Venous Ulcers

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Abstract

This review summarizes current concepts regarding venous ulcers. Venous ulcers are the most common cause of leg ulceration in the western world. The pathophysiology, the mechanism of skin ulceration, and alterations in the healing process are still unknown. This article focuses on the epidemiology, pathophysiology, clinical features, complications, and treatment of venous ulcers.

Introduction

In the United States, chronic venous insufficiency (CVI) is the seventh leading cause of chronic debilitating disease.[1] More than 500,000 people have venous ulcers,[1] and the cost associated with four months of outpatient treatment for leg ulcers has been estimated to be as high as $2,500 per patient.[2,3]

During recent years there has been increased interest in the pathophysiology of venous ulcers with the development of more accurate diagnostic methods and new techniques in wound care.

Epidemiology

Leg ulcers are estimated to affect about two percent of the western population.[4] Venous ulcers are the leading cause of leg ulceration (75-90%),[5-7] and the long-term healing prognosis is poor compared to arterial and diabetic ulcers.[8]

Venous ulcers have traditionally been considered to occur more frequently in females (male:female 1:1.6)[11] and in the elderly. However, 40 percent of patients develop their first ulcer before the age of 50,9,10 and in a recent dual case control study more men were diagnosed with venous ulcers (male:female 1.4:1).[12] In one European study, venous ulceration was more common in lower social classes, but this has not been corroborated by other studies.[12-14]

About 50 percent of all patients with leg ulcers treat themselves.[4,6] In some cases, the care is provided by community nurses or primary care doctors.[10,15] A multidisciplinary approach with different medical specialists such as a dermatologists, vascular surgeons, plastic surgeons, and well-trained nurses has demonstrated increased healing rates with decreased recurrence.[15,16]
Pathophysiology

The venous system in the lower limb is composed of a superficial venous system, a deep venous system within the muscular fascia, and a connecting perforating system. The blood flows from the superficial to the deep system through the perforating veins upward toward the heart; valves impede reflux. Two major pumps propel the blood centrally: the cardiac pump and the muscle pump.

During muscle contraction (systole), the muscles exert high pressure on the deep venous system and milk the blood toward proximal veins. On muscle relaxation (diastole), the pressure falls in the deep system and blood flows from the superficial veins to the deep veins through the communicating veins due to pressure differences. One-way valves in the veins impede outward flow through the perforators during muscle systole and also prevent reflux during diastole.

The calf pump is the most important pump, but the thigh pumps (quadriceps muscle pump, sartorius pump, and hamstring muscle pump) and the foot pump also play roles in blood propulsion. The foot pump does not depend on muscle movements and works even in paralyzed limbs. The plantar veins are stretched during weight bearing, causing them to eject blood.

The venous circulation is a complex system. The integrity of the venous system depends on muscle function, valve competence, and the patient's veins.\(^2\)

Up to 40 to 50 percent of venous ulcers are caused by superficial venous insufficiency and/or perforating vein incompetence alone with normal deep vein.\(^6\) Fewer than 10 percent of venous ulcers are due to deep venous incompetence alone.\(^7\) In a small number of cases, there is obstruction of the deep veins rather than valvular incompetence.\(^8\) Other causes include arteriovenous fistulas, which can be congenital, secondary to trauma or surgery.\(^9,10\) Neuromuscular disorders or arthritis can affect calf muscle pump function. The end point of pump failure is the development of ambulatory venous hypertension that alters the microcirculation, causing ulceration.

The mechanism of skin ulceration is still unknown. There are several hypotheses; Browse and Burnard suggest that venous hypertension leads to capillary distention and leakage of macromolecules (fibrinogen) from the blood to the dermis. The fibrinogen polymerizes to form fibrin cuffs around the capillaries. These cuffs are postulated to act as barriers to oxygen diffusion and nutrient transport that ultimately lead to ulcers.\(^11\) The "trap" hypothesis suggests that other macromolecules leaking into the dermis bind growth factors and matrix materials making them unavailable for tissue repair.\(^12\) The white cell trapping hypothesis suggests that raised venous pressure leads to endothelial cell damage and white cell trapping and activation, releasing proteolytic enzymes, cytokines, and toxic oxygen metabolites that result in damage to the capillaries with leaking of fibrinogen and fibrin deposition.\(^13\) However, none of these hypotheses completely explain the mechanisms of venous ulceration and more research is needed.

Other interesting findings in patients with venous ulcers are increased blood flow in the skin, low TcPO\(_2\), and elevated venous PO\(_2\), which could be explained by the presence of arterio-venous anastomoses (AVA), causing skin hypoxia.\(^14\) Diminished mononuclear cell proliferation in response to mitogens has been found in patients with lipodermatosclerosis, active venous ulcers, and CVI. This could explain the ulceration and the poor healing response present in patients with CVI, as monocyte proliferation is needed for cytokine production, which regulates epidermal regeneration, extracellular matrix production, and tissue repair.\(^15\)

The lymphatic circulation is also abnormal in patients with venous ulcers; the lymphatic vessels are fibrotic and lymphatic drainage is impaired.\(^16\) Alterations in coagulation and fibrinolytic mechanisms have been found in some patients, as well as low levels of protein C, elevated plasma fibrinogen levels, and fibrinolytic products, suggesting an increase in the formation and breakdown of
fibrin. It is not known whether coagulation and fibrinolytic alterations are primary or secondary.[27]

Clinical Features

Obesity, history of leg injury, deep venous thrombosis, and family history of varicose veins are risk factors associated with venous ulcers.[12]

Symptomatically, many patients experience aching discomfort, heaviness, and swelling in the lower limbs that worsen with dependency and as the day progresses. Pain often subsides with leg elevation. Although severe pain has been considered uncommon, in a prospective study of 140 patients with venous ulcers, 64 percent of the patients presented with severe pain, which did not necessarily indicate arterial disease or infection.[24]

The typical location for venous ulcers is the medial malleolus, but lateral and tibial locations can also occur.[29] Ninety-five percent of venous ulcers are located in the gaiter area, between the lower calf and inframalleolar area. Pitting edema of the legs is initially present at the end of the day and later becomes persistent. The skin may have a "woody" consistency (lipodermatosclerosis).[7,29] Lipodermatosclerosis usually starts around the ankle, but can involve the entire lower leg resulting in an "inverted champagne bottle" or "inverted piano leg" appearance. Acute lipodermatosclerosis is a very painful condition that can be misdiagnosed as cellulitis. Sometimes acute lipodermatosclerosis is diagnosed after the "cellulitis" fails to respond to antibiotics.[30]

Varicose veins and telangiectasia may be present in patients with chronic venous insufficiency. Ochre or red-brown pigmentation caused by hemosiderin deposits in the dermis secondary to red blood cell extravasation and post inflammatory hyperpigmentation can also occur (Figure 1). Areas of white sclerotic tissue studded with capillaries (atrophie blanche) may be seen. Ulcers in these areas are often very painful.

The venous ulcer characteristically has irregular borders and the ulcer bed is covered with yellowish fibrinous or red granulation tissue (Figure 2).[7,29]

In all venous ulcer patients, a full history and physical exam should be performed to exclude other causes of leg ulcers or concomitant medical conditions.

Up to 25 percent of patients with venous ulcers also have arterial insufficiency.[31] It is important to measure the ankle-brachial pressure index in all patients by Doppler ultrasound to rule out concomitant arterial disease, as necrosis and gangrene have occurred after compression therapy in patients with undiagnosed arterial insufficiency.[29,31] To perform this test, the patient should be supine with the legs at the level of the heart, the hip in external rotation and the knee slightly flexed. The Doppler probe should be place on the artery (dorsal pedis or posterior tibial) at a 45 degree angle. A cuff is placed around the calf and inflated 20 to 30mm Hg beyond the point where sound disappears. The systolic blood pressure at the brachial artery is then measured.

The ratio between ankle pressure and blood pressure should be greater or equal to 1. An ankle-brachial index (ABI) lower than 0.7 indicates severe arterial disease. A BI greater than 1.3 is suggestive of noncompressible arteries (found in patients with diabetes or end-stage renal insufficiency).[32]

Complications

In venous ulceration, the periwound skin is often eczematous presenting with erythema, scaling, weeping, and crusting with intense pruritus due to venous eczema or contact dermatitis. Frequent contact allergens include topical antibiotics (neomycin, bacitracin), wool fat (lanolin), and adhesives and preservatives (parabens), which are present in many moisturizers and dressings.[4]
Bacterial infections are common in leg ulcers; clinical signs include pain or tenderness, increased drainage, changes in the odor and wound color (black, green, etc.), spreading erythema, poor quality granulation tissue, and failure to heal. Ideally, tissue samples for bacterial culture should be taken by curetting or taking a biopsy of the wound bed. Alternatively, wound fluid can be expressed from the wound borders after rinsing the wound thoroughly with saline solution. A positive wound culture alone does not signify infection. Most ulcers are colonized with bacteria (colonization is the presence of bacterial growth without host response), and bacteria grown from the wound surface may not be representative of the pathogens present in the wound tissue. Some authors suggest that quantitative cultures of tissue or wound fluid with greater than 10^5 bacteria/gram of tissue or millimeter of wound fluid indicate wound infection. Common pathogens causing cellulitis include *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and beta-hemolytic streptococcus.

The presence of large numbers of microorganisms without clinical signs of infection might influence ulcer healing, but this issue is still debated. The eradication of beta-hemolytic streptococci from leg ulcers has been recommended by some authors.

Topical antibiotics should be avoided in venous ulcers due to the high risk of sensitization and increased risk of bacterial resistance. Oral antibiotics should be used for at least 10 days according to sensitivity results when possible. If possible, broad spectrum antibiotics should be avoided since resistant strains can readily develop.

Candidal infections can occur when occlusive dressings are used on chronic wounds. Clinically, candidiasis presents as intense erythema, fragile pustules, and denuded areas.

**Diagnosis**

Using clinical criteria alone, the accuracy in the diagnosis of venous ulceration will be at most 76 percent. For this reason, noninvasive methods are needed for accurate diagnosis and anatomical and functional evaluation.

Color duplex ultrasound scanning is the current gold standard in evaluating venous anatomy and physiology. Other methods include Doppler ultrasound (can be difficult to differentiate superficial from deep venous insufficiency) and air and photo plethysmography (to assess venous reflux, venous-pump function, and potential venous obstruction). Venography is generally reserved for investigation prior to valvular surgery.

**Treatment**

The presence of lipodermatosclerosis, the duration and initial area of the ulcer, age of the patient, deep venous malfunction, and poor mobility are risks for poor healing.

In venous ulceration, compression is the most crucial part of treatment. It facilitates wound healing, reduces venous dermatitis, improves lipodermatosclerosis, and counteracts venous hypertension (Table 1). An external pressure of 35 to 40 mm Hg at the ankle is theoretically required to prevent capillary transudation in legs with venous insufficiency.

There are a number of methods to reduce edema: elastic bandages, Unna's boots, four-layer compression bandages, compression stockings, compression pumps, and orthotic devices (Figures 3 and 4). Insufficient randomized controlled studies have been done to indicate which system is most effective. Patient compliance and ability to apply the device should be considered when
compression is prescribed. Types of compression and their advantages and disadvantages are listed in Table 2. Types of compression stockings are listed in Table 3. Clinical classifications of chronic lower extremity venous disease are listed in Table 4. Compression therapy is contraindicated in arterial disease and it is important to advise the patient to remove compression if there is numbness, increased pain, tingling, or cyanosis of the toes.

Some patients benefit from surgery. Arterial surgery may be indicated in patients with mixed arterial/venous ulcers. It has been confirmed that up to half of all venous ulcers are caused by superficial venous disease. In these patients, surgery has been reported to be curative and prevent recurrence.[44, 47, 49-51] Also, some authors have reported ligation of incompetent perforating veins to be effective in patients with recalcitrant ulcers,[52] but more studies are needed to evaluate nonoperative compared to operative treatments.[50]

Venous eczema improves with adequate compression, moisturizers (petrolatum jelly), and use of topical corticosteroids. Low and mild potency steroids ideally should be used in an ointment base for short periods of time (two weeks) to improve the pruritus and the eczema. If acute dermatitis is present with oozing and weeping, a corticosteroid cream is helpful. Contact dermatitis should be suspected in cases of eczema that do not respond to treatment. In these cases, all topical products should be discontinued and patch tests performed. It is possible that the patient has developed contact dermatitis to the topical steroids.

No dressing of any type has been proven to enhance the healing rate of venous ulcers.[53, 54] However, moist wound dressings have the advantage of relieving pain, debriding necrotic tissue, promoting granulation tissue, and decreasing the cost of wound care. Dressing selection should be based on the status of the wound bed and surrounding skin, the amount of exudate, ulcer depth, and patient compliance.[55] Maceration of the surrounding skin is common due to excess exudate; zinc oxide paste can be applied around the wound to protect the skin. Dressing changes should be minimized to prevent disruption of newly formed epithelial tissue.

Surgical approaches with excision of the ulcer and surrounding liposclerotic tissue and replacement with a free flap has advantages over skin grafting, such as increasing the blood supply to the areas and lower incidence of recurrence.[56] Pinch grafting, keratinocytes grafting, fibrinolytic agents, and allogeneic cultured human skin equivalent have also been used.[56] High doses of pentoxifylline (800mg tid) has shown to accelerate the healing of venous ulcers.[60]

After the ulcer heals, the patient should continue with compression stockings and follow up visits. Ulcer recurrence rates are compliance-related and with the best nonoperative therapy range from 15 to 50 percent or more over intervals of five years.[49, 53] Unfortunately, the cost of the stockings is a major reason for noncompliance.[58, 59]

Patient education regarding skin care, leg elevation at least two hours a day, calf exercises, diet, and compression therapy compliance are essential for successful therapy.

Conclusion

Venous ulceration is the most common cause of leg ulcers. It is a chronic and debilitating condition with a high rate of recurrence. Compression therapy continues to be the cornerstone of the treatment.

References

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