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Review Article

Vascular Pain: A Narrative Review on Venous Leg Ulcers

Matteo L. Giuseppe Leoni[1], Giacomo Farì[2*], Annalisa Caruso[3], Ameen A. Al-Alwany[4], Tran Van Y[5], Phong Van Pham[5], Giustino Varrassi[4,6]

[1]*Department of Medical and Surgical Sciences and Translational Medicine, Sapienza University of Roma, Roma, Italy.*
[2]*Department of Experimental Medicine, University of Salento, Lecce, Italy.*
[3]*Department of Surgery, ASST Lodi, Lodi, Italy.*
[4]*College of Medicine, University of Baghdad, Baghdad, Iraq.*
[5]*Department of Anesthesiology and Pain Medicine, Binh Dan Hospital, Ho Chi Minh City, Vietnam*
[6]*Fondazione Paolo Procacci, 00193 Roma, Italy.*

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Abstract

Background: Venous leg ulcers (VLUs) affect 1-3% of the population and impose substantial pain-related morbidity, yet vascular pain remains under recognized in clinical practice and research.

Objectives: This narrative review synthesizes current evidence on the pathophysiology, clinical manifestations, and management strategies for VLU-associated pain.

Methods: A comprehensive literature search was conducted across PubMed/MEDLINE, Scopus, Embase, and Web of Science (January 2015-July 2025) following SANRA guidelines. Search terms included "vascular pain", "venous leg ulcer", "chronic venous disease" and related terminology. Studies addressing pathophysiology, clinical characteristics, diagnostic approaches, and therapeutic interventions were included.

Results: VLU pain demonstrates complex pathophysiology encompassing nociceptive, neuropathic, and no ciplastic components driven by venous hypertension, chronic inflammation, and central sensitization. Pain prevalence ranges from 50-87% in VLU patients, significantly impacting quality of life and functional status. Evidence supports a five-strategy management framework: (1) treating underlying venous pathology through early ablation, (2) optimized compression therapy achieving ~40 mmHg ankle interface pressure, (3) procedure-specific local anesthesia using topical agents, (4) multimodal systemic analgesia targeting neuropathic features, and (5) adjunctive venoactive drugs. Patient-reported outcome measures reveal substantial psychosocial burden beyond wound-related symptoms.

Conclusion: VLU pain represents a distinct clinical entity requiring mechanism-based, multidisciplinary approaches. Early venous intervention, evidence-based compression protocols, and targeted analgesic strategies show promise for improving outcomes. Critical research gaps include dedicated pain-focused clinical trials, standardized outcome measures, and personalized treatment algorithms. Enhanced recognition and systematic management of vascular pain could substantially improve patient-centered outcomes in chronic venous disease.

Key words: Chronic venous disease; Compression therapy; Pain management; Vascular pain; Venous leg ulcers

Introduction

Pain of vascular origin represents a distinct yet under recognized clinical entity. Chronic venous disease (CVD) and its most debilitating complication, venous leg ulcers (VLUs), represent a prevalent and underappreciated source of vascular pain distinguished by complex pathophysiology and significant impact on quality of life. Venous leg ulcers, which account for approximately 70–90 % of all chronic leg ulcers, affect about 1 % of the Western population during their lifetime, with prevalence rising to 3–5 % among individuals above 65 years of age (1,2). Patients with VLUs commonly experience persistent wound-related pain, with reported prevalence ranging broadly from 50 % to as high as 87 %, reflecting varying methodologies and patient populations (3–5). This pain is multifactorial in origin. Venous hypertension resulting from valve incompetence or obstruction leads to extravasation of plasma proteins, leukocyte trapping, chronic inflammation, and microvascular ischemia. This milieu promotes extracellular matrix degradation and impaired wound healing, while sensitizing both nociceptive and neuropathic pathways (6). Biochemically, the persistent inflammatory state is characterized by elevated proinflammatory cytokines and proteases, compounding nociceptor activation and contributing to perceptual variability

**Corresponding author: dr.giacomofari@gmail.com*

and central sensitization (7). Clinically, pain associated with VLUs often manifests as dull, aching, or burning sensations that may worsen during movement or depend on limb position and can be constant or intermittent (8). Qualitative studies highlight the profound psychosocial burden of VLU-associated pain: patients report embarrassment, interrupted sleep, impaired mobility, and emotional distress, all of which exacerbate pain perception and amplify central nociplastic mechanisms (9). Despite these profound tribulations, vascular pain in the context of VLUs remains underrepresented within pain taxonomy frameworks and is often inadequately addressed in clinical practice. Standard management strategies for VLUs, including compression therapy, leg elevation, wound dressings, and corrective vascular interventions, primarily target ulcer healing but frequently fail to provide adequate analgesia. Moreover, comorbidities such as obesity, immobility, or lipodermatosclerosis may further exacerbate both ulcer chronicity and pain severity (10,11). Emerging therapeutic avenues integrating multimodal approaches offer promise. For instance, addressing both underlying vascular pathology (via compression or endovenous procedures) and neuropathic or inflammatory pain pathways (through pharmacotherapy or neuromodulation) may yield superior outcomes (12). However, mechanistic studies specific to VLU pain remain scarce, and well-designed clinical investigations are lacking.

In summary, pain originating from VLU seems a complex, multifaceted phenomenon encompassing nociceptive, neuropathic, and nociplastic components. The high prevalence and substantial morbidity associated with VLU pain underscore the critical need for enhanced recognition, refined pathophysiological delineation, and targeted therapeutic research. This review aims to synthesize current knowledge and highlight opportunities for future innovation in this underexplored field.

Methods

This review was conceived as a narrative synthesis aimed at providing a comprehensive overview of the epidemiology, pathophysiology, clinical manifestations, diagnostic approaches, and therapeutic strategies related to vascular pain, with particular emphasis on chronic venous disease and VLUs. The methodological approach followed the recommendations of the Scale for the Assessment of Narrative Review Articles (SANRA), which encourages clarity of scope, transparent literature selection, scientific reasoning, and appropriate referencing (13).

Literature Search Strategy: A non-systematic but comprehensive literature search was conducted across multiple databases, including PubMed/MEDLINE, Scopus, Embase, and Web of Science, covering publications from January 2015 to July 2025. Search terms combined controlled vocabulary (MeSH) and free-text keywords related to vascular pain and chronic venous disorders. The primary search string included combinations of the following terms: *"vascular pain"*, *"chronic venous disease"*, *"venous leg ulcer"*, *"ulcer pain"*, *"nociceptive"*, *"neuropathic"*, *"nociplastic"*, and *"pathophysiology"*. Boolean operators and filters were applied to refine results for peer-reviewed original studies, reviews, and clinical guidelines. Reference lists of retrieved articles were also screened to identify additional relevant publications.

Eligibility Criteria*:* Eligible studies were those that provided information on:

1. Pathophysiology of vascular pain (ischemia, microvascular dysfunction, neuroinflammation, nociplastic mechanisms).
2. Clinical characteristics of pain in VLUs, including prevalence, severity, and patient-reported outcomes.
3. Diagnostic approaches integrating vascular and pain assessment.
4. Management strategies, including conservative, pharmacological, interventional, and bioengineering-based approaches.

Both clinical and translational studies were considered. Publications not written in English, conference abstracts without full text, and case reports without broader contextual discussion were excluded.

Data Extraction and Synthesis:

Two authors independently (MLGL, GF) reviewed titles and abstracts for relevance. Full texts of eligible studies were then examined, and relevant data were extracted into structured tables that included study design, population characteristics, main findings, and implications for vascular pain management. Emphasis was placed on identifying recurrent themes across studies rather than conducting quantitative synthesis, in line with the objectives of a narrative review. The search strategy and study selection process are summarized in the PRISMA-style flow diagram (Fig. 1).

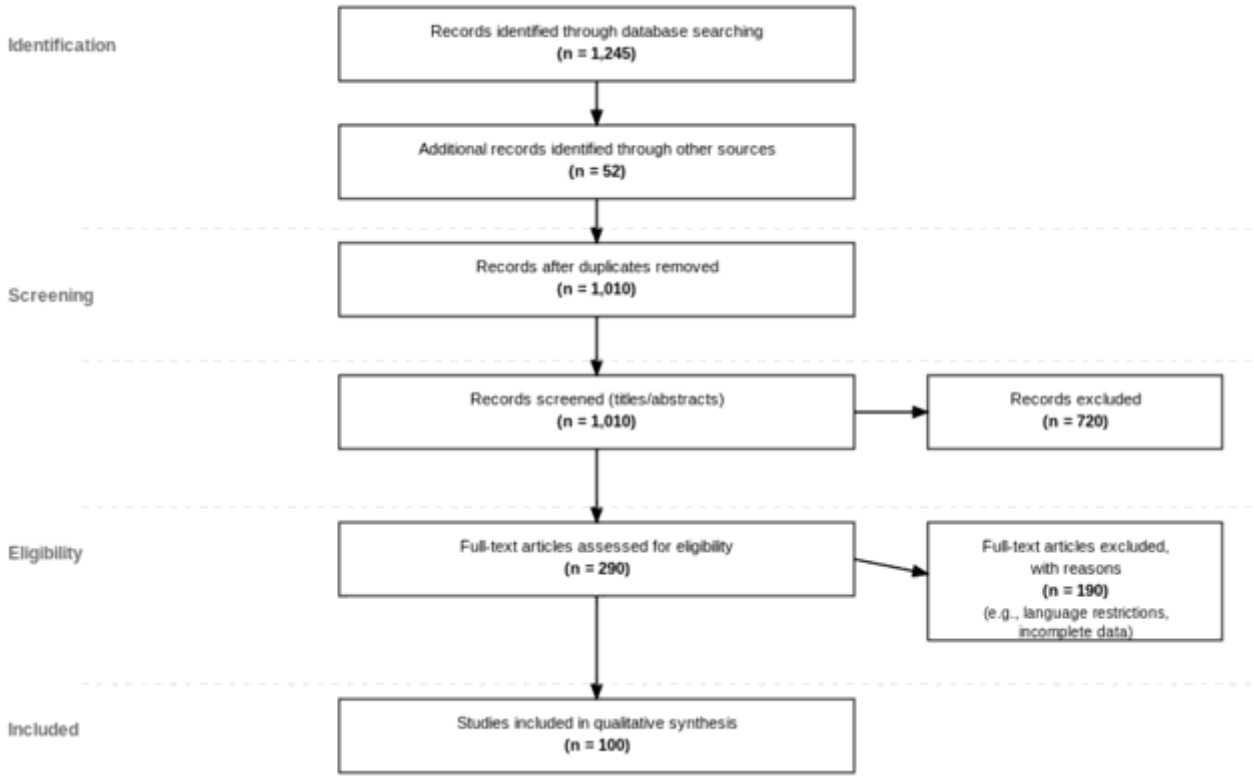

Fig. 1 Flowchart of study selection.

Quality Considerations and Scientific Reasoning
Although no formal risk-of-bias assessment was performed (consistent with the narrative design), care was taken to prioritize high-quality peer-reviewed sources, recent systematic reviews, clinical practice guidelines, and original studies with robust methodology. In accordance with SANRA item 3 (scientific reasoning), studies were critically appraised in terms of internal validity, external applicability, and consistency with existing evidence. Where contradictory findings emerged, these were explicitly discussed with a third researcher (GV) to avoid selective reporting.

Referencing and Transparency: All references were managed using citation software, and reporting adhered to the Vancouver style. Following SANRA item 6 (appropriate referencing), priority was given to recent (2020–2025) publications indexed in major scientific databases. When earlier landmark studies were cited, their relevance was justified in the context of historical or mechanistic insights.

Limitations of Methodology
As this is a narrative rather than a systematic review, potential limitations include selection bias, the absence of quantitative meta-analysis, and possible underrepresentation of non-English language studies. Nevertheless, the adoption of SANRA criteria, transparent description of the search process, and integration of multidisciplinary perspectives mitigate these concerns and strengthen the scientific validity of the review.

Results

Epidemiology and patient-reported burden
VLUs, which comprise approximately 60–80% of all lower-limb ulcers, are closely linked to pain, impaired sleep, psychological morbidity, and functional limitations (14–17). The impact of these symptoms is increasingly assessed using disease- and wound-specific patient-reported outcome measures (PROMs), including VEINES-QOL/Sym, VLU-QoL, Wound-QoL, and the Cardiff Wound Impact Schedule. These instruments capture pain-related interference and broader consequences on daily living, with measurement properties that, while variable, are generally acceptable for comparative analyses at the group level (18–20).

Pathophysiology of VLU pain: Venous hypertension propagates excessive pressure into the microcirculation, leading to capillary dilatation, leukocyte adhesion and degranulation, fibrin cuff deposition, and repeated episodes of hypoxia–reperfusion injury, which collectively maintain a state of chronic inflammation (21–25). Mechanistic studies demonstrate that these processes increase local concentrations of protons, bradykinin, prostanoids, and pro-inflammatory cytokines, thereby sensitizing peripheral nociceptors and amplifying pain signaling. Over time, persistent inflammation, tissue edema, and repeated procedural trauma, such as dressing changes perpetuate both continuous “background” and activity-related “incident” pain. Prolonged ulcer chronicity further contributes to neuropathic alterations and central sensitization, aggravating the pain phenotype (4,21–27). The pathophysiological mechanisms linking venous hypertension to pain sensitization are illustrated in Figure 2.

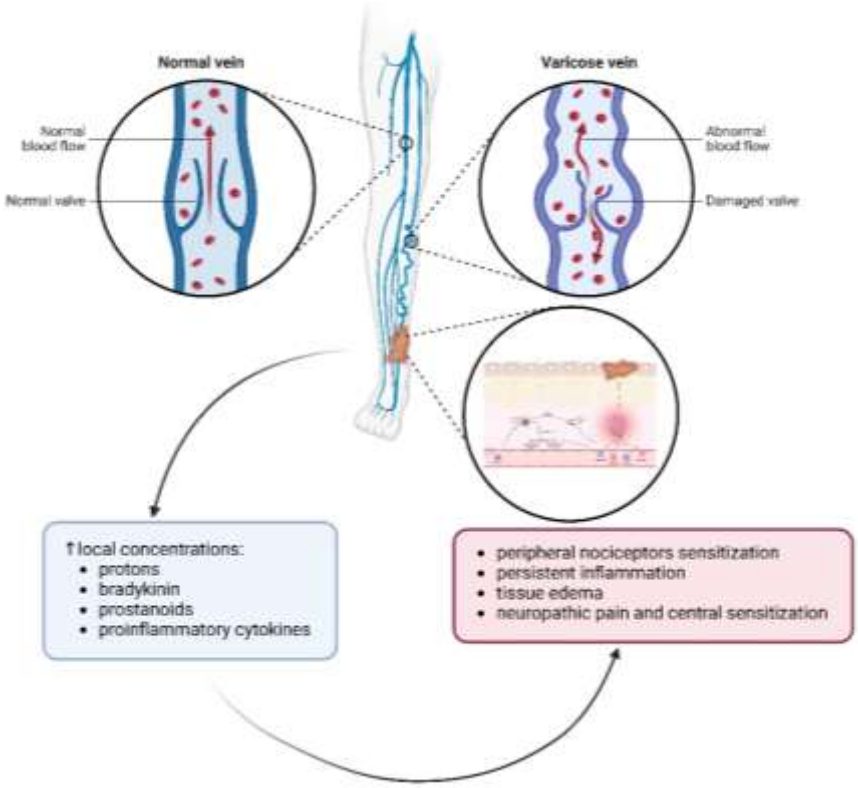

Fig. 2 Mechanistic pathways of venous hypertension and pain in VLU.

Venous hypertension caused by valve dysfunction leads to abnormal microcirculatory pressure, inflammatory mediator release, and tissue injury. These processes increase local concentrations of protons, bradykinin, prostanoids, and cytokines, driving nociceptor sensitization, persistent inflammation, tissue edema, and central sensitization that contribute to chronic pain. Created in https://BioRender.com

Clinical phenotype and assessment: Patients with VLUs typically report a spectrum of pain manifestations, including persistent aching or burning sensations representing "background" pain, movement-evoked or position-dependent "incident" pain, and procedure-related exacerbations during interventions such as debridement or dressing changes (4). Standardized numeric or visual analog scales remain the most widely applied tools to quantify intensity, while neuropathic screening instruments such as DN4 assist in identifying neuropathic descriptors when present (28,29). Comprehensive pain assessment should be integrated with vascular evaluation, including Clinical–Etiological–Anatomical–Pathophysiological (CEAP) classification, duplex ultrasonography, and objective arterial indices such as the ankle–brachial pressure index (ABPI), to ensure safe prescription of compression therapy (30–32). PROMs such as VEINES-QOL/Sym, the Cardiff Wound Impact Schedule (CWIS), and Wound-QoL are frequently employed in active VLUs to capture pain-related interference and broader quality-of-life impact (18–20).

Diagnostic framework (vascular and wound): Accurate diagnostic assessment is fundamental to the safe and effective management of VLUs. All patients should undergo clinical staging using the CEAP classification, which provides a standardized framework for documenting disease severity and guiding intervention. Duplex ultrasonography remains the gold standard for mapping venous reflux and obstruction, enabling precise identification of superficial, deep, or perforator incompetence and informing decisions regarding endovenous or surgical correction (33,34). In parallel, arterial evaluation is indispensable, as undiagnosed peripheral arterial disease (PAD) can render compression unsafe and increase the risk of ischemic complications (3,34). The ABPI is the most widely used screening tool, supplemented by toe pressure or transcutaneous oxygen tension in cases of arterial calcification, diabetes, or inconclusive results (35). The European Society for Vascular Surgery (ESVS) 2022 guideline recommends target ankle interface pressures ≥40 mmHg for active VLUs, recognizing this as the therapeutic threshold for promoting venous return and accelerating healing (30). In patients with mixed arterial–venous disease, modified or reduced compression is advised, while sustained compression is contraindicated if ankle pressure is <60 mmHg, toe pressure <30 mmHg, or ABPI <0.6 (4,25,26). Evidence syntheses highlight inter-guideline variability in safety thresholds, with some recommendations adopting a more conservative cutoff of 0.8 for ABPI (31). This variation underscores the need for individualized clinical

judgment, close patient monitoring, and periodic reassessment during compression therapy.

Emerging studies suggest that dynamic pressure monitoring and novel smart textiles may improve safety and adherence, offering real-time feedback on interface pressures (36). In addition, structured vascular assessment protocols that integrate duplex and ABPI testing into wound care pathways have been associated with earlier diagnosis of mixed disease and improved healing trajectories (37). Overall, thorough vascular staging and arterial assessment remain cornerstones of evidence-based VLU care, ensuring that compression, the mainstay of therapy, is both safe and optimally effective. Figure 3 presents a comprehensive diagnostic flowchart that integrates these assessment components into a systematic workflow for VLUs evaluation and compression therapy decision-making.

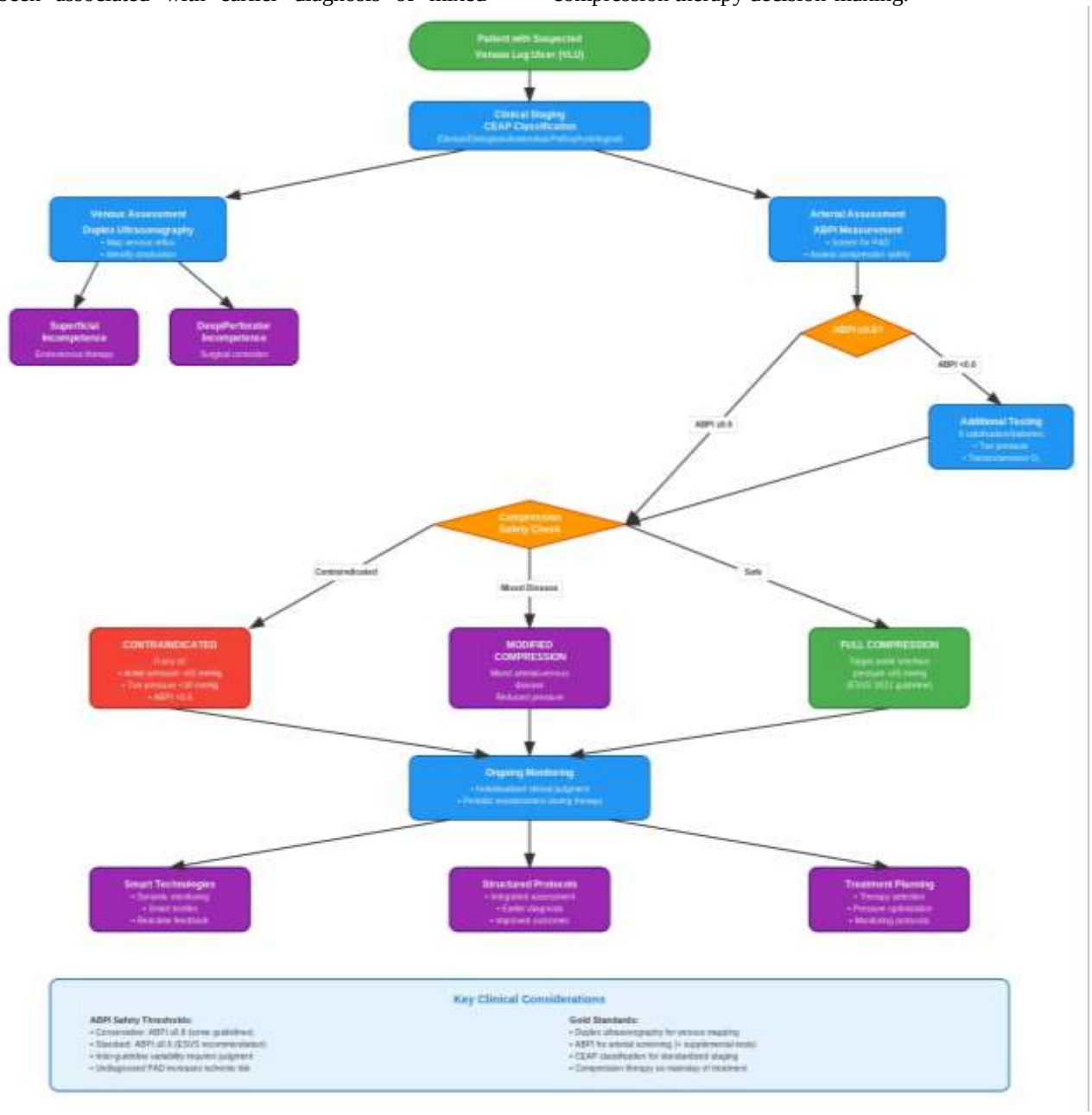

Fig. 3 Diagnostic framework for VLU assessment and compression therapy planning.

The flowchart outlines a structured evaluation pathway, starting with CEAP classification and parallel venous (duplex) and ABPI assessments. Compression is contraindicated with ankle pressure <60 mmHg, toe pressure <30 mmHg, or ABPI <0.6. The framework incorporates ESVS 2022 recommendations for target ankle interface pressures ≥40 mmHg in active VLUs, while noting inter-guideline variability. Emerging tools such as dynamic pressure monitoring and standardized protocols are integrated to optimize outcomes.

Management strategies for pain in VLUs

1) Treat the cause to treat the pain

Pain in VLUs is intimately linked with underlying venous hypertension and superficial reflux. Thus, addressing the root pathology is central to alleviating pain. Early correction of superficial venous incompetence, whether by thermal (endovenous laser

ablation, radiofrequency ablation) or non-thermal (mechanochemical ablation, cyanoacrylate closure) techniques, has been shown to accelerate healing and prolong ulcer-free survival when compared with deferred intervention. The landmark EVRA trial demonstrated that early ablation shortened time to ulcer healing and increased ulcer-free days, while subsequent cost-utility analyses in both UK and US healthcare contexts confirmed its cost-effectiveness (30,38–40). Importantly, improvements in ulcer healing correlated with significant reductions in wound-related pain and meaningful gains in health-related quality of life (QoL) (41). For patients in whom conventional compression is not tolerated or proves insufficient, intermittent pneumatic compression (IPC) has been identified as a useful adjunct, enhancing venous return and promoting healing while also providing symptomatic relief (30).

2) Compression: the cornerstone

Compression therapy remains the cornerstone of both ulcer healing and pain relief in VLU management. High-pressure multilayer or inelastic compression, achieving ankle interface pressures of approximately 40 mmHg, has consistently been associated with accelerated healing, reduced edema, and subsequent pain relief (30). A range of systems is available, including multilayer wraps, short-stretch bandages, adjustable Velcro® devices, and two-piece compression garments (42–44). The choice of modality should be guided not only by hemodynamic efficacy but also by patient comfort, mobility, and lifestyle factors, as adherence is the primary determinant of treatment success. Barriers to consistent wear include discomfort in hot weather, difficulty with donning and doffing, and dermatologic irritation. Structured patient education, individualized garment selection, and provision of donning/doffing aids have been shown to enhance adherence (45–48). Exercise programs designed to improve calf-muscle pump function represent a valuable adjunct to compression, contributing modestly to improved ulcer healing and symptom reduction, though their long-term role in preventing recurrence remains insufficiently defined (30,49).

3) Local wound care to minimize procedure-related pain

Beyond background and incident pain, procedure-related pain, particularly during debridement and dressing changes, constitutes a significant burden for patients with VLUs. Topical anesthetic agents, most notably lidocaine–prilocaine cream (EMLA), applied 30–60 minutes before sharp or mechanical debridement, have demonstrated significant analgesic benefit in multiple randomized controlled trials (50–53). Similarly, the use of ibuprofen-releasing foam dressings has been associated with clinically relevant reductions in pain intensity during wear, without compromising wound healing, with pooled analyses estimating numbers-needed-to-treat between five and seven (54,55). Also, the use of an inhalational anesthetic has been suggested as topical analgesic in these patients (56). Conversely, routine systemic antibiotic therapy is not recommended for uninfected ulcers, as it neither enhances healing nor alleviates pain, and carries unnecessary risks of resistance and adverse effects (30).

4) Systemic and adjuvant analgesia

For patients with persistent pain, a multimodal pharmacological approach is warranted. Baseline analgesia may include short-course non-steroidal anti-inflammatory drugs (NSAIDs) when tolerated. Weak opioids can be considered for short-term management of severe background or procedure-related pain but should always be prescribed with exit strategies to avoid dependence (57). Importantly, some patients develop neuropathic pain features, in which case gabapentinoids or serotonin–norepinephrine reuptake inhibitors (e.g., duloxetine), together with lidocaine patch, may be beneficial (58). Although high-quality, ulcer-specific analgesic trials are scarce, the extrapolation of general neuropathic pain management strategies is currently justified (4,19,47). Non-pharmacological adjuncts, including leg elevation, optimization of sleep hygiene, and cognitive-behavioral interventions, provide additional benefit, highlighting the need for individualized, multidisciplinary care (10,59).

5) Venoactive drugs (adjuncts)

Venoactive drugs, particularly micronized purified flavonoid fraction (MPFF), have demonstrated modest benefits in reducing venous symptoms such as pain, heaviness, and swelling. Randomized controlled trials and meta-analyses suggest that MPFF, when added to compression, may slightly increase ulcer healing rates and improve patient-reported symptoms (60–62). However, guideline recommendations remain cautious, advocating their use only as adjuncts rather than replacements for compression and definitive reflux correction (30).

Figure 4 provides a systematic framework that integrates these five complementary pain management strategies into a clinically practical workflow based on pain type assessment and evidence-based interventions.

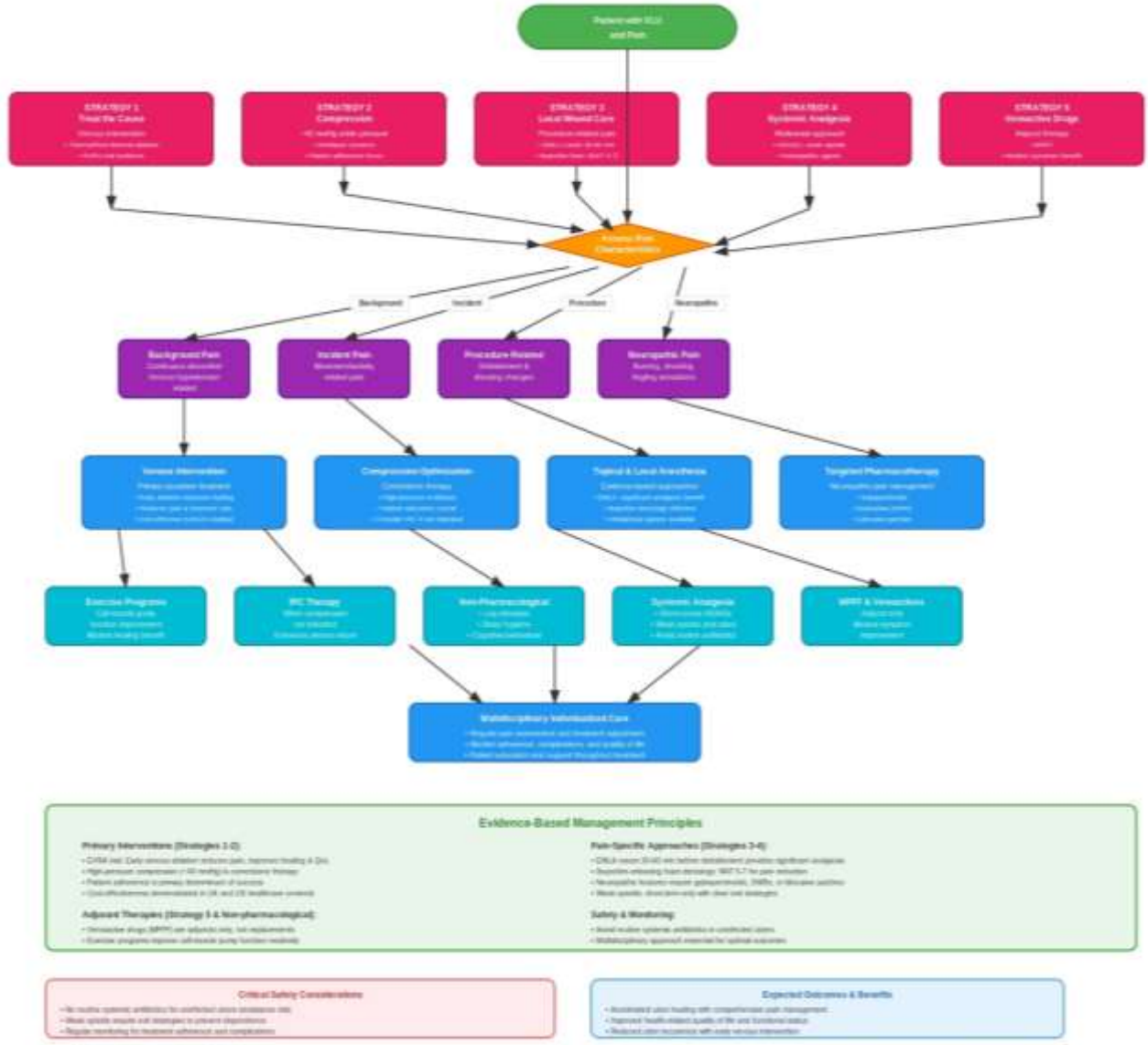

Fig. 4 Evidence-based framework for VLU pain management.

The flowchart outlines five complementary strategies: early venous intervention, compression therapy, local wound care, multimodal analgesia, and adjunct venoactive drugs. Interventions are tailored to pain type (background, incident, procedure-related, neuropathic) and supported by evidence such as EVRA trial outcomes, high-pressure compression, topical anesthetics, and neuropathic pain agents. The approach emphasizes individualized, multidisciplinary care with regular monitoring.

Quality of life, adherence, and person-centered care

Pain in VLUs is not only a localized problem but also a systemic driver of functional decline, contributing to immobility, sleep disturbance, psychological distress, and social isolation (15,16,18–20). QoL has been shown to improve in parallel with ulcer healing and adequate symptom control, underscoring the importance of integrated pain management (19). Patient-centered approaches, such as shared decision-making in compression modality, addressing practical barriers including footwear compatibility, climate-related discomfort, and donning/doffing challenges, and scheduling analgesia before dressing changes, have been shown to enhance adherence (44–48). Structured self-care education, digital adherence tools, and multidisciplinary support further improve patient engagement, long-term outcomes, and recurrence prevention (63,64).

Special populations and comorbidity

Older adults living with VLUs frequently present with multidimensional symptom clusters, most notably persistent pain, chronic fatigue, and sleep disturbance, which interact synergistically to exacerbate disability and psychological distress (65). These clinical manifestations are often accompanied by elevated systemic inflammatory markers, reflecting the interplay between local ulcer pathology and systemic immune activation. Such complexity highlights the necessity for holistic, multidisciplinary management, integrating vascular care, targeted pain control, rehabilitation strategies, and psychosocial support to optimize healing, maintain functional independence, and enhance quality of life in this vulnerable population (35,64).

Evidence gaps and future directions

Despite advances in the management of VLUs, several important research gaps persist. First, there is a striking lack of rigorous randomized controlled trials specifically addressing neuropathic and nociplastic pain phenotypes in VLUs, despite evidence that a subset of patients displays neuropathic descriptors and central sensitization (4,19,47). Second, current VLU trials rarely incorporate standardized pain endpoints, limiting comparability across studies and hindering the development of evidence-based analgesic strategies (53) Third, the comparative effectiveness of different compression modalities on pain outcomes remains poorly defined; while multilayer and inelastic bandages are widely studied, data on adjustable devices and smart compression garments are scarce (30,47,49). Equally important is the need for scalable adherence interventions, such as digital adherence coaching, remote monitoring, and sensor-enabled compression systems, which may improve long-term engagement and outcomes (64,66). Finally, further validation of wound-specific PROMs, including their responsiveness to pain change in active VLUs, is required to ensure accurate assessment in both clinical practice and trials (19,22,30). Addressing these gaps through targeted research will be crucial to advancing patient-centered, mechanism-based care.

Discussion

This narrative review synthesizes current evidence on vascular pain in VLU, revealing both significant advances and persistent challenges in understanding and managing this complex clinical entity. The pathophysiological framework demonstrates that VLU-associated pain represents a multifaceted phenomenon encompassing nociceptive, neuropathic, and nociplastic components, fundamentally challenging traditional pain classification systems (4,21–27). The inflammatory cascade initiated by venous hypertension creates a self-perpetuating cycle of tissue damage, nociceptor sensitization, and central pain amplification that extends well beyond local wound pathology. The evidence presented supports a paradigm shift toward early, comprehensive intervention strategies. The EVRA trial findings (38–40). demonstrate that addressing underlying venous pathophysiology through early ablation not only accelerates ulcer healing but provides meaningful pain relief and quality of life improvements. This aligns with contemporary pain medicine principles emphasizing mechanism-based rather than symptom-focused treatment approaches. However, the integration of vascular intervention with targeted analgesic strategies remains underdeveloped, representing a critical gap between vascular surgery and pain management disciplines. The five-strategy management framework outlined in this review reflects the complexity of VLU pain while providing a structured approach to clinical decision-making. Compression therapy emerges as both cornerstone treatment and potential source of therapeutic conflict—while essential for venous return optimization, adherence challenges frequently arise from compression-related discomfort (42–45,47,48,64). This paradox underscores the importance of individualized approaches that balance therapeutic efficacy with patient tolerability, supported by comprehensive education and adherence support strategies.

Local wound care innovations, particularly the use of topical anesthetics and ibuprofen-releasing dressings(50–55), demonstrate the potential for procedure-specific pain management. However, the predominant focus on healing outcomes in VLU research has resulted in pain being relegated to secondary endpoint status, limiting the development of evidence-based analgesic protocols. The scarcity of dedicated pain trials in VLU populations contrasts markedly with the high prevalence of pain-related morbidity reported in qualitative studies (15–17).

The recognition of neuropathic pain features in VLU patients (4,19,47) challenges conventional understanding of venous ulceration as purely nociceptive. The presence of burning, shooting, or tingling sensations suggests peripheral nerve involvement, potentially through inflammatory mediator-induced sensitization or direct mechanical compression. This mechanistic insight supports the use of gabapentinoids and other neuropathic agents, though specific efficacy data in VLU populations remain limited. The complexity of chronic pain management requires individualized, multimodal approaches that consider patient-specific factors, procedural risks, and available therapeutic modalities (67).

PROMs have evolved to capture the multidimensional impact of VLU pain on QoL, functionality, and psychosocial wellbeing (18–20). The validation of disease-specific instruments represents important progress, yet standardization across clinical trials remains inconsistent. This methodological heterogeneity impedes meta-analysis and comparative effectiveness research, highlighting the need for consensus on core outcome sets for VLU pain studies.

The holistic management approach advocated in this review acknowledges that VLU pain extends beyond the wound itself to encompass sleep disturbance, mobility limitation, and psychological distress (16,35,68). This biopsychosocial perspective aligns with contemporary pain medicine while recognizing the unique challenges posed by chronic wound environments. The integration of cognitive-behavioral interventions, sleep optimization, and social support represents logical extension of multimodal pain management principles to VLU populations.

Limitations

This narrative review has several important limitations that must be acknowledged. First, by design, it does not employ the systematic methodology of a meta-analysis; therefore, risks of selection bias and incomplete retrieval of relevant studies cannot be excluded, despite a broad search

strategy and transparent reporting in accordance with SANRA criteria. Second, restricting the analysis to English-language publications may have introduced language bias and led to the underrepresentation of valuable evidence from non-English sources. Third, although emphasis was placed on recent high-quality guidelines, randomized controlled trials, and systematic reviews, the heterogeneity of available data, particularly regarding pain endpoints, limits the ability to draw firm conclusions about comparative efficacy. Fourth, most studies addressing VLUs pain are secondary analyses of healing-focused trials, rather than rigorously designed pain studies, resulting in underpowered or inconsistent pain outcomes. Similarly, variability in outcome measures and patient-reported instruments hinders comparability across studies. Finally, while multidisciplinary perspectives were integrated, this review inevitably reflects the interpretive synthesis of the authors and may not encompass all nuances of clinical practice globally. Future systematic reviews and dedicated trials with standardized pain outcomes are required to confirm and extend the findings summarized herein.

Future Research Directions: Future research in VLU pain management should focus on elucidating the molecular and neurophysiological mechanisms linking venous hypertension to pain sensitization, with biomarker development to identify patient subgroups and predict treatment response. Well-designed randomized controlled trials with pain reduction as a primary endpoint are urgently needed, evaluating interventions such as early venous ablation, targeted pharmacotherapy for neuropathic features, optimized compression strategies, and novel local anesthetic delivery systems. Technology-enhanced solutions—including smart compression devices, digital health applications, telemedicine, and immersive tools like virtual reality—hold promise for improving adherence, accessibility, and patient comfort (69,70). Personalized medicine approaches that integrate genetic, phenotypic, and biomarker data with advanced machine learning models could guide precision therapies. Finally, healthcare system research is required to determine the cost-effectiveness of comprehensive programs, the impact of multidisciplinary care models, and strategies to implement evidence-based protocols. Collaborative, mechanism-based, and patient-centered research across vascular surgery, wound care, and pain medicine will be critical to close current evidence gaps and transform VLU pain management.

Conclusion

VLU pain is prevalent, mechanistically complex, and clinically consequential. Effective pain control hinges on treating venous pathophysiology (compression, early ablation), minimizing procedure-related pain (topical local anesthetics, atraumatic care), and individualizing systemic/adjunctive therapy—all delivered within a person-centered program that optimizes adherence. Embedding robust pain endpoints in future VLU trials will sharpen guidance and improve patient-level outcomes.

Authors' declaration

We confirm that all the Figures and Tables in the manuscript belong to the current study. Authors sign on ethical considerations.

Conflict of interest

The authors declare that they have no conflicts of interest relevant to this work.

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Authors' contributions

All authors contributed to the study conception and design. Data collection The first draft of the manuscript, Data analysis & interpretation and commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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