Update Management in the Stroke Unit and Early Complications

Symposium Annuel Centre Cérébrovasculaire
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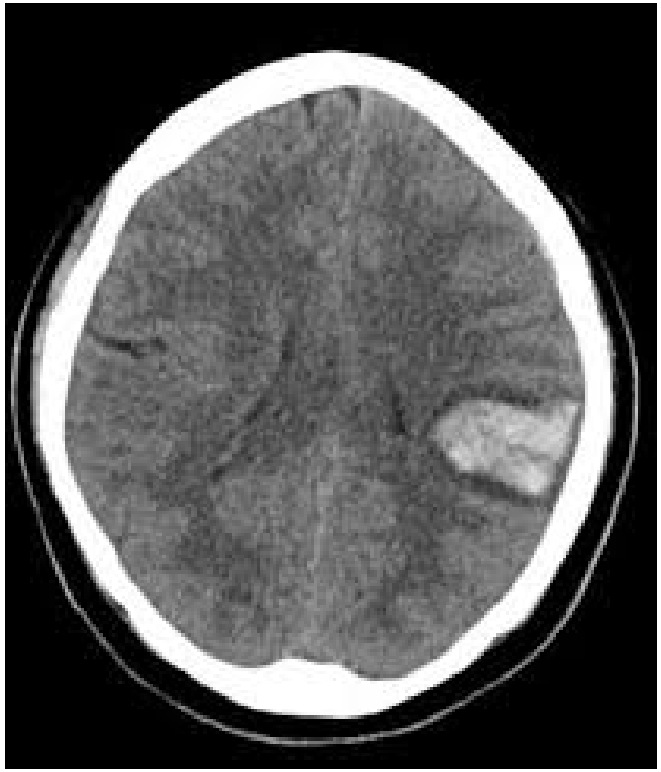
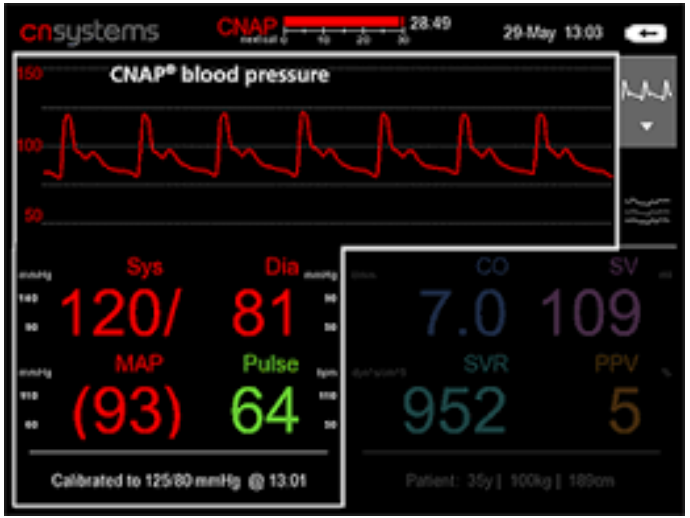
PD Dr. med. Gian Marco De Marchis, MSc
Deputy Head of the Stroke Unit
Neurology Department
University Hospital Basel
Switzerland

Content

1. Blood Pressure Targets in ICH 2019
2. Myocardial Injury in Stroke = Coronary Angiography?
3. Early Recurrent Ischemic Stroke
4. Early Seizure after Stroke: when antiepileptic drugs may be indicated

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CNAP
28:49
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CNAP® blood pressure
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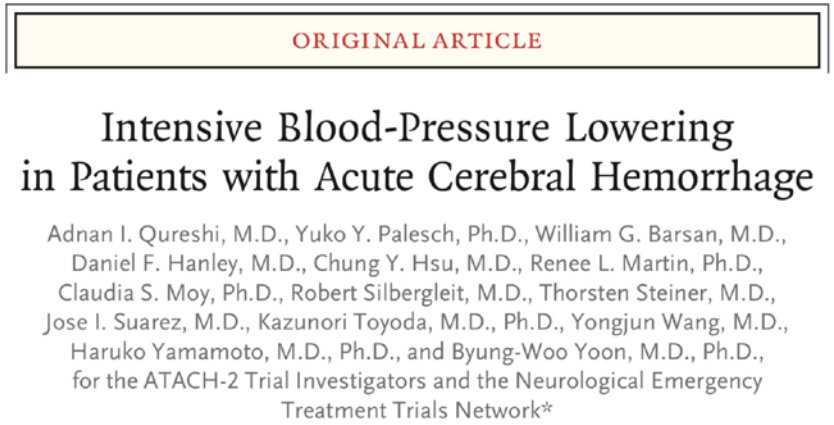
Calibrated to 125/80 mmHg @ 13:01

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 20, 2013 VOL. 368 NO. 25

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jun Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., and John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators*



ORIGINAL ARTICLE

Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D., Daniel F. Hanley, M.D., Chung Y. Hsu, M.D., Renee L. Martin, Ph.D., Claudia S. Moy, Ph.D., Robert Silbergleit, M.D., Thorsten Steiner, M.D., Jose I. Suarez, M.D., Kazunori Toyoda, M.D., Ph.D., Yongjun Wang, M.D., Haruko Yamamoto, M.D., Ph.D., and Byung-Woo Yoon, M.D., Ph.D., for the ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network*

INTERACT–2

- Urapidil (Ebrantil®) = Drug Nr. 1
- Intensive SBP lowering not significant on the primary endpoint (death & disability 3 months after ICH)
- Positive on a series of secondary endpoints

ATACH-2

- Nicardipin used
- Intensive SBP lowering: no benefit
- Excess of renal events

INTERACT: Anderson, C.S., et al. N Engl J Med, 2013.
ATACH-2: Qureshi, A.I., et al. N Engl J Med, 2016. 375(11): p. 1033-1043.

Meta-analysis of both trials on ICH - Blood Pressure Target

Blood pressure control and clinical outcomes in acute intracerebral haemorrhage: a preplanned pooled analysis of individual participant data

Tom J Moullaali, Xia Wang*, Reneé H Martin, Virginia B Shipes, Thompson G Robinson, John Chalmers, Jose I Suarez, Adnan I Qureshi, Yuko Y Palesch, Craig S Anderson*

Moullaali TJ et al, Lancet Neurology 2019; 857-64

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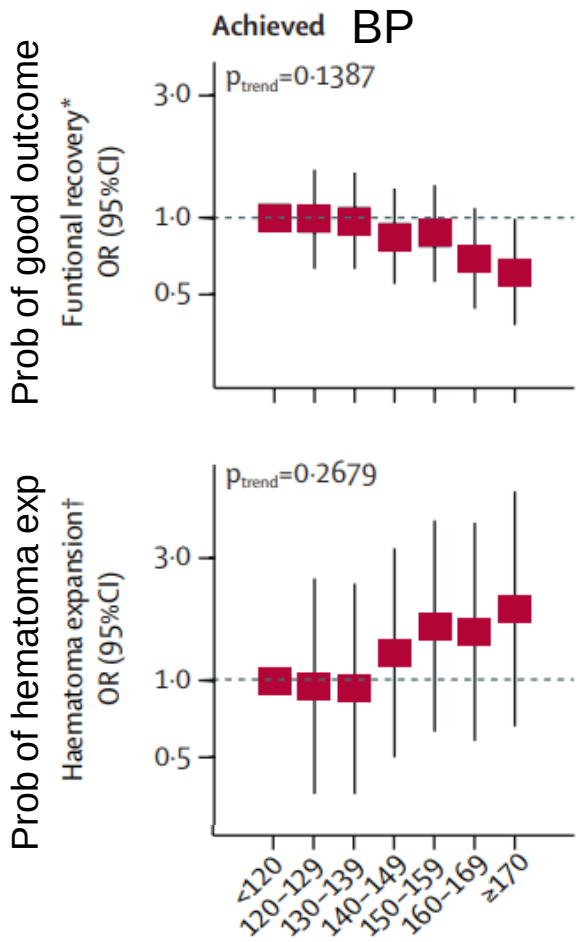
ICH - Blood Pressure Target: What's new?

- Individual patient-level data analysis from INTERACT2 + ATTACH-II (<140mmHg vs. <180mmHg in SBP)
- Endpoint: modified Rankin Scale at 90 days
- 3829 patients, of whom 2/3 Asians
- 3.6 hours median time from symptom onset and randomization
- -29 mmHg: mean magnitude of SBP reduction

Moullaali TJ et al, Lancet Neurology 2019; 857-64



Moullaali TJ et al, Lancet Neurology 2019; 857-64

Intracerebral Hemorrhage – Blood Pressure Targets

↓10% in systolic blood pressure

=

↓ 10% odds of bad outcome

Down to 120-130mmHg

Moullaali TJ et al, Lancet Neurology 2019; 857-64

Safety for renal failure: OK

	Hypotension (n, %)	p value			SAE (
			Cardiac	p value	Renal
Achieved SBP, mmHg					
<120 (n=74)	0 (0·0)	0·0900*	1 (1·4)	0·5204	0 (0·0)
120-130 (n=428)	7 (1·6)		9 (2·1)		4 (0·9)
130–140 (n=854)	3 (0·4)		28 (3·3)		2 (0·2)
140–150 (n=895)	6 (0·7)		21 (2·4)		7 (0·8)
150–160 (n=806)	3 (0·4)		16 (2·0)		4 (0·5)
160–170 (n=474)	5 (1·1)		14 (3·0)		5 (1·1)
≥170 (n=284)	4 (1·4)		10 (3·6)		5 (1·8)

Moullaali TJ et al, Lancet Neurology 2019; 857-64

Magnitude of SBP lowering and functional outcome

Magnitude, baseline - minimum ≤1 hr post-randomisation		
<20 (n=1354)	1·00 (reference)	
20-40 (n=1350)	1·29 (1·06-1·57)	0·0096
40-60 (n=731)	1·23 (0·97-1·55)	0·0853
≥60 (n=381)	0·63 (0·47-0·84)	0·0018

→ “Rapid and large reduction within 1 hour of the initiation of treatment might cause harm”

Moullaali TJ et al, Lancet Neurology 2019; 857-64

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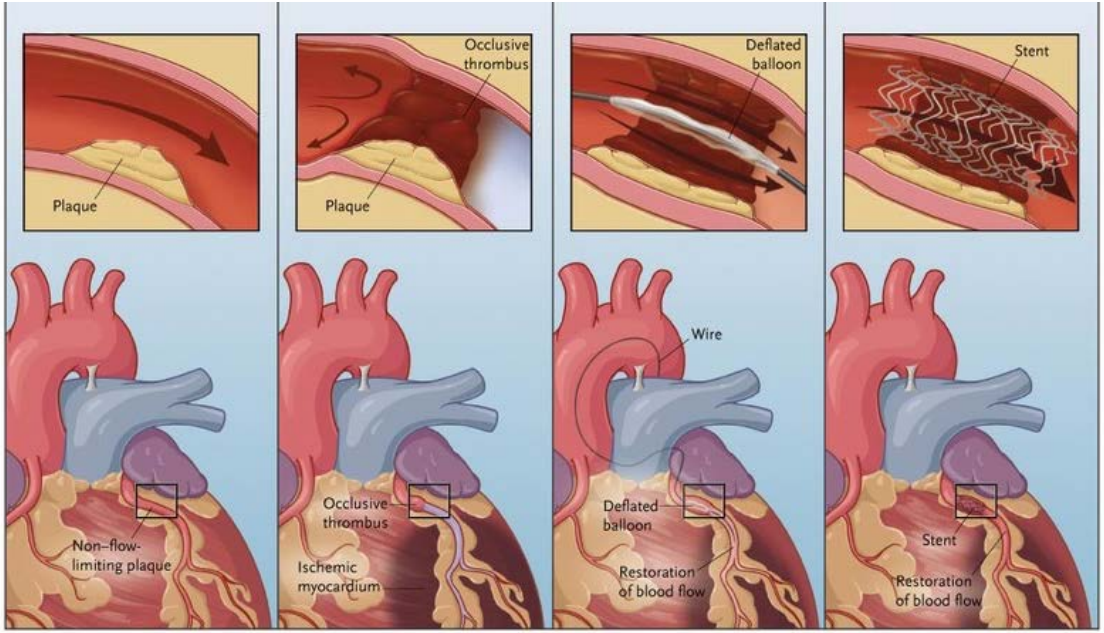
Myocardial Injury after Stroke



Stroke

Coronary Angiographic Findings in Acute Ischemic Stroke Patients With Elevated Cardiac Troponin

The Troponin Elevation in Acute Ischemic Stroke (TRELAS) Study

Hans-Christian Mochmann, MD*; Jan F. Scheitz, MD*; Gabor C. Petzold, MD; Karl Georg Haeusler, MD; Heinrich J. Audebert, MD; Ulrich Laufs, MD; Christine Schneider, MD; Ulf Landmesser, MD; Nikos Werner, MD; Matthias Endres, MD*; Bernhard Witzenbichler, MD*; Christian H. Nolte, MD*; for the TRELAS Study Group

Myocardial Injury after Stroke
TRELAS study

- How often are coronary angiographic findings in acute ischemic stroke patients with elevated cardiac troponin?
- TRELAS Study: Troponin Elevation in Acute Ischemic Stroke
- cTnT assay
  - Reference <14 ng/L
  - For ACS diagnosis >50 ng/L

Mochmann HC et al, Circulation 2016

Myocardial Injury after Stroke : Results
TRELAS study

- 1/7 patients w. an acute ischemic stroke have elevated troponin (cTn>50 ng/L)
- Coronary angiography within 72 hours.
- Compared with patients with Non-ST Elevation ACS (cTnT in the same range!), patients with AIS were:
  - **less likely** to have coronary culprit lesions (24% vs. 79%, P<0.01).
  - **less likely** to undergo revascularizazion (21% vs. 86%, P<0.01)

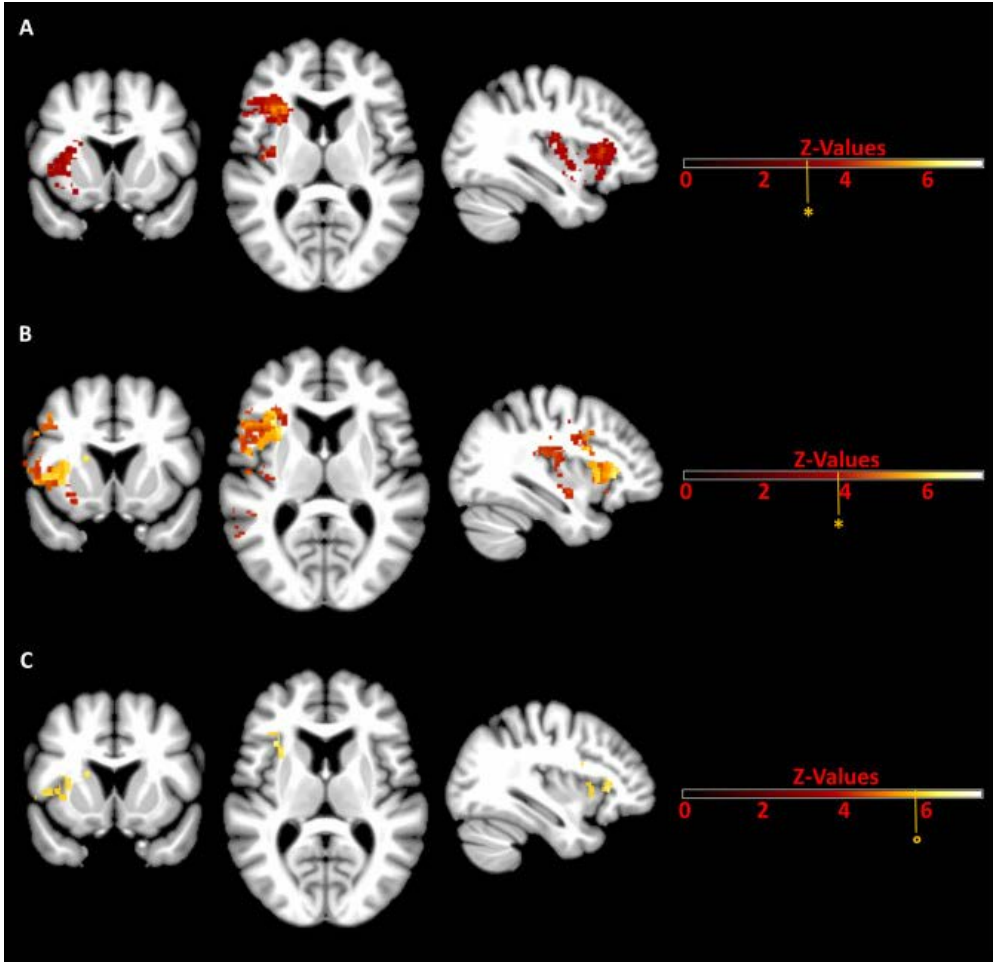
Mochmann HC et al, Circulation 2016

Myocardial Injury after Stroke
TRELAS study

- Although 1 out 7 patients with acute ischemic stroke have elevated cTn, the majority of these patients do not have coincident acute coronary syndrome.
- **Routine invasive diagnostic procedures in AIS patients with elevated cTn do not seem warranted.**
- Echocardiographic wall motion abnormalities (1 pt/7pts)→may warrant cardiac evaluation2

1) Mochmann HC et al, Circulation 2016
2) Yaghi S et al, JNNP 2019

Myocardial Injury after Stroke
Role of right insula



Krause, T., et al. Ann Neurol, 2017. 81(4): p. 502-511.

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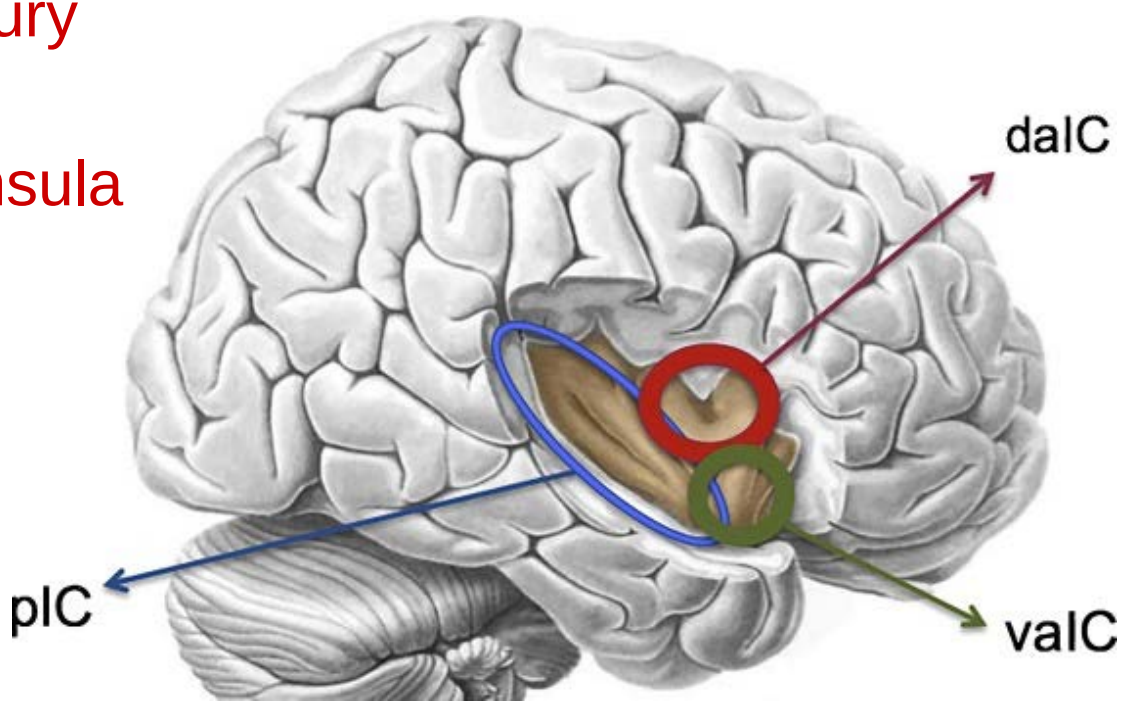
Myocardial Injury after Stroke
Role of right insula



https://doi.org/10.1016/j.dcn.2017.12.006

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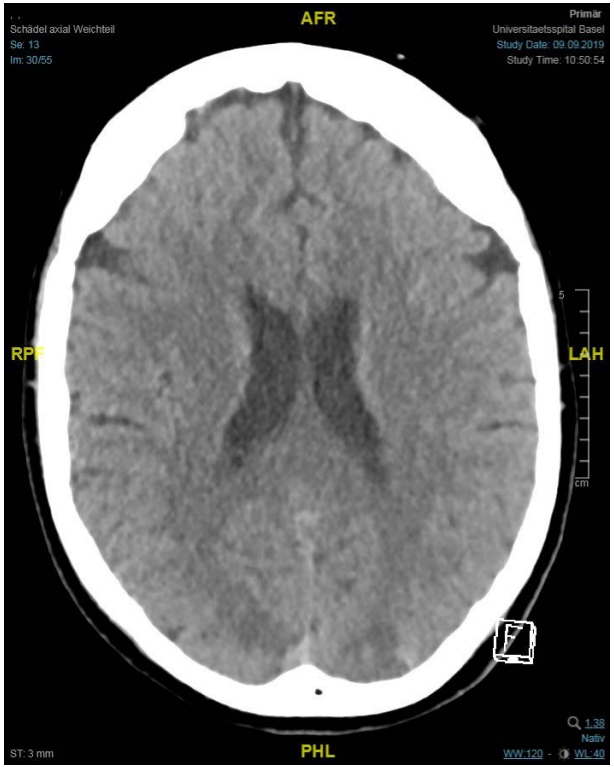
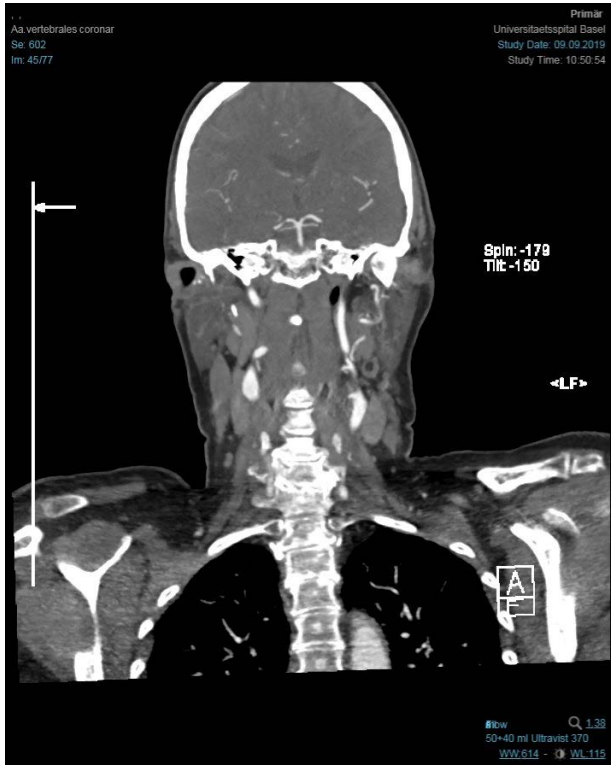
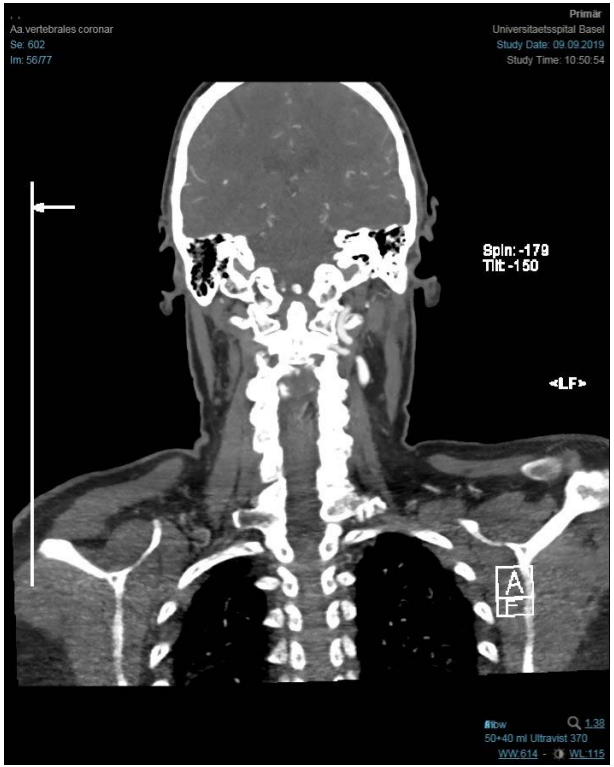
3. **Early Recurrent Ischemic Stroke**
4. Early Seizure after Stroke: when antiepileptic drugs may be indicated

77 y.o. woman with cortical blindness since 12 hours
ECG on admission: atrial fibrillation







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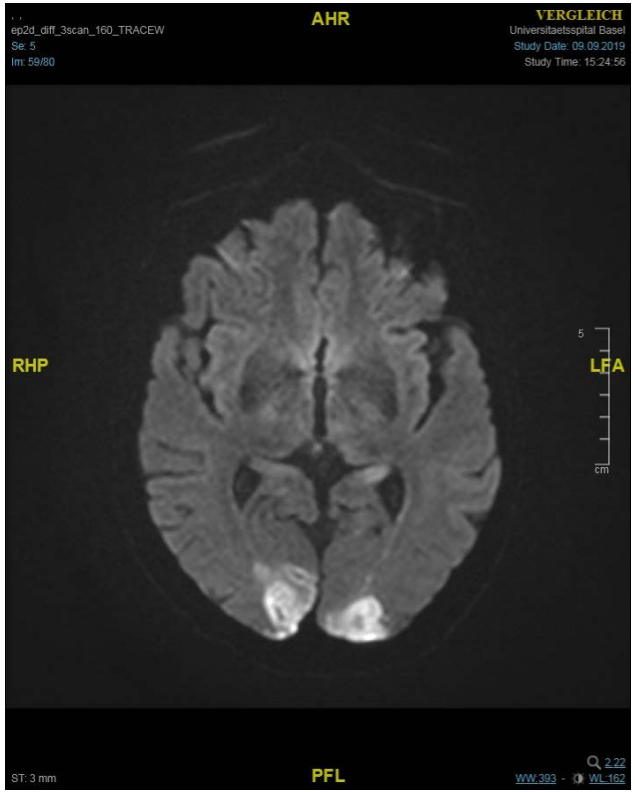
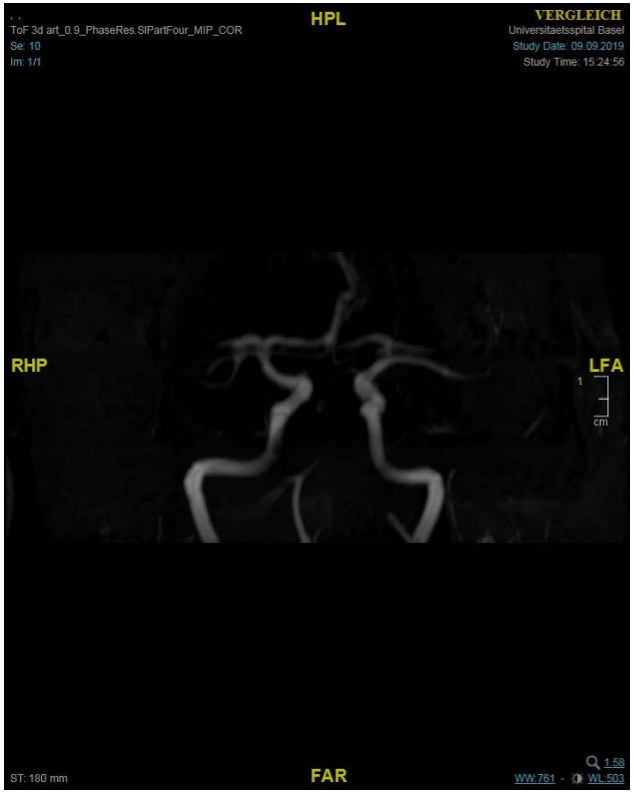
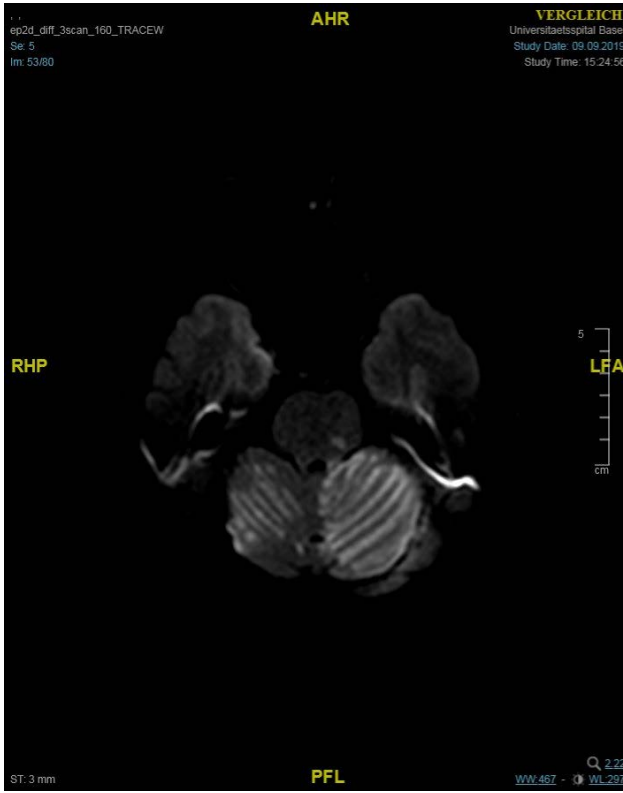
2 hours later: sudden decrease in vigilance



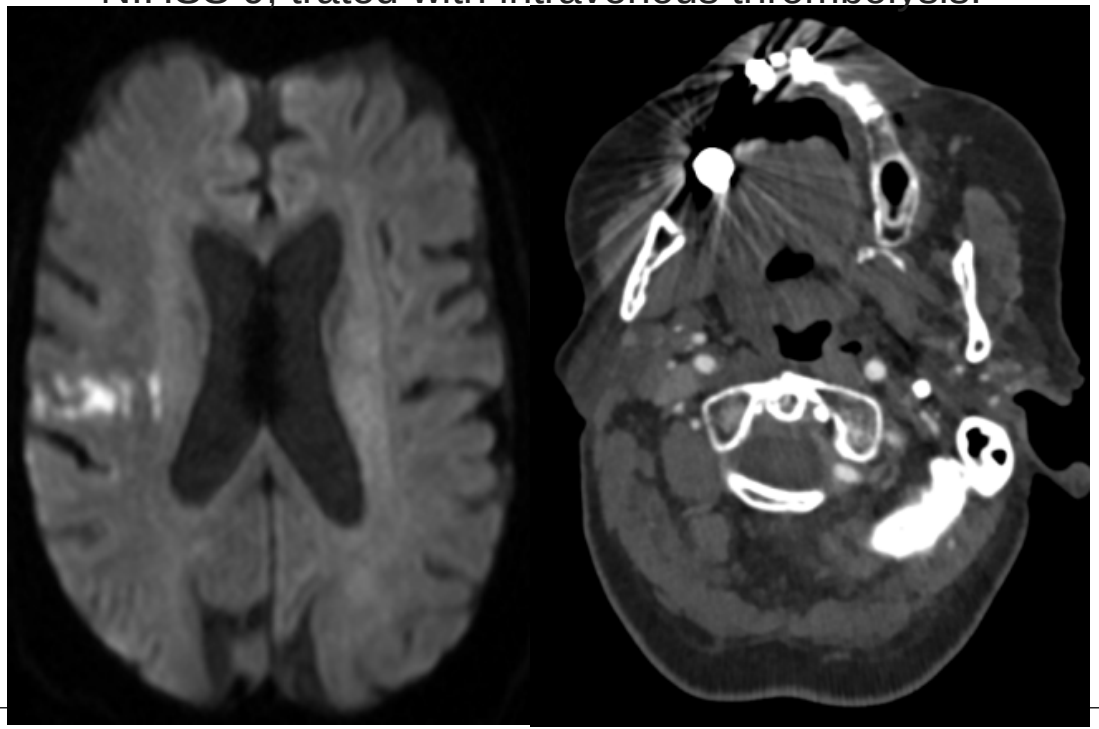




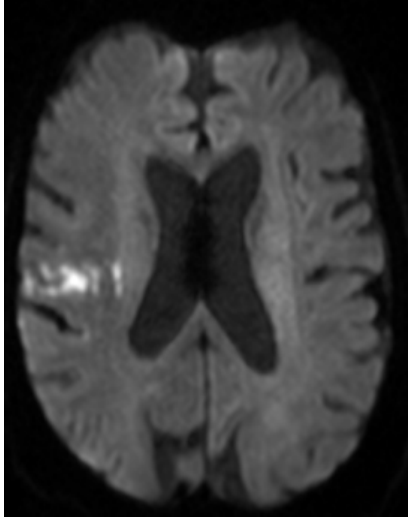
Clinical Vignette #2

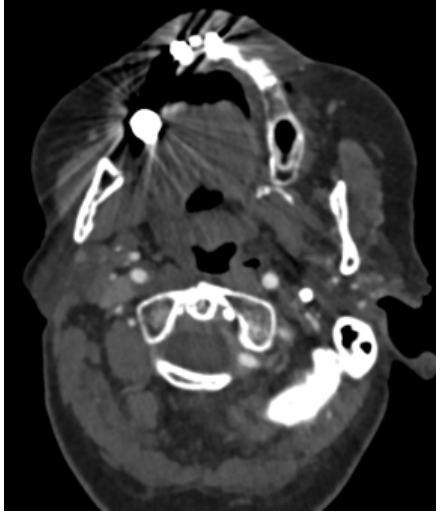
♀, 85 years old, atrial fibrillation under Rivaroxaban 15mg/d (despite normal kidney function...): Acute sensomotor hemisyndrome left with visual hemineglect. NIHSS 9, trated with intravenous thrombolysis.

Admission Day

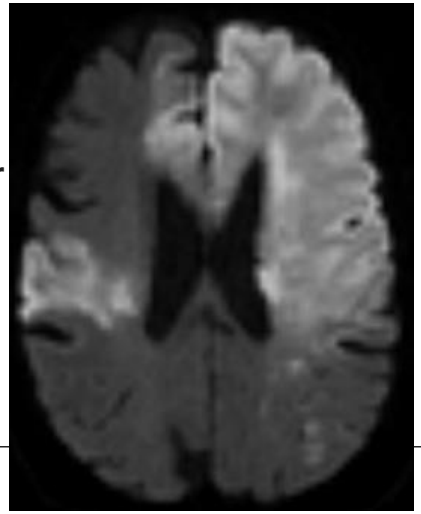


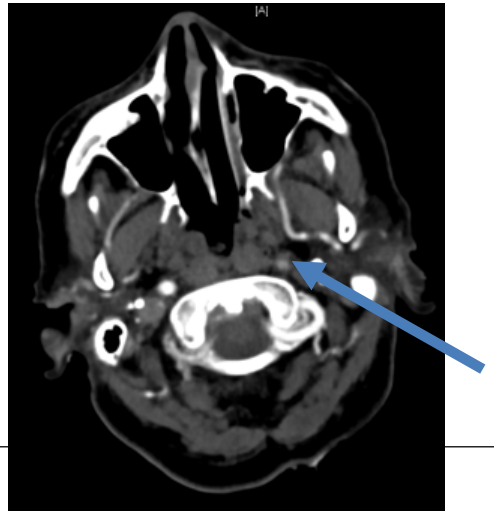
Admission Day





24 hours later





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ARTICLES

Early start of DOAC after ischemic stroke

Risk of intracranial hemorrhage and recurrent events

David J. Seiffge, MD*
Christopher Traenka, MD*
Alexandros Polymeris, MD
Lisa Hert, MD
Nils Peters, MD
Philippe Lyrer, MD
Stefan T. Engelter, MD
Leo H. Bonati, MD‡
Gian Marco De Marchis, MD, MSc‡

Correspondence to Dr. Seiffge: david.seiffge@usb.ch

ABSTRACT

Objective: In patients with recent acute ischemic stroke (AIS) and atrial fibrillation, we assessed the starting time of direct, non-vitamin K antagonist oral anticoagulants (DOACs) for secondary prevention, the rate of intracranial hemorrhage (ICH), and recurrent ischemic events during follow-up.

Methods: We included consecutive patients with nonvalvular atrial fibrillation admitted to our hospital for AIS or TIA (index event) who received secondary prophylaxis with DOAC or vitamin K antagonists (VKAs). Follow-up was at least 3 months. In the primary analysis, we compared rates of ICH and recurrent ischemic events (AIS or TIA) between patients with early (≤7 days since event; $DOAC_{early}$) and those with late (>7 days, $DOAC_{late}$) start of DOAC.

Results: Two hundred four patients were included (median age 79 years, 89% AIS) and total follow-up time was 78.25 patient-years. One hundred fifty-five patients received DOAC with a median delay of 5 days after the index event (interquartile range 3–11) and 49 received VKA. DOAC was started early in 100 patients (65%). We observed one ICH (1.3%/y) and 6 recurrent AIS (7.7%/y). The ICH occurred in a patient taking VKA. No significant difference in the rate of recurrent AIS between $DOAC_{early}$ (5.1%/y) and $DOAC_{late}$ (9.3%/y, $p = 0.53$) was observed.

Conclusions: Even if DOACs are often started early after an index event, the risk of ICH appears to be low. Among all patients receiving anticoagulation, the rate of recurrent events was 6 times higher than the rate of ICH. *Neurology*® 2016;87:1856–1862

Preview – Early vs. Late Start of DOAC

- Individual Patient Data Analysis
- 2550 patients with acute IS linked to atrial fibrillation, in whom a DOAC was started within 30 days
- 30-day risk of recurrent IS (=1.5%) ***7x higher*** than the risk of ICH (=0.2%)

De Marchis GM et al, manuscript in preparation

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2. Myocardial Injury in Stroke = Coronary Angiography?
3. Early Recurrent Ischemic Stroke
4. **Early Seizure after Stroke: when antiepileptic drugs may be indicated**

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Clinical Vignette

- 57 y.o., ischemic stroke in the PCA territory, cortical involvment on DW-MRI, NIHSS 5. Stroke etiology: atrial fibrillation. She suffers a tonic-clonic seizure on day 3.
  - Early seizure (≤7 days): provoked, i.e. not sufficient for the Dx of epilepsy

- Shall we recommend an antiepileptic drug ?
  - If yes, how long?

... like tossing a coin ....

Prediction of late seizures after ischaemic stroke with a novel prognostic model (the SeLECT score): a multivariable prediction model development and validation study

Marian Galovic, Nico Döhler, Barbara Erdélyi-Canavese, Ansgar Felbecker, Philip Siebel, Julian Conrad, Stefan Evers, Michael Winklehner, Tim J von Oertzen, Hans-Peter Haring, Anna Serafini, Giorgia Gregoraci, Mariarosaria Valente, Francesco Janes, Gian Luigi Gigli, Mark R Keezer, John S Duncan, Josemir W Sander, Matthias J Koepp, Barbara Tettenborn

Galovic, M., et al. Lancet Neurol, 2018. 17(2): p. 143-152.

The SeLECT Score

SeLECT Score – Key Numbers

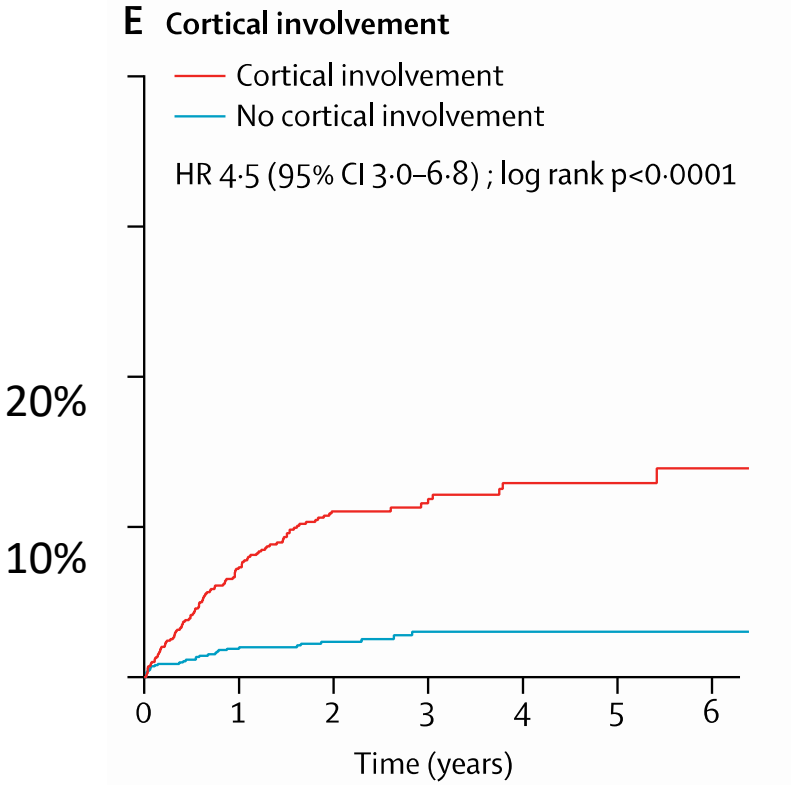
- AED after early seizure: 52%
- Early Seizure (≤ 7 days): 3%
- C–statistics = 0.72
- 1–year risk of seizure: 4%
- →we need ***personalized*** predictions!

The 5 variables associated with time to first late seizure (derivation cohort)

	aHR (95% CI)	p value
Cortical involvement	4·2 (1·9–9·0)	0·0003
Early seizure	4·8 (2·5–9·3)	<0·0001
Stroke severity at admission		
NIHSS ≤3	1 (ref)	..
NIHSS 4–10	1·7 (1·0–3·1)	0·06
NIHSS ≥11	2·7 (1·5–4·9)	0·0008
Territory of MCA involvement	1·8 (0·8–4·1)	0·12
Large-artery atherosclerosis	1·5 (0·9–2·5)	0·15

Galovic, M., et al. Lancet Neurol, 2018. 17(2): p. 143-152.

Seizure after Stroke – SeLECT: Imaging Biomarker



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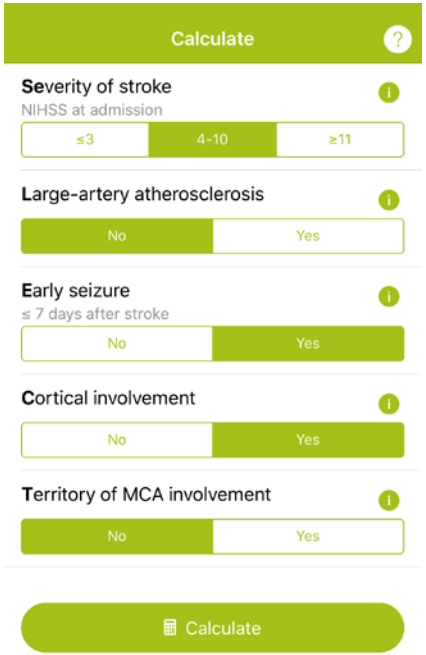
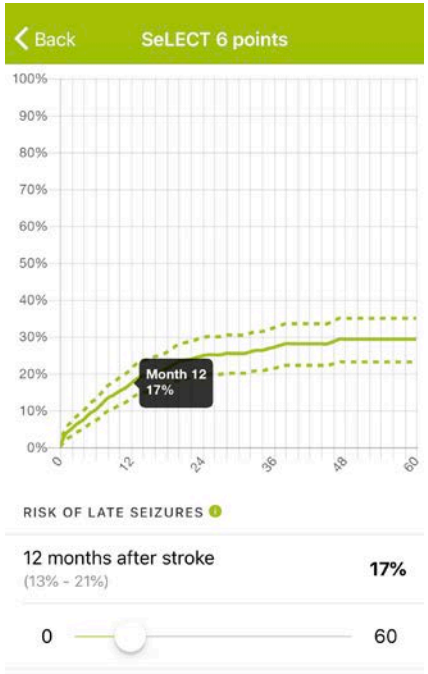
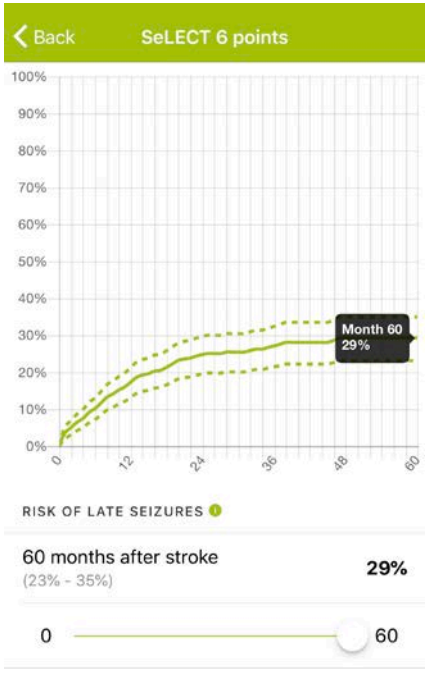
Seizure after Stroke – SeLECT

	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

Galovic, M., et al. Lancet Neurol, 2018. 17(2): p. 143-152.







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  - Early seizure (≤7 days): provoked, i.e. not sufficient for the Dx of epilepsy
- Shall we recommend an antiepileptic drug? **YES**
  - If yes, how long? **Open end**

Content

1. Blood Pressure Targets in ICH 2019
   - Lower is better, avoid sudden BP-drops (>↓60mmHg/hr)
2. Myocardial Injury in Stroke = Coronary Angiography?
   - Not routinely
3. Early Recurrent Ischemic Stroke:
   - More frequent than intracerebral hemorrhage
4. Early Seizure after Stroke: when antiepileptic drugs may be indicated
   - SELECT Score (APP)

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