Best Practice Recommendations For Skin Health and Wound Management 2025

CHAPTER 10

Prevention and Management of Peripheral Arterial Ulcers

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INTRODUCTION

It is estimated that 1.5 million Canadians (older than 40 years) live with symptomatic peripheral arterial disease (PAD).[1]

The Canadian 2022 Society for Vascular Surgery discusses the importance of peripheral arterial disease prevention as it can lead to chronic limb-threatening ischemia (CLTI),[2] resulting in chronic pain, tissue breakdown (ulcers/wounds) or tissue death (gangrene), amputation and death.

This chapter provides information on the prevention and management of PAD, specifically those of the lower extremity. Historically, the main recommendations for the management of peripheral arterial ulcers have focused on two primary objectives: determining if there is adequate blood flow to promote skin health and heal the wound and assessing for signs and symptoms of PAD.[3,4]

Arterial insufficiency that affects skin health also inhibits the wound healing process as tissues are poorly perfused and the delivery of nutritional requirement and systemic antimicrobials is often compromised due to the lack of blood supply to the wound site.[5] Therefore, addressing the underlying PAD is essential when caring for patients who present with lower extremity ulcers.[5]

Prevention of PAD takes a co-ordinated, interdisciplinary team that focuses on screening for risk of atherosclerosis and generalized vascular disease.[6] Teams should work to engage patients and their care partners in managing modifiable risk factors that increase risk, such as smoking, diabetes mellitus, high blood pressure and cholesterol levels,[1] as well as certain lifestyle choices.[7] Non-modifiable factors include age and hereditary.[6] Sex and gender effects on PAD warrant further study.[2]

This chapter will also focus on the most severe form of PAD: chronic limb-threatening ischemia (CLTI). The term *CLTI* is preferred over *critical limb ischemia*, as the latter implies threshold values of impaired perfusion rather than a continuum. CLTI is a clinical syndrome defined by the presence of PAD in combination with rest pain, gangrene or a lower limb ulceration over two weeks' duration.[8] Of concern is the presence of diabetes mellitus, as it increases the incidence of PAD, accelerates disease progression and worsens patient healing and overall outcomes.[5]

Indigenous peoples in Canada face a higher rate of diabetes and complications such as foot ulcers, lower-extremity amputations and peripheral arterial disease.[9,237] In Canada, First Nations are over-represented among persons experiencing a non-traumatic lower extremity amputation.[10] In Saskatchewan, diabetes was the most prevalent factor.[11]

Development of an arterial ulcer may result in gangrene or infection that may ultimately require multiple surgeries or major amputation, which can lead to hastened mortality.[2,5] Of concern is that 15% of patients with PAD will develop CLTI.[5] All patients with suspected CLTI should be referred urgently to a vascular surgeon and an interdisciplinary team.[8] The five-year mortality rate is significant and is higher than some cancer rates.[5] Globally, CLTI is widely believed to be a growing health problem, and more research is urgently needed.[8]

Advancements in medical and wound therapies, along with the establishment of integrated, interdisciplinary wound care centres, have impacted the care of patients with CLTI and, therefore, may have also helped to decrease the overall rate of amputation.[12]

In the United States, the prevalence of PAD in men ranged from 6.5% (aged 60–69 years) to 11.6% (aged 70-79 years) to 29.4% (>80 years). There were similar age-related increases in PAD prevalence in women (5.3%, 11.5%, and 24.7% in these age categories, respectively).[13] Given that the life expectancy of women still exceeds that of men, the overall burden of PAD (total number of individuals affected) is likely to be greater in women than in men. The epidemiology of PAD is likely to be similar in other developed countries, such as the United Kingdom and European nations.[14-16] This staggering increase in PAD prevalence, along with the impact of associated comorbidities, demands a responsive approach to ensure the early detection and treatment of PAD, particularly since arterial insufficiency is identified as the

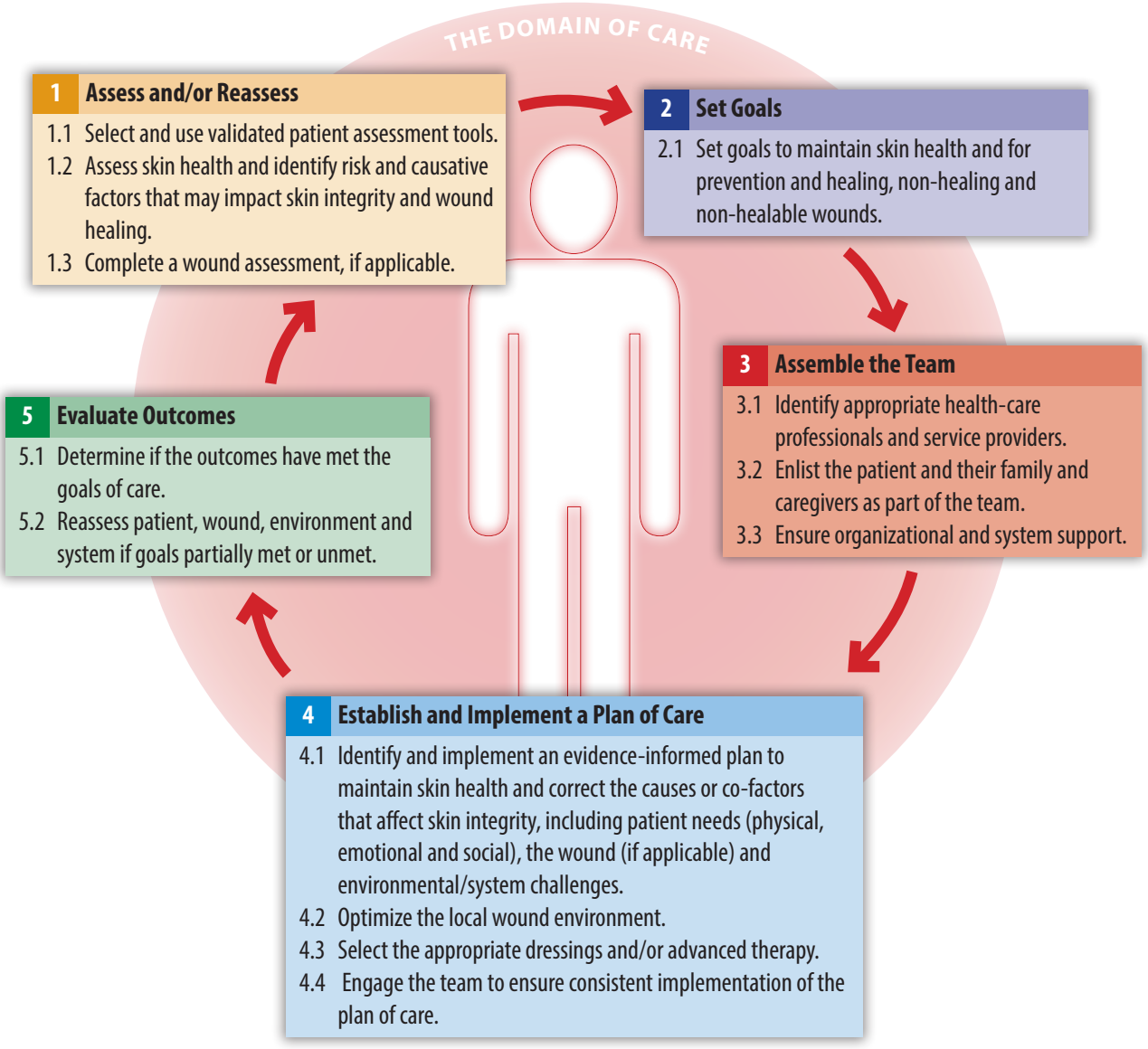
primary causative factor for arterial ulcers.[2,8] Although PAD is a chronic disease that can impact both the upper and lower extremities, it is more common in the lower limbs. Lower extremity arterial disease can also include diseases in the abdominal aorta and in the iliac arteries, which may contribute to, or result in, arterial insufficiency.[8] Of concern is that only 5%-10% of patients with PAD present with classical symptoms of intermittent claudication (IC).[17]

The European Study Group in Diabetes and the Lower Extremity (EURODALE) study, involving a cohort of 1,088 patients with diabetic foot ulcers (DFUs) from 14 different centres in Europe, reported an increase in impaired healing when PAD co-existed with diabetes mellitus (DM).[18] Patients diagnosed with both PAD and DM have been shown to be seven to 15 times more likely to experience major amputation following the development of an ulcer, as compared with those without DM.[19-21]

THE WOUND PREVENTION AND MANAGEMENT CYCLE

This chapter offers a practical, easy-to-follow guide outlining a process, or series of consecutive steps, that supports patient-centred care. This process, called the Wound Prevention and Management Cycle (See Figure 1), guides the clinician through a logical and systematic method for developing a customized plan for the prevention and management of wounds, from the initial assessment to a sustainable plan targeting self-management for the patient.

Figure 1: Wound Prevention and Management Cycle



The recommendations in this chapter are based on the best available evidence and the most current best practice guidelines available worldwide. These recommendations are intended to support members of the health-care team, including the patient and their family, in the planning and delivery of care specific to CLTI, as well as associated arterial ulcers. Two foundational chapters supplement this chapter with additional evidence-informed information and recommendations that are general to all wound types: Chapter 3: Skin: Anatomy, Physiology and Wound Healing[22] and Chapter 4: Prevention and Management of Wounds: An Overview.[23]

The three guiding principles within these BPRs that support effective prevention and management of skin breakdown are as follows:

1. The use of a logical and systematic approach, regardless of the specifics, to prevent and manage skin breakdown,
2. The constant, accurate and multidirectional flow of meaningful information with the team and across care settings, and
3. The patient as the core of all decision making.

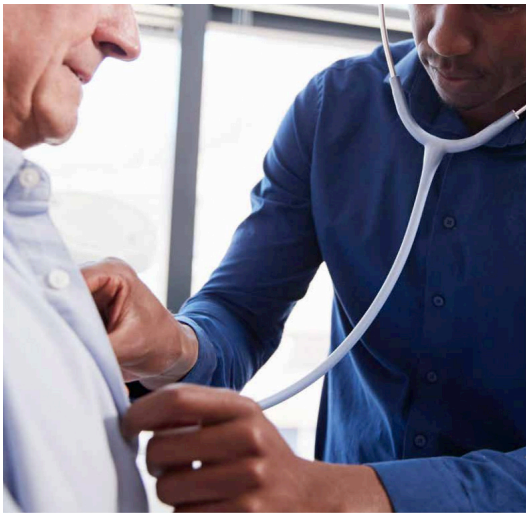
This document is written with the intent to encompass the quintuple aim for health care improvement. This is to enhance the patient care experience, reduce costs, improve population health, improve the clinician experience and enhance equity (See Table 1). This equity piece is particularly important for patients living with skin issues, wounds and, specifically, peripheral arterial ulcers. Ensuring all patients receive care, supplies and ongoing preventative strategies needs to be recognized and communicated to policy makers.[24]

Table 1: Quintuple aim and management of Peripheral Arterial Ulcers

5 components	Applied to Peripheral Arterial Ulcers
Improving population health	Through prevention, education and self-management strategies
Reducing costs	Application of best practice guidelines to ensure most effective treatment Appropriate use of resources - examples: prevention, screening, dressings, devices
Advancing health equity	Application of principles to all those at risk of being affected by peripheral arterial disease
Care team well-being	Providing clinically usable information for front line clinicians
Enhancing the care experience	Creating a process and expectation for care for all those with peripheral arterial issues

Step 1: Assess and/or Reassess

Recommendations
1.1 Select and use validated patient screening and assessment tools



Complete a comprehensive skin assessment as reviewed in Chapter 4: Preventon and Management of Wounds.[23]

According to the global vascular guidelines on the management of chronic limb-threatening ischemia it is recommended that clinicians use a lower extremity threatened limb classification staging system (e.g., Society for Vascular Surgery's (SVS) WIfI classification system that grades the complexity of wounds, including wound extent, degree of ischemia and severity of infection to guide clinical management in all patients with suspected CLTI[8] (See Table 2).

The International Working Group of the Diabetic Foot guidelines (IWGDF, 2023) also recommends use of two classification systems for diabetic foot ulcers that includes ischemic ulcers. The use of these classification systems is important to standardize assessment of ulcers and to improve communication among health-care professionals. The IWGDF recommends use of:

- SINBAD - Site, Ischaemia, Bacterial infection, Area and Depth) classification (first option)
- WIfI - Wound, Ischaemia, foot Infection) systems[25]

The WIfI classification system was developed for use during the initial patient assessment, targeting those who present with ischemic rest pain, diabetic foot ulcers, non-healing lower limb wounds and/or gangrene.[26,27] Similar to the Fontaine and Rutherford classification systems, the WIfI includes scores for varying degrees of ischemia and tissue loss; however, it also adds a score for the presence and severity of infection.[26,27] Although tissue perfusion is considered to be a primary determinant of patient outcomes, the presence and severity of infection can also increase the risk to the limb in regard to potential amputation.[27] Higher WIfI scores also indicate a diagnosis of CLTI and increased risk of lower extremity amputation[26] and survival.[28]

Other existing instruments are available but require confirmed validation. These include: Physical Examination and Chronic Lower-Extremity Ischemia, Intermittent Claudication Questionnaire (ICQ), San Diego Questionnaire, LEGS score based on TASC, Finnvasc and PAD Nomogram.[27,29-33]

Apart from the WIfI classification, the popular Edinburgh Claudication Questionnaire has a 91.3% (95% confidence interval [CI], 88.1-94.5%) sensitivity and 99.3% (95% [CI] 98.9-100%) specificity.[34] The Edinburgh Claudication Questionnaire asks patients:

1. Do you get pain or discomfort in your leg(s) when you walk?
2. Does this pain ever begin when you are standing still or sitting?
3. Do you get it if you walk uphill or hurry?
4. Do you get it when you walk at an ordinary pace on the level?
5. What happens to it if you stand still?
    a. Usually continues more than 10 minutes
    b. Usually disappears in 10 minutes or less
6. Where do you get this pain or discomfort?[2]

A new anatomic scheme for the threatened limb has been proposed by Conte et al. termed The Global Limb Anatomic Staging System (GLASS) for CLTI.[8] This new approach was developed to facilitate clinical decision-making regarding revascularization in CLTI. GLASS incorporates two novel and important concepts, the target arterial path (TAP) and estimated limb-based patency (LBP). The consensus process for developing and assigning GLASS stages was informed by an updated systematic review of revascularization outcomes in CLTI. However, what is important is to always ensure the validity and reliability of assessment tools before using them. More details on chronic limb ischemia tools and ulceration can be found in the global vascular guidelines on the management of chronic limb-threatening ischemia (pages 26S to 30S).[8] Furthermore, more research is needed to study GLASS for CLTI.[35-37]

Table 2 outlines vascular assessment tools.

Table 2: Vascular Assessment Tools*

Tool	Description	Items
Lower Extremity Threatened Limb Classification System: Risk Stratification Based on Wound, Ischemia and foot Infection (WIfI)[25,27]	• Evaluates: - Presence and extent of infection - Degree of ischemia - Tissue loss • Not meant to function as a stand-alone clinical decision-making tool • Validation currently in progress	**W: Wound/clinical** Society for Vascular Surgery (SVS) grades for rest pain and wounds/tissue loss (ulcers and gangrene): 0 (ischemic rest pain, ischemia grade 3; no ulcer), 1 (mild), 2 (moderate), 3 (severe) **I: Ischemia hemodynamics/perfusion** Measure toe pressure (TP) or transcutaneous oxygen pressure ($TcPO_2$) if ankle-brachial pressure index (ABPI) incompressible (>1.3) SVS grades 0 (none), 1 (mild), 2 (moderate) and 3 (severe) **fI: Foot Infection** SVS grades 0 (none), 1 (mild), 2 (moderate), and 3 (severe: limb and/or life-threatening) SVS adaptation of Infectious Diseases Society of America's (IDSA) and International Working Group on the Diabetic Foot's perfusion, extent/size, depth/tissue loss, infection, sensation (PEDIS) classifications of diabetic foot infection
Fontaine Classification[38]	• Identifies clinical presentation of CLTI in 4 stages • Based on clinical symptoms, without other diagnostic tests • Originally in German**	Stage I – Asymptomatic Stage Ia – Mild claudication Stage III – Moderate to severe claudication Stage III – Ischemic rest pain Stage IV – Ulceration or gangrene
Rose Questionnaire[39,40]	• Determines pain experience of patients with cardio-ischemic disease • Standardizes identification of angina to exercise, pain due to myocardial infarction and intermittent claudication • Moderate sensitivity and high specificity[41] • Validated with 2000 subjects to become WHO/Rose Questionnaire	Includes eight questions: 1. Do you get pain in either leg while walking? 2. Does pain begin when standing still or sitting? 3. Do you get this pain in your calf/calves? 4. Do you get it if you walk uphill or hurry? 5. Do you get it when you walk at an ordinary pace on the level? 6. Does it ever disappear while walking? 7. What do you do if you get it while walking? 8. What happens to the pain if you stand still?
Rutherford Classification[41,42]	• Classifies PAD into acute and CLTI • Provides definitions and criteria to standardize: - Severity of PAD - Therapeutic intervention - Outcomes • Approved by the Joint Council of the Society for Vascular Surgery and the North American Chapter of the International Society for Cardiovascular Surgery • Evidence based on other variables (concurrent, predictive and convergent validity) for each clinical symptom	Grades/Categories: • Grade 0 Category 0: Asymptomatic • Grade I Category 1: Mild claudication • Grade I Category 2: Moderate claudication • Grade I Category 3: Severe claudication • Grade II Category 4: Ischemic rest pain • Grade III Category 5: Minor tissue loss, non-healing ulcer, focal gangrene with diffuse pedal ischemia • Grade III Category 6: Major tissue loss extending above trans metatarsal level, functional foot no longer salvageable

Edinburgh Claudication Questionnaire (ECQ)[34]	Updated Rose Questionnaire with improved sensitivity while maintaining high specificity. Also available in French Tested on 300 subjects > 55 years of age. High sensitivity and specificity; high negative predictive and positive predictive value Excellent reproducibility after six months	Include six elements: 1. Pain or discomfort in the legs with walking 2. Pain on sitting or standing 3. Pain going up stairs or hurrying 4. Regular walking pain 5. Pain duration of 10 minutes or more 6. Site of pain

*The decision to employ one of the previously described measurement tools is most often based on personal preference of the specialist or vascular surgeon. There is no current literature or consensus that supports use of one over the other. Even though different vascular measurement tools have been described, they should be used cautiously, and they should never replace a thorough vascular assessment and clinical judgment.
**Clinicians should be aware that measurement tools originally created in another language must have the comparability of translated and adapted scores evaluated to confirm both validity and reliability/precision.[44-46]

Literature review used with permission from Dr. Maryse Beaumier.

A more detailed discussion of validated screening and assessment tools to assess pain, quality of life, nutrition and wound status can be found in Chapter 4: Best Practice Recommendations for the Prevention and Management of Wounds: An Overview.[23]

To support nutritional screening refer to the Canadian Malnutrition Task Force for the most appropriate screening tool based on the population being served: https://nutritioncareincanada.ca/resources-and-tools/hospital-care-inpac/screening

Wound Canada's Nutrition website has additional articles on healthy skin and wound healing: https://www.wound-scanada.ca/health-care-professional/resources-health-care-pros/nutrition

For Indigenous persons refer to Wounds Canada, Professional Guides - Nutrition and Wound Healing for Indigenous Persons for the list of nutrition screening tools:
https://www.woundscanada.ca/doclink/professional-guide-nutrition-and-wound-prevention/eyJ0eXAiOiJKV1QiLCJhbGciOiJIUzI1NiJ9.eyJzdWIiOiJwcm9mZXNzaW9uYWwtZ3VpZGUtbnV0cml0aW9uLWFuZC13b3VuZC1wcmV2ZW50aW9uIiwiaWF0IjoxNjg3MTkyODMwLCJleHAiOjE2ODcyNzkyMzB9.uDzTxlPCXzH1LrIccxmZbl2se3Ee695ZrQzb3LdSaTo

1.2 Assess skin health and identify risk and causative factors that may impact skin integrity and wound healing

The overall health status of an individual has a significant impact on skin integrity, risk for ulceration and the trajectory of wound healing. Awareness and recognition of the presence of CLTI by primary health-care providers has a significant impact on the prevention of arterial ulcers and should be emphasized both in education and in clinical practice.[8]
A national cross-sectional survey of PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program found that PAD afflicts 29% of patients who are ≥ 70 years of age, and 20–29% of those aged 50 to 69 years who report a 10-pack-per-year or more history of smoking.[26,47]

1.2.1 Patient: Physical, emotional and lifestyle

Physical Health and Vascular Status

Risk factors are conditions or diseases that increase the patient's risk of developing issues.[48] Modifiable factors are those that the patient can change and non-modifiable factors are those not under the patient's control. Table 3 lists the major modifiable and non-modifiable risk factors believed to predispose a person with CLTI and to the development of an arterial ulcer.[2,49]

Ongoing reassessment is the key to sustaining healing and optimizing patient outcomes, and to reducing costs.[50] The prevalence of lower extremity amputation is important to monitor as it is an indicator to measure the quality of care patients have received.[51,52]

Table 3: Modifiable and Non-modifiable Risk Factors

Modifiable	Non-modifiable (not under the patient's control)
Glycemic level: hyperglycemia results in delayed wound healing and compromised chemotaxis and phagocytosis[26] Concurrent diabetes and PAD have a three-fourfold increase in mortality and have a rate of amputation that is five times higher than patients without diabetes[2] **Smoking**: increases the risk of wounds through compromised blood flow and delays healing. Smoking increases the risk of PAD two-threefold as well as the risk of stroke, myocardial infarct, and cardiovascular death.[2] **Comorbidities**: Diabetes[2, 86] Dyslipidemia[8,26] Hypertension[26,86] PAD and intermittent claudication[86] Renal failure Abdominal obesity[86] Lack of physical exercise[26] Adverse health-related behaviours: excess use of alcohol and low fruit and vegetable consumption[2]	**Age**: ≥ 65 years old[2,49] **Age:** 50–64 years with risk factors for atherosclerosis (e.g., diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD[8] **Age**: <50 years, with diabetes mellitus and one additional risk factor for atherosclerosis **History**: Individuals with known atherosclerotic disease in another vascular bed (e.g., coronary, carotid, subclavian, renal, mesenteric artery stenosis or abdominal aortic aneurysm) **Family:** History of PAD[2,49]

CLTI and Smoking

The Canadian Cardiovascular Society 2022 Guidelines for Peripheral Arterial Disease indicate smoking is strongly associated with the development and progression of PAD and its complications as major adverse limb events.[2]

The relationship between smoking and PAD has been recognized since 1911, when Erb reported thatintermittent claudication (IC) was three times more common among smokers than among non-smokers.[53] Heavy smokers have a four-fold increased risk of developing IC compared with non-smokers.[53] PAD is most often diagnosed one decade earlier in smokers than in non-smokers.[53]

A strong recommendation with a moderate level of evidence made by the global vascular guidelines on the management of chronic limb-threatening ischemia is to manage all modifiable risk factors in all patients with suspected CLTI.[8,54]

Heavy smoking decreases tissue perfusion by causing peripheral vasoconstriction.[53] Smoking a cigarette decreases arterial blood supply by more than 30% in 45 minutes in specific areas of the body, especially in distal areas.[55] A recent meta-analysis demonstrated that there is now substantial evidence of the association between active smoking and the progression of CLTI.[56] The risk for CLTI is reported as lower among ex-smokers but, nonetheless, significantly increased compared with those who have never smoked.

CLTI and Diabetes Mellitus

Diabetes mellitus (DM) is the second most significant risk factor for developing CLTI and lower extremity ulcers. Up to 50% of patients with diabetes and foot ulceration have concurrent PAD, which confers a significantly elevated risk of adverse limb events and cardiovascular disease.[57]

PAD frequently coexists with peripheral neuropathy.[54] Neuropathy impairs sensory function, which can result in a lower extremity ulcer.[27,58,59] CLTI is more aggressive with DM and frequently coexists with peripheral neuropathy. Peripheral neuropathy can result in a progression of CTLI that goes undetected or is masked. Masked or undetected CTLI increases the risk for ulceration, infection and limb loss.[57]

Individuals with concurrent diabetes and PAD have a three-four fold increase in mortality and have a rate of amputation that is five times higher than patients with PAD without diabetes.[2] According to a meta-analysis of patients with diabetes, every 1% increase of HbA1c corresponds to a 26% increased risk of PAD.[60]

The Inlow 60-second Diabetic Foot Screen is a predictive tool that has since been validated for interrater and intrarater reliability, as well as predictive validity, and can be used to assess for risk factors that increase an individual's risk for ulceration and amputation.[61,62] The updated Inlow's 60-Second Diabetic Foot Screen: 2022 Risk Screening and Plan of Care tool has been augmented to include the IWGDF's classification tool to support the development of appropriate and timely care plans for individuals at risk of developing an ulcer.[63]

Inlow's 60-Second Diabetic Foot Screen: 2022 Risk Screening and Plan of Care is available at: https://www.wound-scanada.ca/doclink/inlow-60-second-diabetic-foot-screen/eyJ0eXAiOiJKV1QiLCJhbGciOiJIUzI1NiJ9.eyJzdWIiOiJpbmx-vdy02MC1zZWNvbmQtZGlhYmV0aWMtZm9vdC1zY3JlZW4iLCJpYXQiOjE2OTMzMjIwNjMsImV4cCI6MTY5MzQwOD-Q2M30.4nAHMINxT5nHQoCl15PpA1uv52fdAmgksSUiaF-oDvM

CLTI and Other Factors

Along with inquiring about diabetes mellitus and smoking, a family medical history is thought to be significant for determining other risk factors and should be obtained during the initial assessment.[2,8] A comprehensive assessment that includes assessing the patient's physical, mental and emotional health, lifestyle, environment and systems enables the health-care team to create appropriate goals and sustainable treatment plans for the prevention and management of arterial ulcers.

An assessment of arterial blood supply using an ankle-brachial pressure index (APBI), a non-invasive test, should be carried out before determining a treatment plan for a person with a lower extremity wound.[2,8,61,64] Blood flow status helps to inform the development of the most appropriate goals of care, such as wound healing, minimizing the risk of infection and preventing further injury. It is important that a clear diagnosis of CLTI be established or eliminated, particularly when other comorbidities exist that may impact the integrity of the skin and tissues of the lower extremities. The presence of PAD is also a marker for systemic atherosclerosis and early death associated with cardiac and cerebrovascular disease and is frequently associated with imminent limb loss.[57] PAD affects 20–29% of individuals over 70 years of age. Most patients do not develop gangrene or require amputations.[26,47] In high-risk coronary patients,

there is no apparent benefit of a systematic detection of asymptomatic extra-coronary atherothrombotic disease and intensified treatment over a two-year follow-up period. More research is needed.[65]

Patients diagnosed with coronary artery disease (CAD) should be screened for PAD.[26] It is recommended that patients over 70 years of age and patients over 50 years of age with atherosclerosis risk factors be screened for a history of walking impairments, claudication, ischemic rest pain and the presence of non-healing wounds on the lower extremities.[66]

Medications

In addition to an overall review of a patient's over-the-counter and prescription medications, special attention should be paid to medications known to interfere with skin health or the healing of arterial ulcers. Medications should be reviewed for continued dose-appropriateness or (temporary) discontinuation.[67-70] As part of this assessment, it is important to consider medications that are prescribed but not consumed by the patient due to costs.[1] Similarly, medications that would be indicated for routine management of CLTI, such as antiplatelet agents, should be assessed for their appropriateness in light of the patient's current health conditions.

Co-morbidities

Conditions such as anemia (iron deficiency)[71] and chronic obstructive lung disease[72] that affect overall tissue perfusion should be taken into consideration. Increased surveillance is required when diabetic neuropathy, venous insufficiency, structural deformities and mobility issues co-exist with an arterial ulcer. These common comorbidities can result in increased risk of injury, skin breakdown and infection when a patient is diagnosed with PAD. As well, assess the patient's history of COVID-19. There is a growing body of research focused on patients who had coronavirus (COVID-19) and have developed post-exertional malaise (PEM) and is similar to myalgic encephalomyelitis/chronic fatigue syndrome.[74,75]

Variations in Presentation PAD/CLTI

The clinical presentation of CLTI may vary significantly in different individuals. More than 50% of patients with PAD are asymptomatic, under-treated and under-recognized, and therefore specific screening and testing are required to diagnose PAD/CLTI.[2] Others may experience significant intermittent claudication, atypical leg pain, rest/night pain, ischemic ulcers and gangrene.[75]

Intermittent claudication affects patient quality of life and increases with age. IC pain affects the patient's calf, and less commonly the thigh and buttock, that is induced by exercise and relieved by rest.[76] Pathophysiology includes muscle ischemia during exercise caused by obstruction of the arterial flow. Symptoms can be described as mild to severe or 'unbearable' by patients.[76] Patients may be less active to avoid triggering the supply-demand mismatch that triggers IC symptoms.[77] Patients may also experience ischemic rest pain; these patients complain of, "burning pain in the soles of their feet that is worse at night."[77] Their sleep is disturbed due to pain and they often sit with their lower legs dangling over the side of the bed in, "an attempt to relieve their discomfort. The slight increase in blood flow due to gravity temporarily diminishes the otherwise intractable pain."[77]

CLTI is classified as symptomatic, asymptomatic or masked. Masked CLTI is a subgroup of asymptomatic PAD/CLTI that remains undetected as a result of the patient's physical inability to walk or the presence of any form of neuropathy that results in a decreased sensitivity to pain.[26] Both diabetic neuropathy and other neurological conditions, such as spinal stenosis, can contribute to masked PAD. Masked PAD, occurring more often in older patients, women and those with multiple comorbidities, should be distinguished from asymptomatic. An assessment of walking capacity is recommended when possible to determine masked PAD.[26]

The 2017 European Cardiovascular Society (ECS) Best Practice Guidelines report that, "While all asymptomatic patients are at risk of CV events, the subgroup with masked PAD is also at high risk of limb events."[26] This explains why an asymptomatic patient can shift rapidly to severe PAD.[26]

Chronic Limb-Threatening Ischemia (CLTI)

Conte et al. propose CLTI be defined to include a broader and more heterogeneous group of patients with varying degrees of ischemia that may delay wound healing and increase amputation risk. A diagnosis of CLTI requires objectively documented atherosclerotic PAD in association with ischemic rest pain or tissue loss (ulceration or gangrene). Ischemic rest pain is typically described as affecting the forefoot and is often made worse with recumbency while being relieved by dependency. It should be present for >two weeks and be associated with one or more abnormal hemodynamic parameters. These parameters include an ankle-brachial pressure index (ABPI) <0.4 (using higher of the dorsalis pedis [DP] and posterior tibial [PT] arteries), absolute highest AP <50 mm Hg, absolute TP <30 mm Hg, transcutaneous partial pressure of oxygen ($TcPO_2$) <30 mm Hg, and flat or minimally pulsatile pulse volume recording (PVR) waveforms (equivalent to WIfI ischemia grade 3). This definition excludes purely neuropathic, traumatic or venous ulcers lacking any ischemic component.[8]

PAD may progress to CLTI,[8] a condition characterized by chronic ischemic rest pain presenting for >two weeks, non-healing ulcers and/or gangrene in one or both lower extremities in conjunction with a clear diagnosis of PAD/CLTI.[53] The diagnosis of CLTI is based on a constellation (a coming together) of signs in lower-limb tissues that include loss of hair on the dorsum of the feet and toes; cool, shiny or dry skin; thickening of toenails; devitalized soft tissue with a dry or wet crust; atrophy of the skin and mummified or dry black toe(s).[8] Another clinical sign, revealed by performing the Buerger's test for thromboangitis obliterans (TAO), is when an elevation of the lower extremity results in pallor, but when the extremity returns to a dependent position the foot is ruborous (often called dependent rubor).[78] This rapid return of colour is called reactive hyperemia and is considered a sign of advanced CLTI.[78]

Pain in advanced CLTI is localized in the toes or the distal foot and not in the calf when the patient is supine. Relief will occur upon sitting or standing.[53] Increased capillary refill time, as well as altered or absent pulses in the lower extremity, may also be indicators of CLTI. However, capillary refill is not a reliable indicator of tissue perfusion.[79] Therefore, a validated assessment tool should be used to provide an accurate measure of peripheral blood flow. The diagnosis of CLTI should be confirmed by diagnostic vascular studies (See Table 7).[53]

Thus, persons with CLTI should always be assessed for the level of risk for amputation.[26] A low ankle-brachial pressure index (ABPI < 0.9) is one of the strongest indicators of CLTI, cardiovascular (CV) risk and associated mortality.[26] Classification systems such as the Fontaine, Rutherford and WIfI are used by clinicians to grade the level of disease, thus the risk of an eventual amputation. In addition to tissue ischemia, the presence of a wound and infection should be considered when determining amputation risk, as presented in the WIfI classification system.[25,26]

Acute Limb Ischemia

CLTI, associated with a progression of PAD/CLTI, should also be differentiated from acute limb ischemia (ALI).[53,80] The clinical presentation of ALI starts with abrupt onset of severe foot pain and the absence of peripheral pulses. Acute arterial occlusion may result from primary arterial thrombosis, arterial embolus or arterial dissection. The heart is the source of the embolus in 85% of episodes. Differentiating between thrombosis and embolic etiology can be difficult. However, a history of claudication points to thrombosis; atrial fibrillation points more to an embolic cause.

The classical 'six Ps' of ALI are strong indicators: pain, pallor, pulselessness, poikilothermia (cold), paresthesia and paresia (paralysis).[53] The presence of paresthesia and paresis favours the diagnosis of ALI, and they should not be present with CLTI. Sometimes patients with some form of symptomatic CLTI will present with acute ischemia; hence the importance of the neurological evaluation of sensation and motor deficit. Assessment by a vascular surgeon is recommended as soon as possible, as this is considered to be a vascular emergency, especially in the interest of limb preservation.[9,58] The three main categories of ALI are viable, threatened and irreversible (See Table 4).

Table 4: Acute Limb Ischemia Classifications[81]

Category	Description
Viable	• Limb not immediately threatened; no sensory loss; no muscle weakness; audible arterial and venous Doppler
Threatened	• Mild to moderate sensory or motor loss; inaudible arterial Doppler; audible venous Doppler • May be further divided into: - IIa (marginally threatened) **or** - IIb (immediately threatened)
Irreversible	• Major tissue loss or permanent nerve damage inevitable • Profound sensory loss, anesthetic • Profound muscle weakness or paralysis (rigor) • Inaudible arterial and venous Doppler

Physical Examination and the Importance of Palpation

Performing a detailed history to determine symptoms, past medical history, and cardiovascular risk factors in all patients with suspected CLTI is a good statement practice of global vascular guidelines on the management of chronic limb-threatening ischemia.[8] Physical examination of a patient with CLTI can confirm the clinical impression and help determine the severity and extent of the disease. The assessment should include a comprehensive examination of the pulses of the lower extremities, along with an inspection of both feet.[49,66]

Examination for vascular status must include palpation of all lower extremity pulses (i.e., femoral, popliteal, dorsalis pedis and posterior tibial), auscultation for abdominal and femoral bruits and inspection of the legs and feet,[8,19,53,82] although pulses can be nonspecific.[8,83]

Arterial palpation can identify a decrease in the amplitude of the pulse pressure, revealing proximal obstruction to blood flow, and can help to identify the disease location.[84,85] For example, finding a normal pulse in the femoral artery and no pulse in the popliteal artery space in a patient with calf claudication would point to a severe stenosis or occlusion of the superficial femoral artery. A decreased femoral pulse signifies aortoiliac disease.[86]

Bruit, a sound heard through a stethoscope placed over the artery, is produced by the turbulence of blood flow in a stenotic arterial segment.[87] The presence of bruit may also be found in the abdomen, indicating aortic, iliac or renal artery stenosis. The lack of bruit, however, does not exclude disease. Any doubt of occlusion or alteration of blood supply should promote further investigations.

When a wound is present, the physical examination should focus on the evaluation of arterial blood flow to determine the degree of healability of the wound site.[2,53]

Diagnostic Studies

Current clinical guidelines recommend performing a comprehensive vascular assessment of lower limbs with the ankle brachial pressure index (ABPI) in patients with a lower limb wound.[25,57,80] However, the validity of this test is known to be suboptimal in the presence of medial wall calcification of the main arteries, especially in the population with diabetes.[25,88,89]

Moreover, noncompressible arteries may affect the ABPI by providing falsely elevated or normal values in patients with diabetes, chronic renal insufficiency, or advanced age[8] leading to inconclusive, distorted results or potentially an overestimation of the actual vascular flow. Therefore, toe pressure is considered more sensitive than ABPI in diagnosing PAD.[8,90]

A strong recommendation is to also measure toe pressure and toe brachial index in all patients with suspected CLTI and tissue loss.[91-93]

Additional diagnostic tests used to screen for and confirm PAD/CLTI include: duplex ultrasound (DUS), pulse volume recording (PVR), transcutaneous oxygen tension ($TcPO_2$), continuous-wave and leg segmental pressure measurements, computed tomography angiography (CTA), magnetic resonance angiography (MRA) and conventional angiography.[26,53,66,94] Some of these investigative methods can also provide valuable information regarding the location, characteristics and severity of occlusive lesions in arterial vessels as a result of CLTI (See Table 5).

Table 5: Diagnostic Tests for Investigating PAD/CTLI

Diagnostic Test	Indications	Contraindications and Limitations	Benefits
Ankle Brachial Pressure Index (ABPI)	First-line test for the screening and diagnosis of PAD/CLTI[26,66,95] May be the only test required to help establish a diagnosis of disease [8,49,53,96] Useful to screen for asymptomatic PAD so that appropriate cardiovascular (CV) prevention strategies can be initiated[66] Useful for surveillance of lower extremity arterial disease after revascularization[26]	Primary limitation is the presence of non-compressible vessels (calcification of the distal arteries in the lower extremities as a result of diabetes),[53,88,90] which may be indicated by an ABPI measure > 1.4026 Requires appropriate diagnostic equipment to be available[26] A trained sonographer is recommended/preferred[26] Use of automated blood pressure (BP) cuffs is **not** recommended[26] Sensitivity is lower in individuals with diabetes	Non-invasive Inexpensive Can be performed resting or with treadmill exercise A strong marker for the presence of CV risk and generalized atherosclerosis[26,96] A two-threefold increase in CV-related death is associated with an ABPI < 0.90[26] Preliminary diagnosis can be made with measures obtained manually with a well-trained clinician[26] but should be interpreted with caution and in the context of a full clinical picture[79]
Ankle Brachial Pressure Index (ABPI) with treadmill exercise	Useful to repeat testing if a normal ABPI measure is obtained with existing IC[26] Performed to rule out asymptomatic or masked PAD[26,66] Useful in differentiating arterial claudication from non-arterial claudication (pseudo-claudication) comparing pre- and post-test measures[66] Useful to detect a proximal lesion on the aorta or iliac artery that contributes to a normal resting ABPI measurement[66]	Requires access to a treadmill in addition to other routine equipment Physical/functional limitations may be a barrier	Better screening for individuals with ABPI measures of 0.91 to 1.30, not exhibiting symptoms of IC, who could be at risk for PAD[8] Useful in assessing functional limitations associated with PAD, and to determine safe parameters for an exercise program[66]

Toe-Brachial Pressure Index (TBPI)	Used when non- compressible vessels exist (calcification of vessels resulting from diabetes)[26] Used to diagnose patients with suspected PAD/CLTI when ABPI >1.40[26,49,80,97-99] Used with normal or borderline ABPI measures when there is the presence of non-healing wounds or gangrene[26] Used to diagnose CLTI[2,8]	Requires appropriate diagnostic equipment to be available[26] A trained sonographer/ technician is recommended[26]	Non-invasive Inexpensive Useful to support the prescribing of compression for cases when significant edema and/or non-compressible vessels hinder reliable ABPI measures Sensitivity and specificity are better than ABPI for patients with diabetes[21,53,90]
Computed Tomography Angiography (CTA)	Can determine the location, characteristics and severity of occlusive lesions in the lower extremities[100] Generally reserved as part of the investigative process when revascularization is being considered[66] Used for patients warranting invasive intervention, such as percutaneous transluminal angioplasty (PTA) or vascular surgery	Requires the administration of nephrotoxic, iodinated contrast medium[8,66] Patients with renal failure, diabetes or dehydration are at risk for contrast- induced renal failure, so caution is warranted[8,66] Image quality may be obscured by the presence of arterial calcification or metallic implants[8] Past or suspected sensitivities to contrast medium should be investigated, along with a review of renal function, prior to test[66]	Can produce a high resolution 3-D visualization of cross sections of vessel lumens, allowing for an accurate determination of vessel diameter and stenosis severity[8] Can be used with end-stage renal patients on dialysis[8] Recommended for optimizing revascularization strategy[66]

Ankle-Brachial Pressure Index (ABPI)

For a detailed description of ABPI and instructions for performing this test, see How-to-Conduct an ABPI.[101] https://www.woundscanada.ca/about-us/68-healthcare-professional/issues/360-2019-vol-17-no-1

For an in-depth discussion of the science underlying the ABPI test, and information about when to use this test, see The Science Behind ABPI.[102]

Health-care professionals should keep in mind that CLTI may affect each of the three primary arterial vessels of the lower extremity in varying degrees. Recent studies show the importance of calculating the ABPI using measures taken from two arteries of each foot.[83] The arterial flow in the foot can be divided into six individual regions, called angiosomes.[103] Recent literature provides some evidence that the specific location of a foot ulcer should be taken into consideration and may provide guidance for vascular and plastic surgery decisions.[83] See Table 6 for interpretation of blood flow and perfusion measures.

Toe-Brachial Pressure Index (TBPI)

A toe-brachial pressure index (TBPI) measure can be obtained similarly to an ABPI. A small, toe-sized cuff is applied, usually to the great toe, instead of the ankle. The availability of the toe cuff is essential. In the case of incompressible arteries, often the result of vessel calcification secondary to DM, a TBPI is a suitable, non-invasive examination that provides an objective indication of distal lower limb vascularization.[104-106]

According to the 2016 American Heart Association (ASA)/American College of Cardiology (ACC) Guideline on the Management of Patients with Lower Extremity Peripheral Artery Disease,[106] when there is possibility of falsely elevated ABPI scores, TBPI with waveforms, along with other appropriate vascular examinations, such as PVR or TcPO2, should be employed to ensure more accurate measures of arterial blood flow.[53,88,107,108]

Arteries in the first digit are narrower and therefore less prone to calcification that may result in false-positive (falsely elevated) measures.[104,105] Current guidelines for PAD/CLTI screening recommend the use of toe pressure with a threshold value <0.70 mmHg to indicate the presence of PAD/CLTI.[21,53]

Obtaining a Transcutaneous Oxygen Tension ($TcPO_2$) Measure

$TcPO_2$ measures are obtained through the use of a transcutaneous oximetry device. The diagnostic test provides information about the supply and delivery of oxygen to the underlying microvascular circulatory system by recording the partial pressure of oxygen at the skin surface.[110] A $TcPO_2$ value of <40 mmHg (at normobaric air) suggests hypoxia sufficient to impair or prevent wound healing (in patients with and without diabetes).[111] Suggested thresholds for arterial wound healing range from 25 to 40 mmHg.[53,111-113]

Table 6: Assessing Arterial Flow and Perfusion

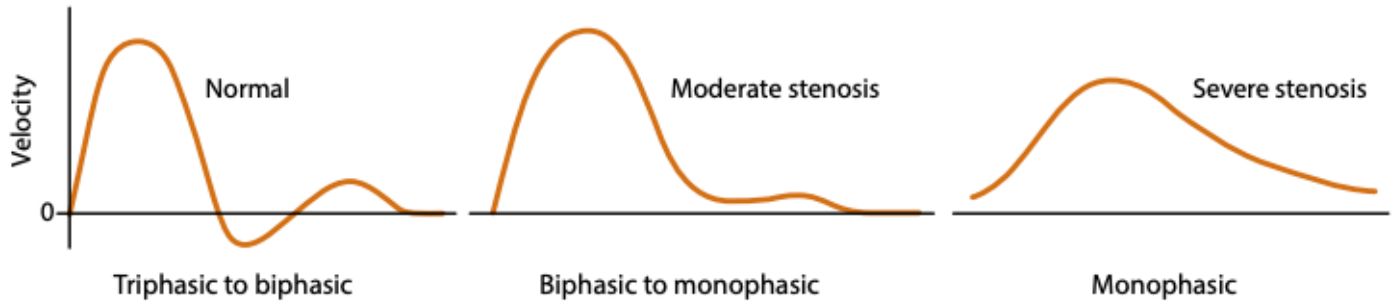
Grade	Ankle-Brachial Pressure Index	Toe Brachial Index	Toe Pressure	Waveforms	Transcutaneous Oxygen Pressure (indicating perfusion)
Non compressible	>1.40 Be aware of possible falsely elevated measures	Preferred when vessels are non-compressible	Preferred when vessels are non-compressible		Preferred when vessels are non- compressible or when localized perfusion may be altered due to previous insult (trauma or surgical repair)
Normal Range	1.0–1.40	>0.7	>70 mmHg	Triphasic	>40 mmHg
Borderline	0.91–0.99	>0.6	>70 mmHg	Biphasic/ monophasic	>40 mmHg
Abnormal: Mild Moderate Severe	<0.90	<0.6	<70 mmHg	Biphasic/ monophasic	<40 mmHg
	0.7–0.9	>0.4	>50 mmHg	Biphasic/ monophasic	30–39 mmHg
	0.41–0.69	>0.2	>30 mmHg	Biphasic/ monophasic	20–29 mmHg
	<0.4 critical limb ischemia (CLI/ CLTI)	<0.2	<30 mmHg	Monophasic	<20 mmHg

Figures 2, 3, 4: Systolic Pressure Measurements for Brachial, Posterior and Posterior Tibial Arteries for Calculating ABPI

Figure 2: Brachial artery	
Figure 3: Left dorsalis pedis artery	
Figure 4: Left posterior tibial artery	

Used with permission from Maryse Beaumier.

Figure 5: Waveforms[109]



Obtaining Continuous-wave and Leg Segmental Pressure Measurements

Obtaining leg segmental limb pressure (CLP) measurements involves a more in-depth process and the availability of appropriate equipment.[114] This diagnostic test requires considerably more time to prepare the patient than a traditional ABPI because it involves the application of inflatable cuffs at multiple levels. Mobility issues and obesity can be hindrances to performing this diagnostic test.

CTA and MRA

Computed tomographic angiography (CTA), magnetic resonance angiography (MRA) and contrast angiography are other diagnostic methods used to determine the location and severity of occlusive lesions in the lower extremities when CLTI exists. CTA examines cross sections of the vessel lumen, allowing for visualization of structures such as vessel diameter and stenosis severity, as well as any existing lesions. The image quality may be obscured by the presence of arterial calcification or metallic implants.

CTA allows a global evaluation of the arterial tree to determine the severity and location of arterial lesions. This information is useful in choosing the revascularization approach—either endovascular, open or hybrid surgery. CTA is often used to intervene in the arteries with balloons and stents. Patients should be screened with appropriate blood work for renal insufficiencies before the CTA is performed.[26] It is generally recommended that patients who have end-stage renal failure have the CTA performed prior to their scheduled dialysis.[26]

MRA requires longer acquisition time and a non-claustrophobic patient. All metal implants such as pacemakers or cerebral clips are contraindication to its use. Finally, a contrast agent in the form of gadolinium must be used. Severe renal insufficiency prevents its use because of the risk of nephrogenic systemic fibrosis.[115]

Conventional Angiography for Diagnostic Purposes

Conventional angiography, a more invasive approach to investigation, provides a comprehensive look at the arterial anatomy through the introduction of a contrast medium (dye) into the arterial system. Contrast angiography is reserved as part of the investigative process for when a patient with PAD is being considered for revascularization.[66] Contrast angiography is used for patients warranting invasive intervention such as percutaneous transluminal angioplasty (PTA) or vascular surgery. Clinicians should be wary of complications related to technique (puncture site hematoma, false aneurysm).

Pain Assessment

Managing pain is a priority for patients with CLTI who are experiencing intermittent claudication , rest pain and/or local wound pain. Therefore, a patient's pain experience should be thoroughly assessed as an essential aspect of the plan of care. Pain assessment requires the use of validated measurement tools, such as the FACES, visual analogue and numerical rating scales.[19] The experience of pain is just one aspect of the differential diagnosis of PAD/CLTI and should be distinguished from other expressions of pain related to other pathologies, such as venous disease and muscular or other neurological conditions.[49,86]

Factors other than ischemic pain and IC may be contributing to the patient's overall pain experience and must be carefully considered and differentiated. For individuals who are likely experiencing IC, the six-minute walk test closely correlates to real-life outdoor walking capacity and quality of life.[116] The distance that the patient can walk in a six-minute period is recorded. As the symptoms of IC decrease, the distance that the patient can walk over the six minutes should increase. Another useful measurement tool is graduated maximal treadmill testing, which records the onset of IC during peak walking times.

Phantom Limb Pain (PLP)

PLP affects up to 80–90% of patients with amputations.[117,118] This type of pain feels like it's coming from a body part that is no longer there, often as a result of surgical amputation secondary to CLTI. In the past it was often thought that this common post-amputation phenomenon was primarily psychological in nature; however, pain experts now recognize that these real sensations originate in the spinal cord and brain.[119]

A characteristic of PLP includes onset within the first few days of amputation, which often affects the part of the limb farthest from the body, such as an amputated foot or leg. PLP may come and go and is often described as shooting, stabbing, boring, squeezing, throbbing and/or burning. PLP may be triggered by pressure on the remaining part of the limb or emotional stress. Finding an effective way to manage PLP can be challenging.[120]

Feet and Footwear Assessment

A thorough assessment of the general condition of the skin and nails of the lower extremities can provide valuable insight into the overall risk level of the patient, particularly when altered skin integrity already exists. Clinicians should look for cool, shiny, dry skin; colour changes (pale, bluish or dark reddish); loss of hair on feet and legs; thickening and brittleness of the toenails; open sores; skin infections or ulcers that will not heal. Clinicians should assess the type(s) of footwear and socks worn for all seasons and multiple uses (employment, leisure, activity, sport).[121]

It is also important to carry out an assessment of the patient's ability to perform foot-related self-care or in partnership with the care partner.[122] For more patient-focused information, please see Wounds Canada's Do It Yourself (DIY) Skin Health Series: Arterial and Leg Ulcers: https://www.woundscanada.ca/patient-or-caregiver/resources/diy-series

As part of integrated team activities, the type and fit of footwear or other custom fabricated orthoses and footwear (orthopedic devices) should be assessed, as they may be a potential source of external pressure and contribute to tissue damage.[66] Burns et al. studied the role of custom foot orthoses in persons with PAD. They report reduction in plantar pressures when compared to 'sham' orthoses[123] (See the Pressure section following for more on pressure and PAD). Clinicians should also assess the ability of the patient to purchase and wear appropriate footwear and receive regular foot care.[53]

Pressure

Patients with PAD/CLTI are at high risk for skin breakdown as a result of poor tissue perfusion. Because of this, pressure over boney prominences on the lower extremities places them at risk for pressure injury and trauma from external forces (See Figure 6). The presence of peripheral neuropathy, with associated loss of protective sensation and/or foot deformity, may further increase the risk for pressure injury.[53,54,124] If there is significant arterial insufficiency, injuries may be unable to heal, potentially leading to infection, CLTI and amputation.

Therefore, it is recommended that a person with CTLI be assessed for level of risk for pressure injury.[80] The Braden Scale for Predicting Pressure Ulcer Risk is one example of a commonly used validated assessment tool for predicting the risk of pressure injury.[125] A 2015 review, Pressure Ulcer Programme of Research (PURPOSE), specified three primary risk factor domains relative to pressure injury risk. These domains were identified as mobility/activity, skin/pressure injury status and tissue perfusion.[126,127]

Quality of Life and Activities of Daily Living

Inquiring about the activities of daily living (ADLs) and instrumental (ADLs), including occupational and leisure tasks, and daily walking patterns provides an indication of a person's overall physical ability and may help to proactively identify potential risk for skin injury. The degree to which a person can participate in everyday activities can impact considerably on their overall sense of health-related quality of life (HRQoL).[94,128] There are several quality-of-life questionnaires available to assess HRQoL, including the Medical Outcomes Study Short-Form 36 General Health Survey.[129,130]

Researchers are working toward developing a quality-of-life tool specific to persons living with PAD titled: Quality of Life Questionnaire for Patients with Peripheral Artery Disease (QOLPAD). Early findings report that the QOLPAD is internally consistent and valid for patients receiving PAD treatment in Germany.[131]

For additional information on QOL tools see Chapter 4: Prevention and Management of Wounds: An Overview.[23]

Figure 6: 63-year-old man, living with type 2 diabetes for 20 years, non-smoker. Ischemic wound created by pressure from work boot; deep tissue infection in progress.

Used with permission from Maryse Beaumier.

1.2.2 Environmental: Socio-economic, care setting, potential for self-management

The socio-economic status of a patient may significantly impact their ability to participate in a treatment plan that has been designed to optimize their sense of wellness and prevent and manage arterial ulcers. A patient's access to items and services to meet needs, their support systems and their educational level (literacy) should be considered when assessing their capacity for self-care and their ability to participate in a plan of care.

Financial concerns, or out-of-pocket expenditures, may restrict the person's ability to take time off from work for medical appointments and to purchase dressing supplies or prescribed medical devices[132] and medications.[1] Poor psychosocial status may be associated with mental health illness, poor well-being, living alone, alcohol or substance use, history of trauma, poor hygiene or malnutrition. All of these factors have been found to be associated with an increased risk of developing an arterial ulcer and should be assessed.[8,53] Current guidelines also recommend that patients with PAD/CLTI be assessed for symptoms of anxiety, depression and hopelessness.[80,133]

1.2.3 Systems: Health-care support and communication

PAD/CLTI is a lifelong medical condition, often requiring surgical intervention and an interdisciplinary team approach.[26,86] Patients suspected of having PAD/CLTI, in conjunction with the presence of a lower extremity ulcer, should be promptly referred to a vascular and wound healing specialists.[8,134,135]

Patients with PAD/CLTI have shortened life expectancies because of severe atherosclerotic disease leading to cardiovascular events and mortality. The five-year survival rate in non-diabetic patients with significant PAD/CTLI is 70%. Patients with both CLTI and renal failure have a two-year survival rate of <50%.[53]

Ensuring that the appropriate interprofessional teams, community-based support services and resources are accessible may be critical to the overall success of a plan of care designed to prevent and manage vascular disease.[8]

1.3 Complete a wound assessment, if applicable

Because arterial ulcers can be the result of multiple disease processes occurring at the same time, clinicians should holistically evaluate the patient, identifying all the underlying and potential external causes (such as trauma) of the tissue damage.[8] An essential aspect of the assessment of an arterial ulcer is the etiology of the wound.[80] It is recommended that wound assessment and local wound care begin with identifying the etiology of the ulcer and minimizing or correcting any other co-factors or conditions that exist.[8]

The assessment of an arterial ulcer should include the location, shape, size, tissue type, presence and nature of wound exudate, presence of malodour, periwound tissue characteristics and wound pain.[80]

Validated assessment tools should be used to measure and describe the characteristics of the local wound environment and surrounding tissues and to determine whether wound healing is taking place. See Chapter 4: Prevention and Management of Wounds: An Overview.[23]

Characteristics of an arterial (ischemic) ulcer include the following:

- Often on the lower extremities; less frequently on the upper extremities, but can occur
- 'Punched out' appearance with well-defined borders (See Figure 7)
- Often associated with little or no exudate or periwound edema
- Often deep, with possible exposure to tendon and/or bone
- Often has yellow slough or black eschar, with minimal or no granulation
- Often associated with moderate to severe pain (See, Figure 8)
- Ischemic regions may appear as dry gangrene (See, Figure 9)
- Periwound tissues may be pale, shiny, dry, with loss of hair and dystrophic nails
- Often appear over boney prominences or other areas being traumatized by external pressures (footwear, pressure, trauma) (See example, Figure 9).

Figure 7: Large, dry arterial ulcer (eschar) on the lower leg of a male, smokes heavily, without diabetes	
Figure 8: 51-year-old female with diabetes, smokes heavily, ischemic pain, TBPI: 20 mmHg	
Figure 9: 57-year-old male with type 2 diabetes with sensitive neuropathy, waiting for revascularization	

Figures 7–9 used with permission from Maryse Beaumier.

After completing a thorough assessment of the local wound site, clinicians should determine the risk of complications, including infection and amputation.

Assessment for Risk of Infection

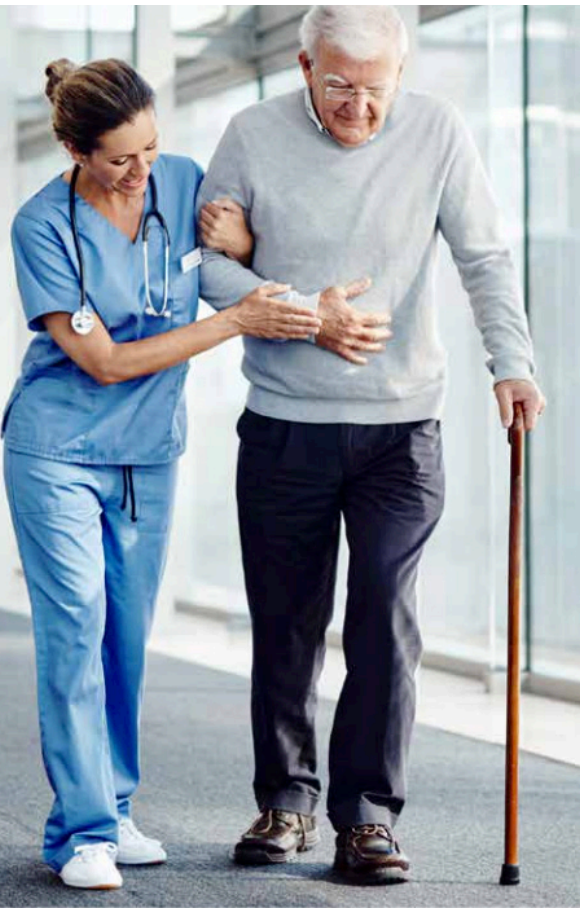
Wound infection is the most common complication of non-healing wounds.[136] Poor arterial blood supply to a wound site, along with the effects of other comorbidities that impact overall tissue perfusion, will contribute to poor resistance to wound infection.[136] Vigilant monitoring of arterial ulcers during the healing process is recommended because inadequate blood flow can suppress signs and symptoms of wound infection and impede the body's ability to fight the infecting pathogens.[136] A clinical diagnosis of wound infection should be determined only after careful consideration of several factors. Assessment should begin with a comprehensive physical exam, followed by a careful assessment of the wound site.

Severe arterial insufficiency inhibits the normal wound healing process because tissues are poorly perfused and the delivery of nutrition and systemic antimicrobials may be less effective due the lack of blood supply to the wound.[8] Inadequate local vascular supply leading to poor tissue oxygenation can favour microbial proliferation, increase the risk of infection and reduce the likelihood of healing.[136] These wounds can appear either with an eschar corresponding to a dry and black skin necrosis or with a heavily exudating and colonized gangrenous stage.

Tips for Obtaining Wound Culture Specimens: Wounds Canada's Chapter 4: Best Practice Recommendations for the Prevention and Management of Wounds: An Overview.[23]

A clinical diagnosis of wound infection is sometimes made based upon clinical signs, patient-reported symptoms and good clinical judgement.[136] However, a more definitive diagnosis of infection can be made with the support of microbiology testing (culture and sensitivity) and blood specimens. Although antimicrobials are sometimes prescribed based on a clinical diagnosis, culture-specific directed care is the preferred approach, because it can identify specific pathogens that may be causing the infection, along with sensitivity guidelines for prescribing specific antimicrobials.

Poor blood flow may suppress inflammatory signs of infection,[137] including erythema, heat and induration.[137] Therefore, a high degree of suspicion may be warranted for PAD/CLTI-related wounds. For detailed information on how to manage PAD-related wound infections, clinicians are referred to the current IDSA guidelines.[137]



Step 2: Set Goals

Recommendations

2.1 Set goals to maintain skin health and for prevention and healing, non-healing and non-healable wounds

Following a comprehensive assessment of the patient, their wound, environment and systems factors, goals for prevention and management can be determined in a collaborative process carried out between the health-care team, the patient and their care partners. Patient-driven goals should be developed based on SMART (specific, measurable, attainable, relevant, timely) principles.[23]

Health-care professionals need to consider the patient's goals, such as: Is the patient's primary goal to close the ulcer? Is it to manage pain? Is it to be able to walk as far as the bathroom? An important aspect of the early stages of treatment is establishing realistic, achievable goals that are mutually understood and agreed upon by the clinicians and the patient.

2.1.1 Identify goals based on prevention or healability

For individuals with PAD/CLTI, goals should be centred around preventing all skin breakdown and the development of wounds.

For individuals with existing wounds, goals should be developed that reflect their healability based on the assessments undertaken by the team (see above). Arterial wounds fall into several healability categories, based in part on tissue perfusion, that can guide realistic goal setting.[21,53,57,138,139] Healability may change over time post-vasculatization. Table 7 identifies examples of goals based on perfusion status.

Adequate perfusion indicates that there is sufficient blood flow to the limb to support tissue viability and wound healing.

2.1.2 Identify quality-of-life and symptom-control goals

Generally, the primary patient-centred goals in the treatment of CLTI are usually to alleviate pain, prevent amputation and improve patient HRQoL, including the healing of any existing arterial ulcers (See Table 8). Patients will often prioritize symptom management, such as alleviating pain, when determining treatment goals. However, health-care professionals should encourage patients to identify HRQoL priorities as well. A decrease in overall sense of wellbeing and HRQoL is often associated with the experience of intermittent claudication, rest/night pain and decreased mobility.[140,141] In patients with pure arterial ulcers, some of the pain may be associated with the ulcer; however, most pain is associated with ischemia. Pain associated with the arterial wound, intermittent claudication and/or ischemia may contribute to patients becoming sedentary.[16]

Table 7: Patient Goal Setting Based on Perfusion

PAD/CLTI Status	Perfusion	Examples of SMART Goals
Borderline*	Adequate	Wound closure within 12 weeks following revascularization Satisfaction with local wound care with every dressing change[142,143] Pain management regimen implemented within 12 hours[2,8,26] Appointment with a vascular surgeon as soon as possible[2,8,26,49,66] Prevention strategies implemented immediately in relation to wound infection[136] Prevent new trauma and pressure injury[2,49,80,66,86]
Post Re-Vascularization	Adequate	Wound closure within 12 weeks following revascularization Pain management regimen implemented within 12 hours[2,8,26] Appointment with a vascular surgeon in accordance with surveillance protocols; potential re-stenosis monitored as per protocol[2,8,26,49,66] Prevention strategies implemented in relation to wound infection[136] Prevention of new trauma and pressure injury[2,49,66,80,86]
Post Re-Vasculari-zation (re-stenosis)	Inadequate	Pain management regimen implemented within 12 hours[2,8,26] Vascular appointment for reassessment (surveillance) and pending revascularization[2,8,26,49,66] Prevention strategies implemented in relation to wound infection[136] Prevention of new trauma and pressure injury[2,49,66,80,86] Satisfaction with local wound care with every dressing change[142,143]
Pending revascularization	Inadequate	Timely and successful revascularization to optimize blood flow[2,8,26,49,66] Prevention strategies implemented in relation to wound infection[136] Prevention of new trauma and pressure injury[2,49,66,80,86] Satisfaction with local wound care with every dressing change[142,143] Ischemic pain controlled in conjunction with primary health-care provider[66]
Not a candidate for revascularization	Inadequate	Wound care appropriate for a non-healing wound initiated immediately[26] Prevention strategies implemented in relation to wound infection[136] Prevention of new trauma and pressure injury[2,49,66,80,86] Satisfaction with local wound care with every dressing change[142,143] Optimization of management of ischemic pain in conjunction with primary health-care provider[66]
Un-determined		Timely vascular assessment[8,26,49,66] Satisfaction with local wound care with every dressing change[142,143] Prevention strategies implemented in relation to wound infection[136] Prevention of new trauma and pressure injury[2,49,66,80,86] Ischemic pain controlled in conjunction with primary health-care provider[2,8,26]

*Borderline would refer to a patient with just enough blood flow for healing; this assessment is difficult to make and should be part of the expert opinion regarding adequate perfusion to heal even though circulation may not be within optimal ranges.

Table 8: Health-related Quality of Life and Symptom-control Goals

Patient Concern	Examples of SMART Goals
Comorbid Conditions	Based on the Canadian Cardiovascular Society 2021 dyslipidemia guidelines[145] • if TG ≤1.5 mmol/L: LDL-C <1.8 mmol/L • if TG >1.5 mmol/L: ApoB <0.7 g/L or non-HDL-C <2.4 mmol/L on maximally tolerated statin dose. Manage lipids, blood pressure and cholesterol to target levels.[2]
Rest and walking pain	• Pain decreased to 1/10–2/10 at rest within one-two weeks. • Taking anticoagulant medication as prescribed within one-two weeks. • Taking maximally tolerated statin as prescribed within one-two weeks to improve walking distance. • Keeping legs in a dependent position (below heart level) as much as possible
Activities of daily living	• Walking 10–15 minutes longer before experiencing PAD claudication symptoms within three - six months of initiating a tailored exercise program • Participating in supervised exercise at a level recommended by a health-care professional within three months • Patients should be instructed to avoid long periods with the hip or knee bent (e.g., gardening). They need to move about every 30 minutes to avoid a thrombosis of the vessel or the graft • Maintaining a healthy diet to support glucose levels that are stable and within the target range and support appropriate body mass index (BMI) and healthy skin within three-four months[144]
Emotional, cognitive, behavioural, mental health factors	• Participating in a smoking cessation program to reduce cigarette consumption to less than one pack a week within three months • Engaging in self-care activities and adhering to a plan of care aimed at prevention and management of ulceration and amputation within one-two months
Infection prevention	• Participating in activities to maintain healthy feet, including not walking in bare feet, daily foot inspections and skin care immediately after assessment with a multidisciplinary team or foot specialist • Regular professional foot care every four-six weeks • Footwear fitted by a qualified health-care professional immediately following the closure of a foot ulcer plus planned follow-up • Follow-up with primary care provider at first sign of ulceration or foot infection • Acquisition of knowledge of signs and symptoms of infection and complications and changes that may be affecting blood flow to the lower extremities • Keeping feet clean and dry; no soaking of feet

Step 3: Assemble the Team

Discussion: Preventing and managing arterial ulcers requires the input of many health-care professionals and service providers. The patient and their care partners are essential members of the integrated team.[2,8]

Recommendations
3.1 Identify appropriate health-care professionals and service providers

Patients with, or at risk for, arterial ulcers have specific concerns and risks that require a team of health-care professionals and supportive services that can work collaboratively with each other, the patient and their care partners.

These team members might include a family physician, vascular surgeon or specialist, orthopedic surgeon, plastic s urgeon, internal medicine specialist, risk reduction and modification specialist (internal medicine physician with a specialty in vascular medicine), infectious disease specialist, nurses specialized in wound and foot care, nurse practitioners, physical therapist, occupational therapist, diabetes educator, pharmacist, dietitian, pedorthist, orthotist, prosthetist, podiatrist or chiropodist, pain management specialist, psychologist, social worker and spiritual care eaders.

See Table 9 for a description of the role each team member plays.

Table 9: Potential Professional Members of the Integrated Team

Team Member	Indication for Referral
Vascular surgeon or specialist	Manage symptoms and reduce risk of ulceration, infection, CLTI and amputation in patients diagnosed with or suspected of having arterial insufficiency[2,8,26]
Hyperbaric medicine specialist	May assist in measurement of localized ischemia via $TcPO_2$ in some cases[135,146147]
Orthopedic surgeon	Support complex surgical interventions resulting from amputation, remodeling/ reconstruction when extensive tissue loss results from CLTI
Plastic surgeon	Consulted when surgical skin flaps and grafts are required post amputation or there is significant debridement of revascularized tissue
Internal medicine specialist and risk-reduction and modification specialists	Consulted regarding the assessment and optimization of systemic comorbidities such as smoking status, lipid lowering, blood glucose, activity and hypertension[2]
Infectious disease specialist	Chronic infection secondary to CLTI may result in acute cellulitis, gangrene and chronic and acute osteomyelitis. Timely consultation with a specialist who has expertise in empirical and culture-specific antimicrobial treatment can support the healing of arterial ulcers[136]
Nurse with specialized wound and foot education	Provide specific clinical and educational support pertinent to the co-ordination of complex plans of care when multidisciplinary efforts are required; pain assessment, wound care planning Provide preventative and maintenance foot care
Physical therapist (PT)	Conservative treatment strategies may include exercise programs aimed at improving symptoms of intermittent claudication[86] Reconditioning and training programs are often required following a surgical amputation associated with CLTI, especially when prosthetics have been prescribed Nonpharmacological treatment of pain Safe exercise intervention to prevent tissue trauma
Occupational therapist (OT)	Pressure risk assessment and pressure redistribution and protection of areas at risk for tissue trauma Activity modification/aides Rehabilitation pertaining to a patient's employment, employability, social and activities of daily living
Diabetes educator, pharmacist, registered dietitian	Assist in identifying and optimizing co-factors such as smoking, hypertension, glycemic control and obesity[80] Assist in appropriate calculations for renal dosing Assist in identifying and managing drug-drug and drug-disease interactions

Pedorthist, orthotist or prosthetist	Manage intrinsic pressure associated with existing foot deformities or extrinsic pressure associated with inappropriate footwear or other mechanical devices[80] In cases where the amputation of a foot or lower limb has occurred, the patient may be a candidate for a prosthetic to aid in ambulation and/or transfers. The risk of falls and other mobility-related injuries should always be taken into consideration. Collaboration with an OT/PT may be beneficial
Physiatrist	Focus on prevention, diagnosis, evaluation, treatment and rehabilitation of the whole person, specifically improving patient functioning through medical and rehabilitation assessment and interventions in partnership with the integrated team: PT, OT, dietitian, speech therapy, spiritual and social works, psychology, and prosthesis, orthoses, engineering and vocational services[148]
Podiatrist, chiropodist	Involved in preventative foot care and regular foot inspection[66] Support treatment of infection in collaboration with infectious disease specialist; prescription of offloading modalities considering bio-mechanics of the foot areas at risk of ulceration; prophylactic surgical offloading correction in carefully selected patients in collaboration with vascular surgeons
Pain management specialist	The level of pain associated with ischemia often requires narcotics and a combination of analgesics and pain management strategies[2,80]
Psychologist, social worker, spiritual leader	Hospital-based, rehabilitation and community-based supports to help patients navigate financial, social, spiritual and relationship, employment concerns
Family physician, primary care provider, nurse practitioner	Participates in decisions concerning choices in pain management and referrals to other specialists for the management of comorbidities, and the ongoing management of this chronic disease

It is common for individuals with CLTI to receive concurrent treatment for other comorbidities. Professional team members need to possess the expertise to manage a variety of co-factors, as well as modify the risk factors that will impact the patient's overall condition. When caring for patients with CLTI, the team should include individuals who are skilled in endovascular and surgical revascularization, wound healing therapies, foot surgery and medical management.

For further information related to assembling a team, refer to Chapter 4: Prevention and Management of Wounds: An Overview.[23]

3.2 Enlist the patient, care partners and family as part of the team

The coming together of ischemic and claudication pain, loss of function and mobility, depression, anxiety, embarrassment, social isolation, financial burden, employment changes, prolonged hospital stay, and chronic morbidity or death are all commonly associated with PAD.[149] In the US, Demas et al. state that though there have been improvements in medical, endovascular and surgical techniques, there continues to be disparities based on sex, race, ethnicity, colonization patterns and socioeconomic status.[149] Therefore, there needs to be a continued effort to increase PAD prevention, advocacy and awareness programs focused on making linkages between smoking, blood glucose and risk of diabetes mellitus, cholesterol, activity and hypertension.[150,151] More work needs to be done to promote prevention, as well as partnerships, in an effort to develop better patient outcomes for people with chronic diseases such as PAD and CLTI.

Engaging individuals who live with PAD/CLTI in the management of their chronic illness is imperative. The Canadian Patient Safety Institute provides a guide focused on strategies to engage patients, families and care partners.[152]

The Chronic Care Model (CCM) is designed to guide teams in delivery of high-quality PAD and CLTI care that aims to improve patient health outcomes. This model of care encourages self-management, use of decision-making tools and delivery of ambulatory care services through several integrated system initiatives designed to make patient-driven, evidence-based care easier to deliver and evaluate.[153-155]

3.3 Ensure organizational and system support

Organizational support for arterial wounds is limited. In 2007, an exploratory study in Quebec revealed the lack of collaboration and consistency among health professionals and difficulty in accessing professionals specialized in complex wound care.[156] In 2013, the Canadian Institute for Health Information (CIHI) looked at the prevalence of compromised wounds in Canada by type, health-care setting and risk factors to inform better prevention and management of wounds.[157] Unfortunately, CIHI reported venous ulcers and arterial ulcers in the same category, not distinguishing wound type clearly enough to provide information relating to specific organizational or system support needs.

In a survey carried out to determine knowledge levels and attitudes regarding lower extremity ulcer care, the following problems were reported: lack of evidence-based clinical practice guidelines for leg ulcer care (82%), absence of evidence-based protocols in home-care agencies (72%), lack of access to wound care products (69%), lack of access to wound care centres (66%) and poor communication among health-care workers (60%).[158] Transfer of knowledge from research to practice is poorly funded, and literature reports that it is a slow and challenging process.[159] Delays in knowledge translation often mean treatments and modalities that have proven beneficial may not be readily available or recognized because the evidence has not yet been incorporated into current health-care policy and procedure.

The 2020 version of this chapter was the first Canadian best practice recommendation dedicated primarily to the prevention and management of arterial ulcers, and even now only a few are available worldwide.[8,16,79]

According to current guidelines for the prevention of lower extremity arterial ulcers, there have been numerous educational efforts, such as national advertising campaigns, designed to promote increased public awareness of PAD/CLTI and the prevention of arterial ulcers. These types of campaigns should be continued more broadly to provide information to patients, care partners and communities:

- Information for patients, care partners and health-care providers in all care settings
- A system to identify at-risk patients
- Risk reduction measures
- Prompt, effective treatment
- Service audits to align local practice with accepted standards of care

Overall, such programs should be built on a structure designed to meet the needs of patients who require chronic care.[8,160] Developing system-supported strategies that focus on the prevention and management of risk factors for arterial ulcers is essential if better patient outcomes are to be achieved. Raising awareness of these risk factors will support early diagnosis and intervention, impacting both the incidence of arterial ulcers and mortality.[8,138]

To support quality of care, health-care systems will also have to generate higher quality data for all long-standing wounds across all health-care settings.[157] Improving recording and reporting of the prevalence and incidence of wounds, the progression of healing and outcomes of all wound types is also significantly important.[157] With better and more consistent data, the process of translating research into treatment and intervention becomes easier, with a stronger influence on improving the overall quality of patient care.[159]

Step 4: Establish and Implement a Plan of Care

An effective plan of care needs to be both evidence-based and allow for patient participation throughout the decision-making process. Successful chronic disease management requires the patient and their care partners to be engaged in a plan of care designed for prevention and management.

Recommendations
4.1 Identify and implement an evidence-based plan to correct the causes or co-factors that affect skin integrity, including patient needs (physical, emotional, social), the wound (if applicable) and environmental/ system challenges

An individual diagnosed with PAD/CLTI may be asymptomatic. In such cases the integrated, interprofessional health team should still work collaboratively to monitor and to manage risk factors and to ensure that appropriate strategies are implemented to prevent the loss of skin integrity. Once the CLTI status is determined treatment plans are developed to reflect goals.

Preventative and management plans of care for a person with PAD often include addressing smoking, nutrition, medications, exercise and activities of daily living, chronic pain, offloading and factors that affect quality of life.[66]
Patients who have been diagnosed with CLTI often require urgent referral to a vascular surgeon to determine the appropriateness of revascularization to restore blood flow in accordance with surveillance protocols.[26,66]

As up to 85% of amputations may be prevented by early detection and appropriate treatment,[53] the principal objectives for a plan of care for a wound should be:

1. to focus on healing process if the blood supply is sufficient and
2. to limit infection if the blood supply is insufficient, or in doubt, during the waiting time for vascular assessment.

For arterial ulcers with sufficient arterial inflow to support healing, use a dressing that will maintain a moist wound-healing environment.[161,162]

Dry gangrene or eschar is best left dry until revascularization is successful.[138] In wounds with insufficient arterial blood supply, PVP-I can also dry out the wound and reduce bacterial load and prevent bacterial infection.[163,164]

Table 10 provides an overview summary of the principal considerations when creating a plan of care based on CLTI status.

Table 10: Summary of Treatment Plan

CLTI Status	Perfusion	Treatment Plan
Prevention	Adequate	• Treat CV risk factors • Manage diabetes mellitus • Smoking cessation • Activity
Borderline*	Adequate	• Treat CV risk factors • Early vascular referral • Offload ulcer site and manage PI risk • Cautious moist wound care
Post revascularization (remains patent)	Adequate	• Treat CV risk factors • Monitor for re-stenosis (surveillance) • Offload ulcer site and manage PI risk • Cautious moist wound care
Post revascularization (re-stenosis)	Inadequate	• Treat CV risk factors • Refer for vascular assessment • Manage ischemic pain • Offload ulcer site and manage PI risk • Monitor vigilantly for infection • Avoid moist wound healing • Keep ulcer clean and dry with antiseptic • Consider adjunctive therapies
Pending revascularization	Inadequate	• Avoid moist wound healing • Keep clean and dry with antiseptic • Offload ulcer site and manage PI risk • Manage ischemic pain • Treat CV risk factors • Consider adjunctive therapies
Not a candidate for revascularization	Inadequate	• Treat CV risk factors • Monitor for increasing symptoms • Manage ischemic pain • Offload site and manage PI risk • Monitor vigilantly for infection • Avoid moist wound healing • Keep ulcer clean and dry with antiseptic • Consider advanced therapies
Undetermined		• Treat CV risk factors • Refer for vascular assessment

* Borderline here refers to a patient with just enough blood flow for healing; this assessment is difficult to make and should be part of the expert opinion judging healability of the wound based on the presence of adequate perfusion to heal even with impaired circulation.

Skin and Nail Care

Peripheral vascular disease increases the risk of foot ulcers and nail changes. PAD/CLTI impacts the layers of the skin, making the tissue susceptible to injury. Therefore, the skin on the lower extremities should be protected from trauma caused through mechanical, chemical and thermal insults;[80] otherwise, even minor injuries can lead to significant tissue loss, infection and failure to heal. Appropriate foot care, including skin cleansing, foot inspection, podiatry care and prompt assessment of lesions, is recommended for an individual diagnosed with PAD/CLTI.[66] Care of the toenails on the limb that has evidence of PAD/CLTI or peripheral neuropathy should be performed by a specialist.[138]

Smoking

Patients and anyone they are living with or regularly visiting the home should be actively encouraged to engage in a smoking cessation program.[2,8] Referral to such a program, along with counselling and pharmacotherapy support, is strongly recommended.[66] Cessation in patients with asymptomatic PAD optimizes the patient's tolerance to ambulation.[2,8] Unless contraindicated, the following pharmaceutical approaches to smoking cessation should be considered: varenicline, nicotine replacement therapy and bupropion.[2,8] When patients are not ready to stop smoking completely, a reduction in smoking by half or the use of an electronic cigarette are recommended as alternative options; however, the long-term safety of electronic cigarettes is unknown.

Glycemic Management/ Control

Effective glycemic management is recommended for patients with asymptomatic PAD.[2,8] For most adults with diabetes, Diabetes Canada proposes a HbA1c target of ≤7.0%. For people with type 2 DM at low risk of hypoglycemia, a lower target of ≤6.5 is recommended. However, a target HbA1c between 7.1% and 8.5% may be the preferred measure in a person with PAD when other comorbidities such as limited life expectancy, recurrent severe hypoglycemia and/ or hypoglycemia unawareness, functional dependency, frailty, advanced age or dementia (delirium, depression) are present.[144]

When poor glycemic control is a suspected factor, patients with CLTI should be encouraged to follow up with their primary health-care provider, diabetes educator or other appropriate specialist for supportive services, technologies or devices that could optimize glycemic control. For more information, please refer to Chapter 11: Prevention and Management of Diabetic Foot Ulcers.

Physical Activity

Assessment of footwear by a foot specialist should be conducted prior to beginning any exercise programs and recommendations made for proper fit and appropriate type for each activity.

Exercise programs should be considered for patients with CLTI as a risk-reduction strategy and as an alternative to revascularization, particularly in the early stages of the disease.[165] Structured, supervised exercise programs are recommended as first-line therapy for the treatment of intermittent claudication.[66] Unsupervised exercise may have some patient benefit when supervised programs are not feasible.[26] These programs aim to manage the symptoms of IC by improving exercise capacity, preventing or minimizing physical disability and reducing the occurrence of CV events. Taking into consideration that patients with CLTI belong to a high-risk population, careful monitoring and evaluation of existing comorbidities is recommended to ensure patient safety during exercise.[49] Take into consideration the patients' history of COVID-19 and risk of long-COVID-19 and post-exertional malaise (PEM).[73,74]

Existing functional limitations associated with claudication pain, along with an evaluation of how well a patient is responding to therapy, are most objectively measured through exercise treadmill tests. Treadmill walking is one example of an exercise program that can be structured and supervised and has demonstrated the best evidence for managing symptoms of IC.[165] Exercise sessions involve selecting a walking speed and degree of incline that will induce symptoms of IC within three to five minutes. When a patient reports moderate claudication pain, they are instructed to stop and rest until the symptoms subside. The exercise cycle is repeated for at least 30 minutes. In subsequent visits, the speed and/or degree of incline of the treadmill can be increased if the patient is able to tolerate walking for 10 minutes or longer at the increased workload without experiencing IC. Exercise sessions longer than 30 to 60 minutes and more often than three sessions per week are considered to have the most benefit.[165] Sessions lasting longer than 12 weeks and up to six months demonstrate the longest-lasting benefit. More research is needed.[165]

Alternative forms of exercise may also benefit the patient, including pain-free walking exercise training, leg-cycling exercise training, aerobic arm exercises, leg-cycling and resistance training.[165] However, current evidence suggests that these are not as effective as treadmill training.

Home-based, self-directed exercise programs are recommended, and may also be of benefit to patients who do not have access to a supervised program.[165] Home-based programs should have a goal of 30 minutes of walking three to five times per week.[49] The presence of lower-extremity wounds and severe IC may potentially exclude a patient from participating in a treadmill exercise training program. As an alternative option, arm ergometry has been shown to improve lower extremity perfusion and alleviate pain in patients with known PAD. Participating in a supervised or home-based exercise program is recommended for patients who have undergone a revascularization procedure.[49]

Medications: Pre-revascularization

Medications prescribed for the treatment of PAD/CLTI are outlined in Table 11; in consideration of four clinical objectives: cardiovascular risk reduction, claudication management, CLTI management and treatment for limb preservation. Cardiovascular risk-reduction medications include lipid-lowering agents, antihypertensive agents, antiplatelet and antithrombotic agents, smoking cessation options and antihyperglycemic and renal agents.

Table 11: Cardiovascular Risk Reduction and Medical Management[2,26,144,166]

For more information see The Canadian Cardiovascular Society 2022 Guidelines for Peripheral Arterial Disease https://ccs.ca/guideline/2022-peripheral-arterial-disease/

Lipid-lowering Agents	
Statins	Recommend maximally tolerated dose of statin for all persons with established atherosclerotic cardiovascular disease (ASCVD), such as PAD/CLTI even if lipid parameters are at target
Ezetimibe	When TG ≤1.5 mmol/L, if LDL-C is 1.8 to 2.2 mmol/L; or when TG >1.5 mmol/L, if ApoB 0.70 to 0.80 g/L or if non-HDL is 2.4 to 2.9 mmol/L, ezetimibe is recommended as second-line therapy (add-on to maximally tolerated dose of statin) When TG ≤1.5 mmol/L, if LDL-C is >2.2 mmol/L; or when TG >1.5 mmol/L, if ApoB >0.80 g/L or if non-HDL is >2.9 mmol/L, ezetimibe is recommended as third-line therapy (add-on to maximally tolerated dose of statin and proprotein convertase subtilisin/kexin type 9 [PCSK9] inhibitor).
Bile acid sequestrant	Does not reduce CV risk but should be considered in persons with PAD/CLTI who are unable to achieve lipid targets in combination with maximally tolerated statin therapy doses with or without ezetimibe
PCSK9 inhibitor	Considered in persons with PAD/CLTI who are unable to achieve LDL-C, ApoB or targets in combination with maximally tolerated statin therapy doses with or without ezetimibe
Fibrate	Does not reduce CV risk, but should be considered in persons with PAD/CLTI and low HDL-C, and/or elevated triglycerides, to reduce the LDL-C values
Anti- hypertensive agents	Considered for selected high-risk patients, aged ≥50 years, and with systolic blood pressure (SBP) levels ≥130 mmHg, intensive management to an SBP ≤120 mmHg[167,168] Patients with diabetes should be treated to attain <130 mmHg SBP and <80 diastolic BP mmHg[169] Other patients should be treated to attain <140 mmHg SBP and <90 mmHg diastolic BP[2,8]
ACE inhibitors	In symptomatic patients with lower extremity PAD/CLTI, these can reduce the risk of adverse CV events, and should be continued even when the person is at blood pressure targets In asymptomatic patients with lower extremity PAD/CLTI, they may reduce the risk of adverse CV events
Cardiovascular and Renal Protective Antihyperglycemic Agents[145,166]	
Glucagon-like peptide-1 receptor agonists (GLP-1 RA)	At doses that have demonstrated cardiovascular and renal protection, are recommended for all people with established atherosclerotic cardiovascular disease (ASCVD), including PAD/CLTI, to reduce the risk of major adverse cardiovascular events (MACE)

SGLT2i therapy	Is contraindicated in CLTI; and SGLT2i therapies are recommended to be stopped during an active wound. However, in the absence of CLTI and when no active wounds are present, SGLT2i should be considered SGLT2i therapy has been shown to reduce the risk of MACE, hospitalization for heart failure and progression of nephropathy in people with established ASCVD, including people with PAD/CLTI
Antiplatelet and Antithrombotic Agents	
1st Line: ASA 75 mg to 325 mg daily	For individuals with symptomatic atherosclerotic CLTI—including those with IC or CLTI—prior to lower extremity revascularization (endovascular or surgical), or prior amputation for lower extremity ischemia to reduce the risk of myocardial infarction (MI), stroke and vascular death
2nd Line: Clopidogrel 75 mg daily	In asymptomatic individuals with an ABPI ≤0.90, consider antiplatelet therapy to reduce the risk of MI, stroke, or vascular death Note: When ABPI is 0.91–0.99, reduction in MI, cerebrovascular accident (CVA) or vascular death in asymptomatic individuals is not well established
Combination: ASA + clopidogrel	Considered for those who are not at increased risk of bleeding and who are at perceived high cardiovascular risk with symptomatic atherosclerotic CLTI, including those with intermittent claudication or CLTI, prior lower extremity revascularization (endovascular or surgical), or prior amputation for CLTI to reduce the risk of CV events
Combination: Warfarin + ASA or clopidogrel Combination: New oral anticoagulants (NOAC) + ASA	NOT RECOMMENDED In the absence of any other proven indication for warfarin, its addition to antiplatelet therapy to reduce the risk of adverse CV ischemic events in individuals with atherosclerotic PAD/CLTI is of no benefit and is potentially harmful due to increased risk of major bleeding The Compass trial evidence recommends rivaroxaban 2.5 mg BID with (ASA 80-100 mg) for symptomatic lower extremity PAD who are at high risk for ischemic events (polyvascular disease, diabetes, history of heart failure, or renal insufficiency) and/or limb amputation, rest pain, ischemic ulcers AND at low bleeding risk. (Strong Recommendation; High-Quality Evidence).In the absence of high-risk limb presentation or high-risk comorbidities and low bleeding risk, they recommend combination treatment with rivaroxaban 2.5 mg twice daily and ASA or single antiplatelet therapy for patients with symptomatic lower extremity PAD (Strong Recommendation; High-Quality Evidence)[2] Caution is warranted given the incremental bleeding risks associated with combination therapy and because existing evidence is inadequate to support a confident recommendation at this time.
Homocysteine-lowering Agents	
Folic acid and vitamin B12 supplements	Effectiveness is not well established in individuals with PAD/CLTI and homocysteine levels ≥14 mmol/L
Oral zinc	Does not appear to aid in healing arterial wounds[170]
Intermittent Claudication Management Considerations	
Statins	Indicated to improve walking distance when prescribed in conjunction with general prevention strategies[26]
Pentoxifylline 400 mg 3x per day	May be considered to improve walking distance in patients with IC. Note: The clinical effectiveness of pentoxifylline as therapy for claudication is marginal and not well established. Not recommended as a useful agent for the treatment of CLTI[66]

Imaging Studies to Optimize the Revascularization Strategy Arterial imaging are not used only to diagnose CLTI. When a revascularization procedure is being considered, advanced imaging may be employed to identify the target vessels (vessels with lesions) and to determine the most appropriate approach to revascularize the limb. If a normal post-exercise ABPI measurement is obtained, arterial imaging is not recommended, in accordance with surveillance protocols.[66]

Medications: Post-revascularization

The presence of asymptomatic or symptomatic CLTI is an ominous sign that widespread atherosclerosis is present. Patients who experience rest pain in a lower extremity, or have developed an arterial ulcer, have a significantly increased risk of myocardial infarction and cardiovascular accident and cardiovascular-related death.[170,171]

Pharmacological management is recommended for risk reduction and can play a significant role in reducing the prevalence of morbidity and mortality.[2,145,167] Even if blood flow has been restored or optimized in a lower extremity, targeted medical therapy is indicated to prevent further cardiovascular events or the progression of CLTI.

Pharmaceutical therapies can be grouped into three categories: thrombosis-directed therapies, cholesterol-lowering therapies and blood-pressure-lowering (anti-hypertensive) therapies. Standard treatment guidelines for medical therapy (including beta blockers, statins, angiotensin-converting enzyme [ACE] inhibitors and calcium channel blockers) will improve outcomes for not only coronary artery disease (CAD), but also arterial ulcers.

The Voyager PAD trial recommends rivaroxaban 2.5 mg twice daily in combination with ASA (80–100 mg daily), with or without short-term clopidogrel use (30 days), for patients with lower extremity PAD after elective endovascular revascularization (Strong Rec; Moderate-Quality Evidence). They also recommend treatment with rivaroxaban 2.5 mg twice daily in combination with aspirin (80–100 mg daily) for patients with lower extremity PAD after elective open revascularization (Strong Rec; High-Quality Evidence).[72]

See Table 12 for a description of these medications.[8]

Table 12: Pharmacotherapy for CLTI and Post-revascularization Medications

Pharmacotherapy for CLTI	
Thrombosis-directed agents	**Antiplatelet Agents** Long-term single antiplatelet therapy recommended for asymptomatic PAD[26] Recommended in accordance with surveillance protocols Recommended for patients with PAD who are symptomatic for IC or have CLTI, to reduce the risk of MI, CVA and vascular death[53,106,180] Recommended for patients with asymptomatic PAD to reverse adverse cardiovascular ischemic events[66] Clopidogrel 75 mg daily is recommended as a safe and effective alternative antiplatelet therapy to ASA to reduce the risk of MI, CVA or vascular death in individuals with symptomatic atherosclerotic PAD.[106] Current guidelines report that clopidogrel may be preferred over ASA Certain high-risk PAD patients benefit from receiving both ASA and clopidogrel; however, it is recommended that this combination therapy be considered on an individual basis, not for patients with high risk of bleeding, and that this combination therapy should be reassessed every six to 12 months to determine if it is still suitable based on the person-centred characteristics No clinical trials have examined the efficacy of newer antithrombotic medications such as prasugrel or vorapaxar to reduce ischemic events in patients with PAD[86] No difference in MACE (major adverse cardiovascular events) and MALE (major adverse limb events, e.g., major amputation) when comparing ticagrelor and clopidogrel[180]
	Anticoagulation Agents There is evidence for prescribing moderate intensity anticoagulation (INR 2-3) in the presence of ASA, suggesting that combining anticoagulant and antiplatelet therapy significantly reduces recurrent CV events; however, this combination also increases the risk of major bleeding

Cholesterol-lowering agents	Strong evidence supports the lowering of cholesterol with statin medications in patients with CLTI to reduce the risk of major vascular events Lipin-lowering therapy with a high-intensity statin at maximally tolerated doses
Antihyper-glycemic agents	Optimizing glycemic control is recommended for patients with CLTI
Anti-hypertensive IVE agents	Treatment of hypertension recommended to reduce cardiovascular events, including congestive heart failure (CHF), CVA and death. There is some evidence to suggest a definite relationship between hypertension and CLTI Effective management of hypertension recommended for patients with asymptomatic PAD[66] Recommended that patients without diabetes who have been diagnosed with PAD and hypertension be prescribed antihypertensive medication to achieve a blood pressure measurement of <140 mmHg systolic[100] Recommended that the treatment goal for PAD patients with diabetes and/or renal disease should be blood pressure of <130 mmHg systolic over 80 mmHg diastolic[66] Treatment with an ACE (angiotensin-converting enzyme) inhibitor medication is recommended to lower CV risk in patients with either asymptomatic or symptomatic PAD[66] Ramipril should be considered as a first-line choice for hypertension treatment in PAD patients; although it should be used with caution in the presence of renal artery stenosis[8] Beta-blockers are widely used for the management of high blood pressure, either alone or combined with other medicines, including diuretics, ACE inhibitors or calcium channel blockers. May be especially useful in people who also have angina or heart failure, or who have had a heart attack There is no available evidence that beta-adrenergic blockers worsen the symptoms of IC
Post-intervention (Revascularization) Medications[90]	
Antiplatelet agents	Clinical evidence does not conclusively support the routine use of antiplatelet agents to improve lower extremity vein bypass graft patency. Long-term single antiplatelet therapy is recommended for patients who have undergone revascularization[26] Use of anticoagulant therapy is still recommended to reduce future cardiovascular ischemic events and incidence of stroke Bypass graft patency may be improved with antiplatelet therapy in patients undergoing prosthetic bypass Antiplatelet therapy recommended for all patients undergoing revascularization for CLTI, and continued post-operatively, unless contraindicated by a pre-existing condition[66]
Anticoagulation agents	The use of warfarin anticoagulation following lower extremity bypass remains controversial Anticoagulation is used selectively in vein bypass procedures when the graft is not considered to be optimal quality or vessels below the graft site are small or diseased Warfarin, in addition to ASA, is prescribed to many patients receiving prosthetic grafts to reduce the ischemic consequences of bypass graft thrombosis Caution is warranted given the incremental bleeding risks associated with combination therapy and because existing evidence is inadequate to support a confident recommendation at this time[8]

Intermittent Claudication (IC): Medical Management versus Revascularization

Patients who experience IC should be considered for medical management before being offered endovascular and surgical therapies. The cornerstones of management for patients who experience intermittent claudication are cardiovascular protection and exercise.[26]

Surgery still plays an important role in the treatment of patients with arterial disease. When PAD results in impairment of normal activities of daily living (ADLs) or incapacitating IC, revascularization should be considered.[26]

If there is severe impairment of ADLs, exercise therapy should be considered, along with revascularization.[26] Choosing the most appropriate intervention, open or endovascular, will depend on the location and distribution of the arterial lesions, as well as the patient's overall condition and comorbidities.

Endovascular therapy is used more commonly than open surgical therapy because of its minimally invasive nature and the reduction of short-term morbidity and mortality. The trade-off, however, is the long-term durability of endovascular repairs.

CLTI and Revascularization

To alleviate pain, improve the patient's HRQoL, close any existing arterial ulcers and prevent amputation, most patients will require some form of revascularization procedure.[53] In addition, an aggressive plan of care aimed at managing all existing cardiovascular risk factors is essential. Revascularization is a fundamental strategy for limb preservation and is the optimal treatment choice for patients with CLTI.[53] However, in some cases, revascularization does not improve limb function and mobility. Cognitive impairment, a non-ambulatory status prior to developing CLTI, and severe comorbidities may lead to a poor prognosis even when revascularization has been performed.

Acute Limb Ischemia (ALI) and Revascularization

When ALI occurs, assessment and emergent revascularization should be carried out if the affected extremity is considered a candidate for preservation.[53,66] In contrast to treating chronic ischemic disease, current guidelines do not recommend investigative tests to determine the vascular anatomy (or sites of occlusion) when the affected limb is not considered a candidate for preservation.[2,8] If a neurological deficit underlies the acute ischemia, urgent revascularization is recommended.[26]

In the case of acute ischemia, treatment with heparin and analgesics to manage pain are recommended as soon as possible.[26]

Managing Pain: Wound Pain, IC and CLTI

The presence of tissue ischemia or neuropathy will require the clinician's careful attention to pain. Management of pain associated with an arterial ulcer should include consideration of local, regional and systemic modalities.[80] One of the primary strategies to reduce pain associated with CLTI is to encourage the patient to position the lower limb in a dependent position to optimize perfusion to the wound. Making appropriate adjustments to sleeping position by increasing foot dependency can optimize rest and reduce night pain but will result in increased swelling of the lower extremities.

The presence of IC and CLTI can cause considerable discomfort and should be managed vigilantly. Current literature reports that the application of an ibuprofen-foam (IBU) dressing may provide some local wound pain relief, as well as increase HRQoL.[174,175] However, there is no available evidence that recommends the routine use of these dressings to treat arterial ulcers,[162] or specifically for the purpose of pain management. More high-quality studies will have to be carried out before any conclusions can be made.[162]

Several studies have reported positive benefits of the use of statins to reduce IC pain.[176,177] A few small studies have demonstrated a benefit of statin therapy to optimize pain-free walking time in patients with IC, although the mechanism of action is not known.[8] However, a 2015 guideline suggests that prescribing ramipril 10 mg once daily should be considered to improve pain-free and maximal walking times in patients with IC.[8]

Pentoxifylline is a medication often prescribed for its action to reduce blood viscosity and platelet aggregation. A 2015 review concluded that there is currently insufficient high-quality data to support the benefits of pentoxifylline for IC.[178] Although pentoxifylline has not been shown to improve arterial ulcer healing,[80] a modest effect in increasing pain-free and maximal walking distance has been demonstrated. This is believed to be a result of improving blood flow and enhancing tissue oxygenation.[179,180]

Although the clinical effectiveness of pentoxifylline for the treatment of IC is not well established,[2] best practice guidelines recommend that pentoxifylline be considered for these patients to improve walking distances.[2]

The use of acetaminophen, in conjunction with opioids, should be considered for the management of pain associated with CLTI.[89] When pain is not adequately controlled, a referral to a specialist with expertise in pain management is recommended, and revascularization should be considered to augment wound healing and limb preservation.[49]

Nutrition

Nutritional counselling may be recommended for patients with PAD and CLTI to determine deficits that may impact the healing of the arterial ulcer.[80] The role of oral zinc to augment the healing of arterial ulcers is not well established.[170] Nutrition must be adequate to provide sufficient protein to support the growth of granulation tissue.[3,8,99,181]

For more information on nutrition, please see Chapter 4: Prevention and Management of Wounds: An Overview.[23]

Psychosocial Factors

Patients with CLTI who are not considered candidates for revascularization have lower reported HRQoL,[128] These lower scores relate specifically to physical pain and a reduction in physical functioning, as well as the ability to participate in activities of daily living. HRQoL scores are reportedly lower in females with CLTI, individuals with a higher body mass index (BMI) and/or reduced ABPI.[182] Social isolation, substance use (alcohol), lower socioeconomic status[1] and poor hygiene and nutrition have been implicated as psychosocial factors that contribute to the development of arterial ulcers. Securing the support of a social worker (medication funding, emotional support, transitions in care), outreach programs, food security and/or a spiritual care specialist may be beneficial to improving HRQoL.[183]

Offloading for Wound Prevention and Healing

As a preventative measure in persons with CLTI, an orthosis, shoe or other offloading device can minimize the pressure over vulnerable areas on the lower extremity. This is particularly important when peripheral neuropathy is present. It is essential that patients with PAD/CLTI receive a biomechanical assessment as soon as possible by a trained foot/footwear professional to ensure the appropriateness of footwear and other orthotic/prosthetic devices that may contribute to extrinsic pressures.[66] Every effort must be made to prevent pressure injury, particularly over boney prominences, and reduce the risk of wounds caused by trauma.[66]

When an arterial ulcer is present it may be necessary to modify the existing offloading device/orthotic to an alternative that will support wound healing and prevent further tissue breakdown.[80]

Consultation with a health-care clinician who is skilled at carrying out a biomechanical assessment of the lower limbs (pedorthist, chiropodist, podiatrist, orthotist) is recommended to determine the most appropriate offloading approach and/or device to use. For further information on offloading devices refer to Chapter 11: Best Practice Recommendations for the Prevention and Management of Diabetic Foot Ulcers.

Limb Amputation

Amputation for chronic ischemia may be performed as the result of a failed revascularization attempt, a lack of suitable conduit or target arteries, severe patient comorbidities, poor functional status or extensive gangrene or infection such that limb preservation is not possible.[184] The goals of amputation are to eliminate all infected, necrotic and painful tissue, to achieve uncomplicated wound healing and to have an appropriate remnant stump that can accommodate a prosthesis.[184]

Major amputation (above the ankle) in patients with CLTI is recommended when there is overwhelming infection that threatens the patient's life, rest pain cannot be controlled and there is extensive tissue loss.[53,185] Amputation should be considered for a patient with significant necrosis on the weight-bearing portions of the foot, non-correctable flexion contracture or very limited life expectancy as a result of comorbidities.[19,21]

Lower limb amputation (LLA) is a disabling and costly condition.[186] Cost estimates are not available for Canada; however, in the United States the costs associated with acute and post-acute care for LLAs exceeds $4 billion USD annually.[186]

A Canadian study on 20,062 patients in Ontario observed a significant increase in the rate of any amputation among patients with diabetes, peripheral arterial disease and both diabetes and periphery arterial disease.[187] In the study, 64% of patients underwent a major (above ankle) amputation. Diabetes was present in 82%, peripheral arterial disease in 94%, and both diabetes and peripheral artery disease in 76%.[187]

Liu et al. assessed whether or not there was a temporal trend in re-amputation rates. They reported higher incidence rates for reamputation to both limbs and to the contralateral limb only. At 12 months, the reamputation rate for all contralateral and ipsilateral reamputations was 19%, and at five years, 37.1%. At five years the contralateral reamputation rate was found to be 20.5%. They found no evidence of a trend in the reamputation rates over more than two decades.[188]

With the increase in the aging population and the expected growth in the number of individuals living with PAD leading to CLTI and lower limb amputation, it is imperative that adequate preventative, rehabilitation resources, lower limb and preventative foot screening and diabetes-management programs are available to this population and are allocated appropriately.[189] In a population-based descriptive study in Canada, Kayssi et al., found that there is variability in the delivery of lower-extremity amputations and postoperative hospital discharges among surgical specialists and regions.[190]

The length of the residual limb has important implications for rehabilitation.[184] Whether the patient has undergone a trans-met amputation (TMA), a below-knee amputation (BKA) or an above-knee amputation (AKA), they will require interventions related to ambulation and mobility, adjustment to new body image, management of phantom limb pain and social and environmental adaptations. A proper assessment is essential to determine whether an amputee is an appropriate candidate for a prosthetic device. Advanced prosthetic technology provides amputees with more choices and new functional designs, and ultralight materials help with independent living.[184] Measuring for and the fitting of a customized prosthetic device should be carried out by a trained professional who has expertise in the biomechanical assessment of the lower extremities, as well as other physiological considerations related to lower-limb amputation. Ulceration is an ongoing concern with the introduction of a prosthetic because the device can be a cause of external pressure injury and discomfort. The patient's overall safety is a priority.

Some important factors to consider in the choice of a prosthetic design are the patient's comfort and sense of safety, appearance of the device, functionality, social circumstances, user-friendliness, cost and maintenance. Collaboration among specialists is essential to support these patients following hospital discharge and to ensure regular servicing of the prosthetic. Regular reassessment may identify a change in the patient's level of function and mobility, weight changes and impact on the fitting of the device, or other concerns regarding safety and comfort.

Phantom Limb Pain (PLP)

Post amputation, the complication of PLP is prevalent (up to 80%) and difficult to manage.[117,191] Various therapies have been explored to determine the best approach to managing PLP; however, none has been found to be highly effective.[120]
Erlenwein et al. in a review explored the use of approaches focused on restoring body scheme and integration of senior-motor inputs. Technology-based applications such as virtual reality, offer options to supplement existing established approaches based on mirror therapy. As well, targeted muscle therapy and prosthesis aids in restoring limb function and reshaping one's body perception.[191]

Currently employed non-invasive and minimally invasive therapies for PLP include medications, exercises and relaxation techniques, transcutaneous electrical nerve stimulation (TENS) and acupuncture.[182,183] More-invasive options include anesthetic and steroid injections, spinal cord stimulation (SCS) and nerve blocks. Surgical stump revision and neurectomy are sometimes considered as a last resort.

Some evidence has been generated for the prevention of PLP before the amputation is performed with the use of pre-operative anesthetic.[120] An RCT by Brunelli et al. studied PLP management after amputation and concluded, "The use of a prolonged postoperative perineural infusion of anesthetic (ropivacaine 0.5%) seems to be an effective therapy for the treatment of phantom limb pain and sensations after lower extremity amputation."[193] Hunt et al. explored the use of perineural infusion of lefobupivaine (n=81) with minimal pain improvements.[194] More research is needed.

Psychological Considerations Following Lower Limb Amputation

Having one or more lower extremities amputated as a result of PAD/CLTI can result in a number of emotional responses, including grief (sense of loss), an alteration in body image and the need to adapt to a new way of life with self and others.[195] Supports are needed to manage associated anxiety and depression.[196] The presence of phantom pain can exacerbate mental health and wellness.[197] Patients are at risk of isolation and negative emotions associated with body image change, each affecting their ability to engage in and carry out activities of daily living.[197] Support is needed to help the patient self-manage and adapt to a new body image and a change in function; these are key to accepting the amputation and enhancing quality of life.[198-200]

Timely referrals to a mental health specialist, Indigenous support worker, psychologist or psychiatrist trained in dealing with amputation can help the patient explore their sense of grief and loss and transition to an acceptance of a new body image and level of functioning within their social, work and community life.[10,61]

Environmental adaptations in the home and place of employment, such as grab bars and modified bathrooms with appropriate signage, can optimize function and foster a greater sense of independence and self-care. This is particularly important when the patient is being considered for, or has been fitted with, a prosthetic limb or is required to mobilize with other devices such as a wheelchair, walker, scooter or vehicle. The support services of a PT and/or OT can optimize the amputee's physical strength, balance and co-ordination, as well as introduce skills and techniques related to transfer and mobilization.[198]

Social workers, psychologists and peer-based programs are helpful in accessing community-based resources and services for the patient to aid in the process of adapting to a new amputation. Supports should include social, psychological and spiritual care approaches relevant to the patient's beliefs and preferences. This includes mindfulness, cognitive behavioural therapy and short- and long-term counselling.[201]

4.2 Optimize the local wound environment

Strategies that are designed to manage the wound should reflect the goals of care for the patient, which have been made, in part by determining the healability of an arterial ulcer in the assessment phase. It is important to remember that healing a wound requires greater perfusion than is needed to maintain intact skin.[4,53]

An arterial wound that has adequate perfusion is considered healable and will need an aggressive approach if the goal is wound closure. The goals for non-healing and non-healable wounds, where blood perfusion is inadequate or factors that impact healing cannot be addressed, will focus on pain control and preventing infection.[4,83,202] Preventing re-ulceration and minimizing further tissue damage should always be a priority with patients who have PAD/CLTI.

It is recommended that dry gangrene or eschar be left dry until revascularization is successful;[79,138] therefore the cleansing of these arterial wounds should be carried out with the daily application of povidone iodine (10% PVP-I) to maintain a dry wound bed.[163,164,203]

4.2.1 Cleansing

For wounds that are considered to have adequate arterial perfusion, pH-balanced, non-cytotoxic skin and wound cleaners should be used to maintain the skin's moisture barrier and acid mantle and promote a moist wound healing environment.[80] Percival et al. state wound cleansers that contain surfactants may enhance wound closure, especially when microorganisms are present that delay wound healing. In wounds complicated by biofilms, persistent inflammation or slough, "The use of surfactants has been shown to aid in the removal of these barriers to wound healing. The use of concentrated surfactant (poloxamer) based wound dressings represent an important component of wound management".[204]

The cleansing of non-healable arterial ulcers that present with dry eschar or dry gangrene is not recommended.[79,88,138] Washing or cleaning a non-healable wound site before the application of 10% PVP-I is not recommended.[80] Gangrenous tissue, if not infected, can form an eschar cap that will progressively shrink as it dries and, eventually, 'mummify'.[53] Protective dressings are required throughout the mummification stage. If the circulation beneath or surrounding the wound is adequate (or improved by a revascularization procedure), a process of auto-amputation may follow.[53]

This process, however, may take considerable time, and pain management, education in bacterial burden, and maintaining a dry wound environment become the priorities.[53,174,203,205]

For further guidance on wound cleansing refer to Chapter 4: Prevention and Management of Wounds: An Overview[23] and Wounds Canada's Product Pickers https://www.woundscanada.ca/health-care-professional/resources-health-care-pros/library/183-resources-industry-partner/288-product-picker

4.2.2 Debriding

Current literature on arterial ulcers is consistent with the practice of not debriding stable black eschar.[80,181,206] Debridement prior to revascularization in poorly perfused extremities should be performed only in a septic foot with or without ischemic signs.[79]

Autolytic and enzymatic debridement may be alternative approaches to consider in cases where sharp debridement may be contraindicated. However, autolytic and enzymatic debridement are contraindicated in the presence of significant PAD.[199] When employing these modalities with an ischemic wound, close monitoring is recommended.[80]

For further guidance on wound debridement refer to Chapter 4: Prevention and Management of Wounds: An Overview.[23]

Surgical debridement of nonviable and non-infected tissue is not recommended until adequate vascular status has been confirmed or restored.[79,207] Without adequate perfusion to heal the wound, debridement may exacerbate tissue ischemia by increasing metabolic demand, leading to increased risk of amputation.[79]

4.2.3 Managing bacterial balance

A progression of PAD often coincides with an increased risk of wound infection.[136] The probability of infection varies directly with increasing bacterial numbers and their relative ability to cause disease (known as virulence) while varying inversely with the host's ability to resist invasion.[136]

The application of topical antimicrobial dressings should be considered to minimize the proliferation of bacteria in the open wound.[136] Povidone iodine (10% PVP-I) is one of the most extensively used broad-spectrum topical antiseptics used to minimize the bacterial burden in long-standing wounds with an inadequate blood supply.[174,205] Hypersensitivity reactions may occur. PVP-I is available in an aqueous solution, as well as being impregnated into products that have a sustained-release delivery system. These newer technologies can support fiscal responsibility by reducing both the frequency of dressing changes and visits with a health-care professional.

However, it is important to consider that formulations of PVP-I, such as liposome hydrogel (3%) and cadexomer-iodine (0.9% iodine), may enhance moist wound healing and may not be appropriate for non-healing arterial ulcers.[205] When it is suspected that an arterial ulcer has become infected, the use of a topical antimicrobial dressing is not considered to be sufficient treatment.[80] Systemic antibiotic therapy is required in patients with CLTI who develop spreading or systemic infection.[53] Clinical signs of infection may be subtler because of the decrease in blood flow to the site of the arterial ulcer.[80] Clinical infection should be suspected when the ulcer becomes more painful, or the local wound site begins to deteriorate or fails to heal.[136] PAD/CLTI-related wound infection is a primary risk factor for major amputation.

For more on maintaining bacterial balance see Chapter 4: Prevention and Management of Wounds: An Overview.[23]

Antibiotic Selection

Rapid assessment and diagnosis of infection associated with PAD, including a consideration of extent and severity of tissue involvement, can facilitate timely intervention.[53] It is recommended that a patient with PAD and CLTI be referred promptly to a vascular surgeon when infection is suspected.[19,66,124] Best practice guidelines recommend that patients with CLTI, skin ulcerations and evidence of limb infection be promptly treated with systemic antibiotics.[64,66,124, 210]

A patient with an infected arterial ulcer should be evaluated as soon as possible by a clinician expert in determining the appropriate culture-guided antimicrobial treatment.[79] Wound cultures and tissue and bone biopsies can guide culture-specific treatment. Where no cultures are available, or prior to culture processing, empiric broad-spectrum antibiotics should be initiated in consultation with an infectious disease specialist whenever possible. Adjustment of antibiotics should be made once the causative micro-organisms and culture and sensitivity have been obtained.[136] Additional caution should be exercised when prescribing antibiotics to a patient with renal insufficiency to ensure effective clearance of these medications. In such cases, consultation with a nephrologist, or pharmacist for renal dose calculations, may be warranted to ensure patient safety. There is a growing practice of engaging a pharmacist for prescription of antimicrobials to treat infection.

Currently, this practice varies from region to region in Canada. The appropriateness of consulting a pharmacist depends on the scope of practice and expertise of individual pharmacists and should be carried out in collaboration with the specialist physician who attends the patient.

4.2.4 Managing moisture balance

Maintaining moisture balance in the local wound environment is recommended for arterial ulcers that are considered to have adequate perfusion to heal or after successful revascularization. Choosing an appropriate dressing can optimize the local wound environment throughout different phases of the wound healing process by helping maintain moisture balance.[4,23]

Careful monitoring is recommended when an arterial ulcer is being treated with a moisture-retentive dressing to ensure that tissues do not become boggy and vulnerable to bacterial growth.[80]

Current BPGs recommend the daily painting of non-healable arterial wounds with 10% PVP-I and covering with a gauze or breathable cover dressing to maintain a dry wound environment.[80,208,209] If sufficient perfusion can be restored through revascularization, the use of moist wound healing principles should be resumed.[80,208] If a dry eschar becomes moist or boggy clinicians should consider the possibility of wound infection.

The progression of infection may be inhibited through surgical wound debridement, and incision and drainage of an existing abscess, before revascularization is carried out.[79,138]

Maintaining a dry wound environment is recommended for non-healable and non-healing wounds, or until adequate blood flow has been re-established or the ischemic digit auto-amputates.[208]

Timely diagnosis and treatment of infection in peripheral arterial wounds is essential to reduce the risk of systemic infection and amputation.[79,138]

For further guidance on maintaining moisture balance refer to Chapter 4: Prevention and Management of Wounds An Overview.[23]

4.3 Select the appropriate dressings and/or advanced therapy

Having a good working knowledge of different classifications and of dressings can assist the clinician in making informed choices so that the wound environment can be optimized at various stages of the healing process.[4,79,136,138,208,210-214]

Currently, there is insufficient evidence to suggest that one particular dressing over another will significantly affect the healing of arterial ulcers.[162,211,215] The healability of the wound and the degree of tissue injury and the patient experience with dressings should always be taken into consideration when choosing the most appropriate dressing.[4]

Moist wound healing and occlusive dressings are not recommended for arterial wounds that do not have sufficient blood flow to heal.[105,216]

However, dressings that provide good ventilation and permit frequent wound inspection are recommended for arterial ulcers.[80]

For further guidance on the different classifications and selection of dressings refer to Chapter 4: Prevention and Management of Wounds An Overview.[23]

For more information about dressing selection, see Wounds Canada's Product Picker: Wound Dressing Formulary and Product Picker: Wound Dressing Selection Guide https://www.woundscanada.ca/health-care-professional/resources-health-care-pros/library/183-resources-industry-partner/288-product-picker

When an ulcer is considered non-healable because of inadequate perfusion, it is strongly recommended that all sources of moisture, such as foot soaks, creams, ointments, saturated footwear/socks be avoided.[26,79,208]

Biologically Active Wound Dressings

Biologically active dressings are believed to influence the levels of proteases and growth factors in the wound environment. There is insufficient literature to support recommending biologically active dressings as a routine treatment for arterial ulcers.

More research is required in this area to determine the benefit that biologically active dressings may have on the healing of arterial ulcers.

Advanced Therapies

There is a lack of strong evidence to support the routine use of advanced therapies—such as electrical stimulation, hyperbaric oxygen therapy, intermittent pneumatic compression, negative pressure wound therapy, spinal cord stimulation, topic oxygen therapy and ultrasound therapy—for arterial ulcers (See Table 13). However, it is recommended that advanced therapies be considered to augment the wound healing progress for patients who are at a high risk for amputation.[80] In other words, advanced therapies should be considered in limited situations when the standard best practice approach to wound healing is not achieving satisfactory outcomes. Access to the advanced therapy, the availability of trained health professionals, cost and appropriateness of treatment are all considerations that should be made prior to the decision to use a particular advanced therapy. It is important to remember that although advanced therapies may support the healing of arterial ulcers, they do not correct the underlying disease. Whenever possible, adequate blood flow should be restored to sustain the healing unless contraindicated.[80] When combined with revascularization, the employment of advanced therapies may improve wound-healing outcomes.[80]

Table 13: Advanced Therapies for the Prevention and Management of Arterial Ulcers

Advanced Therapy	Current Evidence for Use
Electrical stimulation (E-STIM)	Does not replace the benefits or outcomes of revascularization[217-219] Further study specific to arterial wounds needs to be carried out to make any conclusions[220]
Hyperbaric oxygen therapy (HBOT)	Some evidence of benefit in selected patients with ischemic ulcers to augment the wound-healing process[53,79,138,217,221] Currently no evidence in literature to support or refute the use of HBOT to treat arterial ulcers[219,223] May be considered in selected patients with ischemic ulcers who have not responded to, or are not candidates for, revascularization[53] Further research is needed to clarify the benefit for patients without diabetes with arterial or other ischemic ulcers, or for wounds associated with surgical debridement, revascularization or amputation[217,219] Selection criteria should include wounds with hypoxia; tissue hypoxia can be determined with a transcutaneous oximetry measurement ($TcPO_2$) value of <40 mmHg, with reversibility and responsive to oxygen challenge[79,138,218] Some evidence to support consideration in cases of compromised grafts and flaps with concomitant hypoxia and impaired perfusion.[217]
Intermittent pneumatic compression (IPC)	The physiological effects include activating the skin's bioelectrical potential, attracting wound healing mediators, stimulating collagen and blood vessel formation, organizing collagen deposition, reducing tissue edema, improving blood flow and perfusion and generating an antibacterial effect[219,224,225] Thought to aid in the promotion of local circulation by increasing local collateral circulation, enhancing vasodilation, decreasing venous congestion and edema in the extremity[80]
Negative pressure wound therapy (NPWT)	Insufficient evidence to support the routine use for the management of arterial ulcers[226-228] Limited evidence has been obtained to recommend that NPWT may be safe to use on arterial ulcers; conclusions about other outcomes were not made[229] Frequent reassessment should be conducted to ensure ongoing appropriateness and safety of the therapy for a PAD/CLTI-related ulcer[226,227,229]

Spinal cord stimulation (SCS)	Study for the treatment of arterial ulcers is in its early stages[26] Stem cell/gene therapy is not recommended for patients with CLTI[26]
Topical oxygen therapy	Limited evidence to recommend the use of topical oxygen therapy to augment the healing of arterial ulcers. Further study is warranted to make any conclusions regarding its routine use[80]
Ultrasound therapy	No research currently available to recommend the routine use of therapeutic ultrasound to augment the healing of arterial ulcers[230] One limited RCT concluded that ultrasound therapy (MIST therapy) had a significantly higher rate of healing at 12 weeks specifically for ischemic (arterial ulcers[230]

Compression and Arterial Ulcers

There is limited evidence to recommend the cautious use of compression therapy to benefit the healing of ulcers that have been assessed to have mixed etiology (arterial and venous). In such cases, the presence of lower extremity edema is considered to be a barrier to wound healing.[79,138] When advanced CLTI is suspected, a decision to use compression is contraindicated until safe parameters can be determined for the patient, in collaboration with a vascular specialist. Accurate blood flow measures should be determined through appropriate investigations prior to applying compression. A lower level of compression may be appropriate for patients who have a documented ABPI >0.50 to <0.80, but should be avoided for those with an ABPI measure <0.50.[80]

Compression at higher levels may be appropriately used to manage lower limb edema after a successful revascularization procedure has been performed to restore adequate blood flow to the affected extremity.[62] In addition, the prescribing of a lower-level compression (18–30 mmHg) should be considered after lower extremity bypass surgery to manage edema.[80]

For further guidance on various types and indications for advance therapies refer to Chapter 4: Prevention and Management of Wounds: An Overview.[23]

4.4 Engage the team to ensure consistent implementation of the plan of care

A person who has been diagnosed with an arterial ulcer is living with a progressive chronic disease. Engaging the entire team, including the patient and their care partners, is an essential part of preventative care and chronic disease management.

Professional health-care team members who participate in plans of care for patients with CLTI should be actively engaged in educational strategies that teach and promote the prevention of ulceration, infection and amputation. Due to the complexity of PAD and its multiorgan involvement, an integrated team is needed.[231]

There is strong evidence to recommend the use of clinical pathways (structured multidisciplinary care plans) by health teams to optimize clinical outcomes, including a reduction in length of hospital stays, reduced in-hospital complications and costs.

Evans et al. developed an evidence based resource, The Foot Health Pathway for People Living with Diabetes. This pathway is based on population health principles by the Institute for Healthcare Improvement (IHI) and takes a risk-based approach focused on patient outcomes.[59] For more information see: https://www.woundscanada.ca/docman/public/1828-diabetic-foot-complications-b-ltr-1823e-final/file.

For further guidance on engaging the team for better patient outcomes refer to Chapter 4: Prevention and Management of Wounds An Overview[23] and Chapter 11: Prevention and Management of Diabetic Foot Ulcers.

Step 5: Evaluate Outcomes

Recommendations
5.1 Determine if the outcomes have met the goals of care

Regular evaluation of patient outcomes is an important aspect of care to determine whether the goals of care are being met. This should be an ongoing process carried out collaboratively with the patient and other members of the health-care team to ensure the goals of care are clearly understood and shared. When patients with arterial ulcers undergo treatment for PAD/CLTI, the goals of care may need to be modified, depending on the patient's response to treatment. The healability of the ulcer and the overall condition of the patient may change depending on the status of peripheral arterial blood flow and the effects of other comorbidities and other external modalities.

In cases of CLTI, achieving and sustaining optimal perfusion to the affected extremity through revascularization will significantly impact whether the original goals of care can be, or have been, met. When the original goals of care no longer seem achievable, setting new goals is an important step in supporting the patient's challenges in addressing the physical, psychological and emotional burden associated with the presence of CLTI. A conservative approach can be the best option at the terminal stage of CLTI. Patient-directed care that reflects a tailored approach is therefore essential.

5.2 Reassess patient, wound, environment and system if goals are partially met or unmet

When mutually agreed upon goals are not met through the process of arterial wound prevention or management, the team must return to Step 1 and reassess the factors that may be impacting the achievement of these goals. Careful attention should be made to any change in wound and vascular status, the degree and/or type of pain or progression of comorbidities and socio-economic changes in a patient's life that may increase stress and impact their ability to participate in any treatment plan.[79,138]

5.3 Ensure sustainability to support prevention and reduce risk of arterial ulcer recurrence

Ensuring access to ongoing vascular risk screening, foot care and primary health care will support the management of the associated risks for ulceration, recurrent ulceration or wound infection. Clinicians should review the patient's ability to participate in risk factor modification strategies (smoking cessation, medication therapy, appropriate nutrition, exercise programs), other medical therapies and activities that support mental health. Current best practice guidelines recommend that both smokers and ex-smokers be asked about smoking status at every visit with a health-care team member.[66] In addition, it is important to measure changes in the patient's overall condition and functional status in response to a therapeutic plan.

Sustaining adequate blood flow in the lower extremity in patients with CLTI is essential for managing the ongoing risk of arterial ulcers, infection, gangrene and amputation. Because there is a high incidence of re-stenosis when PAD is present, it is recommended that patients who have a prior history of CLTI, or have had a successful revascularization procedure, have scheduled follow-ups with a vascular specialist at least twice a year, or whenever wound progress stalls or deteriorates.[66] In addition, repeating blood flow measurements regularly is recommended after revascularization procedures to ensure ongoing patency of the vessel.[66] Yearly ABPI or TBPI testing may be valuable in providing a measure of disease progression.[49]

Patient and care partner education, in the form of both verbal and written instructions, is recommended to prepare the individual and their care partners on how to detect signs and symptoms of re-stenosis.[66]

Encouraging patients to be advocates for their own health will also enhance ongoing vigilance against recurrence of arterial ulcers. A simple measure of encouraging daily foot and leg inspections can be helpful in detecting early signs of complications associated with CLTI.

The goal of arterial wound care is not always to heal, but to protect from infection until arterial revascularization is achieved, if possible.[83]

Conclusion

The presence of arterial ulcers in the lower extremities can result in serious complications, including reduced quality of life, pain, infection, gangrene, amputation and death. Prevention of PAD that may lead to arterial ulcers and timely treatment of the underlying insufficiency in blood flow are essential. When blood flow cannot be adequately restored, aggressive preventative and management strategies must be employed.

Integrated teams managing the underlying disease process and employing preventative measures to optimize function and ensure the patient's ability to carry out activities of daily living are critical,[212] especially with older adults.[232] Reducing the incidence and recurrence of ulcers has been shown to reduce hospital admissions, the costs associated with treatment for wound infection, and community-based home visits, as well as having a significant impact on health-related quality of life.[233-236] The development of an integrated team is key in ensuring the patient's goals of care are met and through a comprehensive, evidence-based plan of care.

This chapter is intended to be a review and synthesis of the most current best practice guidelines specifically dedicated to the prevention and management of ulcers associated with PAD/CLTI. Currently, too few guidelines exist on this topic. However, the information contained in this and the introductory chapters can support health-care professionals, working in integrated teams, in the development and implementation of plans of care to prevent and manage arterial wounds and minimize unnecessary limb loss.

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