Leçons pratiques apprises des registres AVC

Thrombolysis, Thrombectomy

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Symposium Annuel du Centre Cérébrovasculaire CHUV
September 28th 2023
Day of birth: 2002 “A moment of joy, of thankfulness to patients/their next-of-kin/physicians/nurses/scientists/students and scientist for their tireless support, and of hope to continue to improve patient care and outcomes”

Full Name: The Acute STroke Registry and Analysis of Lausanne

Parents:
Papa (idea, promotor): Patrik Michel

Moral, data and scientific support: George Ntaios, Céline Odier, Matthieu Rutgers, Marc Reichhart
Radiologists: Philippe Maeder, Reto Meuli, Max Wintermark
Technical support: Ali Maghraoui, Alexandre Croquelois

Statistics: Mohamed Faouzi

Acronym «ASTRAL» invented by Matthieu Rutgers
(Belgian fellow, later president of Belgian Stroke Council)
Current Recommendations of IVT/MT in Stroke

Thrombolysis (IVT)

- Symptom onset < 4.5h: IVT
- Symptom onset 4.5 – 9h:
  - Core/Perf. mismatch imaging
  - with target mismatch*: IVT
- Wake-up Stroke (> 4.5h):
  - DWI/FLAIR mismatch: IVT
  - Core/Perf. mismatch: IVT

Thrombectomy (MT)

- Symptom onset < 8h: MT
- Symptom onset < 24h
  - Core/Perf. mismatch imaging
  - DAWN-based selection (clinical/radiological)

Notes:
- Symptom onset < 4.5h: IVT
- Symptom onset 4.5 – 9h: Core/Perf. mismatch imaging
  - with target mismatch*: IVT
- Wake-up Stroke (> 4.5h):
  - DWI/FLAIR mismatch: IVT
  - Core/Perf. mismatch: IVT

- Symptom onset < 8h: MT
- Symptom onset < 24h
  - Core/Perf. mismatch imaging
  - DAWN-based selection (clinical/radiological)

- Infarct core**: < 70ml
  - Mismatch Volume*** > 10ml
  - Mismatch Ratio*: > 1.2
  - ADC < 620um2/s or rCBF < 30%
  - Tmax > 6s

Turc et al., ESO/ESMINT Guidelines MT (ESO 2019)
Berge et al., ESO Guidelines IVT (ESO 2021)
Clinical Translational Neurosciences (CTN) June 2021 https://doi.org/10.1177/2514183X21999228
Whom do we NOT thrombolyse/ thrombectomize and WHY?

**ASTRAL 2003 – 2011 (IVT):**
- 2019 non-thrombolysed patients
  - Admission delays
  - Stroke severity (mostly mild)
  - Advanced Age

**ASTRAL 2003 – 2014 (MT):**
- 17.7% eligible within 6 hours
- Younger age, shorter delays, higher stroke severity were associated with EVT eligibility

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Vanacker et al., Stroke 2016
When is the effect of IVT best?

ASTRAL (n=1730)
Best IVT effect in minor/moderate strokes

NIHSS score at admission

NIHSS score at 24 hours

Best IVT effect in patients with arterial occlusions (CTA)

ASTRAL 2003 – 01/2012
N = 2621

- Prestroke disability (mRS=2) n=227
- Last proof of good health > 4 hours n=1234
- NIHSS < 5 n=1027
- ≥ 50% intracranial obstruction in ischemic territory n=182
- Endovascular treatment / bridging n=45

N=742

- No or insufficient quality CTA n=71
- mRS at 3 months not available n=17

No/minimal arterial obstruction in ischemic territory n=272
Arterial occlusion in ischemic territory n=362

IV-thrombolysis
NMO-T, n=138
NMO-NT, n=154

IV-thrombolysis
O-T, n=263
O-NT, n=119

Ntaios et al., J Neurol 2012
Medlin et al., Stroke 2015
Acute stroke and admission glucose
Clinical outcome at 3 months (n = 1446)

Ntaios et al., Stroke 2010
Early vs. late EVT: more or less dangerous?
ASTRAL retrospective analysis of complications

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Early EVT</th>
<th>Late EVT</th>
<th>P (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural complications</td>
<td>16%</td>
<td>16%</td>
<td>0.90</td>
</tr>
<tr>
<td>(Inguinal access, embolization in non-ischemic territory, dissection, arterial perforation/SAH)</td>
<td></td>
<td></td>
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<tr>
<td>Cerebrovascular complications</td>
<td>17%</td>
<td>20%</td>
<td>0.66</td>
</tr>
<tr>
<td>(Parenchymal hemorrhage, ischemic mass effect, 24h reocclusion)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete recanalisation</td>
<td>8%</td>
<td>9%</td>
<td>0.36</td>
</tr>
<tr>
<td>(TICI &lt;2b)</td>
<td></td>
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</table>

→ Similar risks in early and late thrombectomy

Maslias, Stroke 2021; Maslias Am J Neurorad 2023
Does Imaging selection help IVT/ MT decisions?

Added value of CT-Perfusion (n = 1994)

ASTRAL: N = 273 NCCT

N = 411 NCCT + CTA

N = 1310 NCCT + CTA + CTP

More likely to receive MCTI if:
younger, lower baseline NIHSS, less risk factors, lower creatinine

+ adjustment

Outcome with MCT:
Lower 12-month mortality, fewer unknown stroke mechanisms, no added renal risk.

Bill et al., EJN 2017
What else can we learn from acute stroke CT imaging?

Correlation ASPECTS and CTP core (n= 1046)?

Only moderate correlation. better in late-arriving patients (6-24h) and with LVO

Nanoni et al., AJN 2021
ASTRAL (n=857): what factors determine better collaterals (LMCs)?
- Younger age, dyslipidemia, lower creatinine
- Shorter delay from symptom onset to imaging

Nannoni et al., J Neurol 2019
Predicting outcome: The ASTRAL Score

- ASTRAL, DRAGON, SEDAN outperformed physicians
- Competition of 244 stroke experts against ASTRAL Score to predict mRS > 2 at 3 months
- Experts were accurate in 56.8% while ASTRAL was in 86.5%

Our stroke outcome predictions are often wrong!

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Integer-based prognostic ASTRAL score for the calculation of probability of unfavorable outcome in patients with acute ischemic stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covariates</td>
<td>Score points</td>
</tr>
<tr>
<td>Age: for every 5 y</td>
<td>1</td>
</tr>
<tr>
<td>Severity: for every NIHSS point</td>
<td>1</td>
</tr>
<tr>
<td>Time delay from onset to admission &gt;3 h</td>
<td>2</td>
</tr>
<tr>
<td>Range of visual field defect</td>
<td>2</td>
</tr>
<tr>
<td>Acute glucose &gt;7.3 or &lt;3.7 mmol/L</td>
<td>1</td>
</tr>
<tr>
<td>Level of consciousness decreased</td>
<td>3</td>
</tr>
</tbody>
</table>

Do we get better when including imaging?

Ntaios et al., Neurol 2012
Ntaios et al., Europ J Neurol 2016
We need to show that AI can reach good prediction performance

- 5 Stroke experts (4 Swiss, 1 non-Swiss, 2 different Stroke Centers)
  - 60% female
  - 45 years of experience with acute stroke patient treatment

- 1 CNN model
  - 3 years of experience with stroke data

Herzog et al.: MRI-MCA-M1 Competition. The contenders:
50 Patients with MCA-M1 occlusion und MT

Prediction: 3 months outcome (mRS)

Data either: 1) clinical, 2) imaging or 3) combination of both

222 patients with M1-occlusion: 50% mRS >/= 3

Predict BINARY outcome (mRS good = 0-2 or bad 3-6)

Herzog et al., Stroke 2023
Who performed better?

- Large variability in the prediction of experts
- ACC around 0.6 for experts with clinical data
- ACC around 0.5 for experts with imaging data
- ACC around 0.65 for experts using both data types

- Model outperforms experts when imaging is available

There are more important features in the images. *Deep Learning may help to find them.*
Which variables were important for model and clinicians?

ASTRAL: such different stroke outcomes: Is there inequality in treatments?
Inequalities in Thrombolysis and Thrombectomy

Stroke Severity and Outcome: Socioeconomic factors
- Of 1062 patients: 203 private (PI) and 850 basic insurance (BI)
- Mean NIHSS admission was higher for BI and outcome worse

Rey et al., Eur J Neurol 2011
Spaander et al., Stroke 2017 (TRISP)

Stroke Severity and Outcome: Sex differences
- Women tend to have worse outcomes in stroke despite good IVT effect
- N = 3993 (ASTRAL) N = 9495 (TRISP)
- Women are older at the time of stroke
- After adjusting for age:
  women have higher risk of 3m disability

Future Perspectives:
- Why do Swiss Stroke Centers treat 45% women vs. 55% men?
- Sex-dependent socioeconomic factors

Medlin et al., Eur J Neurol 2020

USZ Universitätsspital Zürich

Spaander et al., Stroke 2017 (TRISP)
What about Chameleons and Mimics?

**Stroke-Chameleons:**
*Strokes that go un-noticed*
- Do not receive appropriate treatment «undertreated»

**ASTRAL:** 47 out of 2200 AIS (2.1%)
- Younger age
- Less typical risk factor profile
- More cerebellar stroke

**Stroke-Mimics**
*Non-Strokes that are falsely treated as stroke*
- Do not receive appropriate treatment «overtreated»

**TRISP:** 100 out of 5581 AIS w. IVT (1.8%)
- Younger age, more females
- Less typical risk factor profile
- Low complication rate of IVT

Suspect a stroke, even if age and lack of risk factors don’t let you think of it. If you treat them unnecessarily: the risk of harm is very low.

Richoz et al., Neurology 2015 | Zinkstok et al., Stroke 2013
ASTRAL teaches us about other special situations…

Chelsea Beck, The Atlantic March 9 2017

Correia et al., Int J Stroke 2016

- N = 10, 60% female HICE (Hairdresser-related cerebrov. events)
- No predilection for posterior circulation
- Only 2 dissections (ICA)
- Hypotension during hot air drying?

Strambo et al., J Stroke and Cerebrovasc Dis 2019

- N = 17 SASs (51 controls)
- Median age 51 years
- 65% dissection (3 with minor falls while skiing)
Preconditioning by Preceding Ischemic Events (PIE) ?

Could preceding TIA or minor stroke be like «preconditioning»
What doesn’t kill you makes you stronger?

Wegener et al., Stroke 2004 (n=65)

ASTRAL: n= 3530; 1001 (28%) >/= 1 preceding cerebral ischemic event
PIE independently associated with reduced severity of stroke; but not with better long-term outcome.
Lessons Learned: We need more data from registries like ASTRAL to:

• Generate hypotheses and derive exploratory knowledge about stroke
• Be more representative (less inequalities)
• Collect Big data (Current Pooling Planned)
• Foster collaborations and joint projects
• Plan prospective clinical trials
ASTRAL- Family
The Future is bright!

Intelligent study design, knowledge of what's important, creativity "out-of-the-box" projects, big power due to large patient numbers, excellent analysis methods, critical and smart interpretation of results, inclusive, collaborative work….

Many things not mentioned:
- Stroke in the posterior territory
- Intracranial dissections
- Many more imaging studies
  
Thank you!