Influence of Nutrition Status and Compression Therapy on Venous Ulcer Healing: A Systematic Review

María Teresa García-Rodríguez, PhD, RN, is Nurse at the Complexo Hospitalario Universitario de A Coruña (CHUAC), Universidade da Coruña, Spain, Rheumatology and Public Health Research Group, Institute of Biomedical Research of A Coruña (INIBIC).

Marta Rodríguez-Parrado, RN, is Nurse at the Complexo Hospitalario Universitario de A Coruña (CHUAC), Universidade da Coruña, Spain.

Rocío Seijo-Bestilleiro, PhD, RN, is Nurse at the Complexo Hospitalario Universitario de A Coruña (CHUAC), Universidade da Coruña, Spain, INIBIC.

Cristina González-Martín, PhD, is Podiatrist at the Complexo Hospitalario Universitario de A Coruña (CHUAC), Universidade da Coruña, Spain, INIBIC.

The authors have disclosed no financial relationships related to this article

Abstract

Objective: To review the literature to determine whether compression therapies and nutrition status influence venous ulcer healing.

Data source: A systematized bibliographic review was carried out by searching PubMed, Scopus, and Cochrane databases for studies published between 2015 and 2020, using descriptors in Spanish and English.

Study selection: After establishing the research question and applying the filters based on inclusion and exclusion criteria, 114 articles were found. After screening, 11 articles were selected for the review: 8 were identified in the literature search, and 3 were added from the bibliographic references of other studies.

Data extraction: The authors developed a data extraction sheet that recorded the following variables: author, country, year of publication, level of evidence, research design, therapy type, initial ulcer size, active ulcer history, pain, healed wounds, wound reduction, therapy tolerance, nutrition assessment method, body mass index, and nutrition disorders.

Data synthesis: Four studies analyzed the relationship between nutrition status and venous ulcer healing, finding that these patients tend to have a high body mass index; a deficit of nutrients such as vitamin A, D, or zinc; and an excess of lipids and carbohydrates. Seven studies compared different types of compression to determine which provided the best results, with two- and four-layer therapy being the most commonly used. Variables such as small wound size and recent onset were associated with better prognosis.

Conclusions: In terms of nutrition, the parameters analyzed are very limited. Although several studies show that two-layer therapy produces the greatest ulcer healing, there is not enough information to recommend one type of therapy over the other. Therefore, more clinical trials are needed to study broader nutrition parameters and compare the types of therapy under matched conditions to determine their influence on ulcer healing.

Keywords

Compression therapy, healing, nutrients, nutrition, review, venous ulcer.

INTRODUCTION

Venous ulcers (VUs) alter microcirculation and macrocirculation and are characterized by their chronic natureand tendency to recur, up to 50% to 70% in as little as 6 months.[1] Moreover, although it is a disorder characteristic of old age, 22% of patients with VUs will develop themby the age of 40 years and 13% by the age of 30 years.[2] In a prevalence study by Escudero Rodríguez et al,[3] 48.5% of patients had chronic venous disease; prevalence was higher in older age groups and women. In addition, 59% of patients required treatment, and 7% had to be referred to specialist consultations. The investigators concluded that chronic venous disease washighly prevalent, but invasive treatments and specialist referrals occurred infrequently.

Among the various treatment options available, compression therapy is the most effective treatment for VUs (Table 1).[1,4] The aims of compression therapy are to increasevenous return, reduce ambulatory venous hypertension,and promote edema reabsorption, thus promoting wound healing and avoiding recurrence.[5]

In caring for patients with VUs, healthcare providers may forget to assess the patient as a whole, overlooking important aspects such as nutrition status. Although scientific evidence shows that nutrition status influences both wound development and wound healing,[4,6,7] there is limited research on nutrition factors in relation to VUs in comparison with ulcers of other etiologies, likely because providers assume that the main factor is the venous disease itself.[6] However, protein requirements increase by up to 250% when a wound occurs, and proteincan also be lost through wound exudate. In addition, various micronutrients are important for wound healing, such as amino acids, vitamins, and minerals.[7–9] Age, high body mass index (BMI), deep thrombosis, and ulcer surface area are also factors associated with delayed healing of VUs.[10] Further, some studies have

shown that older patients with lower limb ulcers experience deficiencies of vitamins, minerals, or protein from inadequate intake.[11,12]

In a systematic review, Barber et al[6] observed that patients with VUs tend to have overweight or obesity but with nutrition deficits. Deficiencies in various nutrients can lead to chronic or worsening VUs or wounds in general. In venous wounds, protein plays a vital role in maintaining oncotic pressure, which stops the expansion of the wound. Vitamin A is important in the inflammatory phase of healing and stimulates epithelialization and collagen production. Vitamin C, besides being an antioxidant, is important for the proliferation of fibroblasts and is involved in the activity of neutrophils and collagen synthesis. Regarding vitamin D, studies show a higher prevalence of deficiency in patients with VUs, although deficiency was not found to influence the wound characteristics.[8,9,13] Other nutrients related to lower limb ulcers in older adults include beta-carotenes; minerals such as zinc, magnesium, or iron; or macronutrients such as protein. Caloric intake is also important.[11,12]

All this, together with other factors such as chronicity and the presence of complications, infection, or skin cancer, can lead to reduced quality of life and increased disability for patients with VUs, resulting in higher healthcare costs due to the frequency of patient care.[1,2,5] Thus, this systematic review aimed to determine the influence of nutrition status and compression therapy on the development of VUs.

METHODS

This review was written following the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) protocol.[14] The

research question was: Do nutrition status and compression therapy influence the evolution and healing of VUs?

The literature search focused on patients with lower-limb VU and the relationship between the nutrition and type of compressive therapy in their healing. The outcomes were categorized as “influence of nutrition status on the state of VUs” and “evolution of VUs by type of compressive therapy” (eg, comparing compression bandaging systems vs or comparing two different compression bandaging systems, etc).

Two nurse researchers identified MeSH terms (varicose ulcer, venous leg ulcer, venous ulcer, compression bandages, compression therapy, nutrition assessment, malnutrition, undernutrition) and used the keywords to develop a rigorous search strategy in PubMed, Scopus, and Cochrane databases. The inclusion criteria were as follows: (1) research reports conducted in adult population with VUs; (2) written in English, Spanish, or Portuguese; (3) published between 2015 and 2020; and (4) relevant for the systematized review. The literature search was conducted in May and June 2020.

Three researchers independently screened the article titles and abstracts to identify those that met the inclusion criteria. Articles that were not excluded were then read in full and assessed for their suitability. Disagreement over the eligibility of studies was resolved through discussion and by a fourth reviewer.

To assess the quality of the articles, the researchers used the scientific level of evidence guideline designed by the Scottish Intercollegiate Guidelines Network[15] because of its simplicity and clarity. The authors developed a data extraction sheet that recorded the following variables: author, country, year of publication, level of evidence, research design, therapy type, initial ulcer size, active ulcer history, pain, healed wounds, wound reduction, therapy tolerance, nutrition assessment method, BMI, and nutrition disorders.

Any differences were discussed, and data were included once consensus was reached. The data were then synthesized and analyzed by the review authors, and discrepancies were solved by consensus.

RESULTS

The bibliographic search revealed 114 articles. Of these, 13 were excluded. The authors assessed the titles and abstracts of the remaining 111 articles, discarding 94 of them because they were duplicates or did not address the questions of interest. The full texts of the remaining 17 articles were read, and 9 articles were excluded because the topic was not relevant. Thus, eight articles were included. However, given the lack of information in the nutrition field, three additional articles were selected from the references of the initial articles. Ultimately, 11 articles were included in this review (Figure).

Of the 11 studies included in the review, 63.6% were conducted in Europe, and the remainder were conducted in the US (18.2%)[23,24] and Australia (18.2%).[25,26] The European studies were conducted in the UK,[16,21] Germany,[22] Poland,[17] Italy,[18] and France.[20] One study was conducted in three countries (France, Germany, and the UK).[19] The majority of the included studies were clinical trials.[16,18–20,25,26] The remaining articles included descriptive cross-sectional studies,[23,24] prospective[17] and retrospective cohort[21] studies, and a case-control study.[22]

According to the Scottish Intercollegiate Guidelines Network model,[15] the level of evidence for most articles would be 1+ with grade of recommendation A,[16–19,25,26] followed by level of evidence 2+ with grade of recommendation C.[21,23,24] The remaining articles had level of evidence 1− with grade of recommendation B[20] and 2++ with grade of recommendation B.[22]

Upon review, four studies analyzed the relationship between nutrition status and VUs.[22–24,26] They show that patients with VUs tend to have nutrition deficiencies, most commonly in vitamins C, D, and zinc.

In addition, seven studies compared different types of compression to determine which provides the best results.[16–21,25] Three of these articles also determined the cost and effectiveness of the different therapies.[16,18,21] The most common compression therapies were two-layer (elastic and inelastic) and four-layer compression therapies.

Results of Individual Sources of Evidence

The main outcomes were categorized as:

- Role of nutrition status on the course of VUs
- Evolution of VUs by type of compression therapy

Role of nutrition status on the course of VUs. Four studies investigated nutrition status in patients with VUs (Table 2).[22–24,26] All four studies used BMI calculations (Table 3), but methods for assessing nutrition status varied. Some nutrition factors such as vitamins, minerals, or protein were taken into account.[22–24] Some of the studies also describe ulcer assessment or development.[22,23]

Renner et al[22] studied two groups of patients: patients with venous ulceration and a control group of patients who had a postsurgical wound following skin cancer removal. The mean size of VUs was 32.5 cm^2, and BMI was higher in the study group than the control group (31.5 vs 27.1 kg/m^2). Nutrition status was assessed using, the Mini Nutritional Assessment and the Nutritional Risk Screening (NRS). Results from these assessments were contradictory: According to the Mini Nutritional Assessment, more patients were at risk of malnutrition in the study group, whereas according to the NRS, patients in the

control group had the highest risk of malnutrition. Patients also underwent biochemical analyses to detect qualitative malnutrition. In the analysis, significantly lower mean values for several parameters were detected in the study group versus the control group, including vitamin B_6 (4.2 vs 9 ng/mL; $P < .0005$), vitamin B_9 (5.19 vs 9.4 ng/mL; $P < .0005$), vitamin C (3 vs 5.2 mg/mL; $P < .007$), zinc (69 vs 87 μg/dL; $P < .006$), and albumin (34.5 vs 40.7 g/L; $P < .000006$). Homocysteine levels were elevated in the study group but in the normal range in the control group (15.1 vs 10.8 μmol/L), and vitamin D levels were deficient in both groups, albeit more so in the ulcer group (9.1 vs 21.3 ng/mL). In the study by Melo et al,[23] ulcers averaged 32.5 cm^2 in size, and mean BMI was 30.93 kg/m^2. Patients' nutrient intake was collected using 24-hour records. Investigators found that 66.7% of the patients had a deficient intake of magnesium, and 100% had a deficient vitamin A intake. On the other hand, 21.2% of patients were overconsuming carbohydrates (resulting from a high intake of sugars in the diet), and 18.2% were overconsuming lipids (from high intakes of monounsaturated, polyunsaturated, and saturated fats). The macronutrient distribution corresponded to the recommendations for healthy individuals, but not for those with chronic wounds, resulting in a hypocaloric and hypoproteic diet. The biochemical parameters analyzed were hematocrit, hemoglobin, albumin, fasting glucose, and C-reactive protein. Although 27.3% (n = 9) of the patients were diagnosed with diabetes, 35.7% of men (n = 5) and 33.3% of women (n = 6) had elevated blood glucose. In addition, 92.9% of men and 84.2% of women had above normal C-reactive protein. The authors considered this increase detrimental to wounds, and suggested that inflammation may exacerbate lower-limb VUs.

McDaniel et al[24] recorded participants' nutrient intake using the Food Frequency Questionnaire. They also calculated BMI and plasma polyunsaturated fatty acid levels. The mean BMI of the participants was 41.28 kg/m^2 and they consumed lower than recommended values for vitamin C, fruits, and vegetables, but higher than recommended values for sodium, saturated fatty acids, and sugar. In addition, participants had an average n6 to n3 ratio of 11.25%, well above the optimal value (4%).

Finally, Bauer et al[26] compared the efficacy of two nutrition supplements in patients with chronic wounds. There was 18 g of protein in the standard supplement and 10.5 g of protein and 9 g of L-arginine in the specific supplement for wounds. Patients' nutrition status was determined using the Patient Generated-Subjective Global Assessment (PG-SGA); protein and energy intake was assessed weekly using the 24-hour recall method, and ulcer characteristics were analyzed using the Pressure Ulcer Scale for Healing (PUSH) system. At baseline, the mean BMI of the specific supplement group was 27.8 kg/m^2, whereas that of the standard supplement group was 25.7 kg/m^2. The PUSH score was slightly higher in the standard feeding group (13.9 in the specific supplement group vs 14.2 in the standard supplement group), as was the energy intake (78 kJ kg^{-1} vs 85.3 kJ kg^{-1}). However, the PG-SGA score was higher in the specific supplement group (11 points) in comparison with the standard supplement group (6.7 points). These data (higher BMI, lower energy intake, and higher PG-SGA) indicated that an intervention to improve symptom management and nutrition choices was urgently needed in the specific supplement group. After 8 weeks, wounds had healed in only three patients in the standard supplementation group; however, their PUSH scores increased more (33.4% vs 4.3%). The PG-SGA score improved more in the specific supplementation group, although the difference was not statistically significant.

Evolution of VUs according to types of compression therapy. Seven articles compared different types of compression therapy (Tables 3 and 4).[16–21,25] Although the majority of them compared two types of therapy,[16,18–20,25] two articles compared multiple types.[17,21] In addition, four of the articles also assessed the cost of the different therapies.[16,18,20,21]

Compression Bandaging Systems Versus Compression Stockings

Ashby et al[16] and Finlayson et al[25] compared compression stockings with four-layer bandaging. In Ashby et al,[16] the average ulcer size in the compression stocking group was slightly larger than in the compression bandage group (4.1 vs 3.7 cm^2); both groups had an ulcer duration of 4 months. There was no difference in healing time between the two types of compression. However, ulcer recurrence was higher in patients with compressive bandage therapy (23%) versus compression stockings (14%). In addition, more patients had to change therapy in the compression stocking group (38% vs 28%). Of these, 42% in the stocking group and 24% in the bandage group were attributable to poor compression tolerance, 17% of patients in the stocking group versus 7% in the bandage group were because of ulcer deterioration, and 2% in both groups were because of increased ulcer area. Compression stocking therapy was more economical because patients did not need to visit the nurse's office as frequently as patients in the compression bandage group.

In contrast, in the study by Finlayson et al,[25] the size of ulcers was slightly larger in the four-layer bandage group (4.6 cm^2) than in the compression stocking group (4.0 cm^2), and the duration of ulcers was longer in the compression stocking group (19 weeks vs 25 weeks). Both groups had similar PUSH scores (10.7 in the four-layer bandage group and 10.0 in the compression stocking group). However, although pain was similar in both

groups at baseline (as measured by the Medical Outcomes Study Pain Measures), at 24 weeks the four-layer bandage group had a lower score (23 vs 34). Ulcer healing was higher in the four-layer bandage group (84%) than in the stocking group (72%), as was ulcer area reduction (96% vs 93%). In addition, healing time was shorter in the bandage versus stocking group (10 vs 15 weeks).

Comparisons of Two Compression Bandaging Systems

Lazareth et al[19] and Gillet et al[20] compared two-layer compression bandaging with four-layer compression bandaging. Lazareth et al[19] concluded that the two-layer bandage therapy was more effective. Total ulcer healing was higher in the bilayer dressing group (48% vs 38% in the four-layer dressing), as was the reduction in wound size (6.6 cm^2 vs 4.9 cm^2). In addition, 47% of wounds treated with bilateral bandaging and 44% of wounds treated with four-layer dressing experienced a relative reduction in wound área greater than 40%. Pain reported with dressing change was higher in patients with the four-layer dressing (40%) than in the bilayer dressing group (27%), as was the incidence of adverse effects (four-layer dressing, 25%; vs bilayer dressing, 17%). The authors also concluded that the two-layer dressing was easier to apply.

Similar results and conclusions were obtained by Gillet et al.[20] After 16 weeks of compression therapy, the healing rate was 48.9% with the two-layer bandage (Biflex Kit; Thuasne Group) and 24.4% with the four-layer bandage (PROFORE, Smith+Nephew). Pain (measured by visual analog scale) was lower at baseline in patients treated with the bilayer bandage, although after 16 weeks of treatment, pain was lower in both groups. Although more adverse effects were found in the bilayer bandage group, mainly consisting of skin reactions (pruritus, eczema, etc), both patients and professionals

reported a greater acceptance of the two-layer bandage because of its softness, breathability, and simplicity of application. They also observed that fewer kits were used with the bilayer bandage (17.6) than with the four-layer bandage (33.2), which implied lower costs with 2-layer therapy.

Mosti et al[18] also compared two types of compression therapy, an adjustable compression bandage (circaid juxtacure; medi USA) and the two-layer inelastic bandage (Coban 2; 3M). The ulcer size was larger in patients in the adjustable compression bandage group (16 cm^2) compared with the inelastic bandage group (12.5 cm^2). Both groups had equivalent pain scores as measured by the visual analog scale, and pain was significantly reduced by compression, regardless of the type of therapy used. The percentage of ulcer healing was higher in the adjustable compression bandage group (78.7% vs 69.6%). In addition, of the patients whose ulcer did not heal at the 12-week follow-up, ulcer size was reduced by 80% in the adjustable compression bandage group and by 71.2% in the inelastic bandage group. Although both compression therapies were well accepted, the adjustable compression bandage therapy was better tolerated. The researchers concluded that in addition to being more effective in healing ulcers, the adjustable compression bandage was also more economical.

Other Comparisons of Compression Systems

The study by Guest et al[21] assessed the clinical outcomes and costs of using a two-layer cohesive compression bandage (Coban 2) versus a two-layer compression system (KTwo; URGO) or a four-layer compression system (PROFORE). At the start of compression, ulcer size was smallest in the cohesive compression system group (41.7 cm), followed by the two-layer compression therapy group (43.9 cm) and the four-layer compression

system group (48.6 cm). After 6 months of study, the two-layer cohesive compression therapy group had the highest percentage of healed ulcers (76%), compared with 70% in the two-layer compression bandage group and 64% in the four-layer compression system group. Further, the length of time from the start of compression therapy to ulcer healing was 1.6 months in the cohesive compression group and 2.0 and 2.1 months in the two-layer compression and four-layer compression groups, respectively. However, the percentage of ulcer reduction was highest in the two-layer compression therapy group (68%; cohesive compression bandage, 65%; and four-layer compression system, 62%). Of the compressive therapies studied, the four-layer compressive therapy was the most expensive, and two-layer cohesive compressive therapy was the least expensive. The authors concluded that the cohesive compression therapy is more effective and less expensive tan the two- or four-layer compression systems.

Dolibog et al[17] compared five types of compression therapy for the healing of VUs. They studied five groups of patients: group A used intermittent pneumatic compression, group B used compression stockings, group C used a multilayer short elastic bandage, group D used a bilayer elastic bandage, and group E used Unna boots. Of the five groups, group E had the smallest ulcer size (18.39 cm), and group B had the largest ulcers (23.12 cm). After 2 months of study, the patients with the highest cure rates were those in groups A (57.14%), B (56.66%), and C (58.62%). The least effective therapies were those used by groups D and E with cure rates of 16.66% and 20%, respectively. The reduction in ulcer size was also greater in groups A, B, and C (48.11%, 41.22%, and 49.02%, respectively) compared with groups D (17.77%) and E (20.48%). Thus, the best performing therapies for the treatment of VUs were the multilayer short elastic bandage, intermittent pneumatic compression, and compression stockings.

DISCUSSION

The Influence of Nutrition Status on VUs

In the management of VUs, nutrition status and deficiencies that may affect the evolution of the wound should be considered. In this study, the authors found four articles [22–24,26] that investigated the nutrition status of patients with VUs.

The healing of any type of wound is influenced by different factors, including nutrition status. For this reason, the presence of nutrition deficiencies at the macronutrient and/or micronutrient level in undernourished or overnourished patients will delay wound healing. In addition, wounds may lose proteins and liquids, requiring a greater supply of nutrients.[27] However, there is not yet enough evidence to determine the nutrition requirements for patients with VUs; the recommendations are based mainly on what has been studied in other types of ulcers.

Researchers have concluded that one of the main risk factors for VUs is a high BMI.[6,28] Patients with VUs in the lower limbs often have obesity or overweight. Adipose tissue is les vascularized and thus may decrease blood flow and nutrients to the wound.[4] Patients with a high BMI have up to three times more risk of developing VUs than do patients who fall within the normal BMI range.[29]

Nutrition Deficiencies

Vitamins. Low values of vitamins B_6, B_9, C, D, and A predominate in patients with VUs.[22–24] Whereas deficits of vitamins B_6, B_9, and C are observed in patients with vascular ulcers, deficits of vitamins D and A are detected in all patients, although more pronounced in patients with VUs. Vitamin D deficiency is associated with age, low sun

exposure, or obesity, whereas vitamin A deficiency is due to a higher metabolic demand (as in the case of a chronic wound) and not only to insufficient intake.[30]

Minerals. Melo et al[23] determined that a normocaloric diet is insufficient for patients with chronic wounds. Magnesium is one of the nutrients that are less consumed but are important for the formation of new tissue and collagen. Magnesium deficiency is related to age and to the homeostasis of vitamin D and calcium.[13] In the study conducted by Renner et al,[22] the authors observed a deficiency in serum zinc. In contrast, McDaniel et al[24] and Melo et al[23] noted that the daily intake of this mineral was within the recommended dietary allowances for healthy individuals. This difference may be because patients with chronic wounds have higher nutrition requirements. Critically, zinc contributes to the transport of vitamins A and C; therefore, its deficiency could influence these vitamins.[13]

Protein. Melo et al[23] reported that daily protein intake was deficient, which could be related to below average grip strength and arm muscle circumference values (grip strength: mean, 25.57 kgF; minimum value, 10 kgF; arm muscle circumference: mean, 26.53 cm; minimum value, 19.84 cm. Meanwhile, McDaniel et al[24] determined that protein intake was adequate (71.37 ± 31.32 g/d) according to recommended dietary allowances (46–56 g/d), and Renner et al[22] observed a normal value for total serum protein (ulcer group median, 68.2 g/L; and control group median, 68.4 g/L; reference range, 66–83 g/L). Finally, in Bauer et al,[26] patients supplemented with only protein had better ulcer healing than did those who were supplemented with both protein and arginine. This may be because more patients had diabetic ulcers in the group supplemented with protein and arginine compared with the protein-only group. In addition, the combined supplement contained less protein than did the protein supplement.

Looking beyond nutrition deficiencies, McDaniel et al[24] and Melo et al[23] also detected an excessive intake of carbohydrates, sodium, or saturated fatty acids, which also interferes with VU healing. The excess of these nutrients implies a risk of developing or worsening comorbidities such as cardiovascular disease, arterial hypertension, or diabetes, in addition to causing an increase in the inflammatory state, which leads to delayed healing of VUs with consequences such as pain or recurrence. Most of the articles found in this section lack information on ulcer size, active history, or healing rate. For this reason, further studies are needed that include information on patients' nutrition status and VU characteristics (healing, reduction in size) with respect to a lower intake of sugars, sodium, and saturated fats.

Evolution of VUs by Type of Compressive Therapy

As seen in Table 5, studies differed in which compressive therapies they investigated and thus recommendations varied as well.

Compression-bandaging systems versus compression stockings. Finlayson et al[25] found better results with four-layer bandaging, whereas Ashby et al[16] observed that there was a higher ulcer recurrence with this type of therapy. Perhaps patients who used stockings continued to use them as a preventive measure after the ulcer healed, leading to a lower ulcer recurrence in this group.

Comparing two compression-bandaging systems. Both Lazareth et al[19] and Gillet et al[20] considered two-layer compression bandaging to be the best therapy. In contrast, Mosti et al[18] found the best results with a self-adjusting bandage because it maintained constant pressure: if the bandage loosened, the patient could readjust it back to the initial pressure,

whereas if the two-layer bandage loosened, it could not be readjusted until the patient returned to the clinic.

Other compression systems comparisons. Guest et al[21] determined that the two-layer cohesive compression bandage was the best therapy, whereas Dolibog et al[17] found that the multilayer short elastic bandage had the best results. Perhaps the two-layer dressing used by Dolibog et al[17] had a lower healing rate because this bandage provided a compression of 25 mm Hg, whereas the two-layer bandages used in the rest of the articles provided a compression of approximately 35 to 40 mm Hg, which was similar to that exerted by the multilayer bandage. In these studies,[17,21] a higher healing rate and reduction in wound size, as well as a lower rate of pain, were observed in the two-layer compression bandage.

Although the articles included in this review all used different compression therapies for the treatment of VUs, their results differ in terms of wound healing, wound reduction, or wound tolerance. This variation may be due to differences between studies in both mean ulcer size and months of active history. For example, in the studies by Ashby et al,[16] Lazareth et al,[19] and Finlayson et al,[25] the wounds were between 4 and 6 cm^2 in area with an active history of approximately 4 months. In the study by Dolibog et al,[17] the wound area was larger than 20 cm^2 with an active history of more than 28 months. Although Guest et al[21] conducted their study on larger ulcers (>40 cm^2), the healing rate was very high—similar or better than that achieved in other studies[16,19,25] in which the ulcer áreas were smaller. The ulcers in the study by Guest et al[21] may have been more recently diagnosed, indicating that the time of ulcer evolution would be a protective factor against older ulcers. Older and larger wounds are more difficult to heal, regardless of the therapy used.

Limitations

Because the authors excluded studies that were not in English, Spanish, or Portuguese, there may be relevant articles written in different languages. In addition, there is a paucity of up-to-date articles providing evidence on the relationship between nutrition status and the development of VUs, and those that appear in this review have a very small sample size. Thus, more research studies are needed to generalize the results.

CONCLUSIONS

Compression therapy is the standard treatment for VUs, and the nurse's skill in performing compression bandaging is fundamental, because it is a determining factor in the reduction and healing of the ulcer. The authors agree with Shi et al31 that it is better to use some form of compressive therapy than none at all, because there is evidence that it reduces pain and increases the rate of ulcer healing. As for the most appropriate type of therapy, two-layer compression or an adjustable compression bandage may be favored because they can maintain adequate pressure and are better tolerated by patients, easy to use, and economical.

In terms of nutrition, different risk factors influence the onset and delayed healing of VUs such as obesity, vitamin deficiencies, or excess sugars. Thus, it is necessary for healthcare staff to look at the patient as a whole and provide education on healthy eating habits. The main recommendation for patients with VUs is to follow a balanced diet that is adequate for their needs. An interprofessional care approach is important, and a registered dietitian and nurse should perform a suitable nutrition assessment and implement an individualized intervention.

Evaluating the nutrition status of patients with VUs can help in wound healing and reduce ulcer recurrence. Consequently, future research should focus not only on determining the most effective type of compression therapy, but also on nutrition status as a fundamental tool in VU healing. The authors recommend that a validated nutrition screening tool (eg, NRS) be used, and although the determination of biochemical parameters is costly, some biochemical indices (total proteins, certain vitamins [A, E, C], or minerals [zinc]) could provide a qualitative and quantitative assessment nutrition status.

REFERENCES

1. Raffetto JD, Ligi D, Maniscalco R, Khalil RA, Mannello F. Why venous leg ulcers have difficulty healing: overview on pathophysiology, clinical consequences, and treatment. J Clin Med 2020;10(1):29.
2. Alavi A, Sibbald RG, Phillips TJ, et al. What's new: management of venous leg ulcers: approach to venous leg ulcers. J Am Acad Dermatol 2016;74(4):627-40.
3. Escudero Rodríguez JR, Fernández Quesada F, Bellmunt Montoya S. Prevalence and clinical characteristics of chronic venous disease in patients seen in primary care in Spain: results of the international study Vein Consult Program. Cir Esp 2014;92(8):539-46.
4. White-Chu EF, Conner-Kerr TA. Overview of guidelines for the prevention and treatment of venous leg ulcers: a US perspective. J Multidiscip Healthc 2014;7:111-7.
5. Bonkemeyer Millan S, Gan R, Townsend PE. Venous ulcers: diagnosis and treatment. Am Fam Physician 2019;100(5):298-305.
6. Barber GA, Weller CD, Gibson SJ. Effects and associations of nutrition in patients with venous leg ulcers: a systematic review. J Adv Nurs 2018;74(4):774-87.
7. Quain AM, Khardori NM. Nutrition in wound care management: a comprehensive overview. Wounds 2015;27(12):327-35.
8. Burkiewicz CJ, Guadagnin FA, Skare TL, do Nascimento MM, Servin SC, de Souza GD. Vitamin D and skin repair: a prospective, double-blind and placebo controlled study in the healing of leg ulcers. Rev Col Bras Cir 2012;39(5):401-7.
9. Burkievcz CJ, Skare TL, Malafaia O, Nassif PA, Ribas CS, Santos LR. Vitamin D deficiency in patients with chronic venous ulcers. Rev Col Bras Cir 2012;39(1):60-3.

10. Labropoulos N, Wang ED, Lanier ST, Khan SU. Factors associated with poor healing and recurrence of venous ulceration. Plast Reconstr Surg 2012;129(1):179-86.
11. Schols JM, Heyman H, Meijer EP. Nutritional support in the treatment and prevention of pressure ulcers: an overview of studies with an arginine enriched oral nutritional supplement. J Tissue Viability 2009;18(3):72-9.
12. Raffoul W, Far MS, Cayeux MC, Berger MM. Nutritional status and food intake in nine patients with chronic low-limb ulcers and pressure ulcers: importance of oral supplements. Nutrition 2006;22(1):82-8.
13. Stechmiller JK. Understanding the role of nutrition and wound healing. Nutr Clin Pract 2010;25(1):61-8.
14. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018;169(7):467-73.
15. Manterola C, Asenjo-Lobos C, Otzen T. Hierarchy of evidence: levels of evidence and grades of recommendation from current use [in Spanish]. Rev Chilena Infectol 2014;31(6):705-18.
16. Ashby RL, Gabe R, Ali S, et al. Clinical and cost-effectiveness of compression hosiery versus compression bandages in treatment of venous leg ulcers (Venous Leg Ulcer Study IV, VenUS IV): a randomised controlled trial. Lancet 2014;383(9920):871-9.
17. Dolibog P, Franek A, Taradaj J, et al. A comparative clinical study on five types of compression therapy in patients with venous leg ulcers. Int J Med Sci 2014;11(1):34-43.
18. Mosti G, Mancini S, Bruni S, et al. Adjustable compression wrap devices are cheaper and more effective than inelastic bandages for venous leg ulcer healing. A multicentric Italian randomized clinical experience. Phlebology 2020;35(2):124-33.
19. Lazareth I, Moffatt C, Dissemond J, et al. Efficacy of two compression systems in the management of VLUs: results of a European RCT. J Wound Care 2012;21(11):553-8.
20. Gillet JL, Guex JJ, Allaert FA, et al. Clinical superiority of an innovative two-component compression system versus four-component compression system in treatment of active venous leg ulcers: a randomized trial. Phlebology 2019;34(9):611-20.
21. Guest JF, Fuller GW, Vowden P. Clinical outcomes and cost-effectiveness of three different compression systems in newly-diagnosed venous leg ulcers in the UK. J Wound Care 2017;26(5):244-54.
22. Renner R, Garibaldi MDS, Benson S, Ronicke M, Erfurt-Berge C. Nutrition status in patients with wounds: a cross-sectional analysis of 50 patients with chronic leg ulcers or acute wounds. Eur J Dermatol 2019;29(6):619-26.

23. Melo PG, Mota JF, Nunes CAB, Amaral KVA, Coelho ASG, Bachion MM. Anthropometric, biochemical, and food consumption parameters are associated with venous leg ulcer area and duration. Adv Skin Wound Care 2020;33(9):476-81.
24. McDaniel JC, Kemmner KG, Rusnak S. Nutritional profile of older adults with chronic venous leg ulcers: a pilot study. Geriatr Nurs 2015;36(5):381-6.
25. Finlayson KJ, Courtney MD, Gibb MA, O'Brien JA, Parker CN, Edwards HE. The effectiveness of a four-layer compression bandage system in comparison with class 3 compression hosiery on healing and quality of life in patients with venous leg ulcers: a randomised controlled trial. Int Wound J 2014;11(1):21-7.
26. Bauer JD, Isenring E, Waterhouse M. The effectiveness of a specialised oral nutrition supplement on outcomes in patients with chronic wounds: a pragmatic randomised study. J Hum Nutr Diet 2013;26(5):452-8.
27. Munoz N, Posthauer ME, Cereda E, Schols JMGA, Haesler E. The role of nutrition for pressure injury prevention and healing: the 2019 international clinical practice guideline recommendations. Adv Skin Wound Care 2020;33(3):123-36.
28. Kreindl C, Basfi-fer K, Rojas P, Carrasco G. Tratamiento nutricional en ulceras por presión y ulceras venosas. Rev Chi Nutr 2019;46(2):197-204.
29. Newell MA, Bard MR, Goettler CE, et al. Body mass index and outcomes in critically injured blunt trauma patients: weighing the impact. J Am Coll Surg 2007;204(5):1056-61.
30. Rojas AI, Phillips TJ. Patients with chronic leg ulcers show diminished levels of vitamins A and E, carotenes, and zinc. Dermatol Surg 1999;25(8):601-4.
31. Shi C, Dumville JC, Cullum N, Connaughton E, Norman G. Compression bandages or stockings versus no compression for treating venous leg ulcers. Cochrane Database Syst Rev 2021;7:CD013397.

Table 1. TREATMENT OF VENOUS ULCERS

Therapy	Types
Compressive	Elastic systems
	Low-elastic systems
	Intermittent pneumatic compression
Topical	Hydrogel
	Hydrocolloids
	Hydrofibers
Pharmacological	Hidrosmin
	Sulodexide
	Pentoxifylline
	Flavonoid fraction purified and micronized

Figure. PRISMA FLOW DIAGRAME

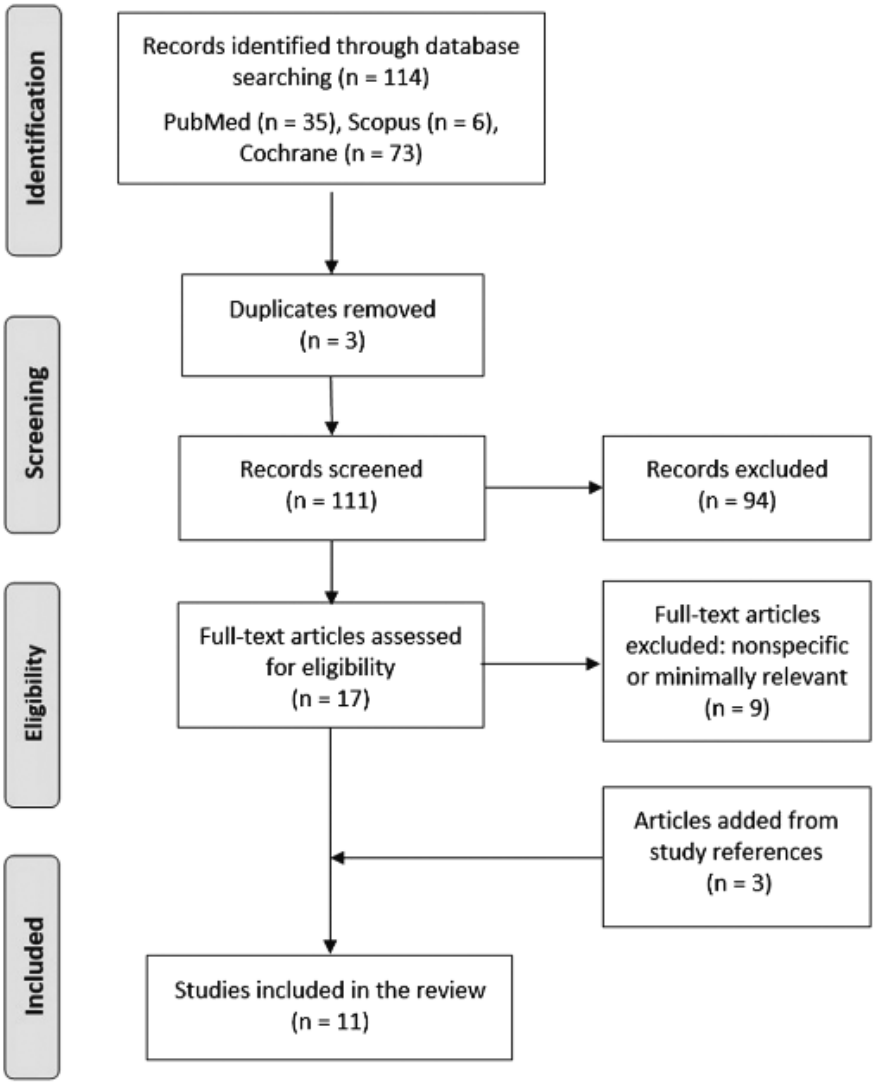

Table 2. RESULTS BY NUTRITION STATE

Author (Year), Country	Level of Evidence	Research Design	Nutrition Assessment Method	Body Mass Index	Nutrition Disorders	Initial Ulcer Size, cm^2	Active Ulcer History, Mo	Healed Wounds, %
Renner et al (2019),[22] Germany	2++	Case-control study	MNA, NRS	Control group: 27.1 kg/m^2 Ulcer group: 31.5 kg/m^2	Vitamins A, B_6, B_9, C, D, zinc; albumin deficiency; elevated homocysteine	Control group: φ Ulcer group: 32.5 cm	Control group: φ Ulcer group: 24 mo	NA
Melo et al (2020),[23] Brazil	2+	Descriptive cross-sectional study	Anthropometric and biochemical measurements, dietary habits	30.93 kg/m^2	Insufficient intake of vitamins A and magnesium; high carbohydrate and lipid intake	12.02 cm	30.97	NA
McDaniel et al (2015),[24] EU	2+	Descriptive cross-sectional study	FFQ, PFA, BMI	41.48 kg/m^2	Insufficient intake of vitamin C, fruit, and vegetables. Excess sugar, sodium, and saturated fatty acids.	NA	NA	NA
Bauer et al (2013),[26] Australia	1+	Prospective, randomized, open-label, clinical trial	PG-SGA, 24-h method	SSG: 27.8 kg/m^2 StSG: 25.7 kg/m^2	NA	NA	NA	SSG: 0% StSG: 25%

Abbreviations: FFQ, Food Frequency Questionnaire; MNA, Mini Nutrition Assessment; NA, not available; NRS, Nutritional Risk Screening; PFA, polyunsaturated fatty acids; PG-SGA, Patient Generated Subjective Global Assessment; SSG, specialized supplement group; StSG, standard supplement group.

Table 3. PATIENT BODY MASS INDEX

	Study, n (%)			
Weight	Renner et al[22]	McDaniel et al[24]	Bauer et al[26]	Melo et al[23]
Normal	3 (12)	1 (9)	—	—
Overweight	9 (36)	1 (9)	—	Men, 12 (85.7) Women, 16 (84.2)
Obesity			3 (25)	
Obesity I	6 (24)	1 (9)		
Obesity II	5 (20)	3 (27)		
Obesity III	2 (8)	5 (46)		

Table 4. RESULTS BY TYPE OF COMPRESSIVE THERAPY

Author (Year), Country	Level of Evidence	Research Design	Therapy Type	Initial Ulcer Size, cm^2	Active Ulcer History, mo	Pain	Healed Wounds, %	Wound Reduction, %	Therapy Tolerance
Ashby et al (2014),[16] UK	1+	Randomized controlled trial	Stockings or 4L bandage	Stockings: 4.1 4L: 3.7	4 mo in both therapies	NA	Stockings: 71% 4L: 70%	NA	Stockings < 4L
Dolibog et al (2013),[17] Poland	1+	Prospective randomized comparative study	Pneumatic compression, compression hosiery, 4L bandage, 2L bandage, or Unna boots	Pneumatic compression: 25.16 Stockings: 24.41 4L: 22.09 2L: 22.44 Unna boots: 21.89	Pneumatic compression: 30.12 Stockings: 32.67 4L: 28.88 2L: 29.81 Unna boots: 29.89	NA	Pneumatic compression: 57.14% Stockings: 56.66% 4L: 58.62% 2L: 16.66% Unna boots: 20%	Pneumatic compression: 48.11% Stockings: 41.22% 4L: 49.02% 2L: 17.77% Unna boots: 20.48%	NA
Mosti et al (2020),[18] Italy	1+	Multicenter, prospective, randomized, controlled clinical trial	Adjustable or nonelastic compressive bandage	Adjustable: 16 Nonelastic: 12.5	Adjustable: 9 Nonelastic: 8	EVA, 5	Adjustable: 78.7% Nonelastic: 69.6%	Adjustable: 80% Nonelastic: 71.2%	Nonelastic < adjustable
Lazareth et al (2012),[19] France, Germany, and the UK	1+	Randomized, controlled, multicenter clinical trial	2L or 4L compressive bandage	2L: 5.94 4L 6.08	2L: 4 4L 3.8	More pain in 4L	2L: 44% 4L 39%	2L: 92.1% 4L 77.6%	NA
Gillet et al (2019),[20] France	1-	Randomized, controlled, multicenter clinical trial	Elastic 2L or 4L compression bandage	2L: 5–25 4L: 5–25	2L: 9.4 4L 6.5	EVA: 2L: 30.8 4L: 34.2	2L: 48.9% 4L 26.3%	NA	Worst tolerated 4L bandage

Table 4. RESULTS BY TYPE OF COMPRESSIVE THERAPY

Author (Year), Country	Level of Evidence	Research Design	Therapy Type	Initial Ulcer Size, cm^2	Active Ulcer History, mo	Pain	Healed Wounds, %	Wound Reduction, %	Therapy Tolerance
Guest et al (2017),[21] UK	2+	Retrospective cohort study	TLCCB, TLCS, FLCS	TLCCB: 41.7 TLCS: 43.9 FLCS: 48.6	TLCCB: 2.1 TLCS: 2.0 FLCS: 2.1	NA	TLCCB: 76% TLCS: 70% FLCS: 64%	TLCCB: 65% TLCS: 68% FLCS: 62%	NA
Finlayson et al (2014),[25] Australia	1+	Randomized clinical trial	4L compression bandage or moderate compression stockings	4L: 4.6 Stockings: 4.0	4L: 4.7 Stockings: 6.3	Baseline pain: 4L: 51.8 Stockings: 50.0	4L: 84% Stockings: 72%	4L: 96% Stockings: 93%	NA

Abbreviations: 2L, two-layer; 4L, four-layer; EVA, visual analog scale; FLCS: 4L bandage; NA, not available; TLCCB, 2L cohesive compression bandage; TLCS, 2L compression system

Table 5. COMPARING COMPRESSIVE THERAPIES

Author	Comparison	Results
Compression bandaging systems versus compression stockings		
Ashby et al[16]	Compression stockings versus four-layer bandaging	No differences in healing time. Compression stockings are lower cost, but ulcer recurrence is higher with compression stockings and poor compression tolerance is noted.
Finlayson et al[25]	Compression stockings versus four-layer bandaging	With four-layer bandages, pain was lower, ulcer healing was higher, there was a greater reduction in ulcer size, and healing time was shorter.
Comparing two compression bandaging systems		
Lazareth et al[19]	Two-layer compression bandaging versus four-layer compression bandaging	Two-layer bandages were easier to apply and led to higher wound reduction and greater ulcer healing. Four-layer therapy had more adverse effects, including higher pain.
Gillet et al[20]	Two-layer compression bandaging (Biflex Kit; Thuasne Group) versus four-layer compression bandaging (PROFORE; Smith+Nephew)	Two-layer compression bandaging had a better healing rate, lower pain, better acceptance, and lower cost. However, there were more adverse effects.
Mosti et al[18]	Adjustable compression bandage (circaid juxtacures; Medi Bayreuth) versus two-layer inelastic bandage (Coban 2; 3M)	Adjustable compression bandage led to better ulcer healing and greater ulcer reduction. It was also lower cost and better tolerated by patients.
Other comparisons of compression systems		
Guest et al[21]	Two-layer cohesive compression bandage (Coban 2) versus two-layer compression system (KTwo; URGO) and four-layer compression system (PROFORE)	-Ulcer healing rate higher with Coban 2 and lower with PROFORE -Healing time was shorter with Coban 2 and longer with PROFORE -Ulcer reduction was higher with KTwo and lower with PROFORE -PROFORE was most expensive; Coban 2 was least expensive
Dolibog et al[17]	Intermittent pneumatic compression, compression stockings, multilayer short elastic bandage, bilayer elastic bandage, and Unna boots	-Healing rate higher with multilayer short elastic bandage and lower with bilayer elastic bandage -Ulcer reduction higher with multilayer short elastic bandage and lower with bilayer elastic bandage