


STUDY PROTOCOL

Open Access



Active legs: Impact of physical activity as an adjuvant treatment in the healing of venous ulcers in primary care: a RCT protocol study

Borja Herrera-Ahijado^{1,2,3,4,5*} , Carmen Folguera-Álvarez^{2,3,4,6,7}, José Verdú-Soriano⁸, Pilar Mori-Vara^{4,9} and Milagros Rico-Blázquez^{2,3,4,9,10}

Abstract

Background Venous ulcers usually present a torpid evolution with a negative impact on patients' quality of life. In primary care, they account for 2.5% of nursing consultations and their treatment represents high costs for national health systems. These patients usually have a low level of physical activity, with muscle pump dysfunction of the lower limbs, which may improve with increased physical activity. The purpose of this study is to analyse the effectiveness of a structured intervention involving physical activity and exercise (Active Legs) as an adjuvant treatment in improving healing of chronic venous ulcers at 3 months follow-up.

Methods A randomized, multicentre clinical trial. A total of 224 individuals receiving primary nursing care with a diagnosis of venous ulcer, with a diameter of 1 cm or greater and an ankle-brachial index between 0.8 and 1.3, able to comply with the study requirements and consenting to participate, will be sequentially included (112 per group).

Both groups will receive the standard treatment in primary care, with cleansing, debridement and healing in a moist environment together with multilayer compression therapy. The intervention group will also receive a structured educational intervention involving lower limb physical exercise and daily ambulation guidelines.

The primary response variables will be complete healing –understood as complete and sustained epithelialisation for at least 2 weeks– and time to healing. The secondary variables will be degree of healing, ulcer area, quality of life, pain and variables related to the healing process, prognosis, and recurrences. Sociodemographic variables, adherence to treatment and satisfaction variables will also be recorded. Data will be collected at baseline, at 3 months and at 6 months follow-up. Survival analysis (Kaplan-Meier and Cox) will be performed to measure primary effectiveness. Intention-to-treat analysis.

Discussion If the intervention is effective, a cost-effectiveness analysis could be conducted and implemented as an additional intervention in the usual venous ulcer treatment in primary care.

Trial registration NCT04039789. [<https://ClinicalTrials.gov>]. 07/11/2019.

Keywords Venous ulcer, Wound healing, Exercise, Nursing, Primary health care, Quality of life, Aging

*Correspondence:

Borja Herrera-Ahijado
borjajesus.herraiz@salud.madrid.org

Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Background

Ulcers of venous aetiology are lesions caused by a process of chronic venous insufficiency [1, 2], with a tendency to a torpid evolution, a low tendency to spontaneous healing [1, 3] and a high recurrence rate [4, 5]. For diagnosis, in addition to the presence of signs of chronic venous insufficiency, it is necessary to assess the ankle brachial index (ABI) [2].

In Spain, lower limb ulcers have a prevalence of 0.1 to 0.3% in the adult population [2] and an incidence of 3 to 5 new cases per thousand people annually (2.6), both values becoming twice as high in the over-65 population segment [2]. Venous ulcers (VU) account for 75–80% of all lower limb ulcers [2, 6] with an average duration of 10.7 months (+ 27 months) and over 50% being recurrent ulcers [1, 2]. They represent 2.5% of primary care consultations and between 1.5 and 3% of total healthcare expenditure in neighbouring countries [1].

In clinical terms, ulcers of venous origin usually show signs such as high levels of exudate, malodour, moderate pain, and infection, causing sleep disturbances, mobility problems, decreased vitality and even dependence in performing basic activities of daily living [7–9]. A negative emotional impact and a low perceived quality of life have also been observed [10, 11].

There are two main components to ulcer treatment. On the one hand, the topical healing of the wound, favouring a moist environment through the use of dressings [1], and on the other hand, the control of chronic venous insufficiency through the use of compression therapy [1, 12].

Recent studies show that these patients suffer from muscle pump dysfunction of the lower limbs [13, 14], resulting in poorer healing rates [5] and decreased ankle mobility [15, 16] associated with a process of fibrosis involving the Achilles tendon [16].

The lack of competence of the muscle pump, together with the decreased ankle mobility and the age at which VUs are most prevalent (over 65 years) could be among the reasons why approximately 50% of patients suffering from VU have an insufficient level of physical activity (less than 10 min of ambulation per day), as suggested by various authors [5, 7, 13, 17].

In recent years, the published studies have demonstrated the positive effects of the daily practice of an exercise and daily ambulation program at home on the functioning of the calf muscle pump [5, 17, 18], the improvement in ankle mobility [16, 19], the significant increase in tissue perfusion parameters [4, 11, 14] and the improvement of more active lifestyle behaviours among patients [7]. Two systematic reviews published in 2018 with a total of 405 patients recommend the use of aerobic

and resistance exercise in the treatment of venous ulcers [20, 21].

With regard to the type of exercises to be performed, there is evidence that a standing position on tiptoe, as well as the flexion-extension of the feet in a seated position, effectively stimulate the calf muscle pump and improve venous return [14, 17, 22]; lower limb resistance exercises also showed benefits in muscle pump functionality and ankle mobility [16, 23] while daily ambulation is also effective as it allows for increased blood pumping from the leg to the heart [11, 14, 17], along with an improvement in the leg muscle pump due to the movement of the ankle joint [5, 14, 16].

Most of the revised studies have been conducted in the United Kingdom, Poland, Brazil, Australia, the Netherlands, and the United States, with small sample sizes. We have not found scientific evidence in Spain on the study of the influence of exercise on the healing of venous ulcers, which justifies the need to conduct this trial, the aim of which is to compare the effectiveness of a structured educational intervention in physical exercise versus the standard practice in the healing of venous ulcers.

Methods/design

Main objective

To evaluate the effectiveness of the “Active Legs” intervention as an adjuvant treatment to standard primary care management of venous ulcers for improving the rate of complete healing at 3 months follow-up compared with the usual practice.

Secondary objectives

To determine whether the Active Legs intervention produces better results than the standard practice on the rate of venous ulcers with complete healing at 6 months follow-up, the degree of healing achieved, the number of recurrences, the quality of life and the pain, as well as to describe the degree of adherence to and satisfaction with the intervention.

Design and setting

A pragmatic, randomized, multicentre, open-label, clinical trial of two parallel groups with 6-month follow-ups. The SPIRIT checklist are available as supporting information (see Additional file 1).

Setting and study population

The study will be carried out in 16 primary care health centres in the Region of Madrid.

It will include participants aged 18 or older, with a diagnosis of venous ulcer recorded in the electronic medical record (ABI greater than 0.8 and less than 1.3; diameter of the lesion greater than or equal to 1 cm) and

under treatment in primary care nursing consultations. The individuals must be able to walk with or without the aid of devices, understand and answer the questionnaires autonomously, be accessible throughout the duration of the study and have expressed their agreement to participate and signed the consent form.

Those who are unable to commute to the health centre, or who reside outside the area where the research is carried out for more than 6 months per year, will be excluded. People with mixed ulcers, deep vein thrombosis (DVT) in acute phase, decompensated heart failure, dermatitis in acute phase, rheumatoid arthritis, undergoing treatment with antineoplastic drugs or with some absolute contraindication for physical exercise will also be excluded.

Withdrawal criteria are set for patients who, during the course of the trial, present a change in their clinical condition that prevents them from further participation, such as inflammation of the locomotor system (with heat, flushing, pain and functional impotence) or trauma due to a fall during the course of program with or without fracture and/or haematoma at both joint and soft tissue level (muscle and tendons) [24], must drop out of the study.

Randomization and masking

Simple random allocation to one of the two study groups via the Electronic Data Collection Notebook.

It is not possible to mask the intervention in this type of trial, although the analysis will be performed by professionals who are unaware of the allocation.

Sample size

Previous studies have obtained 50% complete healing rates at 12 weeks follow-up. Sample size has been calculated considering a relevant post-intervention average difference of 20% of complete healing between the intervention and control groups. Assuming an alpha error of 0.05 and a beta error of 0.02, 93 patients are necessary for each group. Expecting a 20% loss to follow-up after a 3-month period, the required sample size is 224 patients (112 per group).

Recruitment

Study enrolment will be offered during the usual nursing practice, when eligible patients attend for follow-up wound care. They will be sequentially recruited upon signing the consent form.

Interventions

The **control group** will receive the usual treatment following the recommendations for the treatment of skin ulcers of the Madrid Health Service [1], which consists

of assessment, cleansing, antisepsis, debridement, topical treatment (healing in a moist environment through the use of dressings) and multilayer compression therapy.

The **intervention group** will receive the usual treatment together with the “Active Legs” intervention, which consists of an evidence-based, structured, nurse-led educational intervention in health centre consultations. It incorporates a home-based lower limb exercise program and daily ambulation guidelines. Figure 1 shows schematically the different components of both the control and the Active Legs interventions. The home lower limb exercise program consists of four exercises of progressive difficulty, which the patient will perform twice a day, at least 5 days a week. In addition, patients will be required to follow a program of progressive daily ambulation until the target of 150 min/week (30 minutes for 5 days a week) is reached [25]. The detailed intervention is described using TIDieR (see Additional file 2).

Patients will be provided with an “Active Legs” diary containing all the information on the exercise program and a pedometer to record daily steps.

Those who have not reached complete healing at the end of the study will continue with the same treatment until complete healing is achieved and may resume the daily ambulation and exercise program.

In order to avoid possible differences in the application of the Active Legs program, training has been planned beforehand for the nursing professionals participating in the study, including both training in injury assessment and educational intervention.

Outcomes

The **primary outcome** will be complete healing at 3 months follow-up: (yes/no), where complete healing is defined as complete epithelialisation maintained for at least 2 weeks and the time (in days) between the start of the study and complete wound healing.

Secondary variables are defined as complete healing at 6 months follow-up (yes/no), the degree of healing (Resvech 2. 0) which consists of 6 dimensions (depth, size, edges, wound bed, exudate and signs and symptoms of infection) with ascending scoring scales based on the severity of the dimension studied and a total score ranging from 0 to 35 [26]; the ulcer area (cm²), measured by digital photography and subsequent image processing using the open source Java image processing program “The ImageJ ecosystem” [27]; the VAS scale for perceived pain [28]; the level of adherence to the “Active Legs” intervention measured by the combined variable number of steps and time by means of the pedometer record (Yamax PZ270) and patients’ self-reported information on the home exercise program by means of the activity diary and the health-related quality of life measured with

Time	Intervention	Control
Recruitment of nursing professionals	①	①
Training session for nursing professionals	② a	② a
Randomization	Randomization of Patients	
Patient recruitment and baseline visit	③	③
Active Legs intervention	④ ⑤ b c	④ b
Follow-up and outcome measurement	Bi-weekly outcome measurement up to the 3 rd month and at month 6	

①	Recruitment of nursing professionals to participate in the study.
②	120-minute online training: presentation of the project, training in good practices, training in the collection of variables, recording in the electronic data collection notebook and standardisation of the experimental intervention (exercise and daily ambulation programs).
a	Submission of documentation: researcher's dossier.
③	Recruitment of patients, signing of informed consent and collection of baseline variables in both groups.
④	Usual intervention according to the recommendations of the Community of Madrid (wound healing in a moist environment and compression therapy).
⑤	Active Legs Intervention. 1 individualised session lasting 1 hour and bi-weekly follow-ups of the intervention lasting about 15 minutes.
b	Provision of materials: "Guidelines for patients with venous ulcers", of the Community of Madrid, which includes the basic general care of the pathology.
c	Provision of materials: "Yamax PZ270 pedometer" for daily recording of steps and "Active Legs" activity diary, which includes activity guidelines and self-recording tables.

Fig. 1 Components of Active Legs complex intervention vs standard clinical practice

the CCVUQ-e, a questionnaire which in addition to an overall synthetic quality of life score, assesses the following dimensions: pain, depression, social relationships, impairment in performing activities of daily living and body image, with a score of 22 to 112 [29].

Variables related to the healing process are defined as Body Mass Index (kg/cm²); baseline pathology, diabetes mellitus (yes/no); last glycosylated haemoglobin (HbA1) value in the EHR; ABI score; tobacco and alcohol consumption; topical treatments used in existing ulcers; systemic treatments; adherence to multilayer compression therapy (yes/no); and physical activity

level measured by the Minnesota Leisure Time Physical Activity Questionnaire, short version [30] and type of daily ambulation.

Prognostic variables are defined as location of the ulcer at the time of the study, number of ulcers at the time of the study, time (in days) of evolution of the venous ulcers before inclusion in the study and whether they are recurrent ulcers (yes/no).

Variables related to recurrence (measured at 6 months follow-up) are defined as occurrence of recurrence (yes/no), use of compression stockings (yes/no), light/normal/strong compression and hydration of the legs (yes/no).

Additionally, data such as age, sex, living alone (yes/no), employment status and level of education are collected.

Participant timeline

Table 1 shows the participant timeline.

Data collection methods

Patient information will be obtained through clinical interviews, electronic medical records and wound examination in the nursing consultation of the professionals participating in the study. The same information will be collected from participants in the control and intervention groups, except for the level of satisfaction and adherence. Data will be collected every 14 days for the first 3 months or sooner if the ulcers have healed, and at 6 months follow-up.

Patients who refuse to participate in the study, losses and dropouts and their cause, as well as patients who are required to drop out because of withdrawal criteria, will be recorded.

Data management

The information will be recorded in an electronic data collection notebook designed for the study, which contains all the questionnaires and scales, collected in the variables section, for implementation. Photographs of ulcers will be temporarily stored in the electronic notebook until the ulcer area is measured.

Losses in participation

Losses and dropouts during the study and their cause, as well as patients who are required to drop out because of withdrawal criteria, will be recorded. In order to minimise potential losses, as a method of encouraging participation, patients and/or carers will be contacted by telephone to arrange visits.

In the event of dropouts during follow-up, at least 2 telephone calls will be made to record their cause.

Analysis

A descriptive analysis (means, medians, frequencies of distribution) will be performed. The results for the primary outcomes will be analysed on an intention-to-treat (ITT) basis. To analyse the principal effectiveness the incidence rates of completely healed ulcers will be compared with their point estimate and 95% confidence interval. Time to complete healing will be compared using Kaplan-Meier curves (Log-rank test). A Cox regression model will be used to adjust for prognostic factors.

To analyse secondary outcomes, an explanatory model will be fitted with linear or logistic analysis, as appropriate.

Significance will be set at $p < 0.05$. All analyses will be performed using STATA software.

Discussion

The aim of the study is to measure the effectiveness of a structured educational intervention on lower limb physical exercise and daily ambulation (Active Legs) as an adjuvant treatment to topical treatment and compression therapy addressed to individuals with venous ulcers undergoing treatment in primary care.

This research addresses a health problem that affects people of all ages, although its prevalence increases with age, being much more frequent in people over 65 years of age [2].

Venous ulcers can aggravate the prognosis of other pathologies, cause pain, and have a negative impact on patients' wellbeing, self-perception, and perceived quality of life [10, 11]. They also limit the ability to manage daily self-care and impair mobility, thus being a risk factor for dependency and the onset of early frailty [10]. *Research on frailty* is a priority due to the increasing elderly population in many countries, including Spain. Institutions such as the World Health Organisation in its World Report on Ageing and Health [31] stress that population ageing requires a comprehensive public health response, with the development of policies that emphasise the need for healthy and active ageing.

Incorporating a routine of basic lower limb exercises at home and daily ambulation into the self-care of older people with venous ulcers could help them not only to improve wound healing, but also to have a more active and autonomous lifestyle, improving their self-perception, self-concept, and perceived quality of life [7].

This clinical trial follows a pragmatic approach, very close to routine clinical practice, which uses the capabilities of the National Health System. It will be carried out at the primary care level, with the basic resources and means usually available in health centres and does not require additional training of nursing professionals. The study proposes the use of a pedometer as an objective measure of adherence, but this resource would not be necessary for the implementation of the active legs' intervention in clinical practice.

Given that the research team is directly linked to the healthcare activity within the health system, and that the strategic lines of the organisation have seen the need to protocolise the care of venous ulcers in a Protocol for the treatment of skin ulcers in the Community of Madrid, if the intervention were effective it would be easily transferable and its cost-effectiveness and impact on the consumption of healthcare resources could be analysed in the medium term.

The result will in turn lead to a reduction in the cost of treatment, optimising the health system's human and material resources. At the same time, it will contribute to

Table 1 Participant timeline

Study period									
	Recruitment	Allocation	Post-allocation stage						Closing
Timeline	t _x	0	t ₂ weeks	t ₄	t ₆	t ₈	t ₁₀	t ₁₂	t ₂₄ weeks
Recruitment									
Selection screening	X								
Informed consent	X								
Baseline measurement	X								
Allocation		X							
Interventions									
<u>Intervention Group</u>									
Active Legs Intervention		X							
Intervention Reinforcement ^a									
<u>Control Group</u>									
Standard treatment ^a									
Assessments									
Complete healing ^a								X	X
Time to healing ^a								X	X
Resvech 2.0		X	X	X	X	X	X	X	X
Ulcer area		X	X	X	X	X	X	X	X
VAS		X	X	X	X	X	X	X	X
Level of adherence ^b			X	X	X	X	X	X	X
CCVUQ		X						X	X
BMI	X								
Baseline pathology	X								
HbA1	X								
ABI	X								
Tobacco/Alcohol	X								
Multilayer compression treatment	X								
Minnesota Short Version		X						X	X
Type of ambulation	X								
Ulcer location	X								
Number of ulcers	X								
Ulcer evolution time	X								
Recurrent ulcer	X								
Occurrence of recurrence									X
Compression stockings									X
Level of compression									X
Hydration of the lower limbs									X

^a Until complete healing of the wound

^b Intervention group only

homogenise the intervention to be developed for these patients, favouring equity.

Patients will be recruited by their own reference nurses. This may increase variability, which we will try

to minimize by training all participating nurses beforehand and by protocolizing the research, implementing an eDCN specifically designed for the study and providing supporting graphic documentation.

This study, therefore, proposes, through nursing intervention at the primary care level, to address the management of venous ulcers from a different perspective, focusing on the baseline aetiology of the condition as an adjuvant treatment and promoting an active lifestyle to benefit patients' overall health (biopsychosocial model).

Abbreviations

AVH	Ambulatory Venous Hypertension
VU	Venous ulcer
CCVUQ	Charing cross venous ulcer questionnaire
VAS	Visual analogue scale
ABI	Ankle brachial index (ABI)
DVT	Deep vein thrombosis
PCAM	Primary Care Assistance Management
eDCN	Electronic Data Collection Notebook
EHR	Electronic Health Record
CREC	Clinical Research Ethics Committee

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12912-023-01214-y>.

Additional file 1.

Additional file 2.

Acknowledgements

We would like to thank the Research Unit of the Madrid Primary Health Care Management Department for their methodological support. Thanks to the Health Care Directorates and the nurses who form the clinical healthcare group for their involvement in the recruitment of participants and the fieldwork of the study.

Authors' contributions

BJHA, MCFA, JVS, PMV and MRB conceived the study. BJHA, MCFA, PMV and MRB participated in the design of the study. BJHA and MCFA collaborated in the bibliographical search. BJHA, MCFA, PMV and MRB wrote the manuscript. All authors critically evaluated the contents of this paper until the final version was approved.

Funding

This study was funded by the Instituto de Salud Carlos III (ISCIII) through project PI19/00619 and co-funded by the European Union.

Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

All of the participants (patients and nurses) will be duly informed, and their informed consent will be requested in writing. The study respects the basic ethical principles of autonomy, beneficence, justice and non-maleficence, in accordance with the standards of Good Clinical Practice, the Declaration of Helsinki (Fortaleza 2013) and the Oviedo Convention (1997). The processing, communication and transfer of data was carried out in accordance with the provisions of current regulations. The study was approved by the Clinical Research Ethics Committee of the Clinical Hospital San Carlos (16/03/2018) and the Central Research Commission of the Madrid Primary Health Care Management Department (16/05/2018).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Sanchinarro Healthcare Center. Primary Care Assistance Management, Madrid Health Service, Calle San Martín de Porres, 6., Madrid 28035, Spain. ²Research Network on Chronicity, Primary Care and Health Promotion (RICORS-RICAPPS), Instituto de Salud Carlos III, Madrid, Spain. ³Gregorio Marañón Health Research Institute, Madrid Health Service, Madrid, Spain. ⁴Nursing Department. Faculty of Nursing, Physiotherapy and Podiatry, Universidad Complutense de Madrid, Madrid, Spain. ⁵PhD student. Doctoral Program in "Cuidados en Salud", Universidad Complutense de Madrid, Madrid, Spain. ⁶La Paz Healthcare Center. Primary Care Assistance Management, Madrid Health Service, Rivas-Vaciamadrid, Spain. ⁷Research Group on Public Health - Lifestyles, nursing methodology and care in the community environment, Universidad Complutense de Madrid, Madrid, Spain. ⁸Faculty of Health Sciences. Department of Community Nursing, Preventive Medicine, Public Health and History of Science, University of Alicante, Alicante, Spain. ⁹Health Innovation Research Group. Nursing Department. Faculty of Nursing, Physiotherapy and Podiatry, Universidad Complutense de Madrid, Madrid, Spain. ¹⁰Research Unit. Primary Care Assistance Management, Madrid Health Service, Madrid, Spain.

Received: 26 January 2023 Accepted: 20 February 2023

Published online: 10 March 2023

References

1. Servicio Madrileño de Salud. Recomendaciones Para el tratamiento local de las úlceras cutáneas crónicas de la Comunidad de Madrid. Madrid: Comunidad de Madrid. Consejería de Sanidad; 2010.
2. Marinello Roura J, Verdú Soriano J (Coord.). Conferencia nacional de consenso sobre las úlceras de la extremidad inferior (C.O.N.U.E.I.). Documento de consenso 2018. 2ª ed. Madrid: Ergon; 2018.
3. Asociación Española de Enfermería vascular y Heridas. Guía de práctica clínica: Consenso sobre úlceras vasculares y pié diabético. Segunda edición ed. Sevilla: AEEVH; 2014.
4. Jull A, Parag V, Walker N, Maddison R, Kerse N, Johns T. The PREPARE pilot RCT of home-based progressive resistance exercises for venous leg ulcers. *J Wound Care*. 2009;18(12):497–503 Available from <http://www.ncbi.nlm.nih.gov/pubmed/20081574> Accessed 2 Jan 2022.
5. O'Brien J, Finlayson K, Kerr G, Edwards H. Evaluating the effectiveness of a self-management exercise intervention on wound healing, functional ability and health-related quality of life outcomes in adults with venous leg ulcers: a randomised controlled trial. *Int Wound J*. 2017;14(1):130–7 Available from <http://www.ncbi.nlm.nih.gov/pubmed/26817648>: Accessed 2 Jan 2022.
6. Álvarez-Fernández LJ, Lozano F, Marinello-Roura J, Masegosa-Medina JA. Encuesta epidemiológica sobre la insuficiencia venosa crónica en España: estudio DETECT-IVC 2006. *Angiología*. 2008;60(1):27–36 Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0003317008010031>. Accessed 7 Feb 2022.
7. Heinen M, Borm G, van der Vleuten C, Evers A, Oostendorp R, van Achterberg T. The lively legs self-management programme increased physical activity and reduced wound days in leg ulcer patients: results from a randomized controlled trial. *Int J Nurs Stud*. 2012;49(2):151–61.
8. O'Brien JA, Finlayson KJ, Kerr G, Edwards HE. Testing the effectiveness of a self-efficacy based exercise intervention for adults with venous leg ulcers: protocol of a randomised controlled trial. *BMC Dermatol*. 2014;14(1):16.
9. Folguera-Álvarez C, Garrido-Elustondo S, Verdú-Soriano J, García-García-Alcalá D, Sánchez-Hernández M, Torres-de Castro OG, et al. ECAMulticapa: Effectiveness of double-layered compression therapy for healing venous ulcers in primary care: a Study Protocol. *BMC nursing*. 2016;15(1):58 Available from: <http://bmcnurs.biomedcentral.com/articles/10.1186/s12912-016-0179-x>. Accessed 7 Feb 2022.
10. Hopman WM, Vandenkerkhof EG, Carley ME, Harrison MB. Health-related quality of life at healing in individuals with chronic venous or mixed-venous leg ulceration: a longitudinal assessment. *J Adv Nurs*. 2016;72(11):2869–78.
11. Meagher H, Ryan D, Clarke-Moloney M, O'Laughlin G, Grace PA. An experimental study of prescribed walking in the management of venous leg ulcers. *J Wound Care*. 2012;21(9):421–30.

12. Folguera Alvarez MC. Eficacia del vendaje compresivo multicapa en la cicatrización de las úlceras venosas. Alicante: Tesis Doctoral; 2017.
13. Clarke-Moloney M, Godfrey A, O'Connor V, Meagher H, Burke PE, Kavanagh EG, et al. Mobility in patients with venous leg ulceration. *Eur J Vasc Endovasc Surg.* 2007;33(4):488–93.
14. Tew GA, Gumber A, McIntosh E, Kesterton S, King B, Michaels JA, et al. Effects of supervised exercise training on lower-limb cutaneous microvascular reactivity in adults with venous ulcers. *Eur J Appl Physiol.* 2018;118(2):321–9 Available from <http://www.ncbi.nlm.nih.gov/pubmed/29197931>. Accessed 7 Feb 2022.
15. Yim E, Kirsner RS, Gailey RS, Mandel DW, Chen SC, Tomic-Canic M. Effect of physical therapy on wound healing and quality of life in patients with venous leg ulcers: a systematic review. *JAMA Dermatology.* 2015;151(3):320.
16. Szewczyk MT, Jawień A, Cwajda-Białasik J, Cierzniaowska K, Mościcka P, Hancke E. Randomized study assessing the influence of supervised exercises on ankle joint mobility in patients with venous leg ulcerations. *Arch Med Sci.* 2010;6(6):956–63 Available from <http://www.ncbi.nlm.nih.gov/pubmed/22427773>: Accessed 13 Nov 2021.
17. Heinen MM, van der Vleuten C, de Rooij MJM, Uden CJT, Evers AWM, van Achterberg T. Physical activity and adherence to compression therapy in patients with venous leg ulcers. *Arch Dermatol.* 2007;143(10):1283–8.
18. Domingues EAR, Kaizer UAO, Lima MHM. Effectiveness of the strategies of an orientation programme for the lifestyle and wound-healing process in patients with venous ulcer: a randomised controlled trial. *Int Wound J.* 2018;15(5):798–806.
19. Davies JA, Bull RH, Farrelly IJ, Wakelin MJ. A home-based exercise programme improves ankle range of motion in long-term venous ulcer patients. *Phlebology.* 2007;22(2):86–9.
20. Jull A, Slark J, Parsons J. Prescribed exercise with compression vs compression alone in treating patients with venous leg ulcers. *JAMA Dermatology.* 2018;154(11):1304.
21. Smith D, Lane R, McGinnes R, O'Brien J, Johnston R, Bugeja L, et al. What is the effect of exercise on wound healing in patients with venous leg ulcers? A systematic review. *Int Wound J.* 2018;15(3):441–53.
22. Mutlak O, Aslam M, Standfield N. The influence of exercise on ulcer healing in patients with chronic venous insufficiency. *Int Angiol.* 2018;37(2):160–8.
23. Klonizakis M, Tew GA, Gumber A, Crank H, King B, Middleton G, et al. Supervised exercise training as an adjunct therapy for venous leg ulcers: a randomized controlled feasibility trial. *Br J Dermatol.* 2018;178(5):1072–82.
24. Abellán Alemán J, Sainz de Baranda Andujar P, Ortín Ortín EJ. Guía para la prescripción del ejercicio físico en pacientes con riesgo cardiovascular [Internet]. 2 Ed. Murcia: Sociedad Española de Hipertensión; 2014. Available from <https://www.seh-lelha.org/wp-content/uploads/2017/03/GuiaEjercicioRCV.pdf>. Accessed 13 Nov 2021.
25. Muñoz Bellerín J, Calvo Tocado A, Castel C, Perez Boutureira JJ, Lopez de Valdivieso MJ, Aguirre Martín-Gil R, et al. Consejo integral en estilo de vida en Atención Primaria, vinculado con recursos comunitarios en población adulta. Madrid: Ministerio de Sanidad SS e I; 2015.
26. Restrepo Medrano JC. Instrumentos de monitorización clínica y medida de cicatrización en úlceras por presión y úlceras de la extremidad inferior. Desarrollo y validación de un índice de medida [doctoral thesis]. Alicante: Universidad de Alicante; 2010.
27. Chang AC, Dearman B, Greenwood JE. A comparison of wound area measurement techniques: visitrak versus photography. *Eplasty.* 2011;11:e18.
28. Vicente-Herrero MT, Delgado-Bueno S, Bandrés-Moyá F, Capdevilla-García L. Valoración del dolor. Revisión comparativa de escalas y cuestionarios. *Revista de la Sociedad Española del Dolor.* 2018;25(4):228–36.
29. González Consuegra RV. Calidad de Vida y cicatrización en pacientes con úlceras de etiología venosa: adaptación transcultural y validación del "Charing cross venous ulcer questionnaire (CCVUQ)" y del "pressure ulcer scale for Ealing (PUSH)" [doctoral thesis]. Alicante: Universidad de Alicante; 2011.
30. Ruiz Comellas A, Pera G, Baena Díez JM, Mundet Tudurí X, Alzamora Sas T, Elosua R, et al. Validación de una versión reducida en español del cuestionario de actividad física en el tiempo libre de Minnesota (VREM). *Rev Esp Salud Publica.* 2012;86(5):495–508.
31. Organización Mundial de la Salud. Informe Mundial sobre el Envejecimiento y la Salud [Internet]. Estados Unidos (EEUU):OMS; 2015. Available from: <http://envejecimiento.csic.es/documentos/blog/OMS%282015%29InformeMundialSobreEnvejecimientoSalud.pdf>. Accessed 7 Feb 2022.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.