

Chronic ulceration of the leg

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Abstract

The management of patients with chronic leg ulcers represents an enormous burden to healthcare services in the United Kingdom. Most leg ulcers are due to chronic venous hypertension, although arterial compromise, malignancy, vasculitis and other medical disorders are also recognized causes. The assessment of patients with chronic leg ulceration should include a detailed history and clinical examination, supported by relevant investigations. Ankle-brachial pressure index measurement and non-invasive venous (\pm arterial) imaging using colour duplex are the principal investigations. The mainstay of treatment for patients with chronic venous ulceration is compression therapy, applied by trained clinical teams bridging primary and secondary care settings. Prompt endovenous ablation of superficial venous reflux accelerates ulcer venous healing and may have an important role in reducing ulcer recurrence. Patients with arterial compromise may require endovascular or surgical revascularization to promote healing. The causes, assessment and management of patients with chronic leg ulceration are discussed in this article.

Keywords Arterial ulcer; compression bandaging; endovenous ablation; superficial venous surgery; vascular surgery; venous ulcer

Definition

Chronic leg ulceration may be defined as:

- a breach in the epithelial integrity of the skin
- occurring between the knee and malleoli
- of greater than 6 weeks' duration.

Aetiology

The vast majority (>90%) of chronic leg ulcers have a vascular aetiology. Chronic venous hypertension is thought to be the primary cause of around 70% of leg ulcers and a significant contributory factor in a further 15% (Figure 1). In addition to the primary aetiology, other factors may also delay wound healing and should be considered and treated where possible. These include dependent oedema (which is often poorly controlled), medical comorbidities (such as diabetes), poor nutrition, and medications (including steroids or immunosuppressive drugs). Arterial ulceration is usually due to multilevel occlusive peripheral arterial disease causing critical leg ischaemia. Other causes of leg ulceration include vasculitis and malignancy.

Epidemiology

Chronic leg ulceration is generally considered to be a disease of the Western world, with an overall prevalence of ulceration of

around 0.3–1% in the adult population. The female preponderance is more apparent in patients >60 years. The prevalence of chronic venous ulceration is likely to increase as increasing age and obesity are independent risk factors for developing ulceration. Many patients with venous ulcers do have evidence of venous disease (usually reflux, sometimes deep venous occlusion). However, as many patients with varicose veins or previous DVT do not develop ulcers, the correlation between anatomical venous disease and clinical severity is often poor. Ulcers due to arterial disease are more common in men and are rare in patients <50 years.

Pathology and pathogenesis

Venous ulceration

Patients who develop venous ulcers have persistent high pressure in the veins of the leg. This 'chronic venous hypertension' is usually a result of incompetence (or reflux) in superficial and/or deep veins due to faulty valves but may also occur in patients with venous occlusion or recanalization after DVT. Other factors such as immobility, obesity, ankle stiffness, leg dependency and poor calf muscle pump function may also contribute to venous hypertension. In the initial stages, patients with venous hypertension may be asymptomatic, but over time, the skin may become red and inflamed (venous eczema), develop brown pigmentation (haemosiderinosis) or become thickened and scaly (lipodermatosclerosis) and eventually break down resulting in ulceration. The Clinical, Etiologic, Anatomic, Pathophysiological (CEAP) classification is used to describe the severity of venous disease (Table 1).¹ Although the sequence of skin changes is well described, the precise pathogenesis of ulceration due to venous hypertension is poorly understood. Proposed theories include the fibrin cuff theory (observation of peri-capillary fibrin cuffs which may reduce local oxygenation),² the white cell trapping hypothesis (trapped white blood cells may become activated resulting in cytokine release and local tissue damage)³ and the growth factor trapping theory (growth factors important for healing are inhibited by large molecules which have leaked out of capillaries due to venous hypertension).⁴ The typical location for

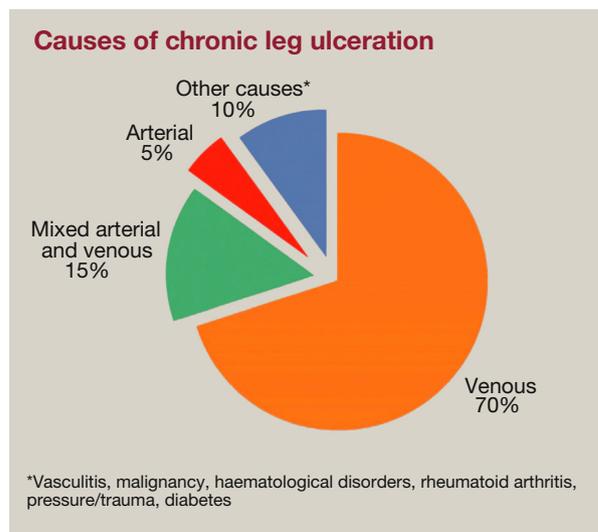


Figure 1

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Clinical, Etiological, Anatomical and Pathophysiological (CEAP) classification of chronic venous disease

CEAP clinical stage	Description
C0	Absence of any signs of venous disease
C1	Reticular veins
C2	Truncal varicose veins
C3	Oedema
C4	Skin changes (pigmentation, lipodermatosclerosis)
C5	Healed ulceration
C6	Open ulceration

Table 1

a venous ulcer is the medial gaiter area of the leg, although lateral leg and foot ulceration (rare) may occur. The perception that venous leg ulceration rarely occurs on the lateral aspect of the leg is false. Other venous skin changes are commonly seen on the ulcerated leg (Figure 2).

Arterial ulceration

Risk factors for occlusive peripheral vascular disease include age, male sex, smoking, dyslipidaemia, diabetes and hypertension. Multilevel arterial stenosis or occlusion may result in critical limb ischaemia and tissue loss. Although arterial ulceration is often seen on the foot (or involving the toes), more proximal leg ulcers may also be seen (Figure 3). Patients with a combination of arterial and venous disease present a unique challenge, as identification of the primary ulcer cause (and main therapeutic target) may be difficult. A combination of clinical, anatomical and haemodynamic assessments can be used to guide patient management. In general, the presence of multiple ulcers, ulcers with a well demarcated or ‘punched-out’ appearance or severely painful ulcers should raise the suspicion for an underlying arterial compromise.

Malignancy

Skin malignancies may present as chronic leg ulcers and should be considered in all ulcers with suspicious features (raised or rolled ulcer edges, exophytic appearance) or poor healing. Basal cell (60%) and squamous cell carcinomas (40%) account for the vast majority. Malignant transformation (squamous cell carcinoma) of chronic venous ulcers (Marjolin’s ulcer) is uncommon.



Figure 2 Typical venous leg ulcer with associated skin changes of chronic venous hypertension.



Figure 3 Leg ulceration in a patient with arterial compromise.

Other causes

Vasculitis, diabetes, rheumatoid arthritis and other systemic conditions (such as sickle cell disease or sarcoidosis) can cause leg ulceration and may be difficult to distinguish from venous ulcers. Biopsy of the ulcer edge for histological examination will usually provide accurate diagnosis of uncommon causes for leg ulceration.

Diagnosis

Clinical history and examination

The aims of clinical assessment are to determine:

- the aetiology of the ulceration
- other contributing factors that may delay healing
- the impact of the ulcer on the patient
- patient expectations from treatment.

A detailed history may provide key clues to the aetiology of the ulcer and should provide strong clinical suspicions to be confirmed by physical examination and appropriate investigations. A history of DVT or varicose veins may indicate chronic venous hypertension, whereas a history of smoking, diabetes, other risk factors or symptoms of peripheral vascular disease may be more suggestive of an arterial component. Advanced patient age, large ulcer size and long ulcer chronicity have been shown to be independent risk factors for delayed ulcer healing and may be useful prognostic indicators.⁵ Previous surgery, co-existing illnesses, medications and patient occupation may be important in planning treatment.

General clinical examination may reveal systemic illness or nutritional deficiencies contributing to poor wound healing. The ulcerated skin should be examined to identify the ulcer location, size, edges, signs of granulation and surrounding skin. Evidence of typical venous skin changes and a granulating ulcer in the medial gaiter area would be consistent with a chronic venous ulcer, whereas a painful punched-out ulcer in a limb with absent pulses may indicate an arterial cause. In order to monitor ulcer progression and response to treatment, ulcer assessment should include details of ulcer morphology, precise location and size. Ideally, serial photography should be used to evaluate clinical status.

Investigations

Ankle-brachial pressure index (ABPI): All patients with chronic leg ulceration should undergo ABPI assessment to

identify underlying arterial compromise (Figure 4). Significant arterial disease may be excluded if ABPI >0.85 , although falsely raised ankle pressures may be present due to calcification in the vessel wall. Although patients with ABPI <0.85 may have arterial compromise and require further specialist investigation or treatment, venous hypertension is the dominant aetiology in the majority of patients.

Colour venous duplex scan: uses a combination of Doppler and B-mode ultrasound to accurately map superficial and deep venous patency and competence in the ulcerated leg. This allows venous ‘mapping’ of the leg. Duplex is widely accepted as the investigation of choice to identify superficial venous reflux potentially amenable to surgery or endovenous intervention. Colour duplex scanning can also identify post-thrombotic scarring and occlusions in iliac and femoral veins.

Ulcer biopsy: As basal cell or squamous cell carcinoma may be a feature in up to 1% or more of chronic leg ulcers, wounds with a suspicious appearance or no evidence of healing after 3 months should be biopsied.⁶ Ulcer edge biopsy may also help identify ulcers due to vasculitis or diabetes, which may be difficult to distinguish from venous or arterial ulcers.

Other investigations: Tests of venous haemodynamic function are generally limited to research studies, but may be of benefit in some cases. Digital and air photoplethysmography techniques provide potentially useful haemodynamic assessments of venous function but are uncommonly utilized in routine clinical practice. Further arterial investigations such as colour duplex or angiography may be necessary where ABPI <0.85 or inconclusive (due to calcified vessels). Further specific investigations may be required in cases suspicious of vasculitis. With a dramatic recent increase in interest in deep venous occlusive disease, specific deep venous investigations such as magnetic resonance venography

(MRV), computerized tomogram venography (CTV) or invasive venography may be useful in some patients. However, the true prevalence of clinical significant venous outflow obstruction in patients with chronic leg ulceration remains unclear.

Management

Patients with chronic leg ulcers are best managed by specialist, multidisciplinary nurse-led teams, ideally bridging the gap between primary and secondary care services. With the regular development and introduction of new wound dressings and products, it is important to emphasize that treatments should be guided by evidence-based, nationally agreed protocols. A number of national and international guidelines have been published to guide the assessment and management of patients with chronic venous disease and ulceration.⁷

The primary aims of treatment are to correct the underlying cause of ulceration and address any exacerbating factors to promote rapid ulcer healing and reduce the risk ulcer recurrence. A multidisciplinary approach involving specialist nurses, vascular surgeons, rheumatologists, dieticians, dermatologists and other health professionals may be required.

Venous ulcers

General measures: Patients should be advised to elevate the limb where possible and continue regular exercise. Measures to stop smoking and improve nutrition may also be beneficial.

Compression therapy: Multilayer graduated compression bandaging applied by trained personnel (providing 40 mmHg of pressure at the ankle and 17–20 mmHg at the upper calf) is accepted as the mainstay of treatment for chronic venous ulceration. Numerous bandaging regimens including short stretch, multilayer systems and double-layered compression stockings have been advocated. A recent randomized trial demonstrated that two-layer hosiery offered similar healing rates to multilayer compression.⁸ In reality, compliance with compression therapy is poor and overstretched primary care nursing teams struggle to keep up with the growing demand of leg ulcer care. Once healed, patients should be advised to wear elastic stockings (class II) to reduce the risk of recurrent ulceration. Difficulty donning and removing stockings are common reasons cited for poor patient compliance and compliance is likely to be worse with higher degrees of compression.⁹

The importance of treating superficial reflux: Our understanding of the importance of treating superficial venous reflux for patients with chronic venous ulcers has increased in recent years. The ESCHAR venous ulcer trial demonstrated that traditional superficial venous surgery offered as an adjunct to compression therapy reduces venous ulcer recurrence.^{10,11} Minimally invasive endovenous interventions have revolutionized the management of patients with chronic venous disease. Endovenous thermal ablation (laser ablation, radiofrequency ablation)^{12,13} have been shown to provide comparable or superior technical success rates in the short and medium-term. Novel non-thermal modalities (cyanoacrylate glue closure and mechanochemical ablation) are exciting techniques, although medium and long-term data are scarce. Ultrasound-guided foam sclerotherapy perhaps represents



Figure 4 Ankle-brachial pressure index (ABPI) assessment.

the ‘least’ invasive endovenous intervention and has gained support from many experts as the treatment of choice in this population.¹⁴ One specific advantage of foam sclerotherapy is the ability to ablate the veins in the sub-ulcer plexus, which may have a key role in transmitting venous hypertension to the ulcerated area (Figure 5). As all of the endovenous ablation (either thermal or chemical) treatment modalities can be offered in an outpatient setting using only local (or no) anaesthesia, they are all likely to be more acceptable than open venous surgery to elderly patients with venous leg ulcers. The recently reported EVRA trial evaluated the role of early endovenous ablation of superficial reflux in patients with chronic venous ulceration. The 450-patient randomized study demonstrated that prompt endovenous ablation with compression therapy accelerated ulcer healing compared to a deferred ablation strategy.¹⁵ For the majority of patients with chronic venous ulceration, there is a strong rationale for early endovenous ablation of superficial reflux to improve ulcer healing and reduce recurrence risk.

Treatment of deep venous disease: There has been a significant increase in the popularity of deep venous stenting procedures in recent years. With the introduction of specific venous stents, promising technical success and patency rates have been reported. While the precise role of deep venous stenting in patients with leg ulcers remains unclear, there are undoubtedly some patients with significant (usually post-thrombotic) deep venous occlusive disease, who may benefit from these novel procedures. Further research is needed to help identify when anatomical occlusion equates to physiological venous outflow obstruction needing intervention.

Other treatments: Wound debridement may be useful in specific cases and can be performed with dressings, larvae or surgery. Healing of larger ulcers may be accelerated using pinch or meshed split skin grafting. The routine use of systemic antibiotics does not improve healing and antibiotic use should be limited to patients with cellulitis. Evidence supporting use of systemic medications or topical growth factors is lacking. Novel and



Figure 5 Ablation of the sub-ulcer venous plexus using ultrasound-guided foam sclerotherapy.

exciting recent developments include ‘spray-on skin’ technology (utilizing autologous dermal cells harvested and administered in a single outpatient visit) and dressings that can deliver topical oxygen. Although early reports have been encouraging, larger studies with long-term follow-up are eagerly awaited. Recent studies have failed to demonstrate a role for aspirin to promote venous ulcer healing.¹⁶

Arterial ulcers

Revascularization is usually indicated where arterial compromise is the primary cause of ulceration. This may be performed by endovascular intervention (angioplasty or stent) or revascularization surgery (endarterectomy or bypass). Management should include aggressive optimization of cardiovascular risk factors and careful diabetic control.

Mixed arterial/venous ulcers

The management of mixed arterial/venous leg ulcers is controversial and should be determined on an individual basis. The use of modified multilayer compression bandaging (25–30 mmHg at ankle) has been shown to be safe for patients with ABPIs between 0.5 and 0.85 within a specialist leg ulcer service with close vascular surgical support.¹⁷ However, patients should be advised to remove bandaging immediately if severe leg pain develops and intensive follow-up is essential in this high-risk group. Where modified compression is not tolerated, revascularization may be necessary to facilitate compression and permit ulcer healing. Careful and regular assessment by a specialist leg ulcer service is particularly important in these high-risk patients.

Other ulcers

Ulcers proven to be malignant on biopsy should be treated by surgical excision with adequate margins and may require skin grafting to facilitate healing. For patients with ulcers secondary to systemic illness (such as vasculitis or diabetes), treatment should aim to address the underlying condition. Adequate oedema control (possibly with compression therapy) is an important component of leg ulcer management, even when chronic venous hypertension is not the primary cause.

Challenges in managing chronic leg ulceration

Despite advances in our understanding of chronic leg ulceration, the management of this patient group remains sub-optimal. A number of studies have demonstrated the benefits of specialist nurse-led community leg ulcer clinics with close links between primary and secondary care services, but the model of leg ulcer care in the United Kingdom remains inconsistent. The majority of patients with leg ulcers are assessed and managed by community nursing staff, usually with appropriate compression bandaging. However, pathways for the assessment and treatment of superficial venous reflux are poorly defined, meaning that patients often do not receive intervention for superficial incompetence despite the unequivocal proven advantages. Despite a strong evidence base, implementation of best practice for patients with chronic leg ulcers is frequently poor. Better education of patients and relatives may improve engagement of the elderly frail population affected by chronic leg ulceration with healthcare services.

Unfortunately, the current NHS reimbursement and funding structure may act as a disincentive against greater involvement of

secondary care services in the management of these patients. Referrals for secondary care are often reserved for patients that fail to respond after many months (or years) of standard leg ulcer treatment. While this may appear to be a logical approach, ulcer chronicity is a major predictor of poor ulcer healing. Therefore, early identification of patients with risk factors of poor ulcer healing (which are well described) and referral for specialist secondary care (such as early treatment of superficial reflux) would seem a more effective approach. In fact, the importance of early endovenous ablation of superficial reflux was clearly demonstrated by the recent EVRA trial.¹⁵ There is a lack of high-profile national initiatives, guidelines or service frameworks for patients with chronic leg ulceration, reinforcing the widely held belief that this is an unglamorous condition affecting a largely elderly, uncomplaining and inconspicuous population.

Prognosis and explanation to patient

Venous ulcers

Healing: In the EVRA trial, 24-week ulcer healing rates were as high as 85.6%. However, 'real-world' healing rates are likely to be much lower. Patients may be advised that around 65% of venous ulcers treated with effective multilayer compression heal within 24 weeks, although reported healing rates range from 36% to 85%. Up to 20% of chronic venous ulcers may remain unhealed after 1 year, despite compression bandaging. Recognized risk factors for delayed healing include advanced patient age, ulcer chronicity and ulcer size.⁵ Scoring systems to predict the probability of healing for individual patients have been described, but are not in widespread use.

Recurrence: One-year venous ulcer recurrence rates as high as 69% have been reported. However, within the ESCHAR trial, recurrence rates for patients treated with compression and venous surgery were 12% at 1 year and 31% at 4 years. These were significantly lower than recurrence rates for patients treated with compression alone (28% at 1 year and 56% at 4 years).^{10,11}

Arterial ulcers

In patients with ulceration due to severe arterial compromise, healing rates are unlikely to exceed 50% despite an aggressive policy of revascularization as these patients are often unfit or unsuitable for arterial intervention.

Mixed arterial/venous ulcers

In a recent observational study, 36-week healing rates of 68% were achieved with modified compression therapy for patients with mixed arterial/venous ulcers and revascularization was performed in only 10% of patients. ◆

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