Treatment of Intracranial Aneurysms

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Epidemiology

• Unruptured intracranial aneurysms:
  – 3.6% in autopsy series
  – 2% in meta-analysis of autopsy/ angiography series
  – female/ male = 1.3
  – peak age: 60-79 years

• Aneurysmal SAH
  – global annual incidence 1:10000
  – 20,000- 30,000 new cases annually in the US
  – mean age: 55 years
  – female/men = 1.6
  – blacks/ whites = 1.6
  – smoking, connective tissue disorders, HTN

• Multiple aneurysms: 15-30%
  – female, smoking, hypertension, post-menopausal, family history
Non-modifiable Risk Factors

• Personal history of SAH
  – risk of new aneurysm 2%
  – annual incidence of SAH 6:10,000

• Family history of SAH/ Familial aneurysms
  – first-degree relatives with 1 affected member: 2-4%
  – first-degree relatives with 2 affected members: 10%
  – multiple, rupture at younger age and have poorer outcome
  – screening with MRA/CTA if 2 first-degree relatives have aneurysms

• Female gender
  – risk less than men until 50s
  – risk increases in post-menopausal women

• Age
  – rare in children
Non-modifiable Risk Factors

• Connective tissue disorders
  – Autosomal dominant polycystic kidney disease
    • 5-10% have aneurysms; screening advised
  – Ehlers-Danlos IV
  – Marfan
  – Neurofibromatosis-1
  – a1-Antitrypsin deficiency
  – Fibromuscular dysplasia

• Anatomic variants
  – persistent trigeminal artery
  – fenestrations
  – azygous ACA
Fenestration
**Modifiable Risk Factors**

- **Smoking**
  - consistently identified in many population studies
  - increased elastase activity
  - larger, multiple, rupture, vasospasm
- **Hypertension**
  - aneurysm formation and SAH
- **Atherosclerosis/ Hypercholesterolemia**
Types of aneurysms

• Appearance or Etiology?

• Saccular (berry)
  – arterial **bifurcation or accentuated curves** of the vessels of the **circle of Willis**
  – > 90% of all aneurysms

• Non-Saccular
  – arise from arterial **trunks** unrelated to branching sites
  – uncommon
  – external trauma
  – weakening from atherosclerosis, dissection, infection, inflammation, neoplasm, radiation
Saccular aneurysms - pathogenesis

• Hemodynamic stress
  – increased flow:
    • 10-20% of patients with AVM have aneurysms
  – increased wall shear stress
    • fragments internal elastic lamina/ initiates aneurysm formation

• Abnormal vascular remodeling
  – structural anomalies in extracellular matrix

• Inflammation
  – intimal thickening proximal and distal to branch points

• Histology:
  – internal elastic lamina is absent; the media is thin or absent
  – sac layers: intima and adventitia
Saccular aneurysms

• Typically found at branch points
  – gap in the media, internal elastic lamina

• Location:
  – Anterior circulation: 90%
    • anterior communicating: ≈30%
    • internal carotid artery: ≈30%
      – posterior communicating
      – ophthalmic artery (female, bilateral 20%, large or giant)
      – terminus
    • middle cerebral: ≈30%
  – Posterior circulation 10%
    • basilar tip: ≈6%

• Multiple lobes:
  – unruptured 9%, ruptured 40%

• Daughter sac:
  – unruptured 16%, ruptured 57%
Natural History

• Juvela et al. 2000
  – unruptured aneurysms diagnosed 1956-1978
  – 142 patients; 18.1 yrs follow-up
  – Annual rate of rupture:
    • Incidental aneurysm with history SAH: 1.3%
    • Incidental aneurysm, no history SAH: 1.0%
    • Symptomatic aneurysm: 2.6%
    • Size:
      – 2 - 6mm: 1.1%
      – 7 – 9mm: 2.3%
      – 10 – 26mm: 2.8%
  – Mortality rate with rupture: 52%
  – Weakness: small number of patients; most (90%) with SAH
Natural History

• Rinkel 1998
  – meta-analysis totaling 3,907 patients
  – overall annual risk of rupture: 1.9%
    • female: 2.6%
    • symptomatic aneurysm: 6.5%
    • asymptomatic, history of SAH: 1.4%
    • posterior circulation: 4.4%
    • ≥10mm: 4.0, <10mm: 0.7

• Morita 2005
  – meta-analysis totaling 3,801 patients (Japan only)
  – overall annual risk of rupture: 2.7%
  – higher risk if ≥10mm, posterior circulation, symptomatic
Natural History

- **International Study of Unruptured Intracranial Aneurysms (ISUIA)**
  - 4,060 patients (history of SAH vs. no history of SAH)
  - mean follow-up 4.1 year

<table>
<thead>
<tr>
<th>Annual rupture rates</th>
<th>&lt;7mm</th>
<th>7-12mm</th>
<th>13-24mm</th>
<th>≥25mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>no prior SAH</td>
<td>0%</td>
<td>0.3%</td>
<td>0.5%</td>
<td>2.9%</td>
</tr>
<tr>
<td>anterior circulation</td>
<td>0%</td>
<td>0.3%</td>
<td>0.5%</td>
<td>2.9%</td>
</tr>
<tr>
<td>posterior circulation</td>
<td>0.5%</td>
<td>0.7%</td>
<td>2.9%</td>
<td>3.68%</td>
</tr>
<tr>
<td>cavernous ICA</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0.6%</td>
</tr>
</tbody>
</table>

Controversial results:
- average size of ruptured aneurysms is 6-7mm
- these rates predict 5600 cases of SAH, instead of true number of 21-33000 cases/ year
- selection bias of the retrospective component?
Diagnosis

• SAH
  – CT: sensitivity decreases with time (and anemia)
  – LP: enough time for xanthochromia to occur?
  – MRI: FLAIR imaging better than CT for older bleeds
    • great for CT (-), LP (+)

• Aneurysm imaging
  – CTA:
    • very high sensitivity, even if SAH
    • sensitivity varies with size
    • negative study requires catheter angiography
  – MRA:
    • no radiation
    • very sensitive >2-3mm
    • flow related artifacts
    • excellent for follow-up after coiling
Catheter Angiography

- Gold standard
- Carries a risk of complications:
  - 0.9% reversible neurologic
  - 0.5% permanent neurologic
  - high-risk patients: carotid atherosclerosis, advanced age, long procedure, hypertension, diabetes
  - Willinsky RA, Radiology 2003
- Detects very small aneurysms
- Detailed evaluation:
  - neck, dome
  - suspected rupture sites
  - collateral circulation distal to the aneurysm
  - hemodynamics
Treatment options

• No treatment
  – monitor
    • imaging (MRA)
    • new headache or cranial nerve palsy
  – modify risk factors (smoking, hypertension)
  – growing or newly symptomatic aneurysms should be treated

• Microsurgery

• Endovascular
Subarachnoid hemorrhage
Subarachnoid hemorrhage grades:

- 0=Unruptured
- 1=Mild H/A
- 2=Severe H/A, neck pain/rigidity, CN palsy
- 3=Lethargy/confusion
- 4=Stupor, hemiparesis
- 5=Deep coma, decerebrate posturing

- Overall mortality rate is around 50%
- About 1/3 of survivors have moderate/severe disability
Symptoms of SAH

- H/A (“worst headache of life”)
  - Sentinel headache in 30-60% patients
- N/V
- Syncope
- Neck pain (meningismus)
- Photophobia
- Focal CN palsy (IIIrd nerve palsy)
- LBP
### Clip or Coil?

<table>
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<tr>
<th><strong>Relative Indications</strong></th>
<th><strong>Relative Contraindications</strong></th>
</tr>
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<tbody>
<tr>
<td><strong>Coil</strong></td>
<td></td>
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<tr>
<td>Poor surgical candidate</td>
<td>Elongated aortic arch</td>
</tr>
<tr>
<td>Favorable aneurysm anatomy</td>
<td>Giant aneurysm</td>
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<tr>
<td>Favorable vascular access</td>
<td>Cervical or intracranial arterial stenosis</td>
</tr>
<tr>
<td>Need for long-term anticoagulation</td>
<td>Aortic, femoral artery occlusion</td>
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<tr>
<td>Posterior circulation aneurysms</td>
<td>Intolerance to iodinated contrast</td>
</tr>
<tr>
<td>Vasospasm</td>
<td>Intolerance to heparin/ antiplatelet agents</td>
</tr>
<tr>
<td><strong>Clip</strong></td>
<td></td>
</tr>
<tr>
<td>Younger patient</td>
<td>Advanced age</td>
</tr>
<tr>
<td>No prior cranial surgery</td>
<td>Giant aneurysm</td>
</tr>
<tr>
<td>Middle cerebral artery aneurysm</td>
<td>Atherosclerotic or calcified aneurysm neck</td>
</tr>
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</table>
Microsurgical clipping
Craniotomy/clipping
Craniotomy/clipping

Fig 7. The carotid cistern, the chiasmatic cistern, the sphenoid compartment of the sylvian fissure and the lamina terminalis cistern.
Endovascular Treatment

- Coils
  - bare platinum
  - coated
- Balloon remodeling
- Stent assisted coiling
- Low porosity stents
- Parent vessel occlusion
- Onyx
Microcatheters

- Soft atraumatic tip
- Steam shapeable
Micro(guidewires)

- Shapeable
- Steerable (Torque)
Detachable Coils
Balloon remodeling
Stent assisted coiling
Flow diversion – Low porosity stents
<table>
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<tr>
<th>Intracranial Aneurysms</th>
<th>Flow Diverter Devices</th>
<th>Endovascular Reconstruction</th>
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**Flow Diverter Devices**

- **Intracranial Aneurysms**
- **Endovascular Reconstruction**
Rabbit 783B06

Pre-Tx  Post-Tx  Sacrifice

Kallmes et al. Stroke 2007
Lumbar Arteries Remain Open

Kallmes et al. Stroke 2007
Jailed Ophthalmic Artery

4 month Follow-up
Endovascular Reconstruction

6 mo FU
Pipeline Embolization Device (PED)

• PITA trial: wide necked unruptured aneurysms (>4mm) with dome/neck <1.5 were enrolled at 4 centers. Aneurysms treated with PED w/w/o adjunctive coiling, clinical analysis at 30 days, 180 days, angiography at 180 days

• Mean aneurysm size 11.5 mm, mean neck 5.8 mm, 38.7% of treated lesions had failed previous endovascular treatment

• 31 aneurysms
  – 28 from ICA, 1 MCA, 1 VA, 1 VB junction
    • 5 cavernous, 15 peri-ophth, 4 sup. hyp, 4 Pcomm
PITA trial

• Successful placement in 30/31 cases (96.8%)
• 2 patients with major periprocedural stroke
• Follow-up angio demonstrated complete aneurysm occlusion in 28/30 cases (93.3%)
• No significant in-stent restenosis at follow-up angio

• These results have been confirmed in both Buenos Aires and Budapest experiences with similar obliteration rates and complication profiles
• PED changes the treatment modality from thinking about packing density in the aneurysm dome to thinking about luminal reconstruction and curative treatment at the level of the aneurysm neck
• This technology is a “game-changing” development for a population of aneurysms that carry a low-curative rate with endovascular coiling alone and a significant peri-operative morbidity with surgical clipping

• Caveats:
  – Perforators and telescoping stents
  – Previous self-expanding stents (Neuroform, Enterprise) and risk of endoleak
  – Ruptured aneurysms given the need for dual anti-platelet adjuvant treatment
  – Bifurcation aneurysms
  – Changes in reperfusion rates in the native vasculature (TJU experience to be published)
Onyx into Aneurysms

Initial presentation

Neck Measures at 7.96mm (green line)
Coil Recanalization: treatment with Onyx

Coil recanalization (66 coils 1070 cm.)

Post Onyx Injection

1.8mL Onyx Injected
Cornell Experience (7/31/2009)

- 516 aneurysms in 504 patients
  - Fusiform: 19, Saccular: 497
  - Saccular aneurysms
    - ruptured: 244
    - unruptured: 253

- Saccular aneurysms treatment: coils/stent
  - GDC alone in 204
  - Matrix alone in 121
  - GDC/Matrix 74
  - Hydrocoil in 24
  - Axium in 26
    - Neuroform/Enterprise stent in 65

- Fusiform Aneurysms:
  - mostly parent artery occlusion
Cornell Experience (7/31/2009)

- Complication rate 8.72%
  - 41 complications:
    - 14 thromboembolic
    - 1 CN III palsy
    - 1 CN VI palsy
    - 10 groin hematomas
    - 2 dissections
    - 8 coil migration,
    - 5 hemorrhage
  - 3 deaths:
    - 2 ruptures
    - 1 migration of coils following by hemorrhage after retrieval of coils

- Retreatment rate: 27/516= 5.2%

- Clinical outcome at six months:
  - Morbidity (Rankin >1) : 7 (1.3%)
  - 3 death (0.6%)
Coils
Coils
Coils/balloon

framing (3D) coil
Coils/balloon
Coils/balloon
Coils/ balloons
Coils/ balloons
Coils/ balloon
Coils/ balloon
Coils/ balloon
Coils/ balloon
Two Catheter Technique
Coiling/Stent
Coiling/Stent
Coils/ balloon/ glue/ stent
Coils/ balloon/ glue/ stent
Retreatment
Deconstruction
Reconstruction
Conclusions

- Multiple ways to treat unruptured aneurysms
  - Observation
  - Microsurgical
  - Endovascular
    - Coil, liquid embolic agent, stent
- Subarachnoid hemorrhage occurs with rupture
  - High morbidity and mortality
- Clipping and endovascular therapies are adjunct treatments to aneurysms, not competing ones
- Tertiary care centers with 24-hour OR, angio, NSICU, neuroanesthesia offer the best outcomes to patients