Impact of ultrasound follow-up to manage in-stent restenosis in femoropopliteal artery.

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Disclosure

Speaker name:
Atsushi Tosaka

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
In-stent restenosis of FP artery has become new problem

Successful FP stenting (738 patients, 915 limbs)

Repeat angioplasty for ISR (137 patients, 157 limbs)
- 21 patients, 24 limbs excluded
  - laser angioplasty
  - additional stenting
  - less than 3 months follow-up after repeat angioplasty

Enrollment (116 patients, 133 limbs)

Classified by visual estimate on angiography

Class I
- Focal ISR group (≤50mm in length)

Class II
- Diffuse ISR group (>50mm in length)

Class III
- Totally occluded ISR group
Class I at risk %
- 39 (100)
- 25 (72.5)
- 11 (50.1)
- 5 (44.5)

Class II at risk %
- 50 (100)
- 28 (65.6)
- 12 (46.7)
- 5 (42.0)

Class III at risk %
- 44 (100)
- 9 (22.7)
- 4 (15.2)
- 2 (15.2)

Follow-up interval (years)
- 0
- 1
- 2
- 3

N=133 limbs

Class I vs II, P=0.66
Class I vs III, P<0.0001
Class II vs III, P=0.0003
Management of FP ISR

Step 1: Avoid in-stent occlusion

A recent study has reported that TASC II C and D lesions and cilostazol administration are independent predictors of stent occlusion after successful FP stenting (3). Early follow-up with duplex ultrasonography for TASC II C/D lesions and cilostazol administration may prevent stent occlusion, and consequently reduce the surgical revascularization rate.

Among ISR classes, class II was related with the highest
Cilostazol reduces restenosis of femoropopliteal lesions

Cilostazol Reduces Angiographic Restenosis After Endovascular Therapy for Femoropopliteal Lesions in the Sufficient Treatment of Peripheral Intervention by Cilostazol Study
Osamu Iida, Hiroyoshi Yokoi, Yoshimitsu Soga, Naoto Inoue, Kenji Suzuki, Yoshiaki Yokoi, Daizo Kawasaki, Kan Zen, Kazushi Urasawa, Hirano, Yusuke Miyashita, Taketsugu Tsuchida, Takaaki Isshiki, Toshimitsu Hara

- OR: 0.26
  (95% CI: 0.13, 0.53)
- P=0.0001

Restenosis rate (%)

49% (38/77)

20% (18/75)
Does DUS FU reduce in-stent occlusion?

Does DUS FU reduce in-stent occlusion?

### Recommendations: Surveillance after interventions for intermittent claudication (IC)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>C</td>
</tr>
<tr>
<td>1</td>
<td>C</td>
</tr>
</tbody>
</table>

6.1. **We suggest** that patients treated with open or endovascular interventions for IC be monitored with a clinical surveillance program that consists of an interval history to detect new symptoms, ensure compliance with medical therapies, record subjective functional improvements, pulse examination, and measurement of resting and, if possible, postexercise ABIs.

6.2. **We suggest** that patients treated with lower extremity vein grafts for IC be monitored with a surveillance program that consists of clinical follow-up and duplex scanning.

6.3. **We suggest** that patients who have previously undergone vein bypass surgery for IC and have developed a significant graft stenosis on DUS be considered for prophylactic reintervention (open or endovascular) to promote long-term bypass graft patency.

Society for Vascular Surgery Lower Extremity Guidelines
Unlike vein graft stenosis, the natural history of stenosis after EVT remains uncertain, making the prediction of which lesion will progress to failure difficult to determine. As previously stated, the lack of reliable data documenting the natural history of the DUS-detected stenosis after EVT makes the practice of prophylactic intervention on the basis of stenosis highly questionable and possibly harmful. Moreover, there may be differences with respect to the behavior of restenoses after angioplasty alone compared with restenoses that develop after stent placement. There are data suggesting that durable salvage of thrombosed superficial FP stents is poor and that occlusion of such stents compromises runoff. Ihnat et al.\textsuperscript{219} analyzing a series of 109 consecutive SFA stents, reported that stent occlusion was associated with a significant worsening of the SVS runoff score from 4.1 to 6.4, amounting to the loss of one runoff vessel for each episode of stent occlusion. If these findings are confirmed in future studies and accurate cutoff criteria predicting progression to clinical failure after SFA stenting can be determined, selective prophylactic reintervention after SFA stenting might be reasonable. At this time, however, no such data exist.

In summary, the natural history of stenotic lesions from EVT remains uncertain, and the benefits of intervention based on duplex findings alone not yet established. Until such criteria are available, patients undergoing EVT should have serial clinical follow-up, including simple hemodynamic measurements, at clinical intervals appropriate for the indication for intervention and the extent of disease treated. In general, those treated for CLI, and with long-segment occlusions should be monitored more closely than those treated for claudication.\textsuperscript{219,261,265} The role of duplex imaging in these patients is currently unclear although useful in determining whether recurrent symptoms are due to stenosis or occlusion and to localize lesions, which might alter the treatment plan. Continued use of duplex may also help to clarify its role further, especially when correlated with clinical presentation, angiographic findings, and ultimate outcome.

Successful FP stenting (199 patients, 247 limbs)

With US FU (198 limbs)  
Without US FU (49 limbs)

Refuse recommended reintervention (one limb)

Complete protocol group (197 limbs)  
Incomplete protocol group (50 limbs)

Follow-up US was planned in 1, 3, 6 and 12 months after FP stenting. When a stent stenosis was identified, recurrent symptom or measurement of peak systolic velocity (PSV) and peak systolic velocity ratio (PSVR) were recorded with lesions having PSV > 300 cm/sec and PSVR > 3.5 considered for reintervention (balloon angioplasty only).
Patient characteristics

<table>
<thead>
<tr>
<th>PATIENT CHARACTERISTICS</th>
<th>COMPLETE PROTOCOL (N=157)</th>
<th>INCOMPLETE PROTOCOL (N=42)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>73.3 ± 0.7</td>
<td>79.0 ± 1.4</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Gender Male</td>
<td>100 (64%)</td>
<td>27 (64%)</td>
<td>0.94</td>
</tr>
<tr>
<td>Hypertension</td>
<td>133 (85%)</td>
<td>37 (88%)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>85 (54%)</td>
<td>13 (31%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>96 (61%)</td>
<td>27 (64%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>45 (28%)</td>
<td>8 (19%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Regular Hemodialysis</td>
<td>34 (22%)</td>
<td>17 (40%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiac History</td>
<td>75 (48%)</td>
<td>25 (60%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Previous Stroke</td>
<td>30 (19%)</td>
<td>11 (26%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Thienopyridines</td>
<td>127 (81%)</td>
<td>35 (83%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>70 (45%)</td>
<td>18 (43%)</td>
<td>0.84</td>
</tr>
<tr>
<td>Warfarin</td>
<td>12 (8%)</td>
<td>5 (12%)</td>
<td>0.56</td>
</tr>
</tbody>
</table>
## Lesion characteristics

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>Complete Protocol (N=197 limbs)</th>
<th>Incomplete Protocol (N= 50 limbs)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre ABI</td>
<td>0.65 ± 0.22</td>
<td>0.70 ± 0.26</td>
<td>0.38</td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>132.7 ± 82.4</td>
<td>129.1 ± 84.7</td>
<td>0.79</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>5.19 ± 0.89</td>
<td>5.35 ± 0.81</td>
<td>0.25</td>
</tr>
<tr>
<td>DS (%)</td>
<td>91.2 ± 11.0</td>
<td>91.6 ± 10.6</td>
<td>0.84</td>
</tr>
<tr>
<td>Total Occlusion</td>
<td>81 (41%)</td>
<td>19 (38%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Below-the-knee run off</td>
<td>1.62 ± 0.98</td>
<td>1.31 ± 1.15</td>
<td>0.06</td>
</tr>
<tr>
<td>CLI</td>
<td>53 (27%)</td>
<td>34 (68%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
Result: Mean follow up period was 499 ± 234 days

Successful FP stenting (194 patients, 247 limbs)

With US FU (198 limbs)  Without US FU (49 limbs)

Refuse recommended reintervention (one limb)

Complete protocol group (197 limbs)  Incomplete protocol group (50 limbs)

Preventive reintervention (with symptom 30 limbs, without symptom 2 limbs)

Without stent occlusion (187 limbs)  Stent occlusion (10 limbs)  Without stent occlusion (42 limbs)  Stent occlusion (8 limbs)
Freedom from stent occlusion

Complete protocol group

Incomplete protocol group

P < 0.001, Logrank

<table>
<thead>
<tr>
<th>Time (M)</th>
<th>Complete protocol at risk (%)</th>
<th>Incomplete protocol at risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0M</td>
<td>197</td>
<td>50</td>
</tr>
<tr>
<td>6M</td>
<td>189</td>
<td>33</td>
</tr>
<tr>
<td>12M</td>
<td>129</td>
<td>15</td>
</tr>
<tr>
<td>18M</td>
<td>64</td>
<td>7</td>
</tr>
</tbody>
</table>

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Freedom from TLR

<table>
<thead>
<tr>
<th>Time (M)</th>
<th>Complete protocol group</th>
<th>Incomplete protocol group</th>
<th>P = 0.145, Logrank</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>94.8%</td>
<td>83.4%</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>83.4%</td>
<td>71.8%</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>77.7%</td>
<td>64.8%</td>
<td></td>
</tr>
</tbody>
</table>

- Complete protocol group:
  - at risk: 197
  - at risk %: 100

- Incomplete protocol group:
  - at risk: 50
  - at risk %: 100
Multivariate predictors of stent occlusion

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>HR (95% CI)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete protocol group</td>
<td>2.47 (1.52-3.94)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Clinically prespecified predictors (age, sex, hypertension, hyperlipidemia, diabetes mellitus, current smoker, hemodialysis, CAD, CVD, thienopyridines administration, warfarin administration, cilostazol administration, pre ABI, lesion length, RVD, %DS, total occlusion, BTK run-off, presence of CLI) with P<0.05 on Cox univariate models were entered into the multivariable Cox regression model.
CONCLUSION

US follow up with preventive intervention for patients with FP stenting will help to reduce in-stent occlusion.

TLR did not increase by performing preventive reintervention.

New technology to improve the treatment for ISR is needed for Japanese patients.
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