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Original

Protocol and algorithm for diagnosis, treatment, and early referral of lower extremity ulcers

Protocolo y algoritmo de diagnóstico, tratamiento y derivación ágil de las úlceras de la extremidad inferior

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Abstract

Venous ulcers are a prevalent disease, especially in elderly patients. They have a negative impact in patients' quality of life and carry a significant economic burden. This article suggests an algorithm for the diagnosis and treatment of lower extremity ulcers in order to optimize their management. There is huge evidence and multiple organizations have published guidelines, consensus documents and treatment recommendations. Nevertheless, there is still a gap between evidence and clinical practice.

Urgo Laboratories proposed the Spanish Phlebology and Lymphology Chapter the creation of a Spanish and Portuguese experts committee the elaboration of an algorithm for diagnosis and treatment and early referral of lower extremity ulcers. A systematic review was performed, considering the current clinical practice guidelines. The algorithm was designed on a simple alphabetic mnemonic rule aiming to easily memorize the key points and most relevant issues of the diagnosis and treatment of these ulcers. All necessary steps from primary care nurses and physicians to Vascular Surgery were considered. With the alphabet letters from A to F in Spanish, all key points were summed up. To confirm ulcer diagnosis *(asegurar el diagnóstico de la úlcera),* best local treatment, compressive therapy, preventive treatment after healing *(tratamiento preventivo de recidiva después de la cicatrización de la úlcera),* surgical strategy *(estrategia quirúrgica)* and pharmacological strategy *(estrategia farmacológica).* An accurate diagnosis, a clinical practice according to the clinical practice guidelines and an early referral to the specialist in order to determine if there is a surgical or interventional strategy are essential to effective resolution and reduction of ulcer healing time, and finally to prevent its recurrence.

Keywords:
Venous leg ulcers. Chronic venous disease. Evidence based practice. Treatment algorithm.

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Resumen

Las úlceras venosas son una patología muy prevalente, especialmente en pacientes de edad avanzada. Repercuten negativamente en la calidad de vida de los pacientes y conllevan un importante consumo de recursos. Este artículo propone un práctico algoritmo para el diagnóstico y el tratamiento de las úlceras en la pierna con el objetivo de optimizar su manejo. Existe una amplia literatura sobre el tema, pero sigue existiendo una brecha entre la evidencia científica y la práctica clínica que seguimos tratando de minimizar.

Laboratorios Urgo propuso al Capítulo Español de Flebología y Linfología la creación de un comité de expertos de España y Portugal para la elaboración de un algoritmo de diagnóstico, tratamiento y derivación ágil de las úlceras en la extremidad inferior. Se realizó una búsqueda bibliográfica sistemática y se tuvieron en cuenta las Guías de Práctica Clínica (GPC).

Se diseñó un algoritmo sobre una regla nemotécnica alfabética que busca ayudar a memorizar los pasos clave del diagnóstico y del tratamiento de estas úlceras.

Se englobaron todos los aspectos prácticos, desde la valoración en Atención Primaria por médicos y enfermeras hasta la atención especializada por el especialista en angiología y cirugía vascular. Con las letras del abecedario de la a hasta la f, resumimos los pasos necesarios para asegurar el diagnóstico de la úlcera, el mejor (best) tratamiento local, terapia compresiva, tratamiento preventivo de recidiva después de la cicatrización de la úlcera y estrategia quirúrgica y farmacológica.

El diagnóstico preciso, la actuación correcta ajustada a las GPC y la derivación temprana para valorar estrategias quirúrgicas o escleroterapia contribuyen a la resolución y a la reducción del tiempo de cicatrización de las úlceras y la mejora de la calidad de vida de los pacientes. Seguir las GPC a través de un algoritmo reduce el consumo de recursos y de gasto, acelerando la cicatrización de la úlcera y previniendo su recidiva.

Palabras clave:
Úlceras venosas. Enfermedad venosa crónica. Práctica basada en la evidencia. Algoritmo diagnóstico.

INTRODUCTION

Venous ulcers represent up to 80% of all lower extremity ulcers with a prevalence increasing with age that stands at 1.69% in the elderly population (1). They take many human, and material resources, and are associated with a tremendous financial burden. This amounts to 2% to 3% of the entire healthcare spending in developed countries (2,3) (and estimated 14.9 billion dollars are spent, each year, in the United States in the management of this entity) (4). These are chronic and recurring ulcers with a mean duration of 12-13 months and up to 60%-70% recurrence (5,6). They have a significant morbidity and negatively impact the patients' quality of life (2).

Chronic venous disease (CVD) is associated with multiple factors like genetics, feminine sex, pregnancy or age, and its management can be complex since patients often complain of difficult scarring and other factors added to chronic venous insufficiency like diabetes mellitus or peripheral arterial disease. A particular case of severe CVD is post-thrombotic syndrome with higher rates of progression into venous ulcers compared to saphenous axes insufficiency-driven CVD. It is estimated that up to 26% of lower extremity ulcers have a mixed etiology (7) (up to half of all extremities with signs of CVD show some degree of underlying arterial lesion). Therefore, these factors need to be taken into consideration for proper management and treatment.

The medical literature available to this date and the clinical practice guidelines are clear regarding the diagnosis, treatment, and referral of lower extremity ulcers. However, numerous problems and diagnostic dysfunctions often arise regarding the referral and overall management of patients with lower extremity ulcers both from primary and specialized care despite the robustness of evidence in the way we should proceed.

There are times that it can take months for ulcers to heal. Causes are varied: erroneous diagnoses, delayed referral to special care, suboptimal or delayed management by primary or special care or no homogenization in its definitive treatment. All these factors translate into a delayed scarring time for the ulcers, which ultimately affects quality of life and increases financial burden considerably.

This gap between evidence and routine clinical practice led the Spanish Chapter of Phlebology and Lymphology (CEFyL) of the Spanish Society of Angiology and Vascular Surgery (SEACV) to build a tool (targeted algorithm) aimed at GPs, nurses, doctors, and specialists to achieve fast diagnoses, prompt referrals, and administer optimal therapies to shorten the ulcers healing time.

MATERIAL AND METHODS

The Spanish Chapter of Phlebology and Lymphology (CEFyL) has created, in collaboration with Urgo medical labs, a committee of experts in angiology and vascular surgery from Spain and Portugal to design an algorithm for the diagnosis, treatment, and prompt referral of lower extremity ulcers.

A systematic bibliographic search was conducted up until January 2022 following the PRISMA declaration in PubMed and Embase with the following strategy: (((("clinical practice guideline*") OR "practice guideline*") OR guideline*) OR recommendation*) AND ((((management) OR diagnosis) OR assessment) OR treatment) AND ((((("chronic venous disease") OR "venous ulcer*") OR "venous leg ulcer*") OR "leg ulcer*") OR "chronic venous insufficiency") OR "chronic wound*").

Reviewers (ML and RR) excluded searches prior to the year 2000, as well as those that were expert consensuses. Searches considered the most adequate ones for the goal proposed were eventually selected.

RESULTS

The search for an easy algorithm for all the sectors involved in the management of these patients triggered the design of an alphabet-based mnemonic rule to simplify and help memorize the key steps or more relevant facets in the diagnostic and treatment of ulcers.

Key aspects included go from primary care assessment to special care by the vascular surgeon. Letters from the alphabet from *a* to *f* are used to summarize the steps needed to achieve diagnosis, clinical examination of lower extremities and ulcers, optimal medical therapy, compressive and preventive treatment of recurrence, and implement surgical and pharmacological strategies. A few explanatory notes are given in each step of the way that should be taken into consideration with selected bibliography that have given rise to these recommendations.

No clinical circumstance surrounding venous ulcers has been left out of the protocol proposed. However, we should mention that arterial ulcers and diabetic foot ulcers have been excluded from this diagnostic-therapeutic algorithm.

The letter a corresponds to achieving diagnosis. Two different sections have been envisioned here: outpatient screening from primary care, and angiology and vascular surgery care. First, it is essential to conduct arterial examination from the very health center including the palpation of distal pulses in extremities (dorsalis pedis and posterior tibial). If the patient shows clear distal pulses (the presence of one of them would be enough), and the appearance and location of the lesion is consistent with a venous ulcer, instrumental diagnosis would not be required.

In the presence of dubious distal pulses, or for the lack of them, the ankle brachial index (ABI) should be used.

ABIs > 0.8 are indicative of enough arterial vascularization to close the venous ulcer, therefore, the protocol should be followed at this point. If the patient's ABI is somewhere between 0.6 and 0.79, his lesions should be categorized as mixed ulcers and preferential referral to the vascular surgery unit for early assessment would be needed.

ABIs < 0.6 are indicative that the ulcer shows a priority arterial component. ABIs > 1.3 indicate that there is a component of arterial calcification making the vessel non-collapsible, meaning that the ABI could be useless, thus giving falsely elevated results. Both groups require early special care.

Regardless of the progression of the ulcer, the minute the patient has been diagnosed with a venous ulcer, referral to an angiology and vascular surgery specialist is advised following the usual ways (letter *e* of the protocol).

The usual thing to do is to reduce the surface of the ulcer nearly 40% in 4 weeks. Should the rhythm of epithelization or granulation be slower than expected by the treating physician, preferential referral should be activated. Direct referral criteria to vascular surgery for patients with decompensated heart failure, peripheral arterial disease or bleeding varicose veins have been included since these groups can benefit from preferential special care.

Early assessment from vascular surgery followed by arterial study should include a complete venous study to confirm diagnosis and assess venous disease anatomically with the use of Doppler ultrasound. Surgical assessment or sclerotherapy will be conducted in all cases based on the results of venous Doppler ultra-

sound and the patient's clinical status. Both venous and mixed ulcers will be moved to steps b and c of the protocol whether they have been diagnosed at the hospital or at a special care center. Arterial ulcers often need revascularization so they can start scarring while those due to causes different than mentioned like vasculitis often require examination by the treating specialist (dermatologist, internist, hematologist, etc.)

Letter *b* refers to the *best* local treatment possible. All lower extremity ulcers should be cleaned locally followed by debridement of devitalized tissue and hyperkeratosis right from the first visit (8). If there are signs of infection, antiseptic solutions should be used followed by silver dressings with antibiofilm and debridement capabilities (9,10). Wound cultures will only be obtained in cases of invasive infection or cellulitis for which specific antibiotics should be indicated based on the results obtained. Topical antibiotics are ill-advised (9,10,11). Signs of infection should be reevaluated at 14 days.

To treat an ulcer without any signs of infection, the selection of the dressing should be based on the best evidence available at the time. Chronic inflammation due to venous hypertension can lead to dermis, collagen, and elastin destructurization, and th destruction of extracellular matrix by an impaired balance between metalloproteinases (MMP) and tissue inhibitors of metalloproteinases (TIMP) (12). On this regard, clinical practice guidelines recommend the use of dressings to provide a matrix for granulation tissue, a wet environment, and impregnation in metalloproteinase modulators like the nano-oligosaccharide factor (sucrose octasulfate).

We should mention that dry healing in the absence of arterial compromise is ill-advised (8). Regarding the surrounding skin, perilesional borders should be protected with barrier cream (13). We should become aware that corticoids aimed at reducing dermatitis, hypergranulation, and eczema due to ulcerous lesion should be used with caution and adapting the dose to the needs of each patient since its prolonged use can have a negative effect on the scarring process (8,14).

C. *Compression* is the pillar of the medical treatment of venous ulcers. It is less used than it should though. There are various reasons for this: ignorance from physicians on the proper prescription of dressings or elastic stockings, lack of availability of proper dressings, low compliance from the patient or even fear of adverse events associated with such dressings. However, these are extremely rare if we take into consideration the existing contraindications and technical details.

With ABIs between 0.6 and 0.79 the compression dressing indicated is the multicomponent one of short and long traction of 20 mmHg. In patients with ABIs between 0.8 and 1.3 multicomponent compression dressings of 40 mmHg are safe.

Overall, multicomponent dressings are preferred over the elastic ones in the early stages of venous ulcers specifically those that combine both elastic and inelastic dressings for being more effective compared to those with one single component (15,16). However, low-elasticity and double component stockings are also indicated in small uncomplicated venous ulcers in eligible anatomies, and if the patient is collaborative (17). Although the evidence available to this date on its effectiveness is still scarce, low-elasticity compression stockings with velcro seem like a good option in patients with unfavorable anatomies or difficulties using standard stockings especially to prevent recurrences (18).

In patients with ABIs < 0.6 systematic compression is ill-advised (18).

The technical details of multicomponent compression dressings are important regarding safety and compliance: protect areas at risk like bone protuberances and the Achilles' tendon, and homogenize leg perimeters, if necessary, to avoid damaging pressure sites (19,20). The skin should be washed and dried before placing the dressing, and hydrated in its surrounding areas with hyper-oxygenated fatty acids (21).

While local compressive therapy is used, the possibility of a coadjuvant interventional therapeutic option should be contemplated too. If feasible and indicated, it should be offered early to speed up scarring times and avoid any recurrences (see letter *e*) (18).

D. Thereafter the ulcer has scarred, compressive therapy should be maintained with the use of an elastic stocking with a certain degree of

compression adapted to the patient's underlying condition (usually 20 mmHg or 40 mmHg) (6). If an expert on angiology and vascular surgery has not performed any evaluation while the ulcer was active, after the wound is close the patient should be referred to this specialist for the examination of his underlying venous disease and establishment of a strategy to prevent recurrences. Skin hydration—hyper-oxygenized fatty acids are advised—is very important to keep proper elasticity and prevent new solutions of continuity (8).

Significant elements that should be taken into consideration are the patient's awareness of his condition (13) to increase compliance to therapy and detect relapses early. Health habits like leading and active life and following a proper diet should be observed too to keep or maintain weight under control.

E. Surgical strategy that should be considered while examining a patient with a lower extremity ulcer. Whether ablation, conventional surgery or sclerotherapy is indicated—which will be individualized for every patient considering factors like age, comorbidities or the state of the skin, among others—the most important thing is that it is performed early(18). Any interventional procedures on patients with ulcers should be prioritized. The faster the patient is referred to vascular surgery the sooner he will benefit from treatment, the sooner the ulcer will scar, and the fewer recurrences will occur. This is an important point that should be made and remembered by all health professionals treating patients with venous ulcers. Clinical practice guidelines (15,19) insist on this, which although is probably the most relevant aspect regarding the effective healing of the ulcer it is also the one with least applied in the routine clinical practice.

F. *Pharmacotherapy*. Drug therapy should be coadjuvant during the scarring process of venous ulcers and should always be associated with compressive therapy and surgical evaluation. Micronized purified flavonoic fraction (MPFF), and sulodexide are indicated to treat CEAP 6 CVD (18,23) (Fig. 1).

DISCUSSION

An algorithm is a sum of instructions designed to develop a specific task that is presented through decisive points that should be dealt with step by step. Treatment algorithms allow stepwise approaches when dealing with complex therapeutic decision-making processes, and provide essential guidance during the entire diagnostic/therapeutic process.

Across the years, numerous protocols and algorithms have been published for the diagnosis and treatment of lower extremity ulcers, which shows how difficult follow-up is on this regard. A comparison among the most important ones has been made in a recent review showing numerous similarities among the different proposals made.

The common ground among the different algorithms available is: to confirm venous etiology and study ulcers in the chronic venous insufficiency severity setting; to rule out the presence of mixed/arterial component using the angle brachial index to decide on the proper degree of compression and discard whether assessment by a different specialist is required; to anatomically locate the dysfunction at stake for targeted therapy prescription on the reflow and obstruction region while making sure that multicomponent dressing and proper wound care are being used.

The primary endpoint is to reduce scarring time. In other medical disciplines it has been confirmed that after the implementation of this kind of algorithms and protocols, efficacy improves (24). In addition, diagnostic process improves as well, the numbers of effective scarring go up, the patients' quality of life is much better, recurrences drop, and fewer cost and resources are needed.

The existence, at the various healing wards of the different health centers, of an algorithm of rapid consultation by the health professional would facilitate the correct implementation of the different therapies available, and raise awareness on how important referral is, as well as early assessment by the vascular surgery team.

The protocol can be downloaded for free in a printable version provided at the official website of the Spanish Chapter of Phlebology and Lymphology: http://www.capitulodeflebologia.org/wp-content/uploads/2020/12/Protocolo-de-derivaci %C3 %B3n-y-tratamiento-ulcera-de-pierna.pdf

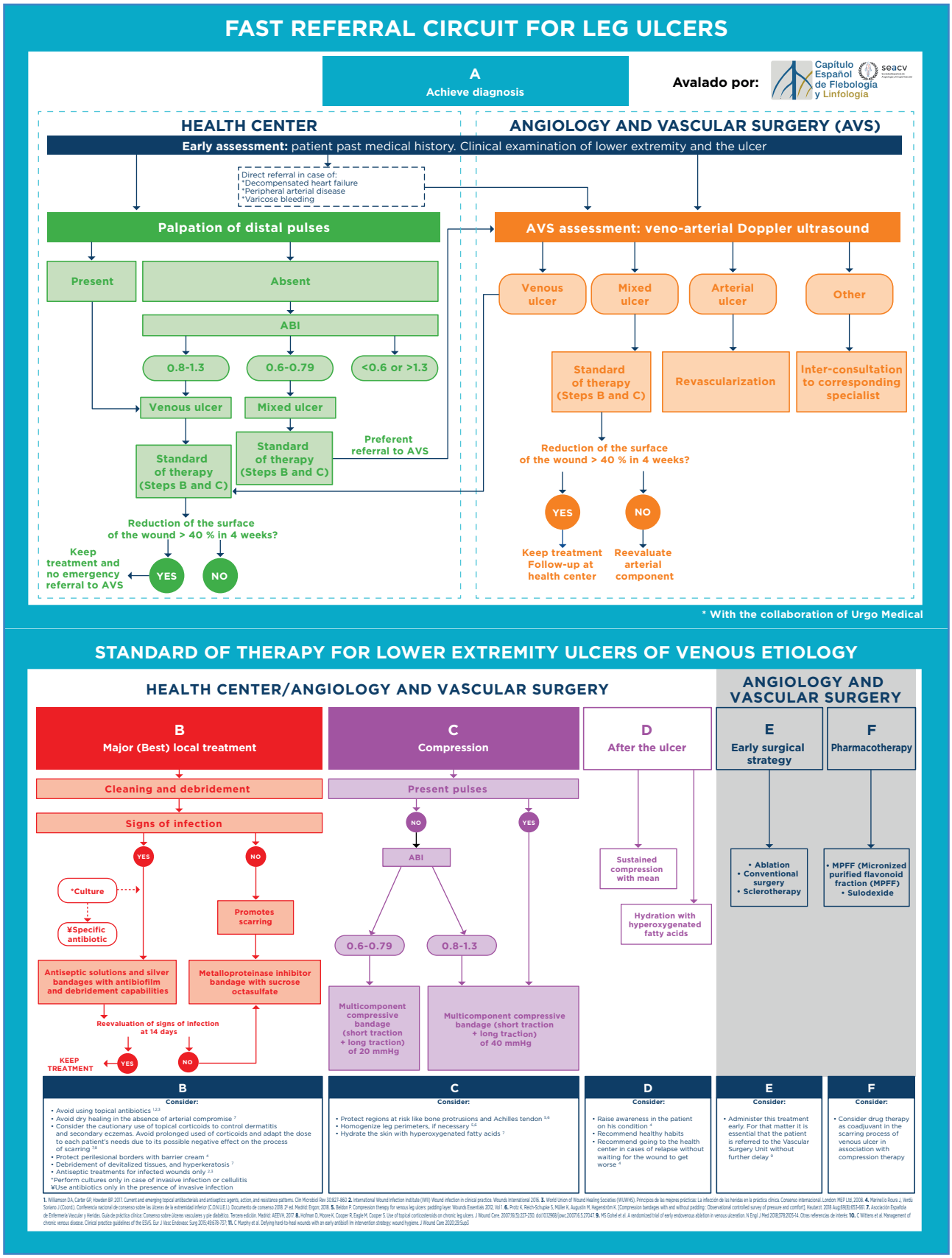

Figure 1. *Protocol.*

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