Critical limb ischemia: Have we made improvement in classifying these patients in a better way?

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Disclosure

Speaker name:

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I have the following potential conflicts of interest to report:

☒ Consulting:

Medtronic, BD BARD, Spectranetics, Intact Vascular, Soundbite Medical, Biotronik, Bayer, Daiichi Sankyo, Böhringer Ingelheim, Astra Zeneca

Improvement in classification?

We all agree:

- Critical limb ischemia (CLI), is the most advanced form of peripheral artery disease
- Clinically, critical limb ischemia (CLI) is defined as ischemic rest pain, tissue loss, or gangrene in the presence of peripheral artery disease (PAD) and hypoperfusion of the lower extremity [1]
- Classifications
  - Rutherford categorization
    - Class IV: Rest pain
    - Class V: Tissue loss
    - Class VI: and/or gangrene
  - Fontaine classification
    - Class III: Rest pain
    - Class IV: Tissue loss or gangrene

BUT

Neither of these classifications incorporates wound size, perfusion assessment, or infection[2]

1 Patel MR et al consensus definitions from Peripheral Academic Research Consortium (PARC). J Am Coll Cardiol 2015;65:931–41.
2 Mills JL Sr, et al.,The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc Surg 2014;59:220–34.e1–2.

Improvement in classification?

Second achilles' heel

- Current hemodynamic cutpoints are likely inaccurate in light of recent publications highlighting the limitation of the ankle–brachial index (ABI) and toe pressure in accurately diagnosing CLI [1,2]

1 Shishehbor MH, Zeller T, et al. An analysis of IN.PACT DEEP randomized trial on the limitations of the societal guidelines recommended hemodynamic parameters to diagnose critical limb ischemia. J Vasc Surg 2016;63: 1311–7.
2 Bunte MC,et al . Curr Cardiol Rep 2013; 15:363.

Improvement in classification?

An analysis of IN.PACT DEEP randomized trial on the limitations of the societal guidelines-recommended hemodynamic parameters to diagnose critical limb ischemia

- Only 14 of 237 patients **(6%)** had an **ABI <0.4**.
- **Abnormal ankle pressure**, defined as <50 mm Hg if Rutherford category 4 and <70 mm Hg if Rutherford category 5 or 6, was found only in 37 patients **(16%).**
- **Abnormal toe pressure**, defined as <30 mm Hg if Rutherford category 4 and <50 mm Hg if Rutherford category 5 or 6, was found in 24 of 40 patients **(60%)** with available measurements. Importantly, 29% of these 24 patients had an ABI within normal reference ranges.

A univariate multinomial logistic regression found no association between the above hemodynamic parameters and the number of diseased infrapopliteal vessels.
However, there was a significant paradoxic association where patients with Rutherford category 6 had higher ABI and ankle pressure than those with Rutherford category 5.
Similarly, there was no association between ABI and pedal arch patency.

1 Shishehbor MH, Zeller T, et al. An analysis of IN.PACT DEEP randomized trial on the limitations of the societal guidelines recommended hemodynamic parameters to diagnose critical limb ischemia. J Vasc Surg 2016;63: 1311–7.

Improvement in classification?

TABLE 1 Overview of the Diagnostic Tools Available in CLI

	Indications/Advantages	Disadvantages
ABI or ankle pressure	• Helps establish a diagnosis and a baseline perfusion • Can be used to monitor efficacy of revascularization • Generally easy to perform	• Can be falsely elevated in noncompressible vessels (advanced age, diabetes, and kidney disease) • Does not localize disease • May be normal or near-normal with isolated infrapopliteal disease
Toe-brachial index or toe pressure	• Useful in noncompressible vessels in which ABI can be nondiagnostic • Generally easy to perform	• Does not localize disease
Leg segmental pressure	• Helps indirectly localize disease • Can be used to monitor efficacy of revascularization • Generally easy to perform	• Can be falsely nondiagnostic in noncompressible vessels
Plethysmography/pulse volume recording	• Can help establish a diagnosis • Can be used to monitor efficacy of revascularization • Useful in noncompressible vessels • May indirectly localize disease	• Might be abnormal in low cardiac stroke volume • Not reliable in inflow disease • Not angiosome-specific
Continuous-wave Doppler ultrasound	• Useful in noncompressible vessels • Generally easy to perform	• Limited sensitivity for proximal disease • Limited in infrapopliteal disease • Limited in localizing the disease • Limited by patient's body habitus
Duplex ultrasound	• Accurate visual assessment of disease and its location • Hemodynamic assessment of degree of stenosis • Used for routine surveillance after bypass • Readily available	• Highly dependent on operator skills • Limited in evaluation of iliac vessels (due to bowel gas and/or obesity) and distal small vessels, especially if heavily calcified • Not well established to assess long-term patency of
CTA	• Provides visual assessment of the disease (stenosis/plaque) and allows the walls of large vessels to be evaluated • May help interventional planning • Three-dimensional imaging • Provide better resolution than MRA	• Iodinated contrast (nephrotoxic) and radiation exposures • Lack of adequate evaluation in the presence of dense calcification or metallic stents • Not very useful for infrapopliteal and pedal arch assessment
MRA	• Provides visual assessment of the disease (stenosis/plaque) and allows evaluation of the walls of small and large vessels • Helps interventional planning • Three-dimensional imaging • Unlike CTA, no radiation or iodinated contrast medium exposure • Unlike CTA and duplex ultrasound, calcifications do not cause artifacts	• Gadolinium exposure; contraindicated if GFR <30 ml/min/1.73 m^2 • Contraindicated in the presence of metallic materials that are not compatible with MRA • Limited evaluation in the presence of certain stents; fair evaluation with alloy ones • Might be limited in the assessment of below-the-knee vessels due to venous artifact. However, time-resolved MRA addresses this limitation • Might require sedation if claustrophobia or agitation exists
Digital-subtraction angiography	• Gold standard • Real-time temporal information augments hemodynamic assessment	• Invasive with risks • Radiation and contrast medium exposure • Two-dimensional imaging
$TcPO_2$	• Assesses microcirculation (regional perfusion) and helps confirm the diagnosis of CLI • Can predict wound healing • May be useful for monitoring efficacy of revascularization	• Limited accuracy in the presence of edema, skin thickness, or infection • Can be falsely normal • Requires skin heating to $\geq 40^\circ$C • Time-consuming
SPP	• Assesses microcirculation, severity of ischemia, and wound healing potential • Can be useful in monitoring efficacy of revascularization • Can be measured in shorter time compared with $TcPO_2$	• Might be insensitive to mild degrees of ischemia • Probe size and shape may affect measurements • Can be painful
Indocyanine green	• May help assess microcirculation • Limited available data for CLI	• Invasive • Not safe in patients with kidney disease • Time-consuming

ABI = ankle brachial index; CLI = critical limb ischemia; CTA = computed tomography angiography; GFR = glomerular filtration rate; MRA = magnetic resonance angiography; SPP = skin perfusion pressure; $TcPO_2$ = transcutaneous oxygen pressure.

We have a huge tool box, but it is a little bit out of fashion

Improvement in classification?

Step forward

- The Threatened Limb Classification System: risk stratification based on wound, ischemia, foot infection (WIfI)
  - WIfI recognizes the multifactorial nature of the threatened limb by accounting for wound size and location, concomitant infection, and the degree of ischemia
  - is intended to provide a more meaningful analysis of outcomes in these high-risk patients

Improvement in classification?

Step forw

- The Threat … fication based on wound, isc…
- Also imple…

a, Estimate risk of amputation at 1 year for each combination

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	L	M	VL	L	M	H	L	L	M	H	L	M	M	H
W-1	VL	VL	L	M	VL	L	M	H	L	M	H	H	M	M	H	H
W-2	L	L	M	H	M	M	H	H	M	H	H	H	H	H	H	H
W-3	M	M	H	H	H	H	H	H	H	H	H	H	H	H	H	H
	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

b, Estimate likelihood of benefit of/requirement for revascularization (assuming infection can be controlled first)

	Ischemia – 0				Ischemia – 1				Ischemia – 2				Ischemia – 3			
W-0	VL	VL	VL	VL	VL	L	L	M	L	L	M	M	M	H	H	H
W-1	VL	VL	VL	VL	L	M	M	M	M	H	H	H	H	H	H	H
W-2	VL	VL	VL	VL	M	M	H	H	H	H	H	H	H	H	H	H
W-3	VL	VL	VL	VL	M	M	M	H	H	H	H	H	H	H	H	H
	f-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3	fI-0	fI-1	fI-2	fI-3

fI, foot Infection; I, Ischemia; W, Wound.

Premises:

1. Increase in wound class increases risk of amputation (based on PEDIS, UT, and other wound classification systems)
2. PAD and infection are synergistic (Eurodiale); infected wound + PAD increases likelihood revascularization will be needed to heal wound
3. Infection 3 category (systemic/metabolic instability): moderate to high-risk of amputation regardless of other factors (validated IDSA guidelines)

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

Component	
W (Wound)	
I (Ischaemia)	
fI (foot Infection)	
Example: A 65-year-old … of general infection/infla… would be 4 (high risk of	

…ressure or $TcPO_2$
≥60
40–59
30–39
<30

…linical/biological sign 2-1). The clinical stage

1 Mills JL Sr, et al The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc Surg 2014;59:220–234.e2.

Improvement in classification?

Steps done

You will hear within this meeting and the next talks, how many efforts have been made to improve classification of CLI patients

- New measurement tools (oxygen sensors…) ar
- New diagnostic tools (perfusion a , are on the way
- Trials are perform techniques
- Inter proach to integrate all stakeholders is no fear anymore
- ing dedicated with regard to CLI are out there (AMP, AMP Europe..)
- Societies have been founded
- Science is more focused on it than ever!

PUBMED(1955-): 5461 hits with regard to CLI: 2017 / 2018 :881

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