Vessel Calcification in BTK Arteries: What is Specific?

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Disclosures

Consultant:

- Abbott Vascular
- Bard Peripheral Vascular
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- Cardiovascular Systems, Inc.
- Cook Medical
- Medtronic
- Spectranetics
- Terumo Medical
- TVA Medical
The Pathogenesis of Arterial Medial Calcification: Accumulation of Senescent Cells

- The majority of senescent cells display the senescence-associated
  1-A-secretory phenotype
  B-pro-calcificatory
  C-associated with osteoblasts,
<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 0</td>
<td>Intimal fibrous thickening (Adaptive)</td>
</tr>
<tr>
<td>Type I</td>
<td>Macrophages, foam cells</td>
</tr>
<tr>
<td>Type II</td>
<td>Intracellular lipid accumulation</td>
</tr>
<tr>
<td>Type III</td>
<td>Foam cells + extracellular lipids</td>
</tr>
<tr>
<td>Type IV</td>
<td>Atheroma: lipid nucleus, foam cells + extracellular lipids (cholesterol crystals)</td>
</tr>
<tr>
<td>Type V</td>
<td>Fibroatheroma - lipid nucleus, covered by fibrous capsule</td>
</tr>
<tr>
<td>Type VI</td>
<td>Wall complication - ulceration, fissure, thrombus, inter-wall hemorrhage</td>
</tr>
<tr>
<td>Type VII</td>
<td>Or intense calcifications</td>
</tr>
</tbody>
</table>
The Pathogenesis of Arterial Medial Calcification: Passive or Active?

- **Passive**: vascular calcification from a mere passive consequence of aging
- **Active**: a tightly regulated, active process featuring a host of factors. Normally, a balance exists between promoters and inhibitors of calcification, but in chronic renal dysfunction, diabetes mellitus, atherosclerosis, and osteoporosis, as well as aging, a dysregulation of calcification can occur
## Types of Vascular Calcification

<table>
<thead>
<tr>
<th>Condition</th>
<th>Location and Features</th>
<th>Associated Condition(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcific atherosclerosis</td>
<td>Intimal; ossification</td>
<td>Atherosclerosis, hyperlipidemia; osteoporosis; hypertension; inflammation</td>
</tr>
<tr>
<td>Calcific medial vasculopathy</td>
<td>Tunica media</td>
<td>Type 2 diabetes mellitus; end-stage renal disease; hyperphosphatemia; amputation</td>
</tr>
<tr>
<td>Elastocalcinosis</td>
<td>Internal elastic lamina</td>
<td>Pseudoxanthoma elasticum; Marfan syndrome</td>
</tr>
<tr>
<td>Calcific uremic arteriolopathy</td>
<td>Microvessels; amorphous</td>
<td>End-stage renal disease; warfarin (?)</td>
</tr>
</tbody>
</table>
Composition of the “calcificates” in the Arterial medial Calcification (AMC)

• Hydroxyapatite \([\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]\) is deposited in the arterial media

• Bone - a biocomposite of structured cellular tissue impregnated with calcium phosphate mineral that aligns with the matrix and with the periodicity of negative charges on collagen.

• Crystals initially form octacalcium phosphate \((\text{Ca}_8\text{H}_2(\text{PO}_4)_6\cdot5\text{H}_2\text{O})\) that re-organizes and seeds epitaxial growth of hydroxyapatite \((\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6)\), the characteristic mineral of bone.

• As in bone, vascular apatitic mineral contains carbonate and magnesium impurities. In both bone and arteries, amorphous mineralization precedes mineralized tissue biogenesis, which follows vascular ingrowth and remodeling

• Mechanisms evolved to limit nucleation and propagation of calcium deposits in vertebrate soft tissues.

• In “Passive” calcification, the apoptotic bodies nucleate dystrophic calcification during tissue necrosis.
It is all in the wall
Circumferential and Semi-Circumferential Medial Calcification

How? Where? Why?

Only way to deliver drugs to the media is creating channels to media which is mixed with the media.

Type of atherectomy devices to do this type of channels are limited to ONLY Diamondback and Caterpillar.
1. Calcified intima;
2. Mild Intimal Hyperplasia
L52045, PT, Lateral plantar, 11-12, 4x

Proximal

1. Media: Calcified;
2. Mild Intimal Hyperplasia
3. No Atheromas
1. Media (between IEL and EEL, arrows): Calcified;
2. Mild Intimal Hyperplasia
3. No Atheromas
1. Media: Calcified;
2. Mild Intimal Hyperplasia
3. No Atheromas
Mid

1. Media: Calcified;
2. Severe Intimal Hyperplasia
3. No Atheromas
L52045, Pop/tibial, 20, 4x

1. Calcified Media;
2. Moderate Intimal Hyperplasia
3. No atheromas
1. Bone and Ca++ above IEL – in Intima(arrow)
Thank You

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