Lower Extremity Revascularization

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Disclosure Information

Douglas E. Drachman, MD, FSCAI

Abbott Vascular, Inc: Advisory Board
Corindus Vascular Robotics: Advisory Board
St. Jude Medical: Consultant
Atrium Medical Corporation: Research Grant Support
Lutonix/BARD: Research Grant Support

Off label use of products will be discussed in this presentation as indicated. Many stents used in the peripheral arterial circulation are indicated for biliary or tracheal application.
Four Main Points

• Atherosclerosis is a “pan-vascular” process
• PVD is underappreciated, but confers profound cardiovascular morbidity
• Early recognition, treatment, and risk reduction are critical
• Endovascular strategies rival longstanding surgical paradigm for revascularization
Atherosclerosis is a “pan-vascular” process

- TIA
- Ischemic stroke
- STEMI
- NSTEMI
- Unstable angina/ACS
- Renovascular hypertension
- Mesenteric ischemia
- Erectile dysfunction
- Claudication
- Critical limb ischemia, rest pain, gangrene, amputation
Meta-Analysis of 34 studies

202 Million with PAD worldwide

23.5% increase between 2000-2010

Figure 3: Estimate of the number of cases, and contributing age groups, in eight WHO regions in the year 2010. LMIC=low-income and middle-income countries. HIC=high-income countries.
Lower extremity claudication: The Tip of the Iceberg

Patients >55 y.o.

Intermittent Claudication
5%

Claudication: Stable
73%

Claudication: Progressive
16%

LE Surgical Revascularization
7%

Non-fatal CV Event
20%

Amputation
4%

5-year Mortality
30%

75% CV Death

CV M&M

PAD: Effect on mortality

Criqui et al. NEJM 1992; 326: 381-386.
Mortality of PAD

![Bar chart showing mortality rates for various conditions](chart.png)

*FIGURE 2. Five-year mortality rates for peripheral arterial disease (PAD) and common types of cancer. (*)Data from the American Cancer Society,20 (+)Data from Vascular Surgery.21*
Treatment of Patients with PAD

- Hygienic and supportive measures to prevent skin breakdown and infection
- Exercise conditioning
- Pharmacotherapy for claudication
- Revascularization
- Most importantly: modification of risk factors
Indications for Revascularization

- Critical limb ischemia
  - Rest pain ("the five Ps")
  - Ulcers, gangrene, necrosis
- Disabling claudication
- Quality of life
Clinical Vignette #1...
68 yo woman with right hip pain, prior steroid injections (pain is worse now)
CT Angiography
Procedure
Angioplasty/Stent
CLEVER RCT: Exercise vs. Stenting
Functional Status & QoL Outcomes

- Mean lesion length = 3.9 cm
- Mean baseline stenosis = 83%
- 38% total occlusions
- 39 CIA and 15 EIA stents

**Screened**
N = 999

**Consented**
N = 183

**Randomized**
N = 119

**Optimal Medical Care**
N = 22
- Withdrawn = 1
- Exited (other) = 1

**Supervised Exercise (SE)**
N = 43
- Withdrawn = 3
- Exited (other) = 1
- Lost to follow-up = 1

**Stenting (ST)**
N = 46
- Withdrawn = 2
- Exited (illness) = 1
- Lost to follow-up = 2

**SE + ST**
N = 8
- Withdrawn = 1

**6-Month Analysis**
- Optimal Medical Care:
  N = 20
- Supervised Exercise (SE):
  N = 38
- Stenting (ST):
  N = 41

Not in 6-Month Analysis
ERASE RCT

- RCT: SET +/- EVR for AI/FP disease (n=212)
- Stable claudication
- Aortoiliac or fem-pop disease
- Randomized 1:1 endovascular revascularization (EVR) + supervised exercise therapy (SET) vs SET alone
- EVR = PTA +/- stent
- SET = 1 hr sessions (2-3/wk x 3 mos or 1-2/wk x 3-6 mos or 1/4wks x 6-12 mos)
- Follow-up @ 1, 6, 12 mos
## ERASE trial: outcomes

<table>
<thead>
<tr>
<th>Functional Performance Measures</th>
<th>Mean (99% CI)</th>
<th>Endovascular Revascularization Plus Supervised Exercise (n = 106)</th>
<th>Between-Group Difference</th>
<th>P Value&lt;sup&gt;a&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Maximum walking distance, m</td>
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<tr>
<td>At baseline</td>
<td>285 (244 to 326)</td>
<td>264 (228 to 300)</td>
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<tr>
<td>1 mo</td>
<td>438 (282 to 595)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1004 (835 to 1174)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>566 (358 to 774)</td>
<td>&lt;.001</td>
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<tr>
<td>6 mo</td>
<td>851 (683 to 1018)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1260 (1076 to 1444)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>409 (183 to 636)</td>
<td>&lt;.001</td>
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<td>12 mo</td>
<td>955 (786 to 1124)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1237 (1058 to 1418)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>282 (60 to 505)</td>
<td>.001</td>
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<td>Pain-free walking distance, m</td>
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<tr>
<td>At baseline</td>
<td>135 (113 to 157)</td>
<td>117 (96 to 138)</td>
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<tr>
<td>1 mo</td>
<td>181 (23 to 339)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>724 (561 to 886)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>543 (340 to 744)</td>
<td>&lt;.001</td>
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<tr>
<td>6 mo</td>
<td>542 (378 to 707)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1071 (900 to 1243)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>529 (315 to 743)</td>
<td>&lt;.001</td>
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<td>12 mo</td>
<td>712 (549 to 876)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1120 (948 to 1293)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>408 (195 to 622)</td>
<td>&lt;.001</td>
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<tr>
<td>Ankle brachial index at rest&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td>At baseline</td>
<td>0.68 (0.64 to 0.72)</td>
<td>0.71 (0.67 to 0.76)</td>
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<tr>
<td>1 mo</td>
<td>-0.02 (&lt;-.07 to 0.02)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.19 (0.15 to 0.23)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.21 (0.15 to 0.27)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 mo</td>
<td>0.04 (&lt;-.01 to 0.09)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.16 (0.11 to 0.20)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.12 (0.05 to 0.17)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>12 mo</td>
<td>0.03 (&lt;-.02 to 0.08)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.16 (0.11 to 0.21)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.13 (0.06 to 0.19)</td>
<td>&lt;.001</td>
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<tr>
<td>Ankle brachial index after exercise&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
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<tr>
<td>At baseline</td>
<td>0.40 (0.34 to 0.46)</td>
<td>0.43 (0.38 to 0.48)</td>
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</tr>
<tr>
<td>1 mo</td>
<td>0.03 (&lt;-.02 to 0.09)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.36 (0.30 to 0.42)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.33 (0.25 to 0.40)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 mo</td>
<td>0.12 (0.06 to 0.18)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.33 (0.27 to 0.39)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.21 (0.13 to 0.29)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>12 mo</td>
<td>0.11 (0.05 to 0.18)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.33 (0.27 to 0.40)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.22 (0.13 to 0.31)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

- VascuQOL
- SF-36

Figure 2. Kaplan-Meier Estimates of the Proportion of Patients Without Additional Intervention During Follow-up

- Endovascular revascularization plus supervised exercise (ER + SE)
- SE only

Log-rank $P = .003$

<table>
<thead>
<tr>
<th>Time Since Randomization, wk</th>
<th>ER + SE</th>
<th>SE only</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>106</td>
<td>106</td>
</tr>
<tr>
<td>10</td>
<td>103</td>
<td>100</td>
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<tr>
<td>20</td>
<td>101</td>
<td>90</td>
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<tr>
<td>30</td>
<td>97</td>
<td>85</td>
</tr>
<tr>
<td>40</td>
<td>93</td>
<td>81</td>
</tr>
<tr>
<td>50</td>
<td>91</td>
<td>73</td>
</tr>
</tbody>
</table>

Aortoiliac Disease: *Surgical Rx*

Aortobifemoral bypass

- **Durable**
  - 5 year primary patency 80.4%
  - 10 year primary patency 72.1%

- **Risk**
  - Operative Mortality 3.3%
  - Systemic Morbidity 8.3%

- **Significant Recovery (weeks)**
Should new techniques and technologies lower our threshold to intervention?

Recommended Therapy of Iliac Artery Stenosis/Occlusion

**Endovascular Treatment of Choice**
- Type A: <3cm
- Types B/C: 3-10 cm, 3-5 cm
- Type D

**Endovascular Therapy, but Insufficient Data**
- 3-5 cm

**Surgical Treatment of Choice**

TASC, J Vasc Surg 2000;31:S1-S296
A 65 year old man with claudication...
Endovascular Therapy for Aortoiliac Disease:  
*Advantages over surgery*

- Less Invasive
- Safer/Fewer Adverse Events
- Similar Efficacy Compared to Surgery
- Shorter Length of Hospital Stay
- Faster return to work
- Potentially more cost-effective
Knee flexed
Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial

Figure 2: Amputation-free survival after bypass surgery and balloon angioplasty

Bands show 95% CIs for survival up to 1, 2, 3, and 4 years of follow-up, which were calculated from the cumulative hazards.

Balloon Angioplasty versus Implantation of Nitinol Stents in the Superficial Femoral Artery

Martin Schillinger, M.D., Schila Sabeti, M.D., Christian Loewe, M.D., Petra Dick, M.D., Jasmin Amighi, M.D., Wolfgang Mlekusch, M.D., Oliver Schlager, M.D., Manfred Cejna, M.D., Johannes Lammer, M.D., and Erich Minar, M.D.
SFA Compressive Forces:
Nitinol Stent Fractures...word of caution

Cross-table lateral knee flexed
Newer scaffolds may offer promise

RSFA stent fracture

LSFA, same patient, “woven” stent
Transradial intervention is possible
Solitary kidney, EVAR, severe EIA/CFA/RSFA PAD
Transradial intervention is possible
Transradial access and benefits
Clinical Vignette #2

• 91 year old woman
• HTN, chol, CVA, CAD, CHF, COPD
• Two months of rest pain, ulceration of right foot, despite supportive care
• ABI: non-compressible vessels
• PVR flat at PT, marginal at DP
Vignette #2: Clinical Course

- Complete resolution of CLI
- Sustained improvement (plethysmography)
- Died of pneumonia 2 years after PTA
Clinical Vignette #3: 60 yo M with IDDM
No straight-line flow to the foot
Aggressive 0.014” wires, then long balloon PTA
Restoration of PT and peroneal flow
Twenty months after PTA...
The value of subintimal angioplasty in the management of critical lower extremity ischemia: failure is not always associated with a rethreatened limb

E. C. Lipsitz, F. J. Veith, T. Ohki

Table 1.—Patency and limb salvage rates on intention to treat basis for series evaluating subintimal angioplasty.

<table>
<thead>
<tr>
<th>Series</th>
<th>#Limbs treated</th>
<th>Technical success</th>
<th>12 month primary patency</th>
<th>12 month assisted primary patency</th>
<th>12 month limb salvage</th>
<th>24 month primary patency</th>
<th>24 month assisted primary patency</th>
<th>24 month limb salvage</th>
<th>% with claudication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yilmaz et al.</td>
<td>67</td>
<td>88%</td>
<td>22%</td>
<td>57%</td>
<td>89%+</td>
<td>9%</td>
<td>19%</td>
<td></td>
<td>67%</td>
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<tr>
<td>Treiman et al.</td>
<td>25</td>
<td>92%</td>
<td>92%</td>
<td>37%</td>
<td>50%**</td>
<td>51%</td>
<td>23%</td>
<td>46%</td>
<td>0%</td>
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<tr>
<td>Laxdal et al.</td>
<td>124</td>
<td>90%</td>
<td>64%</td>
<td>90%***</td>
<td>86%***</td>
<td>84%***</td>
<td>18%</td>
<td></td>
<td>65%</td>
</tr>
<tr>
<td>Lipsitz et al.</td>
<td>39</td>
<td>87%</td>
<td>57%**</td>
<td></td>
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<td>23%</td>
</tr>
<tr>
<td>Shaw et al.</td>
<td>50</td>
<td>78%</td>
<td>27%</td>
<td>86%***</td>
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<td></td>
<td>46%</td>
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<tr>
<td>Tisi et al.</td>
<td>158</td>
<td>85%</td>
<td>51%</td>
<td>83%****</td>
<td>94%</td>
<td>94% (3 years)</td>
<td>9%</td>
<td></td>
<td>18%</td>
</tr>
<tr>
<td>Ingle et al.</td>
<td>70</td>
<td>86%</td>
<td>56%</td>
<td>81%</td>
<td></td>
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<td>38%</td>
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<tr>
<td>Vraux et al.</td>
<td>40</td>
<td>78%</td>
<td>53%</td>
<td>85%</td>
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<td>0%</td>
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<tr>
<td>McCarthy et al.</td>
<td>69</td>
<td>74%</td>
<td>51%</td>
<td>86%+</td>
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<td>38%</td>
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<tr>
<td>Nydahl et al.</td>
<td>28</td>
<td>80%</td>
<td>71%</td>
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<td></td>
<td>0%</td>
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<tr>
<td>London et al.</td>
<td>200</td>
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</table>

*) 82% performed via retrograde popliteal recanalization. **) At 6 months. *** For patients with critical limb ischemia only. **** Freedom from critical limb ischemia. *) Estimated.
Zilver-PTX DES vs. PTA: Event-Free Survival

Zilver-PTX: Provisional DES vs. BMS

89.9%

73.0%

P=0.01 (Log-Rank)

Drug-Coated Balloon Rx: Advantages

- Reduce restenosis
- No chronic implant
  - Chronic inflammation, hyperplasia & ISR
  - Issue of repeat access & subsequent intervention
  - Fracture
- Better treatment of “no-stent” zones
- Treatment option for ISR
- Reduce need for anti-platelet therapy (DAPT)
Punctuated Delivery ➔ Sustained Release

1. Brief (30-second) balloon inflation transfers PTX to endoluminal surface
2. PTX diffuses into the arterial wall from an “endoluminal surface reservoir” (role of the carrier)
3. Over time, therapeutic drug levels are sustained in deep cell layers after endothelial drug levels become sub-therapeutic
4. Drug continues to inhibit restenosis in arterial wall while allowing the lumen to restore and re-endothelialize.
LEVANT-2: outcomes

- Primary patency
  - 65.2% DCB
  - 52.6% PTA
- Freedom from safety endpoint
  - 83.9% DCB
  - 79% PTA
  - P=0.005 (non-inf)

IN.PACT SFA: 2-year outcomes

- Death (none device or procedure-related)
  - 8.1% DCB
  - 0.9% PTA

- Vessel thrombosis
  - 1.5% DCB
  - 3.8% PTA (p=NS)

Laird J, et al. JACC. 2015
Therapies for PAD

Preventing Death
- Antiplatelets
- Cholesterol lowering – “statins”
- ACE Inhibitors
- Beta Blockers

Reducing Symptoms
- Exercise
- Cilostazol
- Catheter-based interventions
- Reconstructive surgery

Saving Limbs
- Catheter-based interventions
- Reconstructive surgery
Conclusions

• Atherosclerosis is a “pan-vascular” process
• PVD is underappreciated, but confers profound cardiovascular morbidity
• Early recognition, treatment, and risk reduction are critical
• Endovascular strategies rival longstanding surgical paradigm for revascularization