How I Use Drug Eluting Devices in my Practice

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Disclosure

Speaker name:
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I have the following potential conflicts of interest to report:

☐ Consulting – Clinical Investigator for Shockwave
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest
• The vast majority of DE device usage outside of the coronary arteries is in infra-inguinal lower limb arteries.

• Patients with femoro-popliteal atherosclerosis present at least 10X more frequently with claudication than they do with critical limb ischemia.\(^1\)

• I’ll focus on the use of DE devices in the treatment of the claudicants with femoro-popliteal disease.

• Briefly discuss DE devices in CLI.

• I do use DE devices for re-stenosis in other locations (renal, mesenteric, subclavian) – not discuss further.

1. Hirsh et al, J Am Coll Cardiol 2006;47:1239-1312
The claudicant population with SFA disease is large.
These patients are 1-2 decades younger than CLI patients (50s – early 70s).
Quality of life is important to these patients and they often have disposable income to try and achieve it.
Intermittent Claudication

- The claudicant population with SFA disease is large
- These patients are 1-2 decades younger than CLI patients (50s – early 70s)
- Quality of life is important to these patients and they often have disposable income to try and achieve it

- Intervention in the SFA in claudicants must be DURABLE as the indication for treatment is lifestyle limiting pain and cardiovascular risk with no limb salvage benefit

Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II)

Norgren L, J Eur J Endovasc Surg 2007
Plain Balloon Angioplasty

- Outcome with POBA is clearly related to lesion complexity and lesion length

Focal stenoses carry a 12 month primary patency of 70-80%\textsuperscript{1,2}
More diffuse disease carries a 12 month primary patency of 30-40%\textsuperscript{1,2}

Table F6. Pooled results of femoral popliteal dilatations

<table>
<thead>
<tr>
<th>Procedure</th>
<th>1-year % patency (range)</th>
<th>3-year % patency (range)</th>
<th>5-year % patency (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA: stenosis</td>
<td>77 (78–80)</td>
<td>61 (55–68)</td>
<td>55 (52–62)</td>
</tr>
<tr>
<td>PTA: occlusion</td>
<td>65 (55–71)</td>
<td>48 (40–55)</td>
<td>42 (33–51)</td>
</tr>
<tr>
<td>PTA + stent: stenosis</td>
<td>75 (73–79)</td>
<td>66 (64–70)</td>
<td></td>
</tr>
<tr>
<td>PTA + stent: occlusion</td>
<td>73 (69–75)</td>
<td>64 (59–67)</td>
<td></td>
</tr>
</tbody>
</table>

PTA — Percutaneous Transluminal Angioplasty.

2. Lofberg et al, J Vasc Surg 2001;34:114-21

24-Month Effectiveness
Primary Patency (PSVR < 2.0): Zilver PTX vs. PTA

Primary Patency (PSVR < 2.0):
- Zilver PTX: 83.1%
- Successful PTA: 32.4% (116 Lesions)
- All PTA: 53.4% (241 Lesions)
- Zilver PTX: 74.8%

p = 0.029

Mean Lesion Length: 66mm +/- 39mm
1. Primary patency – freedom from clinically driven TLR and re-stenosis (PSVR < 2.4)
Is a Stent or Scaffold Necessary in The SFA?

- The femoro-popliteal segment is a challenging environment due to vessel length and mobility.
- The longer and more complex the lesion, the more often a stent is required to treat residual stenosis and flow limiting dissection.
Scaffold Support in the SFA

<table>
<thead>
<tr>
<th>Trial</th>
<th>Trial Type</th>
<th>Indication for “Bail Out” Stent</th>
<th>Incidence of “Bail Out” Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thunder</td>
<td>DEB</td>
<td>Not clearly defined</td>
<td>11.4% (10/87)</td>
</tr>
<tr>
<td>Resilient</td>
<td>BMS</td>
<td>Residual &gt; 30%</td>
<td>40% (29/72)</td>
</tr>
<tr>
<td>Zilver PTX RCT</td>
<td>DES</td>
<td>Residual &gt; 30%</td>
<td>50% (120/238)</td>
</tr>
</tbody>
</table>

- Incidence of “bail out” or “spot” stenting depends on how a significant residual stenosis or dissection is defined
- Longer and more complex lesions consistently have a higher incidence of stenting
Stent Support in the SFA

• In the In.Pact SFA Trial, bail out stenting was 7.3% in the drug coated balloon arm with a lesion length of 8.9cm¹

• However, cases with unsuccessful pre-dilatation were excluded!

• This was also the case for the LEVANTE 2 Trial

• In the Leipzig Real World DEB Registry for extensive SFA lesions treating a mean lesion length of 24cm, the stenting rate was 23.3%.

### Trial Design

1. Screen Failure (treat per std practice)
2. **SUCCESSFUL PRE-DILATATION**
3. **Randomized 2:1**
   - **IN.PACT (220)**
   - **PTA (111)**

**Provisional Stenting?**

- **Secondary Analysis** (331 ITT ALL Subjects)
- **Primary Analysis** (301 ITT NON-Stented Subjects)

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1. With symptoms of claudication and/or rest pain and angiographic evidence of SFA/PPA stenosis
2. Pre-dilatation mandatory for all subjects in IN.PACT SFA II phase only
LEVANT 2 Clinical Trial

PTA Pre-Dilatation
With 1mm undersized Uncoated Balloon

Successful Pre-Dilation

Randomize 2:1

Test Arm:
Dilatation with Drug Coated Balloon
12 Month Follow-up

Control Arm:
Dilatation with Uncoated Balloon
12 Month Follow-up

Suboptimal PTA:
Major flow limiting dissection
OR >70% residual stenosis

Treat per standard practice
30 day follow-up for safety

CAUTION: Investigational Device - Limited by Federal (USA) Law to Investigational Use
Stent Support in the SFA

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2. Andrei Scmidt, Leipzig Real World DEB Registry, LINC 2013
Limitations of Nitinol SES in the SFA

- Patency at 2 years and beyond has been disappointing due to neointimal hyperplasia and instent restenosis
- This is especially problematic in the claudicant where long term patency is required
- Stent fractures in the hostile SFA is also problematic

Figure 3. Primary stent patency rates for fractured and non-fractured stents. Squares = no stent fracture; triangles = stent fracture.

Scheinert et al. JACC; 45(2): 312-315

Absolute Trial, Circulation 2007
24-Month Effectiveness
Primary Patency (PSVR < 2.0): Zilver PTX vs. PTA

- Zilver PTX: 83.1% (Successful PTA: 116 Lesions)
- PTA: 64.5% (All PTA: 241 Lesions)

p = 0.029

Zilver PTX
Successful PTA
All PTA
36-Month Effectiveness
Primary Patency (PSVR < 2.0): Zilver PTX vs. PTA

Zilver PTX 184 lesions

PTA 207 lesions

$p < 0.01$ log-rank
At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to standard care.
3-Year Clinical Impact Event-Free Survival: Zilver PTX vs PTA

Event-free Survival: Freedom from CEC-adjudicated death, amputation, and target lesion revascularization, or worsening Rutherford score (by 2 classes or to class 5 or 6)
At 5 years, Zilver PTX has a superior rate of freedom from persistent or worsening claudication, rest pain, ulcer, or tissue loss.
Challenging Femoro-popliteal Lesions

- Heavily calcified lesions, eccentric polypoid plaque, and instent restenosis remain challenges
- Individualized approach required but strategies to optimize the acute result include atherectomy, high radial force stents and lithoplasty
- Most require an anti-restenosis strategy with DE devices
Drug Elution in CLI

- Majority of CLI patients have tibial disease but a number also have femoro-popliteal disease\(^1\)
- An optimized acute result is probably more important in CLI patients so I have a lower threshold for stenting in the SFA
- Long term patency of SFA and popliteal lesions is just as important in CLI and the use of drug eluting technologies (DCBs, DES) is standard

Drug Elution in CLI

- Less evidence behind primary use of DCBs in tibial disease and there have been some safety concerns
- Some data behind DES in localized proximal tibial disease
- We currently confine tibial DCB use to re-stenosis cases and Rutherford 5/6 cases
Current Approach to Claudicants with SFA Disease

- The vast majority of lesions are initially managed with plain balloon angioplasty (for at least 2 minutes) dilated to NOMINAL.
Current Approach to Claudicants with SFA Disease

- Short lesions (≤ 10cm) that respond well to POBA are then treated with DCB as an anti-restenosis strategy
- Sub-optimal post-angioplasty lesions are all treated with DES (Zilver PTX)
Current Approach to Claudicants with SFA Disease

- Intermediate lesions (10-20cm) are treated with either DCB with spot stenting OR direct DES (Zilver PTX)
- The more complex the lesion (CTO length etc) or poorer result after POBA, the lower the threshold for 1° DES

![Images of angiograms showing stents and balloons inserted in blood vessels.](image)
At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to standard care.
Current Approach to Claudicants with SFA Disease

- Long lesions (> 20cm) in patients with lifetime limiting symptoms are offered surgical bypass if they have a venous conduit
- If not, options include covered stenting or DES
Cost Effectiveness of this Strategy

- Repeat interventions are more complex and costly than primary treatment
- The increased “up front” cost of drug eluting technologies is offset by reduced re-interventions

The Financial Benefits!
of!
Drug Eluting Technology!

Mark W. Burket, MD!
University of Toledo Medical Center!
Toledo, Ohio!
USA!
Zilver PTX – Continued Evolution