doi:10.36849/JDD.7588

 ORIGINAL ARTICLE

Improvement of Chronic Venous Insufficiency Related Leg Xerosis and Dermatitis With Ceramide-Containing Cleansers and Moisturizers: An Expert-Based Consensus

Robert S. Kirsner MD PhD,[a] Anneke Andriessen PhD,[b] Jason R. Hanft DPM FACFAS,[c] Shasa Hu MD,[a] William A. Marston MD,[d] Lee C. Ruotsi MD ABWMS CWS-P UHM,[e] Gil Yosipovitch MD[a]

[a]Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, FL
[b]Radboud UMC Nijmegen, Andriessen Consultants, Malden, The Netherlands
[c]Foot & Ankle Institute of South Florida, South Miami, FL; South Miami Hospital, South Miami, FL
[d]UNC Hospitals Heart and Vascular Center at Meadowmont, Chapel Hill, NC; Wound Management Center, Chapel Hill, NC
[e]Saratoga Hospital Center for Wound Healing and Hyperbaric Medicine, Saratoga Springs, NY

ABSTRACT

Introduction: Chronic venous insufficiency (CVI) may lead to sustained elevated pressure (aka venous hypertension) in the dermal venous microcirculation. Risk factors include advanced age, obesity, female gender, pregnancy, and prolonged standing. CVI in the lower extremities may lead to cutaneous changes such as xerosis and venous leg dermatitis (VLD). This review explores skin barrier restoration using skincare for xerosis and VLD.

Methods: Prior to the meeting, a structured literature search yielded information on fourteen draft statements. During the meeting, a multi-disciplinary group of experts adopted five statements on xerosis and VLD supported by the literature and the authors' clinical expertise.

Results: VLD and associated xerosis is a common condition requiring more attention from healthcare providers. Compression therapy is the standard CVI and should be combined with good-quality skincare to enhance adherence to treatment. Maintaining an intact skin barrier by preventing and treating xerosis using gentle cleansers and ceramide-containing moisturizers may improve the skin sequelae of CVI. Skincare is frequently lacking or overlooked as part of the treatment of patients with CVI and VLD. This skin treatment is an unmet need that can be addressed with ceramides-containing pH balanced cleansers and moisturizers.

Conclusion: Compression therapy is the mainstay of treatment for CVI and VLD. Quality skincare can improve treatment adherence and the efficacy of compression therapy. Using a skincare agent may reduce friction and help patients avoid skin trauma while putting on compression garments. A ceramide-containing moisturizer sustained significant improvements in skin moisturization for 24 hours and may offer synergistic benefits together with compression treatment.

J Drugs Dermatol. 2024;23(2):61-66. doi:10.36849/JDD.7588

INTRODUCTION

Chronic venous insufficiency (CVI) comprises structural and functional pathology of the venous system. CVIs' pathophysiology most commonly results from lower extremity valvular reflux and/ or venous obstruction, which induces sustained elevated pressure (aka venous hypertension) in the dermal venous microcirculation in the dermal microcirculation.[1-4] The prevalence of CVI increases with age and is typically more predominant in women, smokers, obese or pregnant patients, as well as those with hereditary risk factors present.[1] Other risk factors include diabetes mellitus, prolonged sitting or standing, deep vein thrombosis (DVT), heart failure, and chronic lower extremity edema.[5,6] The abnormal venous flow of the lower extremities is observed in ~50% of individuals in the general population, although the estimated prevalence of CVI varies across the population studies reported.[1] A population study by Prochaska and colleagues was performed on 12,423 participants (age range: 40 to 80 years) who were part of the Gutenberg Health Study from April 2012 to April 2017. Using systematic phenotyping of CVI according to established CEAP (Clinical-Etiologic-Anatomic-Pathophysiologic) classification, they found a prevalence of CVI of 40.8% (Table 1).[1] Upwards of 6 million people in the US have advanced forms of CVI, such as leg edema and skin changes, and 2.2 million (PMID: 24625244) have venous leg ulcers.[5] The Edinburgh Vein Study found that the age-adjusted prevalence of CVI was 9% in men and 7% in women.[4] The prevalence of CVI in Asian populations has been reported to be lower than in non-Hispanic white populations. However, the prevalence in South Korea is rising due to the underdiagnosis of CVI, increased obesity, and an aging population.[4]

TABLE 1.

Clinical Staging as Part of the CEAP Classification	
Stage	**Description**
C0	No visible signs of venous disease
C1	Spider veins and reticular varicose veins
C2	Varicose veins with no signs of chronic venous hypertension
C3	Edema
C4	Skin changes
C4a	Pigmentation, dermatitis
C4b	Lipodermatosclerosis, Atrophie blanche
C5	Healed venous leg ulcer
C6	Venous leg ulcer

CEAP (Clinical-Etiologic-Anatomic-Pathophysiologic) classification

FIGURE 1. Venous edema.

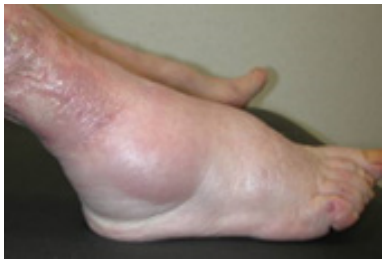
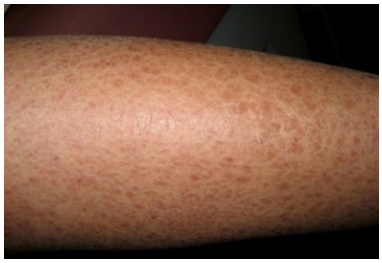


FIGURE 2. Lower leg xerosis.



CVI may lead to spider veins, reticular varicose veins, and edema (Figure 1). CVI induces inflammation and skin changes such as xerosis (Figure 2), pigmentation (Figure 3), dermatitis (Figure 4), lipodermatosclerosis, atrophie blanche, and eventually, venous ulceration (Table 2).[5,6,10,11] Venous ulcers can vary in size, can be difficult to manage and diminish quality of life, particularly if they are painful, complicated with dermatitis and xerosis, or drain profusely.[5,6,10-17] The management of leg ulcers is outside the scope of this review.

FIGURE 3. Pigmentation.

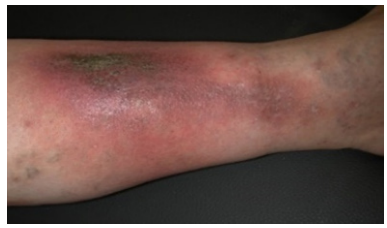
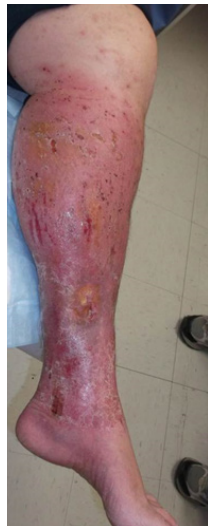


FIGURE 4. Venous dermatitis.



The prevalence of venous leg dermatitis (VLD) in patients >50 years in the US is estimated to be 6-7% (~15-20 million individuals), making this twice as prevalent as psoriasis.[18,19] VLD presents initially as poorly demarcated erythematous plaques of the lower legs bilaterally, classically involving the medial malleolus.[5-9] Duplex ultrasound is useful in demonstrating venous reflux to confirm the clinical diagnosis or when the clinical diagnosis of VLD is inadequate.[5,7]

TABLE 2.

Venous Leg Dermatitis	
Dermatologic presentation	Poorly demarcated erythematous rash, plaques, pitting edema
Associations	Advanced age, obesity, female gender, pregnancy, prolonged standing
Etiology	Venous insufficiency leading to edema and inflammation
Characteristics and location	Gravity-dependent regions such as the lower extremities
Histology	Dermal fibrosis, perivascular lymphocytic infiltrates, extravasated erythrocytes, small blood vessel proliferation
Diagnosis	Clinically, can be confirmed by venous duplex ultrasound
Treatment	Treatment of underlying venous insufficiency, compression stockings, emollients, anti-inflammatory agents

This review explores skin barrier restoration using skincare with gentle cleansers and moisturizers for CVI-related xerosis and VLD.

MATERIALS AND METHODS

The project used a modified Delphi process comprising structured literature searches and face-to-face discussions followed up online.[20,21]

Literature Review

The structured literature searches (01-November 2022) on PubMed and Google Scholar, as a secondary source, of the English-language literature (2010 – October 30, 2022) were performed by a dermatologist and a physician/scientist. They manually reviewed the selected literature for additional resources and prioritized studies on CVI, VLD and xerosis, SC barrier function, and skincare benefits using cleansers and moisturizers. The searches for CVI* VLD** and xerosis*** explored current clinical guidelines, treatment options, and therapeutic approaches using the following terms:

Group 1: *CVI*, VLD**, xerosis**** *AND pathophysiology OR inflammation OR cutaneous changes OR clinical signs OR clinical symptoms OR pruritus OR skin barrier physiology OR function OR dysfunction OR depletion of stratum corneum lipids*

Group 2: *CVI*, VLD**, xerosis**** *AND compression therapy OR skincare OR cleansers OR moisturizers OR emollients OR ceramides OR ce¬ramide-containing skincare OR efficacy OR safety OR tolerability*

The searches yielded 46 papers deemed clinically relevant to CVI, VLD, xerosis, and skin care to promote a healthy skin barrier and potential mitigation of xerosis and VLD using over-the-counter skincare and CER-containing cleansers and moisturizers.

Role of the Panel

The panel of six physicians (advisors) of various specialties (dermatology, vascular surgery, podiatry, and family medicine) involved in treating patients with CVI and resulting skin changes convened for a meeting. Prior to the meeting, a structured literature search yielded information on fourteen draft statements. During the meeting, the authors adopted five statements supported by the literature and the authors' clinical expertise.

RESULTS

Statement 1: *Venous dermatitis is a common inflammatory dermatosis of the lower extremities occurring in patients with chronic venous insufficiency. Risk factors include age, deep vein thrombosis, heart failure, obesity, diabetes, and prolonged sitting/standing.*

CVI leads to sustained venous hypertension (VH) upon ambulation, which causes skin changes and inflammation.[5,7-10] Dilated capillaries may trigger hemosiderin deposition in the dermis, producing hyperpigmentation (both hemosiderin and melanin), predominantly in the gaiter area.[5,7-10] Chronic VH induces thinning of the epidermis, erythema, xerosis, and VLD.[3-9] Patients with CVH frequently have pruritus, leading to scratching, skin markings, lichenification, and excoriations.[5,7-10] Further changes occur through the proliferation of small vessels, edema, spongiosis, mixed inflammatory cell infiltrates, and structural alterations in the papillary dermis.[5,7-10] Studies have shown that expression of matrix metalloproteinases (MMPs) 1, 2, and 13 is altered in the lesional skin of VLD in comparison with healthy skin, which could explain the spongiosis and structural abnormalities observed in the histology of VLD.[24]

Risk factors for developing VLD include advanced age, obesity, female gender, pregnancy, and prolonged standing.[5] Further risk factors associated with VLD include inherited disorders (such as thrombophilia) and prolonged bed rest.[1,5,6]

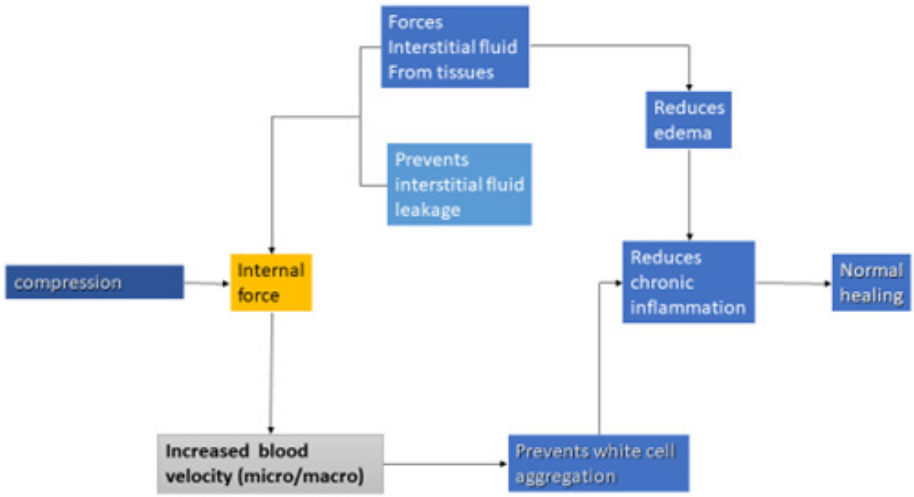
Studies have supported that the pathophysiology of venous and arterial vascular disease are commonalities; however, population-based studies confirming the clinical implications are lacking.[1,22,23] As many patients with leg ulcers never have venous studies, the advisors agreed that the term "venous leg ulcers" may not be appropriate, as the link to the venous system remains unproven in about 40% of leg ulcers.[2,3,5,22,23] Publications and algorithms should distinguish between VLD and swelling leg dermatitis (SLD) as the approach to treatment may differ.[7]

Statement 2: *Compression is the standard therapy for CVI; it has been shown to reduce edema and improve superficial skin lymphatic and venous function and transport.*

Treatment of VLD consists of addressing the VH, usually with compression therapy.[5,6-19]

Clinical guidelines and pathways for patients with CVI-related VLD should include accurate diagnosis and the use of appropriate diagnostic tools.[6] It is important to understand the individual patients' issues to achieve an optimal treatment outcome using a holistic approach.[6,18] Compression is the standard treatment for lowering VH, decreasing edema and inflammation, and enhancing tissue vascularization.[6,10-17] The underlying CVI should be treated with adequate compression that is appropriate and sustainable for the patient.[25] Before applying compression, the ankle-brachial pressure index (ABPI) is to be measured to provide information if sufficient arterial circulation is present for leaving compression safely in place day and night.[6,10-17,26] Lower extremity Doppler examination is recommended as the standard for patients with suspected peripheral arterial disease.[11,26]

FIGURE 5. Mode of action of compression.



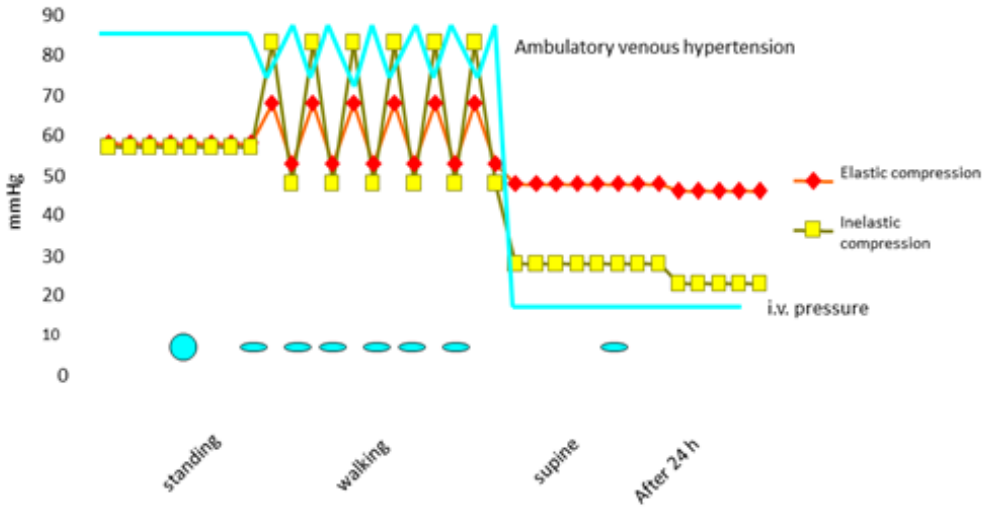
Many guidelines are available on CVI and leg ulcer management using compression.[6,11-17,19] Compression can be delivered using bandages, devices, or stockings and has been shown to reduce edema and inflammation and improve superficial skin lymphatic function and transport within the subfascial system (Figure 5).[6,10-17,25,27] Inelastic short-stretch bandages exert a massage effect during walking, reducing edema and increasing blood flow but inelastic compressions do not compress the legs when patients are at rest.[25,30] Intermittent pneumatic pressure devices have similar effects and may be tolerated in patients with concomitant arterial occlusive disease.[27,28] Elastic compression maintains a constantly high resting pressure independent of body position and has the lowest margin of safety because pressure remains high even when the patient is lying down (Figure 6).[6,30]

Skin damage has been reported even with light thromboprophylaxis stockings. Incorrect application of the bandages or fitting of the compression devices or stockings and lack of daily surveillance are important flaws in patient care, leading to adverse events.[6,29]

Statement 3: *Compression therapy should be combined with good-quality skincare to enhance adherence to and impact of treatment.*

The skin plays a vital role in assisting lymph flow and venous return and acts as a collateral route for lymph drainage.[32] In patients with VH, hyperkeratosis may occur, resulting from the over-proliferation of keratin or reduced desquamation.[34-37] Infrequent skin cleansing and poor skincare may exacerbate

FIGURE 6. Intravenous pressure measured in standing, walking, supine, and after 24 hours when using elastic and inelastic compression.



hyperkeratosis leading to colonization or infection.[34] If left untreated, lesions occur, and there is a risk for invasive infections such as cellulitis.[34-37]

Gentle skin cleansing, exfoliation, and moisturizers as adjuncts to compression or medical treatment should be part of the prevention, treatment, and maintenance of VLD. Hyperkeratosis and papillomatosis should be removed to maintain or restore skin barrier function.[8,9,34] Compression therapy, the standard treatment for patients with VLD, is less effective when hyperkeratosis is left untreated.[34,35] Exfoliation may reduce hyperkeratosis, scabs, and scales in patients with VH and associated VLD.[6-9] Removal of nonvital tissue is an accepted method to decrease biofilms and stimulate healing.[34-37]

There are various methods available for skin cleansing, including mild cleansers with a physiological pH (4-7), scrubbing, or skin massage using monofilament fiber debridement pads.[34-37] In choosing the right cleanser and cleansing device, it is important to consider aspects such as pathophysiology, skin condition, cleansing efficacy, patient tolerance, and interaction between skin condition, skin type, and the cleanser.[34] Further factors to consider are adherence to the treatment, the optimal time and method of cleansing and moisturizing, and the patient's cosmetic perception.[34]

Statement 4: *Maintaining an intact skin barrier by preventing and treating xerosis using gentle cleansers and ceramide-containing moisturizers may improve the skin sequelae of CVI.*

Ceramides, cholesterol, and free fatty acids are essential constituents of the SC.[33,40] They form highly ordered lipid lamellae and fill the space between the corneocytes.[33,40] The composition and structure of the lipid lamellae are critically important to the permeability barrier function of the skin and form an effective waterproof barrier.[33,40] Reductions in SC lipid content may be due to chronic inflammation leading to VLD.[7,8,9,33,40] A healthy skin with good elasticity facilitates an improved surface for compression and exercise in patients with CVI.[34-37] Skin care is important to address the issues associated with inflammation, xerosis, pruritus, and VLD.[8,9,12,31-37] Xerosis and VLD are often associated with pruritus, mainly involving the lower extremities.[18,19,23,31] Pruritus significantly impacts the quality of life and is reported by patients to be equally bothering as skin pain or even worse.[39] Skin changes triggered by CVI make the leg more susceptible to the entry of irritants and allergens through the skin, leading to inflammation and pruritus.[31,40] Scratching can lead to secondary infections, ulcerations, and chronic wounds.[31]

Skincare using cleansers and moisturizers and exfoliation of dry and scaly skin in atopic dermatitis has been reported in an algorithm as a standard measure for AD and may be applicable for VLD.[38] Topically applied steroids combined with moisturizers may be of benefit in acute VLD disease, as is the use of topical nonsteroidal medications such as tacrolimus.[8,9,31] Skin lipids containing moisturizers such as ceramides combat xerosis, restoring skin barrier function and may reduce pruritus.[31,40-45]

Statement 5: *Skincare is frequently lacking or overlooked as part of the treatment of patients with CVI and venous dermatitis. This skin treatment is an unmet need that can be addressed with ceramides-containing pH balanced cleansers and moisturizers.*

Ceramides are essential to the epidermal barrier and help maintain the skin's barrier function.[40] A disturbed composition of ceramides in the epidermis of patients with inflammatory disorders such as AD affects epidermal water loss and reduced water holding capacity.[40,45] It is evident from studies that the qualitative and quantitative difference in ceramide metabolism precipitates cutaneous inflammatory conditions such as dermatitis.[40,45]

Ceramide-containing moisturizers can decrease AD flares, via activation of peroxisome proliferator-activated receptor α, downregulation of inflammatory cytokines, and elevated antimicrobial peptides expression.[46] Ceramides delivered through a multi-vesicular topical product have shown clinically significant results for the management of xerosis.[41-44] Studies demonstrated that ceramide-containing skincare restored skin barrier function, reducing irritation, and was an effective and safe choice for those with xerosis or AD.[41-45]

Currently, skincare for VLD is underused.[5,31] Educating healthcare providers on the pathophysiology of CVI and related VLD is important to promote effective therapy with compression and skin care, improving patient outcomes.[5,18] Training medical assistants and nurses to assess patients for CVI on initial office visit intake may support early intervention.[18] During patient visits, handouts should be given, confirming the information on CVI and the risk of developing it due to comorbid conditions.[18]

LIMITATIONS

Although many studies have looked at atopic dermatitis and the benefits of skincare using gentle cleansers and moisturizers, robust studies on combining compression treatment with skincare for CVI, VLD, and related xerosis are lacking. Moreover, skin treatment is an unmet need for CVI, VLD, and related xerosis that can be addressed with ceramides-containing pH balanced cleansers and moisturizers and should be part of guideless and addressed in education for clinicians and patients as a standard measure.

CONCLUSION

Compression therapy is the standard CVI and VLD and should be combined with good-quality skincare to enhance adherence to

treatment. Maintaining an intact skin barrier by preventing and treating xerosis using gentle cleansers and ceramide-containing moisturizers may reduce friction and help avoid skin trauma while putting on compression garments. A ceramide-containing moisturizer sustained significant improvements in skin moisturization for 24 hours and may offer synergistic benefits together with compression treatment improving adherence to treatment and patient outcomes.

DISCLOSURES

This work was supported by an unrestricted educational grant from CeraVe US.

REFERENCES

1. Prochaska JH, Arnold N, Falcke A, et al. Chronic venous insufficiency, cardiovascular disease, and mortality: a population study. *Eur Heart J.* 2021;42(40)10:4157-4165. doi: 10.1093/eurheartj/ehab495.
2. Chang SL, Huang YL, Lee MC, et al. Association of various veins with incident venous thromboembolism and peripheral artery disease. *JAMA.* 2018; 319:807–817
3. Zygmunt JA. Duplex ultrasound for chronic venous insufficiency. *J Invasive Cardiol.* 2014;26(11):E149–55.
4. Eberhardt RT, Raffetto JD. Chronic venous insufficiency. *Circulation.* 2014;130(4):333–46.
5. Sundaresan S, Migden MR, Silapunt S. Stasis dermatitis: Pathophysiology, evaluation, and management. *Am J Clin Dermatol.* 2017;18(3)6:383-390. Doi: 10.1007/s40257-016-0250-0.
6. Andriessen A, Apelqvist J, Mosti G et al. Compression therapy for venous leg ulcers: risk factors for adverse events and complications, contraindications – a review of present guidelines. *J Eur Acad Dermatol Venerol.* 2017;31(9):1562-1568.
7. Sippel K, Mayer D, Ballmer B, et al. Evidence that venous hypertension causes stasis dermatitis. *Phlebology.* 2011;26(8):361–5.
8. Weedon D. Stasis dermatitis. In: Weedon D, editor. Weedon's skin pathology, 3rd ed. Amsterdam: Churchill Livingstone, Elsevier; 2010.
9. Rapini RP. Stasis dermatitis. In: Rapini RP, editor. Practical Dermatopathology. 2nd ed. Amsterdam: Elsevier; 2012.
10. Marston W, Tang J, Kirsner RS, et al. Wound Healing Society 2015 update on guidelines for venous ulcers. *Wound Repair Regen.* 2016;24(1):136-144.
11. Neumann HA, Cornu-Thenard A, Junger M, et al. Evidence-based (S3) guidelines for diagnostics and treatment of venous leg ulcers. *J Eur Acad Dermatol Venereol.* 2016;30(11):1843-1875.
12. Gloviczki P, Comerota AJ, Dalsing MC, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg.* 2011;53(5 Suppl):2S–48S.
13. Weller CD, Team V, Ivory JD, et al. ABPI reporting and compression recommendations in global clinical practice guidelines on venous leg ulcer management: A scoping review. *Int Wound J.* 2019 Apr;16(2):406-419. doi: 10.1111/iwj.13048.
14. Franks PJ, Barker J, Collier M, et al. Management of patients with venous leg ulcers: challenges and current best practice. *J Wound Care.* 2016;25(Suppl 6):S1-s67.
15. Nelson EA, Adderley U. Venous leg ulcers. *BMJ Clin Evid.* 2016;2016:1902.
16. Marston W, Tang J, Kirsner RS, et al. Wound Healing Society 2015 update on guidelines for venous ulcers. *Wound Repair Regen.* 2016;24(1): 136-144.
17. Sinha S, Sreedharan S. Management of venous leg ulcers in general practice - a practical guideline. *Aust Fam Physician.* 2014;43(9):594-598.
18. Robbins AB. Halting progression of stasis dermatitis: Community perspectives and strategies for prevention. *Family Medicine Clerkship Student Projects.* 2018;326. https://scholarworks.uvm.edu/fmclerk/326
19. Valencia IC, Kirsner RS, Eaglstein WH. Chronic venous insufficiency and venous leg ulceration. *J Am Acad Dermatol.* 2001;44(3):401-421.
20. Trevelyan EG, Robinson N. Delphi methodology in health research: how to do it? Eur J Integrative Med. 2015;7(4):423-428.
21. Brouwers M, Kho ME, Browman GP, et al. AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting, and evaluation in healthcare. *Can Med Association J.* 2010,182:E839-42.
22. Chang SL, Huang YL, Lee MC, et al. Association of various veins with incident venous thromboembolism and peripheral artery disease. *JAMA.* 2018; 319:807–817
23. Vivas A, Lev-Tov H, Kirsner RS. Venous leg ulcers. *Ann Intern Med.* 2016;165:ITC17–32.
24. Wang X, Khalil RA. Matrix metalloproteinases, vascular remodeling and vascular disease. *Adv Pharmacol.* 2018;81:241-330.
25. Wong IKY, Andriessen A, Charles HE et al. Randomized controlled trial comparing treatment outcome of two compression bandaging systems and standard care without compression in patients with venous leg ulcers. *J Eur Acad Dermatol Venereol.* 2012; 26: 102–110.
26. Chesbro SB, Asongwed ET, Brown J, John EB. Reliability of Doppler and stethoscope methods of determining systolic blood pressures: considerations for calculating an ankle-brachial index. *J Natl Med Assoc.* 2011;103(9): 863-869.
27. Moran PS, Teljeur C, Harrington P, Ryan M. A systematic review of intermittent pneumatic compression for critical limb ischaemia. *Vasc Med.* 2015; 20: 41–50.
28. Suehiro K, Morikage N, Yamashita O, Harada T, Ueda K, Samura M, et al. Adherence to and efficacy of different compression methods for treating chronic venous insufficiency in the elderly. *Phlebology. 2*016;31(10):723-28.
29. Dissemond J, Protz K, Hug J, et al. Compression therapy of chronic leg ulcers: Practical aspects. *Z Gerontol Geriatr.* 2017. DOI: 10.1007/s00391-017-1191-9.
30. Partsch H, Menzinger G, Borst-Krafek B, Groiss E. Does thigh compression improve venous hemodynamics in chronic venous insufficiency? *J Vasc Surg.* 2002;36:948-52
31. Purnamawati S, Indrastuti N, Danarti R et al. The role of moisturizers in addressing various kinds of dermatitis: a review. *Clin Med Re.* 2017;14(3-4):75-87.
32. Burian EA, Karlsmark T, Nørregaard S et al. Wounds in chronic leg oedema. *Int Wound J.* 2021; 19(2):411-425. 10.1111/iwj.13642
33. Lynde CW, Tan J, Skotnicki S, Andriessen A, et al. Clinical insights about the role of skin pH in inflammatory dermatological conditions. *J Drugs Dermatol.* 2019;18(12) S-1:1-16.
34. Andriessen A, Wiegand C, Eberlein T et al. Clinical experience using monofilament fiber cleansing and debriding technology for various skin conditions. *J Drugs Dermatol.* 2022;21(11):1-8.
35. Management of hyperkeratosis of the lower limb: Consensus recommendations. London: Wounds UK 2015; 11(4)Suppl 8: Quick guide: Management of hyperkeratosis of the lower limb. *Wounds UK.* 2016; 1-5.
36. Roes C, Morris C, Calladine C. Biofilm management using monofilament fibre debridement technology: outcomes and clinician and patient satisfaction. *J Wound Care.* 2019;28(9):608-622.
37. Schultz G, Bjarnsholt T, James GA et al. Consensus guidelines for the identification and treatment of biofilms in chronic nonhealing wounds. *Wound Repair Regen.* 2017; 25(5):744–757. https://doi.org/10.1111/wrr.12590
38. Lynde CW, Bergman J, Fiorillo L, et al. Clinical insights about topical treatment of mild-to-moderate pediatric and adult atopic dermatitis. *J Cutan Med Surg.* 2019;(6)23(3_suppl):3S-13S.
39. Kini SP, et al. The impact of pruritus on quality of life: the skin equivalent of pain. *Arch. Dermatol.* 2011; 147(10):1153–6.
40. Li Q, Fang H, Dang E, Wang G. The role of ceramides in skin homeostasis and inflammatory skin diseases. *J Dermatol Sci.* 2020;97:2-8.
41. Vender RB, Andriessen A, Barankin B, et al. Cohort using a ceramides containing cleanser and cream with salicylic acid for dry, flaky, and scaling skin conditions. *J Drugs Dermatol.* 2019;18(1):80-85.
42. Danby SG, Andrew PV, Brown K, et al. An Investigation of the skin barrier restoring effects of a cream and lotion containing ceramides in a multi-vesicular emulsion in people with dry, eczema-prone skin: The RESTORE Study Phase 1. *Dermatol Ther (Heidelb).* https://doi.org/10.1007/s13555-020-00426-3
43. Danby SG, Andrew PV, Kay LJ, et al. Enhancement of stratum corneum lipid structure improves skin barrier function and protects against irritation in adults with dry, eczema-prone skin. *British J Dermatol.* 2022;186:875–886.
44. Drealos ZD, Baalbaki NH, Raab S, Colon G. The effect of a ceramide-containing product on stratum corneum lipid levels in dry legs. *J Drugs Dermatol.* 2020;19(4):372-376.
45. Yadav N, Madke B, Das A. Ceramides where do we stand? *CosmoDerma.* 2021;1-44.
46. Lee SE, Jung MK, Oh SJ et al. Pseudoceramide stimulates peroxisome proliferator-activated receptor-α expression in a murine model of atopic dermatitis: Molecular basis underlying the anti-inflammatory effect and the preventive effect against steroid-induced barrier impairment. *Arch Dermatol.* Res 2015;307:781-92.

AUTHOR CORRESPONDENCE

Anneke Andriessen PhD

E-mail:..... ti016762@telfort.nl