Arteriovenous Malformations (AVM) Multimodal Management

Shaye Moskowitz, MD PhD
Boca Raton Regional Hospital
Marcus Neurosciences Institute
Director of Cerebrovascular and Neuroendovascular Surgery
Vascular Malformations

Nonshunting
- Capillary telangiectasia
- Cavernous Malformation
- Developmental venous anomaly

Shunting
- Cerebral AVM/AVF
- Pial AVM/AVF
- Mixed
What is an AVM?

AVMs are congenital lesions develop during the late somite stages of the 4-8th week of embryonic life. The lesion consists of one or more persisting direct connections between the arterial inflow and venous outflow without an intervening capillary bed.
First described in 1850’s and first attempts to ligate feeders in 1890 and resect in 1930
Why do we care?

- Estimated incidence of 0.14% (1/7th of aneurysms)
- Variety of different presenting symptoms may affect patients.
  - Hemorrhage
  - Seizures
  - Vascular steal/ progressive deficit
  - Headache
  - Incidental finding on imaging
Genetics?

• Though developmental in origin, the genetics are poorly understood.
• Vast majority are random with very few familial forms
  – HHT linkage
Rupture risk

• Symptomatic AVM:
  – 2-3% per year
  – Lifetime risk $\approx 105$ – patient age
  – Literature has struggled to truly grasp this

• Asymptomatic AVM:
  – Thought to be $\sim 1\text{-}2\%$ per year based on epidemiologic analyses
  – Better understood with recent RCT
Treatment modalities

- Surgical resection
- Endovascular embolization
- Stereotactic radiosurgery
- Conservative observation
- Modes are usable in any combination
Decisions...
How?

- Consider each individual mode and its benefits and risks overall
- Consider each individual patient and their goals of treatment and make the two match
Treatment modalities

- **Surgical resection**
- Endovascular embolization
- Stereotactic radiosurgery
Surgery

- **Advantages**
  - Instant cure

- **Disadvantages**
  - Infection
  - Brain manipulation
  - Catastrophic bleeding
  - Stroke
  - Reperfusion hemorrhage
Treatment modalities

- Surgical resection
- *Endovascular embolization*
- Stereotactic radiosurgery
Embolic agents

- Variety of materials have been used, some more antiquated than others.
  - Silastic beads
  - PVA particles
  - Platinum coils
  - Ethanol
  - nBCA
  - Onyx (ethylene vinyl polymer)
Embolization

- Advantages
  - Minimally invasive
  - Visualization of the vascular anatomy and changes
  - Immediate effect
  - Independent of nearby functional brain
  - Direct treatment of high risk features
  - Palliation

- Disadvantages
  - Difficult to effect a cure
  - Injury to the vessels
  - Rupture of feeding vessels
  - Stroke
  - Premature embolization of draining veins
  - Radiation exposure
Treatment modalities

- Surgical resection
- Endovascular embolization
- Stereotactic radiosurgery
Radiosurgery

**Advantages**
- Non-invasive
- Minimal risk to neighboring functional tissue
- Minimizes the radiation exposure of adjacent tissue
- Outpatient procedure
- No risk of reperfusion hemorrhage

**Disadvantages**
- Benefit is only seen after two-plus years
- 70% cure rate if the dose is appropriate
- Radiation injury
- Concern for post-SRS hemorrhage rate
Treatment modalities

• Surgical resection
• Endovascular embolization
• Stereotactic radiosurgery

• Observation
Observation

- **Advantages**
  - Can’t hurt a patient you don’t touch

- **Disadvantages**
  - AVMs don’t go away
  - Natural risk remains for the life of the patient
Efficacy

• Surgical resection alone ≈ 100%
• Embolization alone ≈ 10-20%
• Radiosurgery alone ≈ 70%
• Conservative management = 0%

• Can pair these techniques to best match the treatment goals.
Surgical resection

• Concern for neurologic deficit and risk for patients lead to a stratification known quite well as the Spetzler-Martin grading scheme
• Size, eloquence and venous outflow
• Scored 1-5 and proposed to reflect the surgical risk.
• Variety of modifications have been offered.
Features to consider

- Nidal or prenidal aneurysms
- Drainage
- Location (Eloquence)
- Size
- Patient age
- Flow pattern
- Clinical presentation
  - Hemorrhage
  - Steal
Aneurysms

• Increase the risk of hemorrhage
• To what degree? Highly variable…
• Intralinal aneurysms more than prenidal push for a more urgent repair
• Favor surgery and embolization
Eloquence

- Technical risk is higher for surgery
  - Even if temporary
  - Some deficits are easier to tolerate
- Favor radiosurgery

Age

- Longevity means more cumulative risk
Size

- Larger size make curative embolization less likely and technically more demanding.
- Usually associated with a more complex angioarchitecture.
- Less responsive to GKSR unless staged
  - Better as an alternative.
Drainage

• Deep drainage increase the overall hemorrhage risk.
  – Higher complexity but increased natural risk.
• Potentially increase the surgical risk.
  – Less so is the arterial supply is all superficial
  – Vein is last thing to see surgically.
• Potentially reduce the embolization risk as vein may be anatomically discreet.
Flow pattern

- Fistulous drainage are less amenable to GK.
- May be more inclined to treat these with embolization to cut flow and define anatomy.
Clinical presentation

• Hemorrhage
  – More aggressive management overall
  – More aggressive search for a “weak spot” which can be treated with embolization.

• Steal
  – Less common symptom
  – More likely to treat with an aggressive approach
  – Embolization with longer interval between stages.
So how do you match them?

• Try to sum the overall risk by assessing the risk presumed for every option.
• Offer the lowest one.
• When there is treatment equipoise, patient psyche fits in too.
• Have to consider the recent evidence that describes the natural behavior.
51y RHM ICH
24y RHF with incidental AVM
Combined procedure
64y RHF incidental found for headache evaluation
28y RHM incidental AVM
Staged embolization and surgery

He did fine with minor parietal deficits, but this can’t be good for the brain.
So is doing nothing wrong?

- Natural history was not well understood until recently.
- The identification of AVMs previously came with symptoms, though now they are found regularly for unrelated neuro issues.
- But symptomatic vs asymptomatic may not behave with the same longitudinally.
45y LHF, ICH with aphasia and refractory seizures
53yRHM incidental finding
Implications of a bleed…

• The mortality rate associated with the initial bleed is 10%, with the second bleed is 13%, and the rate increases to 20% for each subsequent bleed.

• The incidence of new neurologic deficit occurring with each bleed is 50%.

• Discordant literature though: Northern Manhattan Stroke Study (NOMASS)
### TABLE 2. Rankin Scale Scores of Patients With Incident (n=115) and Both Incident and Recurrent (n=27) Hemorrhages

<table>
<thead>
<tr>
<th>Rankin Scale Score</th>
<th>Incident Hemorrhage</th>
<th>Incident and Recurrent Hemorrhages</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>54 (47%)</td>
<td>13 (48%)</td>
</tr>
<tr>
<td>1</td>
<td>43 (37%)</td>
<td>7 (26%)</td>
</tr>
<tr>
<td>2</td>
<td>13 (11%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>3</td>
<td>2 (2%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>4</td>
<td>3 (3%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>5</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>6</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
New York Islands AVM Study

• Next formal prospective attempt in a relatively confined population to define the incidence in a case-controlled manner.

• 10m people follows for 21m patient-years:
  – 1.34/100k person-years detection rate
  – 0.68/100k person-years hemorrhage rate
Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial

Trial identifiers:
NCT 00389181
ISRCTN 44013133

ARUBA

Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial


- 223 patients unblinded randomized care of observation vs any treatment
  - Funded by NIH/NINDS
  - 114 treated, 109 observed
  - 7 crossed to treat, 3 crossed prior to treat
- Primary: Time to hemorrhage or death
- Secondary: Neurologic deficits
## ARUBA Endpoints

### Patient baseline profiles (n=226 AVM patients)

<table>
<thead>
<tr>
<th></th>
<th>ARUBA cohort n=226</th>
<th>Scotland n=204</th>
<th>Finland n=187</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AVM anatomy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bAVM size &lt;3cm</td>
<td>140 (62%) *</td>
<td>95 (47%)</td>
<td>41 (22%)</td>
</tr>
<tr>
<td>Lobar location</td>
<td>205 (91%)</td>
<td>187 (92%)</td>
<td>137 (73%) *</td>
</tr>
<tr>
<td>Infratentorial location</td>
<td>13 (6%)</td>
<td>7 (3%)</td>
<td>10 (5%)</td>
</tr>
<tr>
<td>Eloquent location</td>
<td>107 (47%)</td>
<td>104 (51%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Spetzler-Martin I</td>
<td>65 (29%) *</td>
<td>30 (15%)</td>
<td>13 (7%)</td>
</tr>
<tr>
<td>Spetzler-Martin II</td>
<td>72 (32%) *</td>
<td>51 (25%)</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>Spetzler-Martin III</td>
<td>64 (29%)</td>
<td>41 (20%)</td>
<td>61 (33%)</td>
</tr>
<tr>
<td>Spetzler-Martin IV</td>
<td>23 (10%)</td>
<td>18 (9%)</td>
<td>46 (25%) *</td>
</tr>
<tr>
<td>Spetzler-Martin V</td>
<td>0</td>
<td>2 (1%)</td>
<td>14 (8%) *</td>
</tr>
</tbody>
</table>

* p<0.001

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ARUBA 3 year

• Spontaneous ICH rate of 2.2%/year
• Complication rate (stroke/death):
  • Observation 10.1%
  • Treatment 30.7%
    • Surgery 29%
    • Embolization 25%
    • Radiosurgery 13%
HR 0.27; 95% CI 0.14-0.54

- Interventional therapy
- Medical management

Event probability (%)

Number at risk
<table>
<thead>
<tr>
<th>Interventional therapy</th>
<th>114</th>
<th>85</th>
<th>71</th>
<th>62</th>
<th>42</th>
<th>38</th>
<th>30</th>
<th>25</th>
<th>19</th>
<th>11</th>
<th>8</th>
<th>5</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical management</td>
<td>109</td>
<td>95</td>
<td>90</td>
<td>72</td>
<td>65</td>
<td>57</td>
<td>43</td>
<td>33</td>
<td>25</td>
<td>17</td>
<td>10</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>
ARUBA 5y
(data presented at ISC 2/2016)

Primary outcome, n=226
“As Treated” (time to 1st stroke or death)

Hazard Ratio, 0.22 (95% CI, 0.12-0.41)
P<0.0001

NNH: 3 (95% CI 2 - 6)
ARUBA 5y
(data presented at ISC 2/2016)

Secondary Outcome
Death or disability (mRS ≥2) at 5 years

B) As Treated

Interventional Therapy (n=42)
Medical Management (n=54)

RR (mRS ≥2): 0.41, 95% CI 0.20-0.82
In sum for ARUBA

- Observation in an asymptomatic AVM is not risk free.
- Treatment choices are riskier.

- NOT concordant with prior data
  - Large meta-analysis published in JAMA
  - 13,698 patients and 46,314 patient-years of follow-up

<table>
<thead>
<tr>
<th></th>
<th>Microsurgery</th>
<th>Embolization</th>
<th>Radiosurgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complication rate</td>
<td>7.4%</td>
<td>6.6%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Efficacy rate</td>
<td>96%</td>
<td>13%</td>
<td>38%</td>
</tr>
</tbody>
</table>
ARUBA

• Concerns include:
  – 13% enrolled
    • 1740 screened, 726 eligible, 323 refused, 177 treated off protocol
  – No standardized treatment arm, no reporting of embo or SRS management details
Summary

• Conservative management carries risk even in asymptomatic AVMs.
• The treatment choices have wide reported efficacy and complication rates, leading to uncertainty in guidance.
• AVMs require the multimodal offerings in management based on patient details, angioarchitecture, clinical presentation and follow-up.
Thank you!