Neurovascular Complications of Diabetes
The Vascular Component

UCSF Vascular Symposium 2016
Alexander Reyzelman, DFM, FACES

Impact

- 15-20% of diabetic patients will have PAD at 10 years
- 45% of diabetic patients will have PAD at 20 year
- One recent survey found a prevalence of PAD in people w/DM >40 years of age to be 20%
- Additional survey showed patients w/DM >50 years of age to be 29%

Neuroischemic ulcers vs Neuropathic ulcers:

Is there a difference?
What defines a wound as neuropathic vs neuroischemic?

“An individual possesses a ‘diabetic foot’ when the diabetic neuropathy and/or arteriopathy of the lower limbs compromise foot function or structure.”

These two situations: neuropathic foot or ischemic foot

- Different entities
- In most patients both co-exist
  - Co-existence termed: neuroischemic


<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Neuropathic</th>
<th>Neuroischemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caused by</td>
<td>Minor trauma, (foot wear)</td>
<td>Spontaneous, s/p trauma</td>
</tr>
<tr>
<td>Mode of occurrence</td>
<td>Fortuitous, patient may be unaware of onset</td>
<td>Sudden with discoloration &amp; pain</td>
</tr>
<tr>
<td>Foot temperature</td>
<td>Normal (warm if AV shunt)</td>
<td>Usually cold</td>
</tr>
<tr>
<td>Foot pulses</td>
<td>Palpable usually bounding</td>
<td>+/- palpable pulse</td>
</tr>
<tr>
<td>ABI</td>
<td>Normal or elevated</td>
<td>&lt;9; possibly elevated</td>
</tr>
<tr>
<td>Doppler waveforms</td>
<td>Usually triphasic</td>
<td>Biphasic/Monophasic</td>
</tr>
<tr>
<td>Edges of ulcer</td>
<td>Raised, calloused 2/2 pressure</td>
<td>Atrophic, depend. rubor</td>
</tr>
<tr>
<td>Site of ulcer</td>
<td>Mostly pressure areas</td>
<td>Edge of foot, toes, heel</td>
</tr>
<tr>
<td>Appearance of ulcer</td>
<td>Indented borders</td>
<td>Gangrene</td>
</tr>
<tr>
<td>Pain during debridement</td>
<td>Mitigated by less sensation</td>
<td>Moderate pain, pure ischemic, exquisite pain</td>
</tr>
<tr>
<td>Patient behavioral response to ulcer pain</td>
<td>Disconnected</td>
<td>Aware of ulcer</td>
</tr>
</tbody>
</table>

How Prevalent are Neuroischemic Ulcers?

- Galkowska et al. reported 42% of ulcers in their clinic to be neuroischemic
- Oyibo et al, study identifying presence of ulcers referred to Manchester Diabetes Center
- 52.3% of ulcers neuroischemic, 36% neuropathic, 11.7% purely ischemic
Emerging Evidence for Neuroischemic Diabetic Foot Ulcers: Model of Care and How to Adapt Practice
Agbor Ndop, MD, and Edward B. Jude MD, MRCP

Neuropathic Ulcer
“Earlier suggestions in the 1980s…neuropathy was the main factor responsible for DFU…”

Neuroischemic Ulcer
“Last two decades have witnessed a paradigm shift from neuropathy… to increasing preponderance of ischemic or neuroischemic ulceration”

Factors related to outcome of neuroischemic/ischemic foot ulcer in diabetic patients
Jan Apelquist, MD, PhD, Targ Elgzyri, MD, Jan Larsson, MD, PhD, Magnus Londahl, MD, PhD, Per Nyberg, MD, PhD, and Johan Thorne, MD, PhD
J Vasc Surg 2011:53

Objective: Prospectively to Identify factors related to healing in patients with DFU and severe PVD

Perspective of the study was to intervene in an earlier phase to achieve healing and to achieve ulcer healing, and hence reduce the risk of amputation.

Methods:
- Patients with DFU
- Systolic toe pressure <45 mmHg or ABI <88 mmHg
- Subjected to angiography, offered vascular procedures when applicable
- F/u until healing

Study Population:
- N=1,151
- Ulcers Wagner 1-5 at or below ankle
- 1984-2006
- All patients fulfilled Fontaine grade 4

Study Design:
- Team: Orthopedic surgeon, Vascular surgeon Podiatrist, RN
- Physical exam performed at inclusion
- Systolic toe and ankle BP measured by standardized strain gauge
- Signs of sensory polyneuropathy tested using Biothesiometer
- Patients were followed for 5 years

Results:
- 1,150 patients included
- 82% toe pressure <45 mmHg
- 49% ankle pressure <80 mmHg
- Subjected to angiography when applicable
- 801 (70%) patients underwent angiography
  - Of these, 63% had vascular intervention
  - 39%, had Percutaneous transluminal angioplasty (PTA)
  - Or reconstructive surgery (24%)
Factors related to outcome of neuroischemic/ischemic foot ulcer in diabetic patients
Jan Apelqvist, MD, PhD, Targ Elgzyri, MD, Jan Larsson, MD, PhD, Magnus Londahl, MD, PhD, Per Nyberg, MD, PhD, and Johan Thorne, MD, PhD

J Vasc Surg 2011:53

Results:

- Healing of DFUs without major amputation in surviving patients was 72%
- Angioplasty and Open bypass surgery increased probability of healing
- Severity of PAD, age, CHF, Dialysis, and extent of tissue destruction were also related to probability of healing

Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study


Aims/Hypothesis

- Outcomes data on individuals with DFUs with and without PAD
- Assess clinical characteristics that best predict poor outcome
- To see if these predictors differ in patients with and without PAD

Methods

- Prospective Cohort study
- N=1,088 DFU, 14 centers in Europe
- Regression modeling used to identify independent predictors of outcome

Results

After 1 yr follow-up, 23% patients had not healed

Healing in patients with PAD was significantly worse.
Predictors of healing were different in patients with and without PAD.

Infection specific predictor of non-healing in PAD patients vs. patients without PAD

In Comparing Patients w/PAD to w/o PAD

69% w/PAD healed
Vs
84% w/o PAD

healed p< 0.001

In Comparing patients with infection

Patients with PAD and infection had higher odds of non-healing than patients without PAD
P<0.001
Conclusion:

Neuopathic and Neuroischemic ulcers are not the same and should be approached differently.

Infection and PAD has worse outcomes than Infection without PAD.

More education and vigilance is needed in promoting earlier recognition of Neuroischemic ulcers.

There's evidence to suggest that Neuroischemic ulcers should be a category in it of itself.

Finding:

Prevalence of LEA in diabetics is 3x higher as in diabetic baseline pop.

This prevalence is 7x higher in non-elderly diabetics with PAD.
Diabetic foot ulcerations are characterized as:

- Purely neuropathic
- Purely ischemic
- Neuroischemic

Prevalence is 35%, 15% and 50% respectively.

Tissues become ischemic from macrovascular disease, becoming further complicated by microvascular disease.

Neuroischemic ulcerations are the least likely to heal without intervention.

If infected, the patients are 90 times more likely to receive a midfoot or higher amputation.

Emerging Evidence for Neuroischemic Diabetic Foot Ulcers: Model of Care and How to Adapt Practice
Aghor Ndop, MD, and Edward B. Jude MD, MRCP

- Understanding difference, neuroischemic vs neuropathic ulceration for identification
- Understand components of vascular exam
  - Non invasive studies
    - ABI, TBI, TcPO2
    - Doppler US waveforms
    - Duplex US scanning
- Treatment
  - Referral, debridement, footwear modifications, treatment of infection
  - Vascular surgery and early referrals
- Minimum assessment
  - Pulse exam
  - Non-invasive studies

Why is it important to distinguish between the Neuropathic vs. Neuroischemic?

Assessment of the need for vascular intervention in patients with ischemic ulcers is frequently based on the presence of rest pain, extent of tissue loss, and disabling claudication. However, pain at rest and claudication in individuals with neuroischemic ulcerations are substantially less frequent than in patients with ischemia without DM.
Prevalence

- 20-30% of patients with PAD have DM
- Condition is often asymptomatic
  - Altered perception of pain
- Duration and severity correlates with incidence and extent of PAD
  - Longstanding diabetes
  - Degree of diabetic control
  - Increase in PAD by 28% for every 1% increase in A1c