Significance Of Calcification In Lower Extremity Arteries Clinically: How To Evaluate It? What Does It Mean For Endo Treatments?

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Y. Gouéffic reports:
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Disclosures

Mediaclelosis / Intimal calcifications

Monckeberg’s medial sclerosis
Atheromatous plaque

Arterial calcifications in atherosclerosis

Steenman, Scientific Reports, 2018
Espitia, PLOSone, 2018

Transcriptomic analysis (microarray) for arterial heterogeneity

Steenman, Scientific Reports, 2018
Espitia, PLOSone, 2018

Calcifications heterogeneity among vascular beds

Steenman, Scientific Reports, 2018
Espitia, PLOSone, 2018

Calcifications is an active cellular process regulated by genes
Assessment of vascular calcifications

Grading scales typically assess:
- based on a single AP or two orthogonal angiographic and/or fluoroscopic views
- the presence of one-sided versus circumferential vessel wall calcification

Drawbacks:
- No distinction between medial and intimal calcifications
- semi quantitative assessment
- not a qualitative assessment of VCs

High resolution CT scan imaging

To determine the pronostic value of calcification types on patients symptomatology

CT Scan on arterial samples (radiology department, OHO Nantes, Jean-Michel Savigny), then high resolution meta CT and serial histology with clinical follow-up

Varga-Szemes, JACC, 2017

What Does It Mean For Endo Treatments?

Animal model are not relevant

• Familial hypercholesterolemic swine (FHS) model
• In-stent restenosis sites treated with an uncoated balloon control (Sterling™, Boston Scientific, n=6) or DCB:
  • Medtronic In.Pact™, 3 µg/mm² (n=6)
  • Bard Lutonix® , 2 µg/mm² (n=6)
  • Ranger™ Boston Scientific, 2 µg/mm² (n=6)

• Angiography Results
  • Neointimal proliferation significantly inhibited, with a smaller increase in percent diameter stenosis for DCB than control.


Ranger™ is not for sale in the U.S. Pre-clinical results may not necessarily be indicative of clinical outcomes.

Lutonix ™ Drug Coated Balloon Catheter is a trademark of C.R. Bard Inc. IN.PACT ™ is a trademark of Medtronic Inc.

Calciﬁcations for interventionalists increase early elastic recoil and prevent nitinol stent expansion

Why could vascular calcifications (VC) could change my strategy?

- VC could destabilize atheromatous plaque and contribute to plaque rupture. (Maldonado et al. 2012, Kelly-Arnold et al. 2013, Maldonado et al. 2014)


  • by early elastic recoil. (capek circulation 1991)
  • by preventing nitinol stent expansion. (Bausback, j endovasc ther, 2011)
  • by limiting the efficacy of drug elution. (Fanelli F, Cardiovasc Intervent Radiol. 2014)
Worse DCBs outcomes

Calcium burden with DCB efficacy

60 patients with SFA stenosis or occlusion treated with DCB

At 1 year, greater calcification was associated with:
- Lower patency
- Lower ABI
- Greater late lumen loss and TLR rate


Impact of arterial calcifications?

<table>
<thead>
<tr>
<th>IN-PACT SFA</th>
<th>LEVANT 2</th>
<th>ILLUMINATE RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Calc</td>
<td>Exclusion</td>
<td>Exclusion</td>
</tr>
<tr>
<td>Rutherford stages</td>
<td>2-4</td>
<td>2-4</td>
</tr>
<tr>
<td>Length</td>
<td>≥10 cm</td>
<td>≤15 cm</td>
</tr>
<tr>
<td>Location</td>
<td>Superficial femoral and proximal popliteal arteries</td>
<td>Superficial femoral or popliteal artery*</td>
</tr>
</tbody>
</table>

* start ≥1 cm below the common femoral bifurcation and terminates distally 5 cm below the tibial plateau AND 1 cm above the origin of the TP trunk


Impact of arterial calcifications on Long
Fracture lipid necrosis Outcomes

VC quantification was performed with a dedicated workstation (EndoSize, Therenva) on the basis of Hounsfield units (HU). The VC%= VC volume / volume of the ROI

Kaladji, Ann Vasc Surg, 2017

Take home messages

- Calcifications is an active cellular process regulated by genes
- Among vascular beds, we observed calcifications heterogeneity
- Imaging improvement is crucial to determine the prognostic value of calcification types on patients symptomatology
- The clinical value of peripheral calcifications is not well established

Kaladji, Ann Vasc Surg, 2017

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Osteoprotegerin (OPG), a decoy receptor, regulates the production of osteoclasts by inhibiting the differentiation of osteoclasts precursors

Davaine, Plos One, 2018
# Atherectomy devices

## DEFINITE AR outcomes

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Denudation</th>
<th>Non-Denudation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure</td>
<td>Analysis</td>
<td>Analysis</td>
</tr>
<tr>
<td>Partial arterial occlusion</td>
<td>9.3% (60/652)</td>
<td>12.4% (95/765)</td>
</tr>
<tr>
<td>Mean grade 2: 1:4</td>
<td>12.1% (76/634)</td>
<td>13.6% (104/765)</td>
</tr>
<tr>
<td>Primary patency vs angioplasty</td>
<td>10.3% (54/523)</td>
<td>11.0% (56/509)</td>
</tr>
<tr>
<td>Primary patency vs balloon</td>
<td>10.6% (58/542)</td>
<td>11.8% (60/518)</td>
</tr>
<tr>
<td>Primary patency vs directional OT</td>
<td>10.3% (53/513)</td>
<td>11.1% (58/534)</td>
</tr>
</tbody>
</table>

No significant difference

P=0.48 and P=0.78

Zeller, Circ Cardiovasc Interv, 2017