Advancements in Neuroendovascular Intervention: Endovascular Management of Subarachnoid Hemorrhage

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Disclosures

- I will show off-label use of devices
- I will show investigational devices
- I am a neurosurgeon – I perform microsurgical clipping and endovascular coiling & flow diversion

Often choosing what to do isn’t Clip \textbf{vs.} Coil, but Clip \textbf{or} Coil.

As attendings, we play to our strength

➢ “If I get in trouble, how will I get out”

\textit{This is what often determines how the \textit{aneurysm will be treated}.}

➢ I am NOT comfortable with bypass techniques
Lecture Overview

1. Epidemiology
2. Diagnosis
3. Treatment
4. Understanding the Literature
5. New Technologies
Three Stroke Types

Ischemic Stroke
- Clot occluding artery
  - 87%

Intracerebral Hemorrhage
- Bleeding into brain
  - 10%

Subarachnoid Hemorrhage
- Bleeding around brain
  - 3%
## Etiologies of non-traumatic SAH

<table>
<thead>
<tr>
<th>Category</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td><strong>Aneurysmal (85%)</strong>, Perimesencephalic hemorrhage (10%), cerebral arteriovenous malformation (AVM), intracranial arterial dissection, carotid-cavernous fistula, cerebral sinus venous thrombosis, eclampsia, spinal AVM, spinal artery aneurysms, moyamoya disease</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>Vasculitis</td>
</tr>
<tr>
<td>Infections</td>
<td>Mycotic aneurysms, gnathostomiasis (parasitic), Lyme vasculitis</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Pituitary apoplexy (adenoma), carcinomatous meningitis</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Coagulopathy, thrombocytopenia, sickle cell disease</td>
</tr>
<tr>
<td>Drugs</td>
<td>Cocaine, amphetamines</td>
</tr>
<tr>
<td>Other</td>
<td>RCVS, eclampsia</td>
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</tbody>
</table>
Diagnosis of Subarachnoid Hemorrhage

- Signs/Symptoms
- CT and MRI
- Lumbar Puncture
- Angiography
Signs and symptoms

Headache: sentinel vs. thunderclap

1.2% of all ED HA complaints (3-6% of those requiring admission, 10% of thunderclap HA, 50% describe as instantaneous, remainder describe as onset of seconds to minutes)

Syncope: 50% of pts
Seizures: 6-16%
Nausea, vomiting, neck stiffness, photophobia, phonophobia
Drowsiness or coma
Cranial neuropathy: CN III palsy, CN VI palsy (elevated ICP)
Impaired upgaze (pressure on midbrain)
CT Imaging

- Sensitivity: 98-100% within 12 hours; 93% within 24 hours; 50% within 7 days
MRI

- Useful if CT head is negative

- T2: 94% and 100% sensitive for detecting subarachnoid blood in the acute and subacute phases

- FLAIR: more sensitive but less specific
Lumbar Puncture

- Avoid if: elevated ICP and herniation
- Sensitivity 100% if done 12 hours to 2 weeks after ictus
- Use spectrophotometry rather than visual examination for xanthochromia
- Hard to interpret if traumatic tap
Workup of suspected SAH

CT \rightarrow LP \rightarrow Observe

Consider further headache workup

Trauma history? Pattern of blood?

Vessel imaging

Aneurysm vs other findings (AVM, vasospasm)
Vessel Imaging

• Computed tomography Angiography
  ➢ Sensitivity: can be high as 95% but 86% if < 3mm
  ➢ poor around bony structures and for posterior circulation aneurysm

• Magnetic Resonance Angiography (MRA)
  ➢ Sensitivity: 55-100%
  ➢ Fairly high sensitivity if >3mm

• Digital subtraction angiography (with 3D rotation)
  ➢ Sensitivity: >95%
CT Angiography – right MCA aneurysm
Angiogram (DSA) – left paraclinoid ICA aneurysm
Angiogram (3D) – left paraclinoid ICA aneurysm
Types of Aneurysms

- Typically berry aneurysms cause SAH but occasionally mycotic or fusiform aneurysms can be cause
- Usually solitary (70-75%)
Aneurysmal Subarachnoid Hemorrhage

- Mean age – 50-60
- Female > male
- African American > Caucasian

Risk Factors

- Smoking
- Hypertension
- Heavy EtOH use
- Inherited Disorders
  - PCKD, Ehlers-Danlos, Marfan’s Syndrome, Osler-Weber-Rendu, Fibromuscular Dysplasia
Aneurysmal Subarachnoid Hemorrhage: Natural History

- Mortality: 15% preadmit, 36% at 1 day, 43% at 7 days, 57% at 1 year
- Overall Mortality estimated at 40-50%
- Higher mortality if: older, female, minority
Aneurysmal Subarachnoid Hemorrhage: Natural History

• Morbidity
  - Disability in survivors: 8-20% with mRS 3-5 as well high incidence of cognitive problems
  - Survivors: 46% report impairment in cognitive function or mood and 7% risk of epilepsy
  - Survivors at 1 year: 46% reported impairment in cognitive function or mood including: impairment were memory (50%), mood (39%), speech (14%), and self-care (10%)

• Poor outcomes if CT shows global edema, IVH, ICH, vasospasm, delayed infarct and concurrent medical issues: hyperglycemia, fevers, anemia, sepsis, pneumonia

• Worse outcomes if: advanced age, increasing systolic BP, fever, rebleeding, DCI and cerebral infarction, large aneurysm size (>10 mm)
Re-bleeding Risk

- 4% within 24 hours
- 20% within 2 weeks
- 50% within 6 months
- 3% per year after 6 months
- 70% fatality for rebleeding events
Aneurysmal Subarachnoid Hemorrhage

- Devastating disease
  - Up to 50% mortality when rupture occurs

- About 40,000 patients treated yearly in the US

- Treatment modalities
  - Endovascular and Microsurgery

Some cases still very challenging!
Historical Perspectives

1761: first pathological correlation between SAH and aneurysm rupture (Morgagni)
1933: first visualization of aneurysm in living patient by angiography (Moniz)
1937: first successful clipping (Dandy)
1991: development of coils for endovascular coiling (Guglielmi)
Why is Coiling usually superior?

• Need to understand the literature.

• ISAT and BRAT
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*

- 2143 patients with ruptured intracranial aneurysms, who were admitted to 42 neurosurgical centers, mainly in the UK and Europe.

- Randomised to clipping (n=1070) vs. endovascular coiling (n=1073)
  ➢ Key: To be “randomized” treating MD had to admit equipoise (obvious selection bias).

- F/U at 1 year

- Relative risk reduction of dependency or death
  ▪ 22.6%

- Absolute risk reduction of dependency or death
  ▪ 6.9% (30.6% versus 23.7%)
**Medium Term**: The early survival advantage was maintained for up to 7 years and was significant (p=0.03).
Re-Bleeding after Treatment

- ~30% of aneurysms will still have a neck after coiling procedure and up to 30% will re-canalize further at follow-up.

- Are these residuals and recurrences dangerous??
Yes...but keep perspective.

- **ISAT Following coil embolization:**
  - 1.9% of cases rebled within 30 days (n=38)
  - 0.6% between 30 days and 1 year
  - 0.2% after 1 year (n=7)

- **ISAT Following Clipping:**
  - 0.7% of cases rebled within 30 days (n=14)
  - 0.3% between 30 days-1 year
  - 0.06% after 1 year (n=2)

- Rest of literature: rebleeding following Coil embo at 1 year 0.9% (notably BRAT was 0%).

Keep in mind the primary outcome takes these rebleeding episodes into account---and coiling is still favored.

***But this is why in my practice I perform Angio at 6mo and INSIST ON PATIENT FOLLOW UP WITH CTA/MRA!!!***
In young patients, age <40, the difference in safety between coiling and clipping is small, and the better long term protection from clipping may give this treatment an advantage.

Take home with re-bleeding: Age **does** matter.

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**TABLE 1**

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>No. w/ Poor Outcomes</th>
<th>Poor Outcome Rate*</th>
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<th>Poor Outcome Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>34 of 186</td>
<td>18.3% (12.4, 24.2)</td>
<td>35 of 174</td>
<td>20.1% (13.2, 27.0)</td>
</tr>
<tr>
<td>40–49</td>
<td>57 of 266</td>
<td>21.4% (15.8, 27.1)</td>
<td>67 of 261</td>
<td>25.7% (19.5, 31.8)</td>
</tr>
<tr>
<td>50–59</td>
<td>71 of 352</td>
<td>20.2% (15.3, 24.7)</td>
<td>121 of 362</td>
<td>33.4% (27.3, 39.5)</td>
</tr>
<tr>
<td>60–69</td>
<td>54 of 198</td>
<td>27.3% (20.2, 34.3)</td>
<td>72 of 194</td>
<td>37.1% (28.4, 45.9)</td>
</tr>
<tr>
<td>≥70</td>
<td>34 of 61</td>
<td>55.7% (37.7, 73.8)</td>
<td>31 of 64</td>
<td>48.4% (31.3, 65.3)</td>
</tr>
</tbody>
</table>

* Calculated according to the Poisson distribution method. Numbers in parentheses represent the 95% confidence limits.
• Age > 65

• For ICA, PCOM, ACOM aneurysms
  ➢ 72% independence vs. 52%

• Seizures
  ➢ Coiling 0.7%
  ➢ Clipping 12.9%
• Cognitive impairment defined as neuropsych scores below the 5th percentile on 2 tests

• Cognitive impairment less common in coiling group
  ➢ 26% in coiling
  ➢ 38% in clipping
BRAT

- A&B days
- “Reflect the real world”
  - (and actually had grade 4s and 5s!)
- **After crossovers:** 280 clipped, 128 coiled (75 – 38%-- cross overs)
  - ***stat analysis was done on originally assigned group***

The intent-to-treat design of the BRAT eliminates any realistic way to “game” the system or to “cherry pick” good-grade patients, and no patients crossed over from coil therapy to surgical clipping because of poor clinical grade. Furthermore, poor outcomes observed in the patients who crossed over continued to be attributed to the original assigned treatment for the primary analysis.

**BRAT Results:**
When patients were assigned to the coil embolization rather than the surgical clipping group, the absolute difference was 10.5%

**TABLE 4: Multivariable analysis of patients with poor outcome (mRS score > 2) at 1 year in the BRAT**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>clipping*</td>
<td>1.72 (1.09–2.76)</td>
<td>0.020</td>
</tr>
<tr>
<td>age &gt;50 yrs</td>
<td>2.03 (1.23–3.42)</td>
<td>0.007</td>
</tr>
<tr>
<td>Hunt &amp; Hess grade &gt;II†</td>
<td>3.51 (2.21–5.68)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* Includes all patients assigned to surgical clipping (intent to treat).
† The Hunt and Hess grade is entered into the regression as a binary variable.
Of 110 coil-treated patients with a 3-year follow-up, 14 (13%) required retreatment compared with 11 (5%) of the 226 clip-treated patients (p = 0.01).
BRAT re-bleeding

- Re-Bleeding:
  - 1 year: none in coiling group, 2 in clipping group (dissecting aneurysms)
  - 2-3 years: None.

- ?more modern coils and equipment contribute?
To sum up the literature:

- A Coil First approach is the way to go, *period*. 
For Brain Aneurysm treatment ...

- Microsurgery is a very mature technique and continues to improve, at slower pace

- Endovascular tools keep evolving, technology driven
New aneurysm treatment technology

**Endoluminal**
- LVS - LVS Jr (FDA approved)
- Pulse Rider (under FDA trial)
- Barrell Stent (under FDA trial)
- NF Atlas (under FDA Trial)
- Enterprise 2 (under FDA trial)
- Liberty (under FDA Trial)
- FRED (under FDA trial)
- Surpass (under FDA trial)
- Pipeline Flex
- Pipeline Flex with Shield (CE mark but not FDA approved)

**Endosaccular**
- WEB
- Medina coil (not FDA approved)
- Luna (not FDA approved)
Background

Thromboembolism is one of the most common endovascular complications.
Low hanging fruit?

- Thromboembolic complications are multifactorial

*How to address that?*

- Coronary stents have been modified to decrease their thrombogenicity
- Neuro intervention could benefit if implants are less thrombogenic or “more blood compatible”
What is Shield Technology™?

Shield Technology™ is a surface treatment where an inert, synthetic phosphorylcholine (PC) polymer is covalently bonded to the strands that make up the Pipeline™ braid.

- PC is the major component on the surface of red blood cells and therefore treating a device with PC results in physiologic mimicry of the cell membrane.

- PC coatings have been successfully used on implanted vascular devices for over 14 years.
Courtesy of: Saleh Lamin, MD
Queen Elizabeth Hospital
Birmingham, UK
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European PED Flex shield Trial

Prospective, single arm, Multicentre European trial

Purpose: assess incidence of safety outcomes in patients treated with PED with shield technology.

Primary endpoint: occurrence of major neurologic complications in the territory supplied by the parent vessel

Secondary endpoint: device related complications at one year.

Aiming for 50 subjects.
CAUTION: Investigational Device. Limited by United States law to investigational use.
Basilar tip aneurysm treated with WEB™

- Img. 1: “Flowering up” of WEB during deployment
- Img. 2: WEB reaching full width at distal position during deployment
- Img. 3: WEB perfectly conforms to the aneurysms shape after deployment

Courtesy Prof. J. Moret, Hôpital Beaujon, France, 2014
79 yo, female
Safety and Efficacy of Aneurysm Treatment with the WEB: Results of the WEBCAST 2 Study


ABSTRACT

BACKGROUND AND PURPOSE: Flow disruption with the Woven EndoBridge (WEB) device is an innovative technique for the endovascular treatment of wide-neck bifurcation aneurysms. The initial version of the device (WEB Double-Layer) was evaluated in the WEB Clinical Assessment of IntraSaccular Aneurysm Therapy (WEBCAST) study, whereas the French Observatory study evaluated both WEB Double-Layer and Single-Layer versions of the device. WEBCAST 2 was designed to evaluate the WEB Single-Layer with Enhanced Visualization.

MATERIALS AND METHODS: Patients with wide-neck bifurcation aneurysms for which WEB treatment was possible were included. Clinical data including adverse events and clinical status at 1 month and 1 year were collected and analyzed. A core laboratory evaluated anatomic results at 1 year following the procedure.

RESULTS: Ten European neurointerventional centers included 55 patients (38 women; 27–77 years of age; mean, 54.4 ± 10.0 years) with 55 aneurysms. Aneurysm locations were the middle cerebral artery in 25 aneurysms (45.5%), the anterior communicating artery in 16 (29.1%), the basilar artery in 9 (16.4%), and the internal carotid artery terminus in 5 (9.1%). Procedural morbidity and mortality at 1 month were, respectively, 1.8% (1/55 patients) and 0.0% (0/55 patients). Morbidity and mortality at 1 year were, respectively, 3.9% (2/51 patients) and 2.0% (1/51 patients). At 1 year, complete occlusion was observed in 27/50 aneurysms (54.0%); neck remnant, in 13/50 (26.0%); and aneurysm remnant, in 10/50 (20.0%) (adequate occlusion in 40/50, 80.0%).

CONCLUSIONS: WEBCAST 2 confirms the high safety and efficacy of WEB aneurysm treatment demonstrated in the WEBCAST and French Observatory studies.

Medina Coil System

CE mark - not FDA approved

- Linear Self Expandable Mesh coil design
- Three-dimensional shape
- Conforms to the aneurysm shape
- Radiopaque Mesh Design
- Linear platinum coil to enhance radiopacity
- Delivered through an .021
- Mechanical detachment system

ENHANCE FILLING
MORE UNIFORM NECK COVERAGE
30 Day Follow Up

Animal CDDCCJ
Left carotid aneurysm
30 day
ANS 1901
Early Experience – Brazil Results
9 aneurysms treated
None on dual antiplatelets
No major clinical adverse event within 30 days
  No stroke
  No hemorrhage
1 case needed stenting for rescue
IIbIIla given intraop
Recurrent Left MCA aneurysm
Single Medina 6 mm Framer
A lot to be learned ...
Conclusions

• Aneurysmal subarachnoid hemorrhage is a critical, life-threatening pathology
• Brain aneurysms should be treated in centers offering all modalities of treatment
• There is still a role for clipping but smaller
• New generations of flow diverters, coil assisting devices, and endosaccular treatment options are coming which will improve outcomes and expand the endovascular armamentarium
THANK YOU!!!