Management of Intracerebral Hemorrhage (ICH)

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Disclosures

• None

Acknowledgements

• Mark Bain MD
• David Fiorella MD PhD
• Henry Woo MD
Learning Objectives

• Define the natural history of ICH
• Review key studies that have influenced the treatment of ICH
• Identify the challenges of the medical and surgical treatment of ICH, including novel treatments
Brain Bleeding

- Multiple types, defined by neurologists and neurosurgeons based on location and etiology
- “Intracranial hemorrhage”
  - Extra-axial
    - Subdural hematoma (SDH), epidural hematoma (EDH), subarachnoid hemorrhage (SAH)
  - Intra-axial
    - Intraparenchymal/intracerebral hemorrhage (ICH), intraventricular hemorrhage (IVH)
Non-Traumatic Intracranial Hemorrhage

• SAH
  – Aneurysm, arteriovenous malformation (AVM)
• IVH
  – Aneurysm, AVM, hypertension, tumor
• SDH
  – Aneurysm, AV Fistula
• Hemorrhagic conversion after stroke
• Intracerebral
  – AVM, cavernous malformation, amyloid angiopathy, anticoagulation, moyamoya, tumors (primary or metastatic), aneurysm, hypertension
Traumatic vs Spontaneous ICH

- Even though the hemorrhage may be similar, many differences exist in diagnosis and management.
- Non-traumatic hemorrhagic stroke often requires more detailed diagnosis (examination and imaging) and management.
ICH

Traumatic * Non-Traumatic

* ER management, ICP control, Critical Care, Surgical Evacuation, AED use, Rehab, etc
• 151 ICH at UF last year
• ICH Accounts for 10-15% of all strokes\textsuperscript{1,2,4}
• 80,000-100,000 cases in US; 2 million worldwide\textsuperscript{2,4}
• 30-day mortality $\sim$50% with majority dead in first 2 days\textsuperscript{3}
• 80% of survivors have severe physical disability and high rates of cognitive impairment\textsuperscript{3}
• 45% of all ICH has a ventricular component (IVH)\textsuperscript{5}

Early Diagnosis

• No one exam finding is definitive
• Index of suspicion and timely imaging are the best tools available
  – Differentiate ischemic from hemorrhagic stroke
  – Stroke diagnosis often delayed without high index of suspicion
  – Early noncontrast CT in all patients with sudden onset severe headache, change in consciousness or neurological changes
  – Advanced neuroimaging if underlying anatomic lesion suspected
ICH Score

• GCS
  – 3-4 (2)
  – 5-12 (1)
  – 13-15 (0)
• Age
  – 80 or above (1)
• Location
  – Infratentorial (1)
• Volume
  – 30 cc or greater (1)
• IVH
  – Positive (1)

• 30 day mortality
  – 0 = 0%
  – 1 = 13%
  – 2 = 26%
  – 3 = 72%
  – 4 = 97%
  – 5 = 100%
ICH Treatment

• Only form of stroke without a clearly effective treatment
Early Management

• Exam (before sedation)

• Intubation – >30% of supratentorial ICH patients and most cerebellar hemorrhages have reduced consciousness requiring airway support
  – O2 saturation <90% or PaO2 <60 = poor outcome

• Blood pressure control
  – Reduce risk of re-hemorrhage with treatment of hypertension
  – SBP <90 = poor outcome

• Labs: CBCP, chemistry, coagulation studies
  • Platelet quantity versus quality
AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage
A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons, the Congress of Neurological Surgeons, and the Neurocritical Care Society

J. Claude Hemphill III, MD, MAS, FAHA, Chair; Steven M. Greenberg, MD, PhD, Vice-Chair; Craig S. Anderson, MD, PhD; Kyra Becker, MD, FAHA; Bernard R. Bendok, MD, MS, FAHA; Mary Cushman, MD, MSc, FAHA; Gordon L. Fung, MD, MPH, PhD, FAHA; Joshua N. Goldstein, MD, PhD, FAHA; R. Loch Macdonald, MD, PhD, FRCS; Pamela H. Mitchell, RN, PhD, FAHA; Phillip A. Scott, MD, FAHA; Magdy H. Selim, MD, PhD; Daniel Woo, MD, MS; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, and Council on Clinical Cardiology

Stroke. 2015;46:000-000. DOI: 10.1161/STR.00000000000000069
ICH Class I Treatment Guidelines

• Correction of coagulopathy or thrombocytopenia (Level 1C)
• SCDs for DVT prevention beginning HD1 (1A)
• For ICH patients with SBP 150-220 and no contraindication to lowering BP, reducing SBP to 140 is safe (1A)
• Initial monitoring and care of patients with ICH should occur in ICU or dedicated stroke unit with physician and nursing neuromedicine experience (1B)
Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D., Daniel F. Hanley, M.D., Chung Y. Hsu, M.D., Renee L. Martin, Ph.D., Claudia S. Moy, Ph.D., Robert Silbergleit, M.D., Thorsten Steiner, M.D., Jose I. Suarez, M.D., Kazunori Toyoda, M.D., Ph.D., Yongjun Wang, M.D., Haruko Yamamoto, M.D., Ph.D., and Byung-Woo Yoon, M.D., Ph.D., for the ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network*

NEJM 375(11), 2016
ATACH-2 Trial

- 1000 patients with ICH and baseline SBP of 200
  - 500 intensive BP control (SBP goal 110-139)
  - 500 standard BP control (SBP goal 140-179)
- Stopped early for futility
- No significant difference in mRS 4-6 at 90 days
  - 38% in both groups
  - 1.6% (intensive) vs 1.2% (standard) AE (NS)
- Renal AE’s 9% (intensive) vs 4% (standard) at 7 days (p=0.002)
ICH Class I Treatment Guidelines

- Glucose should be monitored. Hypo- and hyperglycemia should be avoided (1C)
- Clinical seizures (1A) or EEG abnormality in patients with mental status changes (1C) should be treated with AEDs
- Formal dysphagia screening in all patients (1B)
- BP should be controlled in all patients to prevent recurrent ICH (1A)
- All ICH patients should have access to multidisciplinary rehabilitation (1A)
ICH Class I Treatment Guidelines

- Patients with cerebellar ICH who are deteriorating or who have brainstem compression or hydrocephalus should undergo surgical evacuation of hemorrhage as soon as possible (1B)
Brain Injury after ICH

0-60 min
- Haematoma
  - Neuronal and glial mechanical disruption, oligaemia or ischaemia
  - Glutamate release

0-4 h
- Neuronal and glial mechanical stretch
- Calcium influx, mitochondrial failure
- Sodium accumulation, cytotoxic oedema, necrosis

4 h to 7 days
- Thrombin, ferrous iron, haemin, halotransferrin release
- Microglial activation
  - Oxygen free radicals
- MMP
- Complement factors
- TNFα
  - AQ-4 expression in astrocytes, breakdown of connective tissue in BBB, expression of adhesion molecules
- Interleukin 1β
  - Caspase activation, apoptosis in neurons and glia
- Cytochrome C
- TFKN-α
  - Recruitment of PMNs and macrophages
  - Increased BBB permeability, vasogenic oedema
Time Course of Injury

• EARLY HEMATOMA EXPANSION
  • Initial Tissue Injury, destruction of fiber tracts, increased ICP
  • Can be prevented with reversal of anticoagulation, factor VII
  • ? Impact on outcome

Time Course of Injury

- SECONDARY INJURY
  - Edema
  - Neurotoxicity
  - Inflammation
  - Mass effect
  - Ischemia
Management of Elevated ICP

• Conservative
  – Elevate HOB, avoid hypotonic IVF/hyponatremia, avoid hypoxia and hypotension, treat fever, align neck, control of PC02

• Pharmacologic
  – Analgesia, Sedation, Paralytics
  – Osmotic diuresis
    • Mannitol, hypertonic saline (3% NaCl)

• Surgical
  – External ventricular drain, ICP monitor, evacuation of hematoma / craniotomy for mass lesions, decompressive hemicraniectomy
Hemicraniectomy with Evacuation of ICH

5 DAYS LATER
Surgical Treatment of ICH

Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial

A David Mendelow, Barbara A Gregson, Helen M Fernandes, Gordon D Murray, Graham M Teasdale, D Terence Hope, Abbas Karimi, M Donald M Shaw, and David H Barer for the STICH investigators*

See Comment page 361
STICH

- 1033 patients
- 83 centers
- 503 surgery
- 530 conservative
- 72 hours from ICH
- Early Surgery?
STICH

- Early surgery does not increase death/disability at 6 months
- Moderate clot size
- Reachable/safe location
- “Conscious” patients
- No IVH
ICH

Streptokinase for AMI - GISSI

Prehospital thrombolysis w streptokinase


1987

Coronary angioplasty v thrombolysis

1995 1999 2004

alteplase for AIS approved

Mechanical thrombectomy device approved

NINDS TPA Study for AIS

PROACT2 IA Prourokinase for AIS

MR CLEAN & other EVT studies

STICH I

STICH II AND MISTIE

Prehospital thrombolysis w streptokinase

Surgery for Intracerebral Hemorrhage | March 24, 2017
MISTIE II

• 14% improvement in mRS 0-2
• 38 fewer days in hospital
• $44,000 savings per subject
• 14% decrease in long term care
Original Contribution

ICES (Intraoperative Stereotactic Computed Tomography-Guided Endoscopic Surgery) for Brain Hemorrhage
A Multicenter Randomized Controlled Trial

Paul Vespa, MD; Daniel Hanley, MD; Joshua Betz, MS; Alan Hoffer, MD;
Johnathan Engh, MD; Robert Carter, MD; Peter Nakaji, MD; Chris Ogilvy, MD;
Jack Jallo, MD; Warren Selman, MD; Amanda Bistran-Hall, BS; Karen Lane, CMA;
Nichol McBee, MPH; Jeffery Saver, MD; Richard E. Thompson, PhD; Neil Martin, MD;
on behalf of the ICES Investigators

Stroke Nov 2016
• 14 surgical patients matched with medical patients from MISTIE trial
• MIS endoscopic clot evacuation resulted in 70% clot reduction
• 1 recurrent hemorrhage after surgery
• Trend towards improved mRS 0-3 at 6/12m in surgery vs medical group
  – 43% vs 24% (p=0.19)
Less Invasive Clot Evacuation
Less Invasive Clot Evacuation
Apollo

• Designed for transcranial, minimally invasive, evacuation of blood and tissue

• Fits through the working channel of an endoscope
  – 19F sheath: 6.8 mm diameter
19F = 6.3 mm
Initial Multicenter Technical Experience With the Apollo Device for Minimally Invasive Intracerebral Hematoma Evacuation

BACKGROUND: No conventional surgical intervention has been shown to improve outcomes for patients with spontaneous intracerebral hemorrhage (ICH) compared with medical management.

OBJECTIVE: We report the initial multicenter experience with a novel technique for the minimally invasive evacuation of ICH using the Penumbra Apollo system (Penumbra Inc, Alameda, California).

METHODS: Institutional databases were queried to perform a retrospective analysis of all patients who underwent ICH evacuation with the Apollo system from May 2014 to September 2014 at 4 centers (Medical University of South Carolina, Stony Brook University, University of California at San Diego, and Semmes-Murphy Clinic). Cases were performed either in the neurointerventional suite, operating room, or in a hybrid operating room/angiography suite.

RESULTS: Twenty-nine patients (15 female; mean age, 62 ± 12.6 years) underwent the minimally invasive evacuation of ICH. Six of these parenchymal hematomas had an additional intraventricular hemorrhage component. The mean volume of ICH was 45.4 ± 30.8 mL, which decreased to 21.8 ± 23.6 mL after evacuation (mean, 54.1 ± 39.1% reduction; P < .001). Two complications directly attributed to the evacuation attempt were encountered (6.9%). The mortality rate was 13.8% (n = 4).

CONCLUSION: Minimally invasive evacuation of ICH and intraventricular hemorrhage can be achieved with the Apollo system. Future work will be required to determine which subset of patients are most likely to benefit from this promising technology.

KEY WORD: Intracerebral hemorrhage

Limitations of MIS approach

- Require clot stability for 6-12 h
- Not designed to address active bleeding
- Prolonged clot resolution time
- Poor visualization
- Challenging to remove large percentage of hematoma
73 year old right handed woman

- Altered mental status, global aphasia, right hemiplegia
- NIHSS 20, GCS 10
- MIS clot evacuation on day of admission
- Discharged to rehab on POD#13. Flicker movement on right arm and able to follow commands
- NIHSS 9, GCS 15
- At 10 week follow-up has conversational speech, able to walk with assist, and right arm strength is 4/5
58 year old right handed man

- Sudden onset of headache, right arm and face weakness
- NIHSS 6, GCS 14
- Left gyrus rectus hemorrhage with what appears to be a mass
- IVH but no hydrocephalus
- MIS evacuation / tumor resection on PBD#1
- Pathology: Renal Cell Carcinoma
- Discharged to home on POD#2 with NIHSS 0, GCS 15
49 year old left handed woman

- Severe headache, dysarthria, right hemiparesis
- NIHSS 11, GCS 10
- IVH with hydrocephalus, EVD placed
- MIS evacuation on day of admission
- Immediate post-op right arm and leg strength 4+/5
- Discharged on PBD#7, with NIHSS 0, GCS 15
- Returned to work shortly after
51 year old right handed woman

- Subacute onset headache, blurred vision, tremor
- Lethargic on presentation
- Right frontal EVD placed with improvement
- OR for resection using MIS retractor
- EVD weaned and patient discharged home on POD#3 with normal neurological exam
# Brain Path vs Apollo

<table>
<thead>
<tr>
<th>Brain Path Pros</th>
<th>Apollo Pros</th>
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<tbody>
<tr>
<td>Larger Access</td>
<td>Minimal Access Burrhole</td>
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<tr>
<td>Easy Hemostasis</td>
<td>Less Tissue Disruption</td>
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<tr>
<td>Better Visualization</td>
<td>Not a true “surgical procedure”</td>
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<tr>
<td>Can do in normal OR</td>
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<table>
<thead>
<tr>
<th>Brain Path Cons</th>
<th>Apollo Cons</th>
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</thead>
<tbody>
<tr>
<td>Larger Access</td>
<td>Poor Visualization</td>
</tr>
<tr>
<td>Surgical Procedure, “minimal” is relative</td>
<td>Not designed to achieve hemostasis</td>
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<tr>
<td></td>
<td>Wait for clot stability</td>
</tr>
<tr>
<td></td>
<td>Need angio suite or intra op imaging</td>
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### Trials Summary

<table>
<thead>
<tr>
<th></th>
<th>MISTIE</th>
<th>INVEST</th>
<th>ENRICH</th>
</tr>
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<tbody>
<tr>
<td>Study Size (pts)</td>
<td>500</td>
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<td>300</td>
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<tr>
<td>Randomization</td>
<td>1:1</td>
<td>1:1</td>
<td>1:1</td>
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<tr>
<td>ICH Size (cc)</td>
<td>&gt; 30</td>
<td>20-80</td>
<td>30-80</td>
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<tr>
<td>Stability Scan</td>
<td>Yes, 6h</td>
<td>Yes, 6h</td>
<td>No</td>
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<td>Treatment Window</td>
<td>12hr – 72 hr</td>
<td>&gt;6hs – 72hrs</td>
<td>&lt;24 hrs</td>
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<tr>
<td>Primary Endpoint</td>
<td>mRS ≤ 3 @ 180 d</td>
<td>mRS ≤ 3 @ 180 d</td>
<td>mRS shift @ 180 d</td>
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Thank You!

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