Value of Current Parameters of Hemodynamic Adjustment of CLTI Patients

Peter A. Schneider, MD
University of California San Francisco
Disclosure

Peter A. Schneider, MD

I have the following potential conflicts of interest to report:

☐ Consulting: Philips, Medtronic, Boston Scientific, Intact, PQ Bypass, Cagent, Silk Road Medical, Surmodics, Profusa, CSI
Global vascular guidelines on the management of chronic limb-threatening ischemia

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Level of evidence</th>
<th>Key references</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Definitions and nomenclature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Use objective hemodynamic tests to determine the presence and to quantify the severity of ischemia in all patients with suspected CLTI.</td>
<td>1 (Strong)</td>
<td>C (Low)</td>
<td>de Graaff,16 2003 Brownrigg,17 2016 Wang,18 2016</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Level of evidence</th>
<th>Key references</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 Measure TP and TBI in all patients with suspected CLTI and tissue loss (Fig 3.1 in full guideline).</td>
<td>1 (Strong)</td>
<td>B (Moderate)</td>
<td>Aboyans,21 2008 Salaun,22 2018</td>
</tr>
</tbody>
</table>
Why Do We Need Hemodynamic Assessment?

CLTI=Chronic Limb Threatening Ischemia

• **Pre-procedure:**
  • Severity of ischemia determines urgency and affects prognosis. Used to triage patients.

• **Intra-procedure:**
  • How do you know when you are done? Will this likely fix the problem? How many tibials? Should pedal artery angioplasty be performed?

• **Post-procedure**
  • When to re-intervene? How often to see the patient? How much to worry?
# Global vascular guidelines on the management of chronic limb-threatening ischemia

Global Vascular Guidelines  
J Vasc Surg 2019;June Supplement

## Table 3.1. Comparison of methods of noninvasive testing in patients with chronic limb-threatening ischemia (CLTI)

<table>
<thead>
<tr>
<th>Techniques</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| AP or ABI           | • Simple, inexpensive, quick, widely applicable  
                      • Provides data to predict wound healing and limb survival  
                      • Useful to monitor efficacy of therapeutic intervention | • Because of incompressible tibial arteries, may be falsely elevated or normal in patients with diabetes, renal insufficiency, or advanced age  
                      • Does not provide localization of the disease |
| TP or TBI           | • Simple, inexpensive, quick  
                      • Useful in the presence of small-vessel artery disease  
                      • Useful in noncompressible tibial arteries  
                      • Provides data to predict wound healing and limb survival  
                      • Useful to monitor efficacy of therapeutic intervention | • Generally requires a hallux  
                      • Does not provide localization of the disease |
| Segmental pressures | • Useful in initial anatomic localization of CLTI disease  
                      • Useful in creating therapeutic plan based on disease localization  
                      • Provides data to predict wound healing and limb survival  
                      • Useful to monitor efficacy of therapeutic intervention | • Not accurate in noncompressible tibial arteries |
| TcPo2               | • Useful to assess microcirculation  
                      • Can predict wound healing  
                      • May be useful for monitoring efficacy of revascularization | • Limited accuracy in the presence of edema or infection  
                      • Requires skin heating to ≥40°C  
                      • Time-consuming  
                      • Limited data validation |
| Skin perfusion pressure | • Useful to assess microcirculation and wound healing potential  
                      • May be useful for monitoring efficacy of revascularization  
                      • Can be measured in a shorter time compared with TcPo2 | • Probe size and shape may affect measurements  
                      • Limited data validation |
# Severity of Ischemia Matters

Parameters of Hemodynamic Assessment of CLTI Patients

## Table 3.3. Ischemia grading in Wound, Ischemia, and foot Infection (WIfI) classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>ABI</th>
<th>Ankle systolic pressure</th>
<th>TP, TcPo₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>≥0.80</td>
<td>&gt;100 mm Hg</td>
<td>≥60 mm Hg</td>
</tr>
<tr>
<td>1</td>
<td>0.6-0.79</td>
<td>70-100 mm Hg</td>
<td>40-59 mm Hg</td>
</tr>
<tr>
<td>2</td>
<td>0.4-0.59</td>
<td>50-70 mm Hg</td>
<td>30-39 mm Hg</td>
</tr>
<tr>
<td>3</td>
<td>≤0.39</td>
<td>&lt;50 mm Hg</td>
<td>&lt;30 mm Hg</td>
</tr>
</tbody>
</table>

*ABI, Ankle-brachial index; TP, toe pressure; TcPo₂, transcutaneous oximetry.*

Flat or minimally pulsatile forefoot pulse volume recording is grade 3. Measure TP or TcPo₂ if ABI incompressible (>1.3). Patients with diabetes should have TP measurements. If arterial calcification precludes reliable ABI or TP measurements, ischemia should be documented by TcPo₂, skin perfusion pressure, or pulse volume recording. If TP and ABI measurements result in different grades, TP will be the primary determinant of ischemia grade.
The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIfI)

### Risk of leg amputation at 1 year

<table>
<thead>
<tr>
<th>Wound</th>
<th>Ischemia – 0</th>
<th>Ischemia – 1</th>
<th>Ischemia – 2</th>
<th>Ischemia – 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-0</td>
<td>VL</td>
<td>VL</td>
<td>L</td>
<td>M</td>
</tr>
<tr>
<td>W-1</td>
<td>VL</td>
<td>VL</td>
<td>L</td>
<td>M</td>
</tr>
<tr>
<td>W-2</td>
<td>L</td>
<td>L</td>
<td>M</td>
<td>H</td>
</tr>
<tr>
<td>W-3</td>
<td>M</td>
<td>M</td>
<td>H</td>
<td>H</td>
</tr>
</tbody>
</table>

#### Foot infection

Four classes: for each box, group combination into one of these four classes

- **Very low** = VL = clinical stage 1
- **Low** = L = clinical stage 2
- **Moderate** = M = clinical stage 3
- **High** = H = clinical stage 4

Clinical stage 5 would signify an unsalvageable foot

Validation

Improved ABI = Higher Probability of Wound Healing

**FIGURE 2** Kaplan-Meier Analysis of Wound Healing Post-Procedure According to Change in ABI

The cumulative probability of wound healing was significantly greater in patients with an ankle-brachial index (ABI) increase of at least 0.23 following endovascular revascularization.

Reed et al. JACC Cardiovasc Interv 2017;10:2451
Grades of Ischemia and Amputation Free Survival

One-year AFS lower with decreased toe pressure

Fig 3. Kaplan-Meier amputation-free survival (AFS) by revised toe hemodynamic pressure group. Unadjusted hazard ratio (HR), toe hemodynamic pressure group 1: 1.61; 95% confidence interval [CI], 1.11-2.33; \( P = .01^* \). Unadjusted HR, toe hemodynamic pressure group 2: 3.20; 95% CI, 2.23-4.59; \( P < .0001^* \). Adjusted HR, toe hemodynamic pressure group 1: 1.66; 95% CI, 1.12-2.47; \( P = .01^* \). Adjusted HR, toe hemodynamic pressure group 2: 3.25; 95% CI, 2.22-4.76; \( P < .0001^* \).

Table IV. Kaplan-Meier amputation-free survival (AFS) by revised toe hemodynamic pressure group (N = 282 limbs)

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.64 (0.031)</td>
<td>0.54 (0.032)</td>
<td>0.41 (0.033)</td>
<td>0.28 (0.032)</td>
</tr>
<tr>
<td>TP 31-50 mm Hg (group 0, n = 115)</td>
<td>0.82 (0.040)</td>
<td>0.71 (0.048)</td>
<td>0.58 (0.053)</td>
<td>0.44 (0.056)</td>
</tr>
<tr>
<td>TP 11-30 mm Hg (group 1, n = 82)</td>
<td>0.69 (0.054)</td>
<td>0.53 (0.060)</td>
<td>0.38 (0.060)</td>
<td>0.27 (0.057)</td>
</tr>
<tr>
<td>TP 0-10 mm Hg (group 2, n = 85)</td>
<td>0.36 (0.055)</td>
<td>0.35 (0.055)</td>
<td>0.21 (0.050)</td>
<td>0.08 (0.036)</td>
</tr>
</tbody>
</table>
Improved TBI=Higher Probability of Wound Healing and Lower Probability of MALE

**(A)** The cumulative probability of wound healing was greater in patients with a toe-brachial index (TBI) increase of at least 0.21 following endovascular revascularization. **(B)** Likewise, patients with an increase in TBI of at least 0.21 has a lower probability of major adverse limb events (MALE) during follow-up.
Hemodynamics from IN.PACT Deep Improvement in Toe Pressure=Higher MALE-Free Survival

![Graph showing the probability of MALE-free survival over time with different groups showing varying outcomes and log-rank test significance.](image-url)

Hemodynamic Assessment

• Pressure Measurements
  • ABI, TBI

• Waveforms
  • Continuous doppler waveform, Pulse volume recording

• Morphological Distribution
  • Duplex, CTA, MRA, Angiography

• Regional Tissue Perfusion
  • TCPO2, Skin Perfusion Pressure
  • Fluorescene angiography, Blush assessment techniques
  • Laser doppler, Hyperspectral imaging, SPECT/PET scanning
  • Implantable continuous oxygen sensor
Role of Hemodynamic Assessment
Parameters in CLTI Patients

Fig 3.1. Flow diagram for the investigation of patients presenting with suspected chronic limb-threatening ischemia (CLTI). ABI, Ankle-brachial index; PAD, peripheral artery disease; TBI, toe-brachial index; Wiff, Wound, Ischemia, and foot Infection.
ABI/TBI for initial assessment of patient: subsequent use of physiologic assessment for clinical decision-making is highly variable.

Courtesy: Dr. M. Weinberg
Noncompressible ABIs
Higher Risk of Amputation, also Misleading

Singh et al. Vasc Med 2017;22:210
This will increase as proportion of diabetics and those with renal failure increases.

Table III. Prevalence of patients with a low toe-brachial index (TBI) and a normal ankle-brachial index (ABI)

<table>
<thead>
<tr>
<th>Study (first author)</th>
<th>Year</th>
<th>No.</th>
<th>Low TBI, normal ABI, %</th>
<th>Diagnostic limits</th>
<th>Population</th>
<th>Method</th>
<th>Pretest limb heating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sahli^{47}</td>
<td>2004</td>
<td>303</td>
<td>9^{a}</td>
<td>ABI &gt;0.9, TBI &lt;0.74</td>
<td>Diabetic patients</td>
<td>PP</td>
<td>Yes</td>
</tr>
<tr>
<td>Bird^{15}</td>
<td>1999</td>
<td>423</td>
<td>14^{a}</td>
<td>ABI &gt;0.9, TBI ≤0.7</td>
<td>Patients suspected of PAD</td>
<td>PP</td>
<td>No</td>
</tr>
<tr>
<td>Høyer^{16}</td>
<td>2012</td>
<td>204</td>
<td>17</td>
<td>ABI &gt;0.9, TBI &lt;0.7</td>
<td>Patients suspected of PAD</td>
<td>SGP</td>
<td>Yes</td>
</tr>
<tr>
<td>Crique^{14,60}</td>
<td>1985</td>
<td>613</td>
<td>16</td>
<td>ABI &gt;0.8, TBI ≤0.7</td>
<td>Screening population</td>
<td>SGP</td>
<td>No</td>
</tr>
<tr>
<td>Morimoto^{71}</td>
<td>2009</td>
<td>115</td>
<td>11</td>
<td>ABI &gt;0.9, TBI &lt;0.6</td>
<td>Patients in hemodialysis</td>
<td>OP</td>
<td>No</td>
</tr>
<tr>
<td>Suominen^{7}</td>
<td>2010</td>
<td>2159</td>
<td>27</td>
<td>ABI &gt;0.9, TBI &lt;0.6</td>
<td>Patients suspected of PAD</td>
<td>PP</td>
<td>No</td>
</tr>
</tbody>
</table>

*OP, Oscillometric plethysmography; PP, photoplethysmography; SGP, strain gauge plethysmography.

^{a}Each limb diagnosed independently.
Hemodynamic assessment

TCPO2

- Not point of care
- Time consuming (30 – 45 min)
- Partial validation (TCPO2 > 40) predictive of wound healing
- Clark-type electrode on the skin so that it heats up the skin and provides tcpO2 values
- Noninvasive measurement reflecting the amount of O2 that has diffused from the capillaries, through to the epidermis


Hemodynamic Assessment

Measure Regional Tissue Perfusion

Validation
Quantification
Clinical correlation
Predictive value

Laser doppler
Hyperspectral imaging

Implantable continuous oxygen sensor (potential for remote monitoring)
Conclusion

Parameters of Hemodynamic Assessment of CLTI Patients

• Optimal management of CLTI patients requires assessment of perfusion at multiple time points along the clinical course.
• Previously available methods are inadequate.
• Several promising technologies on the horizon.
• State-of-the-art will be significantly enhanced as these methods become validated and incorporated into clinical trials and practice.
Value of Current Parameters of Hemodynamic Adjustment of CLTI Patients

Peter A. Schneider, MD
University of California San Francisco