UZ GENT

NAH CONGRES
Niet-aangeboren hersenletsel
in Vlaanderen vandaag

Mede mogelijk gemaakt door

EPILEPSIE NA EEN BEROERTE

Prof. dr. Veerle De Herdt

Neurologie UZ Gent

13 oktober 2026

OVERVIEW

Inleiding

Onderliggende mechanismen

Epidemiologie

Geassocieerde factoren

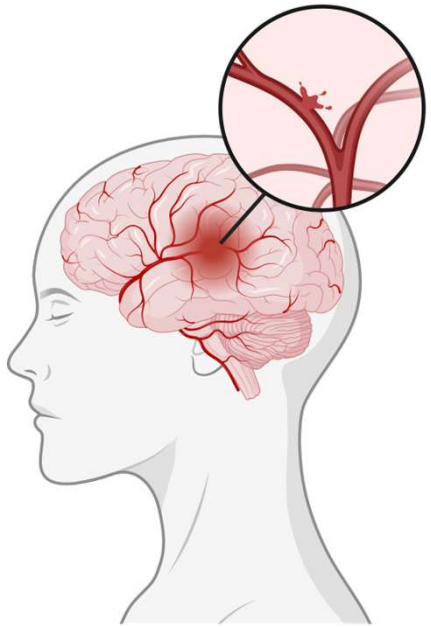
Impact op outcome

Preventie en behandeling

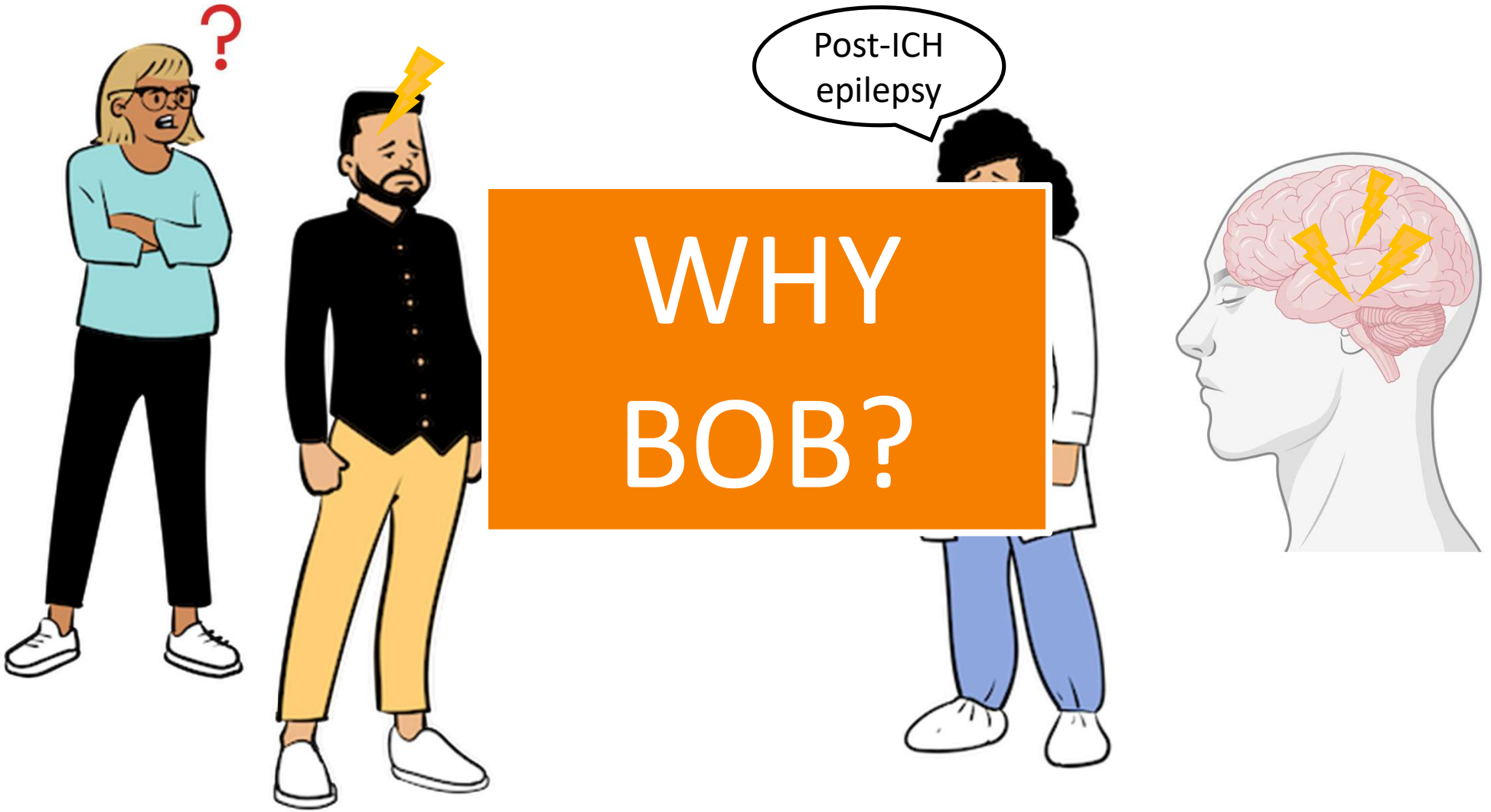
Alice

Bob

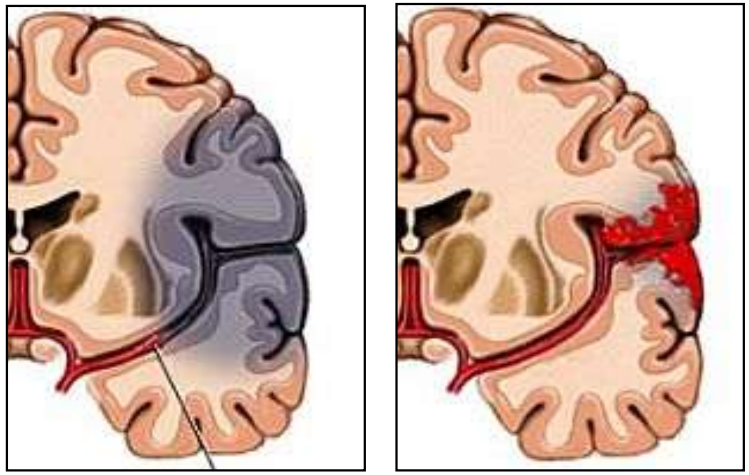
Intracerebral hemorrhage



> 2,000,000 people worldwide per year


?
Post-ICH epilepsy
WHY BOB?

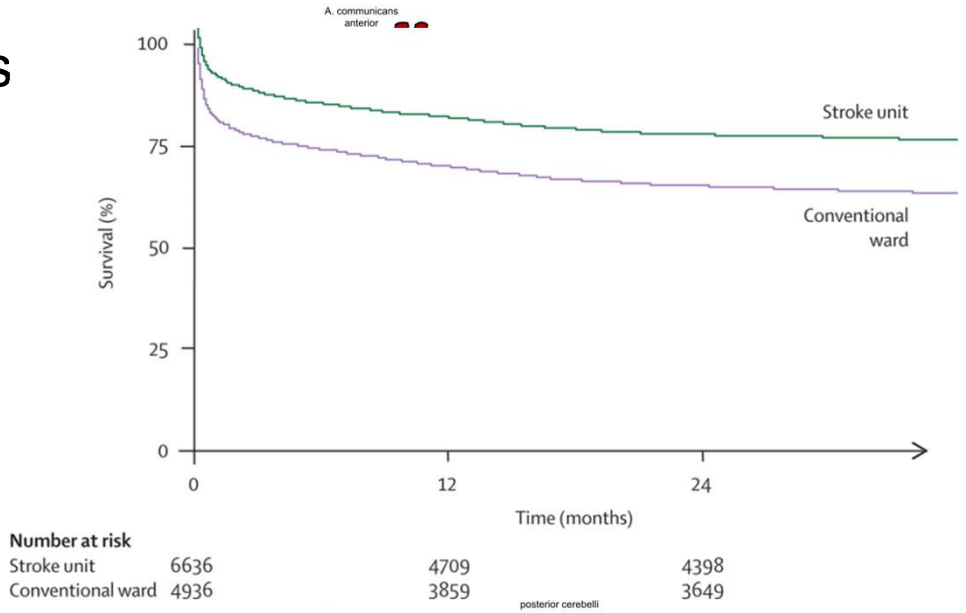
INLEIDING



Beroertes zijn een majeure oorzaak van mortaliteit en invaliditeit en treft in het bijzonder de oudere populatie.

Toenemende groep ouderen + recente vooruitgang in de beroertezorg

→ toename van stroke ‘survivors



Stroke Unit Trialists’ Collaboration 2013

INLEIDING



Epilepsie is een chronische neurologische aandoening.

Tijdens een epileptische aanval is er een abnormale elektrische ontlading van een groep neuronen.

plotse en voorbijgaande verandering in het bewustzijn en /of het gedrag

duur typisch sec tot min

Epilepsie = (herhaald) optreden van epileptische aanvallen.

Men kan de diagnose van epilepsie stellen na 1 epileptische aanval indien het risico op een recidief aanval groter dan 60% wordt ingeschat bv bij aantoonbare hersenschade of in het kader van een epilepsie syndroom.

INLEIDING

Beroerte → voornaamste oorzaak van epilepsie bij volwassenen

- 11% van de epilepsie diagnose bij volwassenen
- 40% bij ouderen

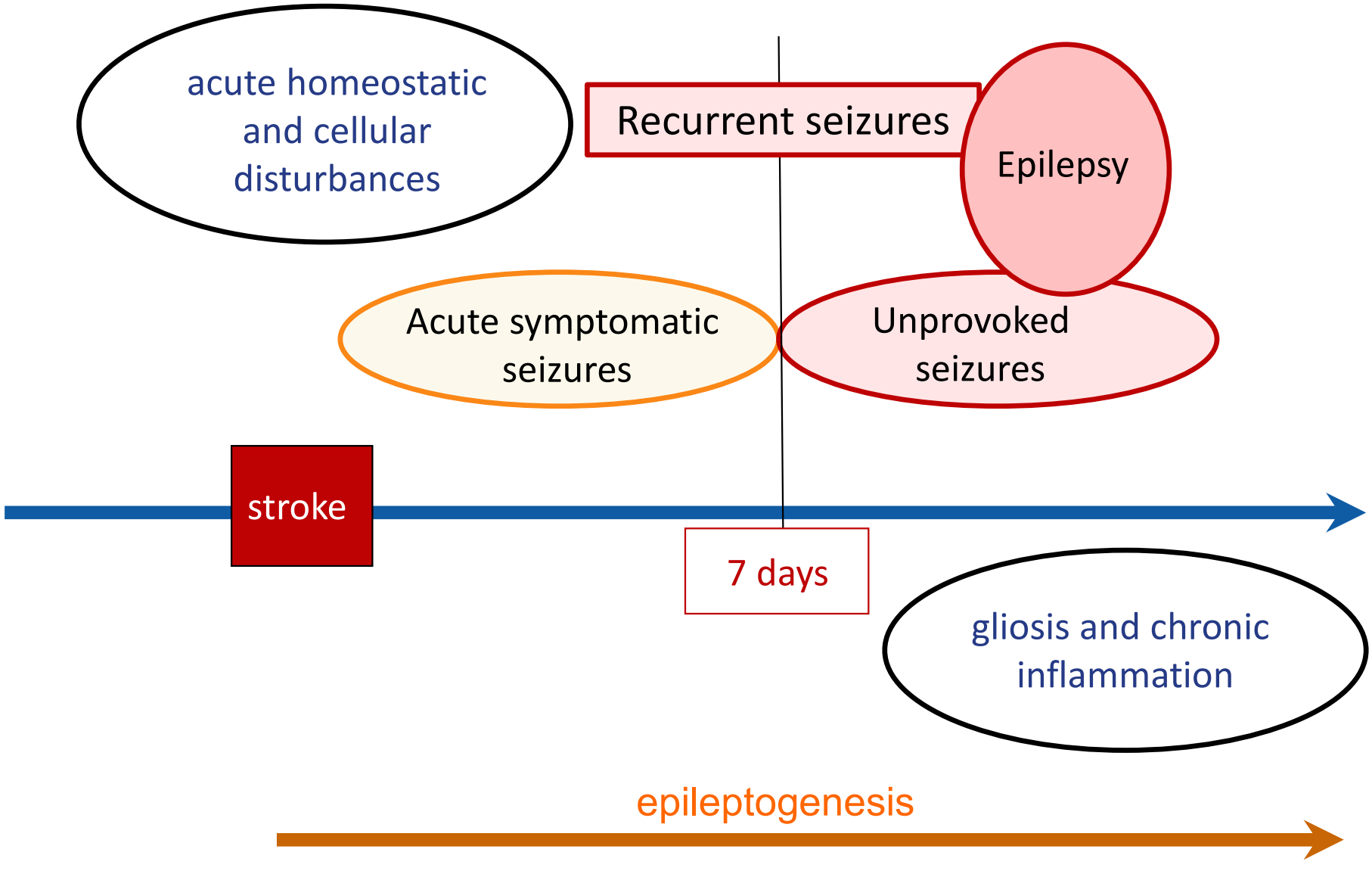
- De incidentie van poststroke aanvallen en de prevalentie van poststroke epilepsie zal toenemen (door een hoger aantal stroke survivors)
- Geen evidentie dat een verbeterde beroertezorg de incidentie van poststroke epilepsie zal doen dalen

INLEIDING

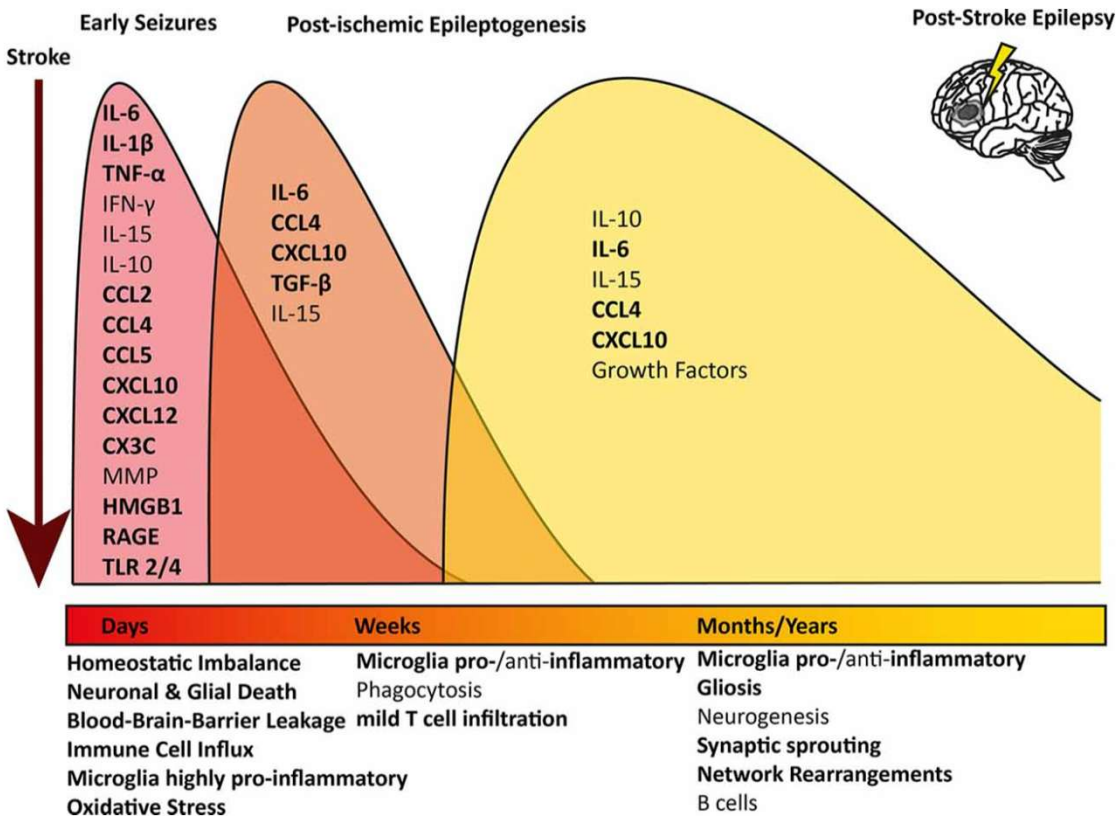
Epilepsie

- heeft een grote impact op alle aspecten van het leven, en de levenskwaliteit
- noodzaakt antiepileptische medicatie met mogelijke bijwerkingen
- verhoogt het risico op comorbiditeiten
- verhoogt de kosten voor zorg
- heeft een mogelijke negatieve impact op outcome na een beroerte
- doet de ‘burden of disease’ toenemen

ONDERLIGGENDE MECHANISMEN



POST-ISCHEMIC CHANGES AND EPILEPTOGENESIS



Blood-brain-barrier leakage, mitochondrial dysfunction, oedema, ion gradient imbalance are post-ischemic pathological changes that may contribute to the stroke lesion as well as to seizure generation.

Troscher A et al. Frontiers Aging Neuroscience, 2021

STROKE AND SEIZURES AND VICE VERSA

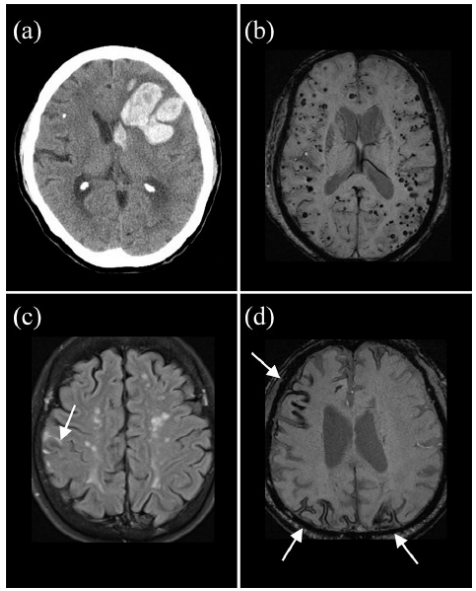
Middle-aged and elderly patients with newly diagnosed epilepsy have a 2 to 3 fold risk to suffer from subsequent stroke within the next couple of years.

→ seizures may be triggered by microvascular changes

→ seizures may be an early biomarker for subsequent stroke

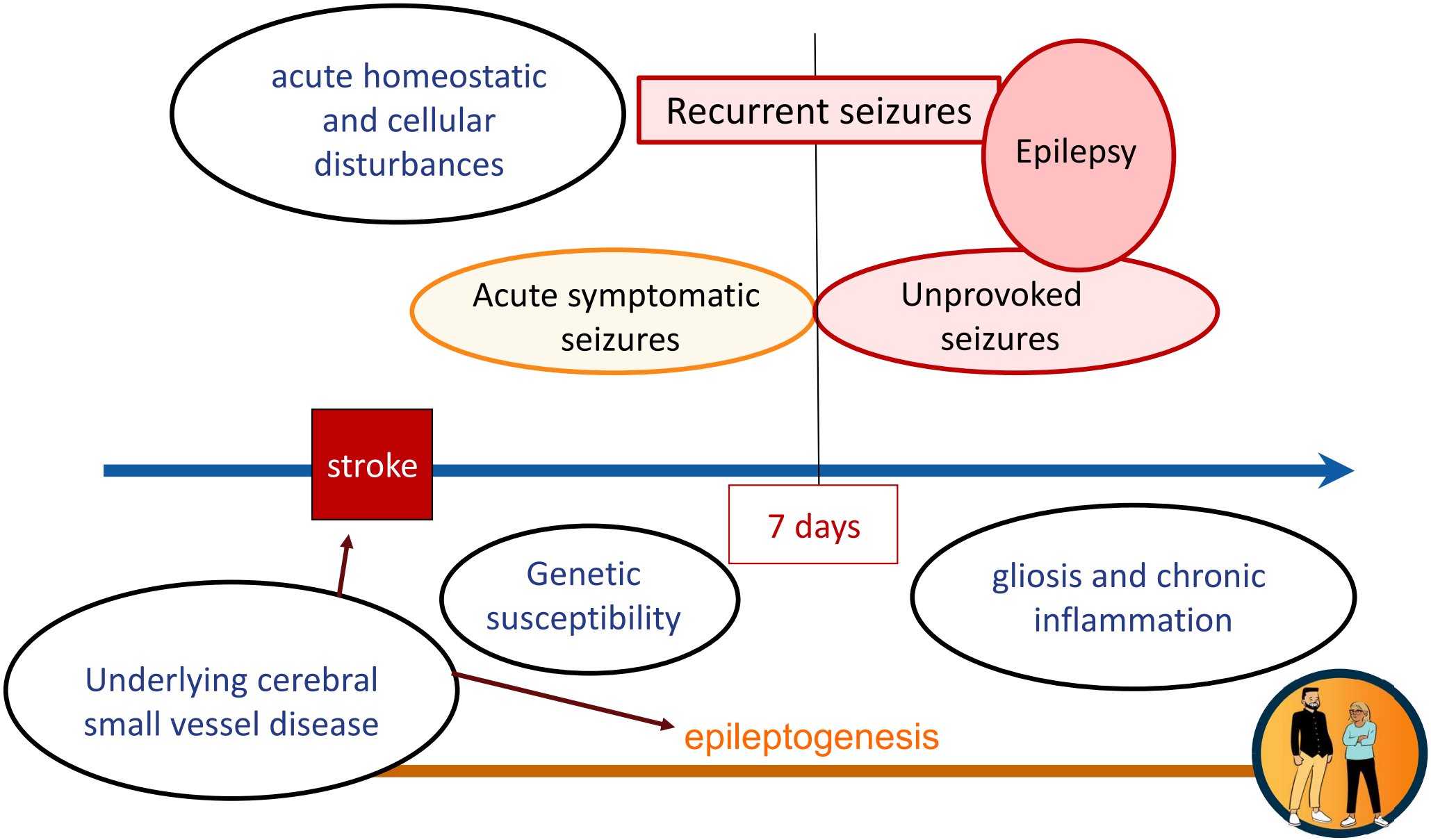
Associated factors for seizures are possibly

linked to the underlying vascular pathology e.g. CAA



Chen et al (2019). Advances in cerebral amyloid angiopathy imaging. Therapeutic Advances in Neurological Disorders. 12.

ONDERLIGGENDE MECHANISMEN



EPIDEMIOLOGIE

Occurence of post-stroke acute symptomatic seizures is estimated

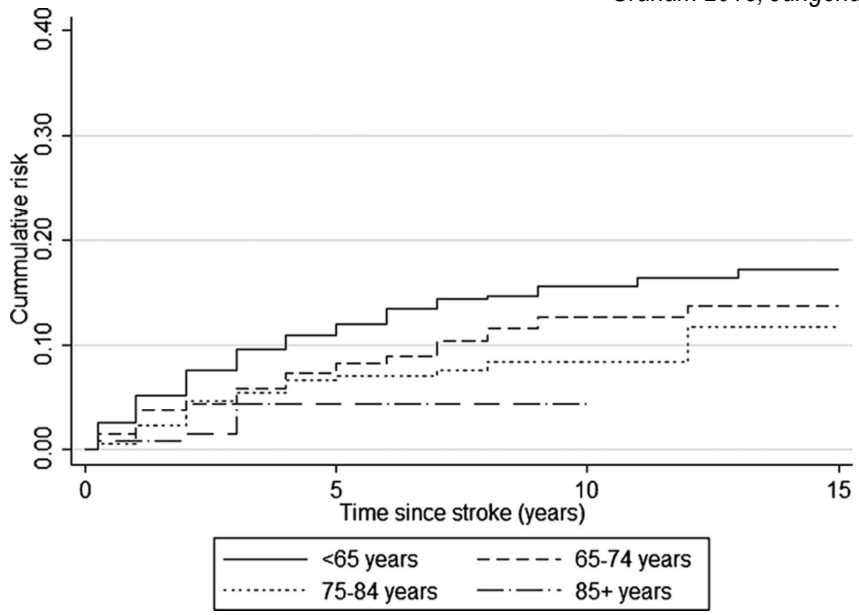
at 3-6% for ischemic stroke

at 10-14% for intracerebral hemorrhage

Pezzini 2012; Beghi 2011; De Herdt 2011; Labovitz 2001, Law 2020

Long-term cummulative risk of unprovoked seizures or post-stroke epilepsy is estimated around 10 %

Graham 2013, Jungehulsing 2013, Rossi 2013, Lahti 2017



American Heart Association.

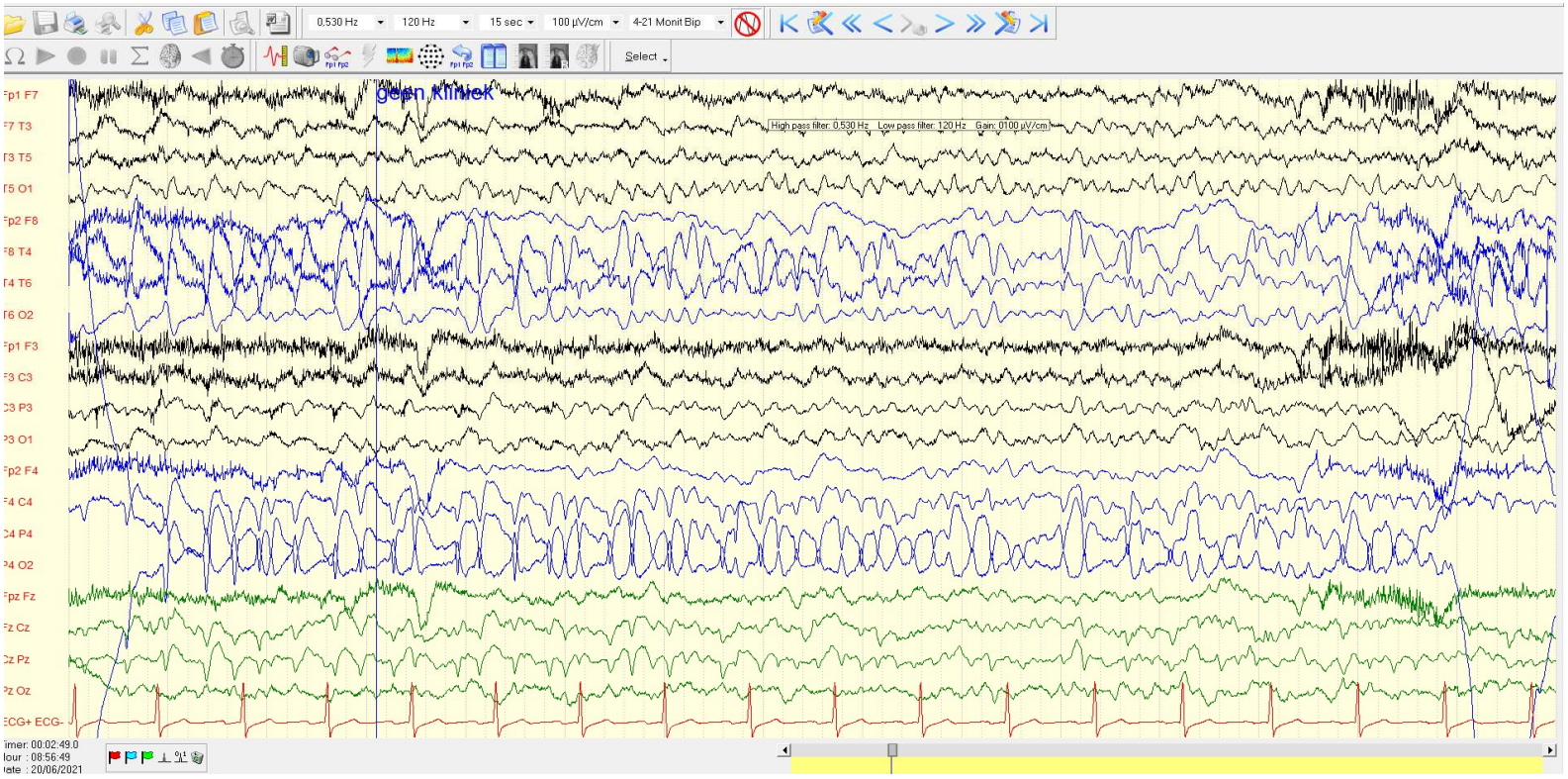
Neil S.N. Graham et al. Stroke. 2013;44:605-611

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EPIDEMIOLOGIE

- Higher incidences when **subclinical and electrographic seizures** are taken into account using continuous EEG monitoring

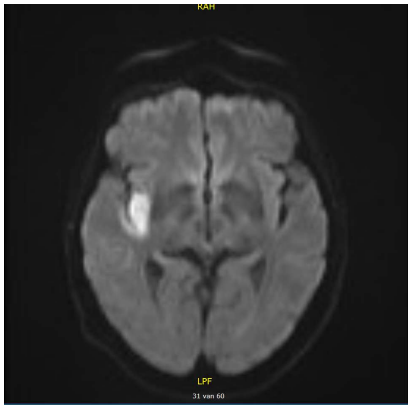
- In intracerebral hemorrhage, epileptic discharges were detected in **16-42%** of patients (*Garrett 2009, Claassen 2007, Vespa 2003, Peter-Derex 2022)*

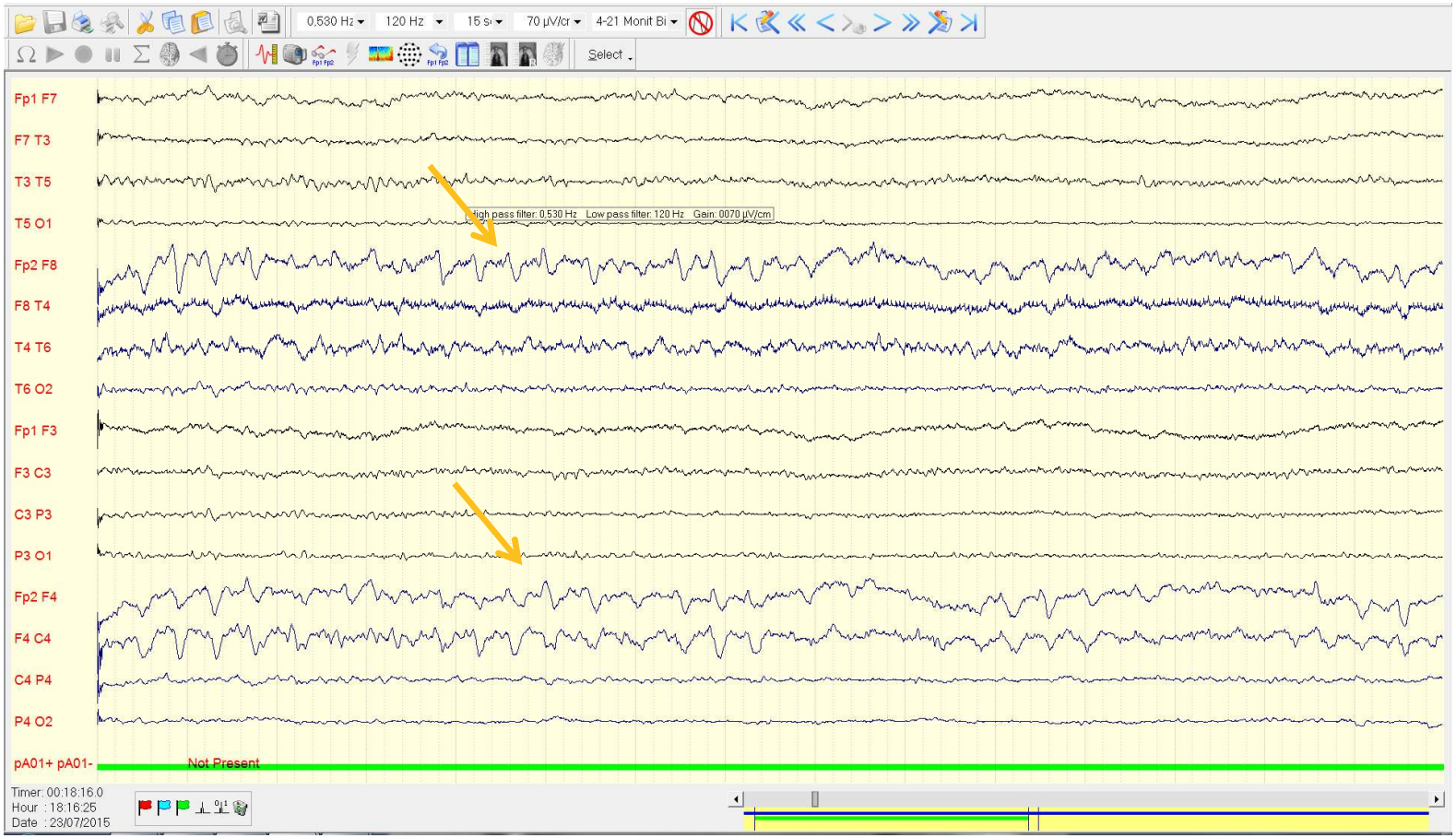


EEG

Golden standard to detect subclinical epileptic activity or clinically unrecognized electrographic seizures (CLUES)

Particularly useful in critically ill patients and patients with altered consciousness + aphasic and confused patients!





GEASSOCIEERDE FACTOREN

Identification of associated factors

> Guide the use of diagnostics in a pre-defined target population

> May help to understand the pathofysiology of post-stroke seizures

> May guide treatment decisions

> can identify a population at risk for clinical research

Stroke 2013

Incidence and predictors of late seizures in intracerebral hemorrhages

Rossi C, De Herdt V, Dequatre-Ponchelle N, Hénon H, Leys D, Cordonnier C

- PITCH database
- Inclusion of MRI biomarkers (BMB, GCA and leukoaraiosis)
- Long-term FU

Results (n=325)

Incidence rate

4 new cases/100 person-years

- Median delay between ICH and LS 9 months (IQR 3-23)

Factors associated with late seizures (n=31)

- Cortical involvement (HR 2.8; 95%CI 1.3-6.1)

MRI biomarkers

- Lobar BMB were predictors of LS, especially when ≥3

ACUTE REPERFUSION THERAPIES

Neurotoxicity of rt-PA and succesfull reperfusion on itself are possible mechanisms for seizure generation.

→ Several studies reported an increased risk of seizures following reperfusion therapies.

→ Larger studies and meta-analyses uniformely demonstrated that recanalisation overall is NOT associated with an increased risk for either ASS or LS *(Lekoubou 2020, Fridman 2021)*

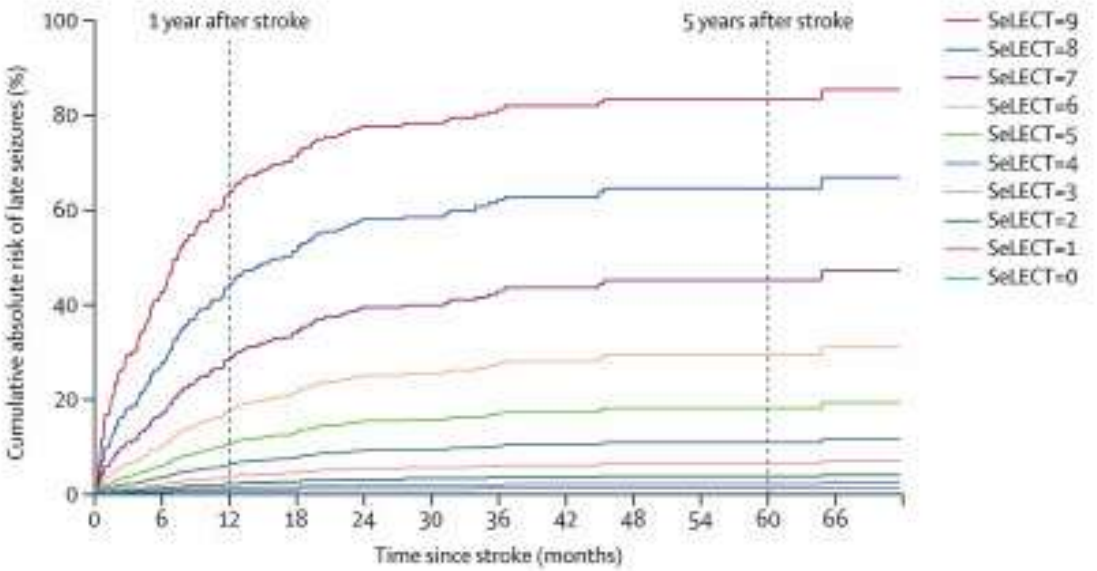
IDENTIFYING PATIENTS AT RISK



a Calculation of SeLECT score

	SeLECT score (points)
(Se) Severity of stroke	
NIHSS ≤3	0
NIHSS 4–10	1
NIHSS ≥11	2
(L) Large-artery atherosclerosis	
No	0
Yes	1
(E) Early seizure (≤7 days)	
No	0
Yes	3
(C) Cortical involvement	
No	0
Yes	2
(T) Territory of MCA	
No	0
Yes	1

b Risk of remote symptomatic seizures



Prediction of remote symptomatic seizures after ischaemic stroke using the SeLECT score. **a** Calculation of the SeLECT score; **b** Kaplan–Meier estimate curves of the risk of remote symptomatic seizures according to different SeLECT values.
From Galovic et al., Lancet Neurology 2018

IDENTIFYING PATIENTS AT RISK



Stroke
Volume 45, Issue 7, July 2014; Pages 1971-1976
https://doi.org/10.1161/STROKEAHA.114.004686

ORIGINAL CONTRIBUTIONS

The CAVE Score for Predicting Late Seizures After Intracerebral Hemorrhage

Elena Haapaniemi, MD, Daniel Strbian, MD, Costanza Rossi, MD, Jukka Putaala, MD, Tuulia Sipi, MB, Satu Mustanoja, MD, Tiina Sairanen, MD, Sami Curtze, MD, Jarno Satopää, MD, Reina Roivainen, MD, Markku Kaste, MD, Charlotte Cordonnier, MD, Turgut Tatlisumak, MD, and Atte Meretoja, MD

a Calculation of CAVE score

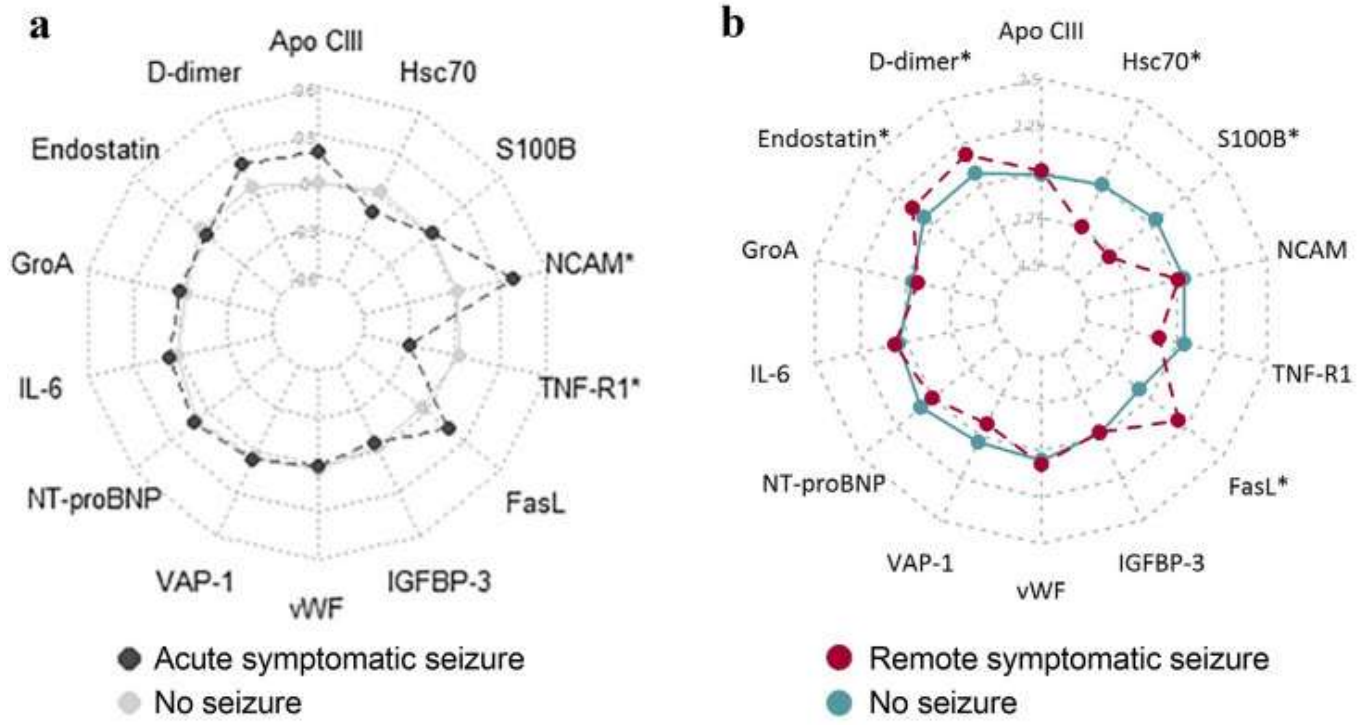
	Points
Cortical involvement	
No	0
Yes	1
Age	
≥ 65 years	0
< 65 years	1
Haemorrhage volume	
≤ 10 mL	0
> 10 mL	1
Acute symptomatic seizure	
No	0
Yes	1

b Risk of remote symptomatic seizures

CAVE score	Seizure risk	
	Derivation	Validation
0 points	0.6%	3.1%
1 point	3.6%	5.0%
2 points	9.8%	15.8%
3 points	34.8%	13.5%
4 points	46.2%	37.5%

Prediction of remote symptomatic seizures after intracerebral haemorrhage using the CAVE score. **a** Calculation of the CAVE score; **b** risk of remote symptomatic seizures according to CAVE score during follow-up in the derivation and validation cohorts. Haapaniemi et al. Stroke 2014.

IDENTIFYING PATIENTS AT RISK

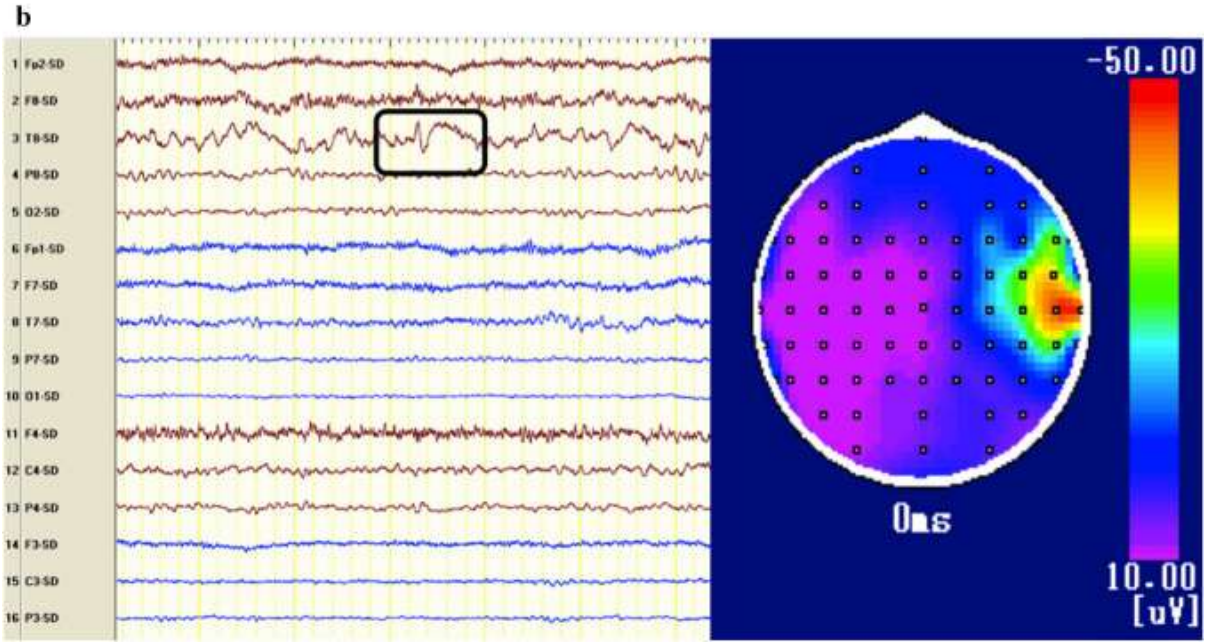


Blood biomarkers of acute and remote symptomatic seizures after stroke. Radar charts of z-scores for biomarkers of **a** acute or **b** remote symptomatic seizures. *ApoCIII*apolipoprotein CIII, *FasL* Fas ligand, *GroA* growth-related oncogene α, *Hsc70* heat shock 70 kDa protein-8, *IGFBP-3* insulin-like growth factor binding protein-3, *IL-6* interleukin 6, *NCAM*neural cell adhesion molecule, *NT-proBNP* N-terminal Pro-B-type natriuretic peptide, *S100B*S100 calcium-binding protein B, *TNF* tumour necrosis factor, *VAP-1* vascular adhesion protein-1, *vWF* von Willebrand factor. Reproduced from Abraira and colleagues. Epilepsia 2020.

IDENTIFYING PATIENTS AT RISK

- Electrographic seizures and LPDs on cEEG in acute brain insult including ICH are associated with further development of new-onset epilepsy (but not with ASS)

(Bentes 2018)



- Early presence of interictal epileptiform activity predicts epilepsy after stroke

(Bentes 2018)

IMPACT OP OUTCOME

Stroke severity is the most important determinant of outcome in stroke patients.

Epileptic discharges could be potentially harmful to acute ischemic tissue:

- Electrical seizures are associated with increased midline shift

  Vespa 2003

- Experimental studies in laboratory animals suggest that frequent early seizures in acute ischemic stroke can increase infarct size and impair functional recovery *Osvaldo and Goldstein 2004*

- 20% of patients with late poststroke seizures developed long-lasting worsening of their neurological sequelae and 50% had transient neurological worsening

  Kumral 2013

Association between seizures after ischemic stroke and stroke outcome: A systematic review and meta-analysis

Xu, Tao; Ou, Shu; Liu, Xi; Yu, Xinyuan; Yuan, Jinxian; Huang, Hao; Chen, Yangmei

Medicine. 95(27):e4117, July 2016.

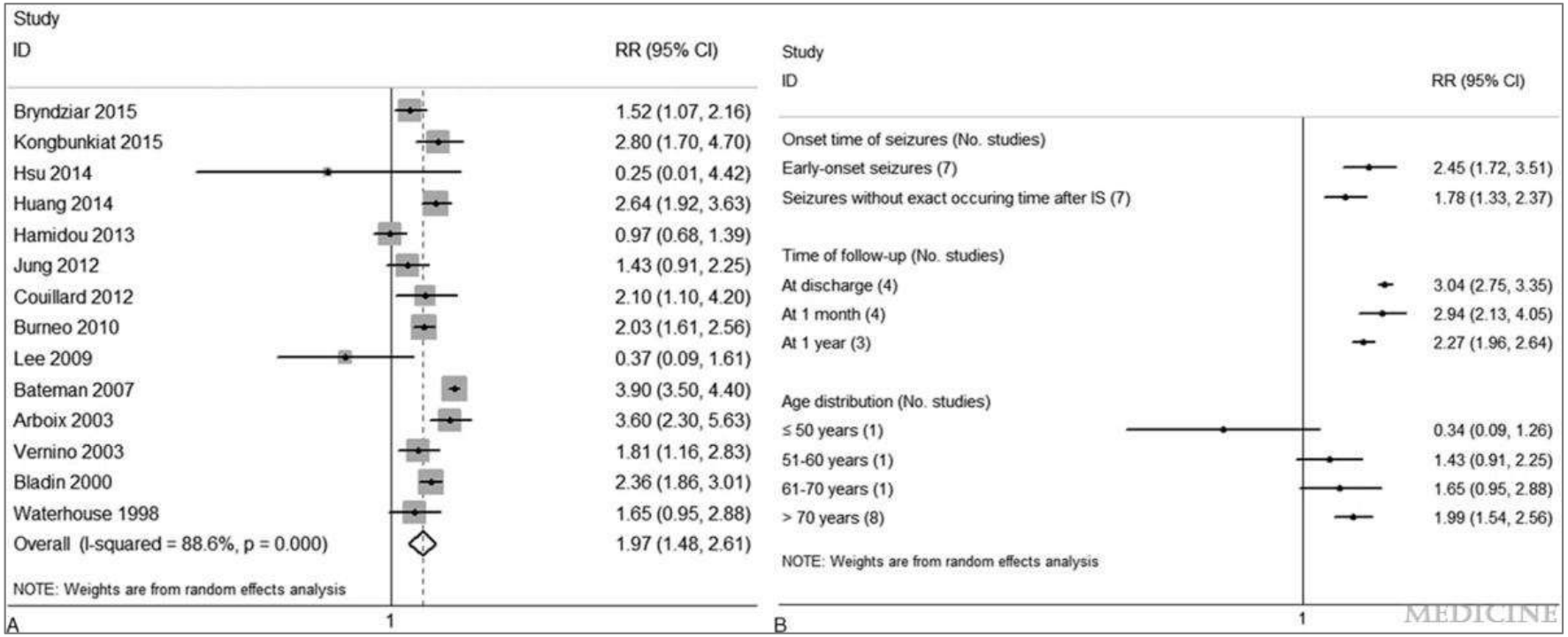


Figure 3. Forest plots of the association between PISS and risk of mortality (A) and the subgroup analyses that were performed to investigate the association between PISS and risk of mortality (B). PISS = post-ischemic stroke seizures.

Wolters Kluwer

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Association between seizures after ischemic stroke and stroke outcome: A systematic review and meta-analysis

Xu, Tao; Ou, Shu; Liu, Xi; Yu, Xinyuan; Yuan, Jinxian; Huang, Hao; Chen, Yangmei

Medicine. 95(27):e4117, July 2016.

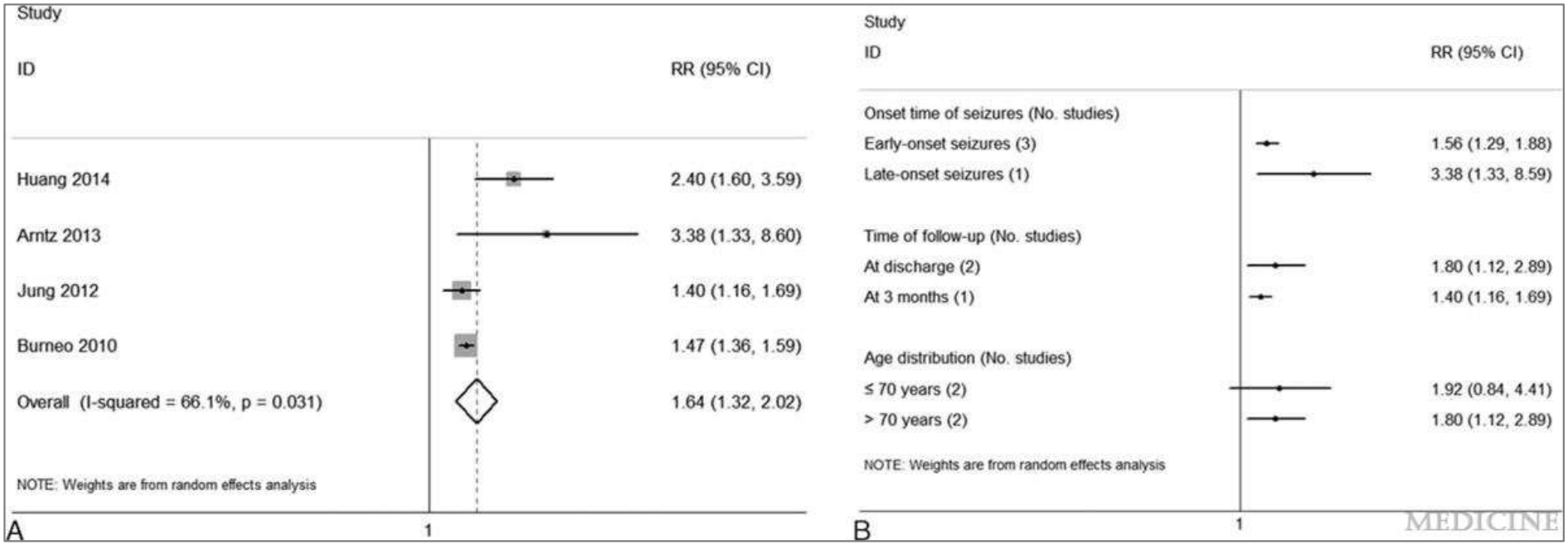


Figure 5. Forest plots of the association between PISS and risk of disability (A) and the subgroup analyses that were performed to investigate the association between PISS and risk of disability (B). PISS = post-ischemic stroke seizures.

Wolters Kluwer

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Early seizures in intracerebral hemorrhage

Incidence, associated factors, and outcome

V. De Herdt, MD, PhD
F. Dumont, MD
H. Hénon, MD, PhD
P. Derambure, MD, PhD
K. Vonck, MD, PhD
D. Leys, MD, PhD
C. Cordonnier, MD, PhD

No Influence on mortality at 7 days and at 6 months

	Mortality at 7 days[μ]		p	Mortality at 6 months[§]		p
	Yes (n=195)	No (n=325)		Yes (n=267)	No (n=241)	
Early seizures	20 (10)	51 (16)	0,092	32 (12)	39 (16)	0,178
Onset seizures	13 (7)	25 (8)	0,754	17 (6)	20 (8)	0,504

Influence of ES on mortality. Results of bivariate analysis.
Data are numbers (%). Analysis using Kaplan-Meier, log rank test. Missing data: μ 2, § 14.

No Influence on functional outcome at 6 months

	mRS ≤2 n=104	mRS>2 n=69	p
Early seizures	16 (15)	10 (14)	0,872
Onset seizures	9 (9)	5 (7)	0,740

Influence of ES on functional outcome at 6 months. Results of bivariate analysis.
Data are numbers (%). Analyses using the χ^2 test. Missing values n=10.

Stroke 2013

Incidence and predictors of late seizures in intracerebral hemorrhages

Rossi C, De Herdt V, Dequatre-Ponchelle N, Hénon H, Leys D, Cordonnier C

- PITCH database
- Inclusion of MRI biomarkers (BMB, GCA and leukoaraiosis)
- Long-term FU

Results (n=325)

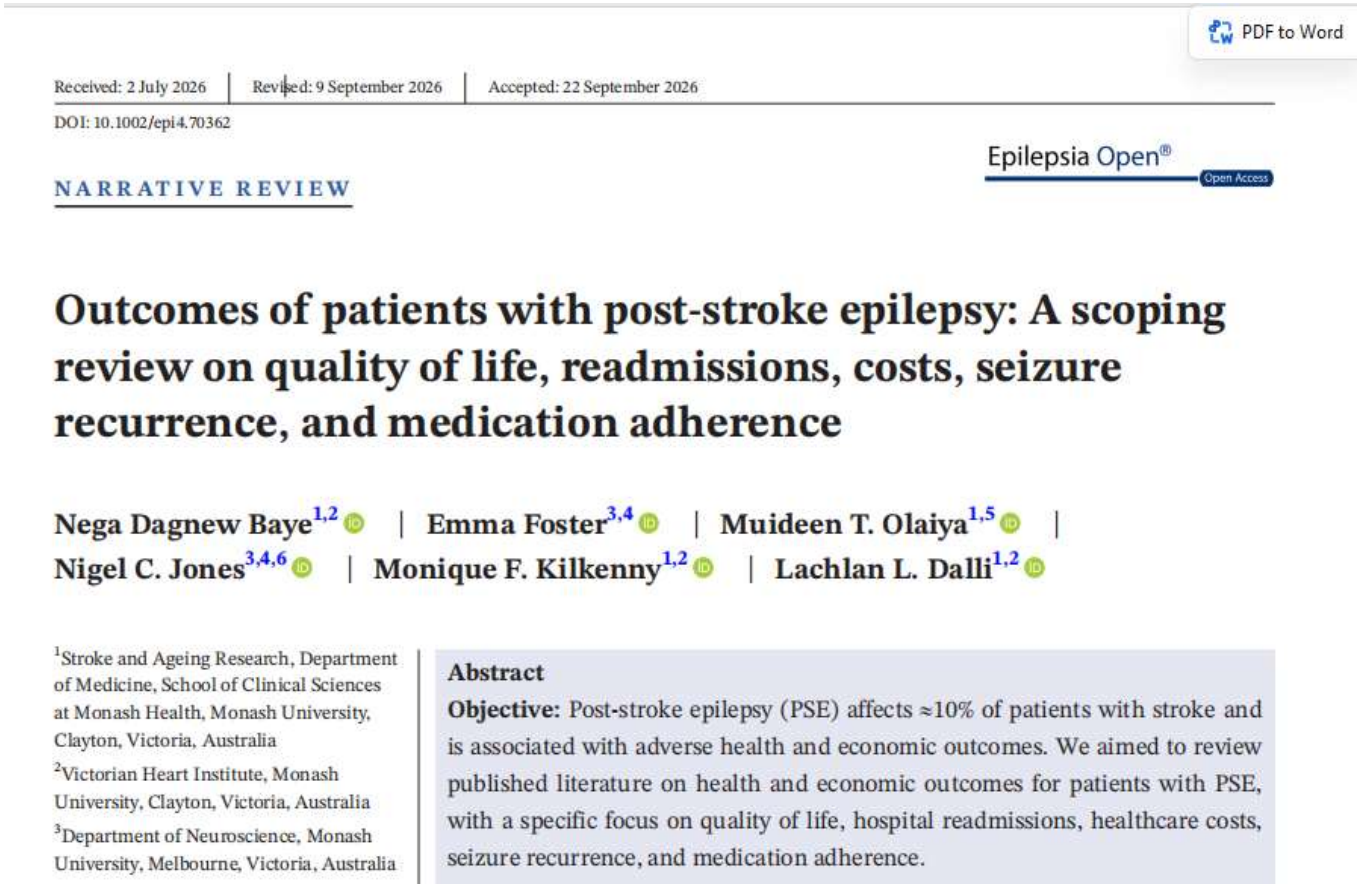
Incidence rate

4 new cases/100 person-years

- Median delay between ICH and LS 9 months (IQR 3-23)

Influence on outcome

- LS were associated with worse functional outcome (mRS≥3) after 3y of FU



PDF to Word

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DOI: 10.1002/epi4.70362

Epilepsia Open® Open Access

NARRATIVE REVIEW

Outcomes of patients with post-stroke epilepsy: A scoping review on quality of life, readmissions, costs, seizure recurrence, and medication adherence

Nega Dagnew Baye[1,2] | Emma Foster[3,4] | Muideen T. Olaiya[1,5] | Nigel C. Jones[3,4,6] | Monique F. Kilkenny[1,2] | Lachlan L. Dalli[1,2]

[1]Stroke and Ageing Research, Department of Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Victoria, Australia

[2]Victorian Heart Institute, Monash University, Clayton, Victoria, Australia

[3]Department of Neuroscience, Monash University, Melbourne, Victoria, Australia

Abstract

Objective: Post-stroke epilepsy (PSE) affects ≈10% of patients with stroke and is associated with adverse health and economic outcomes. We aimed to review published literature on health and economic outcomes for patients with PSE, with a specific focus on quality of life, hospital readmissions, healthcare costs, seizure recurrence, and medication adherence.

PSE was associated with reduced quality of life and greater healthcare costs compared to stroke survivors without epilepsy.
Seizure recurrence was more likely in younger adults. No clear sex differences were noted for any outcomes. Compared to enzyme-inducing antiseizure medications, non-enzyme inducing medications were associated with fewer recurrent seizures and readmissions and less medication discontinuation.

Clinical Neurophysiology 130 (2019) 2282–2286

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Epileptic activity in neurological deterioration after ischemic stroke, a continuous EEG study

P. Scoppettuolo, N. Gaspard, C. Depondt, B. Legros, N. Ligot, G. Naeije *

Department of Neurology, CUB Hôpital Erasme, Université libre de Bruxelles (ULB), Brussels, Belgium

See Editorial, pages 2270–2271

ARTICLE INFO

Article history:
Accepted 15 September 2019
Available online 21 September 2019

HIGHLIGHTS

- Epileptic activities (EA) are found in 44% of acute stroke neurological deterioration.
- Ictal patterns and Periodic discharges (PDs) responds to anti-epileptic drugs.
- Treating ictal patterns and PDs could prevent adverse metabolic consequences of EA.

PREVENTIE EN BEHANDELING

- Does prophylactic treatment prevents seizures and/or influences outcome?
    - up to 30% of physicians report the routine use of prophylactic AED *(Gillmore 2016)*

PREVENTIE EN BEHANDELING

Antiepileptic Drugs to Prevent Seizures After Spontaneous Intracerebral Hemorrhage

A Systematic Review and Meta-Analysis

Federico Angriman ✉, Bharath Kumar Tirupakuzhi Vijayaraghavan, Laura Dragoi, Carmen Lopez Soto, Martin Chapman and Damon C. Scales

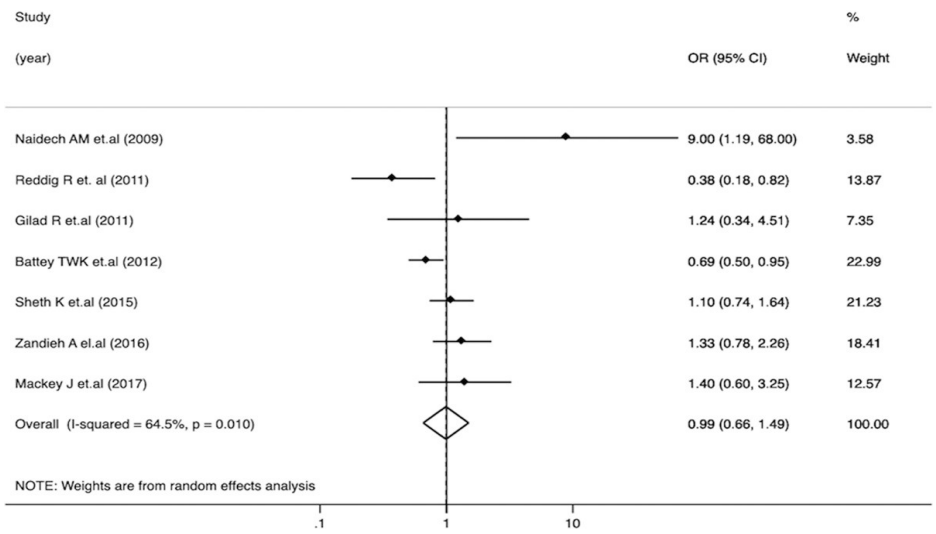
Originally published 2 Apr 2019 | https://doi.org/10.1161/STROKEAHA.118.024380 | Stroke. 2019;50:1095–1099

Table. Characteristics of Included Studies

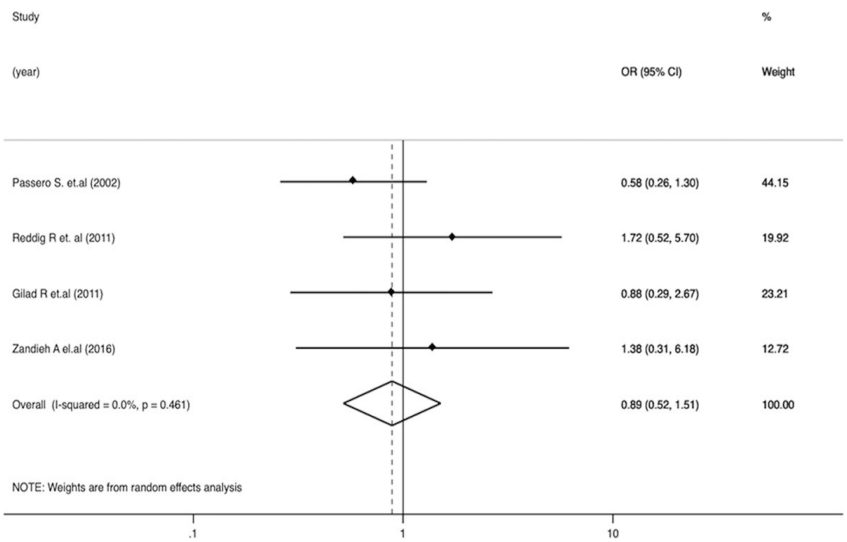
Study (Year)	Year of Publication	Total Sample Size	Design	Main AED Agent	Maximum Follow-Up	Definition of Outcome	Funding
Mackey et al[14]	2017	506	Retrospective cohort	Levetiracetam 97%	Hospital discharge (maximum follow-up 2 mo)	mRS score of ≥4	Non-industry
Sheth et al[15]	2015	744	Retrospective cohort	Levetiracetam 85.8%	90 days	mRS score of ≥4	NINDS
Battey et al[19]	2012	1182	Retrospective cohort	Phenytoin 68%	90 days	mRS score of ≥4	NINDS
Reddig et al[18]	2011	157	Retrospective cohort	Phenytoin 57%	In-hospital (median LOS for AED and non-AED group: 19.1 and 9.2 days)	In-hospital death or hospice discharge	Undisclosed
Zandieh et al[16]	2016	802	Prospective cohort	Phenytoin 58%	90 days	mRS score of ≥4	Undisclosed
Naidech et al[12]	2009	98	Prospective cohort	Phenytoin 100%	90 days	mRS score of ≥4	Departmental funding
Gilad et al[24]	2011	72	Randomized trial	Valproic acid 100%	12 mo	All-cause death	Undisclosed
Passero et al[17]	2002	650	Prospective cohort	Unknown	30 days	Early and late seizures	University of Siena

AED indicates antiepileptic drug; mRS, modified Rankin Scale; and NINDS, National Institute of Neurological Disorders and Stroke.

PREVENTIE EN BEHANDELING



Antiepileptic drug use and poor outcome during long-term follow-up. OR indicates odds ratio.



Antiepileptic drug use and clinical seizures during long-term follow-up. OR indicates odds ratio.

→ Use of profylactic AEDs was not associated with improved outcome or incident seizures

Federico Angriman. Stroke. Antiepileptic Drugs to Prevent Seizures After Spontaneous Intracerebral Hemorrhage, Volume: 50, Issue: 5, Pages: 1095-1099, DOI: (10.1161/STROKEAHA.118.024380)

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PREVENTIE EN BEHANDELING

Journal of Stroke and Cerebrovascular Diseases
Volume 31, Issue 1, January 2022, 106143



Effect of Primary Prophylactic Antiseizure Medication for Seizure Prevention Following Intracerebral Hemorrhage in the ERICH Study

Krupa Savalia MD, PhD [a b], Padmini Sekar MS [c], Charles J Moomaw PhD [c], Sebastian Koch MD [d], Kevin N Sheth MD [e], Daniel Woo MS, MD [c], Douglas Mayson MD [a], ERICH Investigators

- 815 matched pairs of patients treated with prophylactic AEDs
- no significant difference in in-hospital seizure occurence or disability (mRS at 90days)

PREVENTIE EN BEHANDELING

Safety and efficacy of prophylactic levetiracetam for prevention of epileptic seizures in the acute phase of intracerebral haemorrhage (PEACH): a randomised, double-blind, placebo-controlled, phase 3 trial

Laure Peter-Derex, Frédéric Philippeau, Pierre Garnier, Nathalie André-Obadia, Sébastien Boulogne, Hélène Catenoix, Philippe Convers, Laure Mazzola, Michel Gouttard, Maud Esteban, Julia Fontaine, Laura Mechtouff, Elodie Ong, Tae-Hee Cho, Norbert Nighoghossian, Nathalie Perreton, Anne Termoz, Julie Haesebaert, Anne-Marie Schott, Muriel Rabilloud, Christine Pivot, Carole Dhelens, Andrea Filip, Yves Berthezène, Sylvain Rheims, Florent Boutitie, Laurent Derex

Lancet Neurol 2022; 21: 781–91

- Levetiracetam versus placebo
- Used continous EEG monitoring in the acute phase post-ICH

- High incidence of electrographic seizures
- **Number of seizures was significantly lower in the LEV group and duration was shorter**
- No difference on outcome between groups

- underpowered

PREVENTIE EN BEHANDELING

Acute symptomatic seizures

- risk of acute seizure recurrence is 10-20%
- 10-year risk of subsequent US is 30%

(Hesdorffer 2009)

Late unprovoked seizures

Stroke patients with one unprovoked sz have up to 70% risk of sz recurence

(Hauser 1993)

revised ILAE definition of epilepsy

PREVENTIE EN BEHANDELING

- Factors to consider:
  - Elderly population
  - Drug interactions
  - Side effects
  - Seizure control is not always easily obtained, up to 40 % refractory to treatment *Feyissa 2019, Redfors 2020*

→ New generation AEDs are preferred first choice

  - CBZ, VPA, PHT: not first line
    - Low tolerability in elderly
    - Considerable interaction profile
    - E.g. CBZ: decreases DOAC and statin serum concentrations, cause hyponatriemia

PREVENTIE EN BEHANDELING

Lamotrigin

- Moderate antiseizure efficacy
- Well-tolerated
- Mood-stabilising
- Low-interaction profile
- Relatively convenient in use (slow titration)
- CAVE: possible proarrhythmogenic properties (in vitro data)

- randomisation between LTG and CBZ in patients with a first poststroke sz

Gilad 2007

PREVENTIE EN BEHANDELING

Levetiracetam

- High antiseizure efficacy
- Low interaction potential
- IV available
- Well tolerated - irritability and mood swings in <10%

- 2 open label trials with LEV show good efficacy and safety profile in poststroke seizures

  Belcastro 2008; Kutlu 2008

- Multicenter randomized open label study: better efficacy and safety with LEV compared to CBZ, LEV has advantages on cognitive function

  Consoli 2012

PREVENTIE EN BEHANDELING

Lacosamide

- Generally well tolerated
- Good anti-seizure efficacy
- Acceptable interaction profile
- IV available
- CAVE: cardiac conduction disorders

- Lacosamide was well tolerated and effective in pts with epilepsy of cerebrovascular origin
  Rosenow 2020

- IV LCM showed high efficacy and tolerability in NCSE following stroke in pt >70y
  Belcastro 2017

TREATMENT GUIDELINES

ESO guidelines 2017 for the management of post-stroke seizures and epilepsy

→ Only weak recommendations due to very low evidence

- → no (primary) prophylactic AED
- → weak recommendation against AED treatment for ASS
  - → Consider not starting AED treatment

  exception: status epilepticus and recurrent seizures
  - → If started: stop after the acute phase
- → when one late seizure occurs, consider AED treatment, probably lifelong

compounds with a high potential for drug interactions and a high probability of adverse effects on cognition should be avoided

CONCLUSIONS



BESLUIT

- Het onderliggend mechanisme van het ontstaan van poststroke epilepsie is nog onvoldoende gekend.

- Het identificeren van risico groepen voor het ontwikkelen van poststroke epilepsie zou studies met gerichte preventieve behandeling mogelijk kunnen maken.

- Gegevens over het effect van antiepileptica in de acute en chronische fase na een beroerte zou een rationale keuze kunnen ondersteunen.

