Current Management of Cerebral Aneurysms

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Aneurysms....

- Dreaded and horrific
- Death sentence
- Worse than cancer
- Scary
- High risk and high morbidity surgery is mandatory

- Not exactly true
Start with the basics
What are they?
Brain aneurysms
What are they?
Location
Why do we worry?

- Rupture has an overall mortality of 50% and additional morbidity of 25%.
- 1/3 are fatal at presentation.
- Of the survivors:
  - 1/3 are fatal during their hospitalization.
  - 1/3 have significant morbidity.
  - 1/3 return to normal.
Presentation

• **Rupture: most common**
  – Subarachnoid hemorrhage
  – Parenchymal hemorrhage

• **Mass effect: less common**
  – Cranial neuropathy
    • (CN3 from a Pcomm aneurysm)
  – Giant aneurysms with local mass effect

• **Incidental finding: becoming more popular**
Treatment choices

• Conservative
• Definitive repair
  – Clip it
  – Coil it
What is the natural risk?

- About 1 in 20 have an aneurysm
  - Ranges from 1-9% incidence
  - Autopsy studies vs imaging based
- Most never do anything
- Consider unruptured and ruptured separately
Risk factors

• Behavioral
  – Smoking
  – Binge alcohol use
  – Street drug use
  – Hypertension

• Personal
  – Age
  – Gender
  – Family/Personal history

• Anatomic
  – Size
  – Location
  – Morphology
  – Change
Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment

International Study of Unruptured Intracranial Aneurysms Investigators
Lancet 2003 362:103-10
5-year rupture rates

<table>
<thead>
<tr>
<th></th>
<th>&lt;7 mm</th>
<th></th>
<th>7-12 mm</th>
<th>13-24 mm</th>
<th>≥25 mm</th>
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<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cavemous carotid artery (n=210)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3.0%</td>
<td>6.4%</td>
</tr>
<tr>
<td>AC/MC/IC (n=1037)</td>
<td>0</td>
<td>1.5%</td>
<td>2.6%</td>
<td>14.5%</td>
<td>40.0%</td>
</tr>
<tr>
<td>Post-P comm (n=445)</td>
<td>2.5%</td>
<td>3.4%</td>
<td>18.4%</td>
<td>50.0%</td>
<td></td>
</tr>
</tbody>
</table>

AC=anterior communicating or anterior cerebral artery. IC=internal carotid artery (not cavemous carotid artery). MC=middle cerebral artery. Post-P comm=vertebrobasilar, posterior cerebral arterial system, or the posterior communicating artery.

Table 4: 5-year cumulative rupture rates according to size and location of unruptured aneurysm
Ruptured aneurysms

• Different beast entirely
  – Sense of urgency plays a role

• Rerupture rate is substantially higher
  – 4% within 24 hours
  – 1.5% per day up to two weeks (20% total)
  – 50% by 6 months

  – 75% mortality for a re-rupture
Option #1: Conservative management

• Look for growth or change over time
Option #2: Clip it
Option #3: Coil it
How do you decide?

Never this simple...
Past

- First surgical aneurysm treatments were directed extracranially through carotid sacrifice.
  - 1760’s: John Louis Petit
    - Reported carotid occlusion could be tolerated
  - 1800’s: Hunter then Horsley
    - Ligated vessels for downstream aneurysms
  - 1900’s: Cushing
- Aneurysms were first addressed intracranially in 1933 by Dr. Norman Dott with wrapping.
Past

- In 1938, Dr. Dandy clipped the first ICA aneurysm presenting with a CN3 palsy with a malleable silver clip.
- Dr. Olivecrona was the first to clip an aneurysm with a clip that could be repositioned in 1958.
- Following the microscope use, the field evolved rapidly.
  - Clip development
  - Surgical approaches and techniques.
Endovascular History

- Heralded by embolization of peripheral and aortic aneurysms over 2 centuries
- Werner 1941: Transorbital/transluminal coil placement and heating
- Yasargil 1960’s: Endovascular catheterization and magnetically directed iron particles (animal models)
- Serbinenko 1974: First (human) cerebral aneurysm treated endovascularly with detachable balloons
- Dowd and Higashida 1990-1: Described coil embolization
- Guglielmi 1991: Described detachable coil embolization
- FDA approved in 1995
Clip versus coil?

International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial

International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group*

International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion

Andrew J Molyneux, Richard S C Kerr, Ly-Mee Yu, Mike Clarke, Mary Sneade, Julia A Yarnold, Peter Sandercock, for the International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group*

*
ISAT

• Prospective, randomized
• Inclusion:
  – Aneurysmal SAH
  – Treatment modality equipoise
  – Evaluation by INR and microvascular surgeon
• Exclusion:
  – Not a candidate for either modality
  – Randomization 1m after rupture
ISAT

• Outcome goals:
  – Primary endpoint
    • Clinical outcome (reduced mRS 3-6 by 25% at 1y)
  – Secondary endpoints
    • At 1y: rebleed rate, cost, quality of life, epilepsy frequency and neuropsychologic outcome
    • At 5y: clinical outcome
Results

- 9559 patients screened
- 2143 patients randomized
  - 9 crossed to open surgery
  - 38 crossed to coiling
- 1594 patients eligible for initial 12m paper
- 2118 patients eligible for second paper
<table>
<thead>
<tr>
<th></th>
<th>Endovascular treatment (n=1073)</th>
<th>Neurosurgery (n=1070)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male sex</strong></td>
<td>400 (37%)</td>
<td>399 (37%)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>52 (44–60, 18–87)</td>
<td>52 (43–60, 18–84)</td>
</tr>
<tr>
<td><strong>WFNS grade</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>674 (63%)</td>
<td>661 (62%)</td>
</tr>
<tr>
<td>2</td>
<td>269 (25%)</td>
<td>280 (26%)</td>
</tr>
<tr>
<td>3</td>
<td>66 (6%)</td>
<td>68 (6%)</td>
</tr>
<tr>
<td>4</td>
<td>38 (4%)</td>
<td>36 (3%)</td>
</tr>
<tr>
<td>5</td>
<td>11 (1%)</td>
<td>9 (1%)</td>
</tr>
</tbody>
</table>
| 6 (not assessable)
|                  | 15 (1%)                        | 16 (1%)               |
| **Maximum target aneurysm lumen size (mm)** |                      |
| ≤5             | 552 (51%)                      | 572 (53%)             |
| 6–10           | 438 (41%)                      | 426 (40%)             |
| ≥11            | 83 (8%)                        | 72 (7%)               |
| **Number of aneurysms detected** |                      |
| 1              | 836 (78%)                      | 850 (79%)             |
| 2              | 173 (16%)                      | 170 (16%)             |
| 3              | 44 (4%)                        | 35 (3%)               |
| ≥4             | 20 (2%)                        | 15 (1%)               |
| **Time between SAH and randomisation (days)** | 2 (1–4, 0–26)             | 2 (1–5, 0–28)          |

WFNS=World Federation of Neurological Surgeons clinical grading scale.\(^\text{18}\)

*Median (IQR, range). †Patient ventilated and clinical state could not be assessed.

Table 1: Baseline characteristics

<table>
<thead>
<tr>
<th>Aneurysm locations</th>
<th>Right</th>
<th>Midline</th>
<th>Left</th>
<th>Total</th>
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<tbody>
<tr>
<td><strong>Anterior cerebral artery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Anterior communicating</td>
<td>219</td>
<td>549</td>
<td>205</td>
<td>973</td>
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<tr>
<td>Proximal to anterior communicating</td>
<td>9</td>
<td>7</td>
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<td></td>
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<tr>
<td>Pericallosal</td>
<td>46</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td></td>
<td></td>
<td>1084 (50.5%)</td>
</tr>
<tr>
<td><strong>Internal carotid artery</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Proximal or ophthalmic region</td>
<td>12</td>
<td>18</td>
<td></td>
<td>30</td>
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<tr>
<td>Posterior communicating region</td>
<td>313</td>
<td>223</td>
<td>536</td>
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<tr>
<td>Bifurcation</td>
<td>34</td>
<td>45</td>
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<td>79</td>
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<tr>
<td>Other internal carotid</td>
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<td>53</td>
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<tr>
<td>Subtotal</td>
<td>286</td>
<td>304</td>
<td>698</td>
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</tr>
<tr>
<td><strong>Middle cerebral artery</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Proximal to bifurcation</td>
<td>14</td>
<td>14</td>
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<td></td>
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<tr>
<td>Bifurcation</td>
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<td>Distal to main bifurcation</td>
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<td>11</td>
<td></td>
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<tr>
<td>Subtotal</td>
<td>184</td>
<td>119</td>
<td>303</td>
<td>(14.1%)</td>
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<tr>
<td><strong>Posterior circulation</strong></td>
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<td></td>
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<tr>
<td>Basilar bifurcation</td>
<td></td>
<td>17</td>
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<tr>
<td>Basilar trunk</td>
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<tr>
<td>Superior cerebellar</td>
<td></td>
<td>5</td>
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<td></td>
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<tr>
<td>Posterior cerebral</td>
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<td>3</td>
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<tr>
<td>Posterior inferior cerebellar</td>
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<td>22</td>
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<tr>
<td>Subtotal</td>
<td></td>
<td></td>
<td>58</td>
<td>(2.7%)</td>
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<tr>
<td><strong>Total</strong></td>
<td>2143</td>
<td></td>
<td></td>
<td>(100%)</td>
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</table>

Table 2: Aneurysm locations
ISAT

• Results:
  – Primary endpoint
    • 23.5% Dependent/dead for coiled
    • 30.9% Dependent/dead for clipped
    • One year overall mortality 8.0 vs 9.9%
ISAT

• Results:
  – Secondary endpoint
    • Lower seizure risk for coiling
    • Lower rebleed risk for clipping
      – 11 vs 28 within 1st yr
      – 2 vs 7 after 1st yr

Figure 3: Cumulative rebleeding risk from target aneurysm

<table>
<thead>
<tr>
<th>Annual number at risk (rebleeding)</th>
<th>Time since randomisation (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endovascular 1073 (45)</td>
<td>0</td>
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<td>Neurosurgery 1070 (39)</td>
<td>3</td>
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<tr>
<td></td>
<td>6</td>
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<td>9</td>
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<td>69</td>
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<td>72</td>
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<td></td>
<td>75</td>
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<td>78</td>
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<tr>
<td></td>
<td>81</td>
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<tr>
<td></td>
<td>84</td>
</tr>
</tbody>
</table>

Log-rank p = 0.22
Concerns

- Not all aneurysms suitable for either mode
- Bias from higher pre-procedural re-rupture in the surgery arm
  - 6.1% vs 6.3% 2m mortality if exclude pre-treatment re-rupture
- Fewer intra/post-operative angiography to identify residuals in surgical arm (47% vs 89%)
- Coiled aneurysms were less likely occluded
  - 66% vs 82%
  - Since angio was not required, 82% is likely actually higher
- What’s the longevity of coiling? Should age be a consideration?
## Concerns

<table>
<thead>
<tr>
<th></th>
<th>2-12 months</th>
<th></th>
<th></th>
<th>After 1 year</th>
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<tbody>
<tr>
<td></td>
<td>Endovascular</td>
<td>Neurosurgery</td>
<td></td>
<td>Endovascular</td>
<td>Neurosurgery</td>
<td></td>
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<tr>
<td>Complication of severe dependent survival (eg, chest or other infections)</td>
<td>7</td>
<td>15</td>
<td>1</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treated aneurysm rebleeding</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable or definite bleed from another aneurysm</td>
<td>0</td>
<td>0</td>
<td>3*</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other intracranial haemorrhage</td>
<td>0</td>
<td>0</td>
<td>1†</td>
<td>0</td>
<td></td>
<td></td>
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<td>Ischaemic stroke</td>
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<td>0</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
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<td>Cardiac</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>10</td>
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<td></td>
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<tr>
<td>Cancer</td>
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<td>1</td>
<td>9</td>
<td>12</td>
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<td>Suicide</td>
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<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>Renal failure</td>
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<td>0</td>
<td>0</td>
<td>2</td>
<td></td>
<td></td>
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<tr>
<td>Infections not related to dependent survival</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
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<tr>
<td>Other causes (eg, trauma, perforated ulcer, pulmonary embolus, neurodegenerative)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10</strong></td>
<td><strong>21</strong></td>
<td><strong>33</strong></td>
<td><strong>45</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Includes all reported deaths up to November 2004. *See text for details. †Confirmed at autopsy as primary intracerebral haemorrhage.

*Table 3: Causes of death*
BRAT

• Barrow Ruptured Aneurysm Trial
• 725 screened with 500 patients
• At 1 year, 403 were available
• Poor outcomes (mRS $>$ 2) 33.7 vs 23.2%
• At 3 years, outcomes were closer
  – 35.8 vs 30%
• Post hoc analysis noted equipoise for anterior circulation aneurysms
Where do we stand?

• **Aneurysms must be evaluated for either modality**
  – Both approaches must be offered and considered

• Durability of coiling vs disability from craniotomy need to be considered
  – CARAT study confirmed equity at two years

• Constant evolution in endovascular and surgical tools changing the game
What’s changed/changing?

• Adjuvant devices are improving the degree of aneurysm packing and success of treatment
  – Coil material
  – Balloon-assisted embolization
  – Stent-assisted and stand-alone stenting
    • Neuroform
    • Pipeline
    • Complex vascular reconstruction
Coils

- Hydrogel-coated coils which swell to increase the aneurysm filling
- Bioactive coatings
  - Collagens, fibroblasts, growth factors
- Nitinol core providing shape memory to the coils.
Balloon remodeling
Parent vessel protection

Daughter vessel protection

Vessel reconstruction

Aneurysm catheterization

Daughter vessel protection

Rupture protection
Balloon can be used to reshape a frame in place
Creative balloon use for an MCA trifurcation aneurysm

Ultra wide necked MCA trifurcation aneurysm
10.5 x 9.1 x 8.6 mm (6.1 mm neck)
Triple catheterized
Final images
Stent-assisted Coiling

- Neuroform Stent: Available in 2002
  - Introduced as a device to support the coil embolization of wide necked aneurysms
- 60 micron struts
- 6.5-9.0% metal surface area coverage
  - Enough to cause significant flow redirection?
  - Believed to cause endovascular remodeling
Complex reconstructions

- Parent vessel remodeling
- Daughter vessel protection
- Telescoping stents
- Y-stenting
- Trans-PCoA basilar stenting
- Conical stenting into aneurysm
- (In development) Development of intra-aneurysmal stenting
- (In development) Bifurcation stenting
Complex reconstructions

**FIGURE 2.** Diagram demonstrating the sequence (A-C) of deploying two Neuroform stents in the basilar and bilateral PCAs in a Y-configuration before coil embolization.

Pipeline Stenting: Definitive treatment with flow diversion

- Microcatheter delivered, microstent
- Flexible
- Cobalt Chromium and Platinum
Pipeline Embolization Device

- Structure: Metal Surface Area Coverage
  - Neuroform: 6.5 – 9.5%
  - PED: 30-35%
50y male presenting with HA and neck pain
Immediate Post Tx (1/05)

2 Month FU (3/05)
71y female presenting with HA and an incidental aneurysm
Follow up at 4 months
Outcomes

- Initial results from outside the US (Buenos Aires) suggested a low complication rate around 5% with extremely high efficacy.
- Later US data from the post-FDA release suggests higher complication rates around 8.5% with only 68% occlusion at 3 months.
- Much to be understood about flow diversion and its complicated and understudied biology.
Liquid embolics: HD500

- High density polyvinyl alcohol polymer which can fill the aneurysm as a liquid and precipitate into a solid.
Surgical advancements

- Intraoperative imaging
  - Catheter angiography
  - Fluorescent angiography (IC Green)
  - Microdoppler flow analysis
Surgical advancements

• Neuromonitoring
  – EEG intraoperative recording for temporary clip ligation
• Combined trapping with surgical bypass
What does the future hold?

- Better understanding of the biology results greater success in treating aneurysms.
- Through the same efforts, we can work toward better outcomes via balanced approach to treatment modalities and honest appraisal of the risk/benefits.
Thank you

questions?