New Insights into Subarachnoid Hemorrhage

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• I have no disclosures relevant to this presentation

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What’s New in SAH?

• Review of literature over last 12 months:
  – What we learned…
  – What didn’t work…
  – What looks promising…

• Focus on:
  1. Rebleeding
  2. Delayed Cerebral Ischemia

... and try to keep it clinically relevant
SAH: Background

- **Aneurysmal SAH**
  - Up to 10% die before reaching hospital
  - 1/3 of survivors have ‘favorable’ outcome
    - 65% were impaired in at least one cognitive domain

- **Rebleeding**: major early threat to life

- **Delayed Cerebral Ischemia (DCI)**: peak between days 7-10
  - Accounts for 25% of morbidity & mortality

Rebleeding: New Data

- Retrospective cohort of 1205 ruptured saccular aneurysms
- Looked for predictors of rebleeding within 24 hours of ictus
  - Sudden clinical deterioration + ↑ CT blood

Early Rebleeding

- Rebleeding:
  - ≤24 hrs : 5.8%
  - 24-72 hrs : 1.2%
  - Rebleeding mortality : 57%

- Independent predictors:
  - HTN
  - Larger aneurysms
  - WFNS
  - CSF drainage
  - mFisher

Probably underestimated: Missing hyperacute bleeding?
Rebleeding & mFisher Grade

Occurrence of rebleed in patients with low versus high mFisher grade

Log rank p<0.001

mFisher 3-4

mFisher 0-2

van Donkelaar C et al. Stroke. 2015
What Does This Mean?

- Expedite securing aneurysm with large volume bleed
  …especially good clinical grade & high mFisher score

- How can we reduce risk?
  - BP control ?
  - Antifibrinolytics ?
Treating Acute Hypertension

- Conflicting data on association between hypertension and rebleeding
- Okhuma et al.  SBP >160mmHg

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**TABLE 3. Comparison of Systolic Arterial BP in the Rebleed and the Non-Rebleed Groups With Various Cutoff Points**

<table>
<thead>
<tr>
<th>BP, mm Hg</th>
<th>Rebleed Group (n=37)</th>
<th>Non-Rebleed Group (n=236)</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤120</td>
<td>35</td>
<td>221</td>
<td>&gt;0.9999</td>
<td>1.2 (0.3–5.4)</td>
</tr>
<tr>
<td>≤140</td>
<td>31</td>
<td>168</td>
<td>0.1090</td>
<td>2.1 (0.8–5.2)</td>
</tr>
<tr>
<td>≤160</td>
<td>26</td>
<td>100</td>
<td>0.0016</td>
<td>3.1 (1.5–6.8)</td>
</tr>
<tr>
<td>≤180</td>
<td>20</td>
<td>41</td>
<td>&lt;0.0001</td>
<td>5.6 (2.7–11.6)</td>
</tr>
<tr>
<td>≤200</td>
<td>6</td>
<td>5</td>
<td>0.0012</td>
<td>8.9 (2.6–31.0)</td>
</tr>
</tbody>
</table>

“...blood pressure should be controlled with a titratable agent to balance the risk of stroke, hypertension-related rebleeding, and maintenance of cerebral perfusion pressure...”

..The magnitude of blood pressure control to reduce the risk of rebleeding has not been established, but a decrease in systolic blood pressure to 160 mm Hg is reasonable...”
Antifibrinolytics

- Long term: ↓ rebleed but ↑ DCI
- Hillman et al. (TXA for 72 hours)
  - Decreased rebleeds (10.8% → 2.4%)
  - Slight increase in DCI / complications
  - Inconclusive impact on outcome
- Awaiting ULTRA study
  - 1g IV TXA then infusion 24 hrs post SAH

2- Germans MR et al.. Trials. 2013
Summary for Rebleeding

• Rebleeding probably happens more often than we think and carries high mortality

• SBP <160mm Hg in absence of ++hydrocephalus or signs of high ICP

• Awaiting definitive data on antifibrinolytics
  – ?Consider in big bleeds / high risk bleeds
Delayed Cerebral Ischemia

• Delayed ischemic neurological deterioration following SAH
• Usually attributed to angiographic vasospasm
  – Some DCI patients have no large vessel spasm
  – Multiple vascular territories
  – 20%: infarction in absence of clinical Sx

DCI Surveillance

- Transcranial Doppler
- Measure flow velocities
  - Sensitivity 75-90%
  - Specificity >95%

Problems:
- Not all patients with DCI have large vessel spasm
- Many patients with DCI never reach std mFV thresholds

Cerebral Autoregulation

• Measures ability to adapt to changes in BP

• Autoregulation: $M_x$
  – Correlation between MFV and MAP
  – Close to zero: preserved autoregulation
  – Close to 1: fluctuation in FV related to fluctuations in MAP
Autoregulation to Predict DCI

- Large artery vasospasm by TCD and change in Mx:
  - Sensitivity 67%
  - Specificity 92%

Calviere L et al. NeuroCrit Care. 2015;
EEG to Predict DCI / Vasospasm

- cEEG provides continuous information regarding brain function
- Ischemic EEG changes occur at CBF threshold above infarction
- Most Promising:
  - Alpha/Delta Ratio (ADR)
    - Sensitivity 89%
    - Specificity 84%

• Prospective cohort study of 20 SAH pts
• Continual EEG on all patients
• Evaluated 12 different features

• Results:
  – ADR and alpha variability highest association with DCI
  – Median time from cEEG changes to symptoms: 7 hours (IQR 14-117)
EEG to Predict DCI

• Problem:
  – Not generalizable
  – No readily available ADR ‘monitors’
  – Neuro-ICUs in many jurisdictions not staffed by neurologists

EEG to Predict DCI

No Symptoms

Symptoms / DCI

ADR
Topoplot

Follow-up
CT scan

Rots ML.
NeuroCrit Care. 2015.
EEG to Predict DCI

  - Simplified EEG montage
  - Automated processing / algorithm
  - For sustained decrease in Alpha-band power
    - Sensitivity 89%
    - Specificity 77%
  - …but needs further validation

Gollwitzer S. *Clin Neurophys.* 2015.
CT Perfusion

• Look for perfusion defects from DCI
• Especially useful in comatose patients or when other causes of altered LOC
  – Fever
  – Metabolic confounders

• Sensitivity = 84%
• Specificity = 79%

Decision Analysis: CTP

Effectiveness of Diagnostic Strategies in Suspected Delayed Cerebral Ischemia
A Decision Analysis

Sapna Rawal, MD; Carolina Barnett, MD; Ava John-Baptiste, PhD; Hla-Hla Thein, MD, MPH, PhD; Timo Krings, MD, PhD; Gabriel J.E. Rinkel, MD, FRCPE

…in patients who on the basis of clinical assessment are suspected of having DCI, testing for the presence of angiographic vasospasm or perfusion deficits before initiating hypertensive treatment … did not add value to the management of these patients…

Rawal et al. Stroke. 2015;
Take Home Messages

- Rebleeding more common than thought
- Antifibrinolytics if used in high risk / big bleeds should be short trials
- Moderate BP control SBP<160 mmHg
- Better DCI surveillance technology is coming… soon… hopefully
- Start treating DCI when you clinically suspect it - forgo initial imaging
Questions?

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