Clinical impact of zinc oxide compression bandaging in chronic venous disease assessed with ultrasonography and trans-epidermal water loss – preliminary observations

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ABSTRACT

Introduction Chronic venous disease (CVD) affects lower extremities and can lead to serious complications, including venous ulcers. Despite its high prevalence, CVD is often underdiagnosed and undertreated. Compression therapy is essential in managing this condition, with the zinc oxide-based Unna boot providing both compression and anti-inflammatory effects. This study evaluates the Unna boot's effectiveness in reducing lower limb oedema in CVD patients, using advanced non-invasive techniques such as high-frequency ultrasonography (HFUS) and trans epidermal water loss (TEWL).

Materials and Methods We conducted a prospective observational study involving 10 patients with CVD (CEAP classification C3–C6). Participants received treatment with the Unna Boot for four weeks, with assessments at baseline, after treatment, and during follow-up. Key measurements included calf circumference, HFUS for subcutaneous changes, and TEWL to evaluate skin barrier integrity. The Wilcoxon Signed-Ranks Test was used for statistical analysis.

Results Significant reductions were observed in calf circumference (mean decrease of 18.69%, $p<0.05$) and subepidermal low echogenicity band (SLEB) thickness (mean decrease of 37.95%, $p<0.05$) after treatment. TEWL measurements showed no significant changes, likely due to external factors affecting the results.

Conclusion The Unna Boot effectively manages the lower limb oedema in CVD. HFUS provides objective assessments, while TEWL may not accurately reflect skin barrier changes. Further research is needed to explore long-term effects and the Unna Boot's applicability across different CVD stages.

Keywords chronic wounds, zinc oxide bandage, HFUS, TEWL, Unna boot

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INTRODUCTION

Chronic venous disease (CVD) is a common and often debilitating condition that affects the lower extremities. It presents with clinical symptoms ranging from mild telangiectasia, varicose veins to severe complications like venous ulcers, primarily due to venous hypertension, which is caused by valvular dysfunction or venous obstruction.[1,2] The great burden of the disease is related not only to the morbidity and impairment in patient's quality of life, but also to the significant impact on healthcare systems in general.[3,4] Despite its high prevalence, CVD is often underdiagnosed and undertreated. With the progression of the disease, patients may experience debilitating symptoms such as pain, oedema and skin surface changes, eventually resulting in venous ulcers.[5] Standard management of CVD includes both conservative and aggressive management strategies.[6] Conservative treatment generally focuses on compression therapy, which is the gold standard for the management of venous hypertension and its consequences.[7] Among the compression methods, the zinc oxide-based compression bandage, commonly known as the Unna boot, plays a key role for its capability of both providing compression and anti-inflammatory effect.[8,9] Developed by the German dermatologist Paul Gerson Unna, this bandage combines the physiological effects of compression with the healing properties of zinc oxide, in order to promote wound healing and reduce inflammation.[10,11]

The Unna boot has been used extensively for the treatment of venous leg ulcers (VLU), but its role in the management of early CVD, especially in cases of severe oedema, has not been well documented.[12] The aim of the study is to investigate the effectiveness of Unna boot bandaging in the reduction of lower limb oedema associated with CVD using advanced non-invasive methods like high-frequency ultrasonography (HFUS) and trans epidermal water loss (TEWL).[13,14] These diagnostic methods provide detailed assessment of skin integrity and subcutaneous changes, thus giving valuable insights for the evaluation of a therapeutic intervention.[15] Integrating clinical examination with advanced diagnostic imaging could contribute to optimised treatment strategies for patients with CVD.

PATIENTS AND METHODS

We performed a prospective, observational study to evaluate the effectiveness of a zinc oxide-based compression bandage/Unna boot in the management of CVD of the lower limbs. We enrolled 10 patients, followed by the Department of Dermatology of Pisa and diagnosed with CVD. Participants were recruited from December 2023 to April 2024. Inclusion criteria for the study were the following: subjects aged from 18 to 75 years, diagnosis of CVD (C3–C6 according to the CEAP classification),[16] presence of lower extremity oedema, ability to sign informed consent and adhere to treatment plan. Exclusion criteria were having a history of deep vein thrombosis or active venous thromboembolism, ankle-brachial index less than 0.8, skin conditions resistant to zinc oxide application use, such as acne or known allergic dermatitis, inability to sign the consent form, non-adherence with treatment protocol. All the patients were treated, by a medical and nursing staff expert in wound healing with zinc oxide-based compression bandaging/Unna boot.[17]

The bandage was applied from the base of the toes to 2cm below the knee to ensure consistent and appropriate compression. Bandage replacement was performed every week for a total of four weeks. Patient' assessment was conducted at baseline (T0), before bandage application, after four weeks (T1) and at the follow-up (FU) visit after one month, with non-invasive diagnostic tools to evaluate the effects of the Unna boot on lower limb mobility and overall skin integrity. The zinc oxide bandage was maintained until the FU visit, with weekly changes, to assess the therapeutic response over time. All measurements were performed by the same trained operator to ensure consistency and reliability. A fixed anatomical reference point, marked on the skin, was used for all measurements to standardise the location. For each parameter, three separate measurements were taken at the same reference point, and the mean value of the three was used for analysis to minimize variability. The maximum calf circumference was measured with a tailor's tape measure. HFUS using VEVO MD® (FUJIFILM VisualSonics, Toronto, Ontario, Canada) with a 48 MHz probe was employed to assess subcutaneous changes and obtain detailed images of the skin and dermis. US examination was performed on a reference point located on the patient's lower limb, medially from the middle site of the tibial crest and marked with a dermographic pen. A large amount of gel was applied in order to guarantee an adequate distance between the probe and the point of reference. The scan was conducted in B-Mode at a depth of 17.5 mm and in C-Mode (color-Doppler) at a standard speed of 3.7cm/s. Measurements were taken from each scan: the length between the first hyperechoic band, corresponding to the epidermis, and the end of the first hypoechoic band, corresponding to the sub epidermal low echogenicity band (SLEB) in the papillary dermis, was calculated. TEWL measurements were performed using Dermalab® COMBO (Cortex Technology, Hadsund, Danmark) to assess the integrity of the skin barrier providing insights into the gradient of water evaporation through the stratum corneum, which is suggestive of the skin's barrier function. TEWL was expressed in international units (g/m2/h) and ranged from 0 to 250g/m2/h (normal values were 0–25g/m2/h). TEWL values were measured at three specific anatomical sites: one at the ankle level (lower site, L1); one at the midpoint of a segment from the ankle to the knee on the tibial crest (middle site, L2); one below the knee (upper site, L3).

Categorical data were described with absolute and percentage frequencies, while continuous data were described with means and standard deviations. Delta variables were defined as the variance between T1 and T0. To analyse the continuous variables, the non-parametric Wilcoxon Signed-Ranks Test was used, as these variables did not follow a Gaussian distribution, and the sample size was limited. The significance level was set at 0.05. Data processing was conducted using Microsoft Excel 2016.

RESULTS

We enrolled a total of 10 patients (5 males and 5 females), with a mean age of 75 years (standard deviation: 12). Mean values of calf circumference, SLEB and TEWL at T0, T1, and FU of the population are reported in Table 1. The study demonstrated significant clinical and HFUS improvements in patients with CVD following four weeks of treatment with zinc oxide-based compression bandaging/Unna boot.

The mean values of calf circumference were 43.35cm at T0, 35.25cm at T1, and 37.6cm at the FU visit. The mean delta between T1 and T0 is 8.1cm ± 4.40. The non-parametric Wilcoxon Signed-Ranks Test revealed a significant reduction ($p<0.05$) in calf circumference of 18.69%.

HFUS examination showed a reduction in the mean value of SLEB from T0 (1.37mm) to T1 (0.85mm). The mean delta between T1 and T0 is 0.52±0.68. The non-parametric Wilcoxon Signed-Ranks Test revealed a significant reduction ($p<0.05$) in SLEB of 37.95%.

Regarding TEWL measurements, the mean delta between T1 and T0 were 1.98±17.25 g/m^2/h with an average percentage improvement of 9.88% (L1), -6.827±16.50g/m^2/h with an average percentage deterioration of 65.25% (L2) and -0.78±17.57g/m^2/h with an average percentage deterioration of 5.62% (L3). No statically significant change in the TEWL variables before and after the treatment were found.

Table 1. Mean values (N=10) of trans epidermal water loss (TEWL) measured at L3 (below the knee), L2 (tibial crest), L1 (ankle level), C (calf), calf circumference and Sub Epidermal Low Echogenicity Band (SLEB) assessed at Baseline (T0), after four weeks (T1) and during the one month follow-up visit (FU).

	TEWL L3 (g/m2/h)	TEWL L2 (g/m2/h)	TEWL L1 (g/m2/h)	TEWL C (g/m2/h)	Calf Circumference (cm)	SLEB (mm)
T0	13.90	10.46	20.05	7.99	43.35	1.37
T1	14.69	17.29	18.07	6.96	35.25	0.85
FU	7.44	9.88	10.32	8.04	37.6	0.94
p-value	>0.05	>0.05	>0.05	>0.05	<0.05	<0.05

DISCUSSION

The results of this study aligned with previous research, demonstrating the effectiveness of compression therapy in managing CVD. The Unna boot, specifically, has been noted for its dual role in providing both compression and delivering the anti-inflammatory properties of zinc oxide. The significant reduction in lower limb oedema observed in this study is consistent with the known mechanisms of compression therapy, which facilitates the reabsorption of interstitial fluid and reduces capillary leakage.

Specifically, a statistically significant reduction in calf circumference of 18.69% ($p<0.05$) was noted after four weeks of treatment, revealing a decrease in both superficial and deep oedema.

Moreover, the study focuses on the role of incorporating advanced diagnostic tools, such as HFUS and TEWL measurements, into routine clinical practice. These tools provide objective measures of treatment effectiveness, allowing clinicians to monitor the progression of the disease and the impact of therapeutic interventions. The instrumental monitoring of lower limb oedema conducted in this clinical study allowed us to observe an objective reduction in lower leg oedema during therapy with zinc oxide bandaging. In particular, a statistically significant reduction in SLEB thickness of 37.95% ($p<0.05$) was observed after four weeks of treatment. This result highlights how HFUS can be considered a valuable complementary diagnostic tool for objectively assessing changes in oedema in the dermis.[18] Normal values for SLEB thickness in men and women are not well-defined and vary with age, anatomical region and SLEB thickness is subject to fluctuations throughout the day (normal values in healthy people range between 0mm to 0.71mm). SLEB thickness generally increases with age, particularly in sun-exposed areas, as a marker of photoaging and dermal changes such as collagen degradation and water loss. It is typically

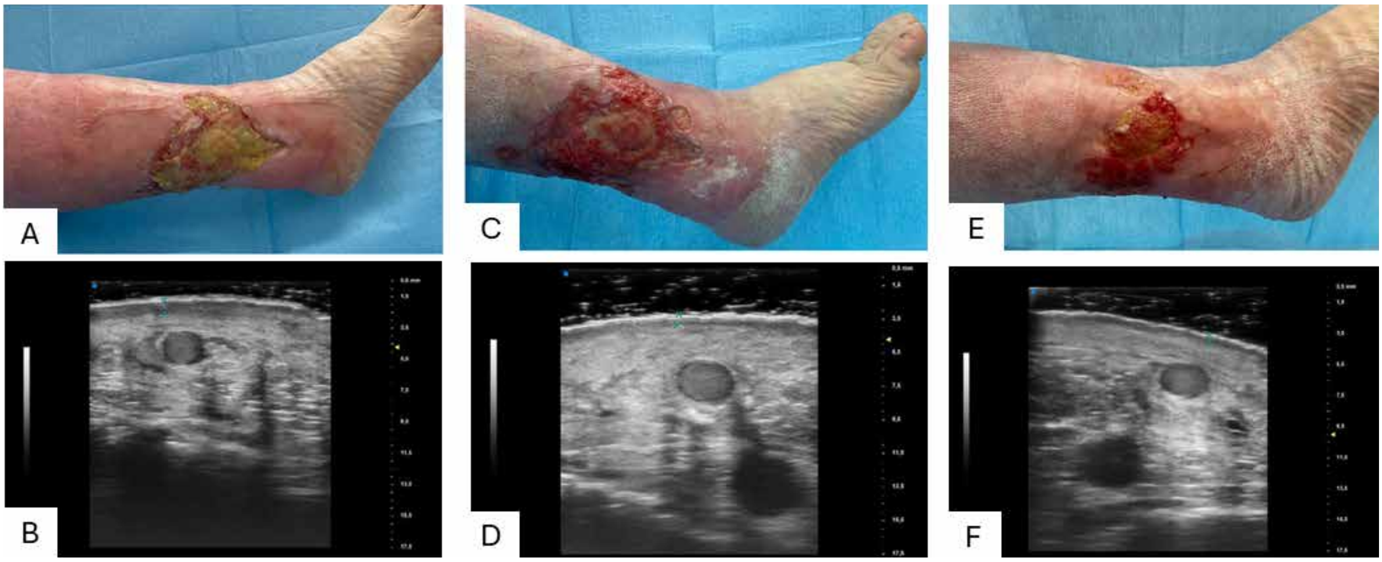

Figure 1. Clinical examination of calf diameter and high-frequency ultrasound (HFUS) assessment of the sub epidermal low echogenicity band (SLEB) in a patient with leg oedema and chronic ulceration. A) Baseline evaluation: calf circumference = 43cm; B) SLEB thickness = 0.88mm; C) After four weeks of treatment with zinc oxide bandage: calf circumference = 40cm ; D) SLEB thickness = 0.66mm; E) At the follow-up visit: calf circumference remains at 40cm; F) SLEB thickness = 0.68mm.

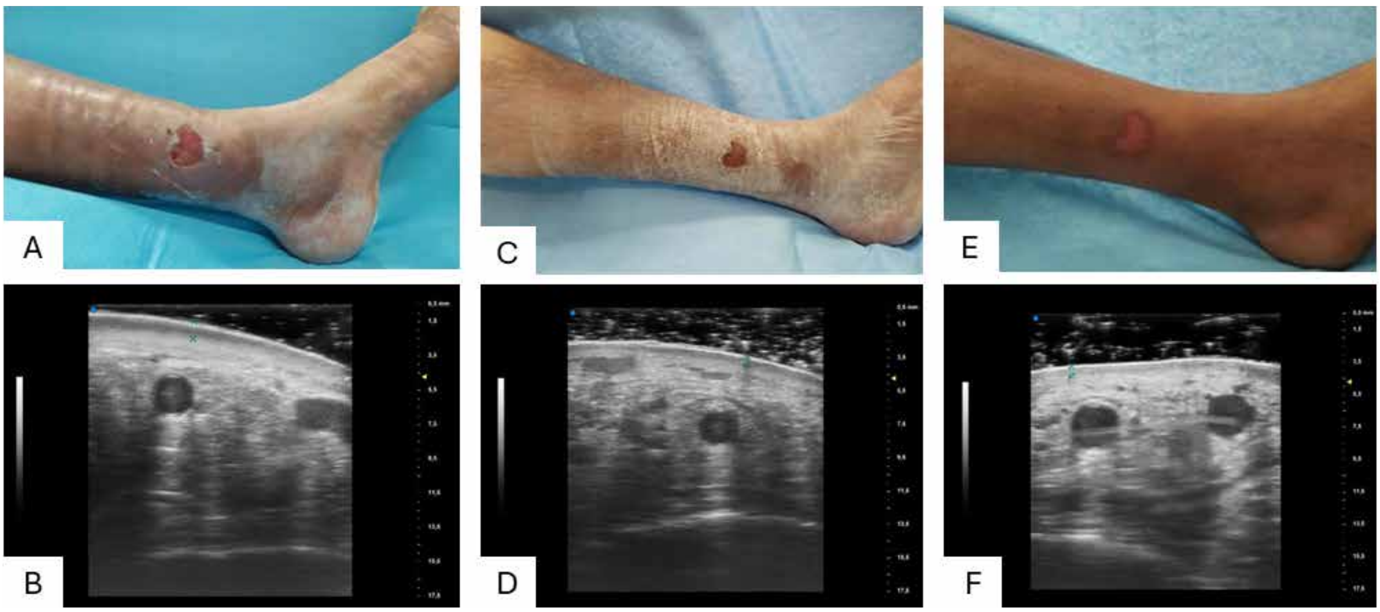

Figure 2. Clinical examination of calf diameter and high-frequency ultrasound (HFUS) assessment of the sub epidermal low echogenicity band (SLEB) in a patient with leg oedema and chronic ulceration. A) Baseline evaluation: calf circumference = 58cm; B) SLEB thickness = 1.03mm; C) After four weeks of treatment with zinc oxide bandage: calf circumference = 40.5cm; D) SLEB thickness = 0.53 mm; E) At the follow-up visit: calf circumference= 40cm; F) SLEB thickness = 0.60mm.

absent in children, appears in adolescents, and becomes prominent in adults.[19–22] Other studies have correlated increased oedema secondary to chronic venous insufficiency with SLEB thickness, finding that it is related to a specific stage of CVD.[23–25] HFUS has been already applied in literature for the evaluation of several dermatological disorder, because of its capability to detect subclinical alteration in the order of micrometers, however, no study has used such diagnostic tool for the precise measurement of the SLEB thickness.[26,27] It is noteworthy that the decrease in calf circumference and SLEB thickness, obtained in T1, was maintained until the FU visit, suggesting that the treatment should be continued for more than four weeks to achieve stable improvement (Figures 1 and 2).

On the other hand, no statistically significant results were observed regarding TEWL measurements. TEWL measurements was used in dermatology to assess the integrity of the skin barrier providing insights into the gradient of water evaporation through the stratum corneum which is suggestive of the skin's barrier function. TEWL was expressed in international units (g/m2/h) and ranged from 0 to 250 g/m2/h (normal values were 0–25 g/m2/h). An increase in TEWL indicates impaired skin barrier function, while a decrease suggests improved barrier integrity.[28] Data presented in literature demonstrated TEWL evaluation as a valid, non-invasive, sensitive, and reproducible tool for objectively measuring the functional state of the epidermal barrier at the stratum corneum level in patients with venous ulcers or chronic venous insufficiency. Particularly, it has been demonstrated that an increase in TEWL values is correlated with the severity of maceration of perilesional skin.[28–31] The conflicting and non-significant results obtained by our study may be due to external factors such as sweating, skin surface temperature and air temperature, which can significantly influence TEWL measurements. Additionally, the presence of zinc oxide on the skin during treatment may have contributed to altering the results.[32,33]

Despite the positive findings, this study has some limitations that should be acknowledged. The relatively short duration of the study (four weeks) may not fully analyse the long-term effects of the Unna boot on CVD. Additionally, the study's small sample size may limit the generalisability of the results to broader populations. Given the exploratory nature of the study, future studies with larger cohorts and extended follow-up periods are necessary to confirm these preliminary findings and explore the long-term benefits of zinc oxide-based compression therapy.

Moreover, some external factors cannot be completely eliminated, for example differences in room ventilation may have led to fluctuations in the TEWL measurement. Therefore, it is recommended that future studies conduct measurements as consistently as possible both subjectively and objectively, in accordance with the guidelines, to minimise the environmental interferences.[32,33]

CONCLUSION

This study demonstrates that zinc oxide-based compression bandaging/Unna boot is effective in reducing lower limb oedema in patients with CVD. After four weeks of treatment, significant reductions were observed in calf circumference and subcutaneous oedema measured by HFUS. On the other hand, TEWL measurements did not show statistically significant changes during the treatment, not providing reliable information about CVD improvement. The findings support the use of Unna boots for managing lower limb oedema in CVD, emphasising the value of incorporating advanced diagnostic tools, like HFUS, to monitor treatment efficacy. Future research with larger samples and longer follow-ups is needed to confirm these preliminary results.

DATA AVAILABILITY

The data supporting the findings of this study are available from the corresponding author on request.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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