY ranged from 0.6% ($SeLECT_{2.0}$ 0 points) to 94% ($SeLECT_{2.0}$ 13 points) after an SFI of 1 month and from 0.2% ($SeLECT_{2.0}$ 0 points) to 53% ($SeLECT_{2.0}$ 13 points) after an SFI 24 months. COSY was below 20% and thus acceptable for private driving already at baseline (ie, SFI 0 months) for $SeLECT_{2.0}$ score values of 0–7 points with the upper border of the 95% CI exceeding 20% for a $SeLECT_{2.0}$ value of 7. COSY declined below 20% following an SFI of 5–14 months for $SeLECT_{2.0}$ values of 8 and 9 points, respectively, and an SFI of 20 months for $SeLECT_{2.0}$ values of 10 points. COSY remained above 20% 2 years after the stroke for $SeLECT_{2.0}$ values of 11–13 points.

Longer SFI was associated with lower COSY (figure 1). Following an SFI of 24 months, COSY declined by factor 3–4 compared with baseline COSY for $SeLECT_{2.0}$ values of 0–9 points. The decline in COSY was less pronounced (factor 1.5–3) for $SeLECT_{2.0}$ values 10–13.

We cross-validated the results using a leave-one-cohort-out strategy (online supplemental table 1). The predictions remained stable when only including recently (after 2014) acquired cohorts (online supplemental table 2). 30% of those with

high SeLECT$_{2.0}$ scores (>6 points) and 67% of those with low scores (0–6 points) had a favourable outcome following stroke (mRS≤2) and could potentially consider driving (online supplemental figure 2). Estimating COSY may help to guide driving regulations in these cases but not in those with severe deficits following stroke (mRS≥3).

To facilitate the calculation of COSY, we implemented the estimates according to SeLECT$_{2.0}$ values and modifiable SFIs in the 'SeLECT score' smartphone application available for iOS and Android (https://predictapps.github.io/select/).

DISCUSSION

Along with stroke-related deficits, for example, neglect, hemianopia, weakness or cognitive deficits, the risk of seizures may impact safe driving following ischaemic stroke. We show that a 'one-size-fits-all' approach may not be adequate to determine the driving ability of stroke survivors at risk of seizures. We assessed the chance of seizure occurrence in the next year (COSY), an essential parameter for determining driving safety in stroke survivors at risk of seizures. The personalised baseline risk of seizures following stroke, determined using the SeLECT$_{2.0}$ score, strongly impacted the predicted seizure risk in the next year. A COSY<20%, viewed as an acceptable risk for driving by many European regulatory agencies, was already achieved at baseline for SeLECT$_{2.0}$ values 0–7 points. Those with SeLECT$_{2.0}$ values of 8–10 points had a COSY<20% after an SFI of 5–20 months while those with higher SeLECT$_{2.0}$ values did not reach a COSY<20% with SFIs of 24 months or less. Thus, the choice of the appropriate SFI is determined mainly by a personalised baseline risk captured using SeLECT$_{2.0}$ score.

Many European regulatory agencies[8 14] recommend a 3-month SFI for those with an acute symptomatic seizure following stroke, which is considerably shorter than the more usual 6–12 months in many jurisdictions in North America and Asia.[9] The regulations typically do not, however, consider other individual characteristics. Those with an acute symptomatic seizure can score 3–13 points on the SeLECT$_{2.0}$ score. According to our data, COSY following a 3-month SFI may range from 3% to 93% for SeLECT$_{2.0}$ scores of 3–13 points. In other words, the risk of seizures in some, but not in all, individuals with acute symptomatic seizures may be acceptable for private driving following a 3-month SFI. These COSY estimates should be interpreted according to local regulations.

Those with acute symptomatic status epilepticus (SeLECT$_{2.0}$ score between 7 and 13 points) had higher COSYs (range 14%–92% after an SFI of 3 months). In these cases, the ability to drive will also likely depend on an individual's characteristics to determine the necessary SFI.

Conversely, our model confirms that stroke survivors without acute symptomatic seizures (SeLECT$_{2.0}$ score between 0 and 6 points) have a low COSY at baseline (range 0.7%–11%), thus not requiring an SFI to reach a low COSY for private driving. This confirms current practice in many countries.

In contrast to an individual's baseline characteristics, SFIs of less than 12 months had a minor impact on COSY. This is understandable, given that stroke survivors in the cohort did not have epilepsy at baseline. Thus, having a first unprovoked seizure requires epileptogenic processes, which may involve long latent periods of several months to years.[15] In other words, a first unprovoked seizure may occur after a few weeks in one individual or after several years in another.

Our work builds on previous research on driving ability in people with seizures. A concept of incorporating CIs alongside risk estimates in regulatory decisions, as visualised in figure 1, challenging the reliance on estimates alone, has been proposed.[5] A 20%–40% cut-off range, with the lower 20% threshold, has been suggested and adopted as a conservative standard by many regulatory bodies.[6] Nonetheless, the sparsity of stroke survivors with acute symptomatic seizures in the SeLECT model underscores the need for a cautious approach, advocating for the use of CIs.

Our study has limitations. We only focused on the predicted risk of unprovoked seizures. Safe driving after a stroke may be impacted by other factors, for example, hemineglect, hemianopia, weakness or cognitive deficits. The SeLECT score does not measure these factors and was not considered when generating our risk-prediction charts. Such deficits require an individualised approach and must be considered in addition to the risk of unprovoked seizures when considering the safety of driving in stroke survivors. Our analysis aimed to assess the potential for stroke survivors to resume driving using National Institutes of Healthy Stroke Scale and mRS data. Despite limited data on these scales' relevance to poststroke driving capabilities, many survivors were functionally independent and might consider driving again (online supplemental figure 2). The individual cohorts in the SeLECT registry had heterogeneous modes of follow-up. In our study, this may have led to slightly uneven prediction estimate curves (eg, a slight increase in risks at month 15 in figure 1 and online supplemental figure 1) due to a clustering of last follow-up visits at predefined time points in some cohorts. The inclusion of a wide variety of cohorts, on the other hand, and the cross-validation of our results support the generalisability of these findings. Further limitations of the SeLECT registry and cohorts are debated in previous publications.[10 11]

Our data questions the current commonly used approach that relies on fixed SFIs only to determine the ability to drive in stroke survivors at risk of having unprovoked seizures. Our results instead support a more personalised approach. We show that an individual's characteristics, which are obtainable within the first 7 days after stroke, significantly impact the conditional risk of unprovoked seizures and should thus be incorporated into decision-making. We provide practical charts to help determine a stroke survivor's predicted risk of seizures and the appropriate SFI to meet driving regulations. These charts can also help stratify the risks associated with other potentially precarious activities, such as working at heights, operating unguarded machinery or participating in certain sports activities.

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Competing interests LA has received personal fees and travel support from UCB Pharma, Eisai, Esteve and Bial and personal fees from Sanofi outside the submitted work. ES has received grants and personal fees from UCB Pharma, Eisai, Esteve and Bial, outside the submitted work. SE received honoraria for consulting and lectures from Allergan/Abbvie, Lilly, Lundbeck, Novartis, Perfood, Teva (past 3 years). FB received fees and travel support from Lusofarmaco, outside the submitted work. CB received a Grant from Sociedade Portuguesa do AVC (sponsored by Tecnifar), honoraria for lectures and support for scientific events from Bial, outside the submitted work. MK received non-financial support from ROCHE and BRAHMS Thermofisher Scientific outside the submitted work. MRK reports grants from UCB and Eisai, outside of the submitted work. BT reports personal fees from Biogen outside the submitted work. JWS reports grants and personal fees from UCB, grants from NIHR and Angelini; and personal fees from UCB and Angelini outside the submitted work. MG received fees and travel support from Arvelle, Advisis, Bial and Nestlé Health Science outside the submitted work. JNW received fees from Boehringer Ingelheim and UCB and travel grants from ROCHE, outside the submitted work. TJvO reports personal fees from Angelini Pharma Österreich; Arvelle Therapeutics, Argenx, Biogen, Eisai GesmbH, GW Pharma, Jazz Pharmaceuticals, LivaNova, und von Zogenix, grants from Boehringer-Ingelheim, outside the submitted work. All other authors declare no competing interests.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but all local ethical committees granted regulatory approval: according to Swiss and German law the regional ethical committees exempted these cohorts from requiring written informed consent. The Austrian and German (1) case–control studies were classified as retrospective service evaluation by the regional ethical committee and informed consent was not required. The retrospective Colombian cohort did not require informed consent by the regional ethical committee. See also Online Supplement. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Who can access the data: Data will be shared on a reasonable request by a qualified investigator, provided consent to share is given by the individual cohorts. Types of analyses: For any purpose on reasonable request by a qualified investigator. Mechanisms of data availability: With investigator support.

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