Management of venous ulcer disease

Wijnand Bert van Gent,1 Esther Dorine Wilschut,1 Cees Wittens2

A venous leg ulcer represents the severe end of the spectrum of chronic venous disease. Venous ulcers are the most common form of leg ulcer. Observational studies have reported the prevalence of venous leg ulcers to be 1-1.5%.1 2 A cross sectional study of a random sample of 1566 people aged 18-64 years from an urban Scottish population estimated the prevalence of venous leg ulcers to be around 1%. The estimated total treatment costs of venous leg ulcers are 1% of the total annual healthcare budget in western European countries.3 In the United States, treatment costs for venous ulcers in more than 6 million patients approach $2.5bn (£1.6bn; €1.8bn), and two million work days are lost annually because of venous ulcer disease.5 A recent prospective study performed in 23 specialised wound centres throughout Germany calculated the mean total cost of a venous ulcer per patient per year to be €9569 (€8658 (92%) direct costs and €911 (8%) indirect costs).6

Treatment is either conservative (bed rest, leg elevation, local treatment, and compression) or surgical (superficial and perforating vein ablation and deep vein reconstruction).

This review examines the prevention and treatment of venous leg ulcers and is based mostly on evidence from observational studies and some reviews and meta-analyses.

SUMMARY POINTS
Venous disease is the most common cause of leg ulcers
Signs of venous hypertension include lower extremity varicosities, oedema, venous dermatitis with hyperpigmentation, and lipodermatosclerosis
Compression is the mainstay of treatment, although surgery can help promote healing
Multi-component compression systems are more effective than single component ones
No specific wound dressing has been shown to be superior
Subfascial endoscopic perforator vein surgery reduces recurrence

SOURCES AND SELECTION CRITERIA
We searched PubMed and the Cochrane Library with the medical subject headings “venous leg ulcers”, “venous ulcer”, “venous ulcers”, and “leg ulcers” combined with “treatment” and “surgery” and “SEPS” and “compression therapy”. The search was limited to the English language. We used evidence from published abstracts from major scientific meetings and textbooks on vascular surgery. We gave priority to evidence obtained from well conducted systematic reviews and large well designed randomised controlled trials.

What is a venous leg ulcer and who gets them?
An ulcer of the skin is a circumscribed inflamed lesion with complete loss of the epidermis and possible loss of part of the dermis and subcutaneous fat. A venous ulcer is an area of epidermal discontinuity that persists for four weeks or more and occurs as a result of venous hypertension and insufficiency of the calf muscle pump. The underlying pathophysiology is venous hypertension caused by reflux, obstruction, or insufficiency of the calf muscle pump, which affects the superficial venous system (greater and smaller saphenous vein), the deep venous system, or the veins that perforate between those systems. Figure 1 shows the superficial and deep system, including perforating veins.

Venous ulcers may supplicate. They are classically found in the gaiter area, from the midcalf to the ankle.

Risk factors for venous ulcer disease are those associated with venous insufficiency: advancing age, male sex (the reported male:female ratio ranges from 1.5:1 to 10:1), deep vein thrombosis, phlebitis, trauma to legs, congestive heart failure, family history of leg ulcers, obesity, higher number of pregnancies, and jobs that involve long periods of standing. Joint or neurological disorders lead to decreased leg activity, which leads to venous insufficiency.

Venous ulcers may be primary or, less often, secondary to an identifiable underlying cause (such as venous...
Healed ulceration

No visible or palpable signs of venous disease

Telangiectases or reticular veins

Signs

Oedema

Active ulceration

Skin changes such as lipodermatosclerosis

Varicose veins

Fig 2 | A venous leg ulcer on the medial aspect of the lower leg (near the medial malleolus). The small ulcer in the centre is surrounded by typical skin changes: thickening and fibrosis of the skin

Fig 3 | A complex venous leg ulcer just above the ankle (upright position). Proximal to the ulcer, the skin is thickened and painful (lipodermatosclerosis). The ulcer covers the complete circumference of the lower leg. Multiple small venous ulcers are seen distal to the larger ulcer

Fig 4 | Venous ulceration on the lower leg. Clinical symptoms are oedema, typical skin changes, and active ulceration (CEAP C3, C4, and C6)

with the changes. Microcirculation studies have shown that hypoxia is not the cause of venous ulceration.9

Venous hypertension leads to extravasation of red blood cells and macromolecules, and this in turn leads to inflammatory changes in the venous microcirculation and leucocyte migration into the dermis. This prompts a cascade of pathological events, in which transforming growth factor β plays an important role, that results in dermal fibrosis, lipodermatosclerosis, and finally ulceration.9 10

How to evaluate a leg ulcer

History

Patients may have symptoms of venous insufficiency, such as aching, heaviness, a feeling of swelling, cramps, itching, tingling, and restless legs. These symptoms are usually worse at the end of the day.

Examination

Signs vary according to the severity of disease. Typical skin changes associated with venous hypertension may be visible before a venous ulcer develops. Skin changes include varicosities of the lower leg, oedema, venous dermatitis usually with hyperpigmentation as a result of deposition of haemosiderosis or haemoglobin in the skin, and lipodermatosclerosis associated with thickening and fibrosis of normal adipose tissue under the skin. Figures 2 and 3 show examples of venous ulcers and the typical skin changes seen.

The examining doctor must note the exact location, size, colour, and degree of necrosis of an ulcer and palpate the peripheral arterial pulses. Rare but severe complications of venous ulcers include osteomyelitis and the development of squamous cell carcinoma in the base of the ulcer.11

Classification

In 1994 the American Venous Forum developed a classification of venous ulcers based on clinical findings, aetiology, anatomical distribution, and pathophysiological dysfunction, the CEAP classification. The clinical classification is based on objective clinical signs of chronic venous disease (C0–6) (fig 4), and further differentiated according to whether the patient is asymptomatic (A) or symptomatic (S). This clinical classification is organised in terms of ascending severity of disease (table 1).

The aetiological classification recognises three categories of venous dysfunction: congenital, primary, and secondary (E1, E2, E3).

The anatomical classification describes the anatomical extent of venous disease—whether in the superficial (A1), deep (A2), or perforating (A3) veins. Disease may involve one, two, or all three systems.

Clinical signs and symptoms of venous dysfunction may be the result of reflux (P1), obstruction (P2), or both (P3).

Investigation

Primary venous ulcers cannot be distinguished from ulcers that are secondary (to trauma or deep vein thrombosis, for example) on history and basic physical examination. If peripheral arterial pulses are absent, investigation of the ankle-brachial index using Doppler ultrasound will help discriminate venous disease from arterial disease.

Table 1 | Clinical classification

<table>
<thead>
<tr>
<th>Class</th>
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<td>C0</td>
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</tr>
<tr>
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</tr>
<tr>
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</tr>
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Compression treatment

Compression is the gold standard conservative approach to treating and preventing ulcers.16 Exactly how compression works is still unknown, but treatment should be adhered to continuously (24 hours a day) until healing is achieved (fig 5). Compression can be applied by using bandages, compression stockings, or combinations of the two methods. Table 2 lists the different types of compression stockings available.

No international standards are available as a guide to which type of compression should be used. In general practice, four layer bandages (an elastic system) are most often used to treat an ulcer and compression stockings to prevent recurrence.

A recent meta-analysis of randomised trials that compared four layer bandages with short stretch bandages showed that four layer bandages, the standard method used in the UK, were associated with significantly shorter time to healing compared with short stretch bandages (multifactorial model based on five trials: hazard ratio 1.31, 95% confidence interval 1.09 to 1.58; P=0.005). Data from two trials that recorded adverse events showed no evidence of a difference in adverse event profiles between the two bandage types. The four layer bandage consists of orthopaedic wool, crepe bandage, elastic bandage, and a final cohesive retaining layer. All layers are applied from toes to knee and normally require weekly renewal, although they can be changed more often if necessary.17 However, another recent meta-analysis of studies that compared a variety of bandages with specifically designed stockings found that leg compression with stockings was better than compression with bandages, that stockings were easier to use, and that patients experienced less pain with stockings.18 A greater proportion of ulcers healed in patients treated with stockings than in those treated with bandages (62.7% v 46.6%; P<0.001). The average time to healing (seven studies, 535 patients) was three weeks shorter with stockings (P=0.001) than with bandages.

Treatment adherence improves the likelihood of healing and will be a contributory factor in any therapeutic study. In a study that followed 113 patients over 15 years, ulcer healing was 97% in patients who adhered to treatment and 55% in those who did not. Mean time to ulcer healing was 5.3 months. Ulcer recurrence was 29% in five years. In the non-adherent group all ulcers recurred by 36 months.5

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Common problems with compression stockings or bandages are pain, discomfort, and itching. A Cochrane review published in 2006 evaluated whether pain occurred more often with specific types of compression. No clear differences were seen between treatment groups.

Table 2 Classification of compression stockings (United Kingdom)

<table>
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According to expert consensus outlined in a document published in 2006 by Union Internationale de Phlébologie, any patient with a venous ulcer should undergo duplex ultrasonography,19 which is the best way to confirm or exclude the presence of venous dysfunction. Duplex scanning can determine whether the deep veins or the greater or lesser saphenous veins and their tributaries are dilated, congested, or incompetent. It can also detect the presence of incompetent perforating veins and whether the problem is caused by anatomical obstruction, reflux, or both.

Although all patients should undergo duplex ultrasonography, few data are available on its sensitivity and specificity in patients with venous ulcer. A small study (20 patients with a venous ulcer) conducted in 1997 found a sensitivity and specificity of duplex ultrasonography for diagnosing venous incompetence in perforating veins of 79.2% and 100%, respectively.14

How are ulcers treated?

Treatment of venous ulcers is either conservative (bed rest, leg elevation, local treatment, and compression) or surgical (superficial and perforating vein ablation and deep vein reconstruction, and more recently subfascial endoscopic perforating vein surgery (SEPS) combined with superficial vein ligation).

The goals of both approaches in patients with chronic venous insufficiency are to control symptoms, promote healing of ulcers, and prevent recurrence. No drugs are available for the treatment of venous leg ulcers.14 The routine use of systemic antibiotics to promote healing in venous leg ulcers is not supported by evidence, and the usefulness of antiseptics is unclear.15

Conservative management

Despite advances in surgery, a non-surgical approach remains the primary treatment worldwide. Strict bed rest and elevation of the affected leg have long been known to be effective in venous ulceration, but this approach is impractical for most patients.

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Despite advances in surgery, a non-surgical approach remains the primary treatment worldwide. Strict bed rest and elevation of the affected leg have long been known to be effective in venous ulceration, but this approach is impractical for most patients.
Stockings may have been associated with less pain than bandages, but the authors concluded that further research was needed. Stockings and bandages should be applied by a trained nurse.

Wound dressings
The box summarises the many types of wound dressings currently on the market. No evidence is available that any one wound dressing confers specific benefit over another. A Cochrane review of 42 randomised trials that evaluated different dressings for venous ulcers advocated that simple, inexpensive, non-adherent dressings be used beneath compression bandages or stockings. Allergic reactions to dressing materials can pose a major clinical problem.

Surgical management
Superficial venous system
In 2007, a randomised controlled trial comparing compression alone with compression plus surgery of the superficial venous system in chronic venous ulceration found that the combined approach did not improve ulcer healing (89% v 93%); it did reduce recurrence at four years (51% v 27%; P<0.01), however, and resulted in a greater proportion of ulcer-free time (78% v 71%; P=0.007 Mann-Whitney U test). Endoluminal laser treatment, radiofrequency ablation, and ultrasound guided foam sclerotherapy are rapidly being used to treat varicose veins, but we have no data on their efficacy in treating venous ulceration.

Perforating veins
The role of perforator vein incompetence in the pathophysiology of chronic venous insufficiency is unclear. Subfascial endoscopic perforator vein surgery is used as a part of the treatment for severe chronic insufficiency. Incompetent perforating veins are ligated by means of an endoscopic procedure in which the incision is made proximal to the ulcer in healthy skin.

A systematic review of outcomes of surgical management incorporating subfascial endoscopic perforator surgery was published in 2004. The search identified 20 studies—one randomised trial and 19 case series—involving 1140 treated limbs. After combining the results the authors found that ulcers healed in 88% (95% confidence interval 83% to 92%) of limbs treated with surgery. The median time to healing was 30-60 days. The ulcer recurrence rate was 16% (11% to 21%; range 0-28%). Mean time to recurrence was 21 months (mean follow-up time of 29 months). Subfascial endoscopic perforator vein surgery combined with superficial vein surgery for leg ulcer treatment has since been evaluated in prospective studies with longer follow-up. Healing rates ranged from 83% to 97% and recurrence rates were between 6% and 27%.

In all studies, subfascial endoscopic perforator vein surgery was combined with ambulatory compression treatment and surgery of the superficial venous system. The role of subfascial endoscopic perforator vein surgery remains unclear.

Deep venous system
No effective treatment is available for deep venous insufficiency in secondary deep venous pathology. Valve repair in primary valve disease, although rare, is the best available.FUTURE RESEARCH AND ONGOING TRIALS
- Future research should be aimed at reducing the prevalence of venous hypertension
- Ambulatory venous compression is the cornerstone of treatment, so ways to increase compliance by improving compression techniques are needed
- The treatment of superficial venous insufficiency is expected to improve quickly with the use of percutaneous techniques (endoluminal laser, radiofrequency ablation, and foam sclerotherapy)
- If treatment for perforator vein incompetence is shown to be effective, minimally invasive perforator vein treatments such as endovenous thermal ablation (laser, radiofrequency, or steam) and chemical ablation will be investigated
- The effectiveness of minimally invasive treatments for deep venous incompetence (insufficiency and obstruction) must be shown to be effective before they are more widely used
- Measures directed at preventing venous ulceration are important to evaluate
- The early surgical removal of thrombus in deep vein thrombosis is being tested in three randomised trials

TIPS FOR NON-SPECIALISTS
- Primary venous ulcers occur in patients with venous hypertension and calf muscle pump insufficiency
- Patients with venous ulceration of the lower leg require evaluation of the deep and superficial venous systems by duplex ultrasonography
- If peripheral arterial pulses are absent, calculate the ankle-brachial index and investigate for peripheral arterial disease
- Four layer compression bandages are better at treating ulcers than single layer bandages, although patients may tolerate elastic stockings better than bandages
- Adherence to 24 hour compression is important to accomplish healing of the ulcer and prevent development of new ulcers

ADDITIONAL EDUCATIONAL RESOURCES
Resources for patients
Resources for healthcare professionals
veinforum.org (http://veinforum.org/index.php?page=medical-professionals)—A forum for healthcare professionals. Contains links to handbooks of venous disorders and journals European Venous Forum (www.europeanvenousforum.org/links.htm)—Up to date links to international standards in venous disease

TYPES OF WOUND DRESSING
Gauze, which may be impregnated with foams or antimicrobials
Hydrocolloids
Transparent films
Hydrogels
Foams
Alginates (derived from seaweed)
Antimicrobials: iodine, silver, alcohol, biguanides, chlorine
Collagen
alternative (level 4 evidence). Several case series have shown promising results for minimally invasive recanalisation of post-thrombotic obstructed deep veins, but the technique needs further study.  

No data are available to support preventive surgery or to identify which patients might benefit from such surgery. Contributors: WVBV drafted the manuscript and is guarantor; EWJ and CW contributed to the manuscript and critically evaluated and revised the manuscript.

Competing interests: All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Provenance and peer review: Commissioned; externally peer reviewed.


Horse sense

It was a hot day in July, and I had taken refuge in the relative cool of my office in the rural medical station where I was serving my mandatory year of general practice before entering specialist training. The hot weather, combined with a peak in agricultural activity (the main occupation and source of income in the area), was keeping the people away from the doctor, so I spent my working hours browsing through textbooks and journals and reading paperback novels.

Suddenly a middle aged peasant, sweating and dishevelled, rushed up the stairs and into the office. “Doctor,” he gasped, “can you do something for the horse?”

Between gasps of air, he gave me the story. He had taken his horse to the field, where he was to spray some pesticide on his crops. He had diluted the toxic powder in a big bucket of water and then turned to get a shoulder-borne spray canister in order to fill it with the solution. The horse, standing nearby and acutely feeling the heat of the day, promptly dipped his muzzle into the bucket and gulped the liquid down thirstily. It was only natural—this was his bucket, and he had been drinking out of it all his working life. How could it suddenly contain death rather than refreshment? Within a few minutes he was writhing on the ground and frothing from the mouth. Was there anything I could do?

I never met my four legged patient. Predictably, the locals were asked to bring the horse to me the next day. The patient lay in a deep slumber, but its ears were pricked and it was writhing as if in discomfort. It could not be touched, and myself and everyone in the room except me (and normally the horse) were kept a few feet away. I administered atropine as I could lay my hands on, and told the peasant to bring it to me to have it injected into its horse immediately.

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I had no veterinary training whatsoever, but there was no expert within reach, and certainly no time to lose. I took a 60 ml syringe, drew as much ampuqle of atropine as I could lay my hands on, and told the peasant to bring it to me to have it injected into its horse immediately.

I never met my four legged patient. Predictably, the poor beast did not survive. His demise was discussed by the locals over coffee and ouzo for days on end, and his master was hauled over the coals by his peers for his total lack of horse sense. The memory of the event has lingered with me all these 25 years.

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