Treatment of ruptured intracranial aneurysm: to clip or to coil?

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Objectives:

- Identify that subarachnoid hemorrhage (SAH) from a ruptured aneurysm represents a form of a stroke
- Discuss what an aneurysm is and what an aneurysmal SAH is
- Identify some of the signs and symptoms of patients presenting with aneurysmal SAH
- Define basic demographic and outcome data related to patients with aneurysms and aneurysmal SAH
- Describe how to use the clinical severity scoring system for patient with SAH: Hunt Hess or WFNS SAH severity scoring systems
- Identify the ISUIA study which is the best natural history study we have for unruptured intracranial aneurysms as well as its shortcomings
- Establish the different treatment modalities for ruptured intracranial aneurysms
- Identify the 2 major randomized, controlled trials for ruptured intracranial aneurysms: ISAT and BRAT
- Explain some of the controversies associated with these studies and their conclusions
- Determine some conditions which favor clipping vs coiling and vice-versa
• Describe some of the controversies associated with treatment of ruptured intracranial aneurysms
Treatment of Ruptured Intracranial Aneurysms: To Clip or Coil?

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Intermountain Healthcare

Neuro-interventional Medical Director
Dixie Regional Medical Center
Disclosures

• Employee of Intermountain Healthcare / Intermountain Medical Group
• No financial relationships with any other medical/surgical/endovascular companies
• I am a neurosurgeon &
• I am a neurointerventionalist
• American Stroke Association
  • Stroke Classifications
    • Ischemic Stroke
    • Hemorrhagic Stroke
      • Subarachnoid Hemorrhage (5% of all Strokes)
      • Intraparenchymal Hemorrhage (IPH)
        • Intracerebral hemorrhage (ICH)
Types of Strokes

- **Ischemic Stroke**: Area deprived of blood.
- **Hemorrhagic Stroke**: Area of bleeding.

**Ischemic Stroke**:
- Obstruction blocks blood flow to part of the brain.

**Hemorrhagic Stroke**:
- Weakened vessel wall ruptures, causing bleeding in the brain.

- Aneurysm
- Blood in subarachnoid space
- Hematoma
- Infarct
- Intracerebral hemorrhage
- Hypertension
Percentage of People Who Were Ever Told They Had a Stroke, 2008

Age-adjusted to the 2006 U.S. standard population.

- □ = 1.0%–2.2%
- △ = 2.3%–2.5%
- ○ = 2.6%–2.9%
- ■ = 3.0%–4.3%
58 yo female with worst headache of her life
Subarachnoid Hemorrhage (SAH)

- Trauma
  - most common cause of SAH
- Spontaneous SAH (5% of strokes)
  - Ruptured intracranial aneurysms (~75%)
  - No cause determined (15%)
    - *perimesencephalic hemorrhages*
  - AVMs (4%)
    - *more commonly ICH/IVH*
- Rare Causes
  - Coagulation disorders
  - Vasculitides
  - Dissection
  - Dural venous sinus thrombosis
Hanging dead Chicken sign
Intracranial Aneurysms

• Weak spot in a vessel -> dilatation or ballooning of an intracranial arterial wall
• Typically at sites of arterial branching or bifurcations
http://drwhitecoat.com/what-is-an-aneurysm/
Intracranial Aneurysms

• Vessels situated in subarachnoid spaces
  • SAH develops when they rupture
• Classification based on shape, size, location
  • Shape
    • Saccular: pouch-like focal distensions of a vessel wall (~96%)
    • Fusiform: tubular distension along a larger diseased segment of a vessel
  • Size: usually in mm or cm
    • Large ≥1.5 cm, Giant ≥2.5 cm
    • Often describe the dome and neck sizes as well
• Location:
  • named after involved vessel or region (e.g. Paraclinoid, ACOM, etc.)
SAH and Aneurysms

• Peak age for aneurysmal SAH is 55-60 yo
• Most common location of aneurysms
  • Anterior circulation (ICA, ACA, MCA)
    • ACoA 30%, P-comm 25%, MCA 20%
• Estimated that 1 in 50 people will develop a brain aneurysm during their lifetime (most will be asymptomatic and never rupture)
• Females : Males (3:2)
• 20-30% of patients with aneurysms have multiple (2 or more)
• Risk Factors for formation, growth, and/or rupture of aneurysms:
  • Environmental/Stimulants/Substances:
    • Nicotine, cocaine, methamphetamines, EtOH abuse
  • Family history of aneurysm
    • First degree relatives
  • HTN, atherosclerosis
  • Collagen vascular disorders/genetic predisposition:
    • Ehlers-Danlos type IV, Marfan Syndrome, Pseudoxanthoma elasticum, Polycystic kidney disease, renal fibromuscular dysplasia,
Signs and Symptoms of SAH

- 30-50% of SAH patients have a “pre-rupture” symptom or warning, most commonly a headache
  - “Sentinel Bleed”
- Severe Headache
  - “worst headache of my life”
- Nausea, vomiting
- Stiff neck or neck pain (meningismus)
- Sensitivity to light (photophobia)
- Blurred vision, double vision, or droopy eyelid
- Pain or pressure behind the eye
- Dilated pupil
- Focal neurologic deficits
- Seizure
- Loss of consciousness or Coma

Greenberg, SNIS
Aneurysmal SAH

• Incidence in western population
  • Approximately 10 per 100,000 population per year
  • US Census Bureau est. population of Utah in 2013 to be 2,855,287
  • Equates to ~286 ruptured intracranial aneurysms in Utah per year
  • 10-15% of patients die before reaching medical care
    • ~ 243 ruptured aneurysms in Utah per year
SAH Outcomes

• 10-15% die before reaching hospital
• Re-rupture = 80% mortality rate
  • 4% rate of re-rupture in first 24-H
  • 20% in first 2-weeks
  • 50% at 6-months
  • Goal of early treatment is to reduce risk of re-rupture
• 50-67% (successful aneurysm clipping) never return to the same pre-op QOL

Deshaiies, Greenberg
• Xanthochromia—yellow coloration of CSF supernatant due to heme pigment released by the breakdown of RBCs.

• Most reliable means for differentiating a traumatic tap from SAH

• Usually not apparent until 2-4 hrs after the bleed

• Remains in 70% pts at 3-weeks and 40% at 4-weeks.
# Clinical Severity of SAH

## World Federation of Neurological Surgeons

<table>
<thead>
<tr>
<th>WFNS Grade</th>
<th>GCS Score</th>
<th>Major Focal Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Unruptured Aneurysm</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>Absent</td>
</tr>
<tr>
<td>2</td>
<td>13-14</td>
<td>Absent</td>
</tr>
<tr>
<td>3</td>
<td>13-14</td>
<td>Present</td>
</tr>
<tr>
<td>4</td>
<td>7-12</td>
<td>+/-</td>
</tr>
<tr>
<td>5</td>
<td>3-6</td>
<td>+/-</td>
</tr>
</tbody>
</table>

## Hunt and Hess

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Unruptured Aneurysm</td>
</tr>
<tr>
<td>1</td>
<td>Asymptomatic or mild HA and/or slight nuchal rigidity</td>
</tr>
<tr>
<td>1a</td>
<td>No acute meningeal irritation but with fixed neuro deficit</td>
</tr>
<tr>
<td>2</td>
<td>Cr Nerve Palsy (CN 3), moderate to severe HA, nuchal rigidity</td>
</tr>
<tr>
<td>3</td>
<td>Mild focal deficit, lethargy or confusion</td>
</tr>
<tr>
<td>4</td>
<td>Stupor, moderate to severe hemiparesis, early decerebrate</td>
</tr>
<tr>
<td>5</td>
<td>Rigidity deep coma, decerebrate rigidity, moribund appearance</td>
</tr>
</tbody>
</table>

Add 1 grade for serious systemic disease (HTN, DM, COPD) or severe vasospasm on angiography.
How do we know when an aneurysm is going to rupture?

http://go-grafix.com/545255.html
ISUIA

Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment

Lancet 2003; 362: 103–10

International Study of Unruptured Intracranial Aneurysms Investigators*

- Best “Natural History” of un-ruptured aneurysms
- 1692 patients followed for at least 5 years
- Cumulative rupture rates per 5 year period were calculated
- Followed surgical vs endovascular outcomes are not comparative (different characteristics and populations)
  - No good randomized/prospective comparative trial for un-ruptured intracranial aneurysms
5-year cumulative rupture rates

- Small aneurysms divided into 2 groups
  - Group 1 = no previous SAH
  - Group 2 = previous SAH

- **Size and location** are the 2 most important prognostic indicators for potential aneurysm rupture
Treatment Options for Ruptured Aneurysms

• Do Nothing
  • Not typically recommended

• Surgery
  • Craniotomy and clip ligation/obliteration
    • Less common
      • Wrap, Trap and bypass

• Endovascular
  • Coil embolization
    • With or without balloon
      • Less Common- OFF LABEL
        • Stent assisted coiling
        • Pipeline Embolization device (Flow Diversion)
Craniotomy & Clip
Ligation/Obliteration

http://www.mayfieldclinic.com/PE-Clipping.htm
Coil Embolization

Aspect Ratio. The length of the dome (D) divided by the length of the neck (N) is the dome:neck ratio. (A) A favorable dome:neck ratio is 2 or greater. (B) A smaller dome:neck ratio may require adjunctive techniques like balloon or stent assistance for best results.
To clip or to coil... that is the question

- Prospective, randomized trials for treatment of aneurysmal SAH
  - Surgical clip ligation vs endovascular coil embolization for ruptured intracranial aneurysms
- 2 Major Trials:
  - ISAT: International Subarachnoid Aneurysm Trial
    - 2002
  - BRAT: Barrow Ruptured Aneurysm Trial
    - 2012
- 2 Smaller Trials
  - Finnish study
    - Koivisto et al. Stroke 2000; 31:2369-2377
International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial

THE LANCET • Vol 360 • October 26, 2002 • www.thelancet.com

International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group*

• Neurosurgeons and neurointerventionalists had to agree that the aneurysm was suitable for either modality
  • Aneurysmal Equipoise
• Randomized 2143 of 9559 screened pts

• Primary outcome
  • Death or dependent living (modified Rankin scale 3-6)
    • 2-months
    • 1-year
    • annually

• Secondary outcomes
  • Seizures
  • Risk of rebleeding
    • Pre-procedural
    • Procedural
    • Post-procedural
  • Retreatment
### ISAT Results

**Table 5: Outcome at 2 months in 1906 patients**

<table>
<thead>
<tr>
<th>Modified Rankin Scale</th>
<th>Endovascular Treatment (n=959)</th>
<th>Neurosurgery (n=947)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 No symptoms</td>
<td>192 (20.0%)</td>
<td>138 (14.6%)</td>
</tr>
<tr>
<td>1 Minor symptoms</td>
<td>275 (28.7%)</td>
<td>245 (25.9%)</td>
</tr>
<tr>
<td>2 Some restriction in lifestyle (0–2 inclusive)</td>
<td>248 (25.9%)</td>
<td>219 (23.1%)</td>
</tr>
<tr>
<td>3 Significant restriction in lifestyle</td>
<td>715 (74.6%)</td>
<td>602 (63.6%)</td>
</tr>
<tr>
<td>4 Partly dependent</td>
<td>95 (9.9%)</td>
<td>172 (18.2%)</td>
</tr>
<tr>
<td>5 Fully dependent</td>
<td>29 (3.0%)</td>
<td>39 (4.1%)</td>
</tr>
<tr>
<td>6 Dead (3–6 inclusive)</td>
<td>48 (5.0%)</td>
<td>55 (5.8%)</td>
</tr>
<tr>
<td></td>
<td>72 (7.5%)</td>
<td>79 (8.3%)</td>
</tr>
<tr>
<td></td>
<td>244 (25.4%)</td>
<td>345 (36.4%)</td>
</tr>
</tbody>
</table>

Data in italics are primary outcome.

**Table 6: Outcome at 1 year in 1594 patients (primary outcome)**

<table>
<thead>
<tr>
<th>Modified Rankin Scale</th>
<th>Endovascular Treatment (n=801)</th>
<th>Neurosurgery (n=793)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 No symptoms</td>
<td>207 (25.8%)</td>
<td>152 (19.2%)</td>
</tr>
<tr>
<td>1 Minor symptoms</td>
<td>217 (27.1%)</td>
<td>220 (27.7%)</td>
</tr>
<tr>
<td>2 Some restriction in lifestyle (0–2 inclusive)</td>
<td>187 (23.4%)</td>
<td>178 (22.4%)</td>
</tr>
<tr>
<td>3 Significant restriction in lifestyle</td>
<td>611 (76.3%)</td>
<td>550 (69.4%)</td>
</tr>
<tr>
<td>4 Partly dependent</td>
<td>80 (10.0%)</td>
<td>106 (13.4%)</td>
</tr>
<tr>
<td>5 Fully dependent</td>
<td>24 (3.0%)</td>
<td>32 (4.0%)</td>
</tr>
<tr>
<td>6 Dead (3–6 inclusive)</td>
<td>21 (2.6%)</td>
<td>25 (3.2%)</td>
</tr>
<tr>
<td></td>
<td>65 (8.1%)</td>
<td>80 (10.1%)</td>
</tr>
<tr>
<td></td>
<td>190 (23.7%)</td>
<td>243 (30.6%)</td>
</tr>
</tbody>
</table>

Data in italics are primary outcome.

- Dead or dependent at 1 year: 23.7% of endovascular arm vs 30.6% in surgical arm
- Relative risk reduction was 22.6% with absolute risk reduction of 6.9%
- 1-year fatality rate was not statistically significant.
ISAT Results

• Higher re-bleed rate in endovascular arm
• No statistical significance in mortality of the re-bleed rates between the two at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Endovascular treatment</th>
<th>Neurosurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before first procedure</td>
<td>14 (7)</td>
<td>23 (16)</td>
</tr>
<tr>
<td>After procedure up to 30 days</td>
<td>20 (10)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>30 days to 1 year</td>
<td>6 (5)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Total up to 1 year</td>
<td>40 (22)</td>
<td>33 (21)</td>
</tr>
<tr>
<td>After 1 year</td>
<td>2 (0)</td>
<td>0</td>
</tr>
</tbody>
</table>

Numbers in parentheses indicate deaths. All deaths from rebleeding occurred within first week except for one at 20 days. Rebleeding was confirmed on CT scanning in all cases.

Table 7: Non-procedural bleeding from target aneurysm

• Seizure rate was significantly higher in surgical arm
  • not shown in graph
ISAT Results

• Retreatment Rates
  • Significantly higher rate of retreatment in the endovascular arm

<table>
<thead>
<tr>
<th></th>
<th>&lt;30 days</th>
<th>30 days -1 year</th>
<th>&gt;1 year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Allocated endovascular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second procedure endovascular</td>
<td>14</td>
<td>30</td>
<td>9</td>
<td>53</td>
</tr>
<tr>
<td>Second procedure neurosurgery</td>
<td>67</td>
<td>10</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td><strong>Allocated neurosurgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second procedure endovascular</td>
<td>24</td>
<td>5</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>Second procedure neurosurgery</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 4: Time to second procedure on same aneurysm
Conclusion

**Interpretation** In patients with a ruptured intracranial aneurysm, for which endovascular coiling and neurosurgical clipping are therapeutic options, the outcome in terms of survival free of disability at 1 year is significantly better with endovascular coiling. The data available to date suggest that the long-term risks of further bleeding from the treated aneurysm are low with either therapy, although somewhat more frequent with endovascular coiling.
Cognition

• Modified Rankin Scale is insensitive to cognitive function

• Is there a difference between the 2 treatments options with regards to patient cognition at 1-year?
• UK patients only, 1 year f/u
• Cognitive impairment was less common in endovascular treatment arm
  • 26.7% endo vs 38.7% surgery
    • P=0.0055, OR=0.58, 95%CI 0.38-0.87
• Incidence of epilepsy higher in surgical group
  • No interaction between incidence of epilepsy on presence of cognitive impairment in this study
Is the 1 year clinical benefit of coiling lost over time if the rate of subsequent re-bleeding is high?
Could late rebleeding overturn the superiority of cranial aneurysm coil embolization over clip ligation seen in the International Subarachnoid Aneurysm Trial?

Patrick Mitchell, F.R.C.S.,¹ Richard Kerr, F.R.C.S.,² A. David Mendelow, F.R.C.S.,¹ and Andy Molyneux, F.R.C.R.,²

¹Neurovascular Research Unit, Nuffield Department of Surgery, University of Oxford and Oxford Radcliffe Hospitals, National Health Service Trust, Radcliffe Infirmary, Oxford; and ²Department of Neurosurgery, Newcastle General Hospital, Newcastle upon Tyne, United Kingdom
• After treatment of first angiogram:
  - Residual aneurysm filling:
    - Coil embolization 34%
    - Clip ligation 18%
  - 89% of patients undergoing coil embolization had a f/u angiogram; 47% of clip ligation patients had a f/u angiogram
Conclusions. When treating ruptured cerebral aneurysms, the advantage of coil embolization over clip ligation cannot be assumed for patients < 40 years old. In this age range the difference in the safety of the 2 procedures is small, and the better long-term protection from SAH afforded by clip placement may give this treatment an advantage in life expectancy for patients < 40 years of age. (DOI: 10.3171/JNS/2008/1083/0437)
Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up

Andrew J Molyneux, Richard S C Kerr, Jacqueline Birks, Najib Ramzi, Julia Yarnold, Mary Sneade, Joan Rischmiller, for the ISAT collaborators


- 6-14 year of f/u (mean of 9 years)
- Reported data as “5” year f/u
- The annual risk of treated aneurysm re-bleeding is higher in the coiling group (10 vs 3), the risk remains low and is at a similar level to the risk of further SAH from another source.
  - No significant difference in mortality rates as a result of re-bleeding

- Risk of death at 5 years significantly lower in coiled group

- No significant difference between % of functional independent patients at 5-years between 2 groups.
• All re-bleeding events from the target coiled aneurysms occurred <5 years
  • Importance of f/u imaging in these pts
• Further treatment after initial coiling had no effect on 5-year outcomes

The question asked in the neurosurgical community about coiling has always been: will the early proven benefit of coiling be lost in the long term? This question was highlighted and modelled in a recent paper and associated commentary. This paper has given rise to controversy, particularly with respect to the management of young patients with ruptured aneurysms (younger than 40 years, who were only a small subgroup in the trial). The level of risk we now report and the absence of an increase in risk of death between the patients treated with coiling and those treated with clipping over what is now a mean of 9 years follow-up would appear not to change the message of our original paper; namely, that for patients with suitable aneurysms, coiling is more likely than clipping to result in improved clinical outcomes at 1 year, and these data suggest that although the early clinical benefits are reduced over time, they are not lost over the subsequent 4 years. We have previously
The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the International Subarachnoid Aneurysm Trial (ISAT)

Andrew J Molyneux, Jacqueline Birks, Alison Clarke, Mary Sneade, Richard S C Kerr

- UK cohort only
- 10 - 18.5 years f/u after ISAT
- Pts in endovascular arm more likely to be alive and independent at 10 years than were patients in the surgical group
- Risk of rebleed from target aneurysm was higher in endovascular group
  - Risk small, similar to risk of rupture of other aneurysms
- At this f/u time point, pts much more likely (40X) to die as a result of other causes than from treatment aneurysm
  - Cancer and Cardiovascular
Criticisms of ISAT

• Only 20% of pts were randomized
  • Not all aneurysms can be deemed equal (to either clip or coil)
  • Is this trial representative? Can it be generalized to all aneurysms?

• Mostly European Centers
  • Prompted a subsequent American trial (BRAT)

• Predominantly low grade hemorrhages

• Predominantly ACOM and PCOM
  • Statistics may have been much different if more basilar artery aneurysms were included

• Predominantly small aneurysms that ruptured
  • Contrast to natural history ISUIA data

• Used CTA to randomize many patients instead of all DSA
  • Hard to distinguish neck anatomy and “coil potential” of an aneurysm

• Only platinum coils used in treatment
  • no bioactive coils, can the recurrence rate and low obliteration rates be generalized to today’s coils?

• Late f/u points used only UK cohort instead of all pts

• Did not have long term angiographic f/u on patients
Distribution of Aneurysm Location

<table>
<thead>
<tr>
<th>Location</th>
<th># pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACOM</td>
<td>973</td>
</tr>
<tr>
<td>PCOM</td>
<td>536</td>
</tr>
<tr>
<td>MCA bifurcation</td>
<td>257</td>
</tr>
<tr>
<td>Basilar</td>
<td>17</td>
</tr>
</tbody>
</table>

-52% of ruptured aneurysms ≤5 mm
-93% of ruptured aneurysms in trial ≤1cm
-89% were WFNS grade 1 or 2 (most were grade 1, 63%)
• Single Center Study.
  • 471 pts: 238 surgical and 233 coil
• Patients were randomly assigned to “clip” or “coil”
• Physician reviewed studies and made a decision to “proceed with assigned” or recommend a “cross over”
  • “Real world decision making”
  • “Right of first refusal”
BRAT

• Primary Outcome
  • mRS 3-6 (death and dependency)
    • 1-year, 3-years and 6-years
  • Intention-to-treat analysis

• Secondary Outcome
  • “As treated” analysis of primary outcome
  • Re-bleeding
  • Retreatment
  • Death
Median aneurysm size = 6mm

Better Distribution of SAH severity

Cross over from coil to clip = 38%
BRAT Primary Outcome

• 1 year
  • Death or dependence (mRS 3-6)
    • Coiling- 23.2%
    • Clipping- 33.7%
      • Odds ratio 1.68 (95% CI 1.08-2.6, p=0.02)

• Coiling benefit remained significant in multivariate logistic regression analysis adjusted for age and HH score
BRAT Secondary Outcomes

• As treated analysis: Death and dependency at 1 year (mRS 3-6)
  • Coil-coil & Clip-Coil (crossovers): 20.4%
  • Clip-Clip & Coil-Clip (crossovers): 33.9%
    • OR 2.01 (95%CI 1.2-3.46, p=0.01)

  • Coiling benefit remained significant in multivariate logistic regression analysis adjusted for age and HH score

• Evaluated intent-to-treat and removed any crossover pts from analysis:
  Death and dependency at 1 year (mRS 3-6)
  • Coil: 18.4%
  • Clip: 33.9%
    • OR 2.28 (95% CI 1.3-4.13, p=0.005)

• Rebleed rate:
  • Coil: no patient treated by coil embolization re-bled after treatment -> 1 year
  • Clip: 2 patients re-bled (1 was originally assigned to coil and crossed over to clip)
Whether evaluated by “intent-to-treat” or “as treated,” there was a significantly higher rate of aneurysm retreatment in the coil group.

**TABLE 6: Retreatment of aneurysms within 1 year in the BRAT**

<table>
<thead>
<tr>
<th>Category*</th>
<th>Total No.</th>
<th>No. w/ Retreatment (%)</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>By Discharge</td>
<td>By 1 Yr†</td>
<td>By Discharge</td>
</tr>
<tr>
<td>assigned to coil group</td>
<td>232</td>
<td>7 (3.02)</td>
<td>16 (6.90)</td>
<td>1.45 (0.39–5.88)</td>
</tr>
<tr>
<td>assigned to clip group</td>
<td>238</td>
<td>5 (2.10)</td>
<td>7 (2.94)</td>
<td></td>
</tr>
<tr>
<td>actual coil Tx</td>
<td>113</td>
<td>3 (2.66)</td>
<td>12 (10.62)</td>
<td>0.72 (0.12–2.97)</td>
</tr>
<tr>
<td>actual clip Tx</td>
<td>245</td>
<td>9 (3.67)</td>
<td>11 (4.49)</td>
<td></td>
</tr>
</tbody>
</table>

* Intent-to-treat and actual treatment categories. For actual treatment, the total number of patients includes only those who were actually treated and in whom follow-up information was available.
† Numbers at 1 year include patients who underwent retreatment during initial hospitalization.
Conclusions. One year after treatment, a policy of intent to treat favoring coil embolization resulted in fewer poor outcomes than clip occlusion. Although most aneurysms assigned to the coil treatment group were treated by coil embolization, a substantial number crossed over to surgical clipping. Although a policy of intent to treat favoring coil embolization resulted in fewer poor outcomes at 1 year, it remains important that high-quality surgical clipping be available as an alternative treatment modality. (DOI: 10.3171/2011.8JNS101767)
• Primary Outcome- Intent-to-treat analysis, Death and disability (mRS 3-6) at 3 years.
  • Coil: 30%
  • Clip: 35.8%
    • OR 1.3, (95% CI 0.83-2.04, p=0.25)

• Effect of clipping on risk of poor outcome observed at 1 year was no longer significant at 3 years
As treated analysis still demonstrated treatment benefit for coiling group at 3-years.
Post hoc analysis

• Location, location, location...

• When outcomes analyzed based on aneurysm location...

• Anterior circulation aneurysms (nearly 80% anterior circulation)
  • No significant difference between 2 assigned groups at any time point (surgery-> 3 years: intent-to-treat)

• Posterior circulation aneurysms
  • Significant benefit to treatment via coiling at 1- and 3-years
BRAT 3-Years: Secondary Outcomes

• Rebleed:
  • No rebleeding between year 1 -> 3 from any patients (coil or clip)
    • Different from ISAT

• Retreatment
  • Coil: 10.6%
  • Clip: 4.5%
    • p=0.03

• Aneurysm Obliteration
  • Coil: 1-year 58%; 3-year 52%
  • Clip: 1-year 85%; 3-year 87%
• Primary Outcome- Intent-to-treat analysis, Death and disability (mRS 3-6) at 6-years
  • Coil: 35%
  • Clip: 41%
    • p= 0.24
  • Similar to 3-year data- no statistical significance between coiling and clipping
BRAT Post hoc analysis

- Similar findings at 6-years
  - When outcomes analyzed based on aneurysm location
  - Anterior circulation
    - No significant difference between 2 assigned groups at 6-years
  - Posterior circulation aneurysms
    - Significant benefit to treatment via coiling at 1-, 3-, and 6-years
BRAT 6-years: Secondary Outcomes

• Rebleed: No rebleeding between year 1-> 6 from any patients (coil or clip)

• Retreatment
  • Coil: 16.4%
  • Clip: 4.6%
    • p=0.0001

• Aneurysm Obliteration
  • Coil: 1-year 58%; 3-year 52%; 6 year 48%
  • Clip: 1-year 85%; 3-year 87%; 6-year 96%
BRAT 6-year Conclusions

CONCLUSIONS  Although BRAT was statistically underpowered to detect small differences, these results suggest little difference in outcome between the 2 treatments for anterior circulation aneurysms. This was not the case for the posterior circulation aneurysms, where coil embolization appeared to provide a sustained advantage over clipping. Aneurysm obliteration rates in BRAT were significantly lower and retreatment rates significantly higher in the patients undergoing coiling than in those undergoing clipping. However, despite the fact that retreatment rates were higher after coiling, no recurrent hemorrhages were known to have occurred in patients undergoing coiling in BRAT who were followed up for 6 years. Sufficient questions remain about the relative benefits of the 2 treatment modalities to warrant further well-designed randomized trials.
BRAT Criticisms

• Study not appropriately powered to detect differences
  • Do the results really matter then?

• Number of Cross over patients from Coil to Clip (38%)
  • Are “intention-to-treat” data valid if 38% weren’t treated that way?
  • Are “as treated” data valid if there are differences between these 2 groups after crossover?
    • Patient characteristics not matched for crossover
      • 280 total clipped, 128 total coiled

• Crossovers demonstrated 2 key points
  • Importance of having a good neurosurgeon who can clip all types of aneurysms
    • many aneurysms do not have “aneurysmal equipoise”
    • Surgery is “only” option for some ruptured aneurysms
  • Confirmed why it was so difficult to randomize in ISAT- equipoise is hard to find

• Matrix Coils – recalled...
Matrix Coils

In terms of technological improvements, first-generation Matrix coils were used in the majority of the BRAT coil embolization procedures. These coils have since been withdrawn from the market because numerous studies have suggested that aneurysms treated with these coils had unacceptably high recurrence rates.\textsuperscript{11,15,16,25,30} It is likely that current endovascular results are, in fact, superior to those reported in this study.
AHA/ASA Guideline

Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

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

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons;
and by the Society of NeuroInterventional Surgery

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Surgical and Endovascular Methods of Treatment of Ruptured Cerebral Aneurysms: Recommendations

1. Surgical clipping or endovascular coiling of the ruptured aneurysm should be performed as early as feasible in the majority of patients to reduce the rate of rebleeding after aSAH (Class I; Level of Evidence B).
2. Complete obliteration of the aneurysm is recommended whenever possible (Class I; Level of Evidence B).

3. Determination of aneurysm treatment, as judged by both experienced cerebrovascular surgeons and endovascular specialists, should be a multidisciplinary decision based on characteristics of the patient and the aneurysm (Class I; Level of Evidence C). (Revised recommendation from previous guidelines)
4. For patients with ruptured aneurysms judged to be technically amenable to both endovascular coiling and neurosurgical clipping, endovascular coiling should be considered (Class I; Level of Evidence B). (Revised recommendation from previous guidelines)
5. In the absence of a compelling contraindication, patients who undergo coiling or clipping of a ruptured aneurysm should have delayed follow-up vascular imaging (timing and modality to be individualized), and strong consideration should be given to retreatment, either by repeat coiling or microsurgical clipping, if there is a clinically significant (e.g., growing) remnant (*Class I; Level of Evidence B*). (New recommendation)

6. Microsurgical clipping may receive increased consideration in patients presenting with large (>50 mL) intraparenchymal hematomas and middle cerebral artery aneurysms. Endovascular coiling may receive increased consideration in the elderly (>70 years of age), in those presenting with poor-grade (World Federation of Neurological Surgeons classification IV/V) aSAH, and in those with aneurysms of the basilar apex (*Class IIb; Level of Evidence C*). (New recommendation)

7. Stenting of a ruptured aneurysm is associated with increased morbidity and mortality, and should only be considered when less risky options have been excluded (*Class III; Level of Evidence C*). (New recommendation)
## Conditions that favor...

### Surgery- clipping
- Younger age (controversial)
- MCA bifurcation/trifurcation
- Mass effect on CN (controversial)
- Hematoma (controversial)
- Small aneurysms 3 mm or less
- Wide neck ruptured aneurysm
- Failed endovascular treatment
- Poor vascular access in groins

### Endovascular- coiling
- Elderly patients
- Poor clinical grade
- Inaccessible (surgically) ruptured aneurysms
- Favorable dome to neck ratio $\geq 2$
- Posterior circulation / basilar
- Patients on Plavix
Controversies

• Consent:
  • Can a neurosurgeon or endovascular specialist adequately represent the other specialty alone in discussing treatment options and recommendations without communication between the 2 specialist?

• Should we be treating smaller, unruptured aneurysms based on ISAT and BRAT small ruptured aneurysm sizes?

• Treatment of un-ruptured aneurysms (surgery vs endovascular)- no current “good evidence” or guidelines for how we should treat un-ruptured aneurysms...
  • Numerous treatment devices/methods available that aren’t available in a ruptured patient
  • Long term outcomes with flow diverters
• What is the natural history of small neck remnants (from either coiling or clipping)?
• Partial coiling of ruptured aneurysm to “protect the dome” then coming back later (week -> weeks) for completion procedure (+/- stent or flow diverter... OFF LABEL)
• Ruptured blister aneurysms
• Ruptured wide necked basilar aneurysms
• Use of balloons for endovascular treatment of ruptured wide necked aneurysms
So Doctor, what would you do if...

• If you had a ruptured intracranial aneurysm would you want it...
  • A: Clipped
  • B: Coiled
  • C: I am still confused
  • D: I don’t know

• Tell me more...
  • CTH
    • hemorrhage pattern, IPH, hydrocephalus, brain edema
  • Angiogram
    • Aneurysm location, size, neck, characteristics, relationship to surrounding vessels, collaterals flow
  • Clinical
    • clinical severity score, timing of symptoms, stability of symptoms, age, medical and surgical history
Sources Cited

- **Handbook of Neurosurgery**. Mark S. Greenberg. 7th ed. Thieme 2010 New York (Greenberg).
- **Neurovascular Surgery**. Spetzler RF, Kalani MYS, Nakaji P. 2nd ed. Thieme 2015 New York (NS Spetzler).
- Society of Neurointerventional Surgeons (SNIS) website www.brainaneurysm.com
Any Questions?
Intentional partial coiling dome protection of complex ruptured cerebral aneurysms prevents acute rebleeding and produces favorable clinical outcomes


Abstract

BACKGROUND: The coiling of ruptured cerebral aneurysms protects against acute rebleeding; however, whether partially coiling a ruptured cerebral aneurysm protects against acute rebleeding has never been demonstrated.

OBJECTIVE: This study was performed to test our hypothesis that intentional partial coiling of complex ruptured cerebral aneurysms, which are unfavorable for clipping and cannot be completely coiled primarily, prevents acute rebleeding to allow for clinical and neurological recovery until definitive treatment and produces favorable clinical outcomes.

METHODS: Data were collected from the prospective databases of three centers. Only subarachnoid hemorrhage patients that were treated with a strategy of intentional partial coiling for dome protection were included. This did not include patients in whom the goal was complete coiling but only subtotal coil occlusion was achieved.

RESULTS: Fifteen patients [aged 51 ± 13 years; HH 3-5 (n = 7); Fisher 3-4 (n = 9)] were treated with intentional partial dome protection. Aneurysm size was 12.8 ± 5.4 mm; neck size 4.9 ± 3 mm; 12 anterior circulation. Four intentional partial coilings were performed with balloon assistance. Definitive treatment was performed 92 ± 90 days later, with no case of rebleeding. Definitive treatment was clipping (n = 8), stent-coiling (n = 5), Onyx (n = 1), further coiling (n = 1). Clinical outcome was favorable in 13 cases (GOS 4-5), fair in one (GOS 3), and death in one (GOS 1).

CONCLUSION: Judicious use of a treatment strategy of intentional partial dome protection for complex aneurysms that are not favorable for clipping and in which complete coiling primarily is not possible may prevent acute rebleeding and produce favorable clinical outcomes.