Endovascular treatment of Cerebral Aneurysms

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Disclosures

NO CONFLICTS OF INTEREST TO DISCLOSE
Objectives

- Review the natural history and treatment options for intracranial aneurysms
- Discuss current endovascular therapy options for treatment of cerebral aneurysms
- Review relevant published literature
- Evaluate future directions for endovascular treatment of brain aneurysm
What is a cerebral aneurysm?
Historical Perspective
Historical Perspective

- 1761 Giovanni Batista Morgagni
  - Published first description of an intracranial aneurysm
- 19\textsuperscript{th} Century approach to cerebral aneurysms
  - Parent vessel ligation for surgical treatment
- 1927 Antonio Egas Moniz
  - Cerebral angiography
- 1937 Walter Dandy
  - Clip ligation of aneurysm neck
- 1962 Operating microscope, clips, anesthesia, NICU
- 1971 Godfrey Hounsfield and Allan Cormack
  - First head CT
- 1976 Paul Lauterbur, Peter Mansfield, and Raymond Damadian
  - First MR scan
- 1990 Guido Guglielmi
  - Detachable coils
Natural History

- **Ruptured intracranial aneurysms**
  - 50% mortality with additional morbidity for survivors
  - Urgent treatment for high risk of re-rupture for patients that have a meaningful prognosis

- **Unruptured intracranial aneurysms**\(^1\)

<table>
<thead>
<tr>
<th>Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment</th>
<th>&lt;7 mm</th>
<th>7-12 mm</th>
<th>13-24 mm</th>
<th>≥25 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavernous carotid artery (n=210)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Anterior cerebral artery, anterior communicating artery, middle cerebral artery, or internal carotid artery (excluding cavernous segment) (n=1037)</td>
<td>0%</td>
<td>1.5%</td>
<td>2.6%</td>
<td>14.5%</td>
</tr>
<tr>
<td>Posterior circulation(\d) or posterior communicating artery (n=445)</td>
<td>2.5%</td>
<td>3.4%</td>
<td>14.5%</td>
<td>18.4%</td>
</tr>
</tbody>
</table>

*No history of subarachnoid haemorrhage. \(1\)History of subarachnoid haemorrhage from a separate aneurysm. \(2\)Any vertebrobasilar or posterior cerebral artery segment aneurysm. Reproduced from Wiebers and colleagues.\(^5\) by permission of Elsevier.

Table 2: 5-year cumulative aneurysm rupture rates according to size and location of unruptured aneurysm

- Additional Risk Factors: Cigarette smoking, family history, hypertension, aneurysm morphology
Unruptured Intracranial Aneurysm: Treatment Options
Clip vs Coil?
Unruptured Intracranial Aneurysm: Treatment Options

Observation vs Treatment
Unruptured Cerebral Aneurysm: Treatment Options

Microsurgical clip ligation

- M/M ranging from < 1% to 50% from small anterior circ to giant posterior circ aneurysms (overall 2.6% mortality, 10.9% morbidity)\(^1\)
- Increased risk for age > 50, aneurysm > 12 mm, and posterior circulation\(^2\)
- Physical manipulation of neural and vascular structures, post-operative recovery time, surgical site, cosmetic, and cognitive complaints

Unruptured Cerebral Aneurysm: Treatment Options

Endosaccular coil embolization:

- **ATENA**¹ (739 aneurysms < 15 mm)
  - 5.4% morbidity and mortality
  - 4.3% aborted procedure
  - 59% complete occlusion, 21.7% neck remnant, 19.3% aneurysm remnant
- Recurrence 16.5-26.4%, more associated with wide neck²;³
- Difficult to treat complex shapes, tortuous anatomy
- Failure to address mass effect

Ruptured Cerebral Aneurysm

WELL, LIKE DUH.
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 Snoe, Julia A Yamold, Peter Sandercock, for the International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group

<table>
<thead>
<tr>
<th>Modified Rankin Scale</th>
<th>2 month outcome</th>
<th>1 year outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Endovascular n=1065</td>
<td>Neurosurgery n=1063</td>
</tr>
<tr>
<td>0 No symptoms</td>
<td>203 (19.1%)</td>
<td>144 (13.6%)</td>
</tr>
<tr>
<td>1 Minor symptoms</td>
<td>310 (29.1%)</td>
<td>273 (25.7%)</td>
</tr>
<tr>
<td>2 Some restriction in lifestyle</td>
<td>274 (25.7%)</td>
<td>254 (23.8%)</td>
</tr>
<tr>
<td>(0-2 inclusive)</td>
<td>787 (73.9%)</td>
<td>671 (63.1%)</td>
</tr>
<tr>
<td>3 Significant restriction in lifestyle</td>
<td>107 (10.1%)</td>
<td>189 (17.8%)</td>
</tr>
<tr>
<td>4 Partly dependent</td>
<td>34 (3.2%)</td>
<td>46 (4.3%)</td>
</tr>
<tr>
<td>5 Fully dependent</td>
<td>62 (5.8%)</td>
<td>73 (6.9%)</td>
</tr>
<tr>
<td>6 Dead</td>
<td>75 (7.0%)</td>
<td>84 (7.9%)</td>
</tr>
<tr>
<td>(3-6 inclusive)</td>
<td>278 (26.1%)</td>
<td>392 (36.9%)</td>
</tr>
</tbody>
</table>

Table 2: Clinical outcome at 2 months and 1 year
Ruptured Acomm Aneurysm
Coil embolization
Adjuncts to Endosaccular Coiling
SAH, Basilar tip aneurysm
Balloon assisted coil embolization
Adjuncts to Endosaccular Coiling
Unruptured Intracranial Aneurysm?
Adjuncts to Endosaccular Coiling

Stent thrombosis

Thrombus cellular components

- Plaque necrotic material
- Platelets
- Neutrophils
- Platelet aggregates

VS

ACS: 30 days < 1 year

ASA +
clopidogrel
prasugrel
ticagrelor

Upstate
Comprehensive Stroke Center
Broad neck Acomm aneurysm
Stent assisted coil embolization
Post stent-coil
Covered Stent for LAD perforation
Critical perforator arteries, Tortuosity

Ophthalmic artery
Anterior communicating artery
Anterior cerebral artery
Middle cerebral artery
Anterior choroid artery
Internal carotid artery
Posterior communicating artery
Posterior cerebral artery
Basilar artery
Superior cerebellar arteries
Posterior inferior cerebellar artery
Vertebral artery
Posterior spinal artery
Anterior spinal artery
Circle of Willis
Porosity: ratio of open area/total stent area
Pore density: the number of pores/area
Metal Coverage: ratio of covered area/total stent area
Porosity: ratio of open area/total stent area
Pore density: the number of pores/area
Metal Coverage: ratio of covered area/total stent area

~10%

~35%
Modeling Flow Diversion (PIV)

Rabbit aneurysm model

D’Urso - Stroke 2011
Kallmes - Stroke 2007
Flow diversion: Theoretical Mechanism of Action

- Creates stasis in the aneurysm
- Stasis favors thrombosis
- Creates a scaffold for endothelium growth
- *Pressure gradient/outflow maintains patency of branch arteries*
Current Flow Diverters

Silk® (CE)

Pipeline Flex® (FDA)

FRED® (CE/IDE)

Surpass® (CE/IDE)
FDA Indications for Use

Indication
The Pipeline® Flex Embolization Device is indicated for the endovascular treatment of adults (22 years of age or older) with large or giant wide-necked intracranial aneurysms (IAs) in the internal carotid artery from the petrous to the superior hypophyseal segments.

Contraindications
Patients with active bacterial infection.
Patients in whom dual anti platelet therapy (aspirin and Clopidogrel/Plavix®) is contraindicated.
Patients who have not received anti platelet agents prior to the procedure.
Patients in whom a pre-existing stent is in place in the parent artery at the target aneurysm location.
# Pipeline: Medical Evidence

## Pipeline® Embolization Device Clinical Results

<table>
<thead>
<tr>
<th></th>
<th>PUFs Trial¹</th>
<th>PITA Trial²</th>
<th>Buenos Aires Experience³</th>
<th>Budapest Experience⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Aneurysms</td>
<td>106</td>
<td>31</td>
<td>63</td>
<td>19</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>104</td>
<td>31</td>
<td>53</td>
<td>28</td>
</tr>
<tr>
<td>Mean Aneurysm Size</td>
<td>18.2 mm</td>
<td>11.5 mm</td>
<td>11.1 mm</td>
<td>16 mm</td>
</tr>
<tr>
<td>Occlusion Rate* - 6 Months</td>
<td>82%</td>
<td>93%</td>
<td>93%</td>
<td>94%</td>
</tr>
<tr>
<td>Occlusion Rate* - 1 Year</td>
<td>86%</td>
<td>Not Reported</td>
<td>94%</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Recurrence Rate</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Major Stroke or Neurologic Death</td>
<td>5.6%</td>
<td>6.5%</td>
<td>0.0%</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

References:
1. Chestnut Medical FDA Panel Presentation
Complications of flow diversion
Complications of flow diversion: Intraparenchymal Hemorrhage
Complications of flow diversion: Late Aneurysm Rupture
Complications of flow diversion: Device stenosis and ischemia
IntrePED (Retrospective Study)

- n = 793 patients, 906 aneurysms, 76 ruptured
- **Neurologic morbidity = 7.4%**
  - Posterior circ = 16.4%, Anterior circ = 4.8%
  - Giant = 25.8%, large = 8.8%, small = 5.4%
- **Neurologic mortality = 3.8%**
  - Posterior circ = 10.9%, Anterior circ = 1.4%
  - Giant = 9.6%, large = 5.0%, small = 1.8%

IntrePED (Retrospective Study)

- **Spontaneous rupture = 0.6% (4/5 within 30 d)**
  - Giant = 4.5%, large = 0.6%, small = 0.0%
- **Intraparenchymal hemorrhage = 2.4%**
  - No subgroup difference, 79% within 30 days
- **Ischemic stroke = 4.7%**
  - Posterior circ = 7.3%, anterior circ = 2.7%
  - Giant = 14.5%, large = 5.0%, small = 2.8%
- **In-stent stenosis = 0.3%**
- **Cranial neuropathy = 0.3%**

Learning Curve
Pipeline versus “traditional” endovascular means
Complete occlusion in 86% of PED vs. 41% of coiled aneurysms (p<0.001)
Retreatment in 2.8% of PED vs. 37% of coiled aneurysms (p<0.001)
Favorable outcome (mRS, 0–2) in 92% of PED group vs. 94% of the coil group (P=0.8)
65 y/o F intractable HA
65 y/o F intractable HA
Endoluminal flow diversion for intracranial aneurysms

- High rates of complete aneurysm occlusion
- *Durable* form of endovascular treatment
- Dual antiplatelet therapy can limit use
- Complications *not insignificant*, but comparable to other treatment modalities and severity of disease
- Powerful tool for complex aneurysms, selective indications
“Hybrid” stent technology

4.5 x 23 mm LVIS® Device
3.5 x 23 mm LVIS® Jr. Device
4.5 x 28 mm Enterprise™ Stent
3.5 x 30 mm NeuroForm™ EZ Stent
Braid Pattern Change

LVIS® Rev. C device

LVIS® Blue device

Larger Angle

Smaller Angle
Visible and shapeable

Radiopaque strands

Pushing

Opening
Ruptured L Carotid aneurysm
Recurrence, Stent-coil LVIS Blue
Recurrence, Stent-coil LVIS Blue
Future Directions
Barrel Stent (Medtronic)
Intrasaccular flow disruption

- WEB intrasaccular flow diversion for treatment of **aneurysm neck** without compromise of parent artery lumen
- Useful for bifurcation lesions, forego antiplatelet therapy

Intrasaccular flow disruption

Woven EndoBridge Intrasaccular Flow Disrupter for the Treatment of Ruptured and Unruptured Wide-Neck Cerebral Aneurysms: Report of 55 Cases

- 52 patients/55 aneurysms, 14 ruptured
- 51/55 treated with WEB device (93%)
- 6/51 (12%) complications, 1/51 rupture, 0/51 M/M
- At 3 months: 34% occluded, 32% residual neck, 34% residual aneurysm (requiring re-treatment)
What goes wrong when stenting?

**FDA Database of Intracranial Neurovascular Stent Complaints 2010-2014**

- **Occlusion within device**: Highest number of complaints.
- **Deployment issue**, **Material separation**, and **Migration of device** follow.
- **Fracture of device**, **Difficult to remove**, and **No code available** are among the least reported problems.

Pipeline Shield Technology (bound synthetic phosphorylcholine)
EM of coated device (+3 nm)
In vitro assays of thrombogenicity
In vitro assays of thrombogenicity
In vitro assays of thrombogenicity
Medina Coil
Future Directions

- Rapidly advancing technology, decreasing technical complications
- Bifurcation lesions, posterior circulation, intrasaccular diversion
- More antiplatelet options/flexibility
- Better outcomes for hemorrhagic cerebrovascular disease!