ICH Management

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Pillar 2 Chair APSS (Acute Care and Emergency Services)
Heart and Stroke Foundation Chair in Stroke Research
Professor
University of Calgary
Epidemiology of ICH

Comprises 15% 10% of stroke in the NA/Europe
30% in the developing world

6 month prognosis
40% dead
40% disabled and dependent
20% independent
Mechanism - ICH

Hypertension
   Treat the hypertension – may NOT be necessary acutely

Drugs (eg. PPA, cocaine)
   Lifestyle changes

Amyloid angiopathy
   No treatment

AVM
   Surgery, radiosurgery, embolization
Investigation of ICH for underlying etiology

Noncontrast CT
+/- CT-angiography

MRI with GRE/SWI

Conventional angiography

Hypertension
Amyloid angiopathy
Arteriovenous malformation
Intracranial aneurysm
Cavernous angioma
Dural venous sinus thrombosis
Intracranial neoplasm
Coagulopathy
Cocaine or alcohol use
Hypertensive Arteriolosclerosis Pattern

Gradient echo imaging
Acute CT for prognosis:
ICH Volume Measurement, IVH, location

\[ \frac{A \times B \times C}{2} \quad A \text{ – greatest width} \quad B \text{ – greatest length} \quad C \text{ – depth} \]
Prognosis

- Size and location of hematoma
- Presence of IVH
- Clinical deficit
“Early Hematoma Growth”

2.5 hours after symptom onset

6.5 hours after onset, with enlargement of the hematoma due to ongoing bleeding
Dripping with each passing minute
Case 1

- 48 year old hypertensive
- Onset 2 hours ago
- Right hemiplegia
- Basal ganglia ICH 20 ml
- Systolic BP 210
Early Achievement of Blood Pressure Lowering and Hematoma Growth in Acute Intracerebral Hemorrhage: Stroke Acute Management with Urgent Risk-Factor Assessment and Improvement-Intracerebral Hemorrhage Study

Yoshitaka Yamaguchi, Masatoshi Koga, Shoichiro Sato, Hiroshi Yamagami, Kenichi Todo, Satoshi Okuda, Yasushi Okada, Kazumi Kimura, Yoshiaki Shioi, Kenji Kamiyama, Ryo Itabashi, Yasuhiro Hasegawa, Kazuomi Kario, Kyohel Fujita, Yasuyuki Kuma, Teppel Kamimura, Daisuke Ando, Toshiiro Ide, Takeshi Yoshimoto, Masayuki Shiozawa, Soichiro Matsubara, Soheil Yoshimura, Kazuyuki Nagatsuka, Kazunori Toyoda, for the SAMURAI Study Investigators

$p$ for trend $= 0.023$

% Incidence of participants with hematoma growth $>6$ mL

- 4.2% at 15 min
- 13.2% at 38 min
- 19.6% at 53 min
- 18.9% at 80 min
- 18.9% at 483 min

Quartiles of time from imaging to target SBP $<160$ mm Hg

$1st$ (n = 48), $2nd$ (n = 53), $3rd$ (n = 56), $4th$ (n = 54)
Primary outcome: death or major disability — no./total no. (%)

Secondary outcomes
Score on the modified Rankin scale — no./total no. (%)

<150 systolic BP lowering marginal in ICH

The NEW ENGLAND JOURNAL of MEDICINE

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jur Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., and John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators

This article was published on May 29, 2013, at NEJM.org.
Degree and Timing of Intensive Blood Pressure Lowering on Hematoma Growth in Intracerebral Hemorrhage

Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial-2 Results

Cheryl Carcel, MD; Xia Wang, MMed; Shoichiro Sato, MD, PhD; Christian Stupf, MD; Else Charlotte Sandset, MD, PhD; Candice Delcourt, MD; Hisatomi Arima, MD; Thompson Robinson, MD; Pablo Lavados, MD, MPH; John Chalmers, MD, PhD; Craig S. Anderson, MD, PhD; on behalf of the INTERACT2 Investigators

![Graph A](image1.png)

**A**

<table>
<thead>
<tr>
<th>Time to target SBP &lt;140mmHg (hour)</th>
<th>Absolute growth (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1</td>
<td>2</td>
</tr>
<tr>
<td>1-6</td>
<td>4</td>
</tr>
<tr>
<td>≥6</td>
<td>6</td>
</tr>
</tbody>
</table>

**P trend 0.029**

![Graph B](image2.png)

**B**

<table>
<thead>
<tr>
<th>Number of times of achieving target SBP &lt;140 mmHg within 24 hours of ICH</th>
<th>Absolute growth (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>2</td>
</tr>
<tr>
<td>3-4</td>
<td>4</td>
</tr>
<tr>
<td>5-8</td>
<td>6</td>
</tr>
</tbody>
</table>

**P trend 0.018**
More aggressive BP lowering in ICH no effect

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment (N = 500)</th>
<th>Standard Treatment (N = 500)</th>
<th>Unadjusted Analysis</th>
<th>Adjusted Analysis†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Relative Risk or Beta Estimate (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Primary outcome: death or disability</td>
<td>186/481 (38.7)</td>
<td>181/480 (37.7)</td>
<td>1.02 (0.83 to 1.25)</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Figure 1. Mean Hourly Minimum Systolic Blood Pressure during the First 24 Hours after Randomization, According to Treatment Group. The dashed vertical line indicates 2 hours, and 1 bars 95% confidence intervals.
Compared with group 1, persons with lower target SBP (group 2) had a higher rate of cerebral ischemia (32% vs 16%; \( p = 0.047 \)), acute neurologic deterioration (19% vs 5%; \( p = 0.022 \)), and length of stay in the neurointensive care unit (median 3 days, IQR 2–4; \( p = 0.014 \)) and hospital (median 7 days, IQR 5–15 vs median 6 days, IQR 3–10; \( p = 0.02 \)) (table 2). The
ICH Management

Table 4  Standardized ICH checklists

- Prehospital care
  - ABCs
  - Determine time of onset and circumstances
  - Perform prehospital stroke screen
  - Brief medical history and medication list
  - Triage to stroke center
  - Perform prehospital notification of pending stroke patient

BP <140 mmHg systolic but not much lower best

Comprehensive stroke centre if severe deficits?
Case 2

- 78 year old afib on warfarin
- Subcortical ICH 6 ml
- Systolic BP 140
Anticoagulation major risk for hematoma expansion

<table>
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<th>Comparison</th>
<th>Four predictors</th>
<th>Four predictors with the addition of CT angiography spot sign</th>
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<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Time from symptom onset to baseline imaging, h*</td>
<td>5.1 vs 1.5</td>
<td>0.50 (0.36–0.70)</td>
</tr>
<tr>
<td>Intracranial haemorrhage volume on baseline imaging, ml*</td>
<td>33 vs 6</td>
<td>7.18 (4.46–11.56)</td>
</tr>
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<td>Antiplatelet therapy at symptom onset</td>
<td>Yes vs no</td>
<td>1.68 (1.06–2.66)</td>
</tr>
<tr>
<td>Anticoagulant therapy at symptom onset</td>
<td>Yes vs no</td>
<td>3.48 (1.96–6.16)</td>
</tr>
<tr>
<td>CT angiography spot sign</td>
<td>Present vs absent</td>
<td>4.46 (2.95–6.75)</td>
</tr>
</tbody>
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Data were calculated on 837 patients from six cohorts (appendix). *Odds ratios for time from symptom onset to baseline imaging and intracranial haemorrhage volume on baseline imaging are for upper quartile vs lower quartile.

Table 3: Multivariable models of predictors of intracerebral haemorrhage growth >6 mL in patients with assessment of CT angiography spot sign, data on antiplatelet therapy, and data on anticoagulant therapy use at symptom onset
Prothrombin Complex Concentrate for Coagulopathy

Clotting factors: FII, VII, IX and X, protein C and S.
**Summary**

**Background** Haematoma expansion is a major cause of mortality in intracranial haemorrhage related to vitamin K.

<table>
<thead>
<tr>
<th></th>
<th>Fresh frozen plasma (n=23)</th>
<th>Prothrombin complex concentrate (n=27)</th>
<th>Treatment effect (95% CI)</th>
<th>p value</th>
</tr>
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<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>INR ≤1.2 within 3 h</td>
<td>2 (9%)</td>
<td>18 (67%)</td>
<td>OR 30.6 (4.7 to 197.9)*</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Secondary clinical outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths at day 90</td>
<td>8 (35%)</td>
<td>5 (19%)</td>
<td>No proportional hazard assumed</td>
<td>0.14†</td>
</tr>
<tr>
<td>Imaging data at 3 h</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Haematoma expansion (mL)</td>
<td>23.7 (28.4)</td>
<td>9.7 (20.9)</td>
<td>16.9 (2.5 to 31.3)‡</td>
<td>0.023</td>
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Prothrombin Complex Concentrate for Coagulopathy

1000U INR 1.5-3
2000U if INR 3-5
3000U if INR >5
Praxbind bolus for Dabigatran associated ICH
ICH Management

ED care

☐ Emergent triage to high acuity area

☐ Perform primary assessment—ABCs

☐ Perform focused neurologic exam (GCS, NIHSS)

☐ Obtain baseline screening labs (CBC and platelet count, electrolytes, INR and PTT, glucose)

☐ Obtain cerebrovascular imaging as soon as possible (non-con CT, stroke CT/CTA/CTP, or MRI)

☐ Obtain brief medical history and medication list

☐ Urine toxicology screen

INR STAT crucial

CT/CTA should be standard
Our Imaging in ICH Philosophy:
Good Quality Plain CT and mCTA brain to view for abnormal arteries/veins and view the leakpoint!
Don’t Leave the ED Without It!
### Summary

**Background** Intracerebral haemorrhage growth is associated with poor clinical outcome and is a therapeutic target for intervention.

**Methods** A systematic review and meta-analysis of individual patient data was performed. Four predictors were considered: time from symptom onset to baseline imaging, intracranial haemorrhage volume on baseline imaging, antiplatelet therapy at symptom onset, and anticoagulant therapy at symptom onset. The addition of CT angiography spot sign was also assessed.

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rFVIIa ICH Trials Failed

Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage

Stephan A. Mayer, M.D., Nikolai C. Brun, M.D., Ph.D., Kamilla Begtrup, M.Sc., Joseph Broderick, M.D., Stephen Davis, M.D., Michael N. Diringer, M.D., Brett E. Skolnick, Ph.D., and Thorsten Steiner, M.D., for the Recombinant Activated Factor VII Intracerebral Hemorrhage Trial Investigators*

Efficacy and Safety of Recombinant Activated Factor VII for Acute Intracerebral Hemorrhage

Stephan A. Mayer, M.D., Nikolai C. Brun, M.D., Ph.D., Kamilla Begtrup, M.Sc., Joseph Broderick, M.D., Stephen Davis, M.D., Michael N. Diringer, M.D., Brett E. Skolnick, Ph.D., and Thorsten Steiner, M.D., for the FAST Trial Investigators*
Logarithmic curve of bleeding with increasing hemostasis then contraction
Logarithmic curve of bleeding with increasing hemostasis then contraction.

ICH volume

Time
Future Directions

- Hemostasis needs to be initiated much earlier
- Spot sign predicts HE but needs refinement
- Hemostatic ICH trial design should focus on:
  - ultraearly time windows (<2h)
  - Deferral or waiver of consent
  - pre-hospital setting (CT ambulance)
Emerging acute tx of ICH

Hematoma expansion prevention therapy

Surgical evacuation of ICH

Thrombolysis in IVH
ICH Surgical Decision Making?

Images A, B, C, D, and E depict various CT scans of the brain. Image A shows a small intracerebral hemorrhage (ICH) in the left hemisphere. Image B highlights a larger ICH with significant mass effect. Image C displays a chronic phase of ICH with surrounding edema. Image D contains two different views of a patient with multiple ICHs, emphasizing the variability in hemorrhage size and location. Image E illustrates a different case with ICH involving the right frontal lobe, showcasing the heterogeneous appearance of hemorrhages on imaging.

These images are crucial for understanding the clinical implications of ICH and guiding surgical decision-making processes, considering factors such as hemorrhage size, location, and mass effect.
When to Operate?

Current practice favours surgical intervention in the following situations:

- Superficial lobar haemorrhage, GCS 9–12, volume 20–80 ml, and/or deteriorating.
- Clot volume between 20 and 80 mls.
- Worsening neurological status.
- Relatively young patients.
- Haemorrhage causing midline shift/raised ICP.
- Cerebellar haematomas > 3 cms &/or causing hydrocephalus.
Safety and efficacy of minimally invasive surgery plus alteplase in intracerebral haemorrhage evacuation (MISTIE): a randomised, controlled, open-label, phase 2 trial

Daniel F Hanley, Richard E Thompson, John Muschelli, Michael Rosenblum, Nichol McBee, Karen Lane, Amanda J Bistran-Hall, Steven W Mayo, Penelope Keyl, Dheeraj Gandhi, Tim C Morgan, Natalie Ullman, W Andrew Mould, J Ricardo Carhuapoma, Carlos Kase, Wendy Tzi, Carol B Thompson, Gayane Yenokyan, Emily Huang, William C Broaddus, R Scott Graham, E Francois Aldrich, Robert Dodd, Cristanne Wijman*, Jean-Louis Caron, Judy Huang, Paul Camarata, A David Mendelow, Barbara Gregson, Scott Janis, Paul Vespa, Neil Martin, Issam Awad†, Mario Zuccarello†, for the MISTIE Investigators†

Summary
Background  Craniotomy, according to the results from trials, does not improve functional outcome after intracerebral

Figure 2: Intracerebral haemorrhage removal
CLEAR IVH Phase 3 trial

tPA instillation
1 mg q8h
dual vent drains

ABOVE: Dual catheters placed bilaterally, $t_1 = 4.5$ hours from Dx.

ABOVE: End of treatment (4 doses given), $t_2 = 48$ hours from Dx.

ABOVE: Extended follow up visit, $t_3 = 17$ days from Dx.
Most ICHs Should Be Care For At CSCs

Calgary serves as the only comprehensive care centre in the south and the primary care centre for an area with over 1.3 million residents (2009)

Legend:
- IV TPA Delivery
- Tertiary Care (Telestroke, Transfers, Education, etc.)
- Comprehensive Stroke Centre
- Primary Stroke Centre
- Proposed Primary Stroke Centre
Key Messages

- ICH 2nd most common stroke
- BP control to systolic ~140 mmHg quickly
- Correction of coagulopathy needed STAT
- Bleeding occurs very early which has limited development of hemostatic tx.
- Surgery offered in moderate sized cerebral or large cerebellar ICH
- Minimally invasive surgery promising
Thank You for your attention