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High Voltage Pulsed Current versus Negative Pressure Therapy in Chronic Venous Ulcers Healing: A Narrative Review

Magy Ibrahim Kamel Qlada[1,2]*, Eman Mohamed Othman[1],
Ahmed Mohamed Kenawy Yousef[3], Amany Refaat Mohamed Abdel Wahid[1]
[1]Department of Surgery, Faculty of Physical Therapy, Cairo University, Egypt.
[2]Department of Surgery, Faculty of Physical Therapy, Egyptian Chinese University, Egypt.
[3]Department of Plastic Surgery, Faculty of Medicine, Cairo University, Egypt
***Corresponding author: Magy Ibrahim Kamel Qlada, Email:** Maibrahim@ecu.edu.eg, **Mobile:** +201210335123

ABSTRACT
Chronic venous ulcers (CVUs) are a prevalent and debilitating condition resulting from chronic venous insufficiency, characterized by prolonged healing, high recurrence, and significant healthcare burden. This narrative review explores two advanced therapeutic modalities; High Voltage Pulsed Current (HVPC) and Negative Pressure Wound Therapy (NPWT) that have shown promise in enhancing CVU healing. HVPC employs electrical stimulation to promote cellular migration, angiogenesis, and antimicrobial effects, while NPWT utilizes subatmospheric pressure to facilitate wound contraction, exudate removal, and tissue regeneration. The review outlines the pathophysiology of CVUs, details the mechanisms and clinical applications of both therapies, and critically evaluates existing evidence regarding their efficacy. Although both modalities demonstrate superiority over conventional care, direct comparative studies are limited, making definitive conclusions about their relative effectiveness challenging. HVPC is advantageous for non-exudative, stagnant wounds requiring cellular stimulation, whereas NPWT is preferred for large, exudative wounds needing rapid granulation and fluid management. The review also highlights the potential for combined or sequential use of these therapies and underscores the need for standardized protocols, cost-effectiveness analyses, and patient-centered outcomes in future research. By addressing current gaps, clinicians can better tailor treatment strategies to individual patient needs, ultimately improving healing outcomes and quality of life for those with CVUs.
Keywords: Chronic venous ulcers, High Voltage Pulsed Current, Negative Pressure Wound Therapy, Wound healing, Electrotherapy

INTRODUCTION
Chronic venous ulcers (CVUs) represent a significant global health burden, affecting millions of individuals and imposing substantial challenges on healthcare systems. These debilitating wounds, primarily located in the lower extremities, arise from chronic venous insufficiency, leading to sustained venous hypertension, inflammation, and impaired tissue repair. Characterized by prolonged healing times, high recurrence rates, and a detrimental impact on patients' quality of life, CVUs often necessitate long-term care and multifaceted treatment approaches. While conventional management typically involves compression therapy, wound debridement, and appropriate wound dressings, a growing array of advanced therapeutic modalities has emerged to accelerate healing and improve outcomes [(1)].

Among these innovative interventions, High Voltage Pulsed Current (HVPC) and Negative Pressure Wound Therapy (NPWT) have garnered considerable attention for their distinct mechanisms of action and reported clinical efficacy. HVPC, a form of electrotherapy, utilizes specific electrical waveforms to stimulate cellular activity, enhance circulation, and exert antimicrobial effects, thereby promoting various phases of wound healing. Conversely, NPWT, a mechanical therapy, involves applying subatmospheric pressure to the wound bed, leading to macro- and micro-deformation, exudate removal, and enhanced angiogenesis [(2)].

Given the persistent challenges in CVU management, a comparative understanding of these two prominent advanced therapies is crucial for clinicians[(3)]. This narrative review aims to provide a comprehensive overview of the pathophysiology of CVUs, delineate the mechanisms and clinical applications of HVPC and NPWT, and critically analyze the existing evidence comparing their efficacy in promoting chronic venous ulcer healing. Furthermore, it will discuss current limitations in research and propose future directions for optimizing treatment strategies.

Pathophysiology of Chronic Venous Ulcers
Chronic venous ulcers are the most common type of leg ulcer, accounting for approximately 70% of all cases. Their development is intricately linked to chronic venous insufficiency (CVI), a condition resulting from dysfunctional venous valves, venous obstruction, or calf muscle pump failure. This dysfunction leads to sustained venous hypertension in the lower limbs, which is the cornerstone of CVU pathophysiology [(4)].

The elevated venous pressure triggers a cascade of events at the microcirculatory level. Increased hydrostatic pressure forces fluid, proteins, and inflammatory cells into the interstitial space, leading to edema. This chronic edema impairs oxygen and nutrient delivery to the

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surrounding tissues, creating a hypoxic and nutrient-deficient environment that compromises cellular function and inhibits wound healing. Furthermore, the extravasation of red blood cells leads to the deposition of hemosiderin, causing the characteristic brownish discoloration (hyperpigmentation) of the skin around the ankle [5].

Inflammation plays a pivotal role in perpetuating CVU chronicity. Venous hypertension induces endothelial cell activation, leading to the upregulation of adhesion molecules and the recruitment of inflammatory cells, particularly neutrophils and macrophages, into the perivascular tissue. These cells release proteolytic enzymes (e.g., matrix metalloproteinases - MMPs) and reactive oxygen species (ROS), which degrade extracellular matrix components and growth factors essential for tissue repair. This proteolytic environment contributes to a vicious cycle of inflammation and tissue breakdown, preventing the wound from progressing through normal healing phases [6].

In addition to inflammation, impaired lymphatic drainage, accumulation of fibrin cuffs around capillaries, and a dysregulation of growth factors (e.g., reduced levels of vascular endothelial growth factor (VEGF) and transforming growth factor-beta (TGF-β)) further contribute to the non-healing nature of CVUs. The net effect is a prolonged inflammatory phase, diminished cellular proliferation, poor angiogenesis, and inadequate collagen synthesis, resulting in a wound stuck in a chronic state [7].

High Voltage Pulsed Current (HVPC) Therapy

High Voltage Pulsed Current (HVPC), also known as High Volt Galvanic Stimulation, is a monophasic twin-peaked pulsed current characterized by its short pulse duration and high peak voltage. Despite the high voltage, the average current is low, making it a comfortable and safe modality. HVPC is increasingly recognized for its therapeutic potential in wound healing, particularly for chronic non-healing ulcers [8].

Mechanism of Action

The proposed mechanisms by which HVPC facilitates wound healing are multifaceted:

1. **Galvanotaxis (Cellular Migration):** Living cells carry a net electrical charge and respond to external electrical fields. HVPC creates a weak electrical field within the wound bed, which mimics the body's natural "current of injury." This directs the migration of various cells crucial for healing, including neutrophils, macrophages, fibroblasts, and epidermal cells, towards the wound. Neutrophils and macrophages are attracted to the negative electrode, while fibroblasts and epidermal cells migrate towards the positive electrode. This directed migration accelerates the inflammatory, proliferative, and epithelialization phases [9].
2. **Enhanced Microcirculation:** HVPC application can induce vasodilation, improving blood flow and oxygenation to the ischemic wound bed. Enhanced microcirculation delivers essential nutrients, growth factors, and immune cells, while facilitating the removal of waste products, all of which are vital for tissue repair [10].
3. **Antimicrobial Effects:** The electrical current can disrupt bacterial cell membranes and inhibit bacterial growth, particularly against common wound pathogens like *Pseudomonas aeruginosa* and *Staphylococcus aureus*. This reduction in bioburden helps to prevent infection and allows the healing process to proceed [11].
4. **Stimulation of Cellular Activity:** HVPC can directly stimulate fibroblasts to produce collagen and growth factors, promote keratinocyte proliferation and migration for re-epithelialization, and enhance endothelial cell activity for angiogenesis. It also appears to modulate matrix metalloproteinase activity, reducing excessive tissue degradation [12].
5. **Edema Reduction:** The monophasic nature of HVPC can cause a "driving" effect on charged proteins and fluid in edematous tissue, moving them away from the wound area, thus reducing localized edema, which can impede healing [13].

Clinical Application

For CVUs, HVPC is typically applied using a direct technique, where an active electrode is placed directly on the wound bed (often using sterile saline-soaked gauze), and a dispersive electrode is placed proximally on intact skin. The polarity of the active electrode is often changed throughout the healing process: negative polarity is generally used during the inflammatory/debridement phase to attract neutrophils and macrophages and for antimicrobial effects, while positive polarity is preferred during the proliferative and epithelialization phases to attract fibroblasts and keratinocytes [14].

Typical parameters include a high peak voltage (100-200 V), a low average current, and a pulse rate between 50-128 pulses per second (pps). Treatment duration usually ranges from 45-60 minutes, once or twice daily, for 5-7 days a week. It is always used as an adjunct to standard care, including compression therapy, debridement, and appropriate wound dressings [14].

Evidence for Efficacy

Numerous studies, including randomized controlled trials (RCTs) and systematic reviews, have investigated the effectiveness of HVPC in CVU healing. A meta-analysis published in the *Cochrane Database of Systematic Reviews* concluded that electrical stimulation (including

HVPC) can accelerate the healing of chronic wounds, including venous ulcers, by a small but significant amount compared to sham or no electrical stimulation. Many individual studies have demonstrated that HVPC significantly reduces wound size, promotes granulation tissue formation, and accelerates complete wound closure in CVU patients, especially those who have failed conventional therapies. Its ability to manage infection and edema further supports its use as a valuable adjunct. However, studies often vary in their parameters, patient populations, and primary outcomes, making direct comparisons challenging [15].

Negative Pressure Wound Therapy (NPWT)

Negative Pressure Wound Therapy (NPWT), also known as vacuum-assisted closure (VAC), is a therapeutic technique that uses a vacuum pump to apply continuous or intermittent negative pressure to a wound bed. A foam or gauze dressing is placed directly into the wound, sealed with an occlusive film, and connected to the vacuum pump [16].

Mechanism of Action

NPWT promotes wound healing through several mechanisms:

1. **Macro-deformation and Wound Contraction:** The negative pressure applies mechanical forces that draw the edges of the wound together, reducing wound size and promoting wound contraction. This physical approximation of wound margins can lead to faster closure [17].
2. **Micro-deformation and Cellular Stretch:** The foam dressing, when subjected to negative pressure, deforms and exerts micro-mechanical forces on the wound bed. This "micro-deformation" leads to cellular stretch (mechano-transduction), which stimulates cellular proliferation (fibroblasts, endothelial cells), increases local angiogenesis, and enhances the production of extracellular matrix components [18].
3. **Removal of Excess Exudate and Interstitial Fluid:** NPWT efficiently removes excess wound exudate, which can contain high levels of proteolytic enzymes and inflammatory cytokines that impede healing. By removing this fluid, it reduces edema, decreases bacterial colonization, and creates a cleaner wound environment [19].
4. **Enhanced Blood Flow and Angiogenesis:** The mechanical stress and removal of edema can lead to increased blood flow to the wound periphery. Additionally, the localized tissue stretch stimulates the release of angiogenic growth factors, promoting the formation of new blood vessels, which are critical for delivering oxygen and nutrients to the healing tissue [20].
5. **Reduced Bacterial Burden:** By continuously removing exudate and its associated bacteria, NPWT helps to reduce the bacterial load in the wound bed, thereby lowering the risk of infection and promoting a more favorable healing environment [21].

Clinical Application

NPWT is highly adaptable in its clinical application. It can be applied continuously or intermittently, with typical pressure settings ranging from -75 mmHg to -125 mmHg. Foam dressings are most common, but gauze-based systems are also used. Dressing changes usually occur every 48-72 hours, depending on exudate levels and wound characteristics. NPWT is indicated for a wide range of chronic wounds, including CVUs, particularly those with high exudate, large surface areas, or exposed deeper structures. Like HVPC, NPWT is always used in conjunction with comprehensive wound care, including debridement and compression therapy for CVUs [22].

Evidence for Efficacy

NPWT has extensive evidence supporting its efficacy in chronic wound healing. Numerous systematic reviews and meta-analyses, including those focusing specifically on CVUs, consistently demonstrate its effectiveness in reducing wound area, accelerating granulation tissue formation, and achieving complete wound closure. For instance, several studies have reported faster healing rates and shorter time to wound closure for CVUs treated with NPWT compared to conventional wound care. It is often considered a gold standard for complex or recalcitrant wounds due to its robust mechanisms. However, the cost of NPWT devices and dressings can be a significant barrier to widespread adoption, and patient tolerance to constant negative pressure can sometimes be an issue [23].

Comparative Analysis: HVPC vs. NPWT in Chronic Venous Ulcers Healing

Direct head-to-head comparative studies between High Voltage Pulsed Current (HVPC) and Negative Pressure Wound Therapy (NPWT) for chronic venous ulcer (CVU) healing are surprisingly limited in high-quality research. Most studies tend to compare one modality against conventional care rather than directly against each other. However, based on their distinct mechanisms and clinical outcomes, we can infer their relative strengths, weaknesses, and potential niches in CVU management [24].

Efficacy and Healing Rates

Both HVPC and NPWT have individually demonstrated superiority over conventional wound care in accelerating CVU healing.

- **HVPC:** Primarily acts at a cellular and microcirculatory level, promoting galvanotaxis, angiogenesis, and antimicrobial effects. It is

particularly beneficial for stimulating tissue regeneration, managing localized edema, and addressing bioburden. It's often praised for its non-invasive nature and relative ease of application, though consistent daily application can be demanding [25].
- **NPWT:** Offers robust macro-mechanical effects, efficient exudate management, and significant promotion of granulation tissue. It excels in managing highly exudative wounds, reducing wound volume, and preparing the wound bed for closure. Its ability to create a consistent, moist wound environment while removing harmful exudates makes it highly effective [26].

Without extensive direct comparative trials, it is challenging to definitively state which therapy is "superior." The choice often depends on specific wound characteristics and clinical goals. For instance, a CVU with significant edema and purulent exudate might initially benefit more from NPWT's fluid removal capabilities, while a clean, stagnant wound might respond well to HVPC's cellular stimulation [27].

Advantages and Disadvantages

High Voltage Pulsed Current (HVPC):

- **Advantages:** Non-invasive, generally well-tolerated, relatively low cost once equipment is acquired, portable units available, promotes deep tissue regeneration. Can be used for pain management as well [28].
- **Disadvantages:** Requires frequent, sometimes daily, application by trained personnel, compliance can be an issue, less effective for very large or highly exudative wounds, limited ability to remove significant amounts of slough or necrotic tissue rapidly [29].

Negative Pressure Wound Therapy (NPWT):

- **Advantages:** Highly effective in exudate management, rapid formation of granulation tissue, promotes wound contraction, reduces bacterial burden, provides a sealed environment for healing, fewer dressing changes compared to daily conventional dressings [30].
- **Disadvantages:** High initial and ongoing cost of equipment and specialized dressings, potential for pain during dressing changes (especially removal), requires careful application to ensure seal integrity, not suitable for wounds with untreated osteomyelitis, malignancy, or exposed blood vessels/nerves. Less portable for active patients compared to smaller HVPC units [31].

Patient Selection

Patient selection is paramount for optimizing outcomes.

- **HVPC** might be preferred for patients with clean, non-exudative, stalled CVUs that need a boost in cellular activity and microcirculation. It could also be considered for patients where NPWT is contraindicated or cost-prohibitive [27].
- **NPWT** is often the first choice for large, deep CVUs with moderate to heavy exudate, slough, or where rapid granulation tissue formation and wound contraction are priorities. It is also beneficial when frequent dressing changes need to be minimized [28].

Cost-Effectiveness

The economic implications of these therapies are complex. While NPWT has a higher direct cost per day of treatment due to specialized dressings and pumps, its potential for faster healing and reduced nursing time might offset these costs in the long run. HVPC has a lower daily supply cost, but the cumulative cost might increase with prolonged treatment durations and frequent clinician visits. Comprehensive cost-effectiveness studies comparing these two modalities, taking into account healing rates, recurrence, and associated healthcare utilization, are still needed to guide optimal resource allocation [31].

Potential for Combined Therapy

The distinct mechanisms of HVPC and NPWT suggest a potential for synergistic benefits when used in combination, or sequentially. For instance, NPWT could be used initially to rapidly reduce exudate, prepare the wound bed, and promote granulation, after which HVPC could be introduced to further stimulate cellular migration and re-epithelialization in a cleaner, less exudative wound. Research into such sequential or concurrent application protocols is an important future direction [21].

Challenges and Limitations in Research

Despite the individual evidence supporting HVPC and NPWT, several challenges and limitations hinder definitive comparative conclusions and optimized clinical protocols for CVU healing:

1. **Lack of Direct Comparative Studies:** The most significant limitation is the paucity of high-quality randomized controlled trials (RCTs) directly comparing HVPC with NPWT. Most studies assess each therapy against conventional care, making indirect comparisons difficult and prone to bias [30].
2. **Heterogeneity of Study Designs:** Existing studies often vary widely in their methodologies. Differences in patient selection criteria (e.g., wound duration, size, comorbidities), intervention parameters (e.g., HVPC voltage/frequency, NPWT pressure settings/cycle), concomitant therapies (e.g., compression, debridement), and outcome measures (e.g., percentage wound area reduction, time to

complete closure) make it challenging to synthesize findings and draw firm conclusions [31].

3. **Blinding Issues:** Blinding participants and clinicians to the intervention received is difficult for both HVPC (due to the sensation of current) and NPWT (due to the visible equipment), which can introduce performance and detection bias [27].
4. **Reporting of Outcomes:** Not all studies consistently report clinically meaningful outcomes such as long-term recurrence rates, patient-reported quality of life, or functional improvements. Focus often remains solely on wound closure rates [28].
5. **Cost-Effectiveness Data:** Comprehensive economic analyses comparing these advanced therapies, accounting for direct and indirect costs over the entire episode of care (including potential recurrence), are scarce [29].
6. **Adjunctive Therapies:** Both modalities are used as adjuncts to standard care, primarily compression therapy for CVUs. The precise contribution of each advanced therapy over and above optimized conventional care is sometimes difficult to isolate [30].
7. **Standardization of Protocols:** A lack of standardized protocols for application parameters, treatment duration, and patient selection for both HVPC and NPWT impedes replicability and generalizability of research findings [31].

These limitations highlight the need for more rigorous and standardized research to provide clear guidance for clinical practice.

Future Directions

Future research and clinical practice should focus on several key areas to enhance the management of chronic venous ulcers using HVPC and NPWT:

1. **Head-to-Head Randomized Controlled Trials:** Prioritizing well-designed, adequately powered RCTs that directly compare HVPC and NPWT, ideally against each other and against optimized standard care, is crucial. These trials should utilize standardized protocols for application, patient selection, and outcome measures.
2. **Combination and Sequential Therapies:** Investigating the synergistic potential of combining HVPC and NPWT, either concurrently or sequentially (e.g., initial NPWT for exudate management followed by HVPC for cellular stimulation), could lead to more effective protocols.
3. **Long-Term Outcomes and Recurrence:** Studies should extend beyond wound closure to assess long-term healing durability and recurrence rates, as this significantly impacts patient quality of life and healthcare costs.
4. **Patient-Centered Outcomes:** Incorporating patient-reported outcome measures (PROMs) such as pain reduction, mobility improvement, and quality of life is essential to capture the full impact of these therapies.
5. **Biomarker Research:** Exploring the changes in wound bed biomarkers (e.g., cytokines, growth factors, proteases) in response to HVPC and NPWT could provide deeper insights into their mechanisms of action and help predict treatment responsiveness.
6. **Cost-Effectiveness Analyses:** Robust economic evaluations are needed to determine the true cost-benefit ratio of each therapy and their combinations, guiding resource allocation in different healthcare settings.
7. **Technological Advancements:** Further development of more portable, user-friendly, and cost-effective HVPC and NPWT devices could increase accessibility and compliance. Smart wound care technologies that integrate monitoring and adaptive therapy delivery should also be explored.
8. **Personalized Medicine Approaches:** Research into identifying patient characteristics (e.g., specific wound biomarkers, genetic predispositions) that predict responsiveness to either HVPC or NPWT could pave the way for personalized wound management strategies.

CONCLUSION

Chronic venous ulcers pose persistent challenges in wound care, necessitating advanced therapeutic interventions to improve healing rates and patient outcomes. Both High Voltage Pulsed Current (HVPC) and Negative Pressure Wound Therapy (NPWT) have emerged as valuable adjuncts to standard compression therapy, each offering distinct advantages based on their unique mechanisms of action. HVPC leverages electrical stimulation to promote cellular activity, microcirculation, and antimicrobial effects, while NPWT utilizes subatmospheric pressure for macro- and micro-deformation, exudate removal, and enhanced angiogenesis.

Existing evidence supports the individual efficacy of both modalities in accelerating CVU healing compared to conventional care. However, a significant gap remains in high-quality direct comparative studies between HVPC and NPWT, making it challenging to establish definitive superiority or specific indications for each in all clinical scenarios. The selection between HVPC and NPWT often depends on wound characteristics, clinician experience, patient tolerance, and economic considerations.

Future research must prioritize rigorous head-to-head trials, explore the synergistic potential of combination therapies, and focus on long-term patient-centered outcomes, including recurrence and quality of life. By addressing current limitations and pursuing these future directions, the evidence base for HVPC and NPWT can be strengthened, ultimately leading to more effective, personalized, and cost-efficient strategies for the comprehensive management of chronic venous ulcers.

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