A new classification on the diabetic ischemic foot promotes a modern approach to treatment

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I hereby have no disclosure for this presentation
First definition of CLI 1982*

"It was generally agreed that **diabetic patients** who have a varied clinical picture of **neuropathy, ischemia and sepsis** make definition even more difficult and it is desirable that these patients be excluded or should be clearly defined as a separate category to allow the analysis of the results in the non-diabetic patients."

SPECIFICITY OF PAD IN DIABETIC PATIENTS

- Same physiopathology **BUT:**
  - **↑** prevalence: 15% after 10y
  - Earlier start / Faster evolution
  - More distal lesions
  - Multilevel disease
  - Medial calcific sclerosis
  - Higher risk of CLI

**WHO**: “Diabetic foot is one of the highest priorities”

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8.9% of total world population

**WORLD**

592 M people living with diabetes in 2035

**increase**

AFR ↑ 109.1%
MENA ↑ 96.2%
SEA ↑ 70.6%
SACA ↑ 59.8%
WP ↑ 46%
NAC ↑ 37.3%
EUR ↑ 22.4%

2013
2035

DIABETIC FOOT ULCER

- Lifetime risk: 25%*
- Result of various risk factors**:
  - Neuropathic foot:
    - 50-70%***
    - Foot deformities
  - Ischemic foot
  - Trauma
  - Impaired resistance to infection

→ Increases morbidity & mortality x1.5:
  - Amputation risk x15
  - After major amputation:
    - 50% mortality at 2y
    - 50% of new amputation at 5y


85% of amputations could be prevented with proper and early treatment.
FIRST CLASSIFICATIONS

- For male smokers with atherosclerosis
  - who did not have diabetes
  - different from ischemic foot with neuropathy and susceptibility to infection

- Pure ischemia classifications:
  - No spectrum of hemodynamics
  - Minimal description of wounds and infection

<table>
<thead>
<tr>
<th>FONTAINE *</th>
<th>RUTHERFORD **</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Clinical</td>
</tr>
<tr>
<td>I</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>IIa</td>
<td>Mild claudication</td>
</tr>
<tr>
<td>IIb</td>
<td>Moderate–severe claudication</td>
</tr>
<tr>
<td>III</td>
<td>Ischemic rest pain</td>
</tr>
<tr>
<td>IV</td>
<td>Ulceration or gangrene</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

602 patients with diabetic foot ulcer and severe PAD
- Not available for revascularization

50% healed primarily with standard wound care or after minor amputation
17% healed only after major amputation
33% died with limbs intact but unhealed wounds

"A validated classification system of diabetic foot ulcers may help clinicians and researchers in everyday assessment, management and development of new therapies."
MODERN APPROACH WITH OPTIMAL CLASSIFICATION

① Classification by ulcer characteristics
② Staging to accurately stratify the risk of amputation
③ Intervention planning

- Allows meaningful comparison of alternative treatment modalities:
  - optimal wound care
  - cell-based therapy
  - open revascularization
  - endovascular intervention

- Allows multidisciplinary approach:
  - Revascularization
  - Wound Control
  - Microbiological control
  - Mechanical control
  - Metabolic control
  - Educational control
**WAGNER SCALE**

*Table 1*

Wagner–Meggitt classification system.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Foot lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No open lesions or cellulitis</td>
</tr>
<tr>
<td>1</td>
<td>Superficial ulcer</td>
</tr>
<tr>
<td>2</td>
<td>Deep ulcer upto tendons and joint tissue</td>
</tr>
<tr>
<td>3</td>
<td>Deep ulcer with abscess, osteomyelitis and joint sepsis</td>
</tr>
<tr>
<td>4</td>
<td>Local gangrene forefoot or heel</td>
</tr>
<tr>
<td>5</td>
<td>Gangrene of entire foot</td>
</tr>
</tbody>
</table>

- **PROS:**
  - Easy to use
  - Evaluates *depth of wound, osteomyelitis presence and gangrene*
  - One of the most widely used classification
  - Capability to predict amputation
    - Wagner grade <3 ($p < 0.001$) related to higher probability of healing**

- **CONS:**
  - Not sufficiently comprehensive: does not evaluate ischemia or infection specifically (when combination of infection and PAD triples the risk of major amputation***)
  - Mainly clinical evaluation (lack of accuracy)

**PEDIS SCALE**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Perfusion</th>
<th>Extent</th>
<th>Depth</th>
<th>Infection</th>
<th>Sensation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No PAD</td>
<td>Skin intact</td>
<td>Skin intact</td>
<td>None</td>
<td>No loss</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>PAD, No CLI</td>
<td>&lt;1 cm²</td>
<td>Superficial</td>
<td>Surface</td>
<td>Loss</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>CLI</td>
<td>1–3 cm²</td>
<td>Fascia, muscle, tendon</td>
<td>Abscess, fasciitis, septic arthritis</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>&gt;3 cm²</td>
<td>Bone or joint</td>
<td>SIRS</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

PAD, peripheral arterial disease; CLI, critical limb ischemia.

Perfusion, Extent, Depth, Infection and Sensation (PEDIS)

- **PROS:**
  - Focused on infection*
  - Predicts accurately adverse outcomes**
  - High sensitivity, specificity and positive likelihood ratios for adverse outcomes**

- **CONS:**
  - Does not categorize ischemic rest pain or gangrene
  - Mainly clinical evaluation

UNIVERSITY OF TEXAS SCALE*

PROS:
- Evaluates presence of ischemia, infection and depth of wound
- Widely used
- Superior in outcome prediction to Wagner scale*

CONS:
- Not sufficiently comprehensive on PAD classification: only +/- no grades or spectrum

Influence of wound scores and microbiology on the outcome of the diabetic foot syndrome

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b Infectious Diseases Unit, San Cecilio University Hospital, Granada, Spain

- 250 diabetic patients
  - 88% type 2, 12% type 1
  - With foot ulcers candidates for IV treatment + debridement
- 42% had prior amputations
- 35% had present distal pulses

« Wagner, Texas and PEDIS scales are associated with minor amputation in univariate analysis
BUT failed to be significant predictors in the multivariate analysis and were not predictors of major amputation »
Wound, Ischemia, and foot Infection [WIFI]

- From the Society for Vascular Surgery Lower Extremity Guidelines Committee
- New intuitive framework for diagnosis and treatment of the threatened limb

- Target population includes any patient with:
  - Ischemic rest pain with objectively confirmed hemodynamic studies (ABI < 0.40, AP < 50, TP < 30, TcPO2 < 20)
  - Diabetic foot ulcer
  - Non-healing lower limb or foot ulceration ≥ 2 weeks
  - Gangrene

Table 1 – Society for Vascular Surgery Lower Extremity Threatened Limb Classification System.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No ulcer</td>
<td>No gangrene</td>
</tr>
<tr>
<td>1</td>
<td>Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx</td>
<td>Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage</td>
</tr>
<tr>
<td>2</td>
<td>Deeper ulcer with exposed bone, joint or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement</td>
<td>Clinical description: Major tissue loss salvageable with multiple (&gt;3) digital amputations or standard transmetatarsal amputation (TMA) ± skin coverage</td>
</tr>
</tbody>
</table>

**I: ISCHEMIA**

Hemodynamics/perfusion: measure TP or TcPO₂ if ABI incompressible (>1.3)

<table>
<thead>
<tr>
<th>Grade</th>
<th>ABI</th>
<th>Ankle systolic pressure, mm Hg</th>
<th>TP, TcPO₂, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≥ 0.80</td>
<td>&gt;100</td>
<td>≥60</td>
</tr>
<tr>
<td>1</td>
<td>0.6–0.79</td>
<td>70–100</td>
<td>40–59</td>
</tr>
<tr>
<td>2</td>
<td>0.4–0.59</td>
<td>50–70</td>
<td>30–39</td>
</tr>
<tr>
<td>3</td>
<td>≤ 0.39</td>
<td>≤50</td>
<td>≤30</td>
</tr>
</tbody>
</table>

**Clinical manifestation of infection**

No symptoms or signs of infection

Infection present, as defined by the presence of at least 2 of the following items:
- Local swelling or induration
- Erythema >0.5 to ≤2 cm around the ulcer
- Local tenderness or pain
- Local warmth
- Purulent discharge (thick, opaque to white, or sanguineous secretion)

Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below).

Exclude other causes of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)
12 limb-salvage experts (Delphi Consensus group) were asked to use the grid to answer two specific questions:

1. what is the perceived risk of amputation for each possible combination?
2. what is the perceived benefit from revascularization for each possible combination?

To define stages of disease that might be useful for clinical decision making and prospective studies.
APPLICATIONS OF WIFI INDEX

- 158 revascularization procedures in 139 patients on a 3y period
- WIfI classification was applied after revascularization (analogous to using the TNM cancer staging system)

<table>
<thead>
<tr>
<th>Wifi clinical stage</th>
<th>Major amputation rates</th>
<th>Wound NON -healing rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3%</td>
<td>8%</td>
</tr>
<tr>
<td>2</td>
<td>10%</td>
<td>19%</td>
</tr>
<tr>
<td>3</td>
<td>23%</td>
<td>30%</td>
</tr>
<tr>
<td>4</td>
<td>40%</td>
<td>63%</td>
</tr>
</tbody>
</table>

« The WIfI clinical stage was predictive of major limb amputation and wound nonhealing and correlated significantly with outcomes predicted by the SVS consensus panel »
201 patients with wounds at presentation on a 2y period
- 93% of diabetes mellitus
- WIfI classifications were calculated at baseline
- Revascularization resulted in a profoundly accelerated wound healing time, especially in clinical stage 3 patients (P < 0.008)

<table>
<thead>
<tr>
<th>WIfI clinical stage</th>
<th>Major amputation rates</th>
<th>1y amputation free survival rate</th>
<th>Wound healing time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0%</td>
<td>100%</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>0%</td>
<td>100%</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>10% (p &lt; 0.001)</td>
<td>92%</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>90% (p &lt; 0.001)</td>
<td>63% (p &lt; 0.001)</td>
<td>264 (p &lt; 0.002)</td>
</tr>
</tbody>
</table>

WIfI is an appropriate classification system and correlates with important clinical outcomes: as the clinical stage progresses, the risk of major amputation increases, 1-year amputation free survival declines, and wound healing time is prolonged. Revascularization especially improves wound healing time in stage 3 patients.
63 threatened limbs in 50 patients
70% diabetic

<table>
<thead>
<tr>
<th>Wifi clinical stage</th>
<th>Major amputation rates</th>
<th>Minor amputation rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>19% (p &lt; 0.01)</td>
<td>6% (p &lt; 0.01)</td>
</tr>
<tr>
<td>4</td>
<td>59% (p &lt; 0.01)</td>
<td>24% (p &lt; 0.01)</td>
</tr>
</tbody>
</table>

Wound score and infection score were associated with major amputation when baseline comorbidities were not. Ischemia score did not correlate with amputation risk in this series but the revascularization approach was aggressive and nearly all revascularizations were successful.
TAKE HOME MESSAGE

- 3 early independent studies on WIfI stratification:
  - risk of amputation with from stage 1 to stage 4

- Clinical care algorithms should be determined after confirmation of those results:
  - to address patients by stratification of risk
  - to better streamline modes of therapy toward specific subgroups of patients
  - BUT WIfI index is not meant to function as a stand-alone clinical decision-making tool

- Patients participating in multicenter trials should be classified using this index
• THANK YOU FOR YOUR ATTENTION
A new classification on the diabetic ischemic foot promotes a modern approach to treatment

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