Arterial Aneurysms: Etiology & Pathophysiology

P. Joshua O’Brien, MD
Duke University

Disclosure

• I have no relationships to disclose.

• I have no unlabeled or unapproved uses of drugs or devices in my presentation.

Outline

• Definition
• Classification
• Etiology
• Pathogenesis
  – Formation
  – Enlargement
• Future
• Summary

Definition

“a permanent localized (i.e., focal) dilation of an artery having at least a 50% increase in diameter compared to the expected normal diameter of the artery in question.”


Classification

• True Aneurysm: dilatation of all three vessel wall layers.

• False Aneurysm: contained by surrounding tissue.
**Etiology**

- Degeneration
  - Infection
  - Poststenotic Dilation
  - Trauma
- Arteritis
- Connective Tissue Defects

**Risk Factors**

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperhomocysteinemia</td>
<td>7.8</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>7.4</td>
</tr>
<tr>
<td>Ever Smoked</td>
<td>5.1</td>
</tr>
<tr>
<td>Low Vitamin B6 Levels</td>
<td>3.15</td>
</tr>
<tr>
<td>Age 75-84 Years</td>
<td>3.3</td>
</tr>
<tr>
<td>Family History of AAA</td>
<td>1.9</td>
</tr>
<tr>
<td>Age (Per 7-Year Increase)</td>
<td>1.7</td>
</tr>
<tr>
<td>Hypertension-Atherosclerosis</td>
<td>1.7</td>
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<tr>
<td>Hypertension-Hyperplasmia</td>
<td>1.4</td>
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<tr>
<td>Waist-to-Hip Ratio</td>
<td>1.22</td>
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<tr>
<td>Waist Circumference</td>
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<tr>
<td>Black Race</td>
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<tr>
<td>Diabetes Mellitus</td>
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<tr>
<td>Female Sex</td>
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<tr>
<td>Age (Per 7-Year Increase)</td>
<td>1.7</td>
</tr>
</tbody>
</table>

**Genesis of an Aneurysm**

- Formation
- Enlargement

**Intima**

- Activation & Translocation of Macrophages, Th1/Th2/8 Lymphocytes
- Smooth Muscle Cell Apoptosis

- Activation/Amplification
  - Cytokines
  - Chemokines
  - Extracellular Proteins
  - Glycoproteins
  - Proteases
**Media**

**PROTEASES**
- MMP-1,-2,-3 (Collagenase)
- MMP-9 (Elastase)
- MMP-12 (Macrophage Elastase)

**ANTIPROTEASES**
- Tissue Inhibitor of Metalloprotease (TIMP)
- $\alpha_1$-antitrypsin

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**The Lamellar Unit**

**Adventitia**

**Loss of Elastin**
- Experimental models with topical elastase produce aneurysm

**Neovascularization (New Adventitial Capillary Formation)**
- VEGF elevated in AAA tissue
- Neovessel formation increased at rupture foci
- Role-player in rupture or just a marker?

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**Enlargement**

- Law of LaPlace
  - Tangential Stress $=$ Transmural Pressure $\times$ Vessel Radius ($T = PR$)

- Multiple vessel shapes with complex radii produces variable foci of wall stresses
- Wall thickness may play a role in rupture
- Hypertension an important risk factor for rupture

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**Enlargement**

- Hypertension an important risk factor for rupture
- Average aneurysm grows 2-3 mm/year
  - Baseline size
  - Smoking
  - Diabetes Mellitus
Familial Aneurysms

- 20-29% of patients with AAA have a first-order relative with AAA.
- Mutant genes produce defects in connective tissue (collagen, etc).
- Autosomal and sex-linked inheritance.
- Develop earlier in life.
- Decreased male-female ratio (2:1).
- Increased risk of rupture.

Summary

- Aneurysm formation is the result of multiple interactive biochemical processes involving all layers of the vessel wall.
- Aneurysm enlargement is the result of physical forces applied to the damaged vessel wall.
- Risk factor modification plays an important role in treatment of aneurysmal disease.
- Ongoing research may provide new targets for earlier intervention.