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REVIEW ARTICLE

Wound Healing Society 2023 update on guidelines for arterial ulcers

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Abstract

The Wound Healing Society guidelines for the treatment of arterial insufficiency ulcers were originally published in 2006, with the last update in 2014. These guidelines provided recommendations, along with their respective levels of evidence, on seven categories: diagnosis, surgery, infection control, wound bed preparation, dressings, adjuvant therapy and long-term maintenance. Over the last 9 years, additional literature regarding these aspects of arterial ulcer management has been published. An advisory panel comprised of academicians, clinicians and researchers was chosen to update the 2014 guidelines. Members included vascular surgeons, internists, plastic surgeons, anaesthesiologists, emergency medicine physicians and dermatologists, all with expertise in wound healing. The goal of this article is to evaluate relevant new findings upon which an updated version of the guidelines will be based.

KEYWORDS

arterial ulcer, arterial-ischemic ulcers, chronic leg ulcers, diabetic ulcers, evaluation of ulcers, leg ulcers, management of leg ulcers

Levels of Evidence

The strength of evidence supporting a guideline is listed as Level I, Level II or Level III, using the following definitions:

- Level I: Meta-analysis of multiple RCTs or at least two RCTs supporting the intervention in the guideline or multiple laboratory or animal experiments with at least two clinical series supporting the laboratory results.
- Level II: Less evidence than Level I, but at least one RCT and at least two significant clinical series or expert opinion papers with literature reviews supporting the intervention. Experimental evidence that is quite convincing but without support from adequate human experience.
- Level III: Suggestive data of proof-of-principle but lacking sufficient data such as meta-analysis, RCT or multiple clinical series.

Abbreviations: CASE S, case series of 3–10 patients; CER, comparative effectiveness research: comparing one or more treatments; EXP, experimental laboratory or animal study; LIT REV, literature review; PATH S, pathological series review; PCOH, prospective cohort study; RCT, randomised controlled trial; RETROS, retrospective study (>10 patients); STAT, statistical analysis, meta-analysis, consensus; TECH, technique or methodology description.

1 | METHODS

1.1 | Data sources and searches

We sought to capture the highest quality of evidence available regarding arterial insufficiency ulcer diagnosis and treatment using a key word search of PubMed, Embase, Google Scholar and Cochrane Library databases. Similarly, the citations of relevant articles were examined by hand. Key terms were generated from the existing guidelines. The search was limited to meta-analyses, systematic reviews, randomised controlled trials (RCTs), retrospective series reviews, clinical case series and expert panel recommendations published between January 2015 and 2023. It was further limited to publications in the English language. The findings of these articles have been divided into one or more of the appropriate categories (diagnosis, surgery, infection control, wound bed preparation, dressings, adjuvant therapy and long-term maintenance) as performed in the original guideline. We have also added new sections on pain control and social determinants of health for this 2023 update.

2 | GUIDELINES FOR DIAGNOSIS OF ARTERIAL INSUFFICIENCY ULCERS

Guideline 1.1: The reliability of capillary refill time as an indicator of tissue perfusion is questionable. (Level II)

Principle: Using the capillary refill test with finger pressure on the dorsum of the dependent foot to measure microcirculatory supply has not been validated. Skin perfusion pressure is a good indicator of lower extremity micro-circulation, and transcutaneous oxygen tension (TcPO2) is a good indicator for critical limb ischaemia (CLIN S & LIT REV).

No updated evidence.

Guideline 1.2: Audio handheld Doppler waveforms are diagnostic of peripheral arterial disease (PAD) and triphasic pulse is reliable to rule out significant PAD. Doppler assessment is commonly used in conjunction with pulse volume recordings (plethysmography) as a screening tool. (Level II)

Principle: Audible Doppler signal sounds can be effective for the detection or exclusion of PAD compared with the ankle brachial pressure index (ABI). Triphasic waveforms from an audio handheld Doppler can rule out PAD in asymptomatic, *low*-risk patients.

Updated Evidence:

1. Aguirre A, Sharma K, Arora A, Humphries MD. Early ABI testing may decrease risk of amputation for patients with lower extremity ulcers. *Ann Vasc Surg*. 2022;79:65-71 [CLIN S].
2. Danieluk A, Chlabicz S. Automated measurements of ankle-brachial index: a narrative review. *J Clin Med*. 2021;10(21):5161 [LIT REV].
3. Mittleider D. Noninvasive arterial testing: what and when to use. *Semin Intervent Radiol*. 2018;35(5):384-392 [LIT REV].
4. Crawford F, Welch K, Andras A, Chappell FM. Ankle brachial index for the diagnosis of lower limb peripheral arterial disease. *Cochrane Database Syst Rev*. 2016;1:CD010680 [LIT REV].
5. Alavi A, Sibbald RG, Nabavizadeh R, Valaei F, Coutts P, Mayer D. Audible handheld Doppler ultrasound determines reliable and inexpensive exclusion of significant peripheral arterial disease. *Vascular*. 2015;23(6):622-629 [CLIN S].

Guideline 1.3: Pulse wave velocity may be useful in screening and evaluating the severity of PAD. (Level III)

Principle: Patients with medial calcinosis and non-compressible arteries, such as in patients with diabetes and end-stage kidney disease, can have significant arterial stiffness independent of an impaired ABI. Increased pulse-wave velocity reflecting upon arterial stiffness shows an excellent correlation with decreased values of brachial artery flow-mediated dilation. Toe brachial index, toe systolic blood pressure and TcPO2 are adjuncts.

Updated Evidence:

1. Hungerford SL, Adji AI, Kapur NK. Interpretation of the central aortic pressure waveform in elderly patients with aortic stenosis. *Am J Physiol Heart Circ Physiol*. 2023;324(6):H697-H712 [LIT REV].
2. Obeid H, Khettab H, Marais L, Hallab M, Laurent S, Boutouyrie P. Evaluation of arterial stiffness by finger-toe pulse wave velocity: optimization of signal processing and clinical validation. *J Hypertens*. 2017;35(8):1618-1625 [RETROS].

Guideline 1.4: Diagnosis of PAD by manual palpation of lower limb pulses is a reliable method when resources are limited. (Level II)

Principle: Primary care physicians and other clinicians may not be well-versed with the use of Doppler for the diagnosis of PAD. It is important to gather information from the history and physical examination to perform a clinical assessment. A history of intermittent claudication and the presence of risk factors such as heart disease (valvular disease, atrial fibrillation and coronary artery disease), stroke or transient ischaemic attacks, hypertension, diabetes, dyslipidaemia, tobacco use and renal insufficiency can increase the pre-test probability of PAD. The detection of ankle systolic pressure by the palpatory method may offer a cheap, simple and useful alternative approach in office care settings for the early detection of PAD. However, a palpable pulse does not rule out PAD, particularly in diabetic patients with medical calcinosis. Given the common occurrence of medial calcinosis in patients with diabetes, toe brachial pressure index is the recommended screening test.

ABI ≤ 0.9 has 75% sensitivity and 86% specificity to diagnose peripheral arterial disease. However, sensitivity is poor in patients with diabetes or end-stage kidney disease because of vessel calcification. Patients with borderline ABI may need further diagnostic tests. Patients with high ABI > 1.4 due to vessel calcification will require alternative tests such as toe-brachial index (TBI), toe pressure or doppler waveform.

Treadmill test—A treadmill test using the Strandness Protocol (speed 3 km/h and 10% slope) can offer objective information about

the patient's functional assessment and unmask moderate stenosis. A post-exercise ankle SBP decrease <30 mmHg or a post-exercise ABI decrease of >20% are diagnostic of PAD.

Updated Evidence:

1. Tehan PE, Santos D, Chuter VH. A systematic review of the sensitivity and specificity of the toe-brachial index for detecting peripheral artery disease. *Vasc Med* 2016;21:382-389 [LIT REV].

Guideline 1.5: Duplex ultrasound (DUS) is usually a first step in vascular workup as it can detect and localise vascular lesions use velocities to quantify lesion extent as well as severity. Doppler Ultrasound provides good information on arterial haemodynamics and it must be combined with ABI measurements. (Level II)

Principle: Information from anatomical imaging tests should always be evaluated in combination with the patient's history, symptoms, clinical examination and hemodynamic tests prior to reaching a final treatment decision. Imaging tests will be discussed under revascularization procedures.

Updated Evidence:

1. Aboyans V, Ricco JB, Bartelink AL EL, Bjorck M, et al. Editor's choice – 2017 ESC Guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery. *Eur J Vasc Endovasc Surg* 2018;55:305-68 [LIT REV].
2. Vlachopoulos C, Xanaplanteris P, Aboynas V, et al. The role of vascular biomarkers for primary and secondary prevention. A position paper from the European Society of Cardiology Working Groups on Peripheral circulation: endorsed by the Association for Research into Arterial Structure and Physiology (ARTERY) Society. *Atherosclerosis* 2015;241:507-532 [LIT REV].

3 | SURGERY OF ARTERIAL INSUFFICIENCY ULCERS

***Preamble*:** In patients with arterial insufficiency ulcers, restoration of blood flow by revascularisation is the intervention that will most likely lead to healing.

Guideline 2.1: Prior to revascularization, an anatomic road map should be obtained. (Level II)

Options include:

- Digital subtraction angiogram
- Duplex angiography, which has a sensitivity of 99% and 80% and a specificity of 94% and 91% for the femoropopliteal and tibial segments, respectively, as compared with arteriography.
- Magnetic resonance angiography
- Contrast tomography angiography[4]

Principle: The goal of revascularisation (open or endovascular) is to restore adequate arterial blood flow to the ulcer, which may be manifested by a pulse in the foot and/or improved ABI. An anatomical roadmap also allows classification of the patient and disease, such as the Wi-Fi and GLASS classifications, allowing risk stratification, optimisation of care, as well as prediction of outcomes.

Updated Evidence:

1. Conte MS, Bradbury AW, Kolh P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg*. 2019;58(1S):S1-S109.e33 [LIT REV].

Guideline 2.2: In the presence of an arterial ulceration with inadequate blood flow, the natural history may be one of disease progression and eventual limb loss, and the treatment options are revascularisation (endovascular or open surgery) or amputation. Adjuvant therapies with pharmacologic intervention or advanced healing dressings may improve the healing of the ulcer but do not correct the underlying vascular disease. They cannot replace revascularisation. Revascularisation is not always successful and durable. Thus, adjuvant therapy may improve the outcome if combined with revascularisation. (Level I)

Principle: Approximately 10%–20% of patients with peripheral arterial occlusive disease will need revascularisation surgery. Bypass surgery has a reported patency rate of 70% for crural-pedal bypass in both diabetic and non-diabetic patients at 5 years (in survivors), a limb salvage rate of 80% with a 1%–2% amputation rate at 2 years in both diabetics and nondiabetics (the same in diabetics), and a limb salvage rate of 80% with a 1%–2% amputation rate at 5 years.[1–3] Surgical results for distal dorsalis pedis bypass: at 5 years, the primary patency is 57%, whereas the secondary patency is 63% and limb salvage is 78% (only 49% alive). At 10 years, the primary patency is 38%, whereas the secondary patency is 42% and limb salvage is 56% (only 24% alive).[2–4] Endovascular results reported an 80% 2-year limb salvage (small series). High-quality evidence supporting the use of adjuvant therapy after revascularisation is still lacking.[5] However, the VOYAGER-PAD trial showed the value of adjuvant therapy after revascularisation with a significantly lower incidence of the composite outcome of acute limb ischaemia, major amputation for vascular causes, myocardial infarction, ischaemic stroke or death from cardiovascular causes.[6]

Updated Evidence:

1. Bonaca MP, Bauersachs RM, Anand SS, et al. Rivaroxaban in peripheral artery disease after revascularization. *N Engl J Med*. 2020;382(21):1994-2004.
2. Hess CN, Norgren L, Ansel GM, et al. A structured review of antithrombotic therapy in peripheral artery disease with a focus on revascularization: a TASC (InterSociety Consensus for the Management of Peripheral Artery Disease) initiative. *Circulation*. 2017;135(25):2534-2555.

Guideline 2.3: The risk of surgery should be weighed against the likelihood of success (of revascularisation and of healing of the ulcer after revascularisation) given a patient's comorbidities. (Level II)

Principle: Revascularisation does not always result in a perfused foot and does not always lead to an adequate inflow of oxygen to guarantee ulcer healing in the foot. For example, patients with heel gangrene and end-stage renal disease may be considered for primary amputation. However, care must be individualised. In some cases, limb preservation may be important to the patient because of issues with body image or in cases where limited function is possible and may still allow the patient to maintain independence with transfers. In addition, the risk of amputation needs to be considered in this complex risk-benefit analysis. Providers should discuss the risks and benefits clearly with the patient and determine the patient's preference.

No updated evidence.

Guideline 2.4: The role of endovascular therapy in revascularisation of the leg is well-established, but how it compares with open surgical procedures is not presently well-defined. The vascular surgeon can use judgement, expertise and local resources to consider the open or endovascular approach. (Level II)

Principle: The BASIL trial was a landmark randomised prospective study examining patients treated with either bypass or a balloon angioplasty approach to revascularisation. This study found no significant difference in either amputation-free survival or overall survival between the groups, but for patients who survived at least 2 years after randomisation, a bypass-first approach was associated with increased survival. BEST-CLI was a randomised, prospective, international study that divided patients with limb threatening disease into open surgical and endovascular cohorts. The trial showed that patients with an adequate great saphenous vein for surgical revascularisation had significantly fewer major adverse limb events or deaths with surgical revascularisation compared to an endovascular approach, suggesting the continued importance of open surgical approaches in appropriate patients.[4]

Updated Evidence:

1. Farber A, Menard MT, Conte MS, et al; BEST-CLI Investigators. Surgery or endovascular therapy for chronic limb-threatening ischemia. *N Engl J Med*. 2022;387:2305-2316 [RCT].

Guideline 2.5: A multidisciplinary approach is recommended for patient care when revascularisation is performed. (Level III)

Principle: Current guidelines are poorly understood and adhered to, with many different treatment strategies and algorithms varying between areas of the world.[1] Treatment appears to be optimised when a multidisciplinary team is involved.[2–4]

Updated Evidence:

1. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. *J Vasc Surg*. 2016;63(2)(suppl 1):3s-21s [LIT REV].

Guideline 2.6: The role of revascularisation of the angiosome is currently unknown, with additional studies needed to determine its importance. (Level III)

Principle: Initial reports documented enthusiasm to treat the angiosomes of the foot. However, these results have not been consistently reproducible. Despite continued enthusiasm for this technique, systematic reviews have not shown consistent results.

Updated Evidence:

1. Forsythe RO, Apelqvist J, Boyko EJ, et al. Effectiveness of revascularisation of the ulcerated foot in patients with diabetes and peripheral artery disease: A systematic review. *Diabetes Metab Res Rev*. 2020;36 Suppl 1:e3279 [LIT REV].
2. Fujii M, Terashi H. Angiosome and tissue healing. *Ann Vasc Dis*. 2019;12(2):147-150 [LIT REV].
3. Stimpson AL, Dilaver N, Bosanquet DC, Ambler GK, Twine CP. Angiosome specific revascularisation: does the evidence support it? *Eur J Vasc Endovasc Surg*. 2019;57(2):311-317 [LIT REV].

Guideline 2.7: The role of stem cell and gene therapy as an alternative method of limb revascularisation is promising but currently undefined. (Level III)

Principle: Stem cell therapy is a promising treatment modality for small vessel revascularisation, with initial success in the TACT trial as well as other small series.[1–3] Recent reports of success have now been documented in small randomised trials. There is no FDA-approved stem therapy for chronic wounds at this time. Additional studies are needed to define the role of this therapy in appropriate populations of patients.

Updated Evidence:

1. Ho J, Yue D, Cheema U, Hsia HC, Dardik A. Innovations in stem cell therapy for diabetic wound healing. *Adv Wound Care*. 2022 [LIT REV].
2. Gorecka J, Kostiuk V, Fereydooni A, Gonzalez L, et al. The potential and limitations of induced pluripotent stem cells to achieve wound healing. *Stem Cell Res Ther*. 2019;10(1):87 [LIT REV].
3. Lopes L, Setia O, Aurshina A, Liu S, et al. Stem cell therapy for diabetic foot ulcers: a review of preclinical and clinical research. *Stem Cell Res Ther*. 2018;9(1):188 [LIT REV].
4. Qadura M, Terenzi DC, Verma S, Al-Omran M, Hess DA. Concise review: cell therapy for critical limb ischemia: an integrated review of preclinical and clinical studies. *Stem Cells*. 2018;36(2):161-171.
5. Forster R, Liew A, Bhattacharya V, Shaw J, Stansby G. Gene therapy for peripheral arterial disease (review). *Cochrane Database Syst Rev*. 2018;10:CD012058 [LIT REV].
6. Peeter Weem SM, Teraa M, de Borst GJ, Verhaar MC, Moll FL. Bone marrow derived cell therapy in critical limb ischemia: a meta-analysis of randomised placebo controlled trials. *Eur J Vasc Endovasc Surg*. 2015;50:775-783 [LIT REV].

Guideline 2.8: The role of the deep vein arterialisation technique for limb revascularisation is promising but currently undefined. (Level II)

Principle: Deep vein arterialisation using open techniques has been historically associated with poor results. However, newer endovascular methods have shown some recent promising results.

Updated Evidence:

1. Shishehbor MH, Powell RJ, Montero-Baker MF, et al; PROMISE II Investigators. Transcatheter arterialization of deep veins in chronic limb-threatening ischemia. *N Engl J Med*. 2023;388(13):1171-1180 [PCOH].
2. Yan Q, Prasla S, Carlisle DC, Rajesh A, Treffalls J, Davies MG. Deep venous arterialization for chronic limb threatening ischemia in atherosclerosis patients – a meta-analysis. *Ann Vasc Surg*. 2022;81:1-21 [LIT REV].

4 | TREATMENT OF ARTERIAL ULCERS: ADJUVANT AGENTS

***Preamble*:** The level of evidence concerning most adjuvant therapies for arterial ulcers is limited; it ranges from a few case reports to controlled studies. Significant arterial disease associated with ulcers should be revascularised. Adjuvant agents cannot replace revascularisation. However, when revascularisation is impossible or unsuccessful or when successful revascularisation does not result in healing, adjuvant agents may be useful. Adjuvant therapy may also be useful in assuring healing in combination with revascularisation. More research is needed to define the proper use (timing, dosage, etc.) of most adjuvant therapies.

While studies have been published in this area since 2014, by and large, they do not change the recommendations made in the 2014 Guidelines. For each of the previous guidelines, new studies are briefly described, along with their impact on the previous recommendations.

Devices

Guideline 3.1: Ultrasound therapy has been extensively studied for both pressure and venous ulcers. There are few, if any, studies specifically on arterial ulcers. Thus, recommendations for use in arterial ulcers cannot currently be made. Further research should be pursued in this area. (Level III)

Principle: Ultrasound may have effects through both thermal and nonthermal properties, including effects on the remodelling phase (thermal) and changing cell membrane permeability (nonthermal). Although there are animal studies and case series that support the efficacy of ultrasound, the lack of RCTs and the variability in settings that have been used in different studies make it difficult to make a recommendation for its use, particularly in arterial ulcers. In a study of a contact and a non-contact ultrasound treatment protocol for lower extremity wounds of any aetiology, including venous insufficiency, diabetic ulcers and peripheral arterial disease, wound metrics of size, volume and granulation tissue were improved. Although this was a small sample pilot study with only 12 wounds studied, it does provide some evidence of benefit in this mixed aetiology wound population.[1] In a RCT multicentre trial conducted to compare outcomes in patients randomised to standard care (SC) alone or SC and 40 kHz noncontact, low-frequency ultrasound (NLFU) treatments 3 times per week for 4 weeks showed an average wound size reduction of 61.6% ± 28.9 in the NLFU+SC compared to 45% ± 32.5 in the SC group ($p = 0.02$). A limitation of the study was that patients with limited arterial flow were excluded from it.

Updated Evidence:

1. Viana L, Pompeo M. Healing rate of chronic and subacute lower extremity ulcers treated with contact ultrasound followed by non-contact ultrasound therapy: The VIP ultrasound protocol. *Wounds*. 2017;29(8):231-239.
2. Gibbons GW, Orgill DP, Serena TE, et al. A prospective, randomised, controlled trial comparing the effects of noncontact, low-frequency ultrasound to standard care in healing venous leg ulcers. *Ostomy Wound Manage*. 2015;61(1):16-29.

Updated Evidence:

Guideline 3.2: Topical negative pressure wound therapy (NPWT) may be promising for mixed ulcers. It may have a role as an adjuvant agent in arterial ulcers, but further study is still required, with no new studies noted. A prospective, single-centre study of 50 patients with ischaemic diabetic foot ulcers was randomised to either percutaneous endovascular angioplasty combined with negative pressure closed drainage or percutaneous endovascular angioplasty combined with depuration. The findings showed that the ulcer healing rate at 180 days post-surgery was significantly greater in the negative pressure group (52% vs. 12%) ($p = 0.002$, <0.05). (Level II—*increased*)

Principle: Topical negative pressure wound therapy has become very popular for many reasons, including the obvious benefit of minimising dressing changes and drainage control. With respect to arterial ulcers, there are at least theoretical reasons to consider effects on blood flow (positive or negative), but updated evidence suggests benefits on healing in the setting of PAD.

Updated Evidence:

1. Dong B, Wang X, Wang W, et al. Effect of percutaneous endovascular angioplasty combined with negative pressure drainage on the "one-stop" treatment of ischemic diabetic foot ulcer. *Ann Vasc Surg*. 2022:S0890-5096(22)00897-4.

Guideline 3.3: Intermittent pneumatic leg compression (IPC) increases blood flow and may be beneficial in limbs with impaired distal perfusion, either before or after revascularisation. A meta-analysis derived from single, small, nonrandomised studies in 2015 showed IPC use was associated with statistically significant improvements in ulcer healing and amputation (OR, 0.14; 95% CI, 0.04–0.55)[1] A retrospective study ($n = 187$) showed a reduction in minor amputations and a decrease in limb pain for patients with CLI. A prospective RCT ($n = 34$) randomising IPC ($n = 18$) to exercise only ($n = 16$) found an improved healing rate of ulcers and a reduced amputation rate. (Level II)

Principle: Intermittent pneumatic compression (IPC) uses external pressure to create gradients that can result in increased blood flow in the setting of PAD.

Updated Evidence:

1. Zaki M, Elsherif M, Tawfick W, et al. The role of sequential pneumatic compression in limb salvage in non-reconstructable critical limb ischemia. *Eur J Vasc Endovasc Surg*. 2016;51(4):565-571.
2. Abu Dabrh AM, Steffen MW, Asi N, Undavalli C, Wang Z, et al. Nonrevascularization-based treatments in patients with severe or critical limb ischemia. *J Vasc Surg*. 2015;62(5):1330-9.e13.
3. Alvarez OM, Wendelken ME, Markowitz L, Comfort C. Effect of high-pressure, intermittent pneumatic compression for the treatment of peripheral arterial disease and critical limb ischemia in patients without a surgical option. *Wounds*. 2015;27(11):293-301.

Guideline 3.4: In patients with non-reconstructable anatomy or whose ulcer is not healing despite revascularisation, hyperbaric oxygen therapy (HBOT) should be considered as an adjuvant therapy. Selection criteria include ulcers that are hypoxic (due to ischaemia), and the hypoxia is reversible by hyperbaric oxygenation. Tissue hypoxia, reversibility and responsiveness to oxygen challenge are currently measured by transcutaneous oximetry (PtcO2), although other methods are under investigation. The majority of data has been collected in patients with diabetes and with arterial ulcers. Studies are required to determine whether these results can be generalised to all ischaemic ulcers and whether post-revascularisation treatment is of benefit. A systematic review and meta-analysis of hyperbaric oxygen therapy for diabetic foot ulcers with peripheral arterial occlusive disease included 11 studies, totalling 729 patients, including 7 randomised clinical trials, 2 controlled clinical trials, and 2 retrospective cohorts, demonstrating significantly fewer major amputations in the HBOT group (10.7% vs. 26.0%; risk difference, −15%; 95% confidence interval [CI], −25 to −6; $p = 0.002$; number needed to treat, 7; 95% CI, 4–20) (Diabetic ischaemic ulcers—Level I; nondiabetic ischaemic ulcers—Level II).

Principle: The benefits of HBOT are clearly related to changing transcutaneous oxygenation with secondary improvements in wound healing.

Updated Evidence:

1. Brouwer RJ, Lalieu RC, Hoencamp R, van Hulst RA, Ubbink DT. A systematic review and meta-analysis of hyperbaric oxygen therapy for diabetic foot ulcers with arterial insufficiency. *J Vasc Surg*. 2020;71(2):682-692.e1.

Systemic Agents

Guideline 3.5: Pentoxifylline does not improve arterial ulcer healing. (Level I) While cilostazol has been shown to improve limb-related and arterial patency-related outcomes in patients with advanced PAD and CLI who are status post revascularisation, its effect on arterial ulcers remains to be evaluated. A meta-analysis by Desai examined the efficacy of cilostazol on limb salvage rates after revascularisation cilostazol improves limb-related and arterial patency-related outcomes in patients with advanced PAD and CLI who are undergoing endovascular and open revascularisation procedures. However, because the data in the literature are limited, wound healing outcome measures, including time to wound healing or completion of wound healing outcomes, were evaluated qualitatively. These studies suggest that patients who use cilostazol have improved wound healing as measured by ulcer wound grade, but the studies did not uniformly standardise their outcome measures and therefore a further sensitivity analysis could not be performed. Additional studies are needed to evaluate the effect of cilostazol therapy on wound healing in patients with advanced PAD. (Level III)

Principle: While there are theoretical reasons to consider pharmacological agents to improve blood flow by changing the physical properties of red blood cells and arterial flow inhibition, only limited data on their benefits has been demonstrated. That being said, weighing potential benefits, risks and options in patient-centred care makes their use and consideration worth discussion in selected patients.

Updated Evidence:

1. Desai K, Han B, Kuziez L, Yan Y, Zayed MA. Literature review and meta-analysis of the efficacy of cilostazol on limb salvage rates after infrainguinal endovascular and open revascularization. *J Vasc Surg*. 2021;73(2):711-721.e3.

Guideline 3.6: There is no evidence supporting the use of prostaglandins (PGE-1) in the treatment of arterial ulcers (Level II). There is high-quality evidence showing that prostanoids have *no effect* on the incidence of total amputations when compared against placebo. (Level II)

Principle: Prostoglandins have theoretical benefits in the setting of PAD but no demonstrated benefit in studies.

Updated Evidence:

1. Vietto V, Franco JVA, Saenz V, Cytryn D, Chas J, Ciapponi A. Prostanoids for critical limb ischaemia. *Cochrane Database Syst Rev*. 2018;1:CD006544.

Topical Agents

Guideline 3.7: There is insufficient evidence to determine whether the choice of topical agent or dressing affects the healing of arterial leg ulcers. Topical oxygen therapy has been advocated for ischaemic wound healing. A non-controlled retrospective analysis of 28 patients with PAD and non-healing ulcers were treated with topical oxygen at home after having vascular intervention revascularisation of the limb and/or debridement where appropriate. Overall, 66% had a reduction of the wound area ranging from 12% to 100%. None had major limb amputation. Eighteen percent underwent toe amputations. Further study is still required to clarify its benefits. (Level III)

Principle: Topical dressings can certainly have benefits or risks with respect to pain and drainage control, but the specific benefits of one over another on arterial ulcers have not been demonstrated. While hyperbaric oxygen therapy has been more robustly studied than topical oxygen therapy, the theoretical benefits, low-risk and availability of topical oxygen are worth discussing. Unfortunately,

consistent benefits on transcutaneous oxygen pressure and healing have not been demonstrated with topical oxygen therapy.

Updated Evidence:

1. Vulakh GM, Hingorani AP, Ascher E, Marks N. Adjunctive topical oxygen therapy for wound healing in patients with peripheral arterial disease. *Vascular*. 2022:17085381221080270.
2. Broderick C, Pagnamenta F, Forster R. Dressings and topical agents for arterial leg ulcers. *Cochrane Database Syst Rev*. 2020;1 (1):CD001836.

5 | WOUND BED PREPARATION

***Preamble*:** Wound bed preparation starts with the identification of wound aetiology and improving associated medical conditions (nutrition, blood flow and awareness). Addressing the general medical condition involves control of diabetes, hypertension, dyslipidaemia, evaluation of immunosuppressive drugs, improvement of nutritional status, smoking cessation and determining if the wound has adequate blood flow (revascularisation, angioplasty, regenerative medicine and others). (Level I)

Guideline 4.1: Debridement is the basis of wound bed preparation. It involves understanding basic concepts as often described by a systematic approach by the TIME acronym (Tissue, Inflammation/infection, Moisture imbalance and Epithelial edge advancement). There are multiple strategies for wound debridement: chemical, mechanical and surgical. Non-surgical debridement involves the use of autolytics (liquefies tissue promoting degradation by host enzymes—hydrogels, hydrocolloids), enzymes (remove devitalised tissue and can cause local irritation, proteolytic/collagenase, papain or fibrinolytic), mechanical (induce separation of tissue and remove debris, may macerate normal skin and remove newly formed tissue—wet to dry dressings, whirlpool, ultrasound, wound irrigation, polyacrylate moist therapy), larval therapy (*Lucilia sericata*—produce enzymes that break down dead tissue and removes all bacteria harbouring wound) and includes efforts to disrupt biofilm. (Level I)

Principle: Debridement of devitalised tissue and the potential benefits of moving a chronic wound to more active healing are well demonstrated, but caution must always be considered the setting of PAD.

Updated Evidence:

1. Goswami AG, Basu S, Banerjee T, et al. Biofilm and wound healing: from bench to bedside. *Eur J Med Res*. 2023;28:157 [LIT REV].
2. Sen CK, Roy S, Mathew-Steiner SS, Gordillo GM. Biofilm management in wound care. *Plast Reconstr Surg*. 2021;148(2):275e-288e [LIT REV].
3. Sibbald RG, Elliott JA, Persaud-Jaimangal R, et al. Wound bed preparation 2021. *Adv Skin Wound Care*. 2021;34(4):183-195 [LIT REV].
4. Granick MS, Tran BNN, Alvarez OM. Latest advances in wound debridement techniques. *Surg Technol Int*. 2020;36:37-40 [LIT REV].
5. Moya-López J, Costela-Ruiz V, García-Recio E, Sherman RA, De Luna-Bertos E. Advantages of Maggot debridement therapy for chronic wounds: a bibliographic review. *Adv Skin Wound Care*. 2020;33(10):515-525 [LIT REV].
6. Weigelt MA, McNamara SA, Sanchez D, Hirt PA, Kirsner RS. Evidence-based review of antibiofilm agents for wound care. *Adv Wound Care (New Rochelle)*. 2021;10(1):13-23 [LIT REV].
7. Harries RL, Bosanquet DC, Harding KG. Wound bed preparation: TIME for an update. *Int Wound J*. 2016;13 Suppl 3(Suppl 3):8-14 [LIT REV].

Guideline 4.2: Surgical debridement involves excision of necrotic/fibrotic tissue to a normal, well-vascularised tissue and removal of infected tissue. Multidisciplinary approaches can be helpful. (Level III)

Principle: While debridement for most chronic ulcers is well established, including patients with, PAD, there are also obvious concerns about creating additional problems in the setting of poor perfusion and oxygenation.

Updated Evidence:

1. Tran DL, Huang RW, Chiu ES, et al. Debridement: technical considerations and treatment options for the interprofessional team. *Adv Skin Wound Care*. 2023;36(4):180-187.
2. Sibbald RG, Elliott JA, Persaud-Jaimangal R, et al. Wound bed preparation 2021. *Adv Skin Wound Care*. 2021;34(4):183-195 [LIT REV].

Guideline 4.3: A moist wound contributes to a healing environment; however, an exudative wound with copious fluid can be detrimental to healing since it harbours substances that will impede cell proliferation (high levels of proteases [MMP] and pro-inflammatory cytokines) and can damage peripheral skin. Many arterial ulcers are too dry related to the poor perfusion in that area. A wound that is too dry can be addressed in multiple ways, including with occlusive dressings, petrolatum-based dressings or topical therapies. Optimisation of the wound environment to enhance cellular (keratinocyte and fibroblast) proliferation to result in epithelialisation requires clinical observation and knowledge of dressing and topical therapy options. For example, depending on the issue to be addressed, a wound might be treated with: hydrocolloids (autolytic debridement, occlusive or semi-occlusive, mild exudates) foam dressings (absorb mild to moderate exudates, insulate the wound, prevent maceration of normal skin and keep a healthy amount of moisture in the wound bed); alginates (absorb moderate exudates, are antibacterial, haemostatic and biodegradable) negative wound pressure therapy (absorbs a large amount of exudates, but is indicated only in non-infected wound bed). There are case studies attempting to optimise wound care with moisture sensors, but the significance of these for routine practice has not been demonstrated. (Level II)

Principle: Balancing the well-established benefits of moist wound healing with the detrimental effects of excessive drainage is difficult to measure but critical to address. Knowledge and experience with topical dressing options as wounds are monitored are critical.

Updated Evidence:

1. Henricson J, Sandh J, Iredahl F. Moisture sensor for exudative wounds – A pilot study. *Skin Res Technol*. 2021;27(5):918-924.
2. Harries RL, Bosanquet DC, Harding KG. Wound bed preparation: TIME for an update. *Int Wound J*. 2016;13 Suppl 3(Suppl 3):8-14 [LIT REV].

Guideline 4.4: Infected wounds (elevated bacterial concentration with a quantitative count $>10^5$ organisms per gram of tissue determined by biopsy of the wound) should be suspected when wounds fail to heal, become more painful, deteriorate or progress to a systemic infection and sepsis. Treatment involves control of medical conditions, debridement of devitalised tissue, and topical antimicrobials (antiseptics—iodine, peroxide, acetic acid, hypochlorous acids, chlorhexidine, silver sulfadiazine, and honey) with systemic antibiotic coverage for microorganisms depending on clinical concern for deeper pathogenic infection. (Level II)

Principle: Managing bacteria to reduce the risk of detrimental and critical infections is always a goal. While a chronic wound will always be colonised with bacteria, understanding the options related to control of physical conditions (e.g., debridement) and bacterial population (topical and systemic antibacterials) is critical.

Updated Evidence:

1. Li S, Renick P, Senkowsky J, Nair A, Tang L. Diagnostics for wound infections. *Adv Wound Care (New Rochelle)*. 2021;10(6):317-327 [LIT REV].
2. Kotronis G, Vas PRJ. Ultrasound devices to treat chronic wounds: the current level of evidence. *Int J Low Extrem Wounds*. 2020;19 (4):341-349 [LIT REV].
3. Haesler E, Swanson T, Ousey K, Carville K. Clinical indicators of wound infection and biofilm: reaching international consensus. *J Wound Care*. 2019;28(Sup3b):s4-s12 [LIT REV].
4. Harriott MM, Bhindi N, Kassis S, Summitt B, Perdikis G, Wormer BA, Rankin TM, Kaoutzanis C, Samaha M, Stratton C, Schmitz JE. Comparative antimicrobial activity of commercial wound care solutions on bacterial and fungal biofilms. *Ann Plast Surg*. 2019;83 (4):404-410 [CLIN S].
5. Jull AB, Cullum N, Dumville JC, Westby MJ, Deshpande S, Walker N. Honey as a topical treatment for wounds. *Cochrane Database Syst Rev*. 2015;2015(3):CD005083 [LIT REV].

Guideline 4.5: Education in management of wound bed.

Principle: It is important to establish a sense of team effort with patients, caregivers and healthcare providers, from the implementation of an action plan, education to an agreement on adherence to treatment. (Level II)

Principle: Evidence-based care that is patient-centred can be enhanced with the healthcare team considering more than one perspective (e.g., clinicians that might include vascular surgeons, orthopaedic surgeons, plastic surgeons, dermatologists, primary care providers, podiatrists, nurses, physical therapists and others). This is not always possible, but the intentional creation of a team with good communication has been demonstrated to enhance patient care.

Updated Evidence:

1. Kim PJ, Attinger CE, Steinberg JS, et al. Building a multidisciplinary hospital-based wound care center: nuts and bolts. *Plast Reconstr Surg*. 2016;138(3 Suppl):241S-247S.

Guideline 4.6: Knowledge of the different dressings (from simple dry gauze to tissue engineered dressings) and that different dressings may be required throughout the healing process depending on wound bed characteristics is important to improve wound healing. (Level II)

Principle: Dry wounds need moisture, exudative wounds need absorption, infected wounds need antimicrobial/antiseptics, necrotic wounds may need debridement (arterial ulcers are special cases in that debridement of tissue with compromised arterial flow can create additional problems with healing). Wound dressings should provide a balance to create a moist environment but also address excess drainage with optimised absorptive capacity. It should also protect the wound from contamination and trauma and minimise pain with dressing changes. Functional and aesthetic considerations should also be addressed when possible.

Updated Evidence:

1. Nuutila K, Eriksson E. Moist wound healing with commonly available dressings. *Adv Wound Care (New Rochelle)*. 2021;10 (12):685-698 [LIT REV].
2. Landriscina A, Rosen J, Friedman AJ. Systematic approach to wound dressings. *J Drugs Dermatol*. 2015;14(7):740-744 [LIT REV].

6 | PAIN MANAGEMENT FOR ARTERIAL ULCERS (NEW)

***Preamble*:** Pain is a common finding in patients with arterial ulcers. Pain in this population can manifest as acute or chronic pain. Acute pain can result from various treatments, including frequent wound debridement, whereas chronic pain can occur secondary to persistent wound and inflammation. Some patients may also have acute pain concurrently with chronic pain. Regardless of the time course, both the physical and psychological aspects of pain should be assessed and treated. No arterial ulcer-specific guidelines have been established to date to guide pain control in this special population. Pain management in this group follows the same strategies as other pain aetiologies with the caveat that patients with arterial ulcers may have co-morbidities, including renal insufficiency, which would require special caution and dose adjustment for certain classes of medications.

Guideline 5.1: Physicians should inquire, recognise and treat pain in patients with arterial ulcers. (Level II)

Principle: Pain is common in patients with arterial ulcers; however, it is thought to be undertreated in this patient population. Untreated or poorly treated pain can lead to neurohormonal changes, which can lead to altered immunity, blood flow, and glucose metabolism, thereby increasing the risk of poor wound healing. Inadequately treated acute

pain from the ulcer can alter neuronal changes, leading to the transformation of acute pain into a chronic pain state. Finally, untreated pain can impair function and mood, and ultimately, quality of life, in these patients. In light of all the adverse physiological and psychological consequences of untreated pain, it is critical for physicals to inquire about, recognise and treat pain in this patient population.

Updated Evidence:

1. Leren L, Johansen E, Eide H, Falk RS, Juvet LK, Ljoså TM. Pain in persons with chronic venous leg ulcers: a systematic review and meta-analysis. *Int Wound J*. 2020;17(2):466-484.
2. Abbade LP, Lastória S, Rollo Hde A. Venous ulcer: clinical characteristics and risk factors. *Int J Dermatol*. 2011;50(4):405-411.
3. Renner R, Seikowski K, Simon JC. Association of pain level, health and wound status in patients with chronic leg ulcers. *Acta Derm Venereol*. 2014;94(1):50-53.
4. Dunwoody CJ, Krenzischek DA, Pasero C, Rathmell JP, Polomano RC. Assessment, physiological monitoring, and consequences of inadequately treated acute pain. *J Perianesth Nurs*. 2008;23 (1 Suppl):S15-S27.
5. Herberger K, Rustenbach SJ, Haartje O, Blome C, Franzke N, Schäfer I, Radtke M, Augustin M. Quality of life and satisfaction of patients with leg ulcers—results of a community-based study. *Vasa*. 2011;40(2):131-138.

Guideline 5.2: Perform a thorough assessment of the pain, including location, distribution, chronicity, and characteristics of the pain. (Level II)

Principle: Optimal pain management requires a thorough assessment of the pain, including its location and distribution, chronicity and nature. Pain localised to a small region can be targeted using topical agents or a peripheral nerve block, whereas widespread pain may be better treated with systemic agents. Understanding the chronicity of pain is important as well. Pain that is temporal in nature (i.e., occurs with dressing change) may be treated with on-demand short-acting analgesics, whereas pain that is chronic in nature should be managed with scheduled analgesics. Finally, the nature of the pain is important. Pain can be nociceptive, neuropathic or mixed. Nociceptive pain is described as sharp, shooting and aching, whereas neuropathic pain is characterised as burning, tingling and pins and needles. While pain from an arterial ulcer may begin as nociceptive pain, it may also exhibit neuropathic characteristics over time. It is important to understand the nature of the pain because neuropathic or mixed pain tends to respond well to medications such as gabapentinoids, tricyclic antidepressants and selective serotonin-norepinephrine inhibitors (SNRIs).

Updated Evidence:

1. Hopf HW, Shapshak, D, Junkins S, O'Neill D. Managing wound pain. In: Bryant RA, Nix DP, eds. *Acute and Chronic Wounds: Current Management Concepts*. 5th ed. Mosby Elsevier; 2015.
2. Fillingim RB, Loeser JD, Baron R, Edwards RR. Assessment of chronic pain: domains, methods, and mechanisms. *J Pain*. 2016;17 (9 Suppl):T10-T20.
3. Pain Management Best Practices Interagency Task Force. *Pain Management Best Practices*. 2019. Accessed September 11, 2023. https://www.hhs.gov/sites/default/files/pain-mgmt-best-practices-draft-final-report-05062019.pdf

Guideline 5.3: Pain management for arterial ulcers should follow a ladder approach. The initial treatment should begin with topical and non-opioid analgesics. Weak and strong opioids should be added sequentially to the regimen if the pain remains uncontrolled. (Level III)

Principle: The World Health Organisation (WHO) Analgesic Ladder is an expert-opinion piece that guides the treatment of cancer pain. This approach may provide guidance for the management of non-malignant pain. The analgesic ladder approach recommends starting therapy with non-opioid medications as the first step, followed by the addition of weak and strong opioids for the second and third steps, respectively. In the case of arterial ulcers, the therapeutics for the first step should include topical agents, including lidocaine-prilocaine cream, lidocaine-tetracaine patches and ibuprofen foam dressings. The use of lidocaine-prilocaine cream or a lidocaine-tetracaine patch can be particularly helpful for managing pain for wound debridement because the local anaesthetic can anaesthetise the wound. Other medications to consider for the first step include acetaminophen and non-steroidal anti-inflammatory agents. If pain is inadequately controlled with agents in the first step, a physician should consider adding weak opioids such as tramadol in addition to agents in the first step. For patients whose pain is refractory to the medications in the first and second steps, a strong opioid should be considered along with agents from the first step. Options for strong opioids include hydrocodone, morphine, oxycodone, hydromorphone and fentanyl. Patients who have neuropathic pain should be started on a neuropathic agent such as gabapentin, pregabalin, tricyclic antidepressants (amitriptyline, nortriptyline and desipramine) and duloxetine. A number of these medications require dose adjustment in the setting of renal or hepatic insufficiency. Physicians should consult the Food and Drug Administration (FDA) package insert or a Chronic Pain Medicine expert for the appropriate dose. For severe pain, especially when initial efforts are not sufficient, referral to a Chronic Pain Medicine expert should be considered. Topical therapy for painful ulcers with narcotics is not established with good evidence.

Updated Evidence:

1. Purcell A, Buckley T, King J, Moyle W, Marshall AP. Topical analgesic and local anaesthetic agents for pain associated with chronic leg ulcers: a systematic review. *Adv Skin Wound Care*. 2020;33 (5):240-251.
2. Centers for Disease Control and Prevention, Public Health Service, U.S. Department of Health and Human Services. Guideline for prescribing opioids for chronic pain. J Pain Palliat Care Pharmacother. 2016;30(2):138-140.
3. Finnerup NB, Attal N, Haroutounian S, McNicol E, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol*. 2015;14(2):162-173.

4. Briggs M, Nelson EA, Martyn-St James M. Topical agents or dressings for pain in venous leg ulcers. *Cochrane Database Syst Rev*. 2012;11(11):CD001177.
5. Stjernswärd J. WHO cancer pain relief programme. *Cancer Surv*. 1988;7(1):195-208.
6. Ventafridda V, Saita L, Ripamonti C, De Conno F. WHO guidelines for the use of analgesics in cancer pain. *Int J Tissue React*. 1985;7(1):93-96.
7. Gutierrez Y, Pourali SP, Kohn AH, Jones ME, Rajkumar JR, Armstrong AW. Topical opioid use in dermatologic disease: a systematic review. *Dermatol Ther*. 2021;34(6):e15150 [LIT REV].

Guideline 5.4: Consider the use of peripheral nerve block to manage pain secondary to extensive wound debridement. (Level III)

Principle: Peripheral nerve block involves injecting local anaesthetic around a nerve or a group of nerves to preferentially anaesthetise a particular site of the body. This approach can be used to anaesthetise the upper or lower extremities and can be helpful when performing extensive wound debridement. A regional anaesthesiologist may be consulted when considering the utility of a peripheral nerve block.

Updated Evidence:

1. Kamel I, Ahmed MF, Sethi A. Regional anaesthesia for orthopaedic procedures: what orthopaedic surgeons need to know. *World J Orthop*. 2022;13(1):11-35.
2. O'Neill DK, Tsui SM, Ayello EA, Cuff G, Brem H. Anaesthesia protocol for heel pressure ulcer debridement. *Adv Skin Wound Care*. 2012;25(5):209-219.
3. Stein BE, Srikumaran U, Tan EW, Freehill MT, Wilckens JH. Lower-extremity peripheral nerve blocks in the perioperative pain management of orthopaedic patients: AAOS exhibit selection. *J Bone Joint Surg Am*. 2012;94(22):e167.

Guideline 5.5: Spinal cord stimulation should be considered to improve pain and blood flow for patients with lower extremity pain secondary to vascular insufficiency. (Level II)

Principle: Spinal cord stimulation (SCS) involves the placement of an electrode in the epidural space that is connected to an internal pulse generator. The internal pulse generator creates electrical impulses that interfere with pain signal transmission from the peripheral to the central nervous system. This technology is used for various painful conditions, including failed back surgery syndrome, painful diabetic neuropathy, pectoris angina, abdominal pain, complex regional pain syndrome and peripheral vascular disease. In the case of peripheral vascular disease, SCS inhibits sympathetic outflow and causes vasodilation. This ultimately leads to improved blood flow to the lower extremities. Additionally, SCS is thought to improve pain by stimulating the release of endogenous opioids and activation of supraspinal pain modulatory centres causing inhibition of pain signal transmission through ascending pathways of the spinal cord. A number of randomised-control trials have shown this technology to be effective for the treatment of painful peripheral vascular disease.

Updated Evidence:

1. Asimakidou E, Matis GK. Spinal cord stimulation in the treatment of peripheral vascular disease: a systematic review – revival of a promising therapeutic option? *Br J Neurosurg*. 2022;36(5):555-563.
2. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. *Eur J Pain*. 2006;10(2):91-101.
3. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine (Phila Pa 1976)*. 2005;30(1):152-160.
4. Fontana F, Bernardi P, Lanfranchi G, et al. Opioid peptide response to spinal cord stimulation in chronic critical limb ischemia. *Peptides*. 2004;25(4):571-575.
5. Erdek MA, Staats PS. Spinal cord stimulation for angina pectoris and peripheral vascular disease. *Anesthesiol Clin North Am*. 2003;21(4):797-804.
6. Myklebust JB, Cusick JF, Boerboom LE, Prieto TE, Khan TA. Vascular effects of spinal cord stimulation in the monkey. *Stereotact Funct Neurosurg*. 1995;64(1):32-39.
7. Cyrek AE, Henn N, Meinhardt F, et al. Improving limb salvage for chronic limb-threatening ischemia with spinal cord stimulation: a retrospective analysis. *Vasc Endovascular Surg*. 2021;55(4):367-373.

7 | PATIENT-REPORTED OUTCOMES AND HEALTH DISPARITIES

***Preamble*:** There is large evidence of physiologic assessments and classifications of peripheral artery disease severity; however, there is a paucity of information on patients' perceptions of their health status, understanding their symptom severity, patient's physical limitations and ultimately their quality of life. For patients with PAD, the main reason for seeking care is their health status (symptoms, function and quality of life); however, patients are largely unaware of the treatment of PAD and what is ahead of them as the disease progresses if left untreated or poorly treated. It is possible that patients who have better insight into their health status will also have better insights into their treatment benefits.

Guideline 6.1: Patient-centred reported health status evaluations have been independently linked to better clinical outcomes. Similarly, clinicians need to better understand the effects of PAD on patients' health status and quality of life when developing treatment strategies. Further research should be conducted to improve the correlation between changes in health status scores treatment modalities for PAD, and outcomes. (Level II).

Principle: Recommendations for use of patient-centred assessment of health status in peripheral arterial ulcers could have a positive impact.

Updated Evidence:

1. Rhymer JA, Mulder H, Smolderen KG, et al. Association of health status scores with cardiovascular and limb outcomes in patients with symptomatic peripheral artery disease: insights from the EUCLID (Examining Use of Ticagrelor in symptomatic Peripheral Artery Disease) trial. *J Am Heart Assoc*. 2020;9:e016573 [PCOH].
2. Smolderen KG, Gosch K, Patel M, et al. PORTRAIT (Patient-Centered Outcomes Related to Treatment Practices in Peripheral Arterial Disease: Investigating trajectories) Overview of design and rationale of an international prospective peripheral arterial disease study. *Circ Cardiovasc Qual Outcomes*. 2018;11:e003860 [PCOH].
3. Johnston A, Vemulapalli S, Gosch KL, et al. Ankle-brachial index in patients with intermittent claudication is a poor indicator of patient-centered and clinician-based evaluations of functional status. *J Vasc Surg*. 2019; 69:906-912 [CLIN S].
4. Bunte MC, House JA, Spertus JA, Cohen DJ, Marso SP, Safley DM. Association between health status and long-term mortality after percutaneous revascularization if peripheral artery disease. *Catheter Cardiovasc Interv*. 2016;87:1149-1455 [CLIN S].
5. Izquierdo-Porrera AM, Gardner QW, Bradham DD, et al. Relationship between objective measures of peripheral arterial disease severity to self-reported quality of life in older adults with intermittent claudication. *J Vasc Surg*. 2005;41:625-630 [CLIN S].
6. Long J, Modrall JG, Parker BJ, Swann A, Welborn MB 3rd, Anthomy T. Correlation between ankle-brachial index symptoms, and health-related quality of life in patients with peripheral vascular disease. *J Vasc Surg*. 2004;39:723-727 [PCOH].
7. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2001;286:1317-1324 [LIT REV]

Guideline 6.2: Emphasis on optimisation of diagnosis and medical management for PAD should be placed on populations at risk. This is particularly true for the African-American population, which faces elevated rates of PAD with subsequent high morbidity and mortality. (Level II)

Principle: The incidence of PAD among African-Americans is 2–3 times the rate of non-Hispanic whites at all age groups. African-American (Black) race is one of the strongest risk factors for the development of PAD, even when controlling for well-known cardiovascular risk factors (hypertension, diabetes, smoking, dyslipidaemia) and non-traditional inflammatory markers (C-reactive protein, D-dimer, fibrinogen, homocysteine and interleukin-6). Although PAD and critical limb ischaemia are more common in the African American population, they are less likely to be offered and receive salvage revascularization procedures. This could be due to unconscious bias or delayed presentation; therefore, improvement in diagnosis and medical management in this population can decrease limb salvage disparities.

Updated Evidence:

1. Bevan GH, Solaru KTW. Evidence-based medical management of peripheral artery disease. *Arterioscler Thromb Vasc Biol*. 2020;40:541-553 [STAT].
2. Durazzo TS, Frencher S, Gusberg R. Influence of race on the management of lower extremity ischemia: revascularization vs amputation. *JAMA Surg*. 2013;148:617-623 [PCOH].
3. Schoenborn CA, Adams PF, Peregoy JA. Health behaviors of adults: United States, 2008-2010. *Vital Health Stat*. 2013;10:1-184 [STAT].
4. Holman KH, Henke PK, Dimick JB, Mirkmeyer JD. Racial disparities in the use of revascularization before leg amputation in Medicare patients. *J Vasc Surg*. 2011;54:420-426e [CLIN S].
5. Ix JH, Allison MA, Deneberg JO, Cushman M, Criqui MH. Novel cardiovascular risk factors do not completely explain the higher prevalence of peripheral arterial disease among African Americans. The San Diego Population Study. *J Am Coll Cardiol*. 2008;2347-2354 [PCOH].
6. Allison MA, Criqui MH, McClelland RL, et al. The effect of novel cardiovascular risk factors on the ethnic-specific odds for peripheral arterial disease in the Multi-Ethnic Study (MESA). *J Am Coll Cardiol*. 2006;481:1190-1197 [PCOH].
7. Hughes K, Seetahal S, Oyetunji T, et al. Racial/ethnic disparities in amputation and revascularization: a nationwide inpatient sample study. *Vasc Endovascular Surg*. 2014;48:34-37 [PCOH].

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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