Abdominal Aortic Aneurysms (AAA): Management in 2012

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• General Considerations
• Pathophysiology
• Epidemiology
• Natural History
• Clinical Presentation
• Treatment
• Outcomes
General Considerations
AAA in 2012

- Definition: Focal dilatation of an artery involving an increase in diameter of at least 50% as compared the expected normal diameter.
- True aneurysms: Have all the vessel wall layers
- False aneurysms: Do not have all of the vessel wall layers
• AAA
  • 75% OF ALL ANEURYSMS
  • 70-90% MALES (esp. white males)
  • 96% DEGENERATIVE
  • 95% BELOW RENALS
  • 98% PROGRESSIVELY ENLARGE
    • Rupture
    • Repair
AAA in 2012

• Responsible for over 15,000 deaths per year in pts. 55 years of age or older
• Approximately 45,000 aortic aneurysm repairs are done yearly
• Greater than 60% of ruptured aneurysm patients never make to the hospital (counting these pts. Mortality from ruptured aneurysms may be > 90%
AAA in 2012

• What do these people have in common?

• George C. Scott
• Harvey Korman
• Lucille Ball
• Albert Einstein
• Conway Twitty
AAA in 2012

• All were celebrities
• None were presidents
• All died with ruptured aortic aneurysms
Pathophysicsology
AAA in 2012

- Aortic wall
  - Smooth muscle
  - Matrix proteins
    - Elastin
    - Collagen
  - Decreasing matrix concentrations from proximal to distal aorta
    - 58% decrease in elastin between supra and infrarenal aorta
  - Elastin is load-bearing protein
    - Resists AAA formation
  - Collagen "safety net"
    - Resists AAA rupture
AAA in 2012

- Elastin is not synthesized in adult aorta
- T-1/2 40 to 70 years
  - Reduced concentrations with aging
  - Increased prevalence of AAA
- Other factors
  - Absent vasa vasorum
  - Hemodynamic effects
AAA in 2012

• Degradation of aortic media
• Up-regulation of matrix metalloproteinases (MMPs)
  • Relative to inhibitors
  • MMP-2,-9, and particularly -12
• Neutrophil elastase, Plasmin also found in high concentrations
AAA in 2012

• Chronic adventitial and medial infiltrate
  • May be related to Chlamydia pneumoniae infection

• Aortic aneurysm antigenic protein (AAAP-40)
  • Collagen associated microfibril/glycoprotein
  • Highest concentrations in abdominal aorta
  • Shares amino acid sequence with
    • Treponema pallidum
    • CMV

• Possibility of autoimmune reaction
  • "Molecular mimicry"
AAA in 2012

• Genetic component
  • Numerous studies noting familial clustering of AAA
  • 15-20% family history
• Single dominant gene with low penetrance (Majumder/Verloes)
• Susceptibility alleles for AAA involving the DRB1 major histocompatibility locus (Tilson)
AAA in 2012

- Complex
- Loss of elastin/collagen
- Up-regulation of MMPs
- Infectious component
- Inflammatory response
- Genetic component
• Abdominal Vascular Disease
  • Aortic Aneurysm (AAA) and Renal Artery Stenosis (aRAS) are the most common conditions.

• AAA share many issues with PAD and the need for secondary prevention measures ..
Epidemiology and Natural History
AAA in 2012

• Epidemiology
  • Largely a disease of elderly white men
    • Male:Female ~6:1
  • Overall prevalence <5%

• Risk Factors
  • Smoking
  • Family History
  • HTN
  • White race

Melton et al
Am J Epidemiol 1984
## AAA in 2012

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
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</thead>
<tbody>
<tr>
<td>Smoking History</td>
<td>5.1</td>
</tr>
<tr>
<td>Family Hx AAA</td>
<td>1.9</td>
</tr>
<tr>
<td>Older Age</td>
<td>1.7</td>
</tr>
<tr>
<td>CAD</td>
<td>1.5</td>
</tr>
<tr>
<td>High Cholesterol</td>
<td>1.4</td>
</tr>
<tr>
<td>COPD</td>
<td>1.2</td>
</tr>
<tr>
<td>Height</td>
<td>1.2</td>
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</tbody>
</table>

*Lederle et al Arch Intern Med 2000*
AAA in 2012

- **Progressive Enlargement**
  - Mean growth 3–4 mm per year
    - Accelerates with increasing size
  - ‘Staccato’ growth 65%
  - Continuous growth in 25%
  - Stable size in 10%

Kurvers et al, J Am Coll Surg, 2004
AAA in 2012

• Eventual outcome (AAA >4cm)
• Repair
  • ~65% at 5 yrs
• Rupture
• Death from other causes

• Rupture Risk by AAA size

<table>
<thead>
<tr>
<th>Size</th>
<th>Risk at 1 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 – 5.5 cm</td>
<td>&lt; 1%*</td>
</tr>
<tr>
<td>5.5 – 5.9 cm</td>
<td>9%</td>
</tr>
<tr>
<td>6.0 – 6.9 cm</td>
<td>10%</td>
</tr>
<tr>
<td>≥7.0 cm</td>
<td>33%</td>
</tr>
<tr>
<td>≥8.0 cm</td>
<td>51%*</td>
</tr>
</tbody>
</table>

Lederle et al, JAMA, 2002
Clinical Presentation
AAA in 2012

• **Asymptomatic**
  • Vast Majority of Patients

• **Symptomatic**
  • Uncommon

• **Ruptured**
  • Uncommon and catastrophic
AAA in 2012

- Asymptomatic Presentation
  - Physical exam
    - Notoriously unreliable
    - 15% PPV
    - Pulsatile mass
  - Incidental finding
    - Increasingly common
  - Screening beneficial and now approved
    - SAAVE act
    - “Welcome to Medicare’ physical
    - Male over age 65 yrs age
    - Any time smoker
- Best test for screening or suspected AAA- Ultrasound
## AAA in 2012


<table>
<thead>
<tr>
<th>Study (Reference)</th>
<th>Patients Invited to Screening, n/n</th>
<th>Uninvited Controls, n/n</th>
<th>OR (95% CI Random)</th>
<th>Weight, %</th>
<th>OR (95% CI Random)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viborg County (21)</td>
<td>6/6339</td>
<td>19/6319</td>
<td>0.31 (0.13–0.79)</td>
<td>7.3</td>
<td></td>
</tr>
<tr>
<td>Chichester (20)</td>
<td>10/3205</td>
<td>17/3228</td>
<td>0.59 (0.27–1.29)</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>Western Australia (23)</td>
<td>18/19352</td>
<td>25/19352</td>
<td>0.72 (0.39–1.32)</td>
<td>16.8</td>
<td></td>
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<tr>
<td>MASS (22)</td>
<td>65/33839</td>
<td>113/33961</td>
<td>0.58 (0.42–0.78)</td>
<td>65.9</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>99/62735</td>
<td>174/62860</td>
<td>0.57 (0.45–0.74)</td>
<td>100.0</td>
<td></td>
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</tbody>
</table>
AAA in 2012

• **Symptomatic Presentation**
  • Acute expansion - manifest as pain

• Compression (very uncommon)
  • Vertebra, IVC, duodenum

• Peripheral embolization
  • Occurs in less than 2-5%
AAA in 2012

- Ruptured
  - Abdominal/ back pain
  - Hypotension/ syncope
  - Abdominal distension
  - Shock
  - Sudden Death
Treatment
• Treatment Options
  • Best Medical Management and Surveillance
    • Secondary CVD prevention
    • Every 6 months US
    • No medical therapy proven to reduce or slow aneurysm growth

• Open Surgical Repair

• Endovascular Repair
AAA in 2012

• When to treat?
  • “Old” Cutoff: 5cm
  • “New” Cutoff?

• ADAM and UK Small Aneurysm Trials
  • Randomized pts to early tx or surveillance
  • 4-5.5cm AAA
  • Extended follow-up
  • Best medical care in both arms

• Surgical Mortality
  • 2.7% in ADAM
  • 5.5% in UK Trial

Powell JT, Br J Surg, 2007; Lederle FA, NEJM 2002
AAA in 2012

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>Surveillance</th>
<th>Immediate repair</th>
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</thead>
<tbody>
<tr>
<td>Surgery</td>
<td>563</td>
<td>488 428 375 318 255 118</td>
</tr>
<tr>
<td></td>
<td>527</td>
<td>466 393 329 261 215 69</td>
</tr>
</tbody>
</table>
AAA in 2012

• Do these results apply to endovascular therapy?

• PIVOTAL trial
  • Industry sponsored
  • 4-5cm AAA
  • Eligible for EVAR
  • Randomized
  • No difference seen for early endovascular repair

• Bottom Line- Size Threshold should be 5.5cm
  • Maybe less with rapid expansion, small female pt.
AAA in 2012

- **Endovascular Repair**
  - Performed using bilateral femoral artery cutdown
  - Performed with high resolution X-ray imaging
  - ICU optional
  - Short hospital stays common
AAA in 2012
AAA in 2012

**Open Surgery**
- The ‘Gold Standard’
- Laparotomy
  - Midline
  - Transverse
  - Flank
- Proximal and distal clamping
- Interposition graft
- ICU postoperatively
Outcomes
AAA in 2012

Early

Acute Complications

- Open complications
  - Adverse CVD events
  - Acute renal injury
  - Colonic Ischemia
  - MSOF
  - Spinal cord injury
  - Embolization

- Endo complications
  - Access related
  - Limb ischemia
  - Renal toxicity
  - Embolization
  - Acute conversion
AAA in 2012

Late

- Open complications
  - Hernias
  - Graft occlusion
  - Pseudoaneurysm formation
  - Aortoenteric fistulae
  - Graft infection

- Endo complications
  - Endoleaks
  - Device Migration
  - Limb occlusion
  - Graft infection

Delayed Complications
EVAR 1
Trial
Enrollment

4799 patients assessed for eligibility
22 refused enrolment
230 pending randomisation by Dec 31, 2003
1423 eligible and offered randomisation
341 refused randomisation
106 preference for EVAR
203 preference for open repair
26 preference for no intervention
6 unknown preference
1082 randomised by Dec 31, 2003
543 assigned to EVAR (intention to treat)
10 died before surgery (3 from AAA rupture) 1 postponed surgery
543 assessed for primary endpoint (2 lost to follow up)
532 AAA repair
517 EVAR (no ruptures)
15 open repair (4 ruptures)
539 assigned to open repair (intention to treat)
13 died before surgery (7 from AAA rupture) 5 refused surgery 1 postponed surgery
539 assessed for primary endpoint (3 lost to follow up)
518 AAA repair
18 EVAR (no ruptures)
500 open repair (3 ruptures)
AAA in 2012

• DREAM Trial
  • Long term results
    • HRQOL after 6 months favors open repair
    • Early mortality advantage for EVAR lost by 1 year
    • High rate of secondary interventions in EVAR group
    • Much higher costs for the EVAR group

• DeBruin et al, NEJM, 2010;362:1881-89.
AAA in 2012

• Open Surgery-Strengths
  • Proven
  • Durable
  • Versatile
  • Definitive

• Endovascular-Strengths
  • Less invasive
  • Lower M&M
  • Shorter recovery
  • Caters to patient preference
AAA in 2012

- Open Surgery-Weaknesses
  - Maximally invasive
  - Significant M&M
  - Prolonged recovery

- Endovascular-Weaknesses
  - Incompletely proven efficacy
  - High re-intervention rates
  - Lifelong surveillance
AAA in 2012

- **Endovascular Grafting for AAA**
  - *Another Tool* For the Vascular Surgeon
  - Excellent results in well selected patients
  - Minimizes serious morbidity and perioperative mortality*
  - Allows for treatment of individuals unfit for open repair
  - Currently 40-60% of AAA are candidates
  - Constantly improving

- **Open Surgical Repair**
  - Excellent, durable results
  - Significant morbidity and recovery times