

**Journal Club:
Surgical Trial in ICH (STICH):
A Randomised Trial**

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**New York City
October 23, 2007**

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Global Objectives

- Improve pt outcome in ICH
- Know how to effectively Rx ICH patients
- Understand current guidelines
- Be aware of future therapies
- Improve Emergency Medicine practice

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Session Objectives

- Examine relevant ICH articles
- Discuss what these articles tell us
- Explore where each article will lead us
- Consider how EM practice might change

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Methodology

- What was the purpose?
- What was the hypothesis?
- What was the data?
- What did the authors conclude?
- What limitations?
- What do we conclude?

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ICH Volume and Outcome

- Broderick: 1993 Stroke
- Key Concept: Hemorrhage volume and GCS predict 30 day mortality
- Data: 60 cc blood, GCS < 9, mort 91%
- Data: 30 cc blood, GCS > 8, mort 19%
- Implications: Simple ED observations allow for a reasonable outcome assessment

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ICH Volume and Outcome

- Broderick: 1993 Stroke
- Data: 3 volumes, 2 GCS strata
- Data: 96% sensitivity, 98% specificity
- Data: 30+cc bleed, 1/71 independ at 30 d
- Implications: EM physicians can know likely outcome, allowing for realistic discussions with family & neurosurgeon

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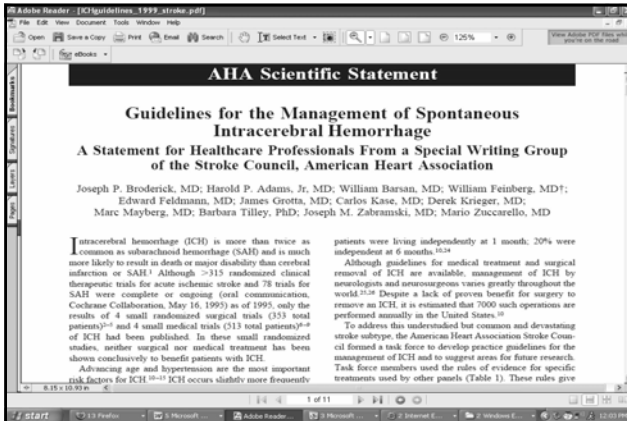


ICH Hemorrhage Growth

- Brott: 1997 Stroke
- Key Concept: ICH volume is dynamic, changes correlate clinically
- Data: 1 hr: 26% had 1/3 growth
- Data: 20 hr: another 12% had 33% growth
- Data: 1/3 growth = drop in NIHSS, GCS
- Implications: Efforts directed at stabilizing hemorrhage volume may impact patient outcome

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ICH Treatment Guidelines

- **ASA Council: 1999 Stroke**
- **Key Concept: ICH guidelines exist**
- **Data: Detailed data on disease, epi**
- **Data: Specific recs on BP, ICP Rx**
- **Implications: This article will enhance the understanding of any EM physician on acute ICH patient management, make care consistent**

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ICH: Surgical Concepts

- **Remember: Only 4 clinical trials!**
- **Total of 353 patients studied in all**
- **Remove clot, reduce pressure**
- **Manage brain trauma and edema**
- **Minimize trauma (superficial clots best)**
- **Minimally invasive approaches now used**
- **75-100% mortality in surgical ICH trials**

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ICH: Surgical Indications

- **Hard to specify...however...**
- **Cerebellar hemorrhage: 3 cm or larger or those that cause mass effect, compression**
- **ICH related to a surgical lesion**
- **Young patients who deteriorate**
- **Other indications less clear**

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STICH ICH Surgical Trial

- **Mendelow: 2005 Lancet**
- **Key Concept: Surgery within 24 hours does not affect 6 month outcome**
- **Data: 25% of pts had a good outcome**
- **Data: Surgery did not change this rate**
- **Implications: ED Rx becomes more important, given lower likelihood of operative neurosurgical intervention**

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STICH ICH Surgical Trial

- Mendelow: 2005 Lancet
- 1033 pts, non-US settings
- Data: early surgery vs. medical, surgical
- Data: Hemorrhage volume: 40 cc
- Data: 81% had GCS 9-15
- Data: Surgical time: 30 hrs, 60 hrs
- Data: Only 16% had surgery < 12 hrs

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STICH ICH Surgical Trial

- Mendelow: 2005 Lancet
- Key concept: This study may not exactly tell the story of US practice
- May still need to consider operative intervention, will need to stabilize patients first

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STICH: Rationale

- ICH 20% of all strokes
- Highest M & M
- Early surgery vs. initial conservative Rx
- Can the ischemic penumbra be preserved?
- Does early surgery fix elevated ICP and low CPP? (CPP = MAP – ICP)

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STICH: Rationale

- Conflicting results from 9 trials
- No firm conclusions
- One meta-analyses included
- Non-randomised trials, one Japan study of 7000 patients
- Improved surgical techniques
- Will death and disability be reduced?

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STICH: Methods

- 1995 study onset
- By 2003, 107 centers
- 1033 patients enrolled
- Consent obtained

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STICH: Inclusion Criteria

- CT evidence of spontaneous ICH
- Within 72 hours of enrollment
- Neurosurgeon uncertain about best Rx
- Hematoma diameter of 2 cm
- GCS score > 4

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STICH: Exclusion Criteria

- Aneurysm due to aneurysm or AVM
- Tumor due to tumor or trauma
- Cerebellar hemorrhage
- Brainstem extension
- Bad outcome likely
- Surgical not possible within 24 hours

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STICH: Surgical Intervention

- Early surgery: in 24 hr of randomisation
- Late surgery: in setting of neurological deterioration
- Left to neurosurgeon discretion

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STICH: Outcome Measures

- Death or disability using the extended Glasgow outcome scale at 6 months after ictus
- Resource use, length off stay

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STICH: Sample Size Calculation

- Prospective sample of 259 patients
- 40% favourable outcome with conservative treatment
- Sample size 800 needed to show a 10% benefit from surgery
- 25% safety margin for protocol violations and crossovers
- Final sample size 1000

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STICH: Statistical Analysis

- Intention-to-treat analysis
- Favourable vs. unfavourable analysis
- Prognosis estimated from formula:
Prognostic score = (10 x GCS) – age – (.64 x ICH volume)
- This lead to a way to define outcome

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STICH: Defining Outcome

- Predicted good prognosis: good outcome was good outcome or moderate disability
- Predicted poor prognosis: good outcome was good outcome, moderate disability, or upper severe disability categories
- *Did they do better than expected?*

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STICH: Defined Subset Analyses

- Age 65 cutoff
- Haematoma volume 50 cc cutoff
- GCS score < 9, 9 to 12, or 13+
- Lobar vs. basal ganglia/thalamic
- Presence of thrombolytic therapy
- Neurological deficit
- Craniotomy vs. other

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STICH: Population

- 1033 patients from 83 centres in 27 countries
- 503 early surgery
- 530 to initial conservative

- Well matched at baseline

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STICH: Characteristics

- Median age 62 years
- Time to randomisation: 20 hour median
- 20% comatose
- 40% GCS 13+
- 40% lobar hemorrhage, 40% BG/T
- Median volume 38 cc, at 1 cm depth
- Time to OR = 30 and 60 hours

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STICH: Surgery

- 6% of early surgery pts received operative intervention after 24 hours
- 26% of conservative patients received operative intervention, usually due to rebleeding or deterioration
- Deterioration usually 3 + GCS points
- Superficial, lobar hemorrhages to OR

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STICH: Main Result

- Prognosis-based dichotomy
- Early surgery: 26% favorable outcome
- Conservative: 22% favorable outcome
- OR = 0.89, ns
- Early surgery 2.3% absolute benefit, 10% relative benefit
- Mortality 36, 37% in the two groups

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STICH: Other Results

- 8% surgery benefit if haematoma less than one cm from surface
- 6% surgery benefit if haematoma evacuated by craniotomy
- If coma, then bad outcome.
- Early surgery in coma patients increased bad outcome risk by 8%

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STICH: Other Results

- Cost analysis, limited numbers
- No clear significant differences
- (Data difficult to digest)

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STICH: Discussion

- Favorable outcome based on prognosis-based indices do not differ
- These trials are hard to conduct and will be harder in the future
- Prognosis-based outcome made it possible to detect more modest amounts of benefit

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STICH: Discussion

- “However, we still cannot give a definitive answer to the questions: can a policy of early surgical intervention for patients with ICH be recommended, and, if so, under what conditions?”

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STICH: Limitations

- Bias in randomisation
- Outcome measure not blinded
- Subgroup analysis uses up statistical power

- Who wan't enrolled and why?
- What happened to these patients?

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STICH: Coma Patient Results

- Uniformly bad outcome
- Surgery is probably harmful
- 40 operations for one good outcome

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STICH: Final Conclusions

- Analyze in context of all trials results
- Can't recommend surgery
- Surgeons should do more studies

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STICH: Some Issues

- Intervention by group a problem
- Time to surgery a problem
- This may not reflect US paradigm

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STICH: Baseline Differences

- The surgical patients differed at baseline in the two groups
- Page 391
- Table 3
- Early surgical patients: less sick
- Conservative patients who received operative: more sick

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STICH: Conclusions

- Study might have concluded: Better than expected outcomes don't occur with or without surgical intervention in ICH patients who are treated many hours after the ictus and who receive delayed operative intervention, often after deterioration

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STICH: What is the Problem?

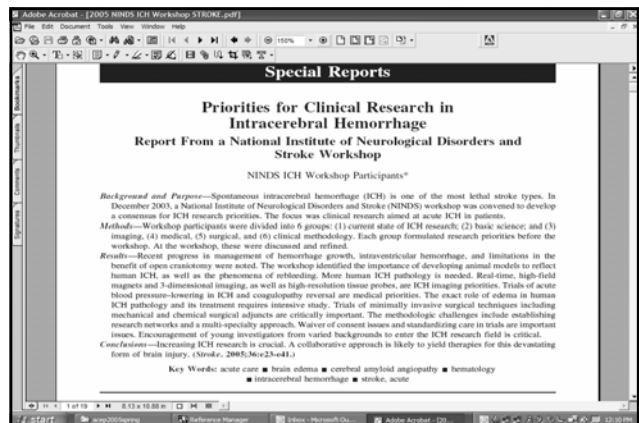
- Generalising the results to a different patient population or treatment paradigm may lead to changes in management that are not indicated
- We should continue to consider operative intervention, given US differences and the conflicting publications, of which this is one

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STICH: What Have We Learned?

- Surgery may not be beneficial in ICH
- Comatose patients (especially those with a large hemorrhage) do poorly and may not warrant surgical intervention
- Superficial hematomas may benefit from surgical intervention
- Research is hard to do
- We have more to do and learn

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NINDS ICH Research Agenda

- NINDS Workshop: 2005 Stroke
- Key Concept: Fundamental questions
Re: ICH treatment and research
- Data: Critical medical, surgical issues
- Data: Extensive info regarding acute Rx
- Implications: Although much theoretical info, an important source of facts that will enhance current clinical practice

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NINDS ICH Research Agenda

- NINDS Workshop: 2005 Stroke
- Key Concept: Landmark article
- Data: 6 writing groups
- Data: 226 references
- Implications: A must for any educator or clinician who wishes to know more about the optimal ED Rx of ICH patients

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Key Learning Points

- Research is a tough business, as is treating ICH patients in the ED
- If the ICH is large and the pt comatose, plan no operative intervention
- In the US, early immediate operative intervention is still an option for smaller, superficial bleeds, especially in viable patients who are not comatose
- We must know how to talk the talk with our neurosurgical consultants
- More work is to be done

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Questions??

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