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2024 TSOC/TSPS Joint Consensus: Strategies for Advanced Vascular Wound Management in Arterial and Venous Diseases

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The Taiwan Society of Cardiology (TSOC) and Taiwan Society of Plastic Surgery (TSPS) have collaborated to develop a joint consensus for the management of patients with advanced vascular wounds. The taskforce comprises experts including preventive cardiologists, interventionists, and cardiovascular and plastic surgeons. The consensus focuses on addressing the challenges in diagnosing, treating, and managing complex wounds; incorporates the perfusion

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evaluation and the advanced vascular wound care team; and highlights the importance of cross-disciplinary teamwork. The aim of this joint consensus is to manage patients with advanced vascular wounds and encourage the adoption of these guidelines by healthcare professionals to improve patient care and outcomes. The guidelines encompass a range of topics, including the definition of advanced vascular wounds, increased awareness, team structure, epidemiology, clinical presentation, medical treatment, endovascular intervention, vascular surgery, infection control, advanced wound management, and evaluation of treatment results. It also outlines a detailed protocol for assessing patients with lower leg wounds, provides guidance on consultation and referral processes, and offers recommendations for various wound care devices, dressings, and products. The 2024 TSOC/TSPS consensus for the management of patients with advanced vascular wounds serves as a catalyst for international collaboration, promoting knowledge exchange and facilitating advancements in the field of advanced vascular wound management. By providing a comprehensive and evidence-based approach, this consensus aims to contribute to improved patient care and outcomes globally.

Key Words: Advanced wound care products • Endovascular intervention techniques • Epidemiology of vascular diseases • Multidisciplinary care approach • Vascular wound management

Abbreviations

ABI	Ankle-Brachial Index
BASIL	Bypass versus Angioplasty in Severe Ischemia of the Leg
CAD	Coronary artery disease
CI	Confidence interval
CKD	Chronic kidney disease
CLTI	Chronic limb-threatening ischemia
CRP	C-Reactive Protein
CVI	Chronic venous insufficiency
ESRD	End-stage renal disease
EVT	Endovascular therapy
FA	Fluorescent angiography
HBOT	Hyperbaric oxygen therapy
HR	Hazard ratio
ICG	Indocyanine green
LEA	Lower-extremity amputation
MACE	Major adverse cardiovascular event
MALE	Major adverse limb event
NIRS	Near-infrared spectroscopy
NSAID	Nonsteroidal anti-inflammatory drug
PAD	Peripheral artery disease
PEDIS	Perfusion, extent, depth, infection and sensation
pO_2	Pressure of oxygen
PTS	Postthrombotic syndrome
RPI	Regional perfusion index
SPP	Skin perfusion pressure
$TcPO_2$	Transcutaneous oxygen pressure
TSOC	Taiwan Society of Cardiology
TSPS	Taiwan Society of Plastic Surgery
VEGF	Vascular endothelial growth factor
WBC	White blood cell
WHO	World Health Organization
WIfI	Wound, Ischemia, and foot Infection

1. INTRODUCTION

Advanced vascular wounds, encompassing a spectrum of conditions, including chronic limb-threatening ischemia (CLTI) and chronic venous insufficiency (CVI), represent a significant and escalating burden on global health and social care systems. These wounds, often more prevalent and complex in nature, can manifest as CLTI — historically known as critical limb ischemia or severe ischemia of the leg — characterized by ischemic resting pain, typically worsening at night, and tissue loss, such as ulceration or gangrene, primarily affecting the foot. The rise in such cases is largely attributed to increased tobacco smoking and the surging incidence of type 2 diabetes. Additionally, CVI contributes to this growing challenge, further complicating the landscape of advanced vascular wound management.[1]

Advanced vascular wounds, a critical complication in the spectrum of diabetes-related health issues, present a significant epidemiological challenge globally. An estimated 19-34% of people with diabetes are expected to develop foot ulcers in their lifetime.[2] They are not only vulnerable to lower-extremity amputation (LEA) but are also affected in terms of long-term life expectancy, with a reduction in life expectancy. In patients with diabetic foot ulcers, the 5-year survival rate of is approximately 55% in both hospital- and community-based studies.[3] The survival rate in patients with diabetic foot ulcers receiving LEA was even worse and poorer than that of patients with common cancers.[4,5] These epidemiological data underscore the critical nature of advanced vascular wounds in diabetic patients. The high risk of amputation or death in patients with CLTI necessitates the consideration of revascularization in virtually all cases, alongside the best medical therapy, to restore the blood supply and reduce the likelihood of severe outcomes.

The scarcity of high-quality evidence, especially regarding advanced vascular wounds,[6] is readily apparent in the published literature and is also reflected in the low strength of recommendations found within various international guidelines.[7] Without timely intervention, the incidence of limb amputation is approximately 25% at 1 year after the diagnosis.[8] Surgical bypass and endovascular therapy are the principal revascularization strategies used to treat advanced vascular wounds. Even after initially successful revascularization, patients with advanced vascular wounds often require multiple procedures to maintain limb perfusion and frequent hospital readmissions for limb-related problems and other comorbidities, most commonly ischemic heart and respiratory disease, which usually coexist in this patient population.

In addition to identifying and addressing vascular insufficiency as the driving force of ischemic ulcerations, a systematic approach to local wound care minimizes the wound-healing time. Local wound management with infection control is also essential for wound healing in addition to revascularization. A multidisciplinary approach involving noninvasive assessment of wound healing followed by prompt revascularization when possible and aggressive wound care are all necessary to improve patient outcomes.

This consensus report addresses approaches to the management of both reperfusion and wound care in adults with advanced vascular wounds. The principles and approaches for achieving this goal are summarized in Figure 1.

Positional Statement 1:

1. The demographic shift toward an aging population has precipitated a notable increase in the incidence of peripheral artery diseases and the prevalence of advanced vascular wounds.
2. The implementation of systematic, evidence-based local wound management protocols, coupled with regular, noninvasive vascular assessments, is paramount in reducing advanced vascular wound-healing durations and averting potential complications.
3. A holistic approach to advanced vascular wound treatment mandates careful consideration and management of coexistent comorbid conditions to optimize overall treatment outcomes.

2. ADVANCED VASCULAR WOUND DEFINITION

Advanced vascular wounds, which include both venous and arterial wounds, are a complex group of wounds that create significant challenges in clinical settings.[9] These wounds often show a lack of response to healing, even after initial treatments such as percutaneous angioplasty, management of venous ulcers, or surgical procedures. The complexity of the wound and the treatment can sometimes lead to considerable tissue loss, muscle deterioration, and nerve damage, which can ultimately affect the function of the limbs.[10]

More specifically, if a wound does not show significant healing progress within a month after these treatments[11] or after the first vascular intervention, the restoration of limb function requires the combined efforts of a team of specialists. In such cases, the wound is identified as an advanced vascular wound.

The term “advanced” in advanced vascular wounds signifies a state of chronicity and complexity that necessitates a more comprehensive and aggressive approach to wound management. The failure of these wounds to heal following initial interventions indicates underlying complexities, such as persistent ischemia, uncontrolled infection, poor venous function, or unaddressed biomechanical stresses.[12]

Persistent ischemia refers to the continuous lack of blood supply to the wound area, which hinders the healing process. Uncontrolled infection, on the other hand, implies that the wound is constantly exposed to harmful bacteria or other pathogens, which can further deteriorate the wound condition. Poor venous function is often due to venous insufficiency or venous hypertension. Unaddressed biomechanical stresses can also contribute to the complexity of the wound-healing process. These stresses can result from factors such as pressure, shear,

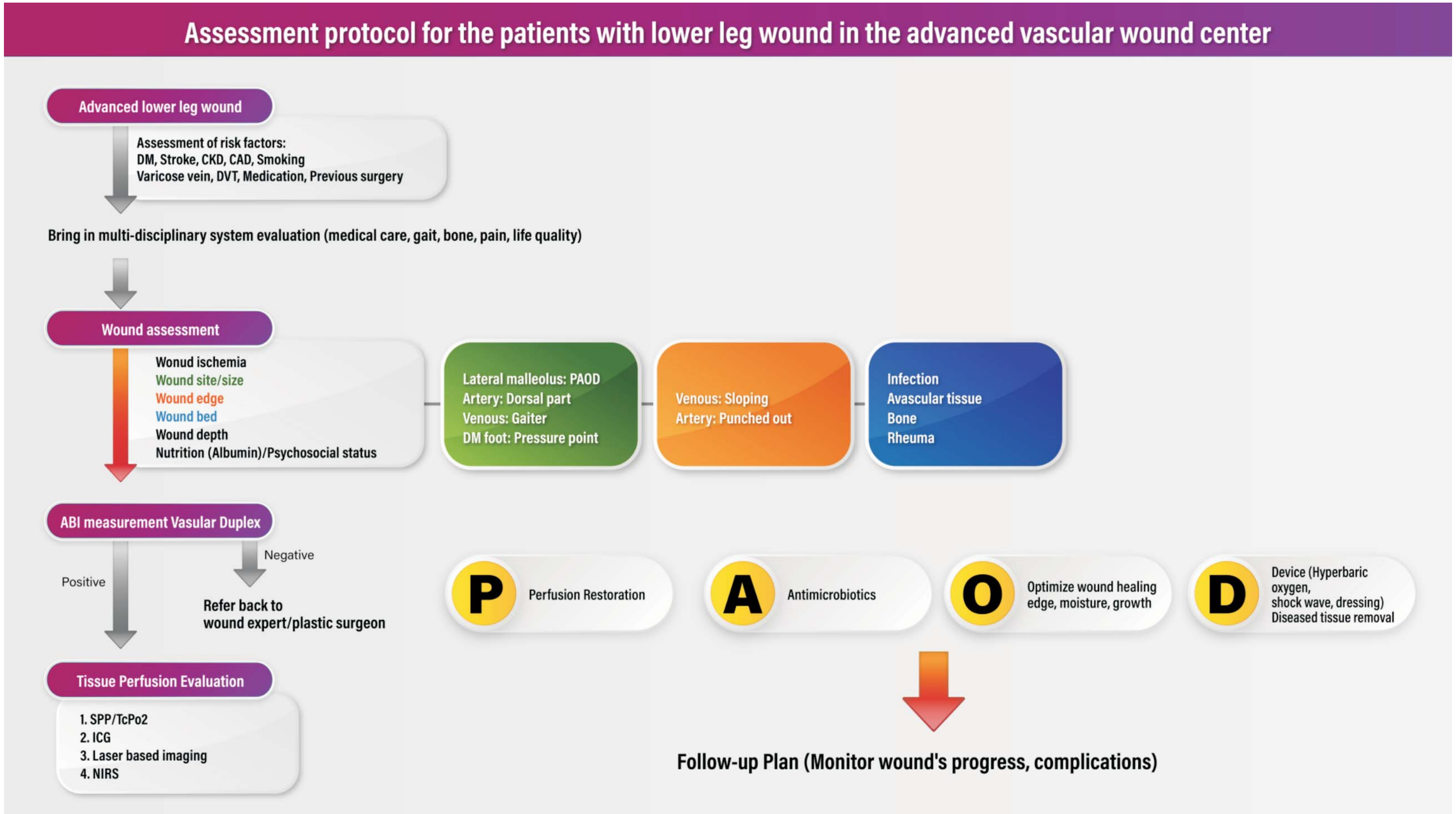

Figure 1. *Assessment protocol for the patients with log leg wound in the advanced vascular wound center. A comprehensive, multi-stage protocol for the management of advanced lower leg wounds in the context of arterial and venous diseases. The protocol initiates with an initial assessment of the wound and identification of risk factors. This is followed by a multidisciplinary system evaluation that integrates various medical specialties for holistic patient care. Key stages include detailed wound assessment, Ankle-Brachial Index (ABI) measurement to evaluate blood flow, and tissue perfusion evaluation to assess vascular health. The core of the protocol revolves around the P-A-O-D framework: [P] Perfusion Restoration – addressing vascular insufficiencies; [A] Antimicrobials – managing infection risks; [O] Optimization of Wound Healing – employing advanced therapeutic techniques; and [D] Device Utilization – integrating medical devices for wound care. This figure encapsulates the strategic approach outlined in the manuscript, emphasizing the sequential and interrelated steps essential for effective management of complex vascular wounds. CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; DVT, deep vein thrombosis; ICG, indocyanine green; SPP, skin perfusion pressure; TcPo2, transcutaneous oxygen pressure.*

or friction that can damage the tissue and impede wound healing.[13]

Furthermore, the complexities of advanced vascular wounds can also involve issues related to tissue, muscle, or other parts of the body. For instance, tissue damage or necrosis can exacerbate the wound condition, making it more difficult to heal.[14] Poor muscle function can impair limb mobility, tissue regeneration, and muscle pump function.[15,16] Other systemic factors, such as diabetes or immune disorders, can also play a role in the complexity of advanced vascular wounds, making them more challenging to manage and heal.[17]

The management of advanced vascular wounds requires a multidisciplinary, team-based approach involving cardiologists, vascular surgeons, plastic surgeons, endocrinologists and other healthcare professionals.[18] This collaborative approach ensures comprehensive care, addressing not only the wound itself but also the underlying vascular pathology, comorbid conditions, and patient's overall health status.

A crucial aspect of managing advanced vascular wounds is a detailed personalized examination of the vascular perfusion or status of the venous system, including venous duplex ultrasound and air plethysmography. This involves noninvasive vascular testing, such as the ankle-brachial index (ABI), quantitative perfusion by indocyanine green (ICG), transcutaneous oxygen pressure measurement, and skin perfusion pressure (SPP),[19] among others. These assessments provide valuable information about the extent of vascular disease and guide the development of a personalized treatment plan.

The impact of advanced vascular wounds extends beyond the physical damage. They significantly affect the patient's quality of life, causing pain, mobility restrictions, and psychosocial distress. The chronicity of these wounds often leads to prolonged treatment durations, frequent healthcare visits, and the need for advanced wound care therapies, all of which contribute to the economic burden for both the patient and the healthcare system.[20]

In conclusion, advanced vascular wounds represent a significant clinical and socioeconomic challenge. A clear understanding of their definition, implications, and the need for a detailed vascular assessment is crucial for all healthcare professionals involved in their management. This knowledge forms the basis for a collaborative, patient-centered approach to care, which is essential for improving clinical outcomes and enhancing the quality of life for patients with these complex wounds.

Positional Statement 2:

1. **Definition of Advanced Vascular Wounds:** Advanced vascular wounds are characterized by their chronic and complex nature, often showing a lack of response to initial treatments such as percutaneous angioplasty or management of venous ulcers within one month. These wounds are identified by significant healing challenges, including tissue loss, muscle deterioration, and nerve damage, necessitating a comprehensive and aggressive approach to treatment.
2. **Socioeconomic Considerations:** Recognizing the significant socioeconomic impact of advanced vascular wounds is essential. Strategies should aim to reduce their burden through cost-effective healthcare solutions and improve patient outcomes.

3. AWARENESS

The current state of advanced vascular wound care reveals a significant gap in the treatment and management of these complex conditions. Despite the severity and impact of advanced vascular wounds on patients' quality of life and economic burden, there is a concerning lack of awareness and undertreatment in many medical facilities.[21]

One of the highlighted gaps is the need for contemporary data on the prevalence of patients with advanced vascular wounds. Accurate data are crucial for understanding the magnitude of the problem and developing targeted interventions. The importance of the lack of detailed examinations of vascular perfusion or the status of the venous system is also critical for adequate treatment plans and wound-healing outcomes.[22]

The lack of a team approach in wound care is another significant issue. The positive impact of a multidisciplinary approach on wound care has been demonstrated in several studies. The opening of an outpatient wound center affiliated with an advanced vascular wound practice team was associated with a 64% increase in lower-extremity interventions and a 59% adjusted risk reduction of major amputation.[23]

Despite these promising results, many medical facilities still lack a team approach to wound care. This lack of a coordinated, multidisciplinary approach can lead to fragmented care, delayed treatment, and ultimately, poorer patient outcomes.[24]

In conclusion, there is a pressing need to raise awareness about the severity and complexity of advanced vascular wounds and to promote a multidisciplinary, team-based approach to their treatment. By doing so, we can improve patient outcomes, reduce the economic burden of these conditions, and ultimately improve the quality of life for patients suffering from advanced vascular wounds.

Positional Statement 3:

1. **Awareness and Data Gaps in Advanced Vascular Wound Care:** There is a critical need to increase awareness and understanding of advanced vascular wounds, particularly in light of the gap in contemporary data regarding their prevalence.
2. **Promotion of Multidisciplinary, Team-Based Care:** Promoting a multidisciplinary, team-based approach to the treatment of advanced vascular wounds is vital. This approach not only improves patient outcomes but also reduces the economic burden associated with these complex conditions.

4. TEAM STRUCTURE FOR THE MANAGEMENT OF ADVANCED VASCULAR WOUNDS

The management of advanced vascular wounds requires a multidisciplinary team approach, emphasizing the importance of a well-structured and collaborative team.[22] This team comprises a cardiologist, vascular surgeon, plastic surgeon, endocrinologist, rehabilitation specialist, specialized nurse, and a wound care specialist. The leadership is typically provided by the cardiologist, plastic surgeon, or vascular surgeon.

The team structure is designed to foster interdepartmental collaboration and communication, which are critical for the successful management of advanced vascular wounds. Importantly, the source of patients with advanced vascular wounds can come from any team members. A plastic surgeon may encounter a wound that requires more specialized vascular care, a cardiologist may identify an ischemic leg during a routine examination, or an endocrinologist may refer a patient with a nonhealing ulcer secondary to diabetes.[25] This underscores the importance of a well-coordinated team where each member understands the roles and capabilities of their colleagues.

Regular multidisciplinary meetings form the backbone of this structure. These meetings provide a platform for team members to discuss patient progress, share insights, and develop comprehensive treatment plans. The leadership role within the team is pivotal. The leader, whether a cardiologist, plastic surgeon, or vascular surgeon, is responsible for coordinating the team's efforts, ensuring effective communication, and making key decisions. They set the direction of the team, ensuring that the care provided is patient-centered and evidence-based.[26]

The team approach allows for the rapid translation of research findings into clinical practice. With a diverse team, new research in any of the relevant fields can be quickly disseminated within the team and applied to patient care. This accelerates the process of bringing new treatments from the laboratory to the bedside. Furthermore, the team approach can lead to the development of personalized treatment plans, which are increasingly recognized as the future of medicine. By considering the patient's condition from multiple perspectives, the team can develop a treatment plan that is tailored to the patient's unique needs and circumstances. This personalized approach can lead to better patient outcomes and improved quality of life.[27]

The team structure also includes mechanisms for feedback and improvement. Regular performance reviews and feedback sessions ensure that the team is constantly improving and adapting to changing patient needs and medical advancements. These sessions provide an opportunity for team members to reflect on their performance, identify areas for improvement, and develop strategies to enhance their practice.

In conclusion, the team structure for the management of advanced vascular wounds is characterized by its collaborative nature, regular multidisciplinary meetings, clear leadership, and fluid roles. The interaction within the team is based on mutual respect and trust, fostering a positive and productive team environment. This structure ensures comprehensive and coordinated care, leading to improved patient outcomes. It is a model that other areas of medicine could benefit from, highlighting the importance of collaboration and communication in health care.

Positional Statement 4:

1. **Multidisciplinary Team Composition:** The management of advanced vascular wounds necessitates a well-structured multidisciplinary team, typically including a cardiologist, vascular surgeon, plastic surgeon, endocrinologist, rehabilitation specialist, specialized nurse, and a wound care specialist. The collaboration among these diverse specialties is pivotal for effective wound management.
2. **Personalized Treatment Plans and Research Translation:** The team approach facilitates the rapid translation of research findings into clinical practice and the development of personalized treatment plans. By considering multiple perspectives, the team can tailor treatment to each patient's unique needs, leading to better outcomes and improved quality of life.

5. EPIDEMIOLOGY OF ADVANCED VASCULAR WOUNDS

5.1 Risk factors

In addition to the consideration of local vascular circulation compromise, caution should be exercised regarding systemic risk factors impairing vascular wound healing.[28]

5.1.1 Age and sex

Age-related changes and delays in wound healing are examined through clinical and animal studies.[29] Although aging causes a temporal delay in wound healing for healthy older adults,[30] it does not impair the quality of healing.[29] Delayed healing in the elderly is associated with slow migration of T cells and phagocytosis of macrophages,[31] along with delayed processes of re-epithelialization, collagen synthesis, and angiogenesis.[32] Various age-related changes in healing capacity have also been identified, including enhanced platelet function, increased secretion of inflammatory mediators, impaired immune cell function, and reduced secretion of growth factors.[29,33] Additionally, exercise has been found to improve wound healing in older adults and aged mice by reducing proinflammatory cytokine levels in wound tissue.[29]

Aged males have been found to experience delayed healing compared to that in aged females. This difference is partly attributed to the effects of sex hormones, including dehydroepiandrosterone, estrogens, and androgens, on the wound-healing process.[34] Estrogen promotes wound healing by modulating genes related to regeneration, matrix production, protease inhibition, epidermal function, and inflammation.[35] Studies suggest that estrogen can improve age-related healing impairments, while androgens have a negative impact on cutaneous wound healing.[34]

5.1.2 Diabetes

Diabetes induces high levels of advanced glycation end-products, leading to impaired wound healing by decreased growth factor production, angiogenesis, keratinocyte and fibroblast migration and proliferation and an abnormal balance between the accumulation of extracellular matrix components and their remodeling by matrix metalloproteinases.[36] Among these factors, insufficient angiogenesis could worsen hypoxia in advanced vascular wounds.[37] Dysfunctions in cellular processes, including T-cell immunity, leukocyte chemotaxis, phagocytosis, and fibroblast and epidermal cell functions, further contribute to inadequate bacterial clearance and delayed repair in diabetic wounds.[36,38] Inadequate angiogenesis and impaired mobilization and homing of endothelial progenitor cells are observed in diabetic wounds, with reduced levels of vascular endothelial growth factor (VEGF).[39] Diabetic neuropathy also plays a role in impaired wound healing. It has been noted that neuropeptides involved in cell chemotaxis and growth factor production are decreased and that leukocyte infiltration is reduced in skin with the loss of sensory nerves.[36,40]

5.1.3 Obesity

Obese individuals are more prone to wound complications such as infections, dehiscence, hematoma, seroma formation, pressure ulcers, and venous ulcers.[41] Factors contributing to these complications include decreased blood flow to adipose tissue, reduced oxygen delivery and antibiotic penetration, increased wound tension, hypovascularity, difficulty in repositioning, microbial colonization in skin folds, and friction from skin-on-skin contact.[42] Systemic factors, such as stress, anxiety, depression, and altered immunity associated with obesity, also contribute to impaired wound healing.[41]

5.1.4 Drugs

Systemic glucocorticoids inhibit wound repair by suppressing inflammation, fibroblast proliferation, collagen synthesis, and hypoxia-inducible factor-1 production, which is an essential transcription factor for wound healing.[43] However, the topical application of low-dose corticosteroids can accelerate wound healing.[44] Nonsteroidal anti-inflammatory drugs (NSAIDs) may have negative effects on healing, including decreased fibroblast numbers, weakened wound strength, delayed epithelialization, and impaired angiogenesis.[45] The impact of long-term NSAID use on wound healing is still unclear.

Chemotherapeutic drugs designed to inhibit cell division, metabolism, and angiogenesis can delay wound healing by decreasing fibroplasia, collagen production, and wound contraction.[46] These drugs also weaken the immune system and increase the risk of infection. Angiogenesis inhibitors that block VEGF receptors or the relevant intracellular signaling pathways have been associated with wound healing complications and wound dehiscence.[47]

5.1.5 Nutrition

Proper nutrition is crucial for wound healing, and deficiencies in nutrients can significantly impact the healing process. Carbohydrates are the main source of energy for wound healing, and this is particularly true of glucose, which provides fuel for cellular activities.[48] Protein is essential for various aspects of wound healing, including capillary formation, collagen synthesis, and immune system function.[49] Amino acids such as arginine and glutamine play important roles in host immunity, collagen deposition, and the inflammatory response.[49] Fatty acids, especially omega-3 fatty acids found in fish oil, may provide benefits for wound healing by influencing inflammation and immunity.[50]

Vitamins and micronutrients such as vitamins C, A, and E, magnesium, copper, zinc, and iron are also critical for optimal wound healing. Vitamin C deficiency impairs collagen synthesis and fibroblast proliferation,[49,51] while vitamin A deficiency affects cellular differentiation and collagen synthesis.[52] Vitamin E acts as an antioxidant and may help reduce excessive scar formation.[51,52] Micronutrients such as magnesium, copper, zinc, and iron serve as cofactors for various enzymes involved in protein synthesis and collagen production.[48,49,51]

5.1.6 Smoking

Tobacco smoke contains over 4,000 substances, including nicotine, carbon monoxide, tar, hydrogen cyanide, nitrogen oxides, N-nitrosamines, formaldehyde, and benzene, which impede healing by reducing tissue blood flow, causing tissue hypoxia, and impairing oxygen metabolism.[53] Smoking-induced vasoconstriction, mainly mediated by nicotine, can decrease blood flow by 40%.[54] In the inflammatory phase, smoking impairs the migration of monocytes and macrophages, reduces lymphocyte and natural killer cell activities, and inhibits bacterial detection by macrophages.[55] This impairs wound healing and increases the infection risk. In the proliferative phase, smoking hinders fibroblast migration and proliferation, impairs wound contraction and epithelial regeneration, decreases production of the extracellular matrix, and disrupts the balance of proteases.[56]

5.1.7 Alcohol

Alcohol diminishes host resistance and affects host defense mechanisms, with acute alcohol exposure resulting in suppressed proinflammatory cytokine release and decreased neutrophil recruitment and phagocytic function.[57] Ethanol exposure also influences the proliferative phase of healing, perturbing re-epithelialization, angiogenesis, collagen production, and wound closure[58] and reducing angiogenesis via a decrease in the expression of VEGF receptors and HIF-1a in endothelial cells.[59] Acute ethanol exposure also leads to impaired wound healing by inhibiting collagen production and altering the protease balance at the wound site.[60]

Evidence regarding the effects of chronic ethanol exposure on wound healing is scarce, although few animal studies have reported that liver cirrhosis might impair inflammatory and proliferative phases of wound healing and epithelialization in experimentally induced cirrhotic rats.[61]

5.1.8 Stress

The disruption of the neuroendocrine immune equilibrium caused by stress affects overall health.[62] It is mediated through the sympathetic-adrenal medullary and hypothalamic-pituitary-adrenal axes, thus increasing levels of hormones such as cortisol, prolactin, epinephrine, and norepinephrine. Psychological stress has been shown to delay wound healing in both humans and animals, as observed in caregivers of individuals with Alzheimer's disease and students experiencing academic pressure.[63] Stress affects the initial inflammatory phase of healing by increasing glucocorticoids and decreasing proinflammatory cytokines (such as tumor necrosis factor-α, interleukin-1α, interleukin-1β, interleukin-6, and interleukin-8) at wound sites.[64]

5.2 Wound fate

5.2.1 Acute phase

Acute wounds involve the disruption of skin integrity and further tissue injury caused by easily identifiable mechanisms, such as trauma. The wound examination should include the size, appearance, location, wound base, and exudate levels. The surrounding region should be examined for erythema, warmth, induration, discoloration, gangrene status, clubbing, cyanosis, capillary refill, and varicose veins.[65] Acute wounds normally heal in the order of four phases: hemostasis, inflammation, proliferation, and remodeling.[66] The cellular response to tissue injury activates keratinocytes, fibroblasts, endothelial cells, macrophages, and platelets, which release many growth factors and cytokines to maintain and achieve wound healing.

5.2.2 Cyanosis

Cyanosis is a pathologic condition with the appearance of a bluish discoloration of the skin or mucous membrane.[67] Peripheral cyanosis, compared to central cyanosis, is usually seen in the upper and lower extremities alone where the blood flow is insufficient or less rapid.[68] Thus, the progression of peripheral arterial disease will cause a mismatch of distal limb perfusion and lead to peripheral cyanosis.

5.2.3 Gangrene

Gangrene is a clinical condition of tissue necrosis due to tissue ischemia caused by circulatory obstruction or decompensation. It is characterized by black discolored tissue followed by sloughing of the superficial skin and deep tissue planes.[31] Wet gangrene and dry gangrene are the two major types of gangrene. Wet gangrene, which is often complicated by a secondary infection, has associated erythema and edema without crepitus. Gas gangrene can be a specific type of wet gangrene resulting from necrotizing infection with edema, crepitus, and gas revealed on radiographs. The involved necrotic lesions may extend into subcutaneous, fascial, and muscle compartments. Therefore, it decreases quality of life and increases the risk of substantial morbidity and mortality.[69] Dry gangrene is dry ischemic tissue primarily caused by diminished or total loss of blood supply and is often a progression of peripheral artery disease (PAD)-related ischemia to distal tissue. Thromboembolic disease and trauma to the vascular system may also result in the cessation of arterial flow. Vasculitis, popliteal entrapment, and Buerger disease (also known as thromboangiitis obliterans) may also contribute to ischemia and the development of gangrene.[70]

5.2.4 Chronic wounds

An ulcer lasting for more than three months is considered a chronic ulcer, in which the wound-healing process is arrested, usually at the inflammatory stage.[28] Thus, chronic wounds are frequently presented with continuous inflammation, which damages the newly developing extracellular matrix.[71] Chronic leg ulcers predominantly include venous ulcers, arterial ulcers and diabetic foot ulcers.

Venous ulcers due to venous hypertension account for 70-90% of leg ulcers. These complications result from venous stasis and venous valve incompetence in the deep veins, leading to distension and stretching of veins to accommodate the additional blood flow.[72]

Arterial ulcers account for approximately 10% of lower extremity ulcers, and the ischemia associated with PAD is the major cause.[73] Ischemic ulcers, which are related to poor perfusion, mostly develop at the most distal sites, such as the toe tips.

Diabetic foot ulcers account for almost 85% of amputations.[74] The causes of diabetic foot ulcers are multifaceted and are essentially related to peripheral neuropathy and ischemia from peripheral vascular disease.[75]

Charcot foot, which is also known as Charcot neuropathic osteoarthropathy, is an uncommon syndrome presenting as bone joint deformity and ulceration of the foot and ankle. The impaired sensation of pain associated with peripheral sensory neuropathy is associated with the development of arthropathy. The main cause of polyneuropathy is diabetes, which is more common than other causes, such as alcohol abuse or malnutrition.[76] Although the arterial blood flow in the foot is initially preserved or even exaggerated, patients with chronic deformities may develop subsequent limb-threatening ischemia.[77]

Therefore, nonhealing ulcers that persist for more than two weeks require an urgent perfusion evaluation for revascularization to prevent further limb loss.[78]

5.2.5 Granulation tissue

The formation of granulation tissue starts in the proliferative phase of wound healing. Granulation tissue develops from two major components: cells and proliferating capillaries. Fibroblasts migrate into the wound and synthesize components of granulation tissue. The growth of new capillaries, called angiogenesis, replaces the damaged vasculature and forms a new circulatory network.[79] These vessels form strawberry-colored granular tissue within the wound bed. The granulation tissue is very fragile and should be protected with dressings or bandages.

5.2.6 Distal amputation

Partial foot amputation and disarticulation can be considered, rather than proximal limb amputation and disarticulation, in selected cases of trauma, diabetic foot, or infection with or without peripheral vascular disease. Partial foot ablations are preferred because direct weight bearing on the residual foot with proprioceptive feedback along normal neural pathways is preserved, rather than ablation at proximal levels. Therefore, preservation of a partial foot is essential to maintain independent ambulation, especially if amputation of the second limb may take place within a few years.

The most common indication for partial amputation is infection with tissue necrosis in diabetic persons.[80]

The major determinant of the amputation level is tissue oxygen perfusion. Vascular recanalization or hyperbaric oxygen therapy (HBOT) should be considered to improve arterial flow or oxygenation if transcutaneous oxygen values are less than 30 mmHg.[81]

5.2.7 Major amputation

Major amputation of the lower extremity is typically defined at the level above the ankle. Acute limb ischemia, trauma, and diabetic foot with infection are the major causes, and amputation is an important treatment option to save lives and proximal limbs.[21] Major amputations are usually performed at the below-knee or above-knee level depending on the level of tissue ischemia, infection or damage. A prosthesis is needed for returning to independent ambulation. However, above-knee amputation poses less opportunity for independent ambulation than a below-knee amputation stump.[82]

5.3 Fate of patients

Vascular wounds pose a significant health concern that can have severe complications, potentially leading to death.[83] In a cohort study conducted in Taiwan, individuals with vascular wounds faced a significantly higher mortality risk than those with claudication, who exhibited an 85% 5-year survival rate. Specifically, half of the patients with vascular wounds did not survive beyond the 5-year mark. The fate of patients with advanced vascular wounds depends on various factors, including the severity of the wound, the presence of comorbidities, and the overall health of the individual. Healthcare providers should work closely with patients to develop personalized treatment plans that address their specific needs and improve their quality of life. By addressing symptoms, managing comorbidities, and promoting rehabilitation, patients with advanced vascular wounds can achieve better outcomes and improved quality of life.

Next, we discuss the fate of patients with advanced vascular wounds, focusing on six factors: asymptomatic wounds, claudication, pain, comorbidity, muscle loss, and walking ability.

5.3.1 Asymptomatic wounds

Asymptomatic vascular wounds are those that do not cause any pain or discomfort. These wounds may be small and superficial. Among long-term diabetic patients, 58% develop symmetric distal polyneuropathy, leading to a loss of protective sensation that can conceal significant symptoms. Combined with anatomical deformities, exposure of the foot to repetitive stress leads to ulcer formation.[84] However, without proper treatment, these wounds can progress and lead to severe complications, such as infections, amputations, and even death.[85] Therefore, it is crucial to monitor and promptly treat asymptomatic vascular wounds to prevent further complications.

5.3.2 Claudication

Claudication is another symptom experienced by patients with advanced vascular disease. It occurs when there is a lack of blood flow to the legs, resulting in pain, cramping, or weakness. This can make it challenging for patients to walk or engage with physical activities. Treatment for claudication may involve lifestyle changes, medications, or revascularization procedures. It is worth noting that patients with vascular intermittent claudication are at 5-year mortality risk of 30%, mostly related to cardiovascular complications.[26]

5.3.3 Pain

Pain is a common symptom experienced by patients with advanced vascular wounds. The pain associated with peripheral vascular wounds can be severe and debilitating, making it difficult to walk, sleep, and perform daily activities. Additionally, pain can be an indication of infection, further complicating the patient's care. Pain management is an essential aspect of treating advanced vascular wounds, and healthcare providers should work closely with patients to develop a personalized pain management plan.

5.3.4 Comorbidity

Comorbidities are often present in patients with advanced vascular wounds. Diabetes is one of the most common comorbidities associated with vascular wounds. Diabetes can affect wound healing in several ways, including reduced blood flow, neuropathy, and increased risk of infection.[85] Hypertension is associated with an increased risk of vascular diseases, including PAD and atherosclerosis, leading to the development and progression of vascular wounds.[21] Coexisting cardiovascular conditions, such as coronary artery disease (CAD) and congestive heart failure, can worsen the prognosis of patients with vascular wounds. These conditions often indicate a more severe underlying vascular disease burden and can increase the risk of complications and mortality.[86] Chronic kidney disease (CKD) can also affect wound healing. This is partially because CKD can lead to anemia, thereby reducing the amount of oxygen that is delivered to the tissues.[87] Malnutrition can also affect wound healing. This is because malnutrition can lead to a deficiency of protein and other nutrients that are essential for wound healing. Managing these comorbidities effectively is crucial to improve the patient's overall health and reduce the risk of complications.

5.3.5 Muscle loss

Muscle loss, or muscle atrophy, can occur in patients with vascular wounds, especially in chronic or severe cases. Skeletal muscle plays a crucial role in wound healing by providing structural support, promoting blood flow, and facilitating tissue regeneration. The loss of muscle mass can delay wound closure and increase the risk of complications. Weakened muscles can affect a patient's ability to perform daily activities, including walking, which can further impact their quality of life and independence. Muscle loss in patients with vascular wounds is associated with an increased risk of wound recurrence. Weak muscles may not provide adequate support to the affected areas, making them more susceptible to the recurrence of injury and the development of new wounds.[88] Monitoring and addressing muscle loss in patients with advanced vascular wounds are essential for prognosis improvement.

5.3.6 Walking ability

Vascular wounds can significantly affect a patient's walking ability by causing pain, reduced blood flow, and tissue damage in the lower extremities. The outcome of the patient's walking ability depends on the type and severity of the vascular wound, the underlying causes, and the treatment received. Exercise therapy, compression therapy, or surgical intervention could improve walking ability, although permanent disability or limb loss may still occur.[87]

5.3.7 Outcomes

Patients with PAD and advanced vascular wounds face complex outcomes, including increased mortality, cardiovascular and noncardiovascular morbidities, and reduced quality of life. The risk of acute myocardial infarction and cerebrovascular accidents is notably higher in this group, linked to the compromised vascular health inherent in PAD.[89] These conditions further heighten the likelihood of gastrointestinal bleeding, especially under antiplatelet or anticoagulant therapy.[90]

Renal complications are also significant, with an escalated risk of acute kidney injury and progression to CKD, often due to impaired blood flow and medication effects.[91] Infections, both at the wound site and systemically, are common, complicating the treatment and recovery process.[92]

Mortality rates are substantially higher, primarily due to cardiovascular causes that are compounded by comorbidities such as diabetes and hypertension. Quality of life is severely impacted by factors such as chronic pain, mobility restrictions, and the psychological strain of chronic illness, emphasizing the need for holistic, patient-centered care to improve outcomes.[1]

Positional Statement 5:

1. Personalized care plans for advanced vascular wound treatment should focus on patient-specific factors (age, sex, diabetes, obesity, drug, nutrition, smoking, alcohol) and lifestyle modifications.
2. Nutritional support and exercise are vital for advanced vascular wound healing, especially in elderly patients.
3. Patients with PAD and advanced vascular wounds face very high cardiovascular risks and reduced quality of life.

6. CLINICAL PRESENTATIONS

Among advanced vascular wounds, diabetic foot wounds are the most common in clinical setting. Assessments of advanced vascular wounds are an important bridge between physicians and surgeons. Such patients are at risk for worsening foot ulceration, which can significantly increase the risk of certain situations for amputation. For effective organization of foot wound assessments, guidelines from the International Working Group of the Diabetic Foot are essential.[93] The Society for Vascular Surgery Lower Extremity Guidelines Committee developed the Wound, Ischemia, and foot Infection (WIfI) Classification System. This system helps categorize the three primary risk factors for amputation.[94]

Accordingly, the key elements of limb status are proposed to readily gauge the severity of the limb threat and to accurately predict the risk of amputation, using the perfusion, extent, depth, infection and sensation (PEDIS) score system and WIfI classification.

6.1 Classifications

The clinical presentation will be described by the scoring system. The grades are defined in Table 1 and Table 2. Table 3 presents a comprehensive summary of various limb and wound classification systems, categorizing them based on the presence of ulceration, gangrene, and infection in the afflicted limb and associated wounds.

6.2 Clinical presentations

6.2.1 Wound with PEDIS 1-2

Case 1: A 72-year-old female diabetic patient with plantar ulcer, ABI: 1.2, no bone or tendon exposure. ABI: 1.08/1.16. with diffuse arterial calcification in the bilateral lower limbs. The series of wound pictures were taken within 4 months [Figure 2A, (P1ED1I1S1), (WIfI: W1I0fI0)]. Case 2: A 58-year-old male with diabetes with end-stage renal disease (ESRD), shallow ulcer at the 5th metatarsophalangeal joint level, X-ray without bony destruction, white blood cell (WBC): 4.8 k/μL, C-Reactive Protein (CRP): 24.35, ABI: 1.49/1.29, patent femoropopliteal arteries [Figure 2B, (P1ED2I1S1), (WIfI: W1I0fI)].

6.2.2 Wound with PEDIS 3

Case 3: A 47-year-old female diabetic patient with a right foot plantar ulcer (Figure 2C). The X-ray showed 2nd metatarsophalangeal joint osteomyelitis (Figure 2C). Circulation is normal (P2ED2I3S2), (WIfI: W2I0fI2). Case 4, An 85-year-old male diabetic patient with CAD post percutaneous transluminal angioplasty, ESRD, right foot progressive gangrene, refused major limb amputation, intravenous antibiotic treatment, WBC: 6.9 k/μL, CRP: 42.27, ABI: 0.88/0.72 (Figure 2D) (P3ED3I3S2), [WIfI: W3I2fI3, no transcutaneous oxygen pressure ($TcPO_2$) data, adjusted scoring data].

6.2.3 Wound with PEDIS 4

Case 5: A 93-year-old male diabetic patient with sepsis, necrotizing fasciitis of the plantar central compartment, and 2nd toe necrosis. WBC: 29.1 K/μL, CRP: 194, ABI: 0.13/0.20. [Figure 2E, (P3ED3I3S2), (WIfI: W3I3fI3)]. Case 6: A 56-year-old female diabetic patient

Table 1. PEDIS scoring system

	Degree of severity			
Grading	I	II	III	IV
Perfusion	Normal: palpable pedal pulses or • ABI: 0.9-1.1 • TBI > 0.6 • TcPO2 > 60 mmHg	Clinical evidence if impaired perfusion: intermittent claudication, • ABI < 0.9 with ankle SBP > 50 mmHg • TBI < 0.6 with toe SBP > 30 mmHg • TcPo2 30-60 mmHg	Critical limb ischemia: resting pain: • Ankle SBP < 50 mmHg • Toe SBP < 30 mmHg • TcPo2 < 30 mmHg • ABI < 0.4	
Extent	Wound size (measured in square centimeters) should be determined after debridement, if possible.			
Depth	Superficial ulcer within the dermis	Ulceration may involve all soft tissue, involving fascia, muscle, or tendon.	Penetrating to bone: osteolytic in X-ray or positive in probe-to-bone test	
Infection	No symptoms or signs of infection	Infection involving the skin and the subcutaneous tissue only (without involvement of deeper tissues and without systemic signs as described below). At least 2 of the following items are present: • Local swelling or induration; • Erythema > 0.5 to 2 cm around the ulcer; • Local tenderness or pain; • Local warmth; and/or • Purulent discharge	Erythema > 2 cm plus one of the items described above (swelling, tenderness, warmth, discharge) or Infection involving structures deeper than skin and subcutaneous tissues such as abscess, osteomyelitis, septic arthritis, fasciitis. No systemic inflammatory response signs, as described below.	Any foot infection with the following signs of a systemic inflammatory response syndrome (SIRS). This response is manifested by two or more of the following conditions: • Temperature > 38 or < 36 Celsius; • Heart rate > 90 beats/min; • Respiratory rate > 20 breaths/min; • PaCO2 < 32 mmHg; • White blood cell count > 12.000 or < 4.000/cu mm; and/or • 10% immature (band) forms.
Sensation	No loss of protective sensation on the affected foot detected, defined as the presence of sensory modalities described below.	Loss of protective sensation on the affected foot is defined as the absence of perception of the one of the following tests in the affected foot: • Absent pressure sensation, determined with a 10 gram Monofilament, on 2 out of 3 sites on the plantar side of the foot, as described in the International Consensus on the Diabetic Foot; and/or • Absent vibration sensation, (determined with a 128 Hz tuning fork) or vibration threshold > 25 V, (using semi-quantitative techniques), both tested on the hallux.		

ABI, Ankle-Brachial Index; SBP, systolic blood pressure; TBI, toe-brachial index; TcPo2, transcutaneous oxygen pressure.

Table 2. WIfI scoring system (wound, Ischemia, and foot Infection)

Wound		
Grade	DFU	Gangrene
0	No ulcer	No gangrene
1	Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx	No gangrene
2	Deeper ulcer with exposed bone, joint or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement	Gangrenous changes limited to digits
3	Extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer ± calcaneal involvement	Extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis ± calcaneal involvement

Ischemia			
Grade	ABI	Ankle systolic pressure (mmHg)	TP, TcPO2 (mmHg)
0	≥ 0.80	> 100	≥ 60
1	0.6-0.79	70-100	40-59
2	0.4-0.59	50-70	30-39
3	≤ 0.39	< 50	< 30

Foot infection	
0	No symptoms or signs of infection
	Infection present, as defined by the presence of at least 2 of the following items: • Local swelling or induration • Erythema > 0.5 to ≤ 2 cm around the ulcer • Local tenderness or pain • Local warmth • Purulent discharge (thick, opaque to white, or sanguineous secretion)
1	Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). Exclude other causes of an inflammatory response of the skin (e.g., trauma, gout, acute Charcot neuro-osteoarthropathy, fracture, thrombosis, venous stasis)
2	Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (e.g., abscess, osteomyelitis, septic arthritis, fasciitis), and no systemic inflammatory response signs (as described below)
3	Local infection (as described above) with the signs of SIRS, as manifested by two or more of the following: • Temperature > 38 °C or < 36 °C • Heart rate > 90 beats/min • Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg • White blood cell count > 12,000 or < 4000 cu/mm or 10% immature (band) forms

ABI, Ankle-Brachial Index; DFU, diabetic foot ulcer; PaCO2, partial pressure of carbon dioxide; SIRS, systemic inflammatory response syndrome; TcPO2, transcutaneous partial oxygen pressure; TP, toe pressure for predicting the outcome of an ulcer in a specific individual.

Table 3. The descriptions of ulcer, gangrene, and infection regarding the affected limb and wound

	Ulcer	Gangrene	Infection
Rutherford	Category 5: minor tissue loss, nonhealing ulcer, focal gangrene with diffuse pedal ischemia	Category 6: major tissue loss above trans-metatarsal level, functional foot no longer salvageable (although in practice often refers to extensive gangrene, potentially salvageable foot with significant effort	
Fontaine	Class IV/IV, ulcer and gangrene grouped together	Class IV/IV, ulcer and gangrene grouped together	
PEDIS	Grade 1: superficial full-thickness ulcer, not penetrating deeper than the dermis; Grade 2: deep ulcer, penetrating below the dermis to subcutaneous structures involving fascia, muscle or tendon; Grade 3: all subsequent layers of the foot involved including bone and/or joint (exposed bone, probing to bone)		Yes, grades 1-4; see IDSA classification
UT	Grade 0: pre- or postulcerative completely epithelialized lesion; Grade 1: superficial, not involving tendon, capsule, or bone; Grade 2: penetrating to tendon/capsule; Grade 3: penetrating to bon		Yes, +/- wounds with frank purulence or > 2 of the following (warmth, erythema, lymphangitis, edema, lymphadenopathy, pain, loss of function) considered infected
Wagner	Grade 0: pre- or postulcerative lesion; Grade 1: partial/full thickness ulcer; Grade 2: probing to tendon or capsule; Grade 3: deep ulcer with osteitis; Grade 4: partial foot gangrene; Grade 5: whole foot gangrene	Ulcer and gangrene grouped together; gangrene due to infection not differentiated from gangrene due to ischemia; also includes osteomyelitis	Included only as osteomyelitis
S(AD)SAD system	Grades 0-3 based on area and depth; Grade 0: skin intact; Grade 1: superficial, < 1 cm^2; Grade 2: penetrates to tendon, periosteum, joint capsule, 1-3 cm^2; Grade 3: lesions in bone or joint space, > 3 cm^2		Yes, 1 = no infection; 2 = cellulitis; 3 = osteomyelitis
Saint Elian	Grades 1-3 based on depth; Grade 1: superficial wound disrupting entire skin; Grade 2: moderate or partial depth, down to fascia, tendon or muscle but not bone or joints; Grade 3: severe or total, wounds with bone or joint involvement, multiple categories including area, ulcer number, location and topography		Grade 0: none; Grade 1: mild, erythema 0.5-2 cm, induration, tenderness, warmth and purulence; Grade 2: moderate, erythema > 2 cm, abscess, muscle tendon, joint, or bone infection; Grade 3: severe, systemic response (similar to IDSA)

Table 3. Continued

	Ulcer	Gangrene	Infection
IDSA			Uninfected, mild, moderate, and severe
SVS lower extremity threatened limb classification	Grades 0-3: grouped by depth, location and size and magnitude of ablative/ wound coverage procedure required to achieve healing	Grades 0-3: grouped by depth, location and size and magnitude of ablative/ wound coverage procedure required to achieve healing	Yes, IDSA system
WIfI	Grade 0: no ulcer; Grade 1: small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx; Grade 2: deeper ulcer with exposed bone, joint or tendon; generally not involving the heel; shallow heel ulcer, without calcaneal involvement; Grade 3: extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer 6 calcaneal involvement	Grade 0 or 1: no gangrene; Grade 2: gangrenous changes limited to digits; Grade 3: extensive gangrene involving forefoot and/or midfoot; full thickness heel necrosis +/- calcaneal involvement	Yes, IDSA system

IDSA, Infectious Diseases Society of America; PEDIS, perfusion, extent, depth, infection and sensation; The S(AD) SAD classification: size (area and depth); sepsis, arteriopathy, denervation; UT, The University of Texas Wound Classification System.

suffered from left foot ischemia, plantar necrotizing fasciitis with resistant-strain pathogen infection, WBC: 19.8 k/μL, CRP: 207.89, ABI: 0.95/0.2 [Figure 2F, (P3ED3I3S2), (WIfI: W3I3fI3)].

6.3 Venous wounds

Venous wounds, also known as venous ulcers, are common and persistent types of chronic wounds that occur in the lower extremities due to poor venous circulation. Venous ulcers are commonly found in the gaiter area of the lower leg and ankle, where venous hypertension and valve dysfunction lead to the development of these ulcers. Clinically, venous ulcers present as shallow, irregularly shaped wounds with a wide base and sloping edges, which set them apart from other types of chronic wounds.[95] The unique presentation is caused by the presence of venous insufficiency in the lower extremities, which results in blood pooling and increased venous pressure.

An important characteristic of venous ulcers is their exudative nature. A moderate to high quantity of exudate is produced by these wounds, which can include serous, serosanguinous, or even purulent fluid in the case of infection.[33] Consequently, excessive moisture from the exudate can lead to maceration of the surrounding skin, posing a challenge for wound healing and posing an increased risk of infection.[10]

In addition to the physical appearance of the wound, venous ulcers are also characterized by specific clinical features that are distinct from other types of wounds. Usually, erythema and warmth are seen around the wound edges as a result of local inflammation (Figure 3). The affected area is frequently tender and uncomfortable, which can further hinder mobility and daily activities. Furthermore, CVI can cause changes in the surrounding skin, such as edema and hyperpigmentation.[96]

It is important to understand the distinct clinical presentation of venous ulcers to make an accurate diagnosis and to manage them effectively. Prompt recognition and intervention are essential to prevent complications, promote optimal wound healing, and improve the patient's overall quality of life.

6.4 Differential diagnosis and comorbidity

An ulcer presenting for more than three months is considered a chronic ulcer. Venous insufficiency is re-

Figure 2. *PEDIS Wound Classification. (A) Illustrates a healing wound classified as PEDIS 1, demonstrating initial stages of recovery. (B) Depicts a healing wound classified as PEDIS 2, showing further progression in the healing process. (C) Presents a wound at the PEDIS 3 stage alongside its corresponding X-ray image, highlighting underlying structural changes. (D) Shows another example of a wound at the PEDIS 3 stage, providing additional insights into this level of severity. (E) & (F) Both depict wounds classified as PEDIS 4, showcasing advanced stages of wound complexity and severity.*

Figure 3. *A venous wound located on the lower leg of a patient. The wound appears as a shallow ulcer with irregular edges and a red, inflamed border. The surrounding skin displays signs of chronic venous insufficiency and stasis dermatitis, such as visible erythema, edema, and hyperpigmentation. Granulation tissue is partially present in the ulcer bed, with areas of yellowish slough seen in the center.*

sponsible for approximately 70% of leg ulcers, arterial disease accounts for 10%, and ulcers of mixed etiology make up 15% of leg ulcer cases. The remaining 5% of leg ulcers are caused by less common pathophysiological factors, presenting significant challenges in terms of diagnosis[75] (Figure 4).

While patient history and clinical examination can often provide sufficient information to determine the underlying cause of an ulcer, understanding the differential diagnoses and initiating early therapy are crucial for ensuring successful treatment outcomes in ulcer patients.

CVI refers to a collection of clinical manifestations affecting the skin and subcutaneous tissue that occur as

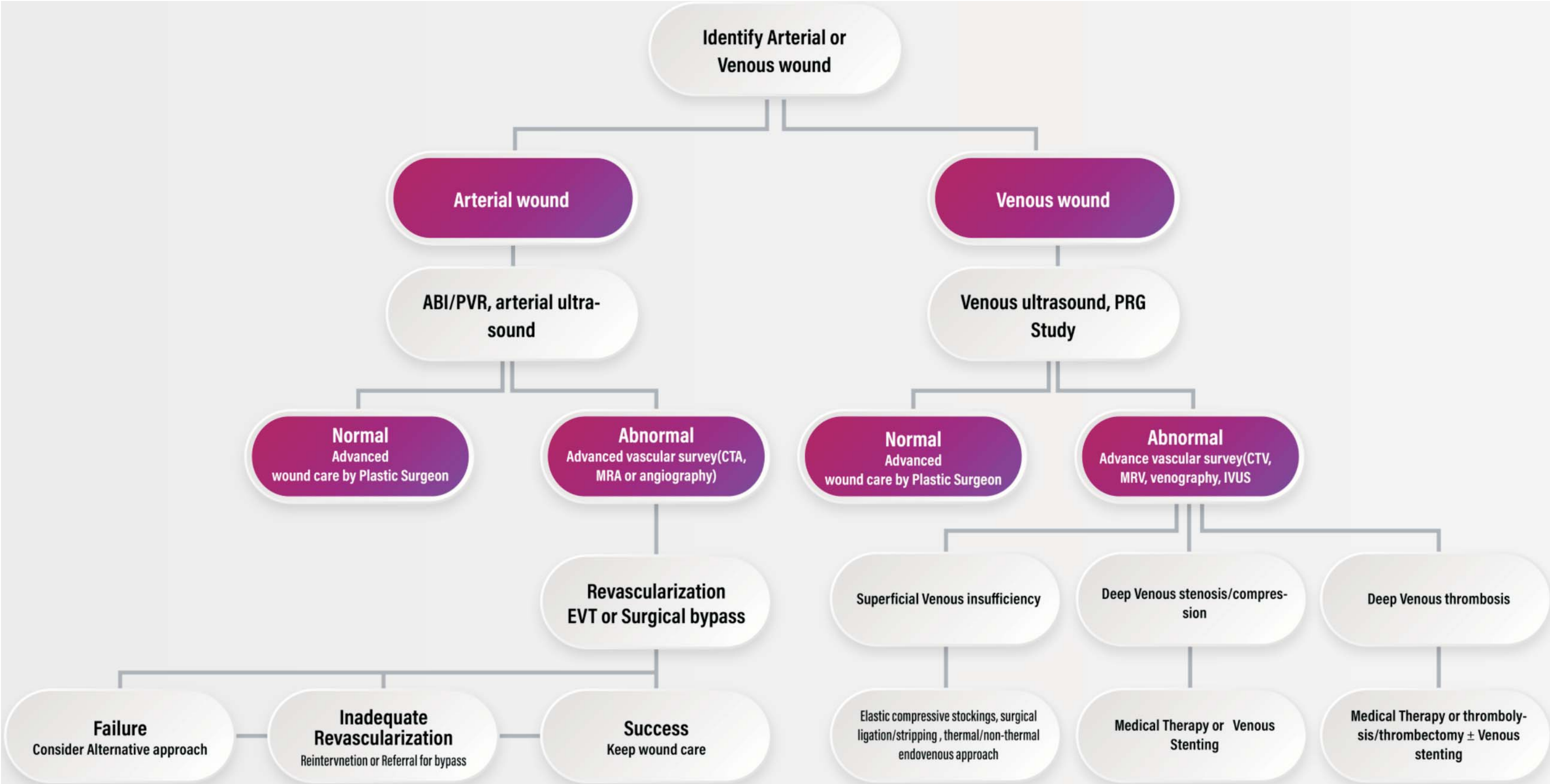

Figure 4. *Distinct treatment algorithms for arterial and venous wounds. Left side of the figure details the treatment algorithm for arterial wounds, emphasizing the importance of restoring blood flow, addressing ischemia, and managing underlying arterial disease. It outlines steps ranging from initial assessment to advanced surgical interventions, tailored to the specific challenges of arterial wound healing. Right side of the figure presents the treatment algorithm for venous wounds. This algorithm focuses on improving venous return, managing edema, and treating venous insufficiency. It includes strategies such as compression therapy, wound debridement, and possibly surgical correction of venous pathology. ABI, ankle-brachial index; CTA, computed tomography angiography; CTV, computed tomography venography; EVT, endovascular therapy; IVUS, intravascular ultrasound; MRA, magnetic resonance angiography; MRV, magnetic resonance venography; PRG, phleborheography; PVR, pulse volume record.*

a result of chronic venous disease. CVI commonly develops due to postthrombotic syndrome (PTS), varicose veins, or arteriovenous malformations. Predisposing factors for CVI include advanced age, genetic factors, pregnancy, and prolonged periods of standing.[97]

It is estimated that approximately 10% of patients with CVI will develop a chronic wound, with a wound-related mortality rate of 2.5%. A venous leg wound generally can be diagnosed by some typical clinical findings, including blow-out veins, edema, corona phlebectatica paraplantaris, atrophie blanche, acroangiodermatitis, lipodermatosclerosis, and stasis dermatitis above the medial malleolus and on the lower leg.

PAD is a medical condition characterized by the narrowing or blockage of arteries that supply blood to the peripheral regions of the body, most commonly affecting the lower extremities. The most common cause of PAD is atherosclerosis. Major risk factors include smoking, diabetes, hypertension, and hyperlipidemia. Other causes of PAD include vasculitis. PAD-related ulcers are commonly found on the lower extremities with irregular shapes, very low healing, and necrotic tissue. Patients often experience intermittent claudication before developing ulcers. Arterial leg ulcers, in comparison to venous leg ulcers, are more frequently associated with severe pain.

Martorell hypertensive ischemic leg ulcers are extremely painful lesions, occurring most often in women rather than men; these wounds commonly involve the lateral-dorsal calf and surrounded by a highly inflammatory rim that may ulcerate with minimal trauma. The patient's arterial diastolic pressure is often continuously higher than 95 mmHg and is associated with hypertension and diabetes.[98]

Primary systemic vasculitis can involve large vessels (giant cell arteritis and Takayasu disease), medium-sized vessels (polyarteritis nodosa and Kawasaki arteritis), and small vessels (Wegener granulomatosis, Churg-Strauss syndrome, microscopic polyarteritis, Henoch-Schönlein purpura, essential cryoglobulinemia, and cutaneous leukocytoclastic vasculitis). Secondary vasculitis is associated with drug reactions, special infections, or neoplasms.

Wegener granulomatosis often manifests with the classical triad of ear, nose, throat, lung and renal involvement with necrotizing granulomatous inflammation and vasculitis. Cutaneous manifestations, including leg ulcers, tend to occur in later stages of the disease in approximately 40% of patients.[99] Detection of anti-neutrophilic cytoplasmic antibodiesis the main test to diagnose Wegener granulomatosis.

While cutaneous manifestations such as malar and discoid rashes are frequently observed in patients with systemic lupus erythematosus, the occurrence of ulceration is uncommon. In a retrospective study, approximately 1.6% (11/670) of patients with systemic lupus erythematosus had ulcers or ischemic lesions.[100] Typical histological findings in cutaneous lupus include vasculitis with necrosis of blood vessel walls and infiltration of polymorphonuclear cells.[101]

In the course of their disease trajectory, approximately 10% of individuals afflicted with rheumatoid arthritis will manifest pedal ulceration.[102] Tissue biopsies of rheumatoid arthritis ulcers may not always reveal clear pathological features of vasculitis. A cohort study of patients with rheumatoid arthritis and ulcers revealed that all had radiographic evidence of erosive disease. However, PAD and CVI may also develop in such patients. Treatment with immunomodulatory agents could also potentially inhibit wound healing or induce vasculitis. Therefore, ulcer presentation in autoimmune disease patients requires a thorough differential diagnosis.

Pyoderma gangrenosum is a rare noninfectious neutrophilic dermatosis that causes painful large ulcers. Pyogenic granuloma is often associated with systemic diseases, such as ulcerative colitis, Crohn's disease, or myeloproliferative disorders. However, approximately 50% of patients do not have underlying diseases.[103] The diagnosis is made clinically after excluding other similar skin disorders. The diagnosis relies on clinical signs and is supported by biopsy for histopathology.

A number of metabolic disorders, such as necrobiosis lipoidica, porphyria cutanea tarda, hyperhomocysteinemia, prolidase deficiency, hyperoxaluria, ulcerative colitis, avitaminosis, cutaneous calcinosis, and calciphylaxis, can lead to leg ulcers. These disorders can contribute to ulcers through various mechanisms, including tissue damage, disrupted blood circulation, chronic inflammation, and calcium deposition.

Hematologic diseases, including sickle cell disease, leukemia, thrombocytosis, thalassemia, hereditary spherocytosis, glucose-6-phosphate dehydrogenase deficiency, essential thrombocythemia, granulocytopenia, polycythemia, monoclonal and polyclonal, and dysproteinemia, can play a role in the development of leg ulcers.[1] These diseases can disrupt the microcirculation and sometimes lead to thromboembolic complications, often as a consequence of PTS. Hematologic conditions such as thrombophilia, platelet dysfunction, or other clotting-related issues can interfere with normal blood circulation in the lower extremities. In such cases, the lower-extremity tissues may experience severe ischemia and necrosis, ultimately leading to ulceration.[104]

External factors could also directly or indirectly contribute to the development of a leg ulcer. Allergic contact eczema, in particular, is commonly observed in patients with leg ulcers, and it often has multifactorial development. Contact sensitization, which refers to an allergic reaction upon contact with certain substances, has been found in a significant percentage of individuals affected by leg ulcers. In rare instances, a leg ulcer can be directly caused by a contact allergy.

Klinefelter syndrome is the best known genetic disorder linked with leg ulcers.[105] Patients with Klinefelter syndrome have a significantly higher incidence of phlebothromboses, up to 20 times more than the general population. Leg ulcers associated with PTS are reported in 6-13% of affected patients. Proposed contributing factors include thrombogenic factors such as vascular abnormalities, increased platelet aggregation, elevated factor VIII activity, and elevated levels of plasminogen activator-inhibitor in the patient's serum.[106]

A comprehensive assessment of the patient, limb, and ulcer is needed to determine the etiology and to formulate an appropriate management plan. During the initial examination of the patient, serologic measurement of blood counts and acute phase reactant agents should be performed. It is also necessary to perform a bacteriological smear as part of the initial examination. Tests to evaluate glycated hemoglobin levels, erythrocyte sedimentation rates, total protein, blood differential, coagulation parameters, and electrolytes are also helpful. A biopsy is recommended if there is clinical suspicion of vasculitis. A Doppler examination and an ABI assessment are fundamental diagnostic procedures that should be conducted in patients suspected of having PAD. These tests help evaluate blood flow and assess the severity of arterial disease. Additionally, computed tomography or magnetic resonance imaging can provide valuable information about the anatomy of blood vessels and aid in the assessment of infectious status. Angiography can be used to evaluate severe arterial disease, providing clarification on the extent and severity of the condition. Additionally, percutaneous transluminal angioplasty can be performed during the same procedure to treat the affected arteries by opening them up and improving blood flow.

7. MEDICAL TREATMENT

7.1 Pain control

Patients with chronic wounds experience pain in different ways, both physically and psychologically, and the pain can be significantly demoralizing. Therefore, pain should be assessed at each patient encounter and should always be taken seriously. Different approaches and considerations should take place during pain management, including local treatment, local anesthetics, psychosocial therapy, and pharmacologic treatment.

7.1.1 Topical treatment and dressing techniques

It is essential for wound care to use a dressing material, which is intended to maintain moisture, limit bacterial overgrowth, keep odor formation at a minimum, and be comfortable to wear. However, it is important to realize that patients with chronic wounds are likely to experience additional pain during dressing removal and wound cleansing.[107] Removal of the adhesive dressing may not only cause pain and trauma but also stimulate the inflammatory process and damage granulation tissues. Therefore, less adhesive and atraumatic dressings are commonly used and recommended to prevent pain and trauma.[108] Compared to traditional dressings, dressings with a soft silicon adhesive have been found to minimize pain and periwound maceration in several studies.[107,109]

Topical analgesics have been proven to be effective in reducing pain when applied before debridement or dressing changes. EMLA (lignocaine/prilocaine) cream and ibuprofen foam are mostly used in these circumstances.[110]

7.1.2 Systematic pain management

Pain management in chronic wounds with PAD should include both nociceptive and neuropathic pain. For pain management in chronic wounds with PAD, incorporating both nociceptive and neuropathic pain components is crucial. Following a modified World Health Organization (WHO) three-step approach, Step 1 involves prescribing a nonopioid analgesic, like NSAIDs, with or without adjuvants such as antidepressants or anticonvulsants. Step 2, applicable when pain persists, recommends adding a carefully selected opioid (e.g., codeine or tramadol) to the regimen. In Step 3, for unresponsive cases, a transition to a stronger oral narcotic is suggested. Throughout this process, especially when introducing opioids, it is vital to exercise caution, considering each patient's risk factors, and ensuring thorough monitoring and education about opioid risks to mitigate potential misuse and dependence. This approach aims to balance effective pain management with the responsibility of minimizing opioid-related complications.

7.2 Pharmacological treatment

7.2.1 Antithrombotic therapy for PAD patients with wounds

Aspirin has been the fundamental pharmacological treatment for atherosclerotic disease, including PAD, to reduce the risk of nonfatal myocardial infarction, nonfatal stroke, or vascular death.[112] Gent et al. conducted the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial, and they found in the subgroup analysis that clopidogrel was more effective than aspirin in reducing major adverse cardiovascular events (MACEs) in patients with PAD alone and PAD comorbid with diabetes.[113] Ticagrelor, a more potent $P2Y_{12}$ inhibitor, was compared to clopidogrel in patients with symptomatic PAD in the EUCLID trial, but no difference regarding MACEs [hazard ratio (HR): 1.02; 95% confidence interval (CI): 0.92-1.13] or major bleeding (HR: 1.10; 95% CI: 0.84-1.43) was found.[114] The strategy of dual-antiplatelet therapy for PAD was tested in a subgroup analysis of the CHARISMA trial,[89] and it failed to reduce all vascular events except for myocardial infarction (HR: 0.63; 95% CI: 0.42-0.95), with the cost of increased fatal or moderate bleeding (HR: 1.99; 95% CI: 1.69-2.34).

Although antiplatelet agents have been used for decades, the benefit has mainly trended toward a reduction in MACEs. There has been no strong evidence to support the benefit of antiplatelet agents in terms of limb outcomes until recently: The COMPASS PAD subgroup analysis, which compared aspirin 100 mg daily plus rivaroxaban 2.5 mg twice daily to aspirin alone, showed a significant 46% relative risk reduction in major adverse limb events (MALEs), including major amputation (HR: 0.54; 95% CI: 0.35-0.82), combined with a 28% relative risk reduction in MACEs (stroke, myocardial infarction, cardiovascular death).[115] Due to this promising result from the COMPASS trial, aspirin once daily plus rivaroxaban 2.5 mg twice daily has been recommended by international guidelines.

7.2.2 Antithrombotic therapy for PAD patients with wounds receiving revascularization

In PAD patients receiving revascularization, the main target is to reduce acute limb ischemia, postsurgical restenosis, target lesion revascularization, and limb salvage. Dual antiplatelet therapy may be more effective than single antiplatelet therapy under this scenario[116] and is recommended for at least 1 month and up to 6 months after endovascular revascularization, irrespective of angioplasty with or without a (bare metal or drug-eluted) stent.[117] In addition, the pivotal result from the YOYAGER PAD trial, testing the same treatment strategy used in the COMPASS trial (aspirin once daily and rivaroxaban 2.5 mg twice daily compared with aspirin alone), with the option to additionally use clopidogrel up to a maximum of 6 months, in PAD patients after receiving revascularization, showed a significant reduction in MACEs and MALEs (HR: 0.85; 95% CI: 0.76-0.96), especially acute limb ischemia (HR: 0.67; 95% CI: 0.55-0.82).[117] The results of the VOYAGER PAD subanalysis indicated that clopidogrel should be prescribed no more than 30 days in combination with aspirin and rivaroxaban due to a trend toward an increased risk of major bleeding.

Cilostazol is effective for improving walking distance by promoting vasodilation and antiplatelet activity with inhibition of phosphodiesterase III and has been recommended by several guidelines.[118] Although there is no evidence to suggest an impact on survival benefit in patients with advanced PAD and CLTI undergoing revascularization procedures, limb-related and arterial patency-related outcomes cannot be overlooked in this patient population.[119] In addition, in PAD patients who are contraindicated for rivaroxaban, such as those with end-stage renal disease, cilostazol may be a reasonable choice to combine with aspirin.[120] Additional studies are needed to evaluate the effect of cilostazol therapy on wound healing in patients with advanced PAD.

The recommended algorithm for antithrombotic management for PAD patients with chronic wounds is shown in Figure 5, modified based on the review from Lee et al.[117]

7.2.3 Risk modification for atherosclerosis

In PAD patients, risk factor control to avoid further disease progression and associated cardiovascular disease is mandatory. Antihypertensive therapy, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics, beta-blockers, or calcium antagonists, should be prescribed to PAD patients with hypertension to reduce the risk of myocardial infarction, stroke, heart failure, and cardiovascular death and to keep systolic blood pressure < 130 mmHg and diastolic blood pressure < 80 mmHg according to the Hypertension Guidelines of the Taiwan Society of Cardiology.[121] Although beta-blockers are not contraindicated in PAD patients, they should be prescribed cautiously in PAD patients with wounds or CLTI.

All patients with PAD should have their serum low-density lipoprotein cholesterol intensively reduced to < 70 or < 55 (preferable) mg/dL because the risk of cardiovascular events is even higher in patients with PAD than in those with CAD.[122] Statin use is associated with lower rates of mortality and major adverse cardiac and cerebral events and increased amputation-free survival in CLTI patients.[123]

PAD patients with concurrent diabetes have a 3-5 times higher risk of mortality and amputation than PAD patients without diabetes. Nevertheless, there is insufficient evidence to establish a significant correlation between rigorous glycated hemoglobin control and a decrease in MACEs or MALEs among patients with PAD.

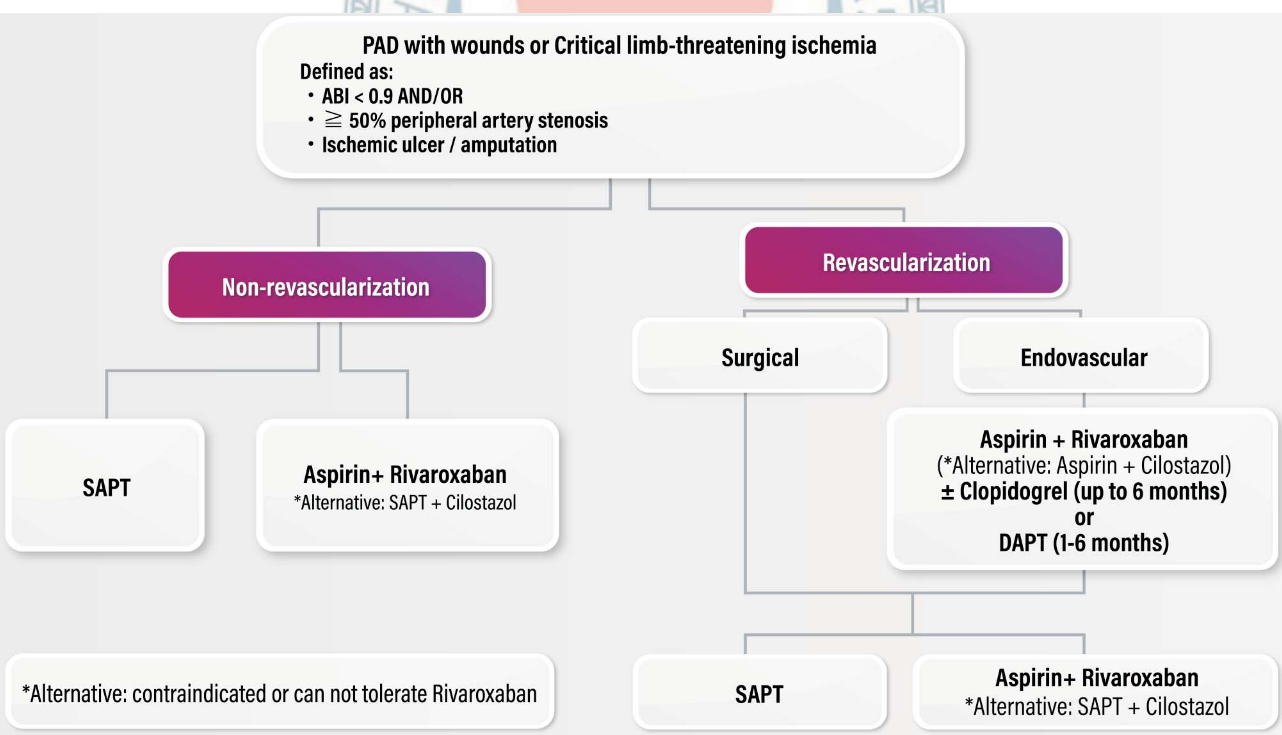

Figure 5. *Algorithm for antithrombotic management. A detailed algorithm for the management of antithrombotic therapy in the context of vascular wound care. It outlines a step-by-step approach for evaluating and managing patients requiring antithrombotic treatment, highlighting key decision points and therapeutic options. The algorithm begins with an initial patient assessment, followed by considerations for various antithrombotic agents, balancing the risks and benefits in the context of wound healing and vascular health. It also incorporates guidelines for adjusting therapy based on patient response and evolving clinical scenarios. This comprehensive flowchart serves as a practical guide for clinicians, ensuring a systematic and evidence-based approach to antithrombotic management in patients with vascular wounds. ABI, ankle-brachial index; DAPT, dual anti-platelet therapy; PAD, peripheral arterial disease, SAPT, single anti-platelet therapy.*

We still propose that maintaining strict glycemic control could offer benefits to patients with both PAD and diabetes.

7.3 Adjuvant therapy

HBOT could play a therapeutic role in CLTI, although the evidence is still controversial. A meta-analysis involving patients with chronic diabetic foot ulcers concluded that HBOT increased the rate of ulcer healing at 6 weeks but not after 1 year.[124] A recent systematic review that examined diabetic foot ulcers occurring in cases of PAD revealed that adjuvant HBOT improves the major amputation rate but not wound healing.[124] Further large-scale clinical trials should be performed for more evidence.

Far-infrared therapy has been widely used for patients with hemodialysis in the maturation and patency of arteriovenous fistula.[125] Some prospective clinical trials of far-infrared therapy showing positive effects in terms of increased foot circulation and ABI values among patients with hemodialysis.[126] The benefits for ischemic wound healing still need to be investigated.

Topical agents are essential for wound care. A recent novel macrophage-regulating drug, ON101 cream (Fespixon®), showed a promising effect on wound healing in patients with diabetic foot ulcers.[127] It may be administered as an additional therapy for diabetes patients with ischemic ulcers after debridement and revascularization.

7.4 Rehabilitation

7.4.1 Exercise in PAD patients

Exercise is important in PAD patients to prevent foot wounds, especially when these are comorbid with diabetes. Physical activity has benefits in controlling vasculopathy and neuropathy through positive effects on endothelial function, oxidative stress, and the inflammatory response.[128] Exercise has also been proven to be effective in improving symptoms, quality of life, and maximal walking distance in PAD patients.[88] However, PAD patients with foot wounds often become immobilized, that is, either bedridden or wheelchair bound. In addition to exercise limitations due to interference by wounds and dressing materials, loading on the affected extremity can also be harmful to wound healing.

7.4.2 Effect of offloading devices

People with diabetic foot ulcers are generally advised to reduce weight-bearing activity to avoid trauma and promote ulcer healing. Therefore, offloading devices, such as nonremovable total contact casts and removable devices, are recommended by international guidelines.[129] Although wound healing is faster with offloading devices, these protective devices could, on the other hand, lead to prolonged immobilization and possible harm to health.

7.4.3 Rehabilitation with chronic PAD wounds

In PAD patients with chronic wounds, the main goals of rehabilitation are to accelerate the healing process of the wounds, to avoid immobility and to prevent further formation of wounds. Recently, a few systematic reviews have tried to determine whether rehabilitation improves the healing of wounds, but there is not enough evidence to conclude that there are better outcomes with rehabilitation.[130] Due to the potential benefits of exercise in some studies, it is still recommended that non-weight-bearing activities, such as ankle-foot range of motion exercise, should be encouraged for the treatment of PAD wounds.[131]

8. TEAM-BASED APPROACH

The management of advanced vascular wounds is a complex, multifaceted process that necessitates a multidisciplinary approach.[25] This approach is characterized by the formation of a well-structured team that includes a cardiologist, plastic surgeon, and other specialists. This section will focus on the collaborative efforts of the cardiologist, vascular surgeon, and plastic surgeon in the management of advanced vascular wounds, including the timing of referral to the team members, personalized vascular wound treatment, and tissue perfusion evaluation. The diagnosis, treatment, and follow-up strategies are outlined in Figure 6.

Accurate timing plays a critical role in the consulting of a reconstructive surgeon or the referral of a patient to the advanced vascular wound team to ensure optimal patient outcomes. Similarly, it is essential to have a clear understanding of the optimal timing for referring a patient to a vascular surgeon or considering hybrid treat-

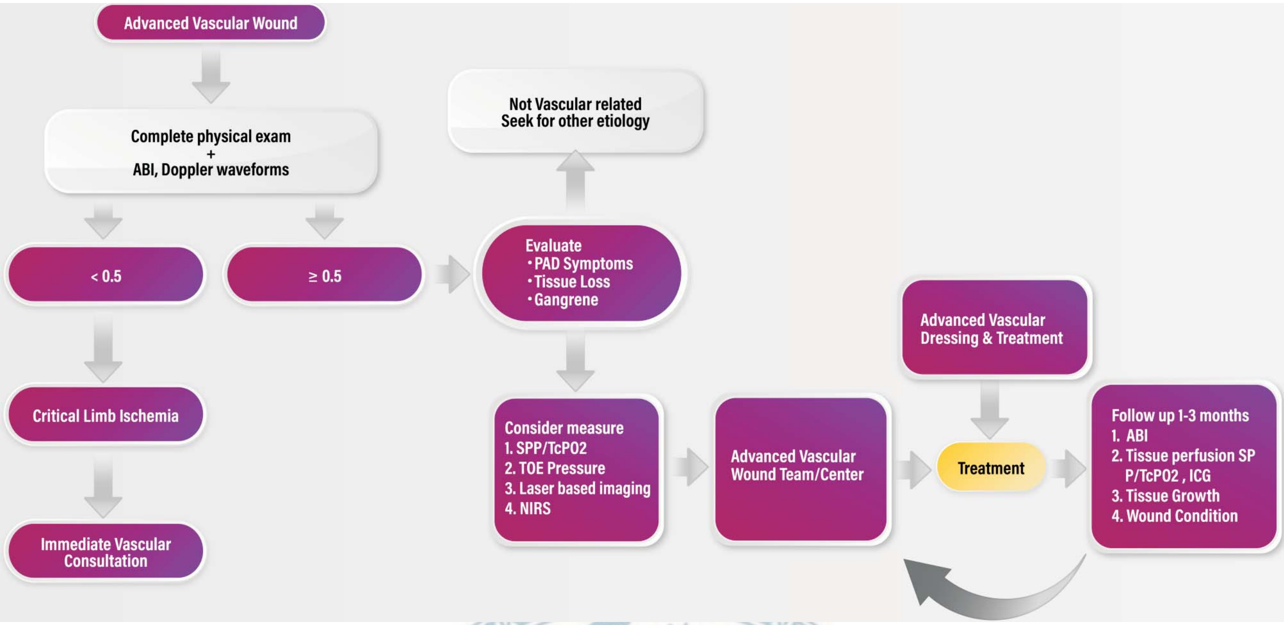

Figure 6. *Treatment algorithm for advanced vascular wounds. This figure presents a comprehensive algorithm for the treatment of advanced vascular wounds, detailing a structured approach based on critical diagnostic and therapeutic parameters. The algorithm begins with an assessment of the Ankle-Brachial Index (ABI), categorizing patients into groups based on a threshold of 0.5. For ABI less than 0.5, indicative of critical limb ischemia, immediate interventions are suggested. Conversely, for ABI greater than 0.5, further evaluation of peripheral arterial disease (PAD) symptoms, tissue loss, and gangrene is recommended. This includes measurements such as skin perfusion pressure (SPP), transcutaneous oxygen pressure ($TCPO_2$), toe pressure, and indocyanine green (ICG) angiography, providing a comprehensive overview of tissue viability and perfusion. The algorithm then guides the clinician towards advanced vascular wound care, recommending referral to a specialized vascular wound team or center. It outlines a sequence of interventions and follow-ups, including vascular dressing applications, targeted treatment modalities, and continuous monitoring. Key follow-up measures include reassessment of ABI, tissue pressure, SPP/$TCPO_2$, ICG, and evaluation of tissue growth and wound condition. This approach ensures a methodical and evidence-based treatment strategy, emphasizing the importance of personalized care and regular monitoring for optimal patient outcomes in advanced vascular wound management.*

ment involving a vascular surgeon.[132]

The consultation with a reconstructive surgeon typically occurs when conventional wound care strategies have failed to promote healing or when a wound is extensive or complex, requiring specialized surgical intervention. The reconstructive surgeon, with their expertise in tissue reconstruction, can provide valuable input on the feasibility and type of reconstructive surgery, such as skin grafts, local flaps, or free flaps.

Referral to the advanced vascular wound team is generally considered when the wound is not responding to initial treatment, recurrent, or associated with significant comorbidities such as diabetes or PAD. The advanced vascular wound team, with their multidisciplinary expertise, can provide comprehensive care, including advanced wound care strategies, revascularization procedures, and reconstructive surgery.

In the management of advanced vascular wounds, referral to a vascular surgeon becomes a crucial consideration when there is evidence of significant vascular disease contributing to the wound. This could include severe PAD, venous insufficiency, or other vascular abnormalities. The vascular surgeon, with their specialized expertise, can provide a comprehensive vascular assessment and perform necessary revascularization procedures.

A unique aspect of this collaboration is the potential for a hybrid approach to vascular treatment. This approach combines the expertise of the cardiologist and the vascular surgeon to provide comprehensive care. For instance, the vascular surgeon can perform a vascular bypass, complemented by the cardiologist performing a vascular intervention. This collaborative approach can optimize blood flow to the wound, promoting healing and potentially saving the limb.[133]

In cases of difficult venous insufficiency, the vascular surgeon and cardiologist can again collaborate, with the vascular surgeon performing hybrid surgery and the cardiologist performing thrombectomy. This combined approach can address both venous insufficiency and any associated thrombosis, improving venous circulation and promoting wound healing.

Moreover, vascular surgeons bring their specialized knowledge and skills in managing extensive vascular diseases to the team. They can provide advanced surgical treatments that may not be within the scope of other team members. This can include complex revascularization procedures, vascular bypass surgery, and other advanced surgical interventions.

In conclusion, the key to effectively managing advanced vascular wounds lies in understanding the appropriate times to consult a reconstructive surgeon or vascular surgeon, and refer a patient to the advanced vascular wound team. These decisions should be based on the patient's clinical presentation, the severity and complexity of the wound, the presence of comorbidities, and the response to initial treatment.

9. ENDOVASCULAR INTERVENTION

9.1 Overview of the current status of endovascular therapy (EVT) for CLTI patients in Asia

EVT has advanced worldwide, but there are several differences in the clinical practice, device systems, treatment strategies, and health reimbursement for endovascular intervention between developed and developing Asian countries.[134] Despite advances in EVT, wound management is often overlooked. Therefore, multidisciplinary, team-based approaches are necessary to effectively treat CLTI.[135] Many Asian countries have a higher incidence of diabetes and ESRD in PAD patients.[136] This has led to an emerging public health issue in Asian countries, including Taiwan. Patients with CLTI who also have diabetes or ESRD represent the most challenging and complicated cases within the PAD subset.[137] For example, these patients may suffer from higher rates of reintervention, amputation, and all-cause mortality than those without diabetes or ESRD.

9.2 Endovascular treatment strategy for CLTI patients

EVT for CLTI is becoming more widespread due to advances in endovascular techniques and devices.[138] According to the literature, multisegment disease is present in approximately half of all CLTI patients.[139] Typically, aortoiliac intervention is known for its durability, while femoropopliteal intervention is still in development. However, there has been no significant advance in infrapopliteal intervention. Ischemic tissue loss generally requires a much greater blood flow to heal than that needed to resolve ischemic rest pain. Since complete wound healing typically takes several months, reintervention with EVT may be necessary in clinical practice to improve clinical outcomes.[140] Frequent, repeat interventions may require further surgical evaluation, particularly if skilled vascular surgeons are available and there is a good vein conduit for bypass surgery. In some cases, a combination of EVT and surgical treatment may be considered a hybrid treatment choice, such as endarterectomy of the common femoral artery combined with femoropopliteal artery endovascular intervention.

To alleviate resting pain and promote healing in mild-to-moderate CLTI cases, the primary strategy is to increase upstream flow as much as possible in patients with multisegment disease.[141] Revascularization should be first considered for patients with significant aortoiliac lesions due to its excellent durability and long-term patency. Femoropopliteal artery disease should also be revascularized if there is insufficient microcirculation in the foot. However, if there is still no clinical improvement after the previous intervention, further intervention, such as tibial or peroneal artery intervention or below-the-ankle intervention, should then be considered. Below-the-ankle intervention is often the last step to be revascularized because of the potential for catastrophic complications associated with endovascular procedures. Nevertheless, it is important to note that these suggestions are only meant as guidance for clinical practice. Each patient with CLTI may have their own unique vascular situation, and physicians should tailor their treatment approach accordingly. In addition, there are several important endovascular therapy strategies for CLTI patients.

9.2.1 Achieve at least one straight-line flow with infrapopliteal intervention

As previously mentioned, infrapopliteal intervention should be considered only if there is insufficient microcirculation in the distal foot or no clinical improvement after upstream revascularization, particularly in cases of poor wound healing or gangrene. Because infrapopliteal artery disease often involves multiple vessels, the goal of infrapopliteal intervention should be to establish at least one straight-line flow to the distal foot. The guidelines for PAD also recommend establishing in-line blood flow to the foot with nonhealing wounds or gangrene.[118,142] Although many long balloons could be used in multisegment stenosis or occlusion of tibial/peroneal intervention, physicians should avoid dilating the nonoccluded segment to prevent balloon-associated vessel injury, spasm, and occlusion, especially during below-the-ankle intervention.

9.2.2 The concept of the angiosome

Although several guidelines for PAD recommend angiosome-directed EVT for patients with CLTI,[78,118,142] there is still debate about the usefulness of angiosome-oriented intervention in infrapopliteal revascularization. The angiosome was first introduced in 1987 for skin healing as a 3D volume of skin, soft tissue, and bone supplied by a single-source artery and its branches.[143] However, due to the multivessel occlusion typically present in symptomatic infrapopliteal artery disease, the use of the angiosome concept may not be appropriate in this context. Additionally, several studies have disagreed with the concept of using laser Doppler flowmetry, SPP, or indigo carmine angiography for perfusion evaluation.[144] In contrast, Iida et al. reported that direct revascularization is better than indirect revascularization in terms of the SPP and limb salvage rate in CLTI patients.[145] For cases with isolated below-the-knee lesions, direct revascularization provides better amputation-free survival and freedom from major amputation and MALEs than indirect revascularization.[146] However, in their subgroup study, a worse limb prognosis was observed for indirect versus direct EVT only in patients with CLTI complicated with wound infection and diabetes.[147]

Nevertheless, in some situations during CLTI treatment, direct revascularization according to the angiosome is extremely difficult. Indirect revascularization should also be attempted to improve blood flow in these cases.

9.2.3 Staged procedure for EVT treatment

A staged procedure is reasonable for patients with ischemic rest pain or nonsevere wounds.[118,142] Treatment for upstream blood flow should be prioritized to improve clinical symptoms. If symptoms persist after inflow treatment, outflow lesions such as infrapopliteal lesions should be addressed. However, for patients with severe nonhealing wounds or gangrene formation, achieving one straight-line flow to the distal foot in a single session is preferred.

9.2.4 Treating as many arteries as a possible strategy for infrapopliteal artery disease

Maximizing the number of opened tibial or peroneal arteries can improve blood flow in severe CLTI cases and potentially lead to improved wound healing.[139,148] Due to high restenosis and reintervention rates in infrapopliteal artery disease, this strategy is reasonable if technically feasible.

9.2.5 EVT or surgical bypass first for CLTI

Both endovascular therapy and surgical bypass can be used to treat patients with CLTI. However, there is an ongoing debate over which treatment should be considered the primary revascularization strategy. In the recent BASIL-2 trial, patients who received vein bypass as the first approach were more likely to require a major amputation or die during follow-up than patients who received endovascular approach as the first strategy.[149] However, the results of the BASIL-2 trial conflict with those from two previous studies (BASIL-1 and BEST-CLI),[150] both of which suggested that a surgical strategy for CLTI may be most appropriate. Therefore, this debate remains unresolved and requires further large studies for clarification.

9.2.6 Awareness of anatomical variants during EVT

Anatomical variations in the lower limb arteries are not uncommon during EVT for CLTI.[151] Therefore, correctly differentiating between vascular occlusion and anatomical variations is a vital step to achieve good outcomes for patients.

9.2.7 Novel endovascular devices and treatment

In recent years, a growing number of endovascular devices have been developed to increase the success rate of procedures and improve possible outcomes. Generally, for femoropopliteal lesions, drug-coated balloons have a better long-term patency rate than uncoated balloons, and drug-eluting stents have a better long-term patency rate than bare metal stents. However, an increased stent length may increase the in-stent restenosis rate, so the strategy of "leaving nothing behind" using drug-coated balloons is preferred over long stenting. Although Katsanos et al. reported that drug-coated devices may increase all-cause mortality in a systematic review and meta-analysis,[152] this mortality signal has gradually disappeared in recent studies.[153] For severe calcified lesions, atherectomy is useful for removing calcified plaques.[154] In Taiwan, Hawkone (Medtronic) and Jetstream (Boston) are currently available. Hawkone is a directional atherectomy device,[155] while Jetstream is a rotational atherectomy device.[154] In addition, a laser can also be used as an atherectomy device.[156] For mild to moderate calcified lesions, chocolate balloons and scoring balloons can be used to dilate the artery and decrease dissection.[157] Shockwave intravascular lithotripsy is another new device that can be used in calcified arteries,[158] but it has not yet been introduced in Taiwan. For untreatable CLTI cases, Limflow is a novel device for percutaneous deep venous arterialization that connects the artery and venous system and increases blood flow to the distal foot.[159] However, this device has not yet been introduced in Taiwan.

9.2.8 CLTI patients with severe infection

There is currently no clear guideline or consensus regarding the best time to perform EVT in patients with CLTI and severe infection. However, if there is severe infection with cellulitis, abscess, or osteomyelitis before or after revascularization, debridement or minor amputation may be prioritized to prevent sepsis. For cases of CLTI with necrotizing fasciitis or gas gangrene, immediate surgical intervention, such as debridement or major amputation, may be necessary to prevent the rapid spread of these infections. Lin et al. studied 90 infected limbs in CLI patients and discovered that lower levels of CRP (< 50 mg/L), which indicate less severe infection, can be a significant predictor of successful outcomes of EVT in diabetic patients with infected foot ulcers.[160] Therefore, it is reasonable to use antibiotics adequately to control infection and inflammation to a less severe status before undergoing EVT if possible.

9.3 Endovascular treatment strategies for patients with CVI

There are various strategies for EVT in the treatment of CVI.[161] For distal venous incompetence that leads to increased pressure, treatment techniques such as ultrasound-guided foam sclerotherapy, laser ablation, and radiofrequency can be used. On the other hand, for proximal stenosis or occlusion, such as nonthrombotic iliac vein lesions or chronic deep vein thrombosis, decompression through angioplasty or iliac vein stenting can be performed.[162] These interventions can help treat lesions and potentially improve wound healing associated with chronic venous disease.

In conclusion, EVT represents a paradigm shift in the treatment of CLTI and CVI. Although there have been great advances in endovascular techniques and devices, endovascular procedures alone cannot guarantee clinical success for patients with severe ischemic wounds complicated by bacterial infections. Regular evaluation of wounds and the microcirculation before and after revascularization can help identify worsening feet and provide prompt intervention and debridement. An adequate nutrition supply is also crucial for post-EVT patients.[163] In addition, comprehensive and multidisciplinary team work is also necessary for treating CLTI and CVI.

10. VASCULAR SURGERY

Advanced vascular wounds are caused by a variety of vascular diseases, including PAD and CVI. These wounds can be challenging to manage and require a multidisciplinary approach to achieve better outcomes. A multidisciplinary approach involving cardiologists, vascular surgeons, and other specialists is pivotal for successful outcomes.

One of the primary roles of vascular surgeons in the management of advanced vascular wounds is the assessment and treatment of underlying vascular disease. PAD and CVI are common underlying conditions that can lead to the development of vascular wounds. However, sometimes it is difficult to identify the definite causes. Vascular surgeons can help to identify and treat these underlying conditions, which can reduce the risk of further wound development or even major amputation.

In patients with PAD, vascular surgery may be necessary to improve blood flow to the affected limb. This can involve procedures such as angioplasty, stenting, or bypass surgery. These procedures can help to restore blood flow to the limb, which can improve wound healing and prevent further tissue damage.

While there is ongoing debate over the primacy of endovascular therapy versus surgical revascularization in CLTI management, recent advancements in endovascular techniques highlight the importance of a patient-centered approach, considering both anatomical and clinical factors. In a previous randomized trial, the Bypass versus Angioplasty in Severe Ischemia of the Leg (BASIL) trial[164] directly compared endovascular therapy to open surgery in CLTI patients. At the 2-year mark, there was no significant difference in amputation-free survival and overall survival between endovascular therapy and surgery. For patients who survived 2 years after randomization, bypass surgery was associated with improved survival (7.3 months, p = 0.02) and amputation-free survival (5.9 months, p = 0.06). However, these data are challenged by more recent endovascular therapy techniques. The two newly published large high-quality clinical prospective trials, the BEST-CLI[150] and BASIL-2[149] trials, may have answered these questions.

In the BEST-CLI trial,[164] the objective was to assess and compare the safety and effectiveness of surgery versus endovascular intervention in patients diagnosed with CLTI. It was a randomized, multicenter trial that enrolled 2100 patients. The trial findings suggest that for patients with CLTI who are suitable candidates for both surgical and endovascular interventions, surgical revascularization using a great saphenous venous conduit is more effective than endovascular intervention in reducing MALEs, including above-ankle amputations, and death. The main driver behind this superiority is the reduction in MALEs. When a great saphenous vein conduit is not an option, the outcomes are similar between surgery and endovascular therapies. The patients in this study had poor baseline health-related quality of life, but those who underwent endovascular intervention showed greater improvements than those who underwent surgery. These results underscore the importance of preprocedure planning, specifically using venous ultrasound to determine the availability of suitable venous conduits. Additionally, the decision-making process should consider surgical candidacy and the preferences/quality of life of the patients.

The BASIL-2 trial included 614 patients with CLTI who were randomly assigned to either the bypass surgery group or the endovascular revascularization group. In patients with CLTI caused by infra-popliteal disease, endovascular treatment outperformed vein bypass. Endovascular treatment was linked to a decrease in the occurrence of death or major amputation. These trial results differ from previous studies (BASIL-1 and BEST-CLI), which indicated that vein bypass yielded better outcomes than endovascular treatment.

For patients diagnosed with CLTI, we advise considering endovascular, open, or hybrid revascularization approaches. The decision should take into account factors such as the anatomical pattern of the disease, patient characteristics, procedural factors, the expertise of the operator, and the availability of resources.

In patients with CVI, vascular surgery may be necessary to amend venous insufficiency. This can involve procedures such as vein ablation or vein stripping. These procedures can help to improve venous blood flow, which can reduce swelling and improve wound healing.[165]

Postsurgical management is critical, involving long-term strategies for lifestyle modification, wound care, and regular follow-ups to monitor signs for a recurrence. This comprehensive care is essential in conjunction with regular endovascular assessments and possible interventions to ensure sustained vascular health. Developing a long-term management plan that includes lifestyle modifications, wound care, and regular follow-up appointments to monitor for any signs of recurrence is important.

Positional Statement 6:

1. **Strategic Surgical Intervention:** Vascular surgeons should leverage their expertise in both open and endovascular surgical techniques, tailoring the choice of intervention (e.g., angioplasty, stenting, bypass surgery, vein ablation) to the specific vascular pathology, while considering the latest clinical trial evidence (such as BEST-CLI and BASIL-2) and individual patient factors such as anatomy, comorbidities, and quality of life implications.
2. **Postoperative Care and Wound Management:** Post-surgical care is critical, and vascular surgeons should take an active role in the ongoing management of the wound. This includes monitoring for complications, optimizing wound healing, addressing factors such as tissue perfusion and oxygenation, and making deci-

sions about adjunct therapies like HBOT, as well as providing guidance on wound care techniques and necessary lifestyle changes to prevent recurrence and promote long-term healing.

11. INFECTION CONTROL

Disruption of the skin reduces the natural defense barrier function in humans, thereby increasing the risk of infection. Any chronic wound is assumed to be infected or considered contaminated by bacteria. Bacteria inside the wound can survive through biofilm formation, and the burden of microorganisms often influences wound healing.[166]

Advanced vascular wounds are prone to infection, leading to compromised wound healing. These infections can present as cellulitis, abscesses, fasciitis, or deep-seated infections such as osteomyelitis. Physicians should suspect wound infection when presented with at least two localized signs of inflammation, such as redness, swelling, warmth, pain, or tenderness, alongside purulent discharge. In some cases, systemic symptoms such as fever may also be present. Bacteriological swabs and cultures can be performed for infected wounds. The most commonly encountered bacteria include *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *hemolytic streptococci*.[10] Physicians may prescribe empirical oral antibiotics initially until culture results or sensitivities are available. In the case of multidrug-resistant bacteria, consulting an infectious disease specialist may be necessary.

For noninfected advanced vascular wounds, the priority is infection prevention. The connection between ulcer infection and wound healing remains unclear, with limited evidence supporting the use of topical antibiotics to improve healing. Routine topical antibiotic use may heighten the risk of drug-resistant microorganisms and skin irritation.[167] Standard wound care requires good hand hygiene practices and the implementation of aseptic techniques as preventive strategies. Aseptic techniques in wound care are applicable in the following scenarios: surgical sutures, wounds involving deep tissues, burns, immunocompromised individuals, diabetes, or other high-risk infection groups.

Healthcare providers performing wound care should follow standard precautions, correctly using personal protective equipment (such as sterile gloves, waterproof gowns, and single-use medical materials) and properly disposing of medical waste. Clean technique principles should be followed for other noncomplicated wounds. This approach does not necessarily require sterile gloves and sterile water for wound irrigation, but other aseptic principles still apply.

12. ADVANCED VASCULAR WOUND MANAGEMENT

12.1 Assessment of tissue perfusion

Assessments of the microcirculation, reviewed in the previous paragraph, include angiography, the ABI or toe-brachial index, lower extremity arterial duplex ultrasonography, and pulse volume recording. Assessments of microcirculation and tissue perfusion, $TcPO_2$ monitoring, SPP, laser-based imaging (laser Doppler and speckle imaging), and ICG, will be reviewed in this section.

Measurement of blood supply has continually evolved over the last 30 years, from simply palpating pulses to angiography to peripheral circulatory measurements based on skin perfusion. Historically, patients may have good macroscopic blood flow but may still have poor skin perfusion, which can be attributed to basement membrane thickening in patients with diabetes and to issues such as microembolism in patients with a history of atherosclerotic disease.[168]

Therefore, other techniques providing information about blood perfusion are also used. Intensive research, such as evaluations of invasiveness or complexity of use, is ongoing. Below, we describe certain reviewed techniques used to evaluate the tissue partial pressure of oxygen (pO_2) and perfusion.

12.1.1 Transcutaneous oximetry

The use of transcutaneous oximetry measuring $TcPO_2$ was developed to overcome the disadvantages of invasive polarographic electrodes. In this method, heated (42-45 °C) electrodes are stitched onto the surface of skin. Heating electrodes modify the surrounding wound environment by "arterialization." The effect of arterialization includes capillary dilation, opening skin pores, decreasing O_2 solubility, and shifting the oxyhemoglobin curve to the right for the ready release of oxygen. Capillary pO_2 is raised toward the arterial level by such modification, and oxygen diffuses across the skin to the electrodes where it is measured. In comparison with the invasive measurement, the O_2 recorded by transcutaneous oximetry is excess oxygen. As the amount of oxygen available for diffusion across the skin depends on oxygen delivery, the release of O_2 greatly exceeds the consumption, and the $TcPO_2$ is closer to the arterial pO_2 with a high cutaneous flow. With a low cutaneous flow, the $TcPO_2$ decreases. Consequently, $TcPO_2$ is a measurement of perfusion and vascular reserve rather than a measurement of oxygenation. With an additional control electrode placed on the infraclavicular skin of the chest, the regional perfusion index (RPI) may be calculated by the periwound $TcPO_2$ divided by the chest $TcPO_2$. The RPI is an important hemodynamic parameter that can be compared to the ABI.[169]

Several disadvantages are still noted. First, transcutaneous measurements do not provide direct data on arterial oxygenation. Second, the electrodes are placed near but not directly inside the wound. Third, the area of placement is limited because electrodes should not overlie bone, ischemic lesions, inflammation, or superficial veins.[169] Finally, heating may induce changes altering the wound environment. However, $TcPO_2$ data are still predictive of wound healing[170] and thus are widely used in clinical practice.

12.1.2 Skin perfusion pressure

SPP predicts wound healing in limb ischemia patients. Three techniques measure SPP: radioisotope clearance, photoplethysmography, and laser Doppler, with laser Doppler being most common due to its noninvasiveness. SPP effectively assesses the wound healing potential with uncertain cutoff values. Unlike other methods such as the ABI, SPP is not affected by factors such as vascular calcification or patient condition. It is a useful predictor, but the optimal cutoff value requires more research.[171].

12.1.3 ICG retention fluorescent angiography (FA)

FA has a longstanding history of use to assess blood flow and tissue perfusion in ophthalmology and surgery. ICG dye-based FA, a newer technology, shows great promise in diverse applications, including breast surgery.[172] ICG FA offers real-time visualization of blood flow and tissue perfusion, aiding the assessment of blood supply adequacy.[173] It identifies poorly perfused or ischemic areas, guiding treatment decisions such as revascularization procedures. ICG FA tracks treatment progress postintervention, ensuring effectiveness and allowing timely adjustments. Promptly identifying inadequate perfusion prevents further tissue loss in advanced arterial ulcer patients, promoting better healing. In surgical cases requiring debridement or grafting, ICG FA directs surgeons to compromised perfusion areas for optimal outcomes. Detailed perfusion information from ICG FA helps reduce complications such as infection and delayed healing.

12.1.4 Laser-based imaging

Laser Doppler imaging and laser speckle imaging are both noninvasive laser-based techniques permitting the study of perfusion.[174] Laser Doppler imaging is a technique that measures blood perfusion in tissue. When coherent light is directed toward a tissue, photons are scattered by moving objects and by static structures. If they encounter moving particles, which in this case are moving red blood cells in vessels, the Doppler effect appears. The photon frequency is therefore modified, and reflected radiation provides information about the speed of red blood cells and consequently about blood perfusion.[175] With a flowmeter, a laser Doppler imager scans an entire region of interest to generate perfusion maps. Despite its simplicity of use and the noninvasive nature of the technique, measurement depths are typically between 1 and 1.5 mm, thus limiting measurements in superficial vascularization.[176] In laser speckle imaging, interference of photons reflected by red blood cells, which causes a speckle pattern, is recorded. A study comparing laser Doppler and laser speckle imaging in human burn scars showed that the results obtained with both techniques correlated well. Laser speckle imaging is more advantageous for clinical applications due to the faster scan time, higher resolution, and reduction in specular reflection artifacts observed using laser Doppler.[177]

12.1.5 Near-infrared spectroscopy imaging (NIRS)

NIRS is a technique whereby light is transmitted to the skin or the surface of a wound. Compared to visible light systems, near-infrared light can penetrate more deeply into tissues. Light at approximately 750 nm is predominantly absorbed by unbound hemoglobin, whereas light at approximately 850 nm is predominantly absorbed by hemoglobin bound to oxygen. By measuring the relative absorption of near-infrared light around those key wavelengths, the ratio of oxygenated to oxygenated plus deoxygenated hemoglobin can be determined. By calculating this ratio, the level of tissue oxygen perfusion can be assessed. Using an array of infrared emitters, the NIRS device can capture data from large areas of skin. However, one limitation to the NIRS device is the need for measuring reflected light, which is scattered by body curvature. When the curvature becomes extreme, such as along the edge of a foot, the images appear to show lower levels of oxygenation. This is an obvious artifact of making measurements over larger areas.[168]

Positional Statement 7:

1. **Comprehensive perfusion assessment:** For the effective management of advanced vascular wounds, it is highly recommended to conduct a comprehensive perfusion assessment using techniques such as transcutaneous oximetry, SPP, ICG FA, laser-based imaging, and NIRS, which are critical in guiding team-based treatment strategies.
2. **Personalize perfusion monitoring techniques:** Tailoring perfusion monitoring techniques to individual patient conditions, considering factors like diabetes and atherosclerotic disease, wound conditions, and treatment options.

12.2. Treatment of wounds

12.2.1 TIME principle of wound treatment

For general treatment of vascular wounds, follow the TIME principle for chronic wound treatment:[178] tissue debridement (except cases with arterial ulcers), infection control, moisture balance, and wound edge care. Once addressed, the ulcer can be accurately diagnosed and classified for appropriate treatment (Table 4).

Debridement, which is crucial in wound treatment, involves removing dead or infected tissue and is the primary step for chronic wounds. A study demonstrated a twofold increase in healing probability with aggressive debridement, and another study affirmed that consistent debridement within one week led to significantly faster healing.[179,180] In addition to debridement, targeting biofilm-cell communities that hinder healing, is also essential for wound healing. Biofilms, which cause 80% of wound infections, are not visible to the unaided eye.[181] Biofilm destruction is crucial to avoid stalling wound healing during inflammation.[180] Various debridement methods include surgical, autolytic, enzymatic, and biologic methods, with surgery being most common and the other methods chosen based on the wound type. Topical agents such as silver, polyhexamethylene biguanide hydrochloride, and cadexomer iodine manage infections, while antimicrobial washes help remove suspected biofilms. Oral or intravenous antibiotics may be needed for cellulitis or systemic infection.

Table 4. Treatments of advanced arterial ulcers

Item	Treatment
Exercise	Planned graduated walking program
Vascular intervention	Angiography, angioplasty (dilatation, stents), or bypass
	By vascular specialist
Wound treatment	Ischemic wound:
	Control infection
	Limit debridement
	Maintain moisture balance
	Vascular evaluation
	Reperfused wound: TIME principle
	Tissue debridement
	Infection control
	Moisture balance
	Edges care
Wound reconstruction	Wound closure (direct or delayed)
	Skin graft (split or full thickness)
	Flap (pedicled or free)

Note: compression is contraindicated for arterial ulcers.

Maintaining moisture balance in wound care is vital.[182] Chronic wounds should not be exposed to air for drying, as this would hamper healing and increase infection risk. Dry wounds require suitable dressings to add moisture, while draining wounds need control to prevent moisture from reaching the periwound. Proper dressings should retain moisture on the wound bed to prevent desiccation. Ensure that the wound edges are free from undermining, and if they are rolled, excise them to promote epithelialization, which is a clear sign of healing.[183]

12.2.2 Treatment of arterial ulcers

For arterial ulcers, addressing the underlying cause is the initial step, often involving vascular consultation and vascular interventions such as angiography, angioplasty (dilation, stents), or bypass by a vascular specialist. Preintervention wound treatment aims to prevent infection and reduce debridement. Following vascular intervention, the TIME principle is applied, and the appropriate dressing is used.[184]

Dressings, typically used with offloading, debridement, and infection control, foster a moist wound environment that promotes cell migration and matrix formation. Dressing selection factors include cost, potential for iatrogenic injury, and exudate management. Dressings should not harm the wound or surrounding tissue by causing maceration or friction injuries. Cost-effectiveness considers healthcare provider time, healing rates, and dressing unit costs. No conclusive evidence from randomized clinical studies favors any specific dressing approach for wound healing.[185]

12.2.3 Wound reconstruction

Severe or large wounds that cause a significant amount of damage to the skin and musculoskeletal system may need surgical treatment to heal properly (Table 4). Reconstructive surgeons use the concept of a "reconstructive ladder" (Figure 7) – the more problematic or larger the wound, the higher the ladder the surgeon must climb. Simple wounds may be closed by primary suturing, sometimes in the primary care setting. However, other wounds may require complex reconstruction, including free tissue transfer.[186]

12.2.4 Direct (primary) closure

After the operative site has been prepared and anesthetized, the wound edges are approximated and closed with sutures. Traumatic wounds are debrided, and the edges of the wound are trimmed and closed. When dealing with skin cancer, after the completion of the excision, the defect is closed respecting the same principles (Figure 7). To minimize tension on closure and cancel dead space, buried dermal sutures are placed. Sutures at the skin level are removed early, a measure facilitated by a secure dermal closure with absorbable sutures.[187] In general, facial sutures are removed in 3 to 7 days; scalp sutures, 7 to 10 days; and lower extremity

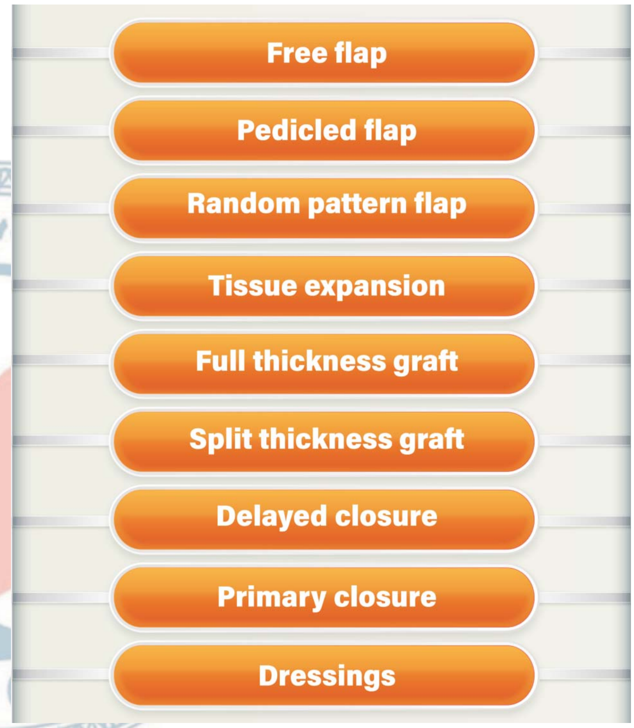

Figure 7. *Reconstructive ladder. 'The Reconstructive Ladder', a systematic approach to wound reconstruction. The ladder metaphorically ascends through increasingly complex treatment options, starting from basic interventions and advancing to sophisticated surgical techniques. It begins with simple dressings, ideal for minor wounds requiring minimal intervention. The next step is primary closure, used for wounds amenable to direct suturing. This is followed by delayed closure, allowing time for edema reduction and contamination control. Subsequent rungs include split thickness grafts and full thickness grafts, chosen based on wound depth and size. Tissue expansion represents a more advanced technique, used to grow extra skin for reconstruction. The ladder then progresses to random pattern flaps and pedicled flaps, suitable for larger or more complex wounds. The pinnacle of the ladder is the free flap procedure, a highly specialized technique involving the transfer of tissue from one body part to another. This comprehensive overview encapsulates the gradual escalation in wound care complexity, highlighting the importance of tailoring treatment to wound severity and patient-specific factors.*

and trunk sutures, 10 to 14 days.

12.2.5 Debridement and delayed (secondary) closure

Primary suture may not be indicated in heavily contaminated wounds, where the risk of infection is high. In such cases, the wound should be debrided, with "delayed closure" subsequently carried out. All contaminated wounds should undergo debridement and thorough irrigation before wound closure. The aim of debridement is to remove all potentially contaminated and devitalized tissue along with foreign material.

12.2.6 Skin grafts

Where skin defects are too large for skin apposition and healing by secondary intention is inappropriate, skin grafts may be used. Free skin grafts are taken from another part of the body and rely on revascularization from a healthy, well-vascularized wound bed. Grafts will not be successful on nonvascularized beds, such as exposed bone or tendon.

Split-thickness skin grafts are defined as grafts involving the epidermis and any part of the dermis and range in thickness from approximately 0.005 to 0.030 inches. They are classified as thin (0.005-0.012 inches), medium (0.012-0.018 inches), or thick (0.018-0.030 inches) grafts, depending on the amount of dermis included.[188] Full-thickness skin grafts are defined as grafts composed of the epidermis and the entire dermis.

The harvesting of a split-thickness graft heals the donor site by secondary intention with minimal morbidity, whereas the donor site for a full-thickness graft usually necessitates primary closure for optimal mitigation of donor site morbidity. Split-thickness grafts are also more amenable to size expansion by meshing techniques, making them more suitable for large wounds.

12.2.7 Flap

Advanced vascular wounds generally occur in the lower leg. Among all wounds, the foot and ankle regions are the most difficult to treat due to the sparse soft tissue and limited flexibility. In the exposure of the underlying tendon, ligament, or bone, which is very common, local flaps, muscle flaps covered with skin grafts, pedicled flaps, or even free flaps would be necessary for reconstruction. The options for reconstruction vary by location and can be categorized into four regions: (1) anterior ankle and dorsal foot, (2) plantar forefoot, (3) plantar midfoot, and (4) plantar hindfoot and medial/lateral ankle. Care should be taken that in patients presenting wounds complicated with occlusive PAD, endovascular angioplasty should be performed previously or in combination.

Local fasciocutaneous flaps are commonly used in defects of the plantar forefoot and plantar midfoot. The flap procedures can be conducted in many forms, such as advancement, rotation, or transposition, depending on the different situations.

Free tissue transfer is almost necessary in large defects of the foot and ankle. Free fasciocutaneous flaps, such as lateral arm flaps and radial forearm flaps, provide thin and pliable tissue, which is especially suitable for the dorsal foot due to proper shoe fitting. The plantar forefoot and plantar hindfoot are weight-bearing parts that require durable soft-tissue coverage while permitting near normal ankle motion. Free muscle flaps surfaced with a skin graft offer a durable and well-contoured reconstruction capable of withstanding the shear forces of repeated ambulation.

Positional Statement 8:

1. In chronic wound treatment, integrate aggressive debridement, moisture balance, infection control, and wound edge management, following the TIME principle. Collaborate with plastic surgeons for advanced techniques in wound debridement and reconstruction.
2. Foster patient education, interdisciplinary collaboration, and continuous adaptation of treatment strategies across all wound care facets, emphasizing the critical role of plastic surgeons in managing advanced vascular wounds.

13. EVALUATION OF THE TREATMENT RESULTS

Wound care is a crucial aspect of health care, requiring a proper evaluation of treatment outcomes. The wound can be assessed through clinical examination, imaging techniques, or specialized tests. It is important to evaluate the five key factors that contribute to the evaluation of treatment results in wound care: perfusion, tissue growth, timeframe, infection control, and rehabilitation (Figure 8).

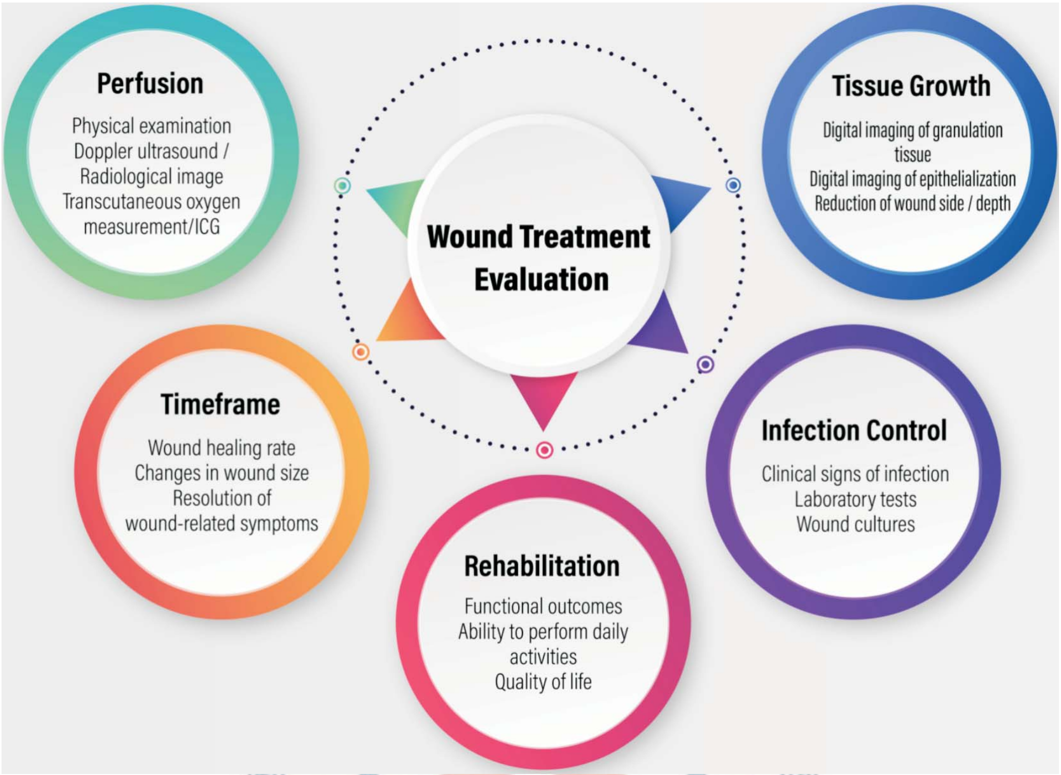

Figure 8. *Evaluation of the wound treatment results. This figure delineates the process and criteria for evaluating the outcomes of advanced vascular wound treatment. It methodically presents the assessment of various critical factors including tissue growth, infection control, rehabilitation processes, timeframe for healing, and perfusion status. The figure provides a comprehensive overview of multiple facets of wound management, emphasizing the importance of a holistic approach in treatment evaluation. This includes monitoring the progress of tissue regeneration, ensuring effective infection management, evaluating patient rehabilitation, and understanding the temporal aspects of wound healing. Additionally, the assessment of perfusion highlights the vital role of vascular health in the overall treatment process. By integrating these diverse elements, the figure underscores the complexity and multifaceted nature of advanced vascular wound care and the necessity of tailored treatment strategies for optimal patient outcomes.*

13.1 Perfusion

Perfusion refers to the blood flow and oxygen supply to the wound area, which is essential for adequate wound healing. Insufficient perfusion can impede tissue repair and delay wound closure. Therefore, evaluating the improvement in perfusion at the wound site is essential when assessing treatment outcomes. The process of wound healing is complex, involving multiple stages, in which perfusion playing a vital role. It facilitates the delivery of necessary oxygen and nutrients needed for tissue regeneration and healing. Therefore, maintaining adequate perfusion holds great clinical significance. Evaluating the effectiveness of a treatment regimen includes assessing whether there has been an improvement in wound site perfusion.

This assessment can be conducted through various approaches. Clinical examination involves physical examination of the wound by healthcare professionals, who assess parameters such as the wound size, exudate, and signs of infection. Imaging techniques such as Doppler ultrasound and magnetic resonance imaging can visualize blood flow in the wound area and evaluate tissue damage and healing extent. Specialized tests such as transcutaneous oxygen measurement and laser Doppler flowmetry provide precise and quantitative measurements of blood flow and oxygenation at the wound site, offering invaluable insights into the wound-healing process. Thus, perfusion plays a critical role in wound management and care, and its evaluation is integral to assessing treatment outcomes. The proper use of various assessment methods ensures that the wound receives adequate blood supply for optimal healing.[184]

13.2 Tissue growth

Successful wound healing relies on the generation of new tissue, specifically robust granulation tissue and epithelialization. A successful treatment methodology should encourage robust granulation tissue development and expedite epithelialization. Evaluation of treatment outcomes involves assessing tissue growth, wound size reduction, and the presence of healthy granulation tissue. The extent to which a treatment stimulates new tissue growth determines its efficacy. Visible indicators include increased healthy granulation tissue, characterized by a fresh, pink or red appearance.

An important treatment outcome is the reduction in wound size, indicating progress in healing. Healthy granulation tissue indicates proper healing and a sufficient blood, oxygen, and nutrient supply. Techniques such as digital imaging capture high-resolution images, providing visual records for assessing tissue quantity and quality. Direct wound measurement tracks size changes, yielding valuable insights into treatment effectiveness. The growth of new tissue is critical in wound healing, and treatment effectiveness depends on its promotion. Evaluating outcomes with techniques such as digital imaging and wound measurements ensures optimal wound management. These methods provide quantitative data and assess tissue growth progress and quality, guiding informed decisions and treatment adjustments.[189]

13.3 Timeframe

The timeframe is an essential consideration in evaluating treatment outcomes for wound healing. Monitoring progress within a specified period of time allows for adjustments and modifications to the treatment plan. Key indicators such as healing rates, reduction in wound size, and resolution of wound-related symptoms provide useful information about treatment effectiveness. Monitoring the timeframe allows healthcare professionals to determine if the treatment plan needs adjustment or modification. To evaluate the effectiveness of a treatment regimen in wound care, it is of great importance to factor in the progress that has been made within a specified timeframe. This involves tracking how quickly the wound is healing over time and noting any significant improvements or potential setbacks. The healing rate can be calculated by examining the speed at which new tissue forms and how quickly the wound size decreases. A rapid healing rate generally signifies that the treatment is effective and that the wound is responding well to care.

A reduction in wound size over time is another vital indicator of progression. A decrease in the dimensions of the wound — its length, width, and depth — usually signals that the wound-healing process is proceeding in a positive direction. If the wound size diminishes steadily within the expected timeframe, this is a good indication that the treatment strategy is working. Additionally, the resolution of wound-related symptoms, including pain, redness, swelling, or exudate from the wound, is also a crucial gauge of treatment effectiveness. Close monitoring of the timeframe not only allows healthcare professionals to keep tracks of the wound-healing process but also enables them to decide if the current treatment plan is serving its purpose or if it requires any adjustments or modifications. If a wound does not heal as expected within the designated timeframe, this might indicate that the treatment plan needs to be revised. By closely observing healing rates, changes in wound size, and the resolution of wound-related symptoms within this timeframe, healthcare professionals can make informed decisions about the care and management of the wound.[190]

13.4 Infection control

Chronic wounds are susceptible to infections, which can hinder the healing process and lead to complications. Thus, infection control plays a vital role in wound healing, particularly in chronic wounds prone to infections. The evaluation of wound treatment results should include an assessment of infection control measures and the reduction of microbial load in the wound. Clinical signs, laboratory tests, and wound cultures can aid in determining the effectiveness of infection control strategies. The overarching concept of infection control emerges as an integral and indispensable element in the progression and successful outcome of wound healing. Within the realm of wound management, infection control assumes a pivotal position, given its potential to significantly influence the course of the healing process. The presence of infection in chronic wounds can be a formidable barrier to healing, causing a significant delay in the recovery process and potentially leading to an array of complications. These complications, in turn, can exacerbate the patient's condition, thereby underscoring the critical importance of effective infection control.

The process of evaluating the efficacy of any treatment protocol necessitates the inclusion of a thorough assessment of the implemented infection control measures. It is essential to ascertain the impact of these measures on the reduction in the microbial load present within the wound. This facet of wound management is of utmost importance, as the reduction in microbial load directly impacts the speed and quality of healing. Therefore, it is vital to ensure that infection control measures effectively reduce the microbial burden within the wound. To determine the effectiveness of the infection control strategies being employed, various tools and techniques can be utilized. Clinical signs serve as valuable indicators, providing tangible evidence of the progression or regression of the infection. Laboratory tests also offer significant insights, facilitating the objective evaluation of the infection status. Additionally, wound cultures represent a robust method for evaluating the microbial burden in the wound. Through these techniques, healthcare professionals can assess and monitor the extent of infection and thereby gauge the efficacy of the infection control measures in place.[191]

13.5 Rehabilitation and follow-up after advanced vascular wound treatment

13.5.1 Overview of rehabilitation posttreatment

Posttreatment rehabilitation for advanced vascular wounds is a critical phase, focusing on restoring function, preventing recurrence, and improving overall quality of life. The rehabilitation process should be tailored to each individual's specific needs, taking into account the nature of the wound, the treatment received, and the patient's overall health status.[138]

13.5.2 Setting rehabilitation goals

Initial rehabilitation goals are set with an emphasis on enhancing mobility, managing pain, and promoting wound healing.[192] These goals are periodically reassessed based on the patient's progress, with adjustments made to ensure that they remain pragmatic. Patient involvement in goal setting is essential for ensuring adherence and satisfaction with the rehabilitation process.

13.5.3 Monitoring progress and adjusting rehabilitation plans

Regular monitoring is vital to assess the progress of rehabilitation. This involves not only tracking wound healing and functional improvements but also evaluating the patient's psychological and emotional well-being. Adjustments to the rehabilitation plan are made as needed, based on these assessments, to address any emerging challenges or changes in the patient's condition.[193]

13.5.4 Incorporation of perfusion assessment in evaluating rehabilitation effectiveness

Evaluating the effectiveness of rehabilitation interventions involves integrating perfusion monitoring tools such as $TcPO_2$ monitoring and ICG fluorescence angiography. These tools provide insights into the vascular health and wound-healing process, complementing traditional functional outcome measures.[194-196] Regular monitoring and comparative analysis of perfusion parameters, alongside patient-reported outcomes, offer a comprehensive view of the recovery process. This approach ensures that rehabilitation strategies are optimally aligned with both functional and vascular health outcomes.

13.5.5 Continuous reassessment and long-term follow-up

Rehabilitation is an ongoing process that does not end with wound closure. Long-term follow-up is essential to monitor for any signs of recurrence, assess vascular health, and ensure that the patient continues to maintain functional gains. This phase may involve periodic reassessments of perfusion metrics and functional status, adjustment of rehabilitation goals, and continued patient education to promote healthy lifestyle choices that support vascular health and wound prevention.

Positional Statement:

1. **Comprehensive Monitoring and Adjustment:** Employ regular physical, psychological, and perfusion monitoring ($TcPO_2$, ICG) to adjust rehabilitation strategies, ensuring alignment with functional and vascular health outcomes.
2. **Perfusion Assessment in Evaluating Rehabilitation Effectiveness:** Maintaining a continuous follow-up for recurrence monitoring, reassessing vascular health, and educating patients on wound care and prevention is critical for long-term outcomes.

14. SOCIOECONOMIC IMPACT OF THE ADVANCED VASCULAR WOUND CENTER AND TREATMENT

Health care disparities, which are significantly evident in vascular disease management, call for setting up advanced vascular wound centers. These centers are pivotal in providing equitable care, especially for economically disadvantaged patients, ensuring that advanced treatments are within reach for all societal sectors.

Advanced vascular wound centers offer more than just direct patient care; they represent a strategic investment for the hospital. Such centers promise financial benefits through innovation in medical technology and sustained patient care programs, which in turn can foster patient loyalty and reduce costly hospital readmissions.

A focused cost-benefit analysis reveals that these centers can reduce the economic burden of chronic wound management. They achieve this aim by providing timely, effective care, which lessens the need for long-term medical support and the indirect societal costs tied to loss of work and long-term disability.

Moreover, as innovation hubs, these centers are poised to lead in the development of new wound care technologies. This serves to enhance patient care while simultaneously establishing the hospital as a leader in medical innovation and research.

In summary, the role of advanced vascular wound centers is twofold: they provide critical care to socioeconomically disadvantaged individuals, improving overall health equity, and they contribute to the hospital's financial and innovative stature. The integration of such centers is therefore not just a moral imperative but a sound economic strategy for healthcare institutions aiming to lead in the delivery of comprehensive and cost-effective care.

15. CONCLUSIONS

The successful management of advanced vascular wounds hinges on a collaborative, team-based approach, encompassing physicians, surgeons, and other healthcare professionals. Central to this strategy is the emphasis on perfusion assessments, such as $TcPO_2$ monitoring and ICG fluorescence angiography, which are instrumental in providing detailed insights into the patient's vascular status and wound healing progress. This integrated approach, combining clinical expertise with advanced diagnostic tools, allows for a more tailored and effective treatment plan, ensuring optimal patient outcomes. Regular follow-up and reassessments are crucial, facilitating timely interventions and adjustments to the rehabilitation process, thereby enhancing long-term patient health and quality of life.

DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

DISCLAIMER

This Joint Consensus was funded by the Taiwan Society of Cardiology, developed following thorough evaluation of current scientific and medical evidence available at the time of their issuance, and reflects the standpoint of the Taiwan Society of Cardiology and the Taiwan Society of Plastic Surgery. Both Societies are not liable for any conflicts, discrepancies, or ambiguities that may arise in comparison with other official recommendations or guidelines from relevant health authorities, particularly concerning the optimal utilization of healthcare or therapeutic approaches. Healthcare professionals should consider this Joint Consensus as a significant reference in their clinical judgment, as well as in developing and implementing preventive, diagnostic, or therapeutic strategies. However, it does not supersede the individual responsibility of healthcare professionals to make informed decisions tailored to each patient's health situation in collaboration with the patient and, when necessary, their caregiver. Furthermore, it does not exempt healthcare professionals from considering other relevant, officially updated recommendations or guidelines by competent health authorities. Healthcare professionals must also ensure they adhere to current rules and regulations regarding medications and medical devices at the time of patient care.

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