Intracerebral Hemorrhage: Update on Contemporary Management

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Disclosures

• I (…unfortunately…) have no financial disclosures relevant to this talk
Overview

• Changing epidemiology
• Importance of critical care
• Interventions:
  – Correct Coagulopathy
  – Blood Pressure Management
  – Surgical Management
Intracerebral Hemorrhage (ICH)

- Incidence:
  - 10% of all strokes in North America
  - Historically more in East Asia
  - Yearly incidence of ~20 /100,000 persons

- Accounts for disproportionate amount of morbidity and mortality from stroke

- Incidence expected to increase in coming decades
Etiology of ICH

- **Hypertension**
- **Amyloid angiopathy**
- **Vascular malformation**
- **Coagulopathy**
- **Hemorrhagic infarction**
- **Venous thrombosis**
- **Septic emboli**
- **Vasculitis**
Changing Epidemiology

• HTN now accounts for only half of ICH
  – Better control of BP
  – Fewer ICH in young
  – More ICH in elderly

• Expect increasing burden
  – Aging population
  – Increased anticoagulation

Lovelock CE et al. Lancet Neurol. 2007 6(6):487.93
Importance of Critical Care

• Deterioration is common after ICH:
  – 20% will ↓ GCS ≥ 2 points before arrival
  – 15% will ↓ GCS ≥ 2 points during first hour in hospital

• Majority survive but lose function

*Early & aggressive ICU care is important*
Targets for Intervention:

- Decrease the size of the hematoma
- Prevent secondary injury
  - Seizures, hypotension, hypoglycemia
  - Complications of critical illness
Early Hematoma Growth

- Hematoma growth is common and occurs over hours
- Prospective study of 103 ICH \(^1\)
  - 38% had hematoma growth (>33% ↑) within 24 hrs
  - 26% within 1 hr
- Strongest predictor of mortality

Potential Interventions

1. Correct Coagulopathy
2. Optimize Blood Pressure
3. Surgical Management
Reversal of Coagulopathy

• Must be done *quickly* and *durably*
  – ICH mortality increases if delayed until patient unconscious
  – SDH mortality increases 30% $\rightarrow$ 80% if surgery delayed $> 4$ h

• Hematoma expansion first 24 hrs
  – $> 50\%$ of warfarin-related ICH
  – 38% non-warfarin spontaneous ICH
Reversal of Oral Anticoagulants

- Frozen Plasma
  - Thawing and infusion times (SLOW!)
- Volume overload
- TRALI

### Predicted Fresh Frozen Plasma Transfusion Volume, Dose, and Expected Factor Increment for Various Target INR Values

<table>
<thead>
<tr>
<th>Initial INR</th>
<th>Volume (L)</th>
<th>Dose (mL/kg)</th>
<th>Factor (%)</th>
<th>Volume (L)</th>
<th>Dose (mL/kg)</th>
<th>Factor (%)</th>
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<th>Dose (mL/kg)</th>
<th>Factor (%)</th>
<th>Volume (L)</th>
<th>Dose (mL/kg)</th>
<th>Factor (%)</th>
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<tbody>
<tr>
<td>6.0</td>
<td>4.5</td>
<td>64</td>
<td>45</td>
<td>3.5</td>
<td>50</td>
<td>35</td>
<td>2.5</td>
<td>36</td>
<td>25</td>
<td>1.5</td>
<td>21</td>
<td>15</td>
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<tr>
<td>5.0</td>
<td>4.3</td>
<td>61</td>
<td>43</td>
<td>2.9</td>
<td>43</td>
<td>30</td>
<td>2.3</td>
<td>32</td>
<td>23</td>
<td>1.0</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>4.0</td>
<td>4.0</td>
<td>57</td>
<td>40</td>
<td>2.5</td>
<td>36</td>
<td>25</td>
<td>2.0</td>
<td>29</td>
<td>20</td>
<td>0.5</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>3.0</td>
<td>3.5</td>
<td>50</td>
<td>35</td>
<td>2.0</td>
<td>29</td>
<td>20</td>
<td>1.5</td>
<td>21</td>
<td>15</td>
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</tr>
<tr>
<td>2.0</td>
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<td>36</td>
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<td>1.5</td>
<td>21</td>
<td>15</td>
<td>0.5</td>
<td>7</td>
<td>5</td>
<td>—</td>
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<td>—</td>
</tr>
</tbody>
</table>

INR, international normalized ratio.

Reversal of Oral Anticoagulants

- Prothrombin Complex Concentrate
  - 25x the vit-K dependent factors of FFP
  - 1000 units (2 vials) for 70kg pt with INR 3.0
  - 2000 units (4 vials) for INR 3.0-5.0
  - 3000 units (6 vials) for INR >5.0

- Give with Vitamin K!
Dabigatran

- Potent direct thrombin inhibitor
- Renal clearance
- No reversal agent
- FFP transfusions do **not** work
- Try:
  - FEIBA or PCC
  - Dialysis
Blood Pressure Management

- Balance of reducing further hemorrhage and achieving cerebral perfusion

- Ischemic penumbra not thought to be major cause of perihematomal injury
  - ?metabolic penumbra

  - If no increased ICP
    - SBP<160 mmHg and MAP<110 mmHg
Blood Pressure Management

• How LOW can we go?

• Preliminary Studies:
  – INTERACT (SBP <140 vs <180)
  – ATACH (SBP 110-140, 140-170, 170-200)

• All appeared safe with suggestion of benefits
ADAPT Study

The Intracerebral Hemorrhage Acutely Decreasing Arterial Pressure Trial

Kenneth S. Butcher, MD, PhD; Thomas Jeerkathil, MSc, MD; Michael Hill, MD, MSc; Andrew M. Demchuk, MD; Dariush Dowlatshahi MD, PhD; Shelagh B. Coutts, MD; Bronwen Gould, BSc; Rebecca McCourt; Negar Asdaghi, MD, MSc; J. Max Findlay, MD, PhD; Derek Emery, MD, MSc; Ashfaq Shuaib, MD; for the ICH ADAPT Investigators

- 75 patients
- Acute ICH
- SBP > 150 mmHg
- Randomized
  - SBP < 180 mmHg
  - SBP < 150 mmHg
- CT perfusion imaging at 2 hours

ADAPT Results

- All patients had focal decreases in CBF
  - Perihematoma relative CBF = 87%

<table>
<thead>
<tr>
<th>Relative to Contralateral Region</th>
<th>&lt;150mmHg Target</th>
<th>&lt;180mmHg Target</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>rCBF</td>
<td>0.86 ± 0.12</td>
<td>0.89 ± 0.09</td>
<td>0.18</td>
</tr>
<tr>
<td>rCBV</td>
<td>0.90 ± 0.14</td>
<td>0.91 ± 0.15</td>
<td>0.73</td>
</tr>
<tr>
<td>Absolute CBF ml/100g/min</td>
<td>38.88 ± 12.98</td>
<td>38.56 ± 10.81</td>
<td>0.91</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative to Ipsilateral Hemisphere</th>
<th>&lt;150mmHg Target</th>
<th>&lt;180mmHg Target</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>rCBF</td>
<td>0.95 ± 0.05</td>
<td>0.99 ± 0.05</td>
<td>0.001</td>
</tr>
<tr>
<td>rCBV</td>
<td>0.98 ± 0.05</td>
<td>0.99 ± 0.06</td>
<td>0.59</td>
</tr>
</tbody>
</table>
Perfusion Maps

Patient 1
<150 mmHg

Patient 2
<180 mmHg
**INTERACT 2**

- RCT from Australia / NZ / China
- Spontaneous ICH within 6 hours with SBP 150-200
- SBP <180 vs. SBP <140
- Any antihypertensive agents
- 2839 patients
INTERACT 2 – Primary Outcome

Odds ratio 0.87 (95%CI 0.75 to 1.01)  P=0.06

Adapted from: Prof. Craig Anderson European Stroke Conference 2013
INTERACT 2 – Functional Status

Odds ratio 0.87 (95% CI 0.77 to 1.00); P=0.04

Adapted from: Prof. Craig Anderson European Stroke Conference 2013
## INTERACT 2 – Safety

<table>
<thead>
<tr>
<th>Serious Adverse Event</th>
<th>Intensive (N=1399)</th>
<th>Standard (N=1430)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct effects of primary ICH event</td>
<td>47 (3.4)</td>
<td>55 (3.8)</td>
<td>0.49</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>37 (2.6)</td>
<td>41 (2.9)</td>
<td>0.72</td>
</tr>
<tr>
<td>ICH</td>
<td>4 (0.3)</td>
<td>4 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Ischemic/undifferentiated stroke</td>
<td>8 (0.6)</td>
<td>8 (0.6)</td>
<td></td>
</tr>
<tr>
<td>Acute MI/coronary event/other</td>
<td>5 (0.4)</td>
<td>5 (0.3)</td>
<td></td>
</tr>
<tr>
<td>Other vascular disease</td>
<td>13 (0.9)</td>
<td>14 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Other cardiac disease</td>
<td>9 (0.6)</td>
<td>12 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Non-cardiovascular disease</td>
<td>160 (11.4)</td>
<td>152 (10.6)</td>
<td>0.49</td>
</tr>
<tr>
<td>Renal failure</td>
<td>5 (0.4)</td>
<td>7 (0.5)</td>
<td></td>
</tr>
<tr>
<td>Severe hypotension</td>
<td>7 (0.5)</td>
<td>8 (0.6)</td>
<td>0.83</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>48 (3.4)</td>
<td>53 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Sepsis (includes other infections)</td>
<td>21 (1.5)</td>
<td>20 (1.4)</td>
<td></td>
</tr>
<tr>
<td>Non-vascular medical /injury</td>
<td>132 (9.4)</td>
<td>125 (8.7)</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: Prof. Craig Anderson European Stroke Conference 2013
No Decrease in Hematoma Growth

- No reduction in hematoma growth
  - 4.5% relative reduction in growth (NS)
  - Proportion of patients with substantial hematoma growth
    26.1% vs. 26.4% (p=0.9)
- Many patients started treatment at 3-4 hours post symptom onset
INTERACT 2 – BP Control

The diagram shows the mean systolic blood pressure (mm Hg) over time for two groups: Guideline group (purple dashed line) and Intensive group (red line). The target level is indicated by the horizontal line at 139 mm Hg. The graph illustrates a significant decrease in blood pressure over time, with statistical significance noted (P < 0.0001 for times >15 min).
INTERACT 2

- Early intensive BP lowering treatment
  - Appears safe - no increase in death or adverse events
  - May be effective
    - Benefit may be smaller than anticipated
    - Functional status and HRQOL

- Awaiting ATACH 2
Surgical Management

- **STICH**
  - 1033 ICH patients
  - Surgical evacuation w/in 72hrs
  - NO difference in outcomes by Glasgow Outcome Scale
  - Deep ICH did worse with surgery

? Superficial ICH may benefit

Mendelow AD. *Lancet*. 2005
STICH 2

- 601 patients with acute superficial ICH
- Randomized to early surgery or initial conservative treatment
- Results:
  - 21% crossover
  - Low mortality in conservative treatment
  - No significant differences
    - Death 18% vs. 24%; p=0.09
    - Favorable outcome 41% vs. 38%; p=0.367
  - Poor prognosis (GCS 9-12) did better with early surgery

ICH Score: Clinical Grading Scale

• Important for:
  – Informed decision making
  – Communication
  – Consistency
  – Identifying patients for research studies

• Similar to:
  – GCS in traumatic brain injury
  – World Federation of Neurological Surgeons in subarachnoid hemorrhage
ICH Score

Predicted Mortality

ICH Score 0: 0%
ICH Score 1: 13%
ICH Score 2: 26%
ICH Score 3: 72%
ICH Score 4: 97%
ICH Score 5: 100%
ICH Score 6: 100%

Hematoma Volume

ICH >= 30 cm³: 1 point
ICH < 30 cm³: 0 points

Intraventricular Hemorrhage

Yes: 1 point
No: 0 points

Infratentorial ICH

Yes: 1 point
No: 0 points

Age

Age >= 80 years: 1 point
Age < 80 years: 0 points

Glasgow Coma Scale

<table>
<thead>
<tr>
<th>GCS 3-4:</th>
<th>2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS 5-12:</td>
<td>1 point</td>
</tr>
<tr>
<td>GCS 13-15:</td>
<td>0 points</td>
</tr>
</tbody>
</table>

ICH Score

Predicts 30 day Mortality  1 Yr Functional Outcome

Take Home Messages

• ICH is a bad disease but aggressive care can make a difference

• PCC and Vitamin K
  – Give enough and give quickly!

• Blood Pressure Targets
  – Consider lower target SBP 140 mmHg

• The ICH score provides prognostic information and consistency
Questions?

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