Clinical Practice Guidelines:
Critical Limb Threatening Ischemia

Acknowledgment

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Abbreviations

ABI: ankle brachial index
*AKA:*above the knee amputation
APSV: Ankle Peak Systolic Velocity
BKA: below-the-knee amputation
CFA: common femoral artery
CLTI: Critical limb-threatening ischemia
CTA: CT angiography
*DAPT:*dual antiplatelet therapy
DM: Diabetes mellitus
*DUS:*duplex ultrasound
*FP:*femoropopliteal
*MRA :*Magnetic resonance angiography
PAD: peripheral arterial disease
PFA: profunda femoris artery
PSVR: peak systolic velocity ratio
Wifi: Wound, Ischemia, and foot Infection

Glossary

Critical limb-threatening ischemia (CLTI) is a clinical syndrome defined by the presence of peripheral artery disease (PAD) in combination with rest pain, gangrene, or a lower limb ulceration >2 weeks duration. CLTI is associated with amputation, increased mortality, and impaired quality of life. All patients with suspected CLTI should be referred urgently to a vascular specialist.

Scope

This Guideline is concerned with the diagnosis and treatment decisions of Critical limb-threatening ischemia (CLTI).

Executive Summary

- Use ABI to determine the presence and quantify the severity of ischemia in all patients with suspected CLTI. **Strong recommendation** .
- Perform a detailed history to determine symptoms, past medical history, and cardiovascular risk factors in all patients with suspected CLTI. **Good practice statement .**
- Perform a complete vascular physical examination of all patients with suspected CLTI, including palpation of carotid, upper extremity, aorta, and lower extremity pulses. **Good practice statement**.
- Perform a complete examination of both feet, including a probe-to-bone test of any open ulcers using sterile equipment, in all patients with pedal tissue loss and suspected CLTI. **Good practice statement**.
- We recommend using DUS imaging, including assessment of Ankle Peak Systolic Velocity (APSV) as the first arterial imaging modality in patients with suspected CLTI. **Strong recommendation**.
- We recommend other noninvasive vascular imaging modalities as CTA or MRA in patients with suspected CLTI who are candidates for revascularization, and who do not suffer impaired renal function. **Strong recommendation**.
- Perform high-quality angiographic imaging of the lower limb using digital subtraction imaging (DSA). This should include the ankle and foot in all patients with suspected CLTI prior to proceeding to revascularization. **Good practice statement**.
- Evaluate cardiovascular risk factors in all patients with suspected CLTI. **Strong recommendation.**
- Refer all patients with suspected CLTI to have all modifiable risk factors including (hypertension, diabetes mellitus, and dyslipidemia), controlled to recommended levels. Strongly advise smoking cessation. **Strong recommendation** .
- Treat all patients with CLTI with an antiplatelet agent. Strong recommendation.
- We recommendclopidogrel as the single antiplatelet agent of choice in patients with CLTI. **Conditional recommendation**.
- We recommendlow-dose aspirin and rivaroxaban, 2.5 mg twice daily, to reduce adverse cardiovascular events and lower extremity ischemic events in patients with CLTI. **Conditional recommendation**.
- We recommend against using systemic vitamin K antagonists for the treatment of lower extremity atherosclerosis in patients with CLTI. **Strong recommendation**.
- We recommend against using low molecular weight heparin for the treatment of lower extremity atherosclerosis in patients with CLTI, except if there is suspicion of acute thrombo-embolic event, or for bridging anticoagulation prior to an invasive procedure. **Good practice statement**.
- We recommend the use of moderate- or high-intensity statin therapy to reduce all-cause and cardiovascular mortality in patients with CLTI. Strong recommendation.
- We recommend the use of metformin as the primary hypoglycemic agent in patients with type 2 DM and CLTI. **Strong recommendation**.
- We recommendwithholding metformin immediately before and for 24 to 48 hours after the administration of an iodinated contrast agent for diabetic patients,

especially those with an estimated glomerular filtration rate <30 mL/min/1.73 m2. **Conditional recommendation**.

- Prescribe analgesics of appropriate strength for CLTI patients who have ischemic rest pain of the lower extremity and foot until pain resolves after revascularization. **Good practice statement.**
- Refer all patients with suspected CLTI to a vascular consultant for consideration of limb salvage unless major amputation is considered medically urgent. **Good practice statement.**
- Offer primary amputation to patients with poor functional status (non-ambulatory), or an unsalvageable limb as judged by a qualified vascular consultant. **Good practice statement .**
- Use an integrated threatened limb classification system (such as WIfI) to stage all CLTI patients who are candidates for limb salvage. **Strong recommendation**.
- Perform urgent surgical drainage including minor amputation, if needed, and commence antibiotic treatment in all patients with suspected CLTI who present with deep space foot infection or wet gangrene. Perform urgent revascularization before or soon after foot surgery. **Good practice statement**.
- Do not perform revascularization in the absence of significant ischemia (WIfI ischemia grade 0). **Good practice statement**.
- Do not perform revascularization based on imaging alone in the absence of tissue necrosis or gangrene. **Strong recommendation**.
- Revascularization could be performed in the absence of significant foot ischemia in exceptional conditions such as isolated region of poor perfusion, which could be the target of angiosome revascularization, if the isolated region of poor perfusion is associated with major tissue loss (eg, WIfI wound grade 2 or 3), and the wound deteriorates despite appropriate infection control, wound care, and offloading. **Good practice statement.**
- We recommendrevascularization to all average-risk patients with moderate ischemia and extensive wounds or extensive tissue necrosis . Conditional recommendation.
- Perform ultrasound vein mapping when available in all CLTI patients who are candidates for surgical bypass. **Strong recommendation**.
- Do not classify a CLTI patient as being unsuitable for revascularization without review of adequate-quality imaging studies and clinical evaluation by a qualified vascular consultant. **Good practice statement**.
- Correct inflow disease first when both inflow and oudlow disease are present in a patient with CLTI. **Good practice statement**.
- Base the decision for staged vs combined inflow and oudlow revascularization on patient risk and the severity of limb threat (eg, WIfI stage). **Strong recommendation.**
- Correct inflow disease alone in CLTI patients with multilevel disease and low-grade ischemia (eg, WIfI ischemia grade 1) or limited tissue loss (eg, WIfI wound grade 0/1) and in any circumstance in which the riskbenefit of additional oudlow reconstruction is high or initially unclear. **Strong recommendation**.
- Restage the limb and repeat the hemodynamic assessment after performing inflow correction in CLTI patients with inflow and oudlow disease. **Strong recommendation**.

- We recommendsimultaneous inflow and oudlow revascularization in CLTI patients with a high limb risk (eg, WIfI stages 3 and 4), or in patients with severe ischemia (eg, WIfI ischemia grades 2 and 3). **Conditional recommendation**.
- Use an endovascular-first approach for treatment of CLTI patients with moderate to severe aorto-iliac disease. **Strong recommendation**.
- We recommendsurgical reconstruction for the treatment of average-risk CLTI patients with extensive aorto- iliac disease, or after failed endovascular intervention. **Conditional recommendation**.
- Perform open CFA endarterectomy with patch angioplasty, with or without extension into the PFA, in CLTI patients with hemodynamically significant (>50% stenosis) disease of the common and deep femoral arteries. **Strong recommendation.**
- We recommenda hybrid procedure combining open CFA endarterectomy and endovascular treatment of aorto-iliac disease with concomitant CFA involvement. **Conditional recommendation**.
- We recommendendovascular treatment of significant CFA disease in selected patients who are deemed to be at high surgical risk or to have a hostile groin. **Conditional recommendation**.
- Avoid stents in the CFA and do not place stents across the origin of a patent deep femoral artery. **Good practice statement**.
- Correct hemodynamically significant (>50% stenosis) disease of the proximal deep femoral artery whenever technically feasible. **Good practice statement**.
- In surgically average-risk CLTI patients with infrainguinal disease, base decisions of endovascular intervention vs open surgical bypass on the severity of limb threat (eg, WIfI), the anatomic pabern of disease, and the availability of autologous vein. **Strong recommendation.**
- Offer endovascular revascularization when technically feasible for surgically high-risk patients with advanced limb threat and significant perfusion deficits (eg, WIfI ischemia grades 2 and 3). **Conditional recommendation**.
- We recommendangiosome-guided revascularization in patients with significant wounds (eg, WIfI wound grades 3 and 4), particularly those involving the midfoot or hindfoot, and when the appropriate target arterial path is available. **Conditional recommendation.**
- In treating femoropopliteal (FP) disease in CLTI patients by endovascular means, We recommendadjuncts to balloon angioplasty (eg, stents, covered stents, or drug-eluting technologies) when appropriate. **Conditional recommendation**.
- Use autologous vein as the preferred conduit for infrainguinal bypass surgery in CLTI. **Strong recommendation**.
- Avoid using a non-autologous conduit for infrainguinal bypass unless there is no endovascular option and no adequate autologous vein. **Conditional recommendation.**
- We recommendperforming intraoperative imaging (angiography, DUS, or both) on completion of open bypass surgery for CLTI and correct significant technical defects if feasible during the index operation. **Strong recommendation**.

- We recommend against usinglumbar sympathectomy for limb salvage in CLTI patients in whom revascularization is not possible, except in carefully selected cases. **Conditional recommendation**.
- We recommendintermibent pneumatic compression therapy in carefully selected patients (eg, rest pain, minor tissue loss) in whom revascularization is not possible. **Conditional recommendation**.
- Do not offer prostanoids for limb salvage in CLTI patients. We recommendoffering selectively for patients with rest pain or minor tissue loss and in whom revascularization is not possible. **Conditional recommendation**.
- Do not offer vasoactive drugs in patients in whom revascularization is not possible. **Strong recommendation**.
- Do not offer hyperbaric oxygen therapy to improve limb salvage in CLTI patients with severe, uncorrected ischemia (eg, WIfI ischemia grade 2/3). **Strong recommendation**.
- The patient should be provided with optimal wound care until the lower extremity wound is completely healed or the patient undergoes amputation. **Good practice statement.**
- Restrict the use of therapeutic angiogenesis to CLTI patients who are enrolled in a registered clinical trial. **Strong recommendation**.
- We recommendtrans metatarsal amputation of the forefoot in CLTI patients who would require more than two digital ray amputations to resolve distal necrosis, especially when the hallux is involved. **Conditional recommendation**.
- Offer primary amputation to CLTI patients who have a pre-existing dysfunctional or unsalvageable limb, or a poor functional status (eg, bedridden), after shared decision-making with the patient and health care team. **Strong recommendation**.
- We recommendsecondary amputation for patients with CLTI who have a failed or ineffective reconstruction and in whom no further revascularization is possible and who have incapacitating pain, nonhealing wounds, or uncontrolled sepsis in the affected limb after shared decision-making with the patient and health care team. **Conditional recommendation**.
- We recommendrevascularization to improve the possibility of healing an amputation at a more distal functional amputation level (eg, AKA to BKA), particularly for patients with a high likelihood of rehabilitation and continued ambulation. **Conditional recommendation**.
- We recommenda BKA or AKA in patients who are non-ambulatory for reasons other than CLTI (ie, bedridden patients with flexion contracture, dense hemiplegia, cancer) and are unlikely to undergo successful rehabilitation to ambulation after shared decision-making with the patient and health care team. **Conditional recommendation.**
- Patients who have undergone amputation for CLTI are instructed to seek medical advice to monitor the progression of disease in the contralateral limb and to maintain optimal medical therapy and risk factor management. **Strong recommendation.**
- Postprocedural care and surveillance of infrainguinal revascularizа%on for CLTI

- Continue best medical therapy for PAD, including the long-term use of antiplatelet and statin therapies, in all patients who have undergone lower extremity revascularization. **Strong recommendation**.
- Promote smoking cessation in all CLTI patients who have undergone lower extremity revascularization. **Strong recommendation**.
- We recommendDAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal prosthetic bypass for CLTI for a period of 6 to 24 months to maintain graft patency. **Conditional recommendation.**
- We recommendDAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal endovascular interventions for CLTI for a period of at least 1 month, alternatively, We recommendAspirin and Rivaroxaban 2.5mg bd. **Conditional recommendation.**
- We recommendDAPT for a period of 1 to 6 months in patients undergoing repeated catheter-based interventions, or alternatively We recommendAspirin and Rivaroxaban 2.5mg bd, if they are at low risk for bleeding. **Conditional recommendation.**
- Patients who have undergone lower extremity vein or prosthesis bypass for CLTI are advised to have a check-up on a regular basis for at least 2 years. We recommendDUS scanning where available. **Good practice statement**.
- We recommendperforming additional imaging in patients with lower extremity grafts who have a decrease in ABI or a decrease in APSV or recurrence of symptoms or a change in pulse status to detect vein graft stenosis. **Good practice statement**.
- Offer intervention for DUS-detected vein graft lesions with an associated PSV of >300 cm/s and a PSV ratio >3.5 or grafts with low velocity (mid-graft PSV <45 cm/s), which may be further documented by CTA, to maintain graft patency. **Strong recommendation.**
- The patient is advised to maintain long-term surveillance after surgical or catheter-based revision of a vein graft, including DUS graft scanning where available, to detect recurrent graft-threatening lesions. **Strong recommendation**.
- Refer for mechanical offloading as a primary component for care of all CLTI patients with plantar wounds, and for continued protection of the healed wound and the foot to include appropriate shoes, insoles, and monitoring of inflammation. **Strong recommendation.**

Introduction

The incidence of PAD has increased over the years due to population aging and the global epidemic of diabetes. Some patients progress to CLTI , an advanced stage of PAD. CLTI is associated with increased mortality, risk of amputation, and impaired quality of life. CLTI is a clinical syndrome defined by the presence of PAD in combination with rest pain, gangrene, or a lower limb ulceration >2 weeks duration.

Purpose

The purpose of this multidisciplinary guideline is to identify quality improvement opportunities in managing CLTI and to create explicit and actionable recommendations to implement these opportunities in clinical practice.

Specifically, the goals are to improve diagnostic accuracy, identify Patients who are most susceptible to CLTI, and educate clinicians and patients regarding the evidence based methods of diagnosis and treatment of different stages and complications of the disease.

The target audience

The guideline is intended for all clinicians who are likely to diagnose and manage patients with CLTI, and it applies to any setting in which CLTI would be identified, monitored, or managed.

Methods

A comprehensive search for guidelines was undertaken to identify the most relevant guidelines to We recommendfor adaptation.

inclusion/exclusion criteria followed in the search and retrieval of guidelines to be adapted:

- *Selecting only evidence-based guidelines (guideline must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence)*
- *Selecting only national and/or international guidelines*
- *Specific range of dates for publication (using Guidelines published or updated 2015 and later)*
- *Selecting peer reviewed publications only*
- *Selecting guidelines written in English language*
- *Excluding guidelines written by a single author not on behalf of an organization in order to be valid and comprehensive, a guideline ideally requires multidisciplinary input*
- *Excluding guidelines published without references as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations*

The following characteristics of the retrieved guidelines were summarized in a table:

- *Developing organization/authors*
- *Date of publication, posting, and release*
- *Country/language of publication*
- *Date of posting and/or release*
- *Dates of the search used by the source guideline developers*

All retrieved Guidelines were screened and appraised using the AGREE II instrument (www.agreetrust.org) by at least two members. the panel decided on a cut-off point or ranked the guidelines (any guideline scoring above 50% on the rigor dimension was retained) . This guideline has been adapted from global vascular guidelines on the management of CLTI (2019)

Evidence assessment

According to WHO handbook for Guidelines we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed information on GRADE is available through the GRC secretariat and on the following sites:

- *GRADE working group: http://www.gradeworkingroup.org*
- *GRADE online training modules: http://cebgrade.mcmaster.ca/*
- *GRADE profile software: http://ims.cochrane.org/revman/gradepro*

Table 1 Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 2 Significance of the four levels of evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Table 3 Factors that determine How to upgrade or downgrade the quality of evidence

Downgrade in presence of	Upgrade in presence of
Study limitations -1 Serious limitations -2 Very serious limitations	Dose-response gradient +1 Evidence of a dose-response gradient
	Direction of plausible bias
Consistency -1 Important inconsistency	+1 All plausible confounders would have reduced the effect
Directness -1 Some uncertainty -2 Major uncertainty	Magnitude of the effect +1 Strong, no plausible confounders, consistent and direct evidence
Precision -1 Imprecise data	+2 Very strong, no major threats to validity and direct evidence
Reporting bias -1 High probability of reporting bias	

The strength of the recommendation

The strength of a recommendation communicates the importance of adherence to the recommendation.

Strong recommendations

With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional recommendations

These are made when there is greater uncertainty about the four factors above or if local adaptation has to account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

When not to make recommendations

When there is lack of evidence on the effectiveness of an intervention, it may be appropriate not to make a recommendation.

Recommendations

Recommendation	Strength of recommendation	Quality of evidence	References
1.Diagnosis			
1.1 Use ABI to determine the presence and to quantify the severity of ischemia in all patients with suspected CLTI	strong	Low	[1] [2] [3]
1.2 Perform a detailed history to determine symptoms, past medical history, and cardiovascular risk factors in all patients with suspected CLTI.	Good practice statement		
1.3 Perform a complete vascular physical examination of all patients with suspected CLTI, including palpation of carotid, upper extremity, aorta, and lower extremity pulses.	Good practice statement		
1.4 Perform a complete examination of both feet, including a probe-to- bone test of any open ulcers using sterile equipment, in all patients with pedal tissue loss and suspected CLTI.	Good practice statement		

1.5 We recommendDUS imaging, including assessment of Ankle Peak Systolic Velocity (APSV) as the first arterial imaging modality in patients with suspected CLTI.	Strong	Moderate	[4]
1.6 We recommendother noninvasive vascular imaging modalities (CTA, MRA) in patients with suspected CLTI who are candidates for revascularization, and who do not suffer impaired renal function.	strong	Moderate	[5] [6] [7] [8]
1.7 Obtain high-quality angiographic imaging of the lower limb using digital subtraction imaging (DSA). This should include the ankle and foot in all patients with suspected CLTI prior to proceeding to revascularization.	Good practice statement		

2. **Medical management**			
2.1 Evaluate cardiovascular risk factors in all patients with suspected CLTI.	strong	Moderate	[9]
2.2 Refer all patients with suspected CLTI to have all modifiable risk factors including hypertension, diabetes mellitus, dyslipidemia, controlled to recommended levels. Strongly advice smoking cessation.	strong	Moderate	[10], [11]
2.3 Treat all patients with CLTI with an antiplatelet agent.	strong	High	[12]
2.4 We recommendclopidogrel as the single antiplatelet agent of choice in patients with CLTI.	Conditional	Moderate	[13],[14]
2.5 We recommendlow-dose aspirin and rivaroxaban, 2.5 mg twice daily, to reduce adverse cardiovascular events and lower extremity ischemic events in patients with CLTI.	Conditional	Moderate	[15]
2.6 We recommend against usingsystemic vitamin K antagonists for the treatment of lower extremity atherosclerosis in patients with CLTI.	strong	Moderate	[15]
2.7 We recommend against usinglow molecular weight heparin for the treatment of lower extremity atherosclerosis in patients with CLTI, except if there is suspicion of acute thrombo-embolic event, or for bridging anticoagulation prior to an invasive procedure.	Good practice statement		
2.8 Use moderate- or high-intensity statin therapy to reduce all-cause and cardiovascular mortality in patients with CLTI.	strong	High	[16] [17]

			[16] [18] [19]
2.9 Use medormin as the primary hypoglycemic agent in patients with type 2 DM and CLTI.	strong	High	[20]
2.10 We recommendwithholding medormin immediately before and for 24 to 48 hours after the administration of an iodinated contrast agent for diabetic patients, especially those with an estimated glomerular filtration rate <30 mL/min/1.73 m2.	Conditional	Low	[21] [22] [23]
2.11 Prescribe analgesics of appropriate strength for CLTI patients who have ischemic rest pain of the lower extremity and foot until pain resolves after revascularization.	Good practice statement		

3. Evidence Based Revascularization (EBR)			
3.1 Refer all patients with suspected CLTI to a vascular consultant for consideration of limb salvage unless major amputation is considered medically urgent.	Good practice statement		
3.2 Offer primary amputation to patients with poor functional status (non-ambulatory), or an unsalvageable limb as judged by a qualified vascular consultant.	Good practice statement		
3.3 Use an integrated threatened limb classification system (such as WIfI) to stage all CLTI patients who are candidates for limb salvage.	strong	Low	[24] [25] [26], [27], [28]
3.4 Perform urgent surgical drainage including minor amputation, if needed, and commence antibiotic treatment in all patients with suspected CLTI who present with deep space foot infection or wet gangrene. Perform urgent revascularization before or soon after foot surgery.	Good practice statement		
3.5 Do not perform revascularization in the absence of significant ischemia (WIfI ischemia grade 0).	Good practice statement		
3.6 Do not perform revascularization based on imaging alone in the absence of tissue necrosis or gangrene.	Good practice statement		
3.7 Revascularization could be performed in the absence of significant foot ischemia in exceptional conditions such as isolated region of poor perfusion, which could be the target of	Good practice statement		

angiosome revascularization, if the isolated region of poor perfusion is associated with major tissue loss (eg, WIfI wound grade 2 or 3), and the wound deteriorates despite appropriate infection control, wound care, and offloading.			
3.7 Offer revascularization to all average-risk patients with severe ischemia and tissue necrosis or gangrene	strong	Low	[29]
3.8 We recommendrevascularization to all average-risk patients with moderate ischemia and extensive wounds or extensive tissue necrosis	Conditional	Low	[25] [26],[27], [28]
3.9 Perform ultrasound vein mapping in all CLTI patients who are candidates for surgical bypass.	strong	Low	[30], [31], [32]
3.10 Do not classify a CLTI patient as being unsuitable for revascularization without review of adequate-quality imaging studies and clinical evaluation by a qualified vascular consultant.	Good practice statement		

4.0 Combined inflow and outflow disease			
4.1 Correct inflow disease first when both inflow and outflow diseases are present in a patient with CLTI.	Good practice statement		
4.2 Base the decision for staged vs combined inflow and oudlow revascularization on patient risk and the severity of limb threat (eg, WIfI stage).	strong	Low	[30] [33]
4.3 Correct inflow disease alone in CLTI patients with multilevel disease and low-grade ischemia (eg, WIfI ischemia grade 1) or limited tissue loss (eg, WIfI wound grade 0/1) and in any circumstance in which the riskbenefit of additional oudlow reconstruction is high or initially unclear.	strong	Low	[30] [33]
4.4 Restage the limb and repeat the hemodynamic assessment after performing inflow correction in CLTI patients with inflow and oudlow disease	strong	Low	[34]
4.5 We recommendsimultaneous inflow and oudlow revascularization in CLTI patients with a high limb risk (eg, WIfI stages 3 and 4), or in patients with severe ischemia (eg, WIfI ischemia grades 2 and 3).	Conditional	Low	[35]

5.0 Aorto-iliac disease			
5.1 Use an endovascular-first approach for treatment of CLTI patients with moderate to severe aorto-iliac disease.	strong	Moderate	[36], [37], [38]

5.2 We recommendsurgical reconstruction for the treatment of average-risk CLTI patients with extensive aorto- iliac disease, or after failed endovascular intervention.	Conditional	Low	[39],[40],[41]

6.0 Common femoral artery disease			
6.1 Perform open CFA endarterectomy with patch angioplasty, with or without extension into the PFA, in CLTI patients with hemodynamically significant (>50% stenosis) disease of the common and deep femoral arteries.	strong	Low	[42],[43]
6.2 We recommenda hybrid procedure combining open CFA endarterectomy and endovascular treatment of aorto-iliac disease with concomitant CFA involvement.	Conditional	Low	[44]
6.3 We recommendendovascular treatment of significant CFA disease in selected patients who are deemed to be at high surgical risk or to have a hostile groin.	Conditional	Low	[45], [46], [47], [48]
6.4 Avoid stents in the CFA and do not place stents across the origin of a patent deep femoral artery.	Good practice statement		
6.5 Correct hemodynamically significant (>50% stenosis) disease of the proximal deep femoral artery whenever technically feasible.	Good practice statement		

7.0 endovascular vs surgical bypass			
7.1 In surgically average-risk CLTI patients with infrainguinal disease, base decisions of endovascular intervention vs open surgical bypass on the severity of limb threat (eg, WIfI), the anatomic pabern of disease, and the availability of autologous vein.	strong	Low	[49]
7.2 Offer endovascular revascularization when technically feasible for surgically high-risk patients with advanced limb threat and significant perfusion deficits (eg, WIfI ischemia grades 2 and 3).	Conditional	Low	[29],[26],[27], [28]
7.3 We recommendangiosome-guided revascularization in patients with significant wounds (eg, WIfI wound grades 3	Conditional	Low	[50],[51],[52], [53], [54]

and 4), particularly those involving the midfoot or hindfoot, and when the appropriate target arterial path is available.			
7.4 In treating femoro-popliteal (FP) disease in CLTI patients by endovascular means, We recommendadjuncts to balloon angioplasty (eg, stents, covered stents, or drug-eluting technologies) when appropriate.	Conditional	Moderate	[55], [56], [57], [58],[49]
7.5 Use autologous vein as the preferred conduit for infrainguinal bypass surgery in CLTI.	strong	Moderate	[49]
7.6 Avoid using a non-autologous conduit for infrainguinal bypass unless there is no endovascular option and no adequate autologous vein.	2(Conditional)	C (Low)	[49]
7.7 We recommendperforming intraoperative imaging (angiography, DUS, or both) on completion of open bypass surgery for CLTI and correct significant technical defects if feasible during the index operation.	strong	Low	[59], [60]

8.0 Non-revascularization treatment of the limb			
8.1 We recommend against usinglumbar sympathectomy for limb salvage in CLTI patients in whom revascularization is not possible.	Conditional	Low	[61]
8.2 We recommendintermibent pneumatic compression therapy in carefully selected patients (eg, rest pain, minor tissue loss) in whom revascularization is not possible.	Conditional	Moderate	[29]
8.3 Do not offer prostanoids for limb salvage in CLTI patients. We recommendoffering selectively for patients with rest pain or minor tissue loss and in whom revascularization is not possible.	Conditional	Moderate	[62]
8.4 Do not offer vasoactive drugs in patients in whom revascularization is not possible.	strong	Low	[63]
8.5 Do not offer hyperbaric oxygen therapy to improve limb salvage in CLTI patients with severe, uncorrected ischemia (eg, WIfI ischemia grade 2/3).	strong	Moderate	[64], [65], [66]
8.6 The patient should be provided with optimal wound care until the lower extremity wound is completely healed or the patient undergoes amputation.	Good practice statement		
8.7 Restrict use of therapeutic angiogenesis to CLTI patients who are enrolled in a registered clinical trial.	strong	Moderate	[29], [67]
9.0 The role of minor and major amputations			
9.1 We recommendtransmetatarsal amputation of the forefoot in CLTI patients who would require more than two digital ray amputations to resolve distal necrosis, especially when the hallux is involved.	Conditional	Low	[68]

9.2 Offer primary amputation to CLTI patients who have a pre-existing dysfunctional or unsalvageable limb, a poor functional status (eg, bedridden), after shared decision-making with the patient and health care team.	strong	Low	[69],[70]
9.3 We recommendsecondary amputation for patients with CLTI who have a failed or ineffective reconstruction and in whom no further revascularization is possible and who have incapacitating pain, nonhealing wounds, or uncontrolled sepsis in the affected limb after shared decision-making with the patient and health care team.	Conditional	Low	[71]
9.4 We recommendrevascularization to improve the possibility of healing an amputation at a more distal functional amputation level (eg, AKA to BKA), particularly for patients with a high likelihood of rehabilitation and continued ambulation.	Conditional	Low	[72]
9.5 We recommenda BKA or AKA in patients who are non-ambulatory for reasons other than CLTI (ie, bedridden patients with flexion contracture, dense hemiplegia, cancer) and are unlikely to undergo successful rehabilitation to ambulation after shared decision- making with the patient and health care team	Conditional	Low	[73] [74]
9.7 Patients who have undergone amputation for CLTI are instructed to seek medical advice to monitor progression of disease in the contralateral limb and to maintain optimal medical therapy and risk factor management.	strong	Low	[75] [76]
10.0 Postprocedural care and surveillance after infrainguinal revascularization for CLTI			
10.1 Continue best medical therapy for PAD, including the long-term use of antiplatelet and statin therapies, in all patients who have undergone lower extremity revascularization.	strong	High	[77], [78], [79], [80], [81]
10.2 We strongly advise smoking cessation in all CLTI patients who have undergone lower extremity revascularization.	strong	High	[82], [83]
10.3 We recommendDAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal prosthetic bypass for CLTI for a period of 6 to 24 months to maintain graft patency.	Conditional	Moderate	[79], [84], [85], [80]
10.4 We recommendDAPT (aspirin plus clopidogrel) in patients who have undergone infrainguinal endovascular interventions for CLTI for a period of at least 1 month, alternatively We recommendAspirin and Rivaroxiban 2.5mg bd.	Conditional	Low	[86], [86], [87], [88]

10.5 We recommendDAPT for a period of 1 to 6 months in patients undergoing repeated catheter based interventions, or alternatively We recommendAspirin and Rivaroxiban 2.5mg bd, if they are at low risk for bleeding.	Conditional	Low	[89], [87], [88]
10.6 Patients who have undergone lower extremity vein or prosthesis bypass for CLTI are advised to have a check up on a regular basis for at least 2 years. We recommendDUS scanning where available.	Good practice statement		
10.7 We recommendperforming additional imaging in patients with lower extremity grafts who have a decrease in ABI or a decrease in APSV or recurrence of symptoms or change in pulse status to detect vein graft stenosis.	Good practice statement		
10.8 Offer intervention for DUS- detected vein graft lesions with an associated PSV of >300 cm/s and a PSV ratio >3.5 or grafts with low velocity (mid-graft PSV <45 cm/s), which may be further documented by CTA, to maintain graft patency.	strong	Moderate	[90],138 2001
10.9 Patient is strongly advised to maintain long-term surveillance after surgical or catheter-based revision of a vein graft, including DUS graft scanning where available, to detect recurrent graft-threatening lesions.	strong	Moderate	[91], [92]
10.10 Refer for mechanical offloading as a primary component for care of all CLTI patients with plantar wounds, and for continued protection of the healed wound and the foot to include appropriate shoes, insoles, and monitoring of inflammation.	strong	High	[93]

Research Needs

1. *Assess the economic benefits of training vascular specialists in open and endovascular techniques and if this lowers the complications rate and saves money*
2. *Is open surgery a really cheaper option or the longer hospitalization and complications will make it most expensive than endovascular techniques*

Clinical indicators for monitoring

Any patient with CLTI should have the following :

1. ABI
2. Duplex ultrasound
3. CTA if revascularization is planned

Updating the guideline

To keep these recommendations up to date and ensure its validity it will be periodically updated. This will be done whenever a strong new evidence is available and necessitates updation.

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Annexes

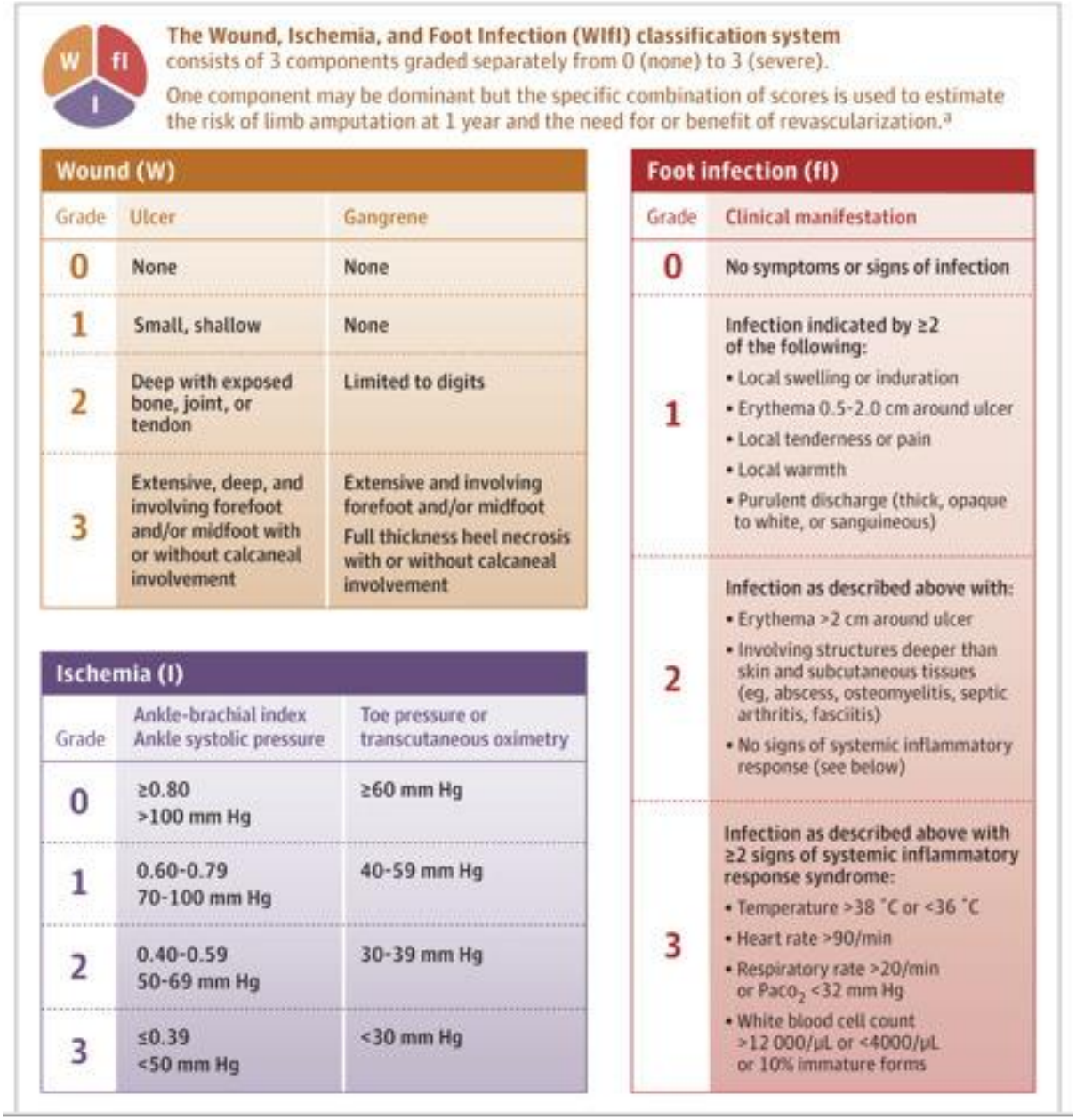

Figure from JAMA 2023 Jul 3;330 1 [94]