Current Vascular and Endovascular Management in Diabetic Vasculopathy

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Peripheral artery disease (PAD)

- Chronic lower extremity ischemia
- Manifestations of PAD (degree of muscle ischemia)
  - Asymptomatic
  - Intermittent claudication (IC)
  - Critical limb ischemia (CLI)

Prevalence of symptomatic PAD
### Stages of chronic limb ischemia

<table>
<thead>
<tr>
<th>Stage</th>
<th>Fontaine</th>
<th>Clinical</th>
<th>Rutherford Grade</th>
<th>Category</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic</td>
<td>0</td>
<td>0</td>
<td>Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
<td>I</td>
<td>1</td>
<td>Mild claudication</td>
<td></td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate-severe claudication</td>
<td>I</td>
<td>2</td>
<td>Moderate claudication</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>I</td>
<td>3</td>
<td>Severe claudication</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
<td>II</td>
<td>4</td>
<td>Ischemic rest pain</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
<td>III</td>
<td>5</td>
<td>Minor tissue loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>IV</td>
<td>6</td>
<td>Ulceration or gangrene</td>
<td></td>
</tr>
</tbody>
</table>

**Critical limb ischemia (CLI)**
Risk factors for symptomatic PAD

- Male gender (cf female)
- Age (per 10 years)
- Diabetes
- Smoking
- Hypertension
- Dyslipidemia
- Hyperhomocysteinemia
- Race (Asian/Hispanic/black vs. white)
- C-reactive protein
- Renal insufficiency
PAD in diabetes

• More common (~x2) intermittent claudication

• PAD in DM
  – 26% increased risk of PAD / 1% increase HbA1c
  – Insulin resistance
  – More aggressive compared to non-diabetes
    • early large-vessel involvement
    • major amputation risk : x5-10
  – Foot ulcers and infections
    • Peripheral neuropathy
    • ↓ resistance to infection
  – Aggressive control of blood glucose levels
    • HbA1c <7.0% or as close to 6% as possible
Characteristics of diabetes vasculopathy

- Diffuse multilevel involvement
- Infragenicular arteries
- Heavy calcification
- Poor collateral developments
- Microangiopathy
- Macroangiopathy
Noninvasive Diagnosis of PAD

- Non-invasive vascular laboratory (혈관검사실)
  - ABI (ankle-brachia index)
  - Toe pressure or toe-brachial index (TBI)
  - Exercise treadmill test
  - Segmental limb pressure
  - Pulse volume recording (PVR)
  - Digital PPG
ABI (Ankle-brachial index)
Toe pressure & toe-brachial index

• Long-standing diabetes, renal failure
  – Incompressible tibial artery
  – Falsely high systolic pressure
  – Non-compressible
    • Ankle pressure ≥250mmHg
    • ABI >1.40

• Toe pressure
  – Useful in DM
  – 30mmHg less than ankle pressure
  – <40mmHg : impaired wound healing
  – Toe-brachial index (TBI) <0.70
  – Limitation :
    • inflammatory lesions, ulceration, tissue loss
Radiologic diagnostic modality

• Duplex scan
  – Easy to perform: accessibility
  – No contrast media and radiation
  – Operator-dependent
  – Calcium in diabetes

• MR angiography
  – No radiation
  – Gadolinium toxicity: nephrogenic systemic fibrosis
  – Overestimate stenosis

• CT angiography
  – Most-frequently used in Korea: cheap, popular, quick
  – Radiation and contrast media use
  – Calcium in diabetes

• Digital subtraction angiography
  – Most accurate in diabetes
  – Radiation and contrast media use
  – Invasive: femoral puncture
  – Pre-intervention purpose: intention-to-treat
Treatment of PAD Claudicants

• Risk factor modification
  – Smoking cessation
  – LDL cholesterol < 100 mg/dL
  – LDL < 70 mg/dL if high risk (eg. DM)
  – HbA1c < 7.0%
  – BP < 140/90 mmHg
  – BP < 130/80 mmHg if diabetic or renal disease
  – Antiplatelet therapy
Treatment of PAD Claudicants

• Supervised exercise therapy
  – Treadmill or track walking
  – Sufficient intensity to bring on claudication, followed by rest
  – Over the course of a 30-60 min session
  – 3 times a week for 3 months

• Pharmacotherapy
  – Cilostazol (Pletaal): 1st drugs
  – Pentoxifylline (Trental)
  – Prostaglandin analogues
Critical Limb Ischemia in diabetes

- Characterized by
  - Occlusive rather stenotic lesions
  - Diffuse, long lesions
  - Multilevel lesions
  - Infrapopliteal lesions

Most PAD in diabetes
1-Year Outcome of CLI

- Alive with amputation: 40%
- Alive without amputation: 40%
- Dead: 20%
Survival of Amputees

Subramanian B, Anesth Analg 2005;100:1241-7
Indications or goals of below-the-knee (BTK) revascularization

• **Indications**
  – Patients with CLI for limb salvage
  – Not simple intermittent claudication

• **Clinical goals**
  – Limb salvage
  – Better wound healing
  – Pain relief
  – Early mobilization
Primary amputation vs. Revascularization

- Lower Extremity Grading System (LEGS) Score
  - Arteriographic findings
    - Stenosis or occlusion
    - Lesion length
  - Presentation
    - Claudication or critical limb ischemia
  - Functional status
    - Ambulatory or non-ambulatory
  - Comorbidities
    - Obesity, CAD, old age
  - Technical factors
    - Redo-procedure, available vein conduit, target vessel status, infection

- Recommended treatment
  - Low score: open surgery
  - Intermediate score: endovascular intervention
  - High score: primary amputation
## WIFI Classification for Risk of Amputation

<table>
<thead>
<tr>
<th>Component</th>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>W (Wound)</td>
<td>0</td>
<td>No ulcer (ischaemic rest pain)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Small, shallow ulcer on distal leg or foot without gangrene</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Deeper ulcer with exposed bone, joint or tendon ± gangrenous changes limited to toes</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Extensive deep ulcer, full thickness heel ulcer ± calcaneal involvement ± extensive gangrene</td>
</tr>
<tr>
<td>I (Ischaemia)</td>
<td>0</td>
<td>ABI ( \geq 0.80 ) Ankle pressure (mmHg) ( &gt; 100 ) Toe pressure or TcPO(_2) ( \geq 60 )</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>0.60–0.79 70–100</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.40–0.59 50–70</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>&lt;0.40 &lt;50</td>
</tr>
<tr>
<td>Fl (Foot Infection)</td>
<td>0</td>
<td>No symptoms/signs of infection</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Local infection involving only skin and subcutaneous tissue</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Local infection involving deeper than skin/subcutaneous tissue</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Systemic inflammatory response syndrome</td>
</tr>
</tbody>
</table>

*J Vasc Surg 2014;59:220–234*
Vascular anatomy of leg

- Aorta
- Iliac arteries
- Common femoral artery
- Profunda femoris
- Superficial femoral artery
- Popliteal artery
- Peroneal artery
- Anterior tibial artery
- Posterior tibial artery
- Dorsalis pedis
- Common plantar artery
- Medial plantar artery
- Lateral plantar artery
- Deep plantar (perforating) artery

Primary pedal arch
Angiosome concept
Revascularization option of PAD

- Endovascular intervention
- Surgical bypass
- Angiogenesis
  - Gene therapy
  - Stem cell
Endovascular Therapy for Limb Salvage

• Relatively new and continually evolving technology
  – Recent advances: DES, DCB hold promise
• Potential advantages
  – Less invasive: mortality and morbidity (?)
  – Fast recovery
• Potential disadvantage
  – Reduced efficacy: hemodynamics, durability
  – Risk of limb deterioration
  – May affect surgical options
  – Cost: frequent repeated treatments, symptom-free intervals
• Outcomes poor for more extensive disease, multi-level disease, major tissue loss, possibly diabetics
Infrainguinal Bypass Surgery for CLI

- Bypass with autogenous vein is the “gold standard”
- Results well documented in hundreds of reports:
  - anecdotal > retrospective > randomized trials
- Versatile: results in complex situations (anatomic, patient related) well established
- Low mortality, good durability
- BUT—there are **limitations** and **risks**:
  - Wound and other complications
  - Prolonged recovery
  - Vein quality and availability
  - Technically demanding procedures
- Outcomes **poorer** for suboptimal conduit, higher medical risk
# 2011 ESC recommendation for PAD

## Critical Limb Ischemia

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Ref&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>For limb salvage, revascularization is indicated whenever technically feasible.</td>
<td>I</td>
<td>A</td>
<td>302, 331, 336</td>
</tr>
<tr>
<td>When technically feasible, endovascular therapy may be considered as the first-line option.</td>
<td>IIb</td>
<td>B</td>
<td>302, 331</td>
</tr>
<tr>
<td>If revascularization is impossible, prostanoids may be considered.</td>
<td>IIb</td>
<td>B</td>
<td>338, 339</td>
</tr>
</tbody>
</table>
National trends in lower extremity bypass surgery, endovascular interventions, and major amputations

Philip P. Goodney, MD, MS, Adam W. Beck, MD, Jan Nagle, MS, RPh, H. Gilbert Welch, MD, MPH, and Robert M. Zwolak, MD, PhD, Lebanon and Hanover, NH; White River Junction, VT; and Chicago, Ill
Angioplasty is not durable

15% need BPG
26% need redo PTA @ 1 yr

41% failure rate

Prior failed ipsilateral percutaneous endovascular intervention in patients with critical limb ischemia predicts poor outcome after lower extremity bypass

Brian W. Nolan, MD, MS, Randall R. De Martino, MD, David H. Stone, MD, Andres Schanzer, MD, Philip P. Goodney, MD, MS, Daniel W. Walsh, MD, and Jack L. Cronenwett, MD, for the Vascular Study Group of New England, Lebanon, NH; and Worcester, Mass

**Table III. Independent predictors of major amputation at 1 year**

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis</td>
<td>2.7</td>
<td>2.2</td>
</tr>
<tr>
<td>Prosthetic conduit</td>
<td>2.1</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>Prior ipsilateral PVI</strong></td>
<td>1.5</td>
<td>1.1</td>
</tr>
<tr>
<td>Prior ipsilateral bypass</td>
<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Tibial target</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>Aspirin</td>
<td>0.8</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Cost-effectiveness

**Best**: Bypass with interventional revisions

Endovascular-first is not cost-effective

Must identify cost-drivers!

- Slow wound healing
- Procedural costs

*J Vasc Surg 2012;56:1015-24*
Surgical Bypass: When Is It Best and Do Angiosomes Play A Role?

Richard F. Neville, MD and Anton N. Sidawy, MD, MPH

Bypass vs Endovascular

Complete Healing

Bypass

Endo

Healed

Failed

76% *

24%

41% *

59%

* Log rank P value = 0.03

Wound healing: Size and Time to healing

### Bypass vs Endovascular Healing based on initial wound size

<table>
<thead>
<tr>
<th>Group</th>
<th>Bypass</th>
<th>Endovascular</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (0–5mm)</td>
<td>84 days</td>
<td>105 days</td>
<td>P = NS</td>
</tr>
<tr>
<td>B (5mm–20mm)</td>
<td>102 days</td>
<td>128 days</td>
<td>P = NS</td>
</tr>
<tr>
<td>C (&gt;20mm)</td>
<td>115 days</td>
<td>164 days</td>
<td>P = 0.01</td>
</tr>
</tbody>
</table>

“Factors influencing wound healing of critical ischemic foot after bypass surgery: is the angiosome important in selecting bypass target artery?”

- 249 distal bypasses: 81% diabetics, 49% ESRD
- Healing rate in indirect revascularization was slower than in direct revascularization, especially in ESRD patients ($P<0.001$)
- No difference after propensity scoring ($P=0.185$)

Conclusion:

"The angiosome concept seems unimportant, at least in non-ESRD cases"

Azuma, Eur J Vasc Endovasc Surg, 2012
CASE 1

• F/61
• CC : infected ulcer, rt. foot (1WA)
• BHx:
  – Known DM patient with insulin (40y, type 1)
  – s/p rt. 4-5 toe amputation d/t trauma (40YA)
Femoral angio via 5F sheath
BTK angio via 4F shuttle
True luminal passage using V18 + microcatheter change to 0.14GW & BAP with 2mm*120mm
BAP with 2.5-3mm*210mm
Final angiography
Post-intervention course

• IV antibiotics
  – Wound culture : MRCNS, Pseudomonas, Citrobacter, Corynebacterium
  – Vancomycin, Tazocin

• Daily I & D at OR

• Ray amputation at POD#7

• Clean wound and well-healed
CASE 2

- M/72
- DM CRF on HD
- HTN
- DM foot at 5th toe
CASE 3

- M/81, Rt. 2\textsuperscript{nd} toe unhealing wound and pain
- HTN, s/p CABG, CRF on HD
- Un-healing wound and pain at Rt. 2\textsuperscript{nd} toe for 4 months
DSA
Infrapop-DPA bypass
Follow-up Duplex scan
CASE 4

- M/81
- DM CRF on HD
- HTN
- Unhealing wound at 1st toe, right

- 2012. 4 endovascular intervention : failed

- 2012. 8 aggravated wound infection after minor trauma
### Recommendations on revascularization of infra-popliteal occlusive lesions

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the case of CLTI, infra-popliteal revascularization is indicated for limb salvage.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>For revascularization of infra-popliteal arteries:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• bypass using the great saphenous vein is indicated</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>• endovascular therapy should be considered.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

CLTI = chronic limb threatening ischaemia.

<sup>a</sup> Class of recommendation.

<sup>b</sup> Level of evidence.

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### CHANGE IN RECOMMENDATIONS

<table>
<thead>
<tr>
<th>2011</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower Extremity Artery Disease</td>
<td>Infra-popliteal lesions</td>
</tr>
</tbody>
</table>

- Endovascular first
- Bypass using GSV
- Endovascular therapy

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Updated 2017 ESC guideline for PAD
Summary

• All diabetic patients with ischemic symptom or unhealing ulceration
  – objective testing for PAD

• Early identification of PAD at risk
  – Essential for limb salvage

• Multidisciplinary approach
  – Organized and systematic management for PAD in diabetics
  – Diabetic foot clinic
Thank you for your attention

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