

Venous ulcer

Venous ulcers are wounds that are thought to occur due to improper functioning of venous valves, usually of the legs (hence **leg ulcers**).^{[1]:846} They are the major occurrence of chronic wounds, occurring in 70% to 90% of leg ulcer cases.^[2] Venous ulcers develop mostly along the medial distal leg, and can be painful with negative effects on quality of life.^[3]

Exercise together with compression stocking increases healing.^[4] The NICE guidelines recommends that everyone with a venous leg ulcer, even if healed, should be referred to a "vascular service" for venous duplex ultrasound and assessment for endovenous surgery.^[5]

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Signs and symptoms

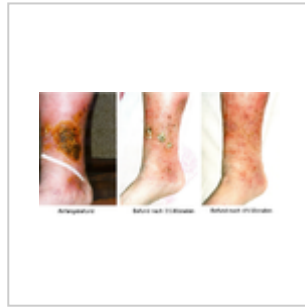
Signs and symptoms of venous ulcers include:

Venous ulcer	
Other names	Venous insufficiency ulceration, stasis ulcers, stasis dermatitis, varicose ulcers, ulcus cruris
	
Venous ulcer on the back of the right leg.	
Specialty	Dermatology 

- Moderate pain, which improves on elevation (unlike arterial ulcers which worsen with elevation)
- Irregular, sloping edges
- Associated oedema, due to increased hydrostatic pressure, which contributes to 'atrophie blanche'
- 'Atrophie blanche', localised loss of skin pigmentation due to death of erythrocytes and scarring
- Lipodermatosclerosis, a hardening of the skin which can lead to an "inverted champagne bottle" appearance to the leg
- Associated superficial varicose veins or "ankle flare", a collection of small, dark, engorged superficial veins^[6]



Venous ulcer before surgery



Healing process of a chronic venous stasis ulcer of the lower leg



Healing venous ulcer after one month

Pathophysiology

The exact cause of venous ulcers is not certain, but they are thought to arise when venous valves that exist to prevent backflow of blood do not function properly, causing the pressure in veins to increase.^{[7][8][9][10]} The body needs the pressure gradient between arteries and veins in order for the heart to pump blood forward through arteries and into veins. When venous hypertension exists, arteries no longer have significantly higher pressure than veins, and blood is not pumped as effectively into or out of the area.^{[7][8][9][10]}

Venous hypertension may also stretch veins and allow blood proteins to leak into the extravascular space, isolating extracellular matrix (ECM) molecules and growth factors, preventing them from helping to heal the wound.^{[7][10]} Leakage of fibrinogen from veins as well as deficiencies in fibrinolysis may also cause fibrin to build up around the vessels, preventing oxygen and nutrients from reaching cells.^[7] Venous insufficiency may also cause white blood cells (leukocytes) to accumulate in small blood vessels, releasing inflammatory factors and reactive oxygen species (ROS, free radicals) and further contributing to chronic wound formation.^{[7][10]} Buildup of white blood cells in small blood vessels may also plug the vessels, further contributing to ischemia.^[11] This blockage of blood vessels by leukocytes may be responsible for the "no reflow phenomenon," in which ischemic tissue is never fully reperfused.^[11] Allowing blood to flow back into the limb, for example by elevating it, is necessary but also contributes to reperfusion injury.^[8] Other comorbidities may also be the root cause of venous ulcers.^[9]

It is in the crus that the classic venous stasis ulcer occurs. Venous stasis results from damage to the vein valvular system in the lower extremity and in extreme cases allows the pressure in the veins to be higher than the pressure in the arteries. This pressure results in transudation of inflammatory mediators into the subcutaneous tissues of the lower extremity and subsequent breakdown of the tissue including the skin.

Wounds of the distal lower extremities arising from causes not directly related to venous insufficiency (e.g., scratch, bite, burn, or surgical incision) may ultimately fail to heal if underlying (often undiagnosed) venous disease is not properly addressed.

Diagnosis

Classification

A clinical severity score has been developed to assess chronic venous ulcers. It is based on the CEAP (clinical, etiology, anatomy, and pathophysiology) classification system developed by an expert panel. A high score gives a poor prognosis.^[12]

Distinction from arterial ulcer

A venous ulcer tends to occur on the medial side of the leg, typically around the medial malleolus in the 'gaiter area' whereas arterial ulcer tends to occur on lateral side of the leg and over bony prominences. A venous ulcer is typically shallow with irregular sloping edges whereas an arterial ulcer can be deep and has a 'punched out' appearance. Venous ulcers are typically 'wet' with a moderate to heavy exudate, whereas arterial ulcers are typically 'dry' and scabbed. The skin surrounding a venous ulcer may be edematous (swollen) and there may be evidence of varicose veins; the skin surrounding an arterial ulcer may be pale, cold, shiny and hairless. Both venous and arterial ulcers may be painful, however arterial ulcers tend to be more painful, especially with elevation of the leg, for example when in bed.

Differential diagnosis

Leg ulcerations may result from various pathologic processes. Common causes of leg ulcerations include inadequate blood flow and oxygen delivery to tissues as seen in peripheral arterial disease and venous stasis ulcerations. Additional causes include neutrophilic dermatoses such as pyoderma gangrenosum or Sweet's syndrome; vasculitic processes such as cryoglobulinemia; calciphylaxis (often seen in people with end-stage kidney disease but may also occur with medications such as warfarin); cancers such as squamous cell carcinoma (Marjolin's ulcer) or myelodysplastic syndrome; neuropathy (e.g., diabetic peripheral neuropathy); or atypical infections such as nocardiosis, sporotrichosis, or mycobacterial infections.

Prevention

Compression stockings appear to prevent the formation of new ulcers in people with a history of venous ulcers.^[13]

Treatment

The main aim of the treatment is to create such an environment that allows skin to grow across an ulcer. In the majority of cases this requires finding and treating underlying venous reflux. The National Institute for Health and Care Excellence (NICE) recommends referral to a vascular service for anyone with a leg ulcer that has not healed within 2 weeks or anyone with a healed leg ulcer.^[14]

Most venous ulcers respond to patient education, elevation of foot, elastic compression, and evaluation (known as the Bisgaard regimen).^[15] Exercise together with compression stocking increases healing.^[4] There is no evidence that antibiotics, whether administered intravenously or by mouth, are useful.^[16] Silver products are also not typically useful, while there is some evidence of benefit from cadexomer iodine creams.^[16] There is a lack of quality evidence regarding the use of medical grade honey for venous leg ulcers.^[17]

The recommendations of dressings to treat venous ulcers vary between the countries. Antibiotics are often recommended to be used only if so advised by the physician due to emergence of resistance of bacteria to antibiotics. This is an issue on venous ulcers as they tend to heal slower than acute wounds for example. Natural alternatives that are suitable for the longer term use exists on the market such as honey and resin salve. These products are considered as Medical Devices in EU and the products have to be CE marked.^{[18][19]}

Compression therapy

Non-elastic, ambulatory, below knee (BK) compression counters the impact of reflux on venous pump failure. Compression therapy is used for venous leg ulcers and can decrease blood vessel diameter and pressure, which increases their effectiveness, preventing blood from flowing backwards.^[7] Compression is also used^{[7][20]} to decrease release of inflammatory cytokines, lower the amount of fluid leaking from capillaries and therefore prevent swelling, and prevent clotting by decreasing activation of thrombin and increasing that of plasmin.^[2] Compression is applied using elastic bandages or boots specifically designed for the purpose.^[7]

Regarding effectiveness, compression dressings improve healing.^[21] It is not clear whether non-elastic systems are better than a multilayer elastic system.^[21] Patients should wear as much compression as is comfortable.^[22] The type of dressing applied beneath the compression does not seem to matter, and hydrocolloid is not better than simple low adherent dressings.^{[23][24]} Recently there have been clinical studies on a multi-functional botanical-based ointment in combination with compression therapy in the treatment of difficult-to-heal wounds, including venous leg ulcers.^[25]

Intermittent pneumatic compression devices may be used, but it is not clear that they are superior to simple compression dressings.^[26]

It is not clear if interventions that are aimed to help people adhere to compression therapy are effective.^[27] More research is needed in this field.

Medications

Pentoxifylline is a useful add on treatment to compression stockings and may also help by itself.^[28] It works by reducing platelet aggregation and thrombus formation. Gastrointestinal disturbances were reported as a potential adverse effect.^[28]

Sulodexide, which reduces the formation of blood clots and reduces inflammation, may improve the healing of venous ulcers when taken in conjunction with proper local wound care.^[29] Further research is necessary to determine potential adverse effects, the effectiveness, and the dosing protocol for sulodexide treatment.

An oral dose of aspirin is being investigated as a potential treatment option for people with venous ulcers. A 2016 Cochrane systematic review concluded that further research is necessary before this treatment option can be confirmed to be safe and effective.^[30]

Oral zinc supplements have not been proven to be effective in aiding the healing of venous ulcers, however more research is necessary to confirm these results.^[31]

Treatments aimed at decreasing protease activity to promote healing in chronic wounds have been suggested, however, the benefit remains uncertain.^[32]

Skin grafts and artificial skin

Two layers of skin created from animal sources as a skin graft has been found to be useful in venous leg ulcers.^[33]

Artificial skin, made of collagen and cultured skin cells, is also used to cover venous ulcers and excrete growth factors to help them heal.^[34] A systematic review found that bilayer artificial skin with compression bandaging is useful in the healing of venous ulcers when compared to simple dressings.^[33]

Surgery

A randomized controlled trial found that surgery "reduces the recurrence of ulcers at four years and results in a greater proportion of ulcer free time".^[35]

Local anaesthetic endovenous surgery using the thermoablation (endovenous laser ablation or radiofrequency), perforator closure (TRLOP) and foam sclerotherapy showed an 85% success rate of healing, with no recurrence of healed ulcers at an average of 3.1 years, and a clinical improvement in 98% in a selected group of venous leg ulcers.^[36]

Dressings

It is not certain which dressings and topical agents are most effective for healing venous leg ulcers.^[37] Silver-containing dressings may increase the probability of healing for venous leg ulcers.^[37] A clinical trial was successfully performed with a mixture of 60% sugar or glucose powder and 40% vaseline^[38].

Prognosis

Venous ulcers are costly to treat, and there is a significant chance that they will recur after healing.^{[2][7]} one study found that up to 48% of venous ulcers had recurred by the fifth year after healing.^[7] However treatment with local anaesthetic endovenous techniques suggests a reduction of this high recurrence rate is possible.^[36]

Without proper care, the ulcer may get infected leading to cellulitis or gangrene and eventually may need amputation of the part of limb in future.

Some topical drugs used to treat venous ulcer may cause venous eczema.^[39]

Research

The current 'best' practice in the UK is to treat the underlying venous reflux once an ulcer has healed. It is questionable as to whether endovenous treatment should be offered before ulcer healing, as current evidence would not support this approach as standard care. EVRA (Early Venous Reflux Ablation) ulcer trial – A UK NIHR HTA funded randomised clinical trial to compare early versus delayed endovenous treatment of superficial venous reflux in patients with chronic venous ulceration opened for recruitment in October 2013. The study hopes to show an increase in healing rates from 60% to 75% at 24 weeks.^[40]

Research from the University of Surrey and funded by the Leg Ulcer Charity is currently looking at the psychological impact of having a leg ulcer, on the relatives and friends of the affected person, and the influence of treatment.^[41]

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External links

<p>Classification ICD-10: I83.0 (http://apps.who.int/classifications/icd10/browse/2016/en#/I83.0), I83.2 (http://apps.who.int/classifications/icd10/browse/2)</p>
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	016/en#/I83.2), L97 (http://apps.who.int/classifications/icd10/browse/2016/en#/L97) • ICD-9-CM: 454.0 (http://www.icd9data.com/getICD9Code.ashx?icd9=454.0) • MeSH: D014647 (https://www.nlm.nih.gov/cgi/mesh/2015/MB_cgi?field=uid&term=D014647) • DiseasesDB: 29114 (http://www.diseasesdatabase.com/ddb29114.htm)
External resources	MedlinePlus: 000834 (https://www.nlm.nih.gov/medlineplus/ency/article/000834.htm)

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