Difference of tissue characters of early and late femoropopliteal in-stent restenosis evaluated by high resolution intravascular imaging, optical coherence tomography.

Osaka Saiseikai Nakatsu Hospital
*Kobe University Graduate School of Medicine

Amane Kozuki, Toshiro Shinke*, Ken-ichi Yanaka*, Junya Shite
Disclosure

Speaker name: Amane Kozuki

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

☑️ I do not have any potential conflict of interest
Background

• In-stent restenosis (ISR) in femoropopliteal (FP) artery is still **unsolved** problem.
• In coronary artery stent, **smooth muscle cell proliferation** caused early ISR and **neoatherosclerosis** leads to late ISR.
• In femoropopliteal stent ISR, however, underline mechanisms of early and late ISR and its impact on outcomes have not been clarified.

Optical Coherence Tomography (OCT) is a light-based imaging modality that uses near infrared light and interferometry to image intracoronary microstructures at high resolution.

- **High Resolution**: 15~20μm
- Very clear observation of the lumen and intracoronary tissue
- Established method for stent follow-up
Objective

The aim of this study was to evaluate and explore the mechanism of FP ISR using OCT.
Material and Method

Study Design and Patients

• Multi-center retrospective study
  ✓ Osaka Saiseikai Nakatsu Hospital
  ✓ Kobe University Graduate School of Medicine
• Study period: May 2013 – Sep 2016
• FP ISR lesions were enrolled
• OCT was performed before EVT
• EVT was performed with scoring balloon or POBA
• No atherectomy device nor DCB was reimbursed at study period in Japan
Morphology of ISR tissue

**Homogeneous:**
uniformly signal-rich

**Heterogeneous:**
predominantly signal-poor lesion containing multiple spots of various signal strength

**Layered:**
signal-poor with a high-signal band adjacent to the surface

Gonzalo N. American Heart Journal 2009;158:284-93
Intra-stent thrombus: irregular mass protruding beyond the stent strut into the lumen

Jang IK. Circulation 2005;111:1551-5
Macrophage accumulation:
high-intensity band, which exceed the intensity of intra-tissue speckle noise, with high backscattering within the fibrous-cap

Tearny GJ. J Am Coll Cardiol 2012;59:1058-72

Zilver PTX stent

Misago stent
Result

• **44** stents, **30** limbs

• Stent type:
  - **BMS**: 32
    - Misago 16
    - SMART Control 13
    - Zilver 5
  - **DES (Zilver PTX)**: 12

• Average period after implantation:
  - **514** days (min 204, max 1099)

Early (<1y) ISR: n=17

Late (≥1y) ISR: n=27
## Baseline characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early ISR n=17</th>
<th>Late ISR n=27</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69.2±8.4</td>
<td>70.7±9.0</td>
<td>0.60</td>
</tr>
<tr>
<td>Sex (Men; n)</td>
<td>12 (71%)</td>
<td>17 (63%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.1±4.3</td>
<td>21.1±2.6</td>
<td>0.41</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>15 (88%)</td>
<td>23 (86%)</td>
<td>0.57</td>
</tr>
<tr>
<td>Dyslipidemia (n)</td>
<td>13 (77%)</td>
<td>23 (86%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Diabetes mellitus (n)</td>
<td>5 (29%)</td>
<td>7 (26%)</td>
<td>0.53</td>
</tr>
<tr>
<td>Hemodialysis (n)</td>
<td>2 (12%)</td>
<td>1 (4%)</td>
<td>0.33</td>
</tr>
<tr>
<td>History of Smoking (n)</td>
<td>11 (65%)</td>
<td>23 (85%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Variable</td>
<td>Early ISR n=17</td>
<td>Late ISR n=27</td>
<td>P value</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td>Rutherford class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/3/4</td>
<td>3/14/0</td>
<td>5/20/2</td>
<td>0.51</td>
</tr>
<tr>
<td>Critical limb ischemia (n)</td>
<td>0 (0%)</td>
<td>2 (7%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Chronic total occlusion (n)</td>
<td>9 (53%)</td>
<td>18 (67%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>5 (29%)</td>
<td>6 (22%)</td>
<td>0.75</td>
</tr>
<tr>
<td>TASC Ⅱ classification</td>
<td></td>
<td></td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>A/B</td>
<td>1 (6%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>C/D</td>
<td>16 (94%)</td>
<td>26 (96%)</td>
<td></td>
</tr>
</tbody>
</table>
### OCT result
- Quantitative analysis -

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early ISR n=17</th>
<th>Late ISR n=27</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal lumen area (mm$^2$)</td>
<td>3.8 ± 2.2</td>
<td>4.3 ± 4.7</td>
<td>0.67</td>
</tr>
<tr>
<td>Stent area at MLA (mm$^2$)</td>
<td>25.1 ± 4.7</td>
<td>28.2 ± 7.0</td>
<td>0.12</td>
</tr>
<tr>
<td>Minimal stent area (mm$^2$)</td>
<td>24.1 ± 5.0</td>
<td>26.3 ± 8.0</td>
<td>0.31</td>
</tr>
<tr>
<td>Reference lumen area (mm$^2$)</td>
<td>15.9 ± 5.8</td>
<td>14.9 ± 6.4</td>
<td>0.74</td>
</tr>
<tr>
<td>Variable</td>
<td>Early ISR n=17</td>
<td>Late ISR n=27</td>
<td>P value</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>----------------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Minimal lumen area plaque character</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homogeneous</td>
<td>3 (18%)</td>
<td>3 (11%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Layered</td>
<td>11 (65%)</td>
<td>10 (37%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>3 (18%)</td>
<td>14 (52%)</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Neoatherosclerosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid</td>
<td>4 (24%)</td>
<td>7 (26%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Plaque rupture</td>
<td>4 (24%)</td>
<td>7 (26%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Calcification</td>
<td>0</td>
<td>2 (7%)</td>
<td>0.47</td>
</tr>
</tbody>
</table>
OCT result

Intra-stent thrombus

- Early ISR: 0%
- Late ISR: 48.1%

P = 0.001
OCT result

Macrophage accumulation

Early ISR: 29.4%
Late ISR: 81.5%

P=0.001
1 year re-TLR free survival

Early ISR: 71%
P = 0.00

Late ISR: 18%
Early ISR
-Misago 8m-
Late ISR
-SMART Control 30m-
This review is mostly based on pathology from coronary artery, \textit{not from FP artery}\footnote{Yahagi K, J Cardiovasc Surg (Torino). 2014 Jun;55(3):307-23}. Major cause of FP ISR is the proliferation of smooth muscle cell.
Frequency of intra-stent thrombus

**SFA non-ISR 8m**
- **BMS:** 0%
- **DES:** 13%

_Kozuki A, J Cardiol. 2016 May;67(5):424-9._

**Coronary 2nd DES ISR**
- **Early (≤1y):** 3.5%
- **Late (>1y):** 10.5%

_Song L, EuroIntervention. 2017 Jun 20;13(3):294-302._
Cilostazol improves patency

Soga Y, J Am Coll Cardiol 2009;53:48–53
Discussion

• Anti-thrombotic and anti-atherosclerotic intervention may have a potential to reduce the incidence of cardiovascular event and ISR after femoropopliteal stent implantation.

Aboyans V, Eur Heart J 2017 in press
Annand SS, Lancet 2017 in press
Conclusion

✓ Intra-stent thrombus and macrophage accumulation were frequently observed in late ISR suggesting underlying mechanism of early and late ISR might be different.

✓ Further studies are warranted to explore the effectiveness of long-term anti-atherothrombotic interventions to improve clinical outcome in PAD patients.
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