The Foot Doctor: The Front Line to Diagnose Atherosclerosis

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How Far We’ve Come
How Did We Get Here
What Did We Do
Where Are We Going
How Far We’ve Come

We can now identify occlusive disease prior to going to the Cath lab
Occlusion of the posterior tibial artery including medial and lateral plantar arteries
Near occlusion posterior tibial (PT) artery
Occlusion of the (DP) doralis pedis artery
Stenosis/occlusion medial plantar artery
Blockage of anterior tibial artery
How Did We Get Here

BY REALIZING OUR EARLY EVALUATIONS WERE INADEQUATE
What are/were the real problems in dealing with PAD?

- Delayed and Late Diagnosis
- Delayed and Late Intervention
- Only recognized as a problem when CLI presents
Delayed and Late Diagnosis

- Early clinical evidence diagnosed and treated as neuropathic disease
- Early treatment is symptomatic
- Missed opportunity to convert patients to being PROACTIVE, NOT REACTIVE early on in their disease
Suppressing the symptoms allows disease to progress, sometimes to the point of amputation.
Delayed and Late Intervention

- Progression of distal disease
- Progression of cardio-vascular disease
- Delayed physician intervention in dealing with metabolic syndrome
- Delayed patient involvement in their own disease – most often told neuropathy is chronic, un-treatable and to just live with condition
Missed opportunity to shift patients from being REACTIVE to PROACTIVE early in the process
Only recognized as a problem when CLI presents

Observing early evidence without intervention of PAD gives physician a **ringside seat** to the development of non-reversible disease
If you ignore a patient’s feet, they will go away.
Study: Mandatory Foot Exam

Impact of mandatory foot exam for a population at risk:

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATIENTS SEEN PRE-CLINIC VISITS</td>
<td>13,896</td>
<td>14,464</td>
<td>14,281</td>
</tr>
<tr>
<td>PATIENTS SEEN IN THE FOOT UNIT</td>
<td>9,596 (69%)</td>
<td>11,616 (80%)</td>
<td>12,984 (91%)</td>
</tr>
<tr>
<td>FOUND ULCERS</td>
<td>84</td>
<td>83</td>
<td>36</td>
</tr>
</tbody>
</table>

In summary: Going from 60% to 90% of patients receiving a comprehensive diabetic foot exam appears to have reduced the number of ulcers by more than half.

Data from SALSAmigo Mohamad al Derwish in Riyadh presented at the ISDF 2015 in The Hague By, David G. Armstrong, DPM, MD, PhD, Director, Southern Arizona Limb Salvage Alliance (SALSA)
Early Diagnosis + Early Intervention = Better Outcomes
What Did We Do

We recognized that the diagnostic process needed to be changed
Podiatric physicians are in the unique position of being the primary care physician of the lower extremity.

Podiatrists are often times in the first position to spot the early signs of disease.

Early detection gives the patient the benefit of early treatment leading to significantly better outcomes.

Conversely, we know that conditions that are left undiagnosed and untreated can lead to disaster.
Step 1: Listen to the Patient

Hear what the patient’s symptoms are actually telling you
Step 1: Listening to the Patient

- 75% of patients with PAD are either asymptomatic or unaware of the signs of PAD.
- Diabetics with neuropathy have absent classic symptoms of PAD which is only revealed by questioning that their lower extremity fatigue when walking but relieved by a few minutes of rest.
- PAD symptoms most commonly occur first in the foot as decreased arterial flow results in a cascade of negative effects.
• Exercise induced – easily recognized
  • Pain, aching or cramping with activity
  • Relieved by rest, only to be repeated upon activity

• Elevation induced – often diagnosed as neuropathy or fibromyalgia
  • Pain, aching, cramping or feeling of coolness in foot, leg, thigh or buttocks after getting into bed or elevation of feet
  • Relieved by standing up
Step 2: Improve In-Office Evaluation

Expand scope of physical assessment
Traditional In-Office Evaluation

Typical Exam

- Check Pulses
- ABI - ankle brachial index

Shortfalls

- Generally palpated only in 1 area
- Measures peripheral flow to the level of the ankle
Step 2: Expanded Evaluation

Next Level Exam

- Check quality of pulses
- Check volume of dorsal venous structures
- Check temperature gradient
- Elevation dependency to check venous refill
- Xerosis
- Skin Turgor
- TBI
- Stethoscope with ultrasound

Advantages

- May be bounding proximal to occlusion and may be absent distal to blockage
- Decreased arterial in-flow = less out-flow
- Drop off in temperature from ankle to toe can indicate occlusive disease
- Indicates the need for additional testing
Step 3: MRA

Why it’s important
What We’ve Found

- MRA with Long Leg Run Off of the foot has correlated with vascular deficits involving either the medial and lateral plantar arteries or both, and/or the dorsalis pedis artery.
- Subjective findings correlated with the area of symptomatology
Step 3: MRA

Why it's important

- Some patients show stenosis/occlusion of PT or DP arteries at ankle level and may respond to:
  - Pharmacologic therapy
  - Supervised exercise and nutritional programs
  - Percutaneous transluminal angioplasty
  - Combination of any or all of the above

- Patients physically seeing the stenosis/occlusion of pedal arteries are transformed from being **PASSIVE TO PROACTIVE** in their disease

- Patients that are actively involved in the tx of their disease have better outcomes
Maybe it’s NOT Neuropathy
Assessment of the Integrity of Vascular Pedal Inflow in Patients with Neuropathic Pain

Study presented at: Cardiovascular Disease Management: A Case-Based Approach, 2014
120 consecutive patients diagnosed with neuropathy

All had idiopathic pain

All had abnormal clinical exam

16 patients were unable to have MRA - excluded

**Interesting Findings**

<table>
<thead>
<tr>
<th>Co-morbidities</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>26</td>
</tr>
<tr>
<td>Hypertension</td>
<td>69</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>55</td>
</tr>
<tr>
<td>Previous Failed Treatment</td>
<td>53</td>
</tr>
<tr>
<td>Claudication</td>
<td>65</td>
</tr>
<tr>
<td>Elevation-induced</td>
<td>29</td>
</tr>
<tr>
<td>Exercise-induced</td>
<td>17</td>
</tr>
<tr>
<td>Both</td>
<td>19</td>
</tr>
</tbody>
</table>
MRAs Showing Pedal Disease:

Typical MRA findings in over 95% of patients diagnosed with neuropathy

- Significant occlusion of med. & lat. plantar arteries. Focal occlusion of peroneal artery after bifurcation into the anterior perforating and lateral calcaneal branches
- Subtotal occlusion of distal PTA with reconstitution distally with both plantar arteries occluded beyond origin
- Distal popliteal moderate stenosis
- Single vessel runoff, anterior tibial artery w/multiple high-grade stenosis
- Tibio-peroneal trunk heavily diseased w/multiple near occlusions
- PT artery occluded majority of calf
- Common plantar artery occluded
- Severe occlusive disease
- Popliteal artery occluded
- Tibio-peroneal trunk occluded
- Reconstitution of anterior tibial artery w/dominant runoff vessel
- PTA occluded throughout its length
  DP occluded at mid foot
Occlusive disease involving the dorsalis pedis at the level of the mid-tarsal joint, pulses & ABI normal, elevation induced pain
Percutaneous trans-luminal angioplasty dorsalis pedis
Case Study #1

- 62 year old white female
  - Chronic venous stasis ulcers, duration 12-15 years
  - Non-healing ulcer measured 4.1cm x 2.5cm x .3cm, duration 2 years

- Risk Factors for Coronary Disease
  - Remote smoking history
  - Family history of heart disease

- Treatment
  - First seen at wound care center, January
  - Patient states she had
    - Cardiovascular work-up Normal
    - Arterial work-up Normal
    - Cardiac catheterization Normal
### Case Study #1

#### Podiatric Consultation Revealed

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>134/75</td>
</tr>
<tr>
<td>Pulse</td>
<td>70 and regular</td>
</tr>
<tr>
<td>Weight</td>
<td>135 pounds</td>
</tr>
<tr>
<td>Height</td>
<td>5’ 4”</td>
</tr>
<tr>
<td>O2 Saturations</td>
<td>100%</td>
</tr>
<tr>
<td>Cardiac exam</td>
<td>Unremarkable</td>
</tr>
<tr>
<td>Femoral pulses</td>
<td>Good</td>
</tr>
<tr>
<td>Dorsalis pedal pulses</td>
<td>Good, bilateral</td>
</tr>
<tr>
<td>ABI</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>1.12</td>
</tr>
<tr>
<td>Left</td>
<td>.92</td>
</tr>
</tbody>
</table>
Case Study #1

- In spite of non-invasive test being negative, patient had arteriogram and long leg runoff all normal with the exception of:
  - right posterior tibial 100% occluded
  - diminished pedal flow
  - no significant collaterals

- Successful laser recanalization of PTA
Posterior Tibial Artery Occluded Distally

Courtesy Dr. R. Heuser
Recanalization of Posterior Tibial Artery

Wire successfully crossing into the pedal vessels

Angiogram confirming pedal vessel

Courtesy Dr. R. Heuser
Patency to the pedal vessel after ballooning – this corresponds to the area of the ulcer.
Where We Are Going

New Thoughts on Dealing with Residual Pedal Insufficiency/Microangiopathy after Recanalization
“The reality is that heart disease is not only acquirable, it’s preventable and it’s reversible.”

Richard Heuser, MD
Growth Factors

A Post Procedure Adjunct to Transluminal Angioplasty & In Conjunction With Previous Instituted Procedures
Biologics to stimulate the induction of vascular angiogenesis
Growth Factors

- Protein molecules which are quite versatile & promote cell growth
- Function to regulate cell division & cell survival in numerous different specific cell types
- Bind to receptors on the cell surface, resulting in activation of cellular proliferation
- Synonym for cytokines which function like regulatory signals
- Play a role in maintenance and repair of tissues
Growth Factors Pertinent to this Discussion

Transforming growth factors (TGFs)
Nerve growth factor (NGF)
Platelet-derived growth factor (PDGF)
Vascular endothelial growth factor (VEGF)

Epidermal growth factor (EGF)
Fibroblast growth factor (FGF)
Placental growth factor (PGF)
Most Influential:
Placental Growth Factor (PGF)

- A protein encoded by the *PGF* gene
- PGF is a member of the VEGF (vascular endothelial growth factor) sub-family - a key molecule in angiogenesis and vasculogenesis
Why PGF?

PGF Supports:
- Angiogenesis denotes formation of new blood vessels from pre-existing ones
- Vasculogenesis denotes formation of new blood vessels where there are no pre-existing ones

For example:
If a monolayer of endothelial cells begins sprouting to form capillaries, angiogenesis is occurring.
Vasculogenesis, in contrast, is when endothelial precursor cells (angioblasts) migrate and differentiate in response to local cues (such as growth factors and extracellular matrices) to form new blood vessels. These vascular trees are then pruned and extended through angiogenesis.
Sprouting angiogenesis: The Stages

- **Stage 1**: Angiogenic growth factors (AGF) activate receptors on endothelial cells present in pre-existing blood vessels.

- **Stage 2**: Activated endothelial cells begin to release proteases that degrade the basement membrane to allow endothelial cells to escape from the original (parent) vessel walls.

- **Stage 3**: Endothelial cells proliferate into the surrounding matrix forming solid sprouts connecting neighboring vessels.

- **Stage 4**: As sprouts extend toward the source of the angiogenic stimulus, endothelial cells migrate in tandem, using adhesion molecules called integrins.
Sprouting angiogenesis: The Stages

- Stage 5: The sprouts then form loops becoming a full-fledged vessel lumen as cells migrate to the site of angiogenesis.

- Stage 6: Sprouting occurs at a rate of a couple millimeters per day, enabling new vessels to grow across gaps in the vasculature.

- Stage 7: Potential to re-vascularize ischemic tissues to reverse hypoxia and provide nutrition.
Case Study #2

• 77 year old Caucasian male
  • Numbness, coldness, and both elevation and exercise induced claudication, duration 5+ years
  • Left foot more involved than right foot

• Risk Factors for Coronary Disease
  • Family history of diabetes
  • Family history of heart disease
  • Known diagnosis
    • Dyslipidemia
    • Hypertension
    • Type II Non-insulin dependent DM with neuropathy

• Treatment
  • Gabapentin, approximately 3 years
## Case Study #2

**Podiatric Consultation Revealed**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>166/89</td>
</tr>
<tr>
<td>Pulse</td>
<td>59</td>
</tr>
<tr>
<td>Weight</td>
<td>184</td>
</tr>
<tr>
<td>Height</td>
<td>5'10'</td>
</tr>
<tr>
<td>Dorsalis pedal pulses</td>
<td>Markedly diminished Bilaterally</td>
</tr>
<tr>
<td>Posterior tibial pulses</td>
<td>Absent Bilaterally</td>
</tr>
<tr>
<td>Temperature Gradients</td>
<td>Warm to Cool</td>
</tr>
<tr>
<td>Capillary Refill</td>
<td>Markedly diminished</td>
</tr>
</tbody>
</table>
Case Study #2
Case Study #2
Preliminary Application & Findings

Ultrasound of PT Artery & Nerve

Before PDA Injection

After PDA Injection
Utilizing growth factors increases vascular supply with resolution of symptomatology
Elevation induced claudication with occlusion of the Posterior Tibial Artery.

Claudication in calf resolved, foot pain and neuropathy persisted.

Proceeded with growth factor injection to PT artery. Immediate positive response noted.

At 11 weeks post injection, foot pain gone and neuropathy slowly resolving proximal to distal.
Preliminary Application & Findings

Before PDA Injection

After PDA Injection

Ultrasound of DP Artery
Moving Forward

- Continue with pre and post injection ultrasound when using placental derived amnion for residual pain and neuropathy 2nd to vascular deficiency
- Will obtain ABI & TBI pre and post injection with PDA for residual pain and neuropathy 2nd to vascular deficiency. Early preliminary results positive
- Will re-evaluate with ultrasound and ABI & TBI at appropriate intervals to gather long term information
TOGETHER WE CAN SAVE BOTH LIMBS AND LIVES