

Modern Concepts In Management Of Patients With Critical Limb Ischemia

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***CLI can be defined as ;**

arterial blood flow that is inadequate to accommodate the metabolic needs of resting tissues in the limbs. (Dick ,et al. 2007)

Criteria for diagnosis include either one of the following :

a- More than two weeks of recurrent foot pain at rest that requires regular use of analgesics

b- An ankle-brachial index of 0.4 or less

c- An ankle systolic pressure of 50 mm Hg or less

d- A toe systolic pressure of 30 mm Hg or less

e- Tissue necrosis, with similar hemodynamic measurements

- * These patients would be classified in the more severe ends of the Fontaine classification (stage III-IV) or the Rutherford classification (grades 4-6) (Table I) .
Table 1. Classification schemes of peripheral arterial disease (TASC II)

<i>Classification</i>	<i>Stage</i>	<i>Clinical description</i>
Fontaine	I	Asymptomatic
	II a	Mild claudication
	II b	Moderate to severe claudication
	III	Rest pain
	IV	Ulceration or gangrene
Rutherford	0	Asymptomatic
	1	Mild claudication
	2	Moderate claudication
	3	Severe claudication
	4	Rest pain
	5	Minor tissue loss
	6	Severe tissue loss or gangrene

* Chronic subcritical (subclinical) limb ischemia is a poorly recognized stage of critical limb ischemia. It represents a subgroup of patients with critical limb ischemia who are asymptomatic with severely reduced circulation to the foot and ankle pressures (White, Rutherford and Ryjewski, 2007).

While critical limb ischemia may be due to an acute condition such as an embolus or thrombosis, most cases are the progressive result of a chronic condition, most commonly atherosclerosis. (White, Rutherford and Ryjewski, 2007).



CLI is associated with both a significantly reduced life expectancy and an elevated risk of major amputation of the involved extremity if improvement in distal arterial flow is not established. (Naidoo and Steve. 2009)

it has almost always multilevel occlusive disease which often includes occlusions of arteries in the leg and foot.(Veith et al . 1990)

Risk Factors include;(age, tobacco use, diabetes, dyslipidemia, hypertension ,chronic renal insufficiency and elevated homocysteine levels)

DIAGNOSTIC STUDIES *

Hematologic Studies, Lipid Profile, C-Reactive Protein, Hypercoagulable States, Homocysteine.

Cardiac and Cerebrovascular Evaluation

ECHO, Carotid duplex and CTA

Vascular Laboratory and Imaging Studies

A/B Index, TcPO₂

color-guided duplex imaging,

gadolinium-enhanced magnetic resonance imaging (MRA),

computed tomographic angiography (CTA), and intra-arterial subtraction

angiography (DSA) are the most frequently used imaging modalities for the delineation of arterial anatomy. (carbon dioxide angiography—COPD) Moos, et al: 2011.



The care of many patients with CLI is not always a straight forward plan. It has to be tailored for every individual patient according to his or her clinical , radiological findings, and according to the accompanying co-morbidities as well (Vinit, Melissa, and Melina .2010)

Decision making for CLI commonly poses three dilemmas: whether to treat medically or with intervention; if treating with intervention, whether to amputate or revascularize; and if revascularizing, whether to employ endovascular intervention or open surgery.

Medical Management *

A-Risk Factors Modification

Regardless of the modality of treatment, risk factors and comorbidities should be identified and controlled.(Hankey , Norman and Eikelboom. 2006)

B- Exercise therapy .

C- Pharmacotherapy.

D- Intermittent Pneumatic Compression

* Pharmacotherapy.

1-Clopidogrel (Plavix, Bristol-Myers Squibb, New York, NY) is the only antiplatelet agent approved by the FDA for the secondary prevention of atherosclerotic vascular disease, including PAD.

2-PICOTAMIDE

An inhibitor of thromboxane A₂ synthase and thromboxane- endoperoxide receptors.

The Drug Evaluation in Atherosclerotic Vascular Disease in Diabetics (*DAVID*) study demonstrated that picotamid was more effective than aspirin alone in reducing overall mortality at 24 months in patients with PAD and type 2 diabetes.

3- Aspirin

(pentoxifylline and cilostazol) have achieved FDA approval for the treatment of intermittent claudication in the United States.

However, a number of other medications have been investigated, with varying degrees of evidence supporting their efficacy .

These include :

A- Changers in tissue metabolism (*naftidrofuryl, levocarnitine*)

B-Enhancers of nitric oxide production (*L-arginine*)

C-Vasodilators (*statins, buflomedil, prostaglandins, ACE inhibitors and K-134*).

* Intermittent Pneumatic Compression

Intermittent pneumatic compression (IPC) in combination with appropriate risk factor modification may be a viable method of treatment for :

A- Unreconstructable vascular disease

B-Patients physiologically unfit for surgical intervention

TECHNIQUE :

Sequential inflation and deflation of pneumatic pressure cuffs positioned at the foot or calf. Inflation-deflation rates vary according to the system used, each applying a pressure up to 120 mm Hg for 2 to 3 seconds before deflating.

This sequence is continued at a rate of three cycles per minute throughout the treatment session.

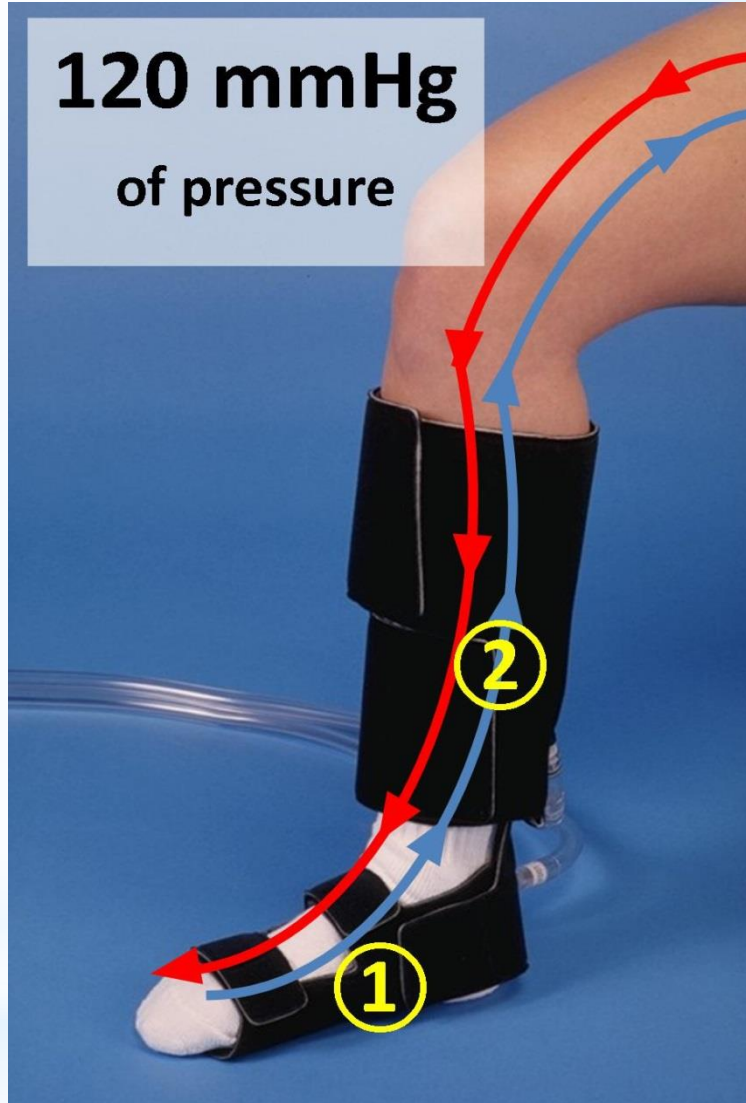
The physiologic effects of IPC are; (Chang, et al, 2012.)

1- An increase in the arteriovenous pressure gradient

2-Reversal of vasomotor paralysis

3-Enhanced release of nitric oxide

**120 mmHg
of pressure**



Limb salvage with complete wound healing was achieved in 14 of 24 patients (54%) who underwent IPC. Kavros et al, 2010 .

* Surgical Management

A- Endovascular revascularization .

B- surgical revascularization procedures.

C- local amputations .

A- Endovascular revascularization *

Recent improvements in catheter, guide wire, stent, and stent - graft technology have transformed the treatment of critical lower limb ischemia from a primarily open surgical (bypass) modality supplemented by some catheter - based treatments to a primarily endovascular modality

B- surgical revascularization procedures *

Primarily vein and prosthetic arterial bypasses above or below the inguinal ligament.

These may on occasion be supplemented with localized endarterectomies or patch angioplasties, although these operations have largely fallen into disfavor and alone are rarely enough to save a severely ischemic limb. at least 20 - 30% of patients with critical ischemia will be primary option from the outset.

C- local amputations of toes and other portions of the foot and control infection(in patients with good circulation as manifested by collaterals.)

Reoperation or Reintervention *

some patients need reoperation or reintervention because they developed a failed (thrombosed) or failing (threatened but patent) graft from a lesion in their graft or its inflow or outflow tract (Veith et al .1984)

This is due to both intimal hyperplasia, largely a reaction to vascular injury, and progression of the arteriosclerotic process..

The first line in these patients is endovascular techniques, (Norgren, et al; 2007.) .

Similarly, bypass operations or partially open thrombectomy will be required after early or late failure of endovascular treatment or prior bypasses in patients in whom no further endovascular options are available (Gargiulo, et al . 2010).

Lipsitz, et al . 2003 ,observed the duration of patency following more than 3 bypasses was substantial and resulted in more than 3 years of extended limb salvage in more than 50% of the patients who would otherwise have required an amputation

• Therapeutic angiogenesis for critical limb ischemia *

a naturally occurring phenomenon in response to tissue ischemia, and is promoted by proangiogenic factors, including VEGF, fibroblast growth factor, hypoxia-inducible factor-1 α , and hepatocyte growth factor. (Makino, et al, 2012.)

Such therapies may be particularly valuable for the treatment of CLI in patients with physiologic or anatomic contraindications for revascularization. Preliminary findings, to date, are encouraging.

Stem Cell Therapy

Stem cell therapy is another developing technique to induce therapeutic angiogenesis. (Tongers, Roncalli and Losordo, 2008.)

- a- Autologous Cells
- b- Allogenic Cells



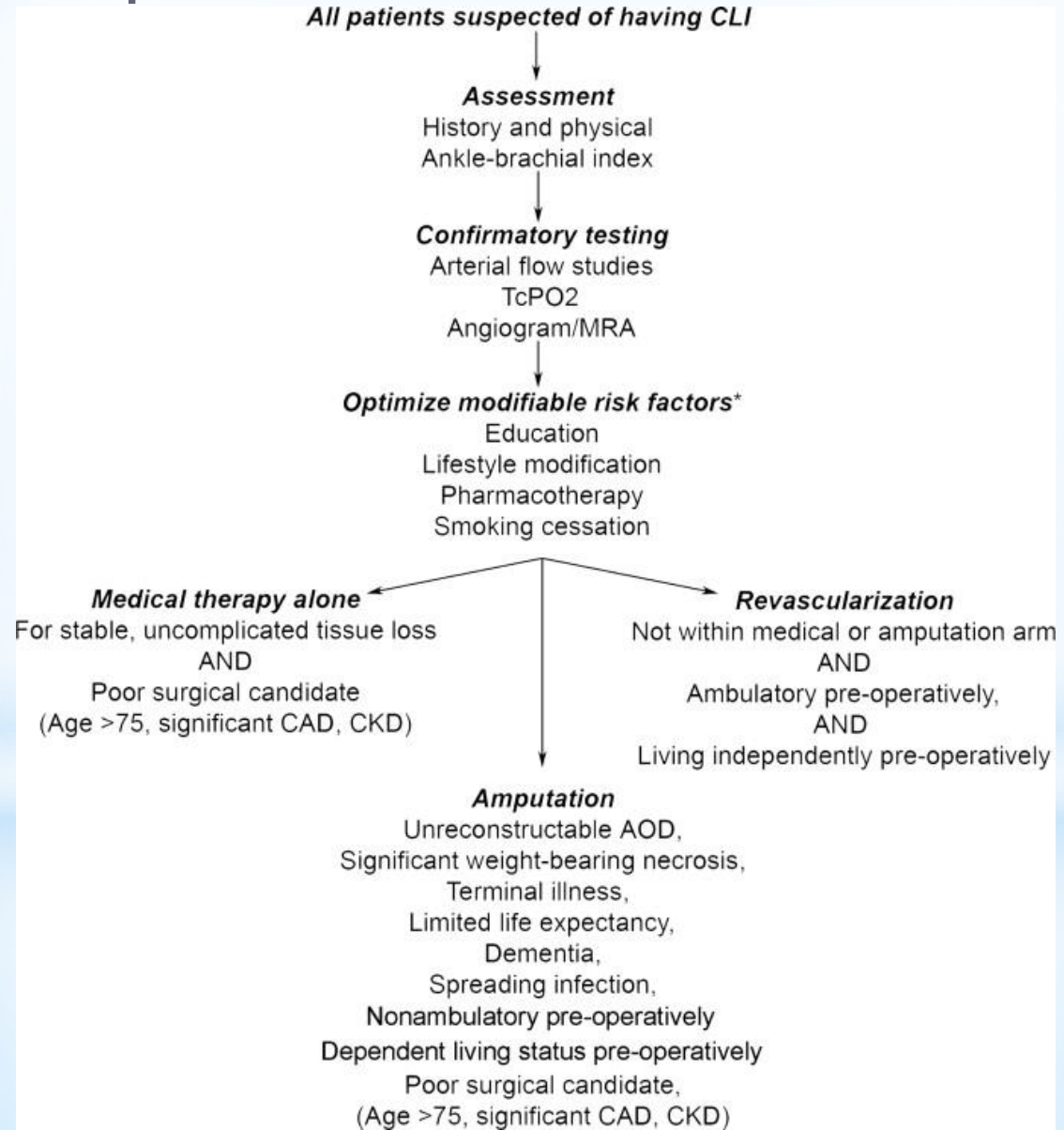
- **Angiosome-directed revascularization for critical limb ischemia**

An angiosome is a three dimensional anatomic block of tissue fed by a specific artery.

Although arterial connections exist between angiosomes, the angiosome theory posits that superior results can be achieved by revascularizing the vessel that directly feeds an angiosome in the region where there is tissue loss, rather than relying on indirect flow from arteries that feed adjacent angiosomes.



This algorithm explain the Proposed mechanism for the approach to the patient with CLI.



everything possible should be done even Multiple redo *
procedures. to

salvage the threatened foot in these elderly, sick patients who do not walk well after one major amputation and certainly do not do so after bilateral amputations, which 25% of this population may otherwise require at some point in their course.(Lipsitz, et al . 2003)

Thank you