

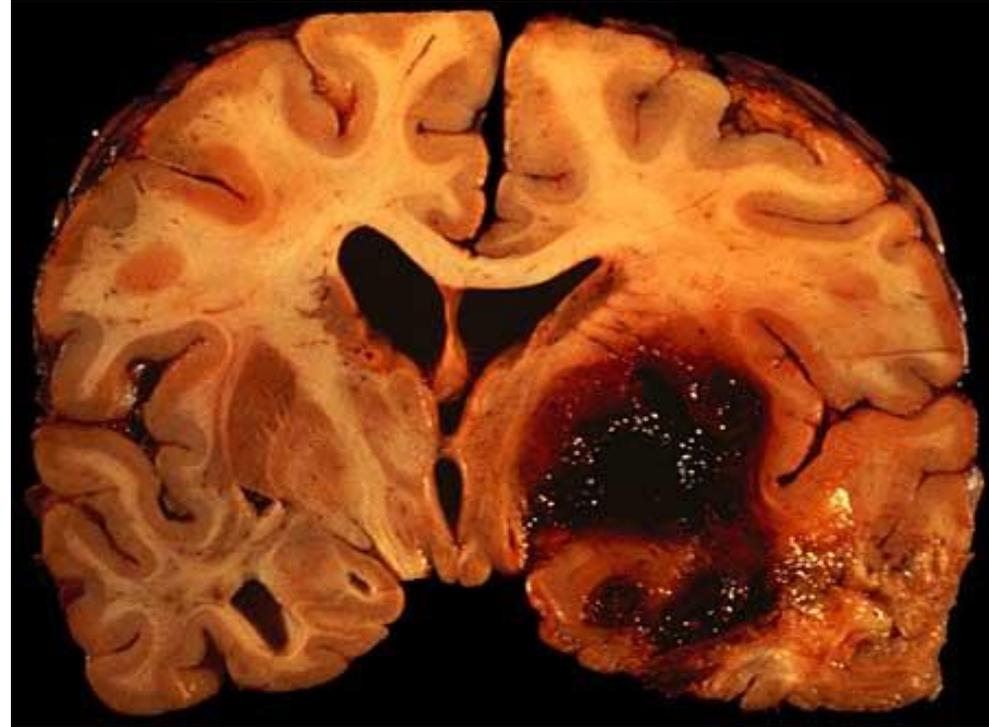
The management of ICH when to operate when not to?



Rush Center for
Neuroendovascular surgery

ICH is a Bad Disease

- High Incidence
 - Accounts for 10-15% of all strokes^{1,2,5}
 - 80,000 cases in US; 2 million WW^{2,5}
 - Incidence doubles for African-Americans and Asians^{1,2,3}
- High Mortality/Morbidity
 - 30-day mortality ~50% with majority dead in first 2 days³
 - Substantial disability; only 20% of survivors live independently at 6 months³
- **45%** of all ICH has a ventricular component (IVH)⁷



Source:

¹ Qureshi AI, Tuhim S, Broderick JP, Batjer HH, Hondo H, Hanley DF. Spontaneous intracerebral hemorrhage. *N Engl J Med.* 2001;344:1450-1460. doi:10.1056/NEJM200105103441907.

² Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. *Lancet.* 2009;373(9675):1632-1644. doi:10.1016/S0140-6736(09)60371-8.

³ Broderick JP, Adams HP Jr, Barsan W, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A Statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. *Stroke.* 1999;30:905-915. doi:10.1161/01.STR.30.4.905.

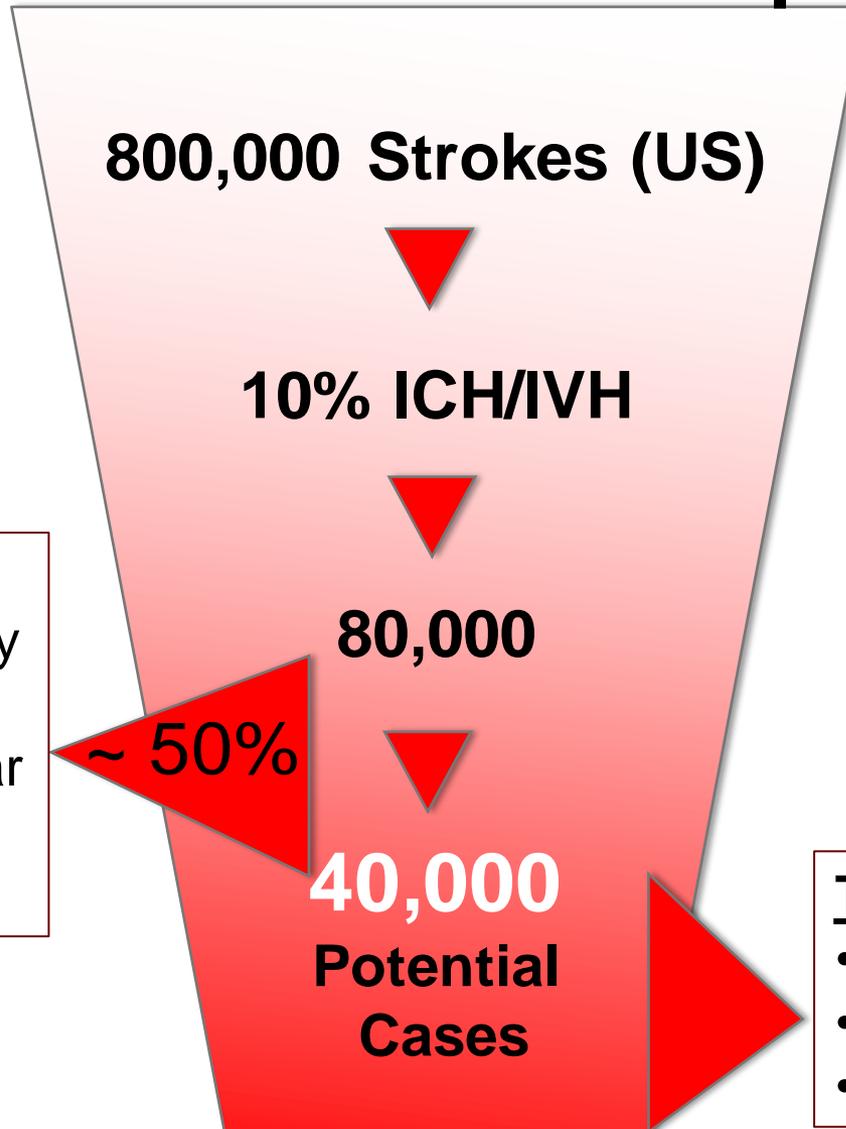
⁴ Thrift AG, Geoffrey DA, McNeil JJ. Epidemiology of intracerebral hemorrhage. *Epidemiol Rev.* 1995;17(2):361-381.

⁵ Towfighi A, Greenberg SM, Rosand J. Treatment and prevention of primary intracerebral hemorrhage. *Semin Neurol.* 2005;25(4):445-452.

⁶ Sahni R, Weinberger J. Management of intracerebral hemorrhage. *Vasc Health Risk Manag.* 2007;3(5):701-709.

⁷ Morgenstern LB, Hemphill JC III, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: A Guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2010;41:2108-2129, published online before print July 22 2010. doi:10.1161/STR.0b013e3181ec611b.

ICH intervention = Can Help Thousands



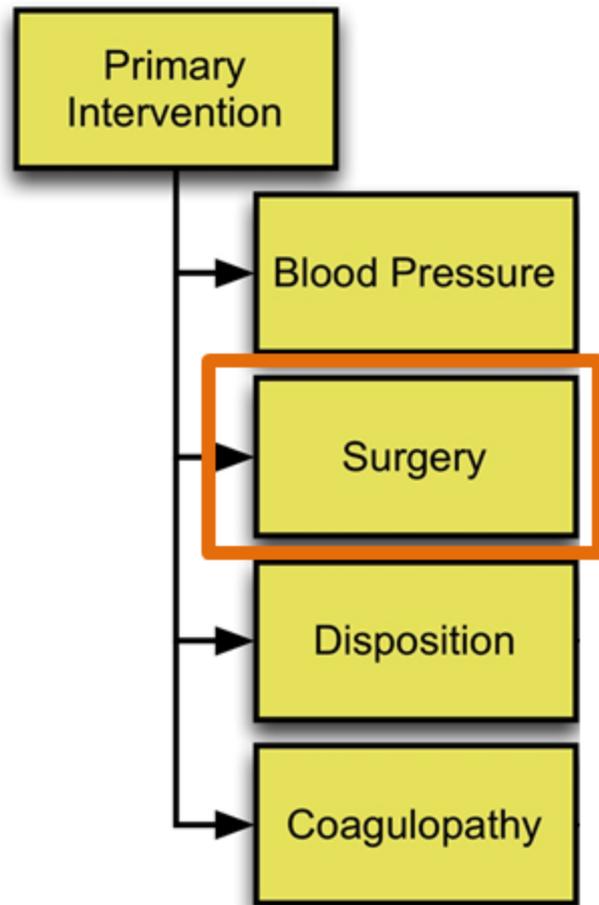
Not Targets:

- Acute mortality
- < 20 cc clot
- Amyloid, Lobar
- Subdural
- Subtentorial

Target:

- Anterior, Ventricular
- Hypertensive
- > 20 cc clot

Role of Surgery



Location	Surgery urgently:
Cerebellum	<ul style="list-style-type: none">• Declining neuro exam• Size > 3 cm, or• Compressive effects brainstem, or• hydrocephalus
Lobar	ICH causing mass effect/herniation in severely affected but salvageable patient and as a life-saving measure

V. Procedures/Surgery

Craniotomy for Posterior Fossa Hemorrhage

- Deterioration can occur quickly in cerebellar hemorrhage
 - Obstructive hydrocephalus
 - Mass effect on brainstem
- Nonrandomized studies suggest that patients with cerebellar hemorrhage that is:
 - > 3 cm in diameter
 - Associated with brainstem compression
 - Associated with hydrocephalushave better outcomes with surgical decompression
- Attempting to control ICP via means other than hematoma evacuation is not recommended and may be harmful

V. Procedures/Surgery



Craniectomy for ICH

- Potential of decompressive craniectomy (DC) to improve outcomes has not been well studied.
- STITCH trial suggests improved outcomes with DC in patients with:
 - Coma (GCS < 8)
 - Significant midline shift
 - Large hematomas
 - ICP that did not normalize with medical management
- Systematic review suggests that DC with hematoma evacuation might be safe and improve outcomes.



Intraparenchymal hemorrhage



Intraparenchymal hemorrhage

- Current management strategy
 - Blood pressure control and monitor
 - Surgical evacuation by craniotomy
 - Placement of external ventricular drainage

- STICH trial
 - Randomized prospective study looking at effectiveness of early surgery (within 24 hours of randomization) versus initial medical therapy
 - STICH trial did not show significant difference in outcome between surgical arm and medical therapy
 - Subgroup analysis showed that superficial hemorrhages (< 2 cm from the surface) benefited from evacuation

V. Procedures/Surgery



Craniotomy for Supratentorial Hemorrhage

- STITCH trial
 - Early surgery vs conservative management for supratentorial ICH when clinical equipoise is present
 - “early surgery” = within 24 hours of randomization
 - There was no overall statistically significant difference in mortality or functional outcome between the two groups
- STITH II trial
 - Early surgery vs conservative management for conscious patients with superficial lobar hemorrhage (10-100 mm³ within 1 cm of cortical surface), without IVH, and admitted within 48 hours of onset
 - 41% in early surgery vs 38% in conservative group with favorable outcome
 - 21% of conservative management ultimately underwent surgery
 - No advantage to early surgery for patients in good prognosis group
 - Non-significant survival advantage in the surgical group



Intraparenchymal hemorrhage

- STICH showed us that evacuation of deeper hemorrhages through craniotomy was not more beneficial than conservative measures
- The question of evacuation through less invasive methods has not been tested
- What about early evacuation with less invasive methods?

V. Procedures/Surgery



Minimally Invasive Surgical Evacuation of ICH

- Recent randomized studies suggest better outcomes with less invasive approaches compared to standard craniotomies
- MISTIE II trial
 - Minimally invasive surgery plus rt-PA for intracerebral hemorrhage evacuation vs medical management (small study)
 - Significant reduction in perihematomal edema in evacuation group
 - Trend towards improved outcomes in evacuation group
- MISTIE III trial in currently in progress



Intraparenchymal hemorrhage

- MISTIE II trial

Objectives & Purpose: The purpose of this trial is to determine the safety of using a combination of minimally invasive surgery plus clot lysis (using rt-PA) to remove ICH. The MISTIE trial uses image-based surgery (MRI or CT) to provide catheter access to ICH. This study tested if the intervention facilitates more rapid and complete recovery of function and decreased mortality compared to conventional medical management without subjecting the patient to craniotomy. The specific objective of this trial is to test safety and assess ability to remove blood clot from brain tissue.

MISTIE II Trial (complete)

Medical Management + Clot Drainage Catheter With tPA vs. Medical Management Alone

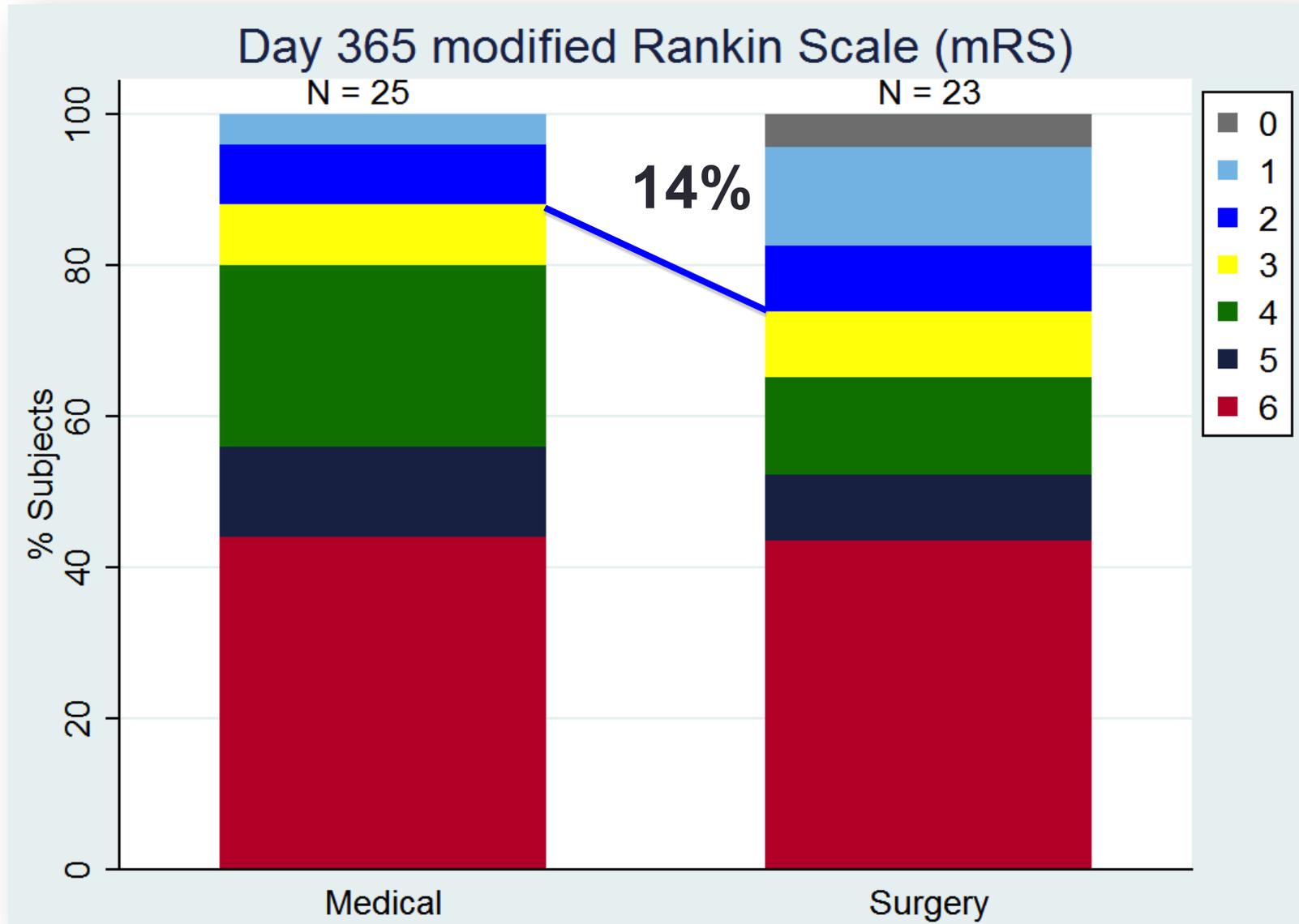
- **Inclusion:** Spontaneous, supratentorial Intracerebral Hemorrhage $\geq 20\text{ml}$, with a GCS ≤ 14 or a NIHSS ≥ 6 .
- **n** = 96 patients randomized
- **Therapy:** 1 mg of tPA administered via drainage catheter every 8 hours for up to 72 hours (3 days)

Intraparenchymal hemorrhage

- MISTIE II

Conclusions: Minimally invasive surgery plus rt-PA enhances survivor functional outcomes for independence. MISTIE treatment may benefit ICH patients because effective removal occurs and there appears to be limited tissue injury. These clinically significant benefits should be tested in a Phase III trial. These results could lead to a major change in practice. Now, the majority of ICH patients do not undergo surgical removal of the ICH.

MISTIE II Long Term Outcomes

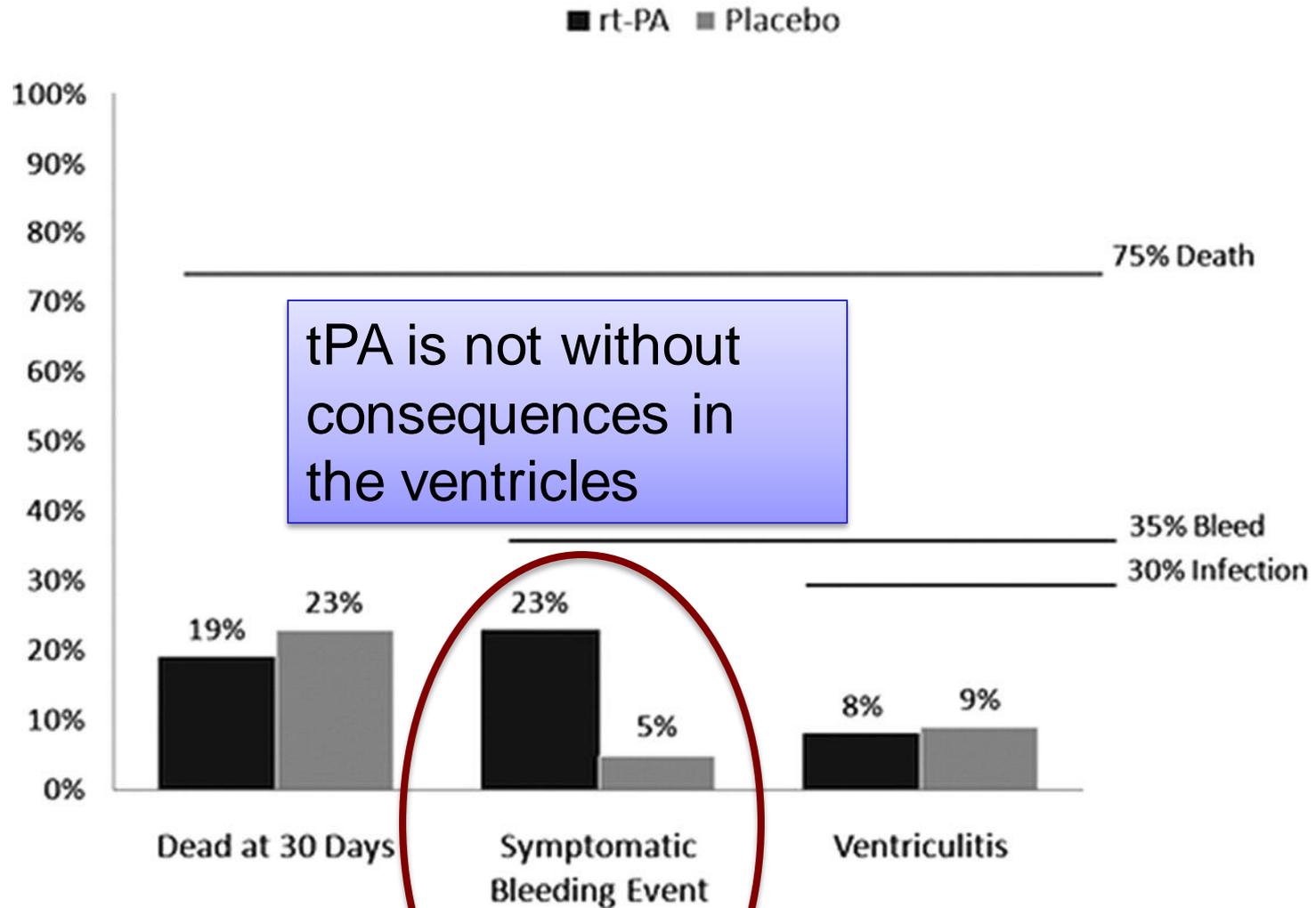


CLEAR II Trial (complete)

EVD + tPA vs. EVD + placebo

- **Inclusion:** small supratentorial ICH (≤ 30 ml) with massive IVH with an EVD already placed for treatment of obstructive hydrocephalus, per standard of care
 - Median ICH volume: 7.5 ml
 - Median IVH volume: 52.7 ml
- **n** = 48 patients randomized
- **Therapy:** Subjects were randomized to receive either 3 mg of rtPA or 3 ml of normal saline injected via the EVD into the ventricular spaces every 12 hours until clot resolution.
 - **10.2 \pm 8** days in ICU for rtPA and **12.7 \pm 8.4** days in ICU for placebo

CLEAR II Outcomes



Naff N et al. Stroke 2011;42:3009-3016

Intraventricular hemorrhage

- Intraventricular and intracerebral hemorrhage have a morbidity and mortality rate of 50-80%
- Animal models have demonstrated that in IVH intracranial pressure control is important but to the change in neurological outcome, removal of IVH is important
- IVH has been shown to increase tissue inflammation and the more of the blood removed, the more decrease in inflammatory factors

Current management of IVH

- Observation and monitoring of neurological status, control blood pressure
- Placement of External Ventricular Drainage system
- Placement of EVD plus or minus infusion of TPA
- Surgical evacuation

- CLEAR trial
 - Multicenter blinded prospective safety trial comparing best medical care with aggressive ventricular drainage with TPA injected into ventricular catheters at a dose of 3 mg every 12 hours
 - Study enrolled 48 pts
 - Symptomatic bleeding was 23% in t-PA group versus 5% in placebo group
 - Mortality was 19% in t-PA group versus 23% in placebo group
 - Clot resolution was 18% in t-PA group versus 8% in placebo group

Intraventricular hemorrhage

- t-PA group underwent earlier removal of EVD catheters due to clot obstruction and there were less exchanging of EVD catheters due to clot obstruction
- There was also clinical improvement by an increase in GCS scores at 4 days in t-PA group
- This was an initial safety study and not designed to assess long-term functional outcome.

Intraventricular hemorrhage

- CLEAR III trial is a current ongoing trial that will assess functional

Inclusion:

- ▶ Age 18-80
- ▶ Symptom onset less than 24 hrs prior to diagnostic CT scan
- ▶ Spontaneous ICH less than or equal to 30 cc or primary IVH
- ▶ IVH obstructing 3rd and/or 4th ventricles
- ▶ ICH clot stability at 6 hours or more post IVC placement
- ▶ IVH clot stability at 6 hours or more post IVC placement
- ▶ Catheter tract bleeding stability 6 hours or more post IVC placement
- ▶ EVD placed per standard medical care
- ▶ SBP less than 200 mmHg sustained for 6 hours prior to drug administration
- ▶ No test article may be administered until at least 12 hours after symptom onset
- ▶ Able to randomize within 72 hours of diagnostic CT scan
- ▶ Historical Rankin of 0 or 1

- CLEAR III

Exclusion:

- ▶ Suspected or untreated ruptured cerebral aneurysm, arteriovenous malformation (AVM), or tumor
- ▶ Presence of a choroid plexus vascular malformation or Moyamoya
- ▶ Clotting disorders. Subjects requiring long term anti-coagulation are excluded.
- ▶ Use of Dabigatran prior to symptom onset.
- ▶ Platelet count less than 100,000, international normalized ratio (INR) greater than 1.4
- ▶ Pregnancy
- ▶ Infratentorial hemorrhage
- ▶ Thalamic bleeds with apparent midbrain extension with third nerve palsy or dilated and non-reactive pupils.
- ▶ Subarachnoid hemorrhage (SAH) at clinical presentation
- ▶ ICH/IVH enlargement that cannot be stabilized in the treatment time window
- ▶ Ongoing internal bleeding
- ▶ Superficial or surface bleeding
- ▶ Prior enrollment in the study
- ▶ Any other condition that the investigator believes would pose a significant hazard to the subject if the investigational therapy were initiated
- ▶ Planned or simultaneous participation (between screening and Day-30) in another interventional medical investigation or clinical trial
- ▶ No subject or legal representative to give written informed consent

Current Treatment Options

Medical Management

- Ineffective in randomized trials to improve patient outcomes. (BP lowering, Corticosteroids, Glycerol, Mannitol, Hemodilution)

Open surgery

- No evidence of improved outcomes in randomized trials; STICH I & II

Minimally invasive drainage

Recent trials have shown mixed results

- MISTIE I & II: promising; phase III underway
- CLEAR I & II: tPA elevates symptomatic hemorrhage; phase III underway

Clinical Conclusions

- MISTIE II and CLEAR II show positive trend of evacuating clot in patients with ICH / IVH to reduce mass effect and hemotoxicity.
- Both trials show trends toward better outcomes if the clot burden can be reduced quickly
- Thrombolysis is not without consequence in terms of bleeding events and ICU stay days.

Apollo

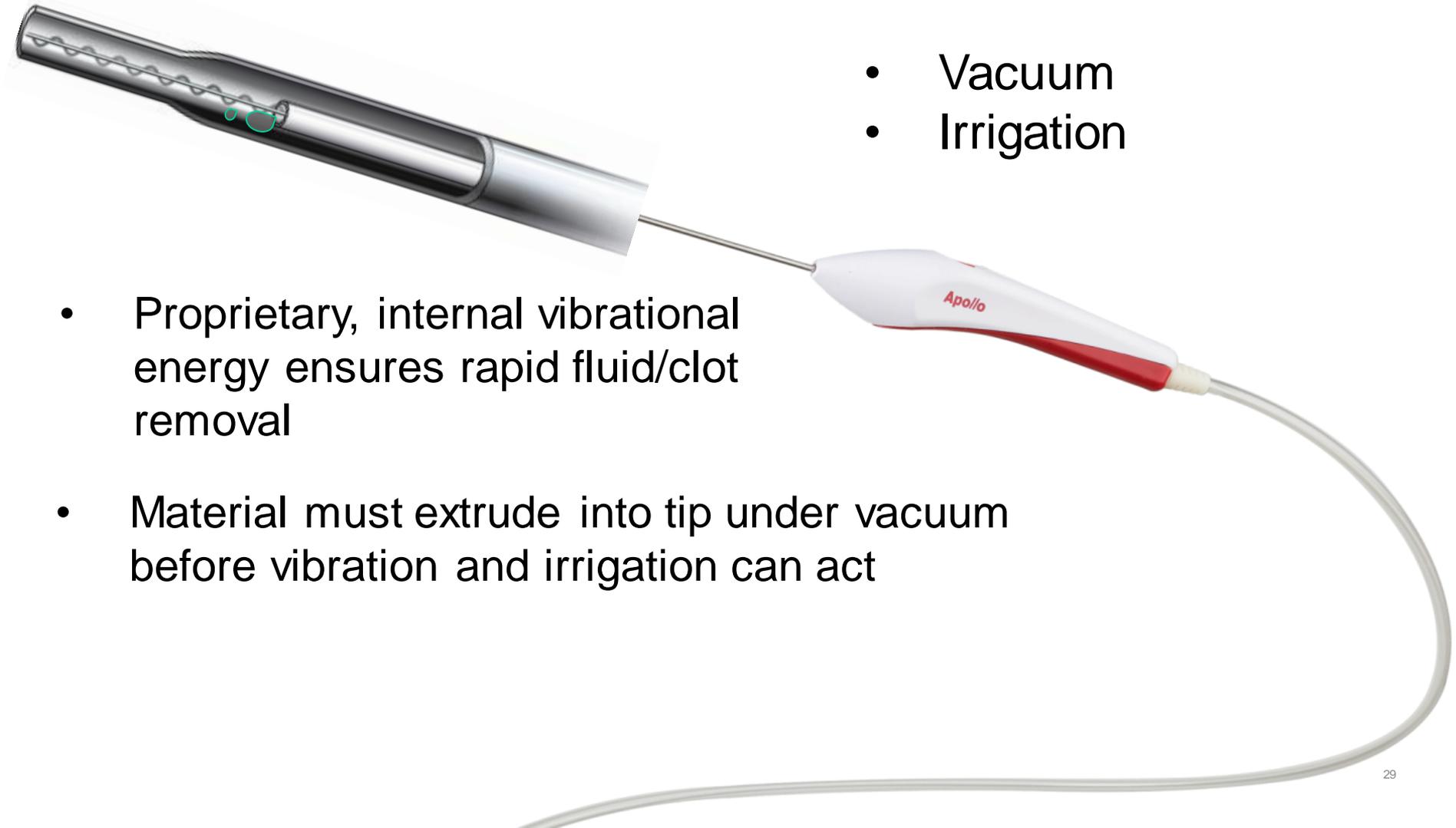
A minimally invasive device that is primarily indicated for intraventricular hemorrhage but its use in intraparenchymal hemorrhages might have a role in the future

The Apollo™ System

- Dedicated hardware components deliver
 - Vacuum, irrigation, vibrational energy
- All components physician controllable, precise, and gentle
- Compatible neuroendoscope enables:
 - Fluid/clot vs. brain differentiation
 - Hemostasis confirmation



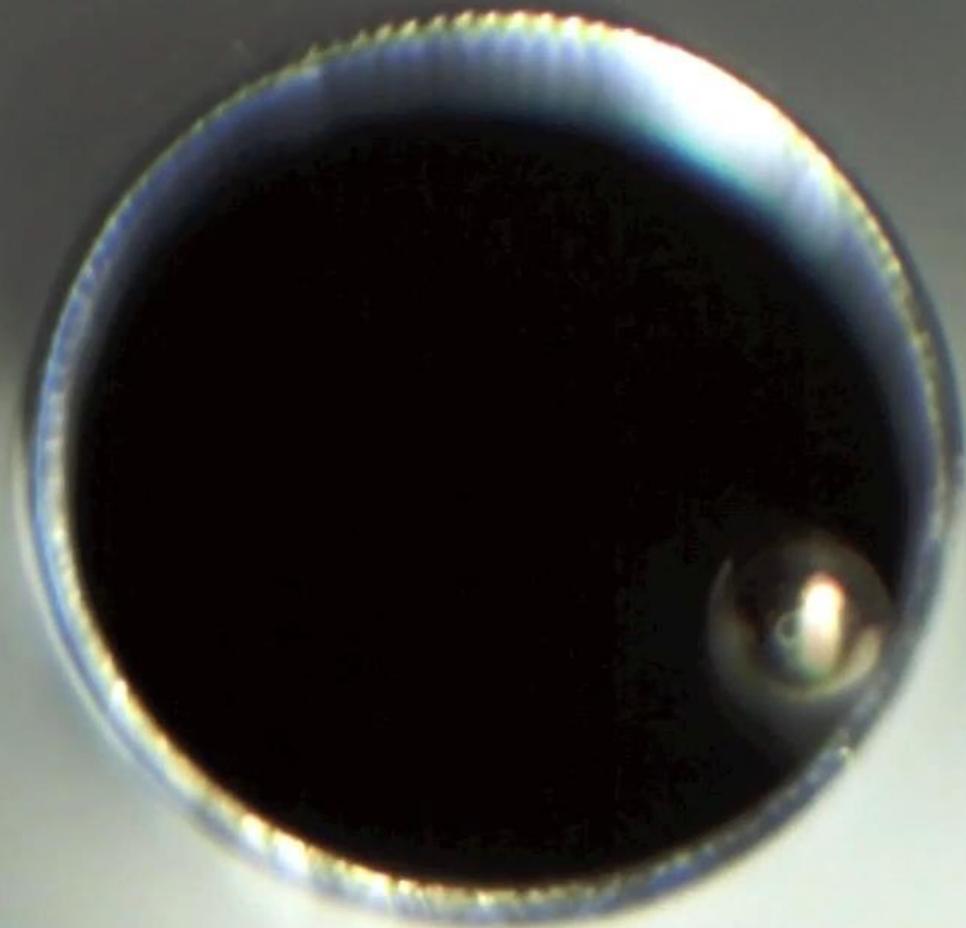
The Apollo™ System Wand



- Vacuum
 - Irrigation
- Proprietary, internal vibrational energy ensures rapid fluid/clot removal
 - Material must extrude into tip under vacuum before vibration and irrigation can act



20x power view
of Apollo Wand tip



Adjunctive Technologies

- Access
 - Burr Hole, mini-craniotomy
 - 19F Peel away sheath
- Neuronavigation: Trans-dural Ultrasound, Stealth
- Direct Visualization: Storz Neuroendoscope
- Location: OR

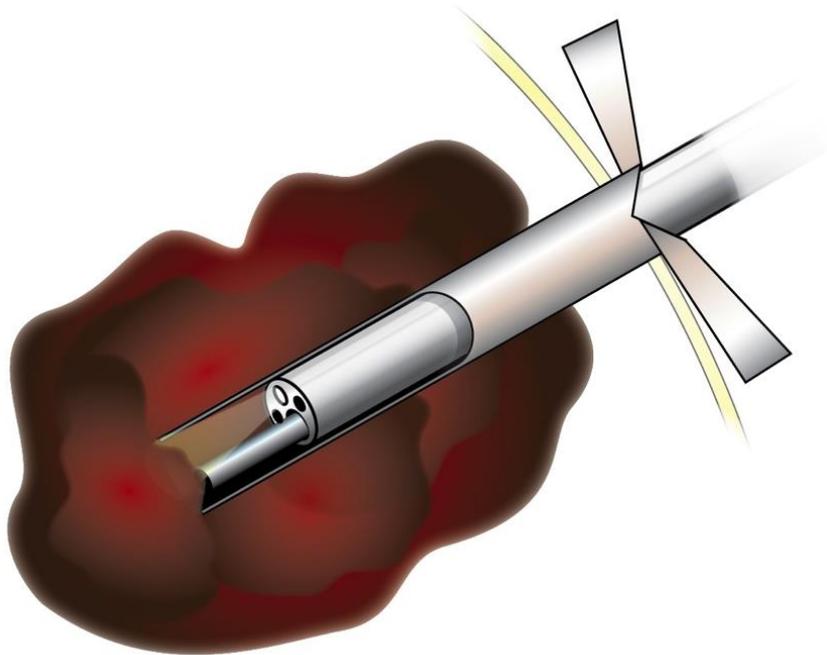


Apollo case

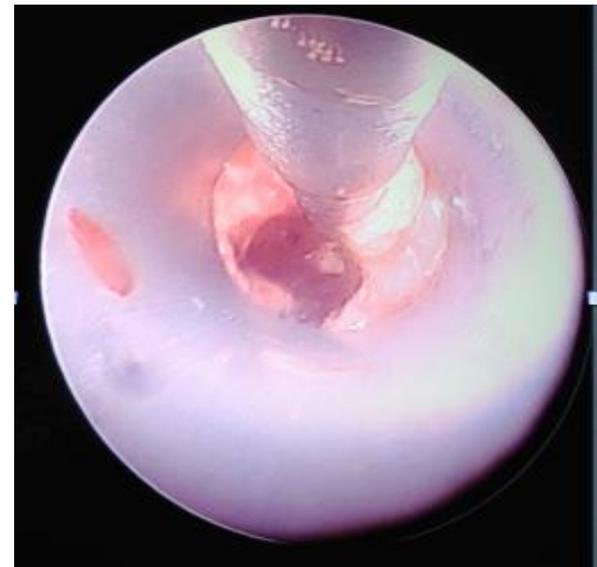
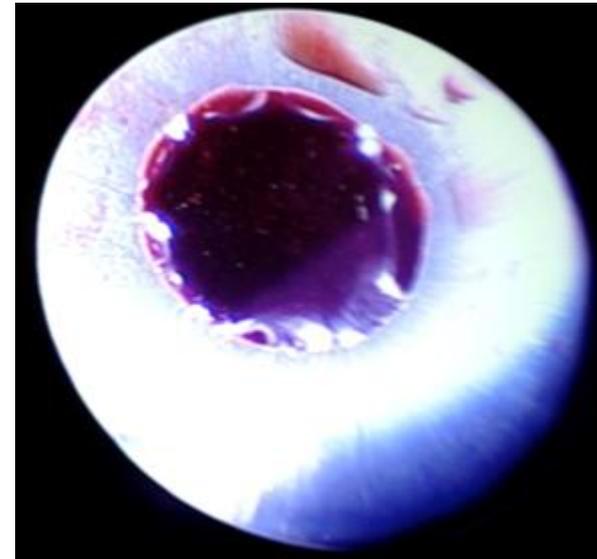


Procedure: Endoscopy

- Important to create a working space within the sheath away from clot at tip



- Evacuate the hematoma until tissue differentiation is seen.
- Exit sheath later in case.



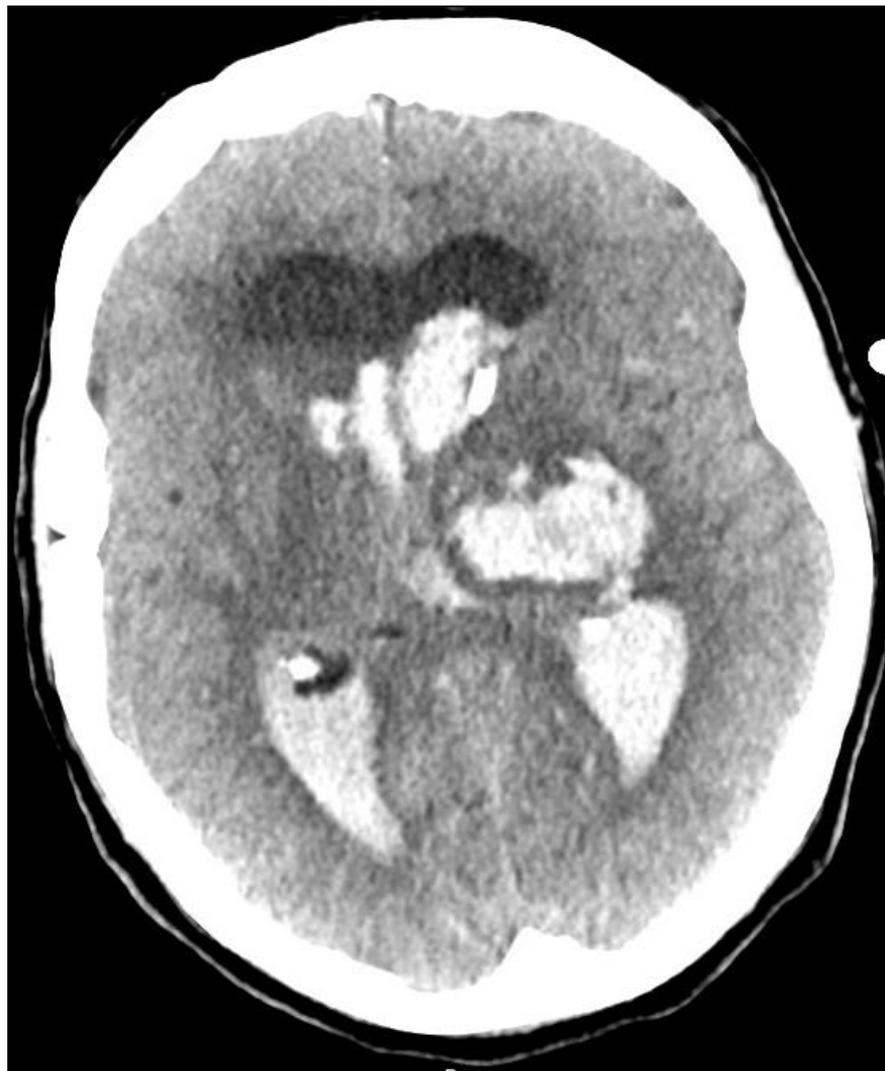
Setup: Room Orientation

- Apollo™ System near patient's head, behind physician
- Endoscopy tower and neuronavigation at patient's feet
- If using intraop CT, need short drapes, minimize other equipment near head

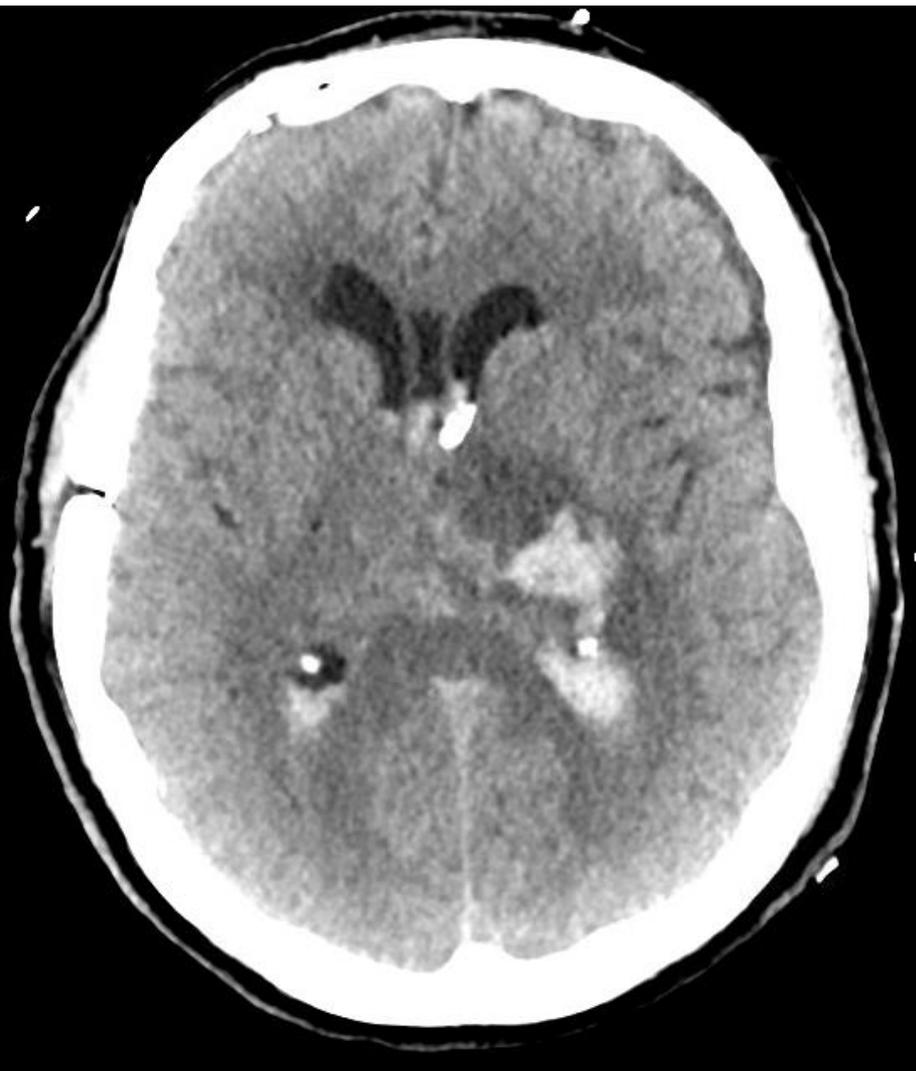


- 51y F found unresponsive at home
 - Exam
 - GCS 4T
 - Intubated
 - Pupils 2mm, non-reactive
 - Localizing lt UE
 - CT: Lt BG ICH/ IVH
 - OR: Apollo aspiration

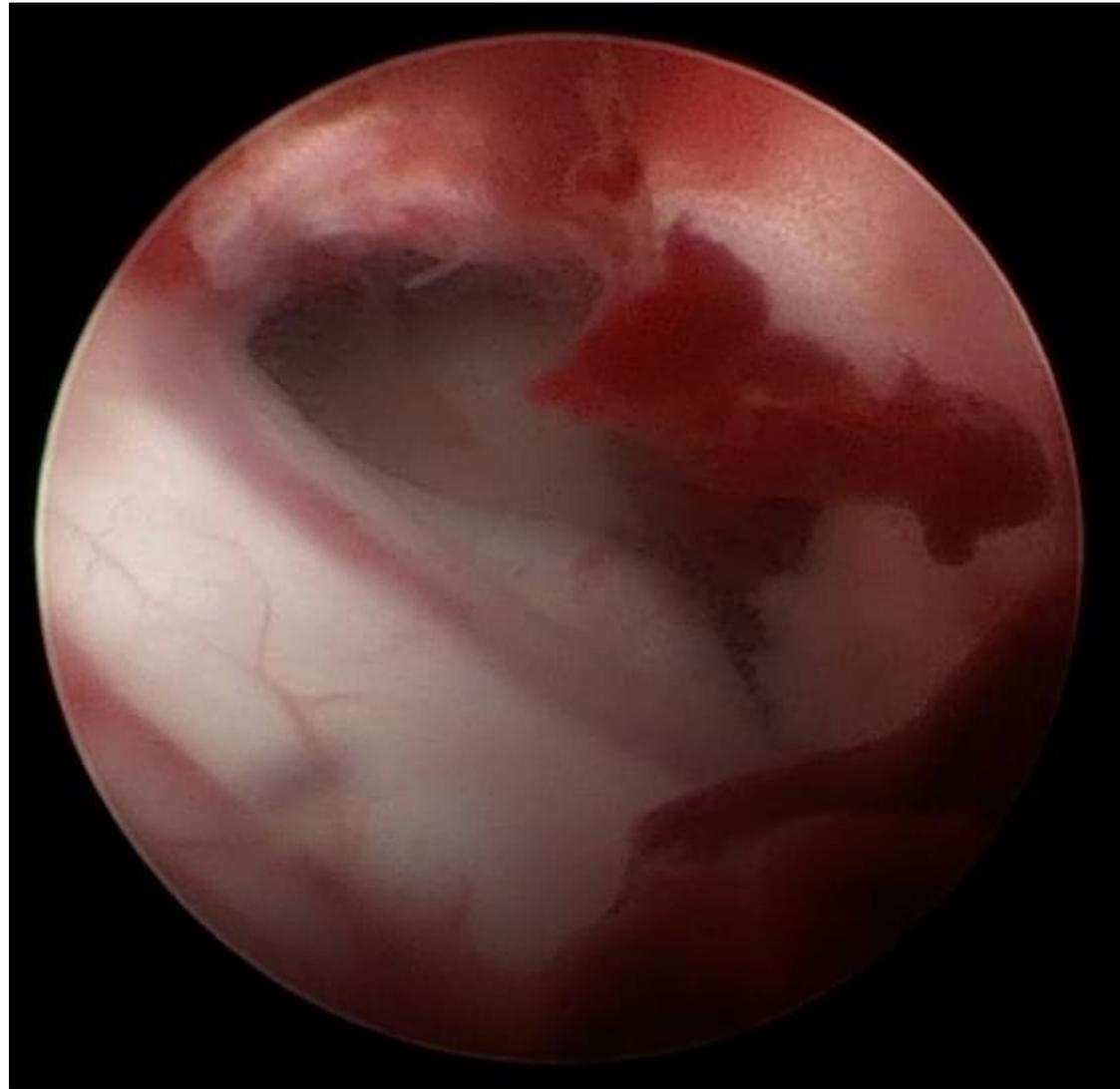
PRE



POST



Patient B Endoscope Video



Apollo case



Apollo case



Outcome

- Patient extubated following commands
- No need for VP shunt

- 49y M woke up w HA, emesis
 - Exam:
 - GCS 7T
 - Intubated
 - Localizing in all extremities
 - CT head:
 - Rt caudate ICH w IVH
 - OR:
 - Apollo aspiration
 - Permanent Shunt: None

PRE



POST





- 53y F found unresponsive
 - Initially GCS 8 at OSH, there decompensated to 4T
 - Exam:
 - GCS 4T
 - Intubated
 - Pupils 3mm, sluggish
 - Localizes rt UE
 - CT: pan IVH
 - OR: Apollo aspiration
 - Permanent Shunt: Yes

PRE



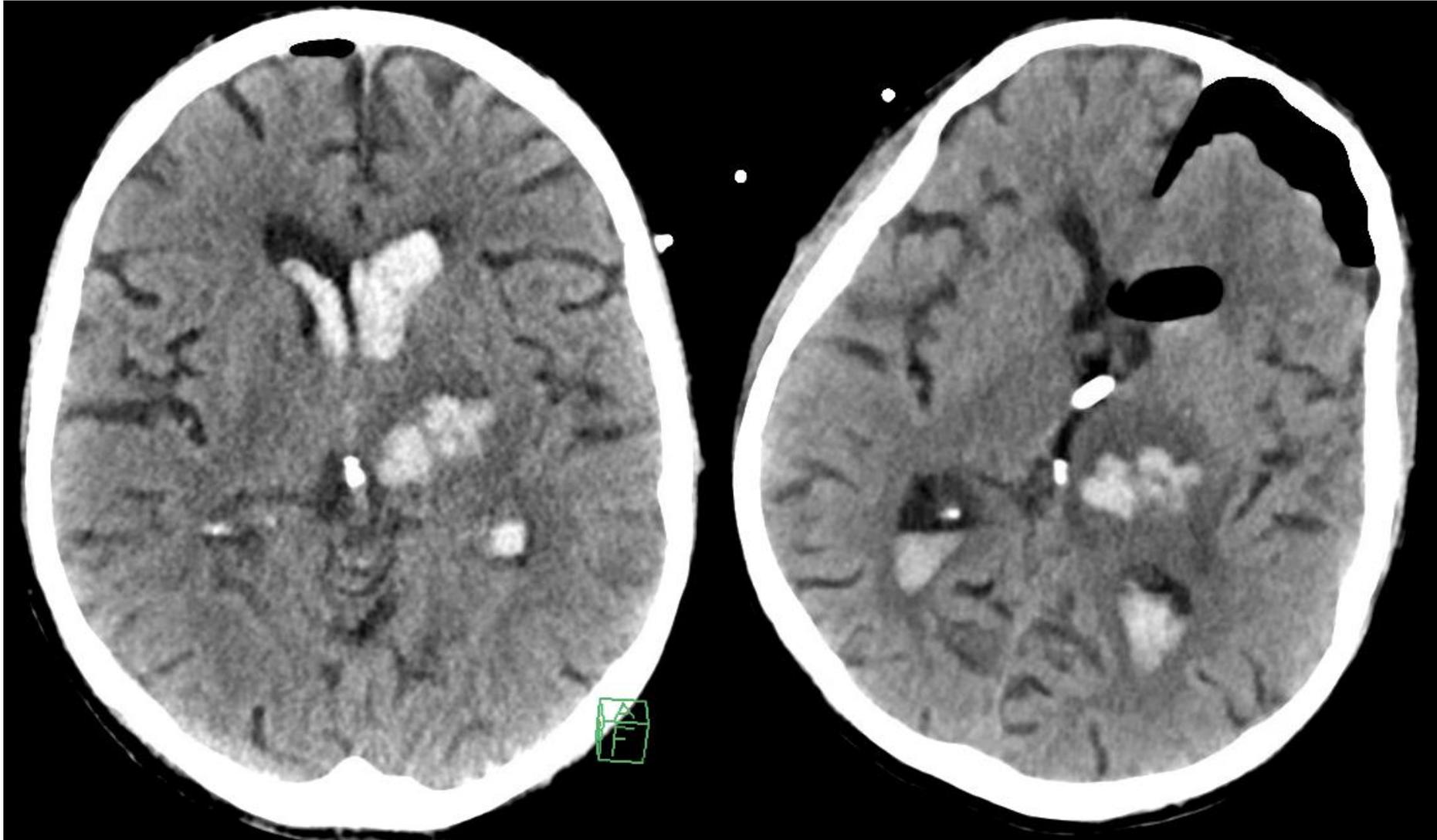
POST



- 56y M presented with confusion, rt sided weakness
 - Exam:
 - GCS 14
 - Dysarthric
 - Plegic on Rt
 - CT: lt thalamic ICH/ IVH
 - OR: Apollo aspiration
 - Permanent Shunt: None

PRE

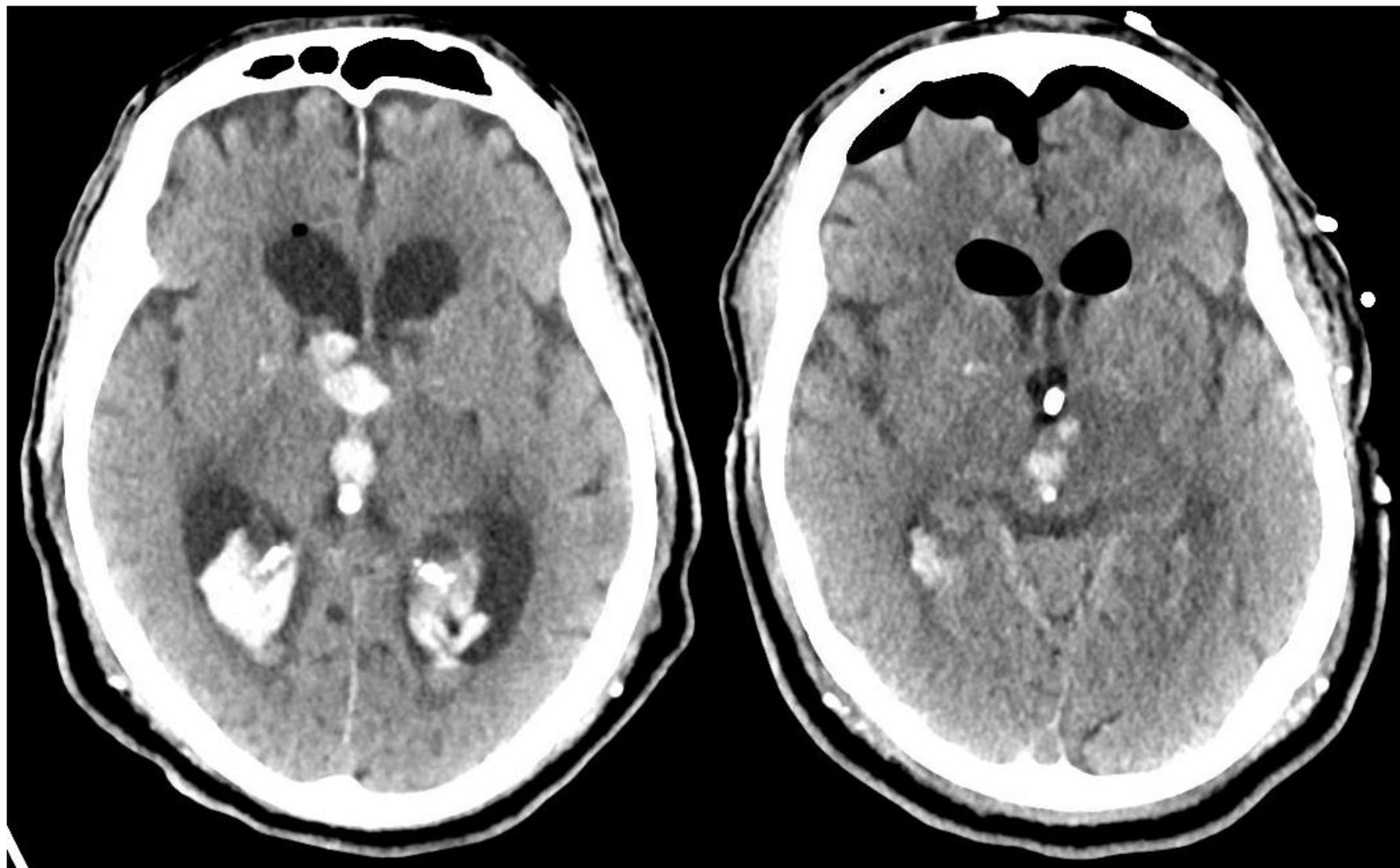
POST



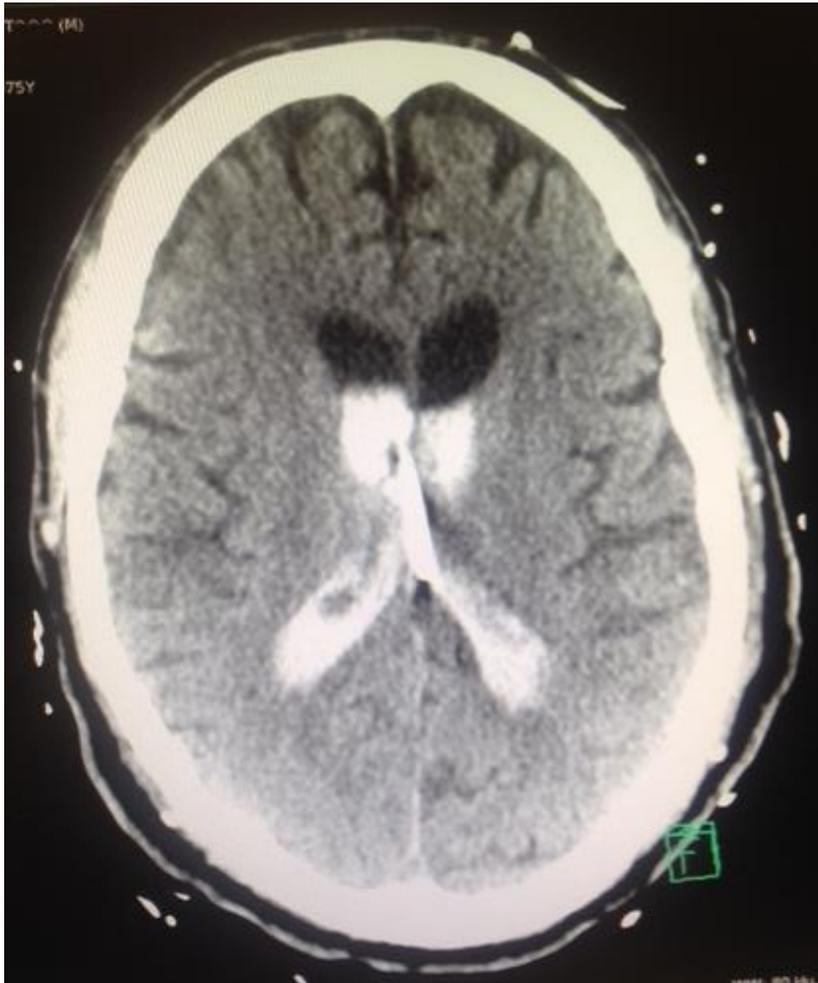
- 76y M found unresponsive
 - Exam
 - GCS 3T
 - Eyes closed to painful stimuli
 - No movement of extremities to deep painful stim
 - CT: Lt thalamic ICH w IVH
 - OR: Apollo aspiration
 - Permanent Shunt: None

PRE

POST

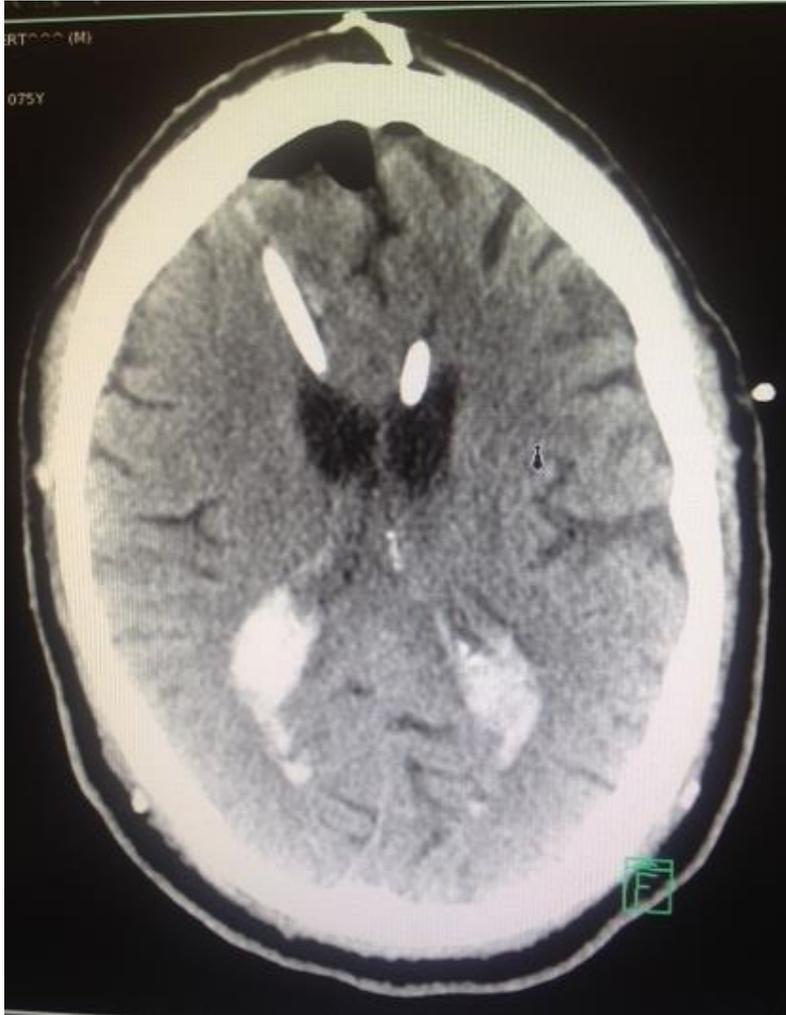


Pre-Op



- 64YO male, sudden headache, loss of consciousness
- Corneal reaction only, extending posturing upon arrival
- Immediate EVD insertion resulted in opening eyes to stimulation after several days.
- Bi-lateral, frontal burr holes for Apollo evacuation

Post-Op

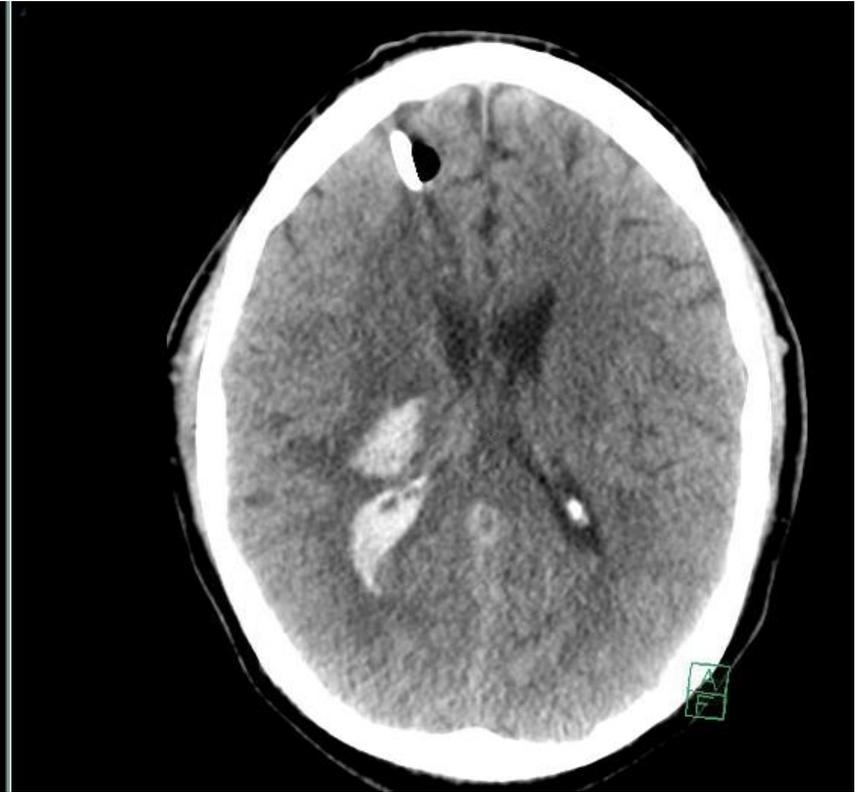


- Frontal horns cleared along with Foramen of Monro to restore circulation.
- Patient stable post-op.

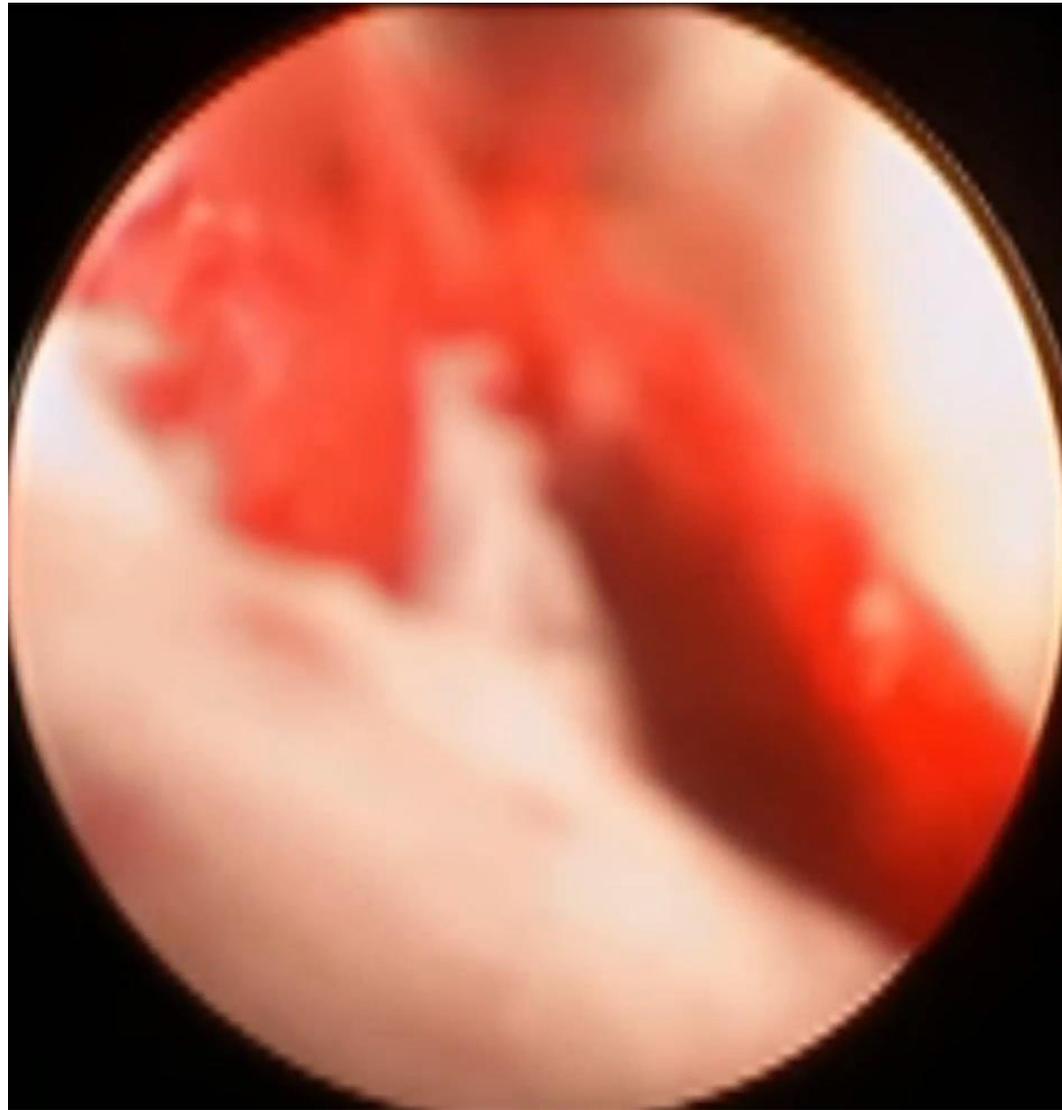
Pre-Op



Post-Op



- Surgical goal was removal of obstruction from frontal horn and Foramen of Monro



V. Procedures/Surgery – Surgical Treatment



Class I Recommendations	Class, Level of Evidence (LOE)
<p>Patients with cerebellar hemorrhage who are deteriorating neurologically or who have brainstem compression and/or hydrocephalus from a ventricular obstruction should undergo surgical removal of the hemorrhage as soon as possible. <i>(Unchanged from previous guideline)</i></p>	<p>Class I, LOE B</p>
Class II Recommendations	Class, Level of Evidence (LOE)
<p>For most patients with supratentorial ICH, the usefulness of surgery is not well established <i>(Revised from previous guideline)</i> <i>Specific exceptions and potential subgroup considerations are outlined below:</i></p>	<p>Class IIb, LOE A</p>
<p>A policy of early hematoma evacuation is not clearly beneficial compared to hematoma evacuation when patients deteriorate <i>(NEW recommendation)</i></p>	<p>Class IIb, LOE A</p>
<p>Supratentorial hematoma evacuation in deteriorating patients might be considered as a life-saving measure. <i>(NEW recommendation)</i></p>	<p>Class IIb, LOE C</p>



V. Procedures/Surgery – Surgical Treatment



Class II Recommendations, cont'd	Class, Level of Evidence (LOE)
<p>Decompressive craniectomy with or without hematoma evacuation might reduce mortality for patients with supratentorial ICH who are in coma, have large hematomas with midline shift, or have elevated ICP refractory to medical management. <i>(NEW recommendation)</i></p>	Class IIb, LOE C
<p>The effectiveness of minimally invasive clot evacuation utilizing stereotactic or endoscopic aspiration with or without thrombolytic usage is uncertain. <i>(Revised from previous guideline)</i></p>	Class IIb, LOE B
Class III Recommendations	Class, Level of Evidence (LOE)
<p>Initial treatment of these patients (see Class I recommendation above) with ventricular drain rather than surgical evacuation is not recommended. <i>(Unchanged from previous guideline)</i></p>	Class III, LOE C



V. Procedures/Surgery



Surgical Treatment of ICH (Clot Removal)

- Role of surgery for most patients with spontaneous ICH remains controversial.
- Randomized trials comparing surgery (hematoma evacuation) to conservative management have not demonstrated a clear benefit.

V. Procedures/Surgery



Timing of Surgery

- Timing of surgery for ICH remains controversial
- Some trials suggest improved outcomes with early surgery (pooled analysis indicated within 8 hours of hemorrhage)
- Ultra-early (within 4 hours) craniotomy was found to increase the risk of rebleeding in a small study.

V. Procedures/Surgery



Craniotomy for Supratentorial Hemorrhage

- Early hematoma evacuation has not been shown beneficial in the two largest randomized trials.
- Unclear whether surgery may benefit specific groups with supratentorial ICH.

Why do we care about ICH?



NEUROLOGICAL INJURY AFTER ICH

- Stage 1: Mechanical Disruption
 - Immediate mechanical destruction of neurons
- Stage 2: Local Ischemia
 - Local mass effect limits regional perfusion around the hematoma

NEUROLOGICAL INJURY AFTER ICH

Stage 3: Hemotoxicity

- Hours, days even weeks after hemorrhage
- Direct toxic effects of blood product degradation on surround brain tissue

ICH TREATMENT

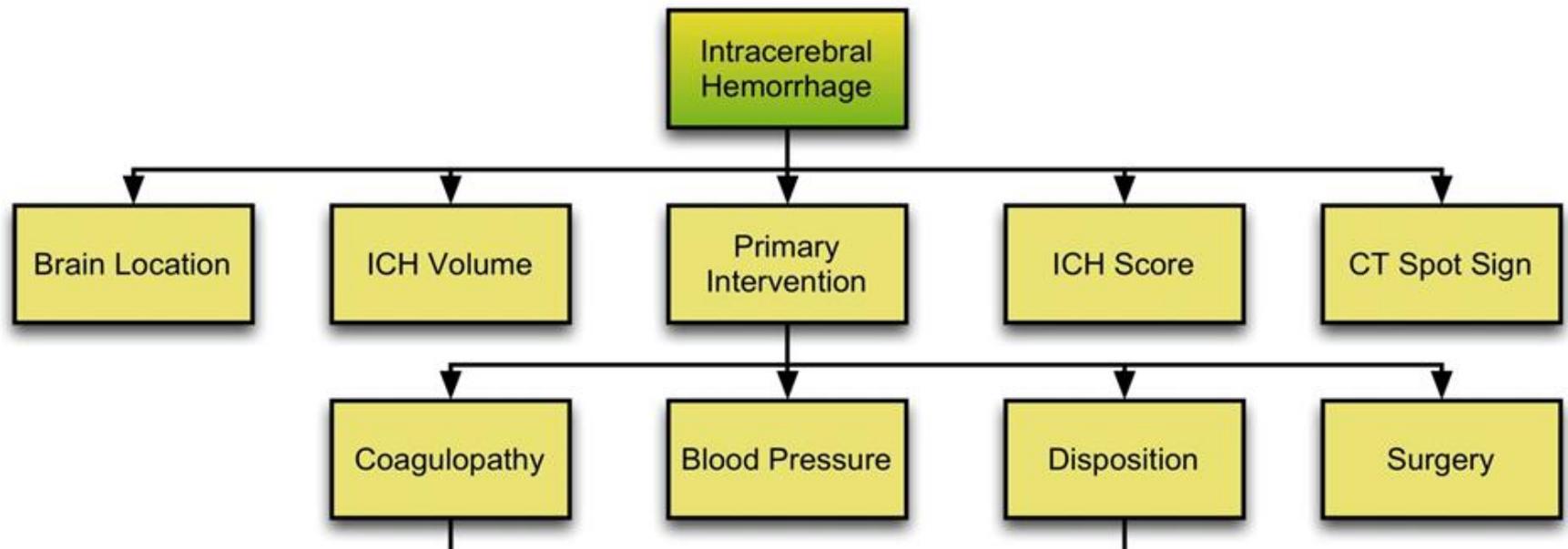
- Removal of blood products could improve outcomes
 - Relieve local ischemia
 - Remove hemotoxic material
- Must be accomplished without any additional injury to the adjacent normal brain

Rush Center for Neuroendovascular surgery



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Intracerebral Hemorrhage



Minimally Invasive Surgery Plus Recombinant Tissue-type Plasminogen Activator for Intracerebral Hemorrhage Evacuation **Decreases Perihematomal Edema**

W. Andrew Mould, BA*; J. Ricardo Carhuapoma, MD*; John Muschelli, ScM; Karen Lane, CCRP; Timothy C. Morgan, MPH; Nichol A. McBee, MPH; Amanda J. Bistran-Hall, BS; Natalie L. Ullman, BS; Paul Vespa, MD; Neil A. Martin, MD; Issam Awad, MD; Mario Zuccarello, MD; Daniel F. Hanley, MD; for the MISTIE Investigators

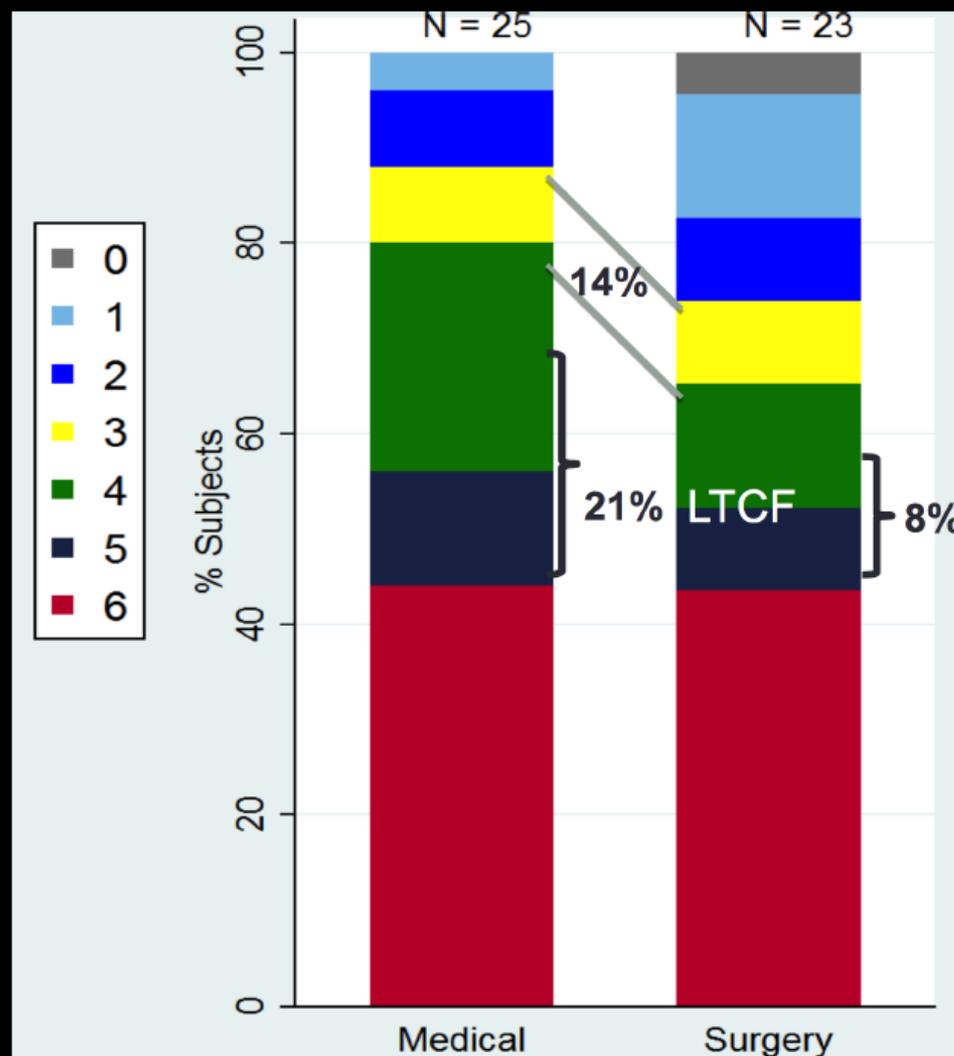
Background and Purpose—Perihematomal edema (PHE) can worsen outcomes after intracerebral hemorrhage (ICH). Reports suggest that blood degradation products lead to PHE. We hypothesized that hematoma evacuation will reduce PHE volume and that treatment with recombinant tissue-type plasminogen activator (rt-PA) will not exacerbate it.

Methods—Minimally invasive surgery and rt-PA in ICH evacuation (MISTIE) phase II tested safety and efficacy of hematoma evacuation after ICH. We conducted a semiautomated, computerized volumetric analysis on computed tomography to assess impact of hematoma removal on PHE and effects of rt-PA on PHE. Volumetric analyses were performed on baseline stability and end of treatment scans.

Results—Seventy-nine surgical and 39 medical patients from minimally invasive surgery and rt-PA in ICH evacuation phase II (MISTIE II) were analyzed. Mean hematoma volume at end of treatment was $19.6 \pm 14.5 \text{ cm}^3$ for the surgical cohort and $40.7 \pm 13.9 \text{ cm}^3$ for the medical cohort ($P < 0.001$). Edema volume at end of treatment was lower for the surgical cohort: $27.7 \pm 13.3 \text{ cm}^3$ than medical cohort: $41.7 \pm 14.6 \text{ cm}^3$ ($P < 0.001$). Graded effect of clot removal on PHE was observed when patients with $>65\%$, 20% to 65% , and $<20\%$ ICH removed were analyzed ($P < 0.001$). Positive correlation between PHE reduction and percent of ICH removed was identified ($\rho = 0.658$; $P < 0.001$). In the surgical cohort, 69 patients underwent surgical aspiration and rt-PA, whereas 10 underwent surgical aspiration only. Both cohorts achieved similar clot reduction: surgical aspiration and rt-PA, $18.9 \pm 14.5 \text{ cm}^3$; and surgical aspiration only, $24.5 \pm 14.0 \text{ cm}^3$ ($P = 0.26$). Edema at end of treatment in surgical aspiration and rt-PA was $28.1 \pm 13.8 \text{ cm}^3$ and $24.4 \pm 8.6 \text{ cm}^3$ in surgical aspiration only ($P = 0.41$).

Conclusions—Hematoma evacuation is associated with significant reduction in PHE. Furthermore, PHE does not seem to be exacerbated by rt-PA, making such neurotoxic effects unlikely when the drug is delivered to intracranial clot. (*Stroke*.

MISTIE II Trial Results: 365-Day Outcome and Cost-benefit

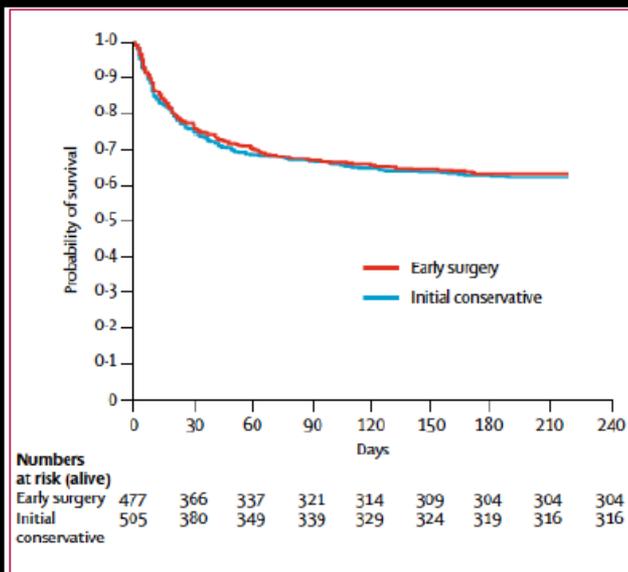


Early surgery versus initial conservative treatment in patients with spontaneous supratentorial intracerebral haematomas in the International Surgical Trial in Intracerebral Haemorrhage (STICH): a randomised trial

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*

Findings 1033 patients from 83 centres in 27 countries were randomised to early surgery (503) or initial conservative treatment (530). At 6 months, 51 patients were lost to follow-up, and 17 were alive with unknown status. Of 468 patients randomised to early surgery, 122 (26%) had a favourable outcome compared with 118 (24%) of 496 randomised to initial conservative treatment (odds ratio 0.89 [95% CI 0.66–1.19], $p=0.414$); absolute benefit 2.3% (–3.2 to 7.7), relative benefit 10% (–13 to 33).

Interpretation Patients with spontaneous supratentorial intracerebral haemorrhage in neurosurgical units show no overall benefit from early surgery when compared with initial conservative treatment.

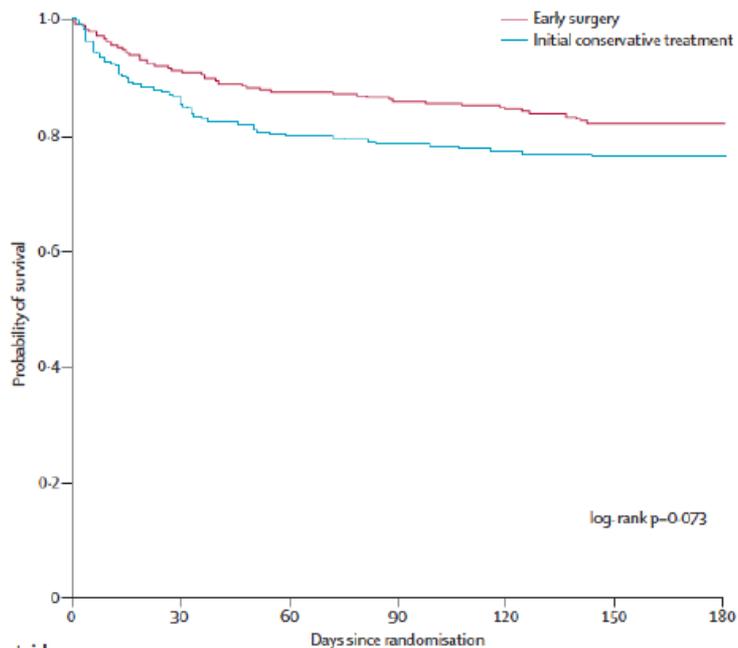


Early surgery versus initial conservative treatment in patients with spontaneous supratentorial lobar intracerebral haematomas (STICH II): a randomised trial

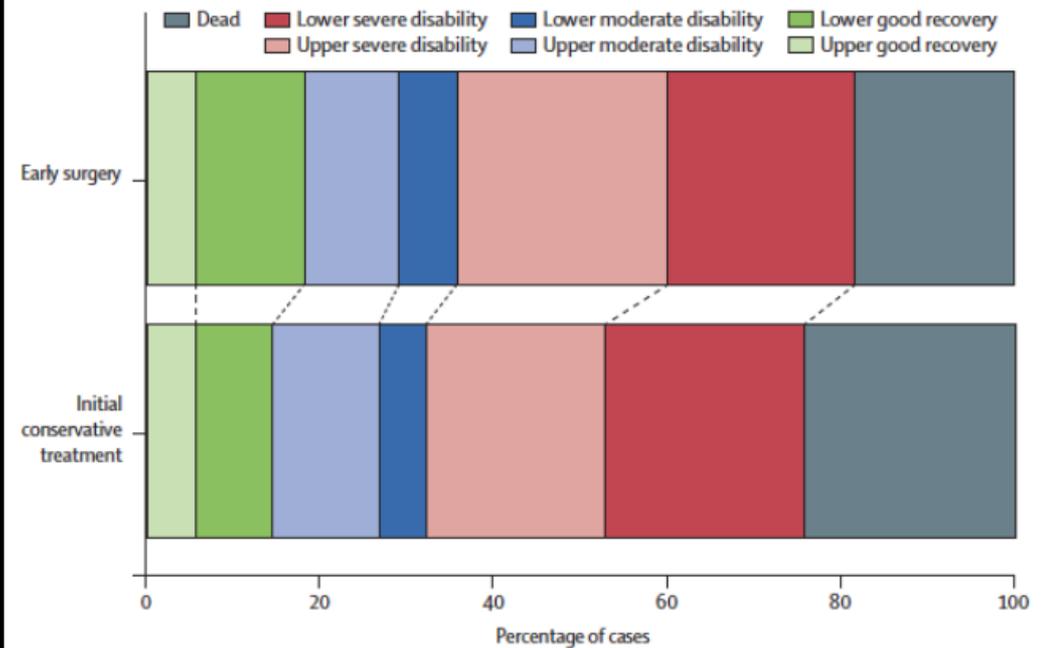
A David Mendelow, Barbara A Gregson, Elise N Rowan, Gordon D Murray, Anil Gholkar, Patrick M Mitchell, for the STICH II Investigators

Findings 307 of 601 patients were randomly assigned to early surgery and 294 to initial conservative treatment; 298 and 291 were followed up at 6 months, respectively; and 297 and 286 were included in the analysis, respectively. 174 (59%) of 297 patients in the early surgery group had an unfavourable outcome versus 178 (62%) of 286 patients in the initial conservative treatment group (absolute difference 3.7% [95% CI -4.3 to 11.6], odds ratio 0.86 [0.62 to 1.20]; $p=0.367$).

Interpretation The STICH II results confirm that early surgery does not increase the rate of death or disability at 6 months and might have a small but clinically relevant survival advantage for patients with spontaneous superficial intracerebral haemorrhage without intraventricular haemorrhage.



Number at risk	0	30	60	90	120	150	180
Early surgery	300	271	260	255	251	231	169
Initial conservative	292	252	232	237	222	202	148





***M*inimally *I*nvasive **S**ubcortical *P*arafascicular **A**ccess for
Clot *E*vacuation**

MISPACE

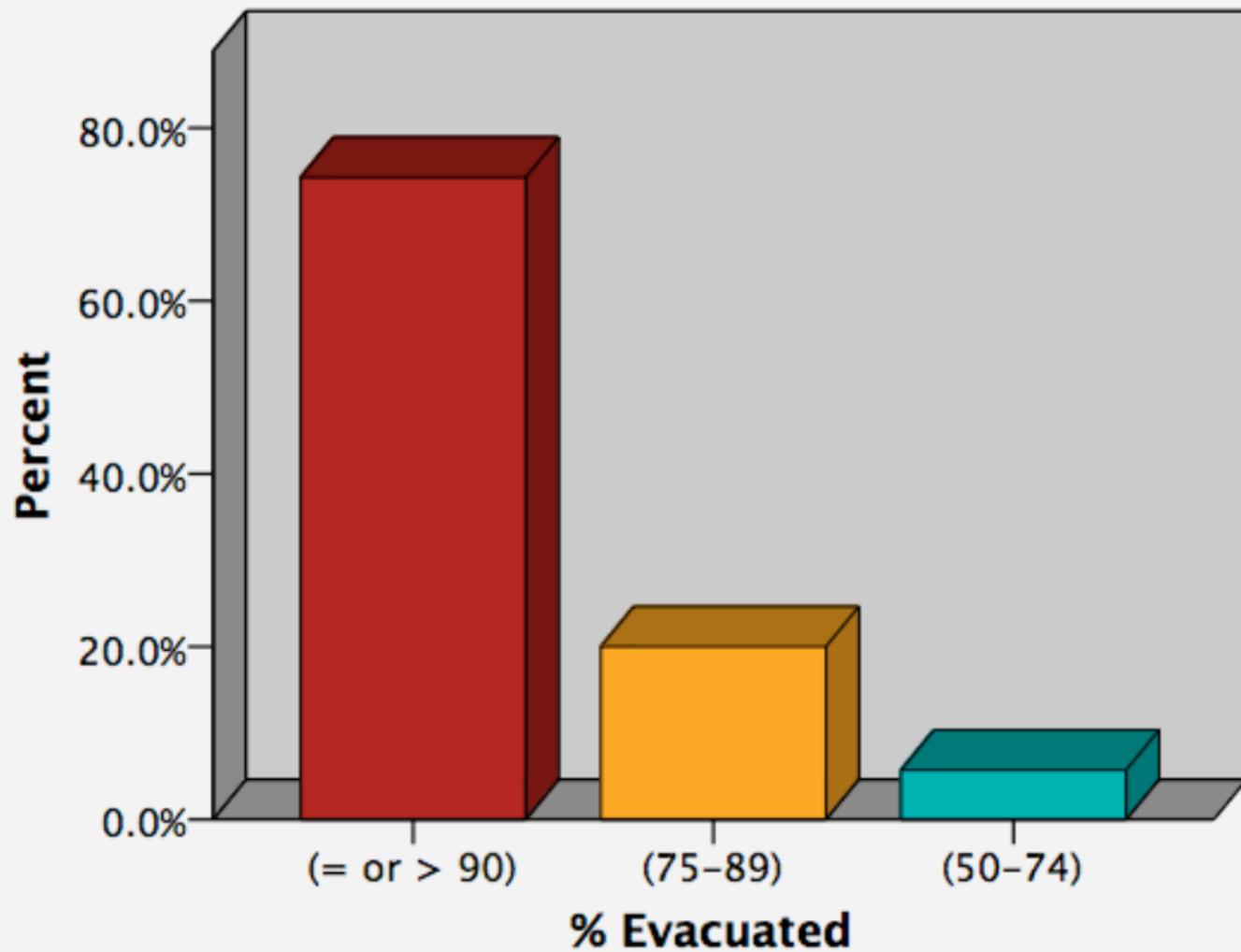
Maximize Clot Removal
+
Minimize Tissue Disruption

Methods

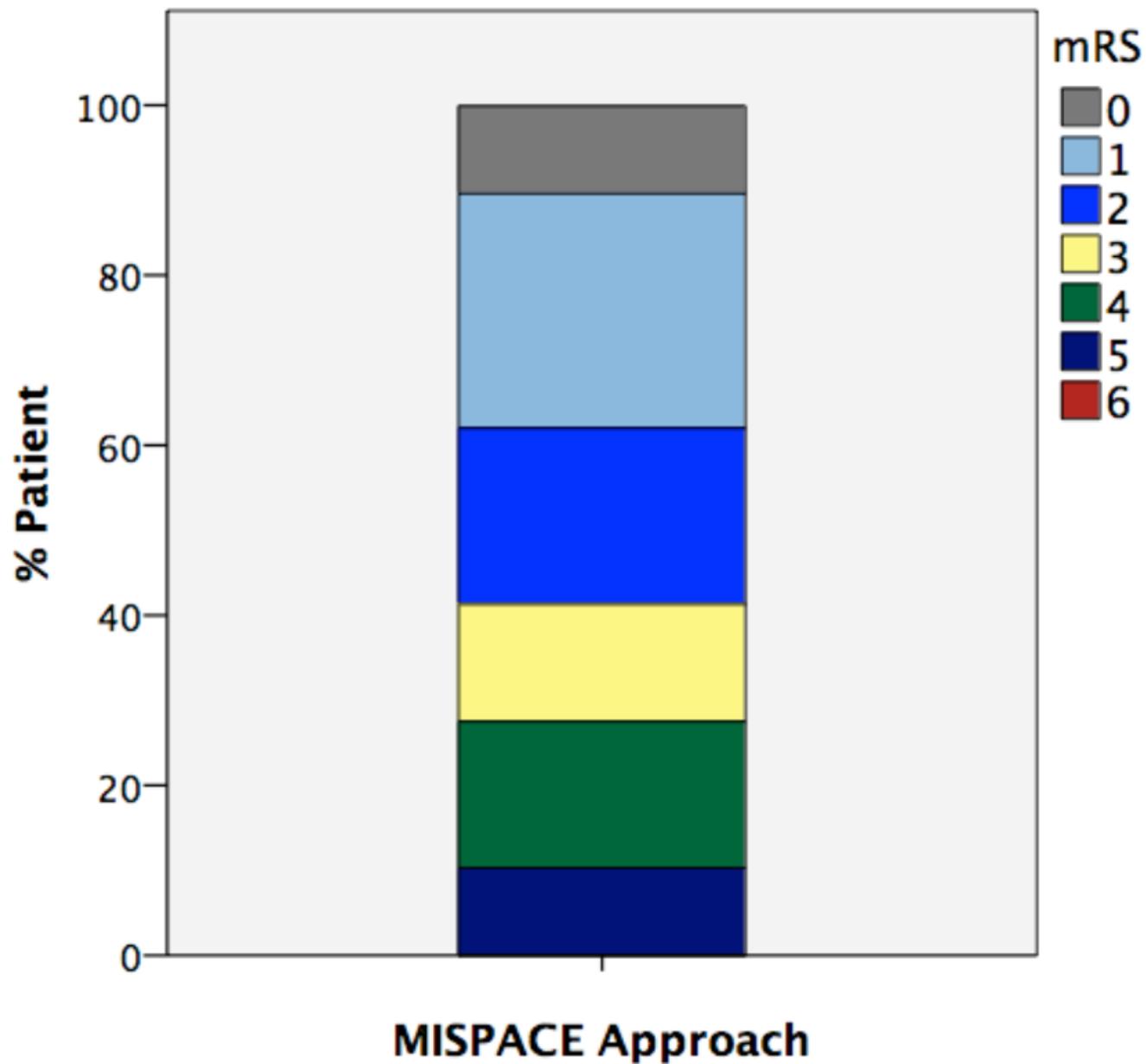


- Retrospective study
- Study time: 2 years
- 10 North American Centers
- 11 Surgeons, CME accredited course

Percentage of Hematoma Evacuated



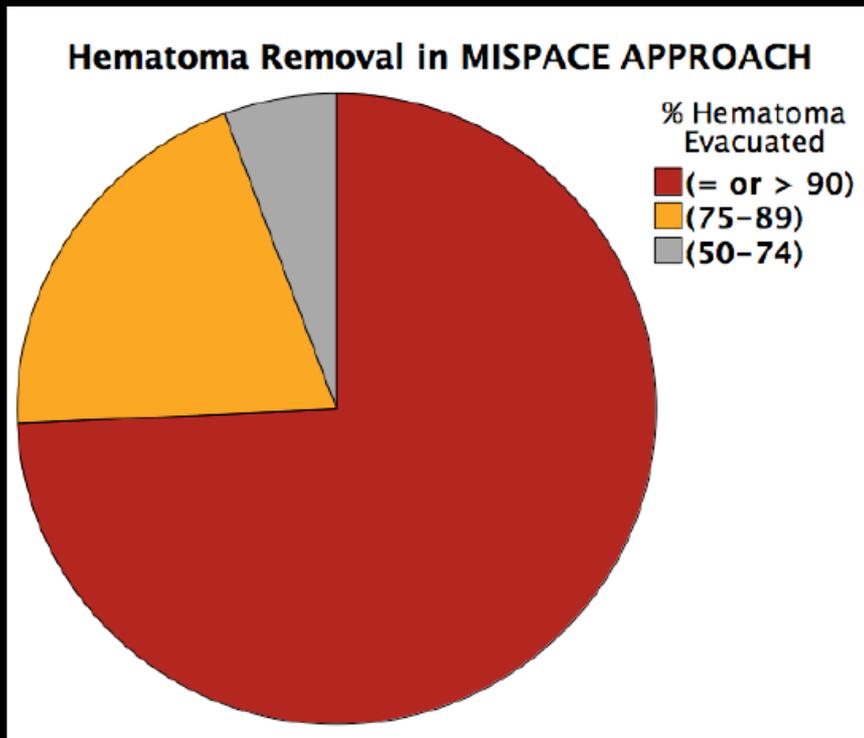
Post-Op mRS



MISPACE Approach

N= 35

Average Clot Reduction ≈ 89%



Mortality rate: 0.0%

Penumbra Apollo Approach

N= 29

Average Clot Reduction ≈ 54%

No Significant Change in GCS

Mortality rate: 13.8%

PREVALENT DISEASE

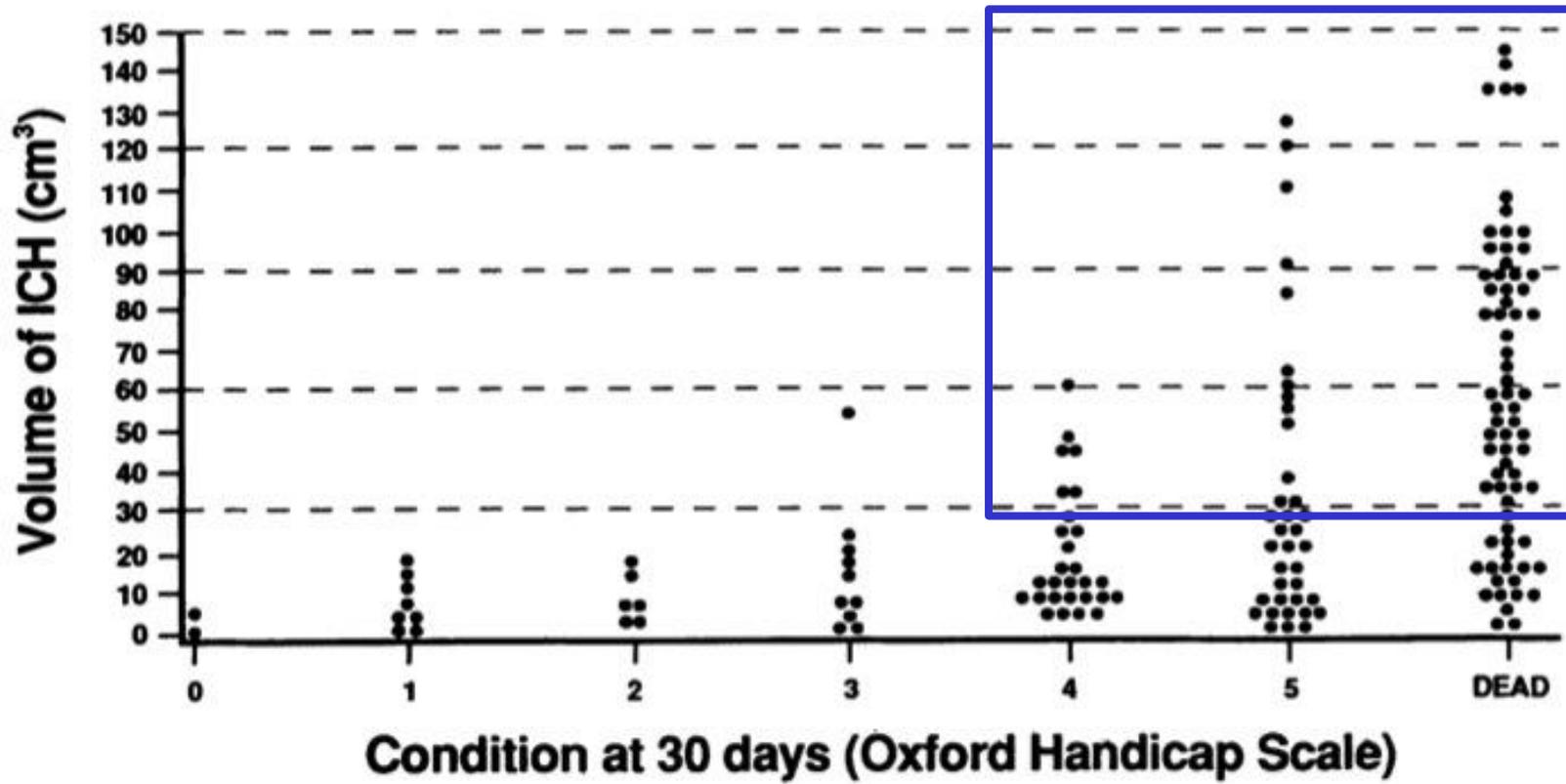
- Accounts for 10-15% of all strokes
- Much more common than SAH
- Affects 80,000 in the US, 2M WW

CLINICALLY DEVASTATING DISEASE

- Highest rates of morbidity, mortality, and economic burden of any of the stroke subtypes
- 30-day mortality of ~45%, majority dead in first 2 days
- IVH extension raises mortality to 50 – 80%
- Majority of survivors are severely disabled
- Only 20% of survivors live independently at 6 months

BRODERICK et al., STROKE 1993

- 99% of patients with >30cc hemorrhage have an Oxford Handicap score of 4 or greater



NO EFFECTIVE TREATMENTS

- While the major advances have occurred in the treatment of other forms of stroke...
- **NO MEDICAL OR SURGICAL TREATMENT HAS BEEN SHOWN TO BE BENEFICIAL IN THESE PATIENTS**

ORPHANED POPULATION

- Reimbursements for the medical management of ICH patients are poor and their care is time and resource intensive
- ICH has become an orphaned disease

CURRENT STATUS

- ICH patients are an optimal cohort for new and innovative (although unproven) therapies

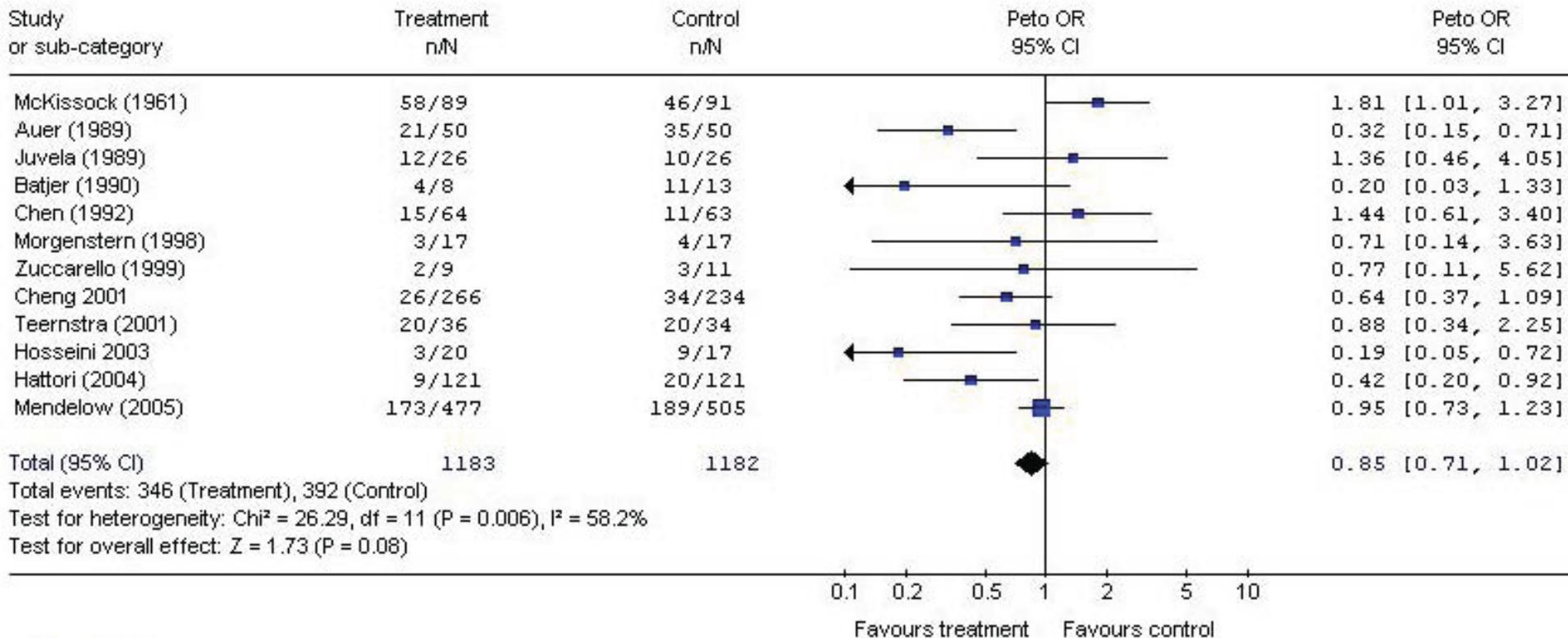
**Early hematoma
evacuation...why
would it be beneficial?**

OPEN SURGERY IS NOT EFFECTIVE

- Meta-analysis of 2186 cases from published literature (1985-2009)
- Presumably because injury to the surrounding brain during surgery negates the benefits of hemorrhage evacuation

NO BENEFIT FOR MORTALITY AFTER SURGERY

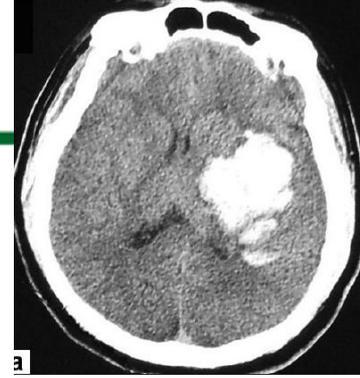
Review: Surgery in Intracerebral haemorrhage
 Comparison: 01 Surgery v Control
 Outcome: 02 Death



EVIDENCE FOR MIS

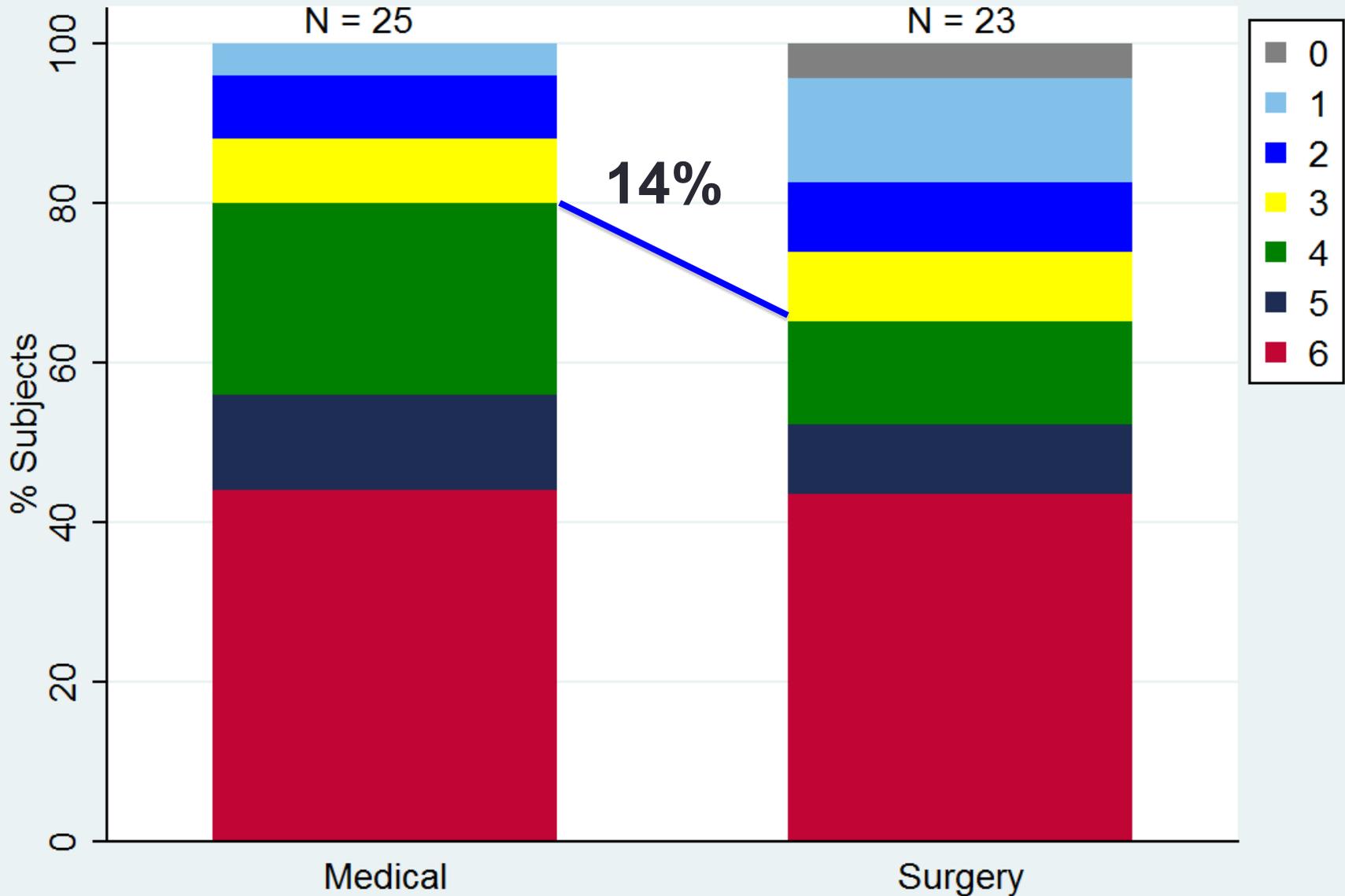
- Zhou et al., Stroke 2012 Meta-analysis of 12 high quality MIS trials involving 1955 patients
 - MIS vs. Medical Management
 - MIS reduced death or dependence at end of follow up (OR, 0.54, $P < 0.00001$)
 - MIS reduced death at the end of follow up (OR, 0.53, $P < 0.00001$)

MISTIE II (ICH)

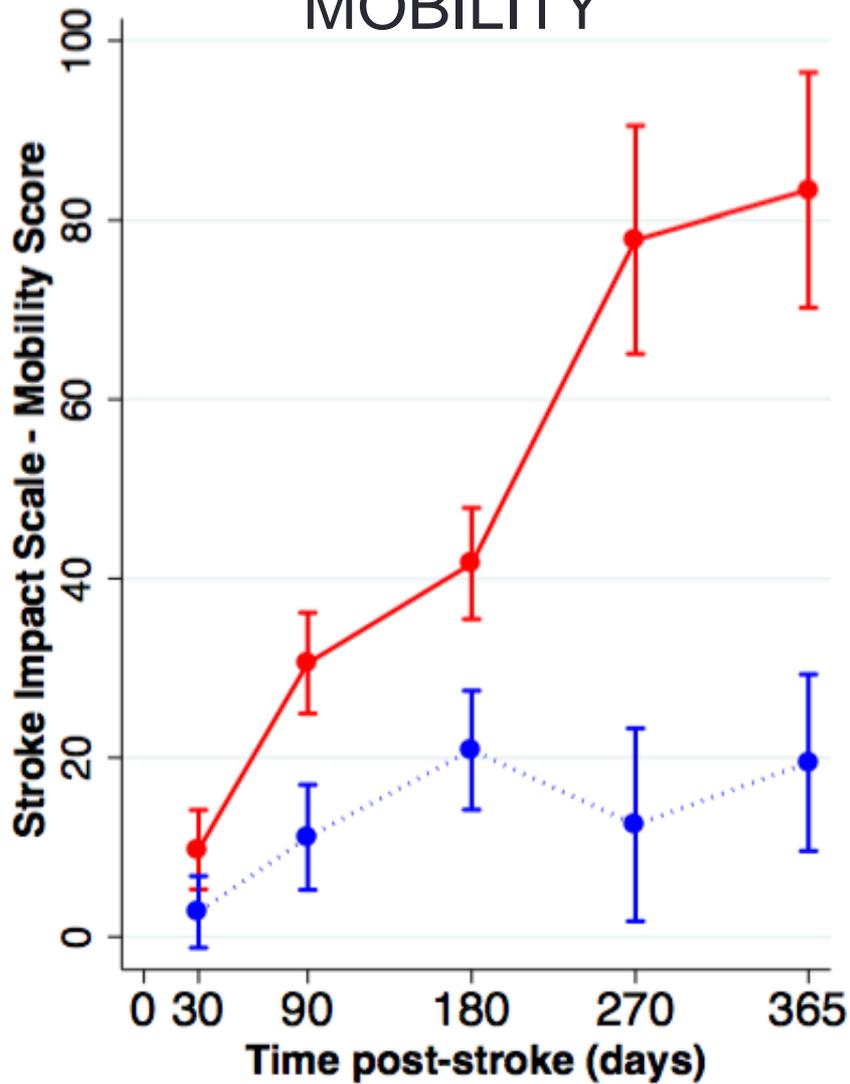


- Phase II trial of minimally invasive stereotactic hematoma aspiration followed by catheter placement and t-PA irrigation for up to 4 days
- Significant reduction in peri-hematomal edema (PHE)

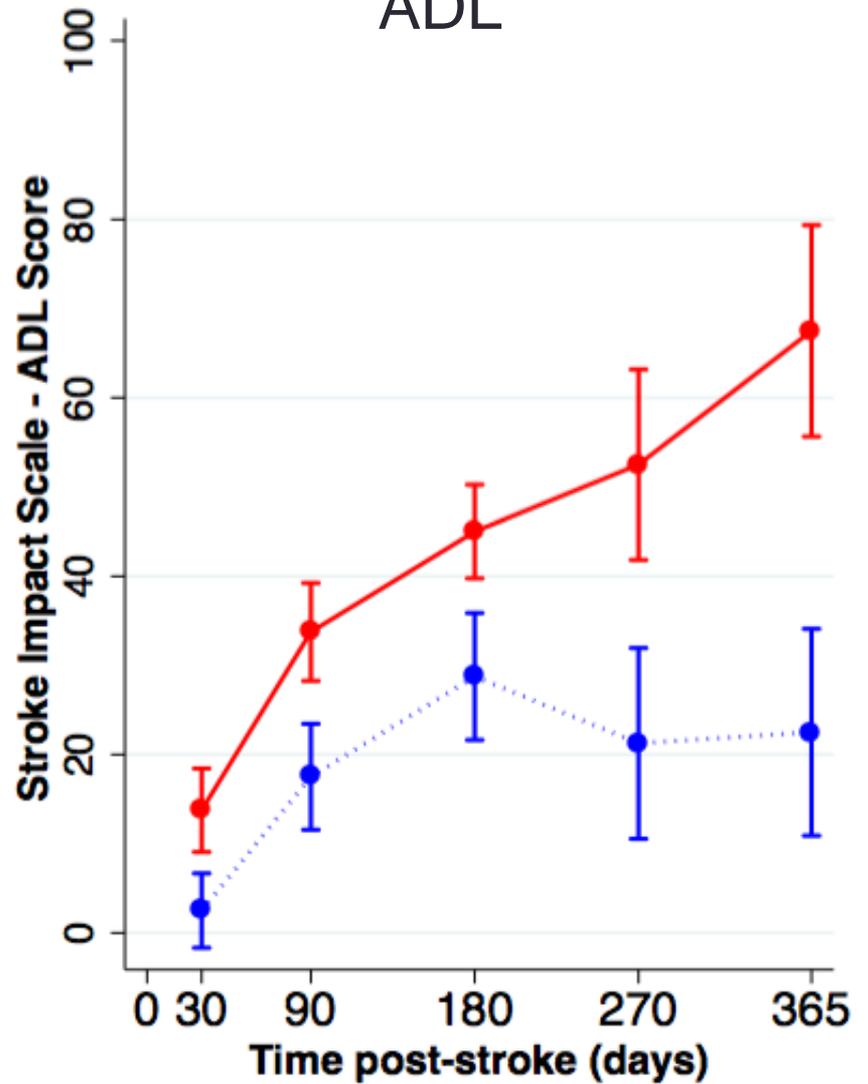
Day 365 modified Rankin Scale (mRS)



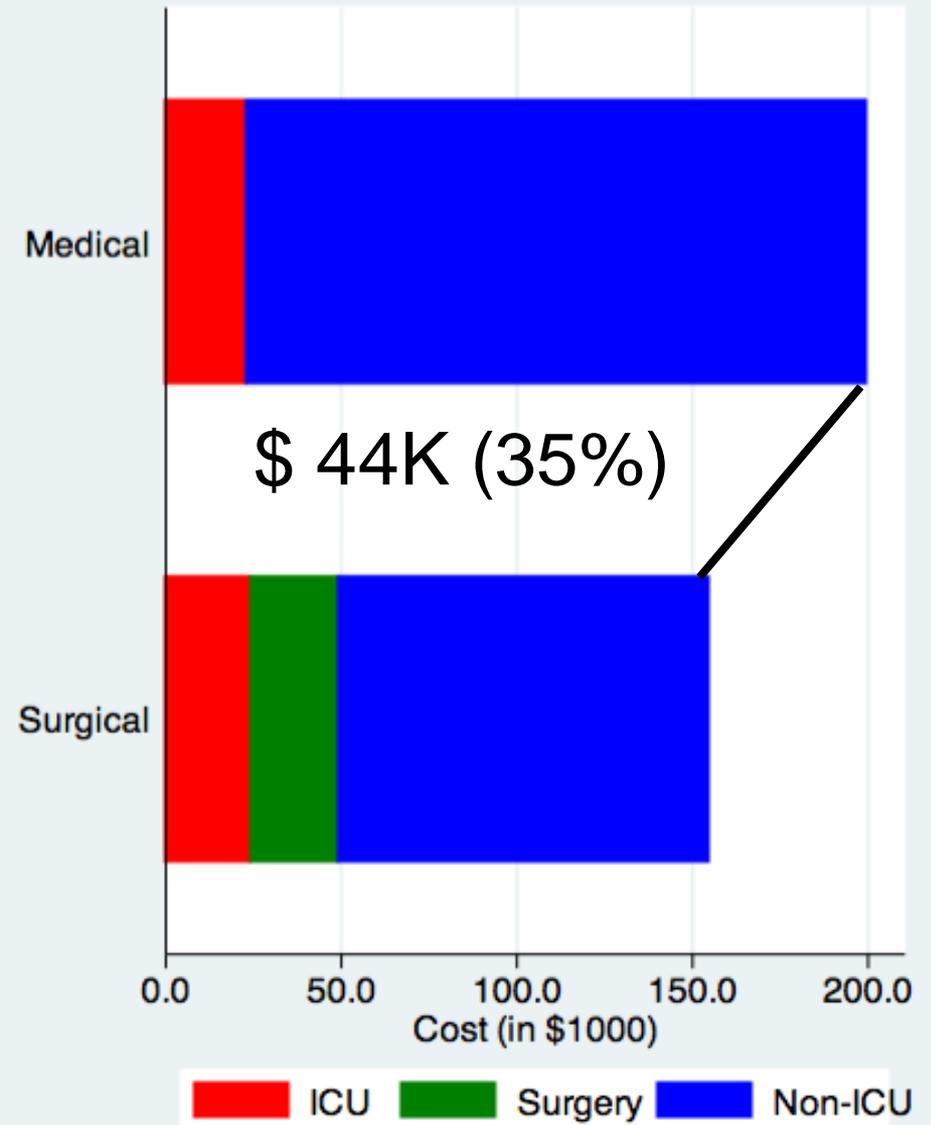
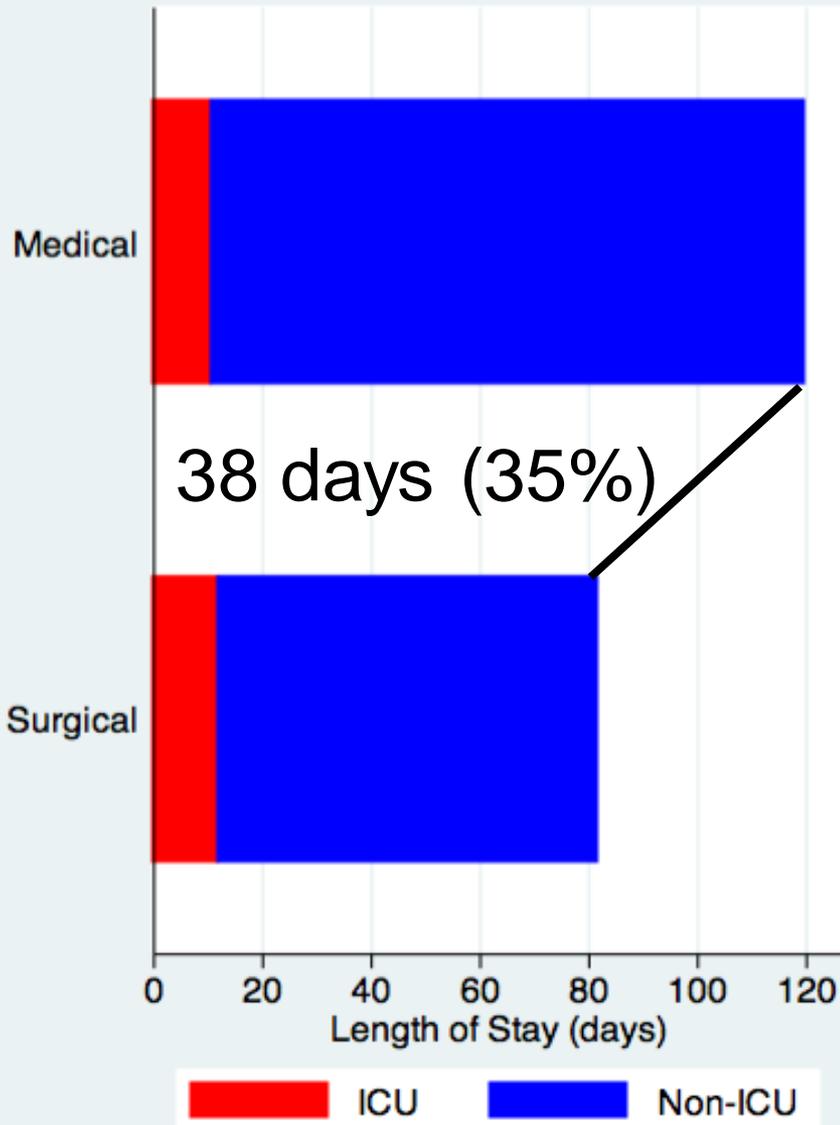
MOBILITY



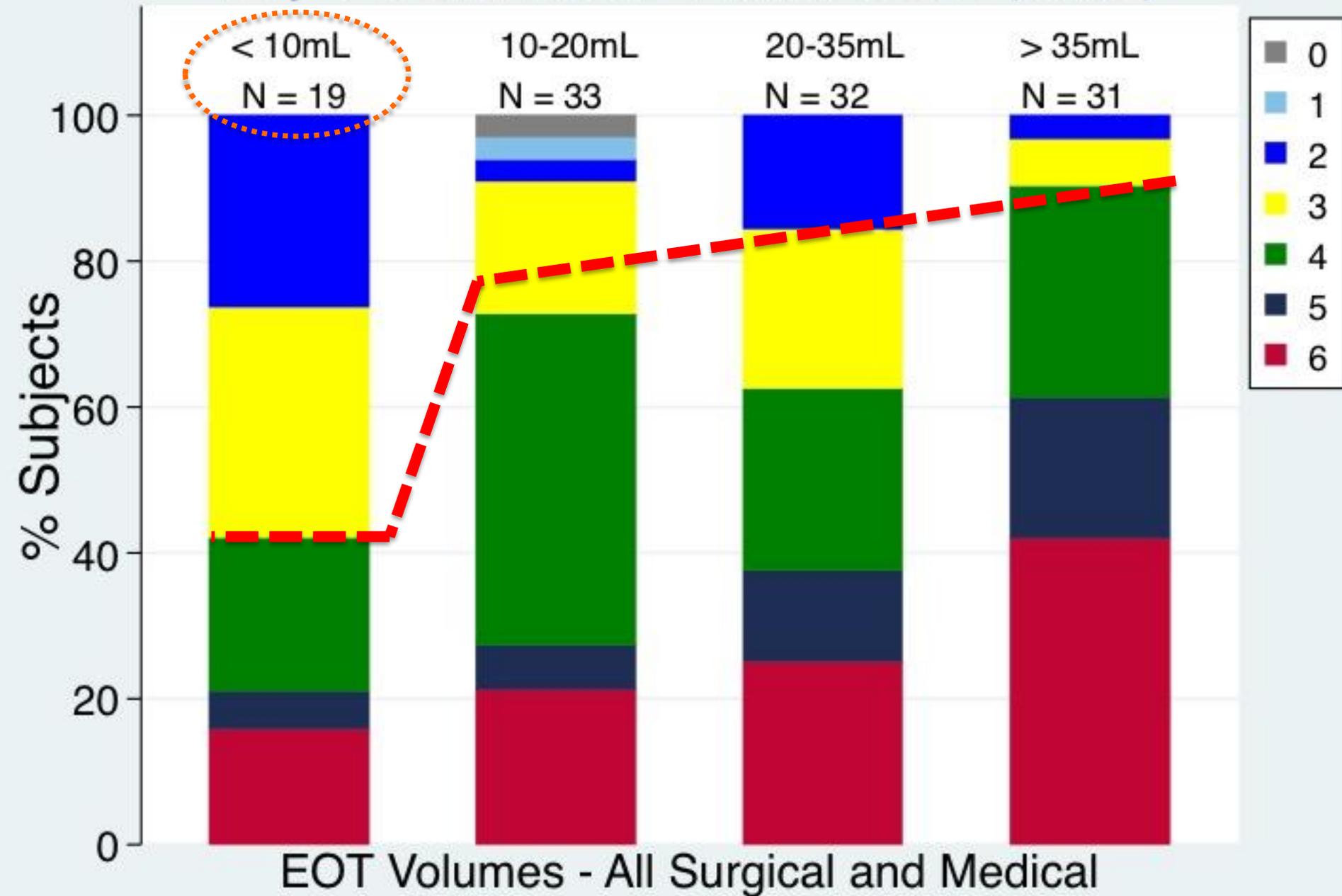
ADL



Length of Stay and Cost by Treatment Arm



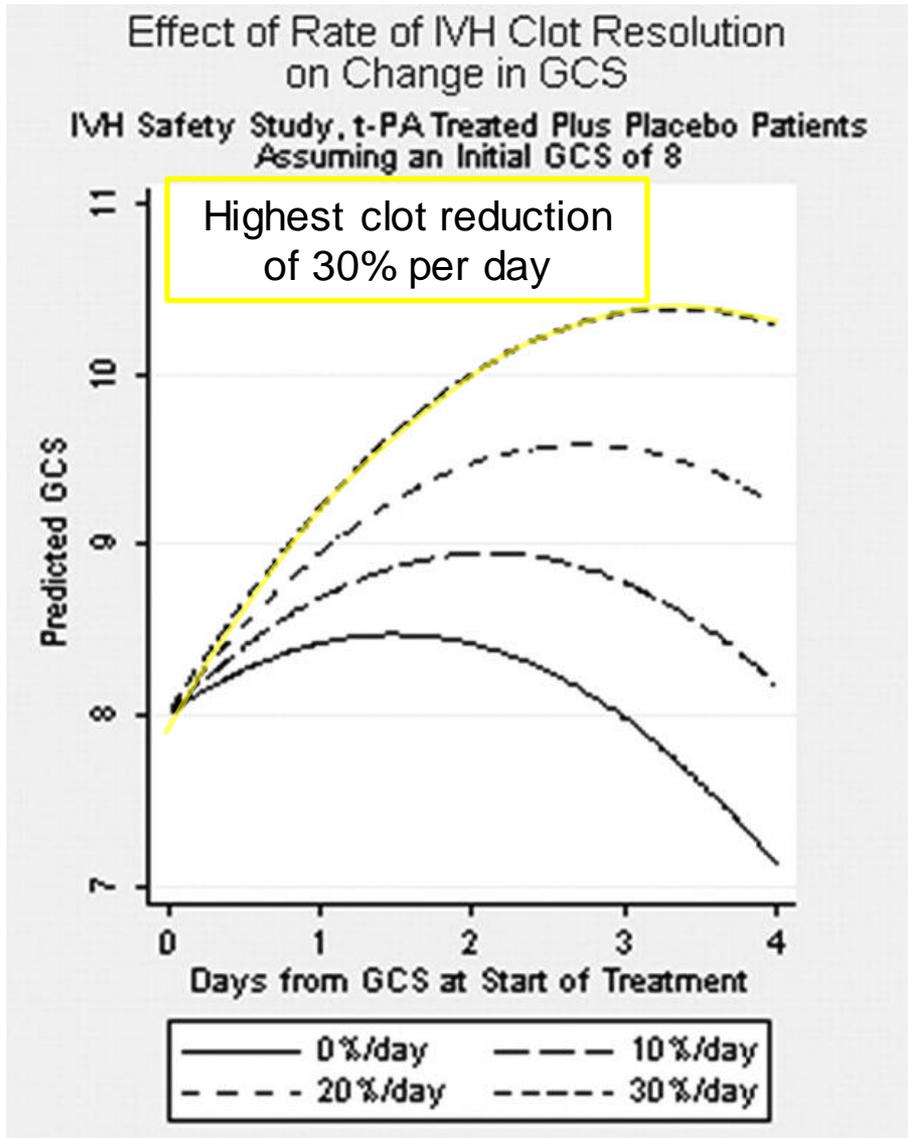
Day 180 modified Rankin Scale (mRS)



CLEAR II

- 48 patients were randomized to receive either 3 mg of rtPA or 3 ml of normal saline injected via the EVD into the ventricular spaces every 12 hours until clot resolution

CLEAR II OUTCOMES



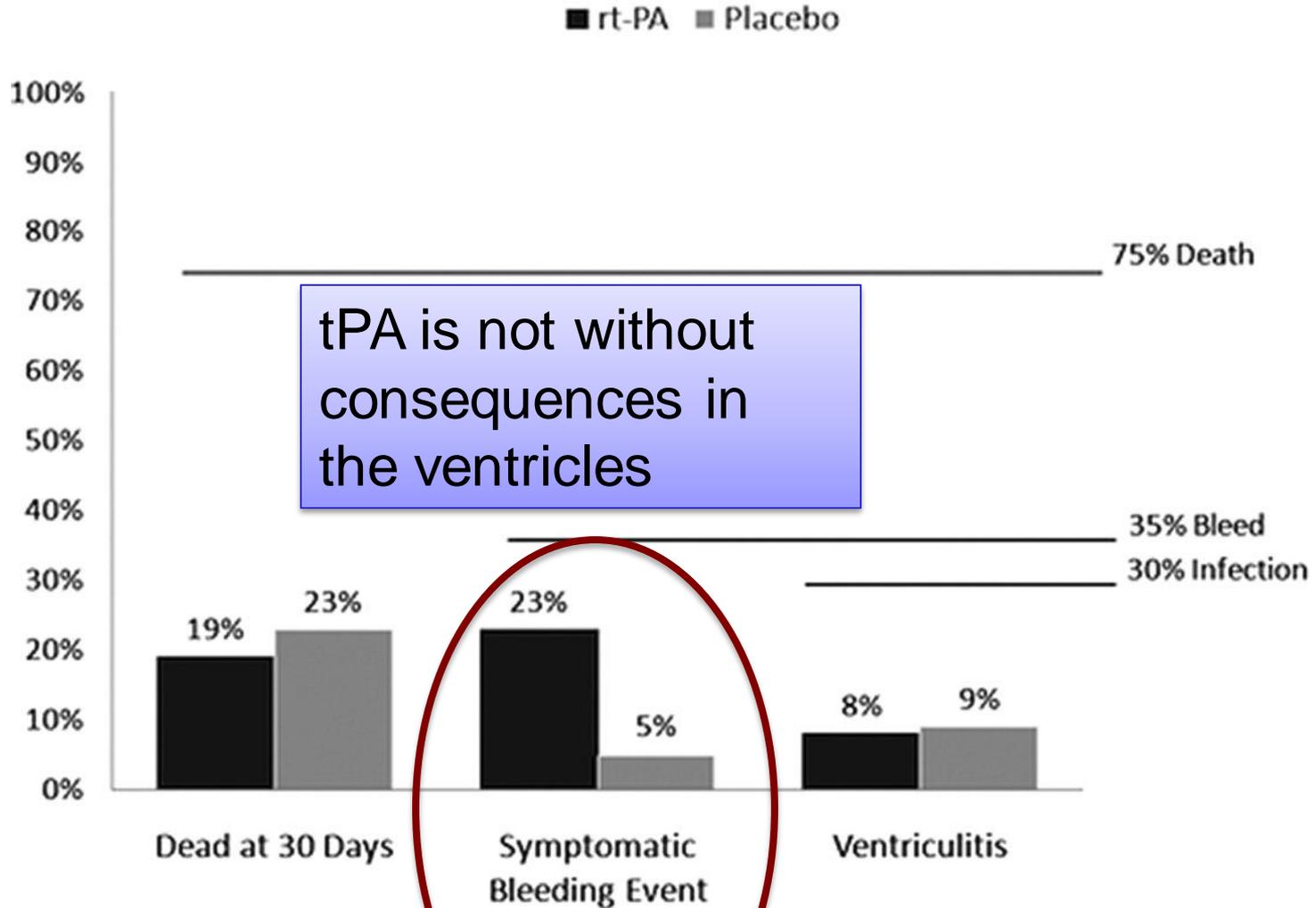
- Patients whose clot resolved faster showed better GCS at 96 hours ($p < 0.001$)
- GCS score not only improved more quickly but also did not show a decline on day 3

CLEAR II OUTCOMES

- Patients whose clot resolved faster showed better clinical outcomes (p value <0.001)
- The faster the hemorrhage was reduced, the better the patients fared

Outcome	rtPA	Placebo
mRS score ≤ 4	52%	27%
NIHSS ≤ 10	54%	29%

CLEAR II OUTCOMES



Naff N et al. Stroke 2011;42:3009-3016

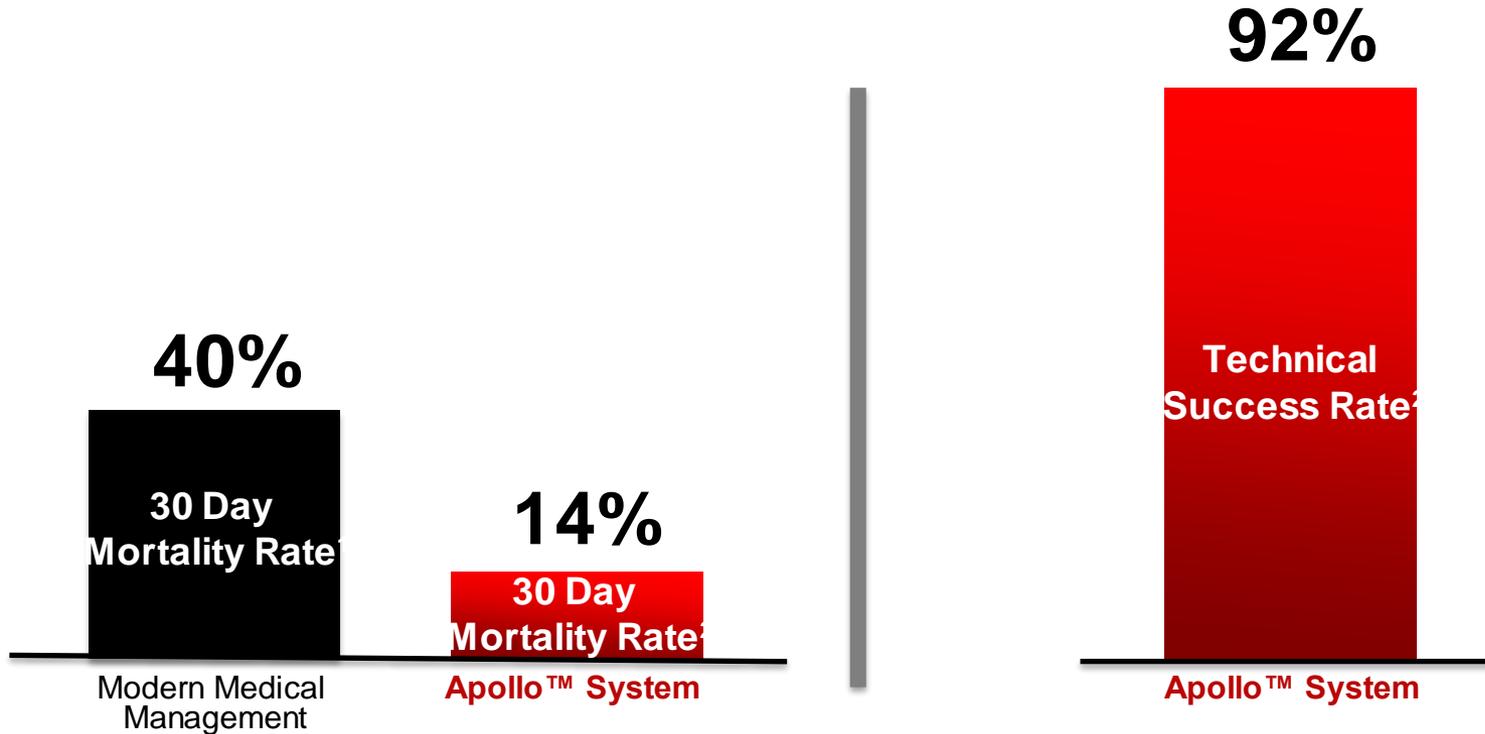
CONSIDERATIONS OF CURRENT MIS TREATMENTS

- Catheter drainage with tPA can be slow and can increase symptomatic hemorrhage
- MISTIE treatment effect driven by patients with $< 10\text{cc}$ of blood left after procedure
 - Minority of patients in MISTIE
 - Required days to achieve
 - Multiple serial CT scans
- Fast and complete mass effect reduction is key

ADVANTAGES OF A PURELY MECHANICAL CLOT EVACUATION

- IMMEDIATE, predictable, reduction of hematoma volumes to < 10 cc in most all cases
- No need for tPA infusions or post-procedure catheter placement

EARLY EXPERIENCE: APOLLO™ SYSTEM



- Further evidence generation is planned

OBSERVATIONS TO DATE

- Case experience indicates that substantial hemorrhage evacuation is technically feasible in most cases
- Without a requirement for catheter drainage or t-PA irrigation

CONCLUSIONS

- MIS for ICH is where thrombectomy for AIS was ~ 10 years ago
- Compelling preliminary data
- New devices to facilitate the procedure
- Randomized clinical trials are required