INTRACEREBRAL HEMORRHAGE

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Introduction

ICH
- Presentation
- Outcome
- Neuroimaging
- Complications
  - Hematoma expansion
  - Management of ICP/edema
    - IVH: EVD, IT-tPA
    - Osmotic therapy
- Surgery
- Reversal of coagulopathy
ICH: presentation

- Rapid onset
- Headache frequent
- Decreased LOC common
- Often accompanied by early rigidity in paretic limb
ICH: presentation

50% CAA
50% Other

Majority HTN

Qureshi; N Engl J Med 2001;344:1450-60
ICH: presentation

PRIMARY ICH

Hypertensive
Cerebral amyloid angiopathy
Cryptogenic

SECONDARY ICH

Trauma
AVM
Intracranial aneurysm
Coagulopathy
Hemorrhagic conversion of ischemic stroke
Dural sinus thrombosis
Intracranial tumor
Cavernous malformation
Dural AV fistula
Venous angioma
Cocaine use
CNS vasculitis

Mayer; Lancet Neurol 2005; 4(10): 662-72
ICH: identifying blood

<table>
<thead>
<tr>
<th>Evolution of blood</th>
<th>Oxygenated Hb</th>
<th>Deoxy Hb</th>
<th>Intracellular Meth-Hb</th>
<th>Extracellular Meth-Hb</th>
<th>Hemosiderin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperacute (&lt;12 h)</td>
<td>Hyperdense</td>
<td>Isointense or mildly hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hypointense rim</td>
</tr>
<tr>
<td>Acute (12 h to 2 d)</td>
<td>Hyperdense</td>
<td>Isointense or hypointense</td>
<td>Hypointense</td>
<td>Hypointense</td>
<td>Hypointense rim that gradually progresses to centre</td>
</tr>
<tr>
<td>Early subacute (2–7 d)</td>
<td>Hyperdense</td>
<td>Hyperintense</td>
<td>Hypointense</td>
<td>Hypointense</td>
<td>Hypointense</td>
</tr>
<tr>
<td>Late subacute (8 d to 1 m)</td>
<td>Isodense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hyperintense</td>
<td>Hypointense</td>
</tr>
<tr>
<td>Chronic (&gt;1 m)</td>
<td>Hypodense</td>
<td>Isointense or hypointense</td>
<td>Hypointense</td>
<td>Hypointense</td>
<td>Slit-like hyperintense or isointense core that is surrounded by a hypointense rim</td>
</tr>
</tbody>
</table>

_Table: Appearance of blood on CT and MRI by stage_
# ICH: utility of diagnostic tests

<table>
<thead>
<tr>
<th>CT</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid initial eval</td>
<td>Cerebral amyloid angiopathy</td>
</tr>
<tr>
<td>Location of bleed</td>
<td>AVM</td>
</tr>
<tr>
<td>HCP/IVH</td>
<td>Hemorrhagic transformation</td>
</tr>
<tr>
<td><strong>CTA/CTP</strong></td>
<td>Tumor</td>
</tr>
<tr>
<td>Spot sign</td>
<td>Sinus thrombosis</td>
</tr>
<tr>
<td>AVM</td>
<td>Cavernous malformation</td>
</tr>
<tr>
<td>Tumor</td>
<td><strong>CATH ANGIO</strong></td>
</tr>
<tr>
<td>Sinus thrombosis</td>
<td>DAVF</td>
</tr>
<tr>
<td></td>
<td>Small AVM</td>
</tr>
<tr>
<td></td>
<td>Small aneurysm</td>
</tr>
</tbody>
</table>

Kidwell; Lancet Neurol 2008;7:256-67
ICH: diagnostic utility of MRI

ACUTE HEMATOMA

HEMATOMA OLD BLEED MICROBLEED

LOBAR MICROBLEEDS
ICH: diagnostic utility of angiography

- Cerebral angiography
  - To make the etiological diagnosis in cases of:
    - Aneurysms
    - AVM’s
    - Vasculitis
    - Dural AV fistula
  - In young patients (< 45 y/o) w/o risk factors for ICH, the yield of angiography can reach 48% in putaminal, thalamic and posterior fossa ICH.
  - In young patients with lobar ICH, yield of angiography can reach 65%.
  - The yield of cerebral angiography in primary IVH is high regardless the age of the patient (63 to 67%).
  - In patients > 45 y/o and hypertension with ICH in “classic” locations, the yield of angiography is 0.
ICH: Hematoma expansion

38% > 33% growth over 24h
73% some growth over 24h
Independent predictor of bad outcome

Davis; Neurology 2006; 66(8): 1175-81
ICH: Hematoma expansion

CTA spot sign

<table>
<thead>
<tr>
<th>Spot Sign Characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of spot signs</td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>1</td>
</tr>
<tr>
<td>≥3</td>
<td>2</td>
</tr>
<tr>
<td>Maximum axial dimension</td>
<td></td>
</tr>
<tr>
<td>1–4 mm</td>
<td>0</td>
</tr>
<tr>
<td>≥5 mm</td>
<td>1</td>
</tr>
<tr>
<td>Maximum attenuation</td>
<td></td>
</tr>
<tr>
<td>120–179 HU</td>
<td>0</td>
</tr>
<tr>
<td>≥180 HU</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Accuracy Parameter</th>
<th>Hematoma Expansion* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>88 (75–94)</td>
</tr>
<tr>
<td>Specificity</td>
<td>93 (89–95)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>69 (57–79)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>98 (95–99)</td>
</tr>
<tr>
<td>Positive likelihood ratio</td>
<td>12.4 (8.2–18.7)</td>
</tr>
<tr>
<td>Negative likelihood ratio</td>
<td>0.13 (0.07–0.27)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>92</td>
</tr>
</tbody>
</table>

*Hematoma expansion defined as >30% or >6 mL increase from the initial ICH volume.
ICH: diagnosis summary

* Diagnostic approach…

- CT/CTA on presentation
  - Noncon CT:
    - bleed versus stroke
    - Hydrocephalus/herniation/IVH
  - CTA
    - spot sign
    - identifies most vascular etiologies
- MRI/MRA/post-con MRI if diagnosis uncertain
  - Best for: amyloid, tumor, stroke with transformation
- Cath angio in young patients, those without risk factors, lobar hemorrhage through middle age, primary IVH, and combined ICH + SAH or SDH
ICH: Hematoma expansion

**FAST**  Placebo vs. rFVIIa (20µg/kg or 80µg/kg) within 4hr  
\[n=841\]

<table>
<thead>
<tr>
<th>Variable</th>
<th>rFVIIa, 20 µg/kg (N=276)</th>
<th>rFVIIa, 80 µg/kg (N=297)</th>
<th>Placebo (N=268)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume of intracerebral hemorrhage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline — ml</td>
<td>24±26</td>
<td>23±26</td>
<td>22±24</td>
</tr>
<tr>
<td>Estimated milliliters of increase from baseline — mean (95% CI)</td>
<td>4.9 (2.9 to 7.0)</td>
<td>3.7 (1.7 to 5.7)</td>
<td>7.5 (5.4 to 9.6)</td>
</tr>
<tr>
<td><strong>P value vs. placebo</strong></td>
<td>0.08</td>
<td>0.009</td>
<td>—</td>
</tr>
</tbody>
</table>

**Hematoma expansion**  
No difference in good outcome, bad outcome or death

**Functional outcome**  
ICH volume<60mL; Age≤70; ≤2.5h to treatment; IVH<5mL

ICH: Hematoma expansion

**INTERACT**

SBP < 180 vs. SBP < 140 within 6 hr

*n* = 404

<table>
<thead>
<tr>
<th>Hematoma expansion (&gt;33% or 12.5cc)</th>
<th>40/172 (23%)</th>
<th>26/174 (15%)</th>
<th>36% (0 to 59%)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Functional outcome</th>
<th>&lt;140</th>
<th>&lt;180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or dependency†</td>
<td>95 (49%)</td>
<td>95 (48%)</td>
</tr>
<tr>
<td>Death</td>
<td>25 (13%)</td>
<td>21 (10%)</td>
</tr>
<tr>
<td>Dependency</td>
<td>70 (36%)</td>
<td>74 (37%)</td>
</tr>
<tr>
<td>Median mRS score‡</td>
<td>2 (1-4)</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>Median NIHSS score§</td>
<td>2 (1-5)</td>
<td>2 (1-5)</td>
</tr>
</tbody>
</table>

ICH: Osmotic Therapy

**HS or mannitol**  ICP; Tissue shifts; Cerebral edema

23.4% HS for transtentorial herniation  
\[ n=68 \text{ (29 ICH)} \]

ICP reduced from 23 to 14 at 1h

Transtentorial herniation reversed in 75%

Koenig; Neurology 2008;70:1023-1029
ICH: IT tPA

CLEAR-IVH Resolution of IVH in ICH and primary IVH

1g bid or tid IT until clot 80% gone or 12 doses given

n=52

Expected mortality 50-80%; observed mortality 8%
Symptomatic rebleed 8%
Bacterial ventriculitis 0%

Morgan; Acta Neurochir Suppl 2008; 105:217-20
ICH: Surgery

**STICH** RCT of early (24h) vs. conservative treatment for ICH
Equipoise: eligible if unclear which treatment better
27% crossover to surgery
n=1033
ICH: Surgery

Meta-analysis of RCTs for treatment of lobar hemorrhage

<table>
<thead>
<tr>
<th></th>
<th>Surgery n/N</th>
<th>Control n/N</th>
<th>Peto OR 95% CI</th>
<th>Peto OR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auer (1989)</td>
<td>11/24</td>
<td>15/21</td>
<td></td>
<td>0.36 (0.11-1.16)</td>
</tr>
<tr>
<td>Teernstra (2001)</td>
<td>12/16</td>
<td>7/9</td>
<td></td>
<td>0.86 (0.13-5.63)</td>
</tr>
<tr>
<td>Mendelow (2004)</td>
<td>56/110</td>
<td>71/113</td>
<td></td>
<td>0.62 (0.36-1.05)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>150</td>
<td>143</td>
<td></td>
<td>0.58 (0.36-0.92)</td>
</tr>
</tbody>
</table>

Total events: 79 (surgery), 93 (control)
Test for heterogeneity: $\chi^2 = 0.87$, df=2 (p=0.65), $I^2=0$
Test for overall effect: $Z=2.30$ (p=0.02)
ICH: Surgery

MINIMALLY INVASIVE CRANIOPUNCTURE

RCT minimally invasive surgery for basal ganglia ICH

Cannula placed inside clot and 10,000U-50,000U urokinase injected followed by aspiration (dose based on hematoma volume)

n=465

90d outcome

<table>
<thead>
<tr>
<th></th>
<th>+tx</th>
<th>-tx</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRS 0-2</td>
<td>63%</td>
<td>41%</td>
</tr>
<tr>
<td>Dead</td>
<td>8%</td>
<td>9%</td>
</tr>
</tbody>
</table>

http://www.strokecenter.org/trials/TrialDetail.aspx?tid=690
ICH: Reversal of coagulopathy

Warfarin-associated cerebral hemorrhage

- Associated with larger hematoma and higher frequency of hematoma expansion

- 3x higher mortality than ICH without coagulopathy

- Vitamin K + FFP 4-6U (up to 15cc/kg) + rFVIIa 40-80µg/kg expect INR to rebound

- PCC (prothrombin complex concentrates) 30U/kg or FIX complex may be available soon
**ICH: Reversal of coagulopathy**

Table 1  Selected studies of time to correction of INR using fresh frozen plasma and vitamin K in warfarin associated intracranial hemorrhage

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Time to correct INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brody et al. [21]</td>
<td>12</td>
<td>32 h (median)</td>
</tr>
<tr>
<td>Lee et al. [23]</td>
<td>45</td>
<td>30 h (median)</td>
</tr>
<tr>
<td>Goldstein et al. [22]</td>
<td>69</td>
<td>1/6 of high INRs not corrected at 24 h</td>
</tr>
<tr>
<td>Huttner et al. [18]</td>
<td>18</td>
<td>INR corrected within 2 h in 39%</td>
</tr>
<tr>
<td>Siddiq et al. [24]</td>
<td>9</td>
<td>Only 33% reached target INR in 3 h. Mean time to reach target INR $&gt;8$ h</td>
</tr>
</tbody>
</table>
ICH: impact of neurocritical care

Crit Care Med 2004 Vol. 32, No. 11

Journal of Neurosurgical Anesthesiology
Vol. 13, No. 2, pp. 83–92
ICH: treatment summary

* Treatment approach…

- Stabilize
  - Reverse herniation
  - EVD
- Stop hematoma expansion
  - BP control
  - FVIIa probably doesn’t help in unselected patients
    - FVIIa or PCC or FIX complex in warfarin-associated
    - platelets/DDAVP if platelet problem
- Surgery
  - Posterior fossa
  - Selected lobar
  - ?minimally invasive
- Good comprehensive critical care matters
ICH: Cliff Notes

- ABC’s
- Diagnosis of bleed: CT (with CTA and post-con CT)
- Reversal of coagulopathy:
  - factor VII, FFP, vit K
  - Platelet/ddavp
- Management of ICP/edema/mass effect
  - Acute:
    - pCO2 30-35; mannitol 1-2g/kg or 3% 250cc; or 23.4% 50cc
    - EVD
    - Hemicraniectomy
    - Clot evacuation
      - Cerebellar: >30cc, acute hydrocephalus, posterior pontine compression
      - Lobar hemorrhage < 1cm from surface
  - Subacute:
    - hypertonic saline gtt or scheduled mannitol
    - IT tPA
Blood pressure management: SBP < 140 (or 160)
- Nicardipine 0-15mg/hr or labetalol gtt
- Early aggressive transition to orals: ACE-I, Beta blocker, calcium channel blocker, ARB, clonidine, minoxidil

Critical care: euglycemia, euthermia, DVT prophylaxis @ 48hr if no EVD

Diagnosis of etiology
- MRI with GRE during admission and repeat at 6wks if still unclear etiology
- EKG, echo to look for LVH; UTOX
- DSA if lobar + few RF’s, primary IVH, young; may need to repeat at 2-6 wks