Screening for Ischemia in the Diabetic Foot: What is the Best and How to Use the Information

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Which one is false?
Diabetics have a pattern of atherosclerotic disease typically characterized by:

1. Severe inflow disease
2. Severe tibial disease
3. Sparing of the pedal vessels
4. Medial calcification (Monckeberg's sclerosis)
5. Suboptimal collateralization

In diabetic patients with neuropathy, which screening tool has the highest sensitivity?

1. Pulse exam by a vascular surgeon
2. Ankle-brachial index
3. Ankle-brachial index with exercise
4. Toe-brachial index
5. Pulse-volume recording
Screening for Ischemia in Diabetics

1. Is important,
2. Is best accomplished with a specific set of tools,
3. The results of which can be used to optimize management.
Diabetes and PAD

- >23 million diabetics in US, >350 million worldwide
- DM increases the risk of CAD, cerebrovascular events, and PAD by up to 4 fold
- One out of three patients with DM age >50 has PAD
  - DM and neuropathy: 7-10% will develop an ulcer annually
  - DM, neuropathy and PAD: 25-30% will develop an ulcer annually
- Nearly 70% of amputations in US are in diabetic patients
  - #1 cause of amputations
- Age-adjusted risk for amputation is 28-fold higher

Overall, diabetics with PAD are at significantly increased risk for mortality and limb loss.

Critical Limb Ischemia (CLI)

Fate of Patients With CLI After Initial Treatment
Summary of 6-month outcomes from 19 studies

Diabetic + CLI = Mortality at 6 months ~50%

PAD increases the risk of death and CV events beyond that of CAD

Grenon et al, QCOR Meeting, Atlanta 2012
Risk to Limb Much Higher for Diabetics

Diabetes and PAD: Anatomic and Pathologic Correlates

- Diabetics have a unique pattern of peripheral atherosclerosis
  - Less frequent inflow (aorto-iliac) disease; SFA may be spared
  - Severe tibial disease; pedal vessels often spared
  - Less chance of collateralization
  - Stenosis in the collaterals

- Pathology
  - Atherosclerosis
  - Medial calcification (Monckeberg’s sclerosis)

- Coexistent neuropathy has profound effects on the diabetic foot which are chronic and progressive

Metabolic aberrations:
- Chronic hyperglycemia
- Insulin resistance
- Dyslipidemia
PAD is a different, and more virulent disease in the diabetic patient.

Screening for Ischemia in Diabetics

1. Is important, because PAD is a different, and more virulent disease in the diabetic patient, with worst outcomes (morbidity and mortality)
2. Is best accomplished with a specific set of tools,
3. The results of which can be used to optimize management.

Goals of Non-Invasive Screening

1. Confirm the presence of disease
2. Provide reproducible physiological data concerning disease severity
3. Document the location and hemodynamic importance of vascular lesions
4. Prepare a plan in case intervention is needed
5. Provide serial measurements over time to follow disease progression and results of treatment

Cao et al, EIVES 2011
“For one mistake made for not knowing, ten mistakes are made for not looking”

–Andrew Boulton

The First Tool to Screen for PAD: Physical Examination

Pulse intensity should be assessed and should be recorded numerically as follows:

- 0, absent
- 1, diminished
- 2, normal
- 3, bounding

The ischemic foot may appear pink and relatively warm even in the presence of ischemia because of arteriovenous shunting.

Methods for Assessing Arterial Insufficiency

- Hemodynamic/Physiologic measurements
  - ABI, TBI
  - Segmental doppler pressures
  - Pulse volume recordings

- Tissue perfusion
  - TcPO2
  - Skin perfusion pressure (SPP)
  - Hyperspectral tissue oxygenation

- Anatomic imaging
  - Ultrasound, CTA, MRA, angiography

The American Diabetes Association consensus statement on PAD recommends screening of diabetic patients over 50 years of age, as well as younger insulin-dependent patients with other vascular risk factors utilizing ankle-brachial index (ABI) determinations.

These traditional tests continue to provide a simple, risk-free, and cost-effective approach to establishing the PAD diagnosis as well as to follow PAD status after procedures.
The ABI

- Normal range: 0.91-1.31
- Cut-off for diagnosis: <0.90
- Cut-off in diabetes to get the highest sensitivity and specificity: 1.0-1.1
- Intra-observer variability: 7.3%-12%
- Eight different methods for calculation of measure ABIs
- Recommendations from Societies: highest pressure in the leg by the highest pressure in the arm to obtain the greatest reproducibility (TASC II Working Group and American Diabetes Association)

Interpreting the ABI in Diabetics

- Sensitivity and specificity drops:
  - Sensitivity: 95% → 63-100%
  - Specificity: 99% → 85-97%

- With neuropathy, as low as (Cao et al, EJVES 2011):
  - Sensitivity: 50-71%
  - Specificity: 30-96.8%

- The most significant factor affecting the validity of the ABI is diabetes (OR 4.36 for false-negative results)
  - Chung et al, Angiology 2010

Toe-Brachial Index Measurement

- The toe-brachial index (TBI) is calculated by dividing the toe pressure by the higher of the two brachial pressures.
- Digital cuff, PPG probe
- Useful for noncompressible vessels (ABI>1.3)
- Normal >0.75
- TBI values ≤ 0.7 are usually considered diagnostic for lower extremity PAD
- Severe ischemia <0.25
- Absolute pressure <30 mm Hg associated with poor healing rates

Segmental Pressures (mm Hg)

- Allow localization of areas of disease
- Generally 4 cuffs placed on leg
- More than 20 mm Hg gradient indicates significant disease in the intervening segment
**Pulse Volume Recordings**

- Thigh, calf, transtarsal cuffs
- Arterial waveform generated by volume change in the limb beneath the cuff
- Not influenced by calcification
- Transtarsal waveform predictive of foot healing

**Tissue Perfusion**

- TcPO2
  - Probes placed on multiple sites on foot, leg with reference on trunk
  - Takes 20-30 minutes to stabilize
  - Normal 60 mm Hg, <20 predicts poor healing, >35-40 good.
  - Rise >10 said to positively predict benefit of HB02

- Skin perfusion pressure (SPP)
  - Laser doppler and cuff, takes 5 minutes or less
  - Blood pressure that restores capillary flow
  - 30 mm Hg appears to be a threshold value for healing
  - Modest PPV and NPV

**TBI or not TBI: that is the question. Is it better to measure toe pressure than ankle pressure in diabetic patients?**

B. Brooks*†, R. Dean*†, S. Patel*†, B. Wu*, L. Molyneaux* and D. K. Yue*†

Diabetic Medicine 18, 528-532, 2001

“In the majority of patients with diabetes, assessment of TBI conveys no advantage over ABI in determining perfusion pressure of the lower limbs.
Only in those patients with overt calcification, which gives an ABI >1.3, are toe pressure measurements superior.”
Screening tools that are effective in screening PAD in the nondiabetic population are less efficacious in diabetes particularly with peripheral neuropathy. Qualitative waveform analysis and the TBI are more effective screening methods than the ABI and foot pulses particularly in high-risk limbs with peripheral neuropathy.

Other Imaging Tests for PAD

- Useful for planning revascularization – not so much to predict wound healing
  - Contrast enhanced magnetic resonance angiography (CE-MRA);
  - Computed tomographic angiography (CTA);
  - Digital subtraction angiogram - gold standard

Color Duplex Ultrasonography

- Duplex ultrasound of the extremities is useful to diagnose anatomic location and degree of stenosis of peripheral arterial disease.

Systolic Pressure Predicts Healing of Foot/Toe Lesions

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Probability of Healing (%)</th>
<th>Probability of Healing (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO Diabetes</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Ankle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Above 90</td>
<td>100</td>
<td>85</td>
</tr>
<tr>
<td>55-90</td>
<td>85</td>
<td>45</td>
</tr>
<tr>
<td>Below 55</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Toe</td>
<td></td>
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<td>Above 90</td>
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</tr>
<tr>
<td>55-90</td>
<td>100</td>
<td>75</td>
</tr>
<tr>
<td>Below 55</td>
<td>70</td>
<td>45</td>
</tr>
</tbody>
</table>

Probability of Healing in a Diabetic Foot Ulcer

- An ulceration on the foot in diabetes
  - will generally heal if the toe pressure is >55mm Hg, whereas healing is usually severely impaired if the toe pressure is <30mm Hg.
  - Will generally heal if the TcPO2 is >50mmHg, whereas healing is usually severely impaired when TcPO2 is <30mmHg.

Lepantalo et al, EJVES, 2011

TO REMEMBER...

- If a diabetic patient has a foot ulcer and there are no palpable pulses (even if doppler signals are present) then the patient should be worked up for vascular disease
- If an ulcer in a diabetic patient is stagnant – then there is a high likelihood there is vascular insufficiency and/or underlying necrosis
- Trust the ABI when low, but not high.
- In case of a normal or high ABI, in the presence of diabetes, other investigations should be carried: toes pressures, perfusion assessment.

Screening for Ischemia in Diabetics

1. Is important,
2. Is best accomplished with a specific set of tools, to be used based on local expertise, protocols, and status of patient's vessels, i.e. calcifications.
3. The results of which can be used to optimize management.

Screening for Ischemia in Diabetics

1. Is important,
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3. The results of which can be used to optimize management.
**ACC/AHA Guideline for the Management of PAD: Diagnosis and Treatment of Asymptomatic PAD**

- **Individual at PAD risk: No leg symptoms or atypical leg symptoms**
  - Consider use of the San Diego Walking Impairment Questionnaire

- **Perform a resting ankle-brachial index measurement**
  - ABI ≥ 1.30 (abnormal)
  - ABI 0.91 to 1.30 (borderline & normal)
  - ABI ≤ 0.90 (abnormal)

- **Pulse volume recording Toe-brachial index (Duplex ultrasonography)**
  - Abnormal results

- **Confirmation of PAD diagnosis**
  - Decreased post-exercise ABI

- **Evaluate other causes of leg symptoms**

- **Obtain prompt vascular specialist consultation:**
  - Diagnostic testing strategy
  - Creation of therapeutic intervention plan

- **Ongoing vascular surveillance**
  - Written instructions for self-surveillance

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**ACC/AHA Guideline for the Management of PAD: Diagnosis and Treatment of Critical Limb Ischemia (1)**

- **Severe lower extremity PAD documented:**
  - ABI less than 0.4; flat PVR waveform; absent pedal flow

- **Systemic antibiotics if skin ulceration and limb infection are present**

- **Obtain prompt vascular specialist consultation:**
  - Diagnostic testing strategy
  - Creation of therapeutic intervention plan

- **Patient is not a candidate for revascularization**
  - Medical therapy or amputation (when necessary)

- **Patient is a candidate for revascularization**

- **Revascularization possible:**
  - (see treatment text, with application of thrombolytic, endovascular, and surgical therapies)

- **Revascularization not possible:**
  - Medical therapy; amputation (when necessary)

- **Ongoing vascular surveillance**
  - Written instructions for self-surveillance

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**ACC/AHA Guideline for the Management of PAD: Diagnosis and Treatment of Critical Limb Ischemia (2)**

- **Patient is a candidate for revascularization**

- **Imaging of relevant arterial circulation (noninvasive and angiographic)**

- **Revascularization possible:**
  - (see treatment text, with application of thrombolytic, endovascular, and surgical therapies)

- **Revascularization not possible:**
  - Medical therapy; amputation (when necessary)

- **Ongoing vascular surveillance**
  - Written instructions for self-surveillance
Guidelines from American Diabetic Association

- HbA1C < 6.5%
- Fasting total cholesterol < 175mg/dL (4.5mmol/L)
- Fasting triglycerides < 150mg/dL (1.7mmol/L)
- SBP < 130mmHg & DBP < 80mmHg
- Ace-inhibitors for microalbuminuria
- Low dose aspirin

Intensive Glycemic Control and Cardiovascular Outcomes: ADVANCE

Primary Outcome: Microvascular plus macrovascular (nonfatal MI, nonfatal stroke, CVD death)


HR=0.90 (0.82-0.98)

Significant reduction in primary endpoint (a reduction in microvascular outcome-nephropathy)

Intensive Glycemic Control and Cardiovascular Outcomes: ACCORD

Primary Outcome: Nonfatal MI, nonfatal stroke, CVD death


HR=0.90 (0.78-1.04)

- No difference in primary outcome
- Increase in mortality
- Halted early
The Diabetic Rapid Response Acute Foot Team: 7 Essential Skills for Targeted Limb Salvage

Ryan H. Fitzgerald, DPM, Joseph L. Mills, MD, Warren Joseph, DPM, and David G. Armstrong, DPM, PhD
Southern Arizona Limb salvage Alliance and College of Medicine, University of Arizona, Tucson

1. The ability to perform hemodynamic and anatomic vascular assessment with revascularization if necessary
2. The ability to perform neurologic workup
3. The ability to perform site-specific culture technique
4. The ability to perform wound assessment and staging/grading of infection and ischemia
5. The ability to perform site-specific bedside and intraoperative incision and debridement
6. The ability to initiate and modify culture-specific and patient-appropriate antibiotic therapy
7. The ability to perform appropriate postoperative monitoring to reduce risks of re-ulceration and infection

Eplasty 2009;9:e15

Tissue perfusion-based algorithm for vascular workup at the SFVAMC

Screening for Ischemia in Diabetics

1. Is important,
2. Is best accomplished with a specific set of tools
3. The results of which can be used to optimize care, including risk factors management, appropriate referral and surgical revascularization.
Take-Home Message

- Patients with diabetes are at high risk for PAD
- Early referral and intervention are crucial to improve diabetic foot ulcer healing and to prevent amputation
- Non-invasive vascular testing is recommended in all patients with diabetes and a foot ulcer
- Image if non-invasive tests indicate ischemia or when conservative treatment does not achieve ulcer healing
- Ensure that medical treatment is optimized
- Revascularize to improve distal perfusion and promote ulcer healing when indicated

Acknowledgement

- Dr. Christopher Owens
- Dr. Eveline Oestreicher Stock

Exercise ABI Testing

- Confirms the PAD diagnosis
- Assesses the functional severity of claudication
- May “unmask” PAD when resting the ABI is normal
- Aids differentiation of intermittent claudication vs. pseudoclaudication diagnoses

Thank you
Exercise ABI Testing: Treadmill

- Indicated when the ABI is normal or borderline but symptoms are consistent with claudication;
- An ABI fall post-exercise supports a PAD diagnosis;
- Assesses functional capacity (patient symptoms may be discordant with objective exercise capacity).

Amputation Prevention Centers

- Focus on high-risk patients
- Multidisciplinary team approach
- Vascular surgery and podiatry key players
- Coordinated inpatient and outpatient management

The angiosome concept

- The Angiosome Concept: Direct v. Indirect revascularization. Does it matter?
- Does it matter?

UCSF Center for Limb Preservation

www.ucsfhealth.org/heart
Direct vs. Indirect Endovascular Revascularization based on the Angiosome Concept

Diabetes Control and Complications Trial (DCCT): Cumulative Incidence of the First of Any of the Predefined Cardiovascular Disease Outcomes

UKPDS: Intensive Blood-Glucose vs. Conventional Treatment in Patients With Type 2 Diabetes

Treatment guidelines
Individuals “At Risk” for Lower Extremity PAD

- Age less than 50 years with diabetes, and one additional risk factor (e.g., smoking, dyslipidemia, hypertension, or hyperhomocysteinemia)
- Age 50 to 69 years and history of smoking or diabetes
- Age 70 years and older
- Leg symptoms with exertion (suggestive of claudication) or ischemic rest pain
- Abnormal lower extremity pulse examination
- Known atherosclerotic coronary, carotid, or renal artery disease