Update Management in the Stroke Unit and Early Complications

Symposium Annuel Centre Cérébrovasculaire
CHUV, 26.09.2019

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Switzerland
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
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
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

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
Achieved BP

Prob of good outcome

Prob of hematoma exp

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

<table>
<thead>
<tr>
<th>Achieved SBP, mmHg</th>
<th>Hypotension (n, %)</th>
<th>p value</th>
<th>Cardiac</th>
<th>p value</th>
<th>SAE (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120 (n=74)</td>
<td>0 (0.0)</td>
<td>0.0900*</td>
<td>1 (1.4)</td>
<td>0.5204</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>120-130 (n=428)</td>
<td>7 (1.6)</td>
<td></td>
<td>9 (2.1)</td>
<td></td>
<td>4 (0.9)</td>
</tr>
<tr>
<td>130–140 (n=854)</td>
<td>3 (0.4)</td>
<td></td>
<td>28 (3.3)</td>
<td></td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>140–150 (n=895)</td>
<td>6 (0.7)</td>
<td></td>
<td>21 (2.4)</td>
<td></td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>150–160 (n=806)</td>
<td>3 (0.4)</td>
<td></td>
<td>16 (2.0)</td>
<td></td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>160–170 (n=474)</td>
<td>5 (1.1)</td>
<td></td>
<td>14 (3.0)</td>
<td></td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>≥170 (n=284)</td>
<td>4 (1.4)</td>
<td></td>
<td>10 (3.6)</td>
<td></td>
<td>5 (1.8)</td>
</tr>
</tbody>
</table>

Moullaali TJ et al, Lancet Neurology 2019; 857-64
## Magnitude of SBP lowering and functional outcome

**Magnitude, baseline - minimum ≤1 hr post-randomisation**

<table>
<thead>
<tr>
<th>Magnitude</th>
<th>n</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>1354</td>
<td>1.00 (reference)</td>
<td></td>
</tr>
<tr>
<td>20-40</td>
<td>1350</td>
<td>1.29 (1.06-1.57)</td>
<td>0.0096</td>
</tr>
<tr>
<td>40-60</td>
<td>731</td>
<td>1.23 (0.97-1.55)</td>
<td>0.0853</td>
</tr>
<tr>
<td>≥60</td>
<td>381</td>
<td>0.63 (0.47-0.84)</td>
<td>0.0018</td>
</tr>
</tbody>
</table>

→ “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
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
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 revascularization (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 evaluation

1) Mochmann HC et al, Circulation 2016
2) Yaghi S et al, JNPP 2019
Myocardial Injury after Stroke
Role of right insula

Myocardial Injury after Stroke
Role of right insula

Content

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77 y.o. woman with cortical blindness since 12 hours
ECG on admission: atrial fibrillation
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, treated with intravenous thrombolysis.
Early start of DOAC after ischemic stroke
Risk of intracranial hemorrhage and recurrent events

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; DOACearly) and those with late (> 7 days, DOAClate) 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 DOACearly (5.1%/y) and DOAClate (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
Content

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Clinical Vignette

- 57 y.o., ischemic stroke in the PCA territory, cortical involvement 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


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)

<table>
<thead>
<tr>
<th>Variable</th>
<th>aHR (95% CI)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>Cortical involvement</td>
<td>4.2 (1.9–9.0)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Early seizure</td>
<td>4.8 (2.5–9.3)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Stroke severity at admission</td>
<td></td>
<td></td>
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<tr>
<td>NIHSS ≤3</td>
<td>1 (ref)</td>
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<tr>
<td>NIHSS 4–10</td>
<td>1.7 (1.0–3.1)</td>
<td>0.06</td>
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<tr>
<td>NIHSS ≥11</td>
<td>2.7 (1.5–4.9)</td>
<td>0.0008</td>
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<tr>
<td>Territory of MCA involvement</td>
<td>1.8 (0.8–4.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Large-artery atherosclerosis</td>
<td>1.5 (0.9–2.5)</td>
<td>0.15</td>
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Seizure after Stroke – SeLECT: Imaging Biomarker

E  Cortical involvement

- Cortical involvement
- No cortical involvement

HR 4.5 (95% CI 3.0–6.8); log rank p<0.0001

Seizure after Stroke – SeLECT

<table>
<thead>
<tr>
<th>SeLECT score (points)</th>
<th>(Se) Severity of stroke</th>
<th>(L) Large-artery atherosclerosis</th>
<th>(E) Early seizure (≤7 days)</th>
<th>(C) Cortical involvement</th>
<th>(T) Territory of MCA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NIHSS ≤3</td>
<td>No</td>
<td>No</td>
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<td>No</td>
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<td></td>
<td>NIHSS 4–10</td>
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- Shall we recommend an antiepileptic drug? YES
  - If yes, how long? Open end
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)
Merci beaucoup!