Mycotic Aortic Aneurysms – Epidemiology and management

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FACULTY DISCLOSURE

• Use of Investigational Devices
  IDE for physician-modified endografts for treatment of complex aortic aneurysms

• Consulting
  Medtronic, Inc.
  L.W. Gore
Objectives

• Discuss the clinical presentation of infected native mycotic aortic aneurysms and aortic grafts infections

• Review outcomes of medical management alone vs medical + surgical repair

• Discuss the role, if any, of endovascular therapy in the management of pts with aortic mycotic aneurysms

Historical Perspective

• Described by William Osler – noticed during autopsies of pts who died of endocarditis

• At the time he used the term “micrococcus” to describe this infection …that was likely due to TB, or syphilis but it is unclear since (in his discourse) he describes the Gramm’s technique to stain tissue
Mycotic Aneurysms: 2 groups

Primary mycotic aneurysm

Graft related mycotic aneurysms

Aorto-enteric fistulae

Aortic graft erosion

Overview- Aortic graft erosions and fistulae

• Aorto-enteric fistula is different from graft erosions

• A "fistula" communicates two cavities – must be blood flowing into the viscus
Etiology- Primary Mycotic Aneurysm

- Usually, a result of bacteremia and subsequent "super-infection" of the diseased or irregular aortic surface
  - Atherosclerotic
  - Aortic ulcer
  - Aortic aneurysm

- Forms pseudoaneurysms that are unstable

Etiology- Primary Mycotic Aortic Aneurysm

- However, source can also be from extra vascular infection
  - Spine (osteomyelitis)
  - Pyelonephritis
  - UTI
  - Perforated viscus
  - Colonoscopy
  - BCG treatment for bladder cancer
  - Aneurysms/dissection can erode into the esophagus, spine, ureter or bowel

- Can also indolent
Overview- Primary Mycotic Aortic Aneurysm

- Very rare condition – 0.65% to 2% of all aortic aneurysms

- Most are saccular and often multifocal
  - Syphilis (Treponema pallidum): historically

- However…..

Salmonella spp (esp enteritidis) in the East

Staphylococcus aureus, Streptococcus pyogenes and S. Pneumoniae in the west
MICROBIOLOGY – Mayo Clinic Experience

<table>
<thead>
<tr>
<th></th>
<th>n = 54</th>
<th>Percent</th>
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<td>Culture positive</td>
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<tr>
<td>Polymicrobial infections</td>
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<td>Streptococcus viridans</td>
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<td>Candida sp.</td>
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<td>Lactobacillus</td>
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</table>

Enterococcus sp.  Klebsiella sp.  E. coli  Staph Coag Negative  Bacteroides fragilis
Enterobacter sp.  Proteus Mirabilis  Staph aureus  Nocardia sp.  Rothia mucilaginosa
Pseudomonas sp.  Peptostreptococcus  Eikenella corrodens  Corynebacterium sp.  Catoblebacter sp.

Primary Mycotic Aortic Aneurysm: distribution

Infected aortic aneurysms: Aggressive presentation, complicated early outcome, but durable results

Gustavo S. Oderich, MD, Jean M. Panneton, MD, Thomas C. Bower, MD, Kenneth J. Cherry Jr., MD, Charles M. Bawden, MS, Andrea A. Noel, MD, John W. Hallett Jr., MD, and Peter Gloviczki, MD, Rochester, Minn.
Treatment

- Antibiotics

- Hospital mortality is 36% to 82%

- A series of 22 “high-risk pts” had a 50% hospital mortality with most pts dying within 2 wks of hospital admission and the rest who made it out died within 2 wks of discharge

- Aneurysm related mortality was 77%
  - Generally considered worse in Salmonella sp. or other G-negative bacteria

Is this the best we can offer?

How about surgery?
Surgical approaches

• As in any other instance, wide debridement and removal of infected tissue is better than leaving this tissue in place.
• Question remains, however.....
  – What do you replace it with
    • Prosthetics will get infected
    • Aortic ligation has been attempted in the 20s and 30s but consequences are not acceptable
• And if replaced, can mortality & morbidity in this already vulnerable population be lower than medical management?
• Perhaps.... But what conduit?
• How about cadaveric vessels?
Surgical approaches: Cadaveric Grafts

- Used to replace a carotid artery in 1903
  - First used for the aorta by Gross in 1948 (Coarctation)
  - Dubost in 1952 used it to replace infrarenal aorta
- Remains useful to this date

Use of Cryopreserved Aortoiliac Allograft for Aortic Reconstruction in the United States

Vascular LFDC
Low-Frequency Disease Consortium

Cryopreserve arterial Allografts

- 220 patients treated at 14 academic centers

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<th>n</th>
<th>%</th>
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<tr>
<td>Initial aortic procedure</td>
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<td>Open reconstruction</td>
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<td>Endovascular</td>
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<td>Indications</td>
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<td>Primary prosthetic graft infection</td>
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<tr>
<td>Infected aortic aneurysms</td>
<td>44</td>
<td>20</td>
</tr>
<tr>
<td>Graft enteric fistula/erosion</td>
<td>33</td>
<td>15</td>
</tr>
</tbody>
</table>

- 30-day mortality, 9%
- Length of stay, 24 days

Late Results

Mean follow-up, 30 ± 3 months (Range, 1 to 160 months)

Patients at risk: 122, 91, 65, 54, 46, 35, 27, 22, 21
Neoaortic reconstruction with Xenografts (Bovine patch)

Due to the high cost of cryopreserved graft, a group in Norfolk, UK evaluated making their own graft and went on to treat 6 patients:

- Kept all 6 pts on antibiotics
- 30-day mortality: 0%
- At 13 months, there were NO reinfection AND
- 100% survival rate

How about using a regular graft?

It will get reinfecte.

CAN WE PREVENT GRAFT INFECTION?
This has been tried!
Rifampin-soaked Dacron grafts

• To mitigate the risk of graft infection, antibiotics were added to Dacron and tested for resistance in the 1980’s.

In situ rifampin-soaked grafts with omental coverage and antibiotic suppression are durable with low reinfection rates in patients with aortic graft enteric erosion or fistula.

• The best concentration both in-vivo and in-intro is 60 mg/mL as it was found to be 100% resistant to intravascular inoculation of gram + organism (S. aureus) at 7-10 days, 80-100% in 10 days.

• Very popular
Rifampin-soaked Dacron grafts

Drawings – courtesy of Gustavo Oderich, MD
Rifampin-soaked Dacron grafts

- Included 54 pts with aortic graft erosion or fistula
- Presentation
  - GI hemorrhage: 33 pts
  - Fevers: 25 pts
  - Hemorrhagic shock: 10 pts
- Operative mortality 2.3% in stable pts and 40% in pts in hemorrhagic shock
- HLOS: 20 ±18 days
- 5-year survival was 59 ± 8%
  - No late graft related death
  - Two pts (4%) had a graft reinfection

“NAIS” Procedure

- George P. Clagett, MD - UT Southwestern in Dallas, Tx.
- Noted high thrombosis (43% patency at 3 years and 33% amputation rate) and reinfection of prosthetic grafts
- Described the technique of “NAIS”- neo aortoiliac system using femoral vein in 1993
“NAIS” Procedure

Has Excellent patency and limited risk of infection
Some have advocated “staging” the procedure – same outcomes

Extra-Anatomic bypass

• Aims to revascularize the lower extremities before removing the infected aorta in the middle

• Several alternations
  – Axillo-femoral bypass is the most common
  – Ascending or descending aorta to bilateral common femoral arteries
Infected aneurysm of the thoracic aorta

- Rare cases – experience limited to case series
  - Mortality: 30%-50%
- Largest series was by Hsu et al (25 pts -13 in the arch)

- Medical treatment results in near 100% long-term mortality (57% in hospital mortality)

- Surprisingly, surgical repair had a 12%

- However, aneurysm-related mortality was 28% in the surgical group
- Late graft re-infection – 16%

Considerations in pts with Thoracic Mycotic Aneurysms

- Does it involve the arch?
  - Pt will need hypothermic arrest
  - This adds to complexity and increased mortality

- Is there an actual fistula to the esophagus/trachea/bronchus
  - Worse outcome
    - Cancer
    - Bleeding
    - Aged pts

- What do you replace it with?
47 y.o. male with Marfan syndrome and Type B AD
How do we address patients with infected TAAA?
Jeffery L. Ballard, MD

Vascular surgeon from Loma Linda University who was interested in perfusing the intestines while repairing a TAAA (Type III-V) without using extracorporeal pump

Ballard Technique
Ballard Technique

Infected aortic aneurysms: Aggressive presentation, complicated early outcome, but durable results

- A series of 43 pts treated with open repair at the Mayo Clinic
- Operative mortality was 21%
- Average length of stay was 25 days (6-119)
- Late deaths were mostly:
  - cardiovascular disease (39%)
  - cancer in 22%
- Graft related complications were low and similar to non-infected pts (90% freedom at 5 years)
Surgical management - Taiwan Experience

- A series of 56 pts treated with open repair from Taiwan
- In-hospital mortality was 23%
- HLOS: 45 days (5-149)
- Death after discharge were all re-infection-related (4/4)
- Late surgical-related complications were low (16%)
- 1 year survival:
  - Infrarenal: 82%
  - Thoracic: 47%

### CONTEMPORARY RESULTS

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
<th>% 30-d Mortality</th>
<th>% Graft reinfection</th>
<th>% Primary patency</th>
<th>% Limb salvage</th>
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<tbody>
<tr>
<td><strong>Axillo-femoral bypass</strong></td>
<td></td>
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<tr>
<td>Yeager (1999)</td>
<td>60</td>
<td>18</td>
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<td>73</td>
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<td>Seeger (2000)</td>
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<td>19</td>
<td>3</td>
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<td><strong>Femoro-popliteal vein</strong></td>
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<td>Clagett (1993)</td>
<td>41</td>
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<td><strong>Arterial allograft</strong></td>
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<td>Verhelst (2000)</td>
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<td>Harlander (2014)</td>
<td>220</td>
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<td>4</td>
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<tr>
<td><strong>Rifampin-soaked</strong></td>
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<td>Oderich (2006)</td>
<td>52</td>
<td>8</td>
<td>12</td>
<td>89</td>
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<tr>
<td>Oderich (2011)</td>
<td>54</td>
<td>9</td>
<td>4</td>
<td>92</td>
<td>100</td>
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</table>
Clearly outcomes of these open repairs are underwhelming....

IS THERE AN ENDOVASCULAR OPTION?

Endovascular Enthusiasts must have a say...

- **Semba et al.** in 1998:
  - 0% 30-day mortality in 3 pts

- **Patel et al.** – TEVAR in 14 cases of infected thoracic aneurysms:
  - Early survival: 86%
  - 3-year survival: 58%
  - Re-infection: 25%

- **Kan et al.** (*J Vasc Surg 2007*) - reviewed of 48 pts:
  - 30-day mortality: 11%
  - 20% had persistent infection
  - 3-year survival of 30% with persistent infection

- Why even offer open repair with such great outcomes???
So, Why not use an endograft?

- Well… think about it…
- If you place a prosthesis into an infected aorta, it will ultimately become infected
- This is particularly true if you are not removing all infected material
- Surgical principles dictate that you **HAVE** to immediately repair or exclude the duodenum, esophagus or ureter in the aorto-enteric fistulae and remove all dead tissue to enhance survival

52 y.o. male with an aortic dissection and multiple sternotomies presented with an aorto-trachial fistula
Infected infrarenal endograft

- 60 y.o. male with back pain and infrarenal penetrating aortic ulcer
- Underwent EVAR at an OSH
- Returned with fevers, chills and worsening abdominal, worsening abdominal pain and in renal failure
- Started on broad spectrum antibiotics for presumed graft infection and transferred
Endovascular outcomes

- Endovascular management is considered as a "temporizing" measure

- Recently, there's been new/resurrected enthusiasm about endovascular repair

National Study of Treatment of Mycotic Abdominal Aortic Aneurysms Comparing Open and Endovascular Repair

- 132 patients (mean age, 70±9) treated in Sweden for infected AAA
So, why this increased interests in endovascular therapy? What’s fueling it?

- 44 yo male IV drug user with S. aureus endocarditis and bacteremia
- Previous aorto-bifemoral bypass that is now occluded, iliac stents and multiple laparotomies for intestinal obstructions
- Has ileostomy and short bowel syndrome
- CTA and PET scan showed a >2 cm mycotic aneurysm
Obviously, you have to fix this

- Tried open repair but couldn’t
- The idea of an endograft becomes more appealing
- He added:
  - 3 amps of 60 mg/dL Rifampin
  - 30 cc sterile water
So, if you can’t do this, what do you do in a case when the patient’s too sick or you just can’t get in???

- 44 yo male IV drug user with S. aureus endocarditis and bacteremia
- Previous aorto-bifemoral bypass that is now occluded, iliac stents and multiple laparotomies

Rifampin soaking dacron-based endografts for implantation in infected aortic aneurysms--new application of a time-tested principle

Guillermo A Escobar 1, Jonathan L Elision 2, Justin Hurie 3, Shipra Arya 4, John E Rectenwald 2, Dawn M Coleman 2

Mortality after endograft for infection

- Most recurrences appear to happen at 1-2 years
- After 2 years, chance of long-term survival is good, much better than open repair
- So, how do we get pts to this 2 year mark?

Optimizing the chance of success of endovascular therapy

- What if we can drain the abscess after endografts for pts who are not candidate for open surgery?
- Described by Belair in 1998
- Literature review of 29 pts with infected endografts
- Hospital mortality was 21% (6 pts)
- Another 7 died within a year so 45% 1-year mortality
- Only 41% of pts got antibiotics and the rest had a drain placed
- Mortality was 50% in drained or not, especially if there was a fistula

Moulakakis KG et al. J Endovasc Ther 2014; 21:448-455
So…. Drains don’t work

NOT SO FAST!!!!

What if we add antibiotics to drain/lavage?

- 10 pts with graft infection treated with drainage and irrigation
- Using a solution of Gentamycin, Penn G and Metronidazole
- Irrigated until sterile culture – how long?
- Only 2 were known to reinfec – 80% survival
- Even on VRE
- Drain placed in the aortic sac and irrigated with linezolid for 28 days
- At 7 months show resolution clinically and on CT

Conclusions

• Mycotic aortic aneurysms are rare but deadly

• Medical management **ALONE** results in nearly 100% mortality

• Open surgical repair is better than conservative management, but still carries a high mortality (>20%) and morbidity (up to 50%)

• Endovascular treatment is gaining popularity for **primary** infected aneurysms in pts **without enteric contamination**

• It **may be used as a “bridge” to open surgery** in pts with massive hemorrhage, or as a definitive treatment in conjunction with antibiotics in high-risk pts with no evidence of enteric erosion

Thank You!