Management Of Leg Ulcers

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Abstract

In the United States, leg ulcers present a significant clinical problem, occurring at a rate of approximately 600,000 new cases per year. (1) The most common types are venous, arterial, and neuropathic ulcers. Venous hypertension is the primary culprit in venous ulcerations. Peripheral vascular disease due to atherosclerosis with microvascular or macrovascular changes leads to ischemic ulcers. Sensory impairment with loss of protective sensation in the foot and repetitive trauma lead to neuropathic ulcers. Unusual causes of leg ulcers must be considered in the differential diagnosis. To arrive at the diagnosis, the clinician must perform a thorough history and physical examination, and order relevant investigative studies. Good management of chronic leg ulcers depends on correction of identified underlying conditions, long-term multidisciplinary care effort, and integrating traditional and new wound-healing technologies. Most patients with chronic leg ulcers benefit from the use of compression bandaging at a level appropriate to their vascular status. Venous ulcers must be managed with an arsenal of strategies to control venous insufficiency, heal the wound, and prevent recurrence. Surgery with revascularization remains the treatment of choice for chronic ischemic leg ulcers. In the absence of vascular compromise, up to 90 percent of neuropathic ulcers will heal with proper ulcer debridement, treatment of infection, saline wet-to-dry dressings, and relief of weight from the ulcerated area. The available armamentarium for wound care includes over 2000 wound dressing products and elastic compression wraps. Chronic leg ulcer treatment options have been expanded by alternatives available to treating these wounds. These alternatives include hyperbaric oxygen therapy, bioengineered skin substitutes, recombinant platelet-derived growth factors and vacuum assisted wound closure. Patients with large leg ulcers may benefit from skin grafting. Other patients may benefit from ligation and stripping of superficial veins or subfascial interruption of perforating veins.

MANAGEMENT

In the last few years there have been many new wound dressings, topical products, and skin equivalents made available. It is necessary to tailor wound care plan to the etiology of the ulcer. The use of cost-effective methods is strongly recommended for long term treatment plans. ([24])

VENOUS ULCER MANAGEMENT

Venous ulcers should be debrided of necrotic and fibrinous material to allow a healthy granulation tissue to develop. (Picture 6) In the absence of apparent local wound infection, antibiotics seem to have little effect in treating venous ulcers. Although povidone-iodine, acetic acid, sodium hypochlorite, and hydrogen peroxide have been shown to be toxic to cultured fibroblasts, they are helpful and remain in use. ([25]) At concentrations that preserve fibroblast function these products can be used as debriding and topical antibacterial agents. ([26]) Moistened saline gauzes may be appropriate for initial management of all types of leg ulcers but moisture retentive dressings are preferred. The latter help debride necrotic tissue, relieve pain and reduce the frequency of dressing change. ([27]) They also are more cost-effective. (24)

Figure 1

Picture 6: Wound debridement with a curette

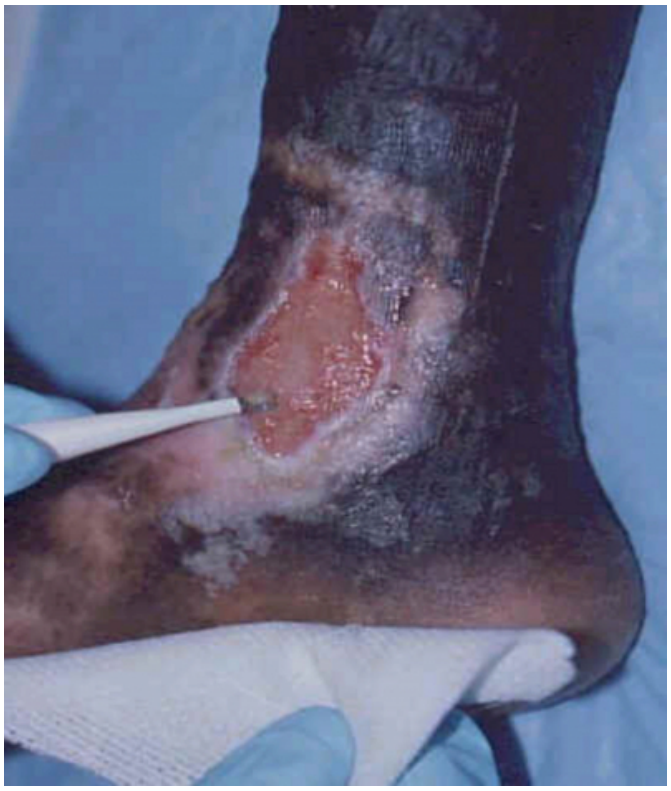
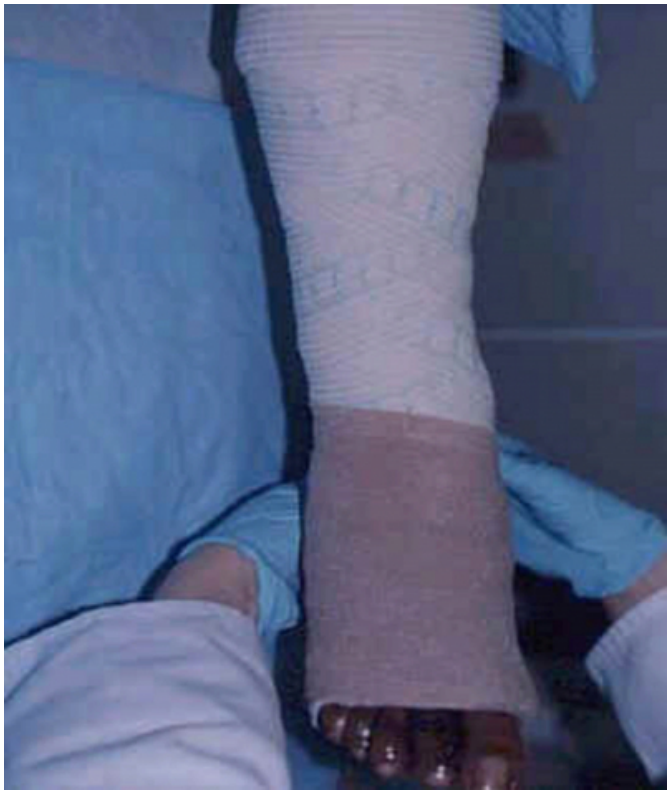


Figure 2

Picture 7: Application of a multilayer compression system



Patients with venous insufficiency are advised to elevate their legs above the heart level while sleeping, and to avoid standing for long periods. The mainstay of venous ulcer management is compression to achieve an external pressure between 30-40 mm Hg at the ankle, this is required to prevent capillary transudate. For compression bandaging to be safely applied the ankle brachial pressure index must be at least 0.8. (16,25) The bandages should be changed once or twice a week. A summary of common compression systems is included in Table 3.

The healing rate depends on the initial size of the ulcer, but 65-70% of venous ulcers heal within six months. (16) The five-year recurrence rate of healed venous ulcers can be as high as 40%. Other predictive factors for venous ulcer healing include duration of the ulcer, size, a fibrinous ulcer bed, the presence of lipodermatosclerosis, along with history of venous surgery, hip or knee replacement, and ankle brachial pressure index of less than 0.8. ($_{28}$) Surgery to correct superficial venous incompetence, as well as the ligation of incompetent perforating veins may be beneficial, curative, and may prevent recurrence. (16) At the present time, venous surgery should be reserved for patients who fail to respond to conservative treatment measures and who are adherent to medical treatment. In patients with healed ulcers who have not had surgery, the mainstay of preventing recurrence is graduated elastic compression stockings.

ARTERIAL ULCER MANAGEMENT

In daily wound care a sharp wound debridement is not recommended. Compression therapy is contraindicated in arterial disease. The mainstay of treatment of arterial leg ulcers is surgical. The aim is to restore blood supply to compromised limbs. An optimal control of associated predisposing factors, such as hyperlipidemia, hypertension, and diabetes, as well as smoking cessation and an exercise program should be included in the management plan.

NEUROPATHIC ULCER MANAGEMENT

The goal of wound dressings is to provide a warm, moist environment that is free of external contamination. Saline wet-to-dry dressings and several types of commercially available occlusive dressings (eg, hydrocolloids, alginates, foams, and films) are effective. However, none is ideal for every situation.

Various growth factors show promise. Becaplermin (Regranex), a recombinant human platelet-derived growth factor formulated into a gel, increases the incidence of and

decreases the time needed for complete wound closure. All dressings and other wound care products are only adjuncts to careful local treatment measures, including reduction of pressure, sharp debridement of damaged tissues and control of infection. (7)

Restoration or optimization of blood supply, treatment of any active infection, and protection of the ulcerated areas should also be an integral part of the management. Off-loading the foot often requires the use of a protective plaster boot with a window cut out at the site of the ulcer. After complete healing of the wound, patients should be fitted with footwear designed to minimize trauma and protect bony prominences.

Patient education about avoiding leg and foot problems is important in preventing recurrence after ulcer closure.

LEG ULCER TREATMENT MODALITIES

DRESSINGS

Over 2000 types of dressings are available. See table 4 for a summary.

Figure 3

Table 4: Selected dressings and some of their properties

Dressing types	Brand names	Dressing properties	Indications for use according to ulcer characteristics					
			Mild exudate	Moderate exudate	Heavy exudate	Dry necrotic	Clean wound	Superficial granulating
Films	Bioclusive Opsite Polyskin Tegaderm	Adhesive, thin, transparent, impermeable.	+				+	
Hydrocolloids	Comfeel Curaderm Duoderm Cutinova	Adhesive, waterproof, hydrophilic, promote granulation tissue formation.	+	+				
Foams	Hydrosorb Allevyn Curafoam Lyofoam	Highly absorbent, soft, opaque, adhesive or non-adhesive, helpful in cushioning bony prominences.		+	+			
Hydrogels	Curagel Vigilon Hypergel Elastogel	Available in gels or thin sheets, help breakdown of necrotic tissue by autolytic debridement.				+		
Alginates	Kaltostat Sorbsan Algisorb Dermacea	Absorbant, biodegradable, derived from seaweed		+	+			
Collagen dressings	Fibracol Medifil Nugel	Provide a collagen matrix for cellular migration.					+	
Hydrofibers	Aquacel	Pads or ribbon dressings, form a soft gel that maintain moist environment.	+	+				
Hydropolymers	Tielle	The absorbant material is a synthetic material. It can be molded around awkward areas.						+
Super-absorbents	ConvaDerm Polymen	Highly absorbant, may be used under Unna boot with a weekly dressing change.		+	+			

PENTOXIFYLLINE

Pentoxifylline is FDA approved for the treatment of intermittent claudication. Its use in venous leg ulcers was evaluated. Pentoxifylline 800 mg three times a day appears to be an effective adjuvant to compression bandaging for treating venous leg ulcers.([29])

CILOSTAZOL (PLETAL)

Cilostazol was approved by the FDA in 1999 to treat intermittent claudication but not for the treatment of leg ulcers. It is a type 3 phosphodiesterase inhibitor. In 4 randomized placebo controlled studies enrolling 1534 patients with claudication Cilostazol 100 mg twice daily was found to improve both pain-free and maximal treadmill walking distance. ([30])

HORSE-CHESTNUT SEED EXTRACT (HCSE)

Bielanski ([31]) reviewed 16 randomized controlled trials using HCSE in the treatment of chronic venous insufficiency (CVI). A total of 1083 patients were included. Of these trials, 8 were placebo controlled, and 5 compared HCSE with a reference medication. None of the studies evaluated HCSE effect on venous ulcers. The studies were all short term, ranging from 2 to 12 weeks in duration. The authors concluded that HCSE may have some effect in reducing short-term symptoms of CVI, but further well-designed studies of longer duration are necessary to answer this question.

HYPERBARIC OXYGEN (HBO)

HBO was first used to assist wound healing in 1965. Many of its past uses had little or no scientific support. Hypoxic tissue, reperfusion injury, compartment syndrome, crush injury, failing flaps, burns and necrotizing infections have all been shown to respond favorably to HBO. It is used for chronic wounds, especially diabetic foot infections and leg ulcers caused by arterial insufficiency, more than for any other indication.

HBO-- 100 percent oxygen at two to three times the atmospheric pressure at sea level -- can result in arterial oxygen tension in excess of 2000 mm Hg, and oxygen tension in tissue of almost 400 mm Hg. HBO treatments at 2.0 to 2.5 atmospheres for 90 to 120 minutes are used.

There is controversy in the literature about convincing evidence of HBO's beneficial effect on healing of chronic leg ulcers. In 1999 the American Diabetes Association stated, "There are no randomized controlled trials to support the use of hyperbaric oxygen therapy to treat neuropathic diabetic foot wounds". (7) HBO is a relatively expensive treatment modality. It is considered unnecessary in simple,

well-perfused wounds, but can be used successfully in hypoxic or ischemic wounds. London et al. (16) suggested that HBO should not be considered as treatment for lower leg ulcerations.

VACUUM-ASSISTED CLOSURE (VAC)

The FDA recently approved VAC, an innovative technique using negative pressure, for closure of chronic wounds. The technique consists in placing an open-cell foam dressing into the wound cavity and applying a controlled subatmospheric pressure (typically 125mm Hg below ambient pressure). This will remove chronic edema, and leads to increased localized blood flow resulting in enhanced formation of granulation tissue. Small studies with a total of 34 participants provide weak evidence suggesting that VAC may be superior to saline gauze dressings in healing chronic wounds. ([32]) The VAC may be used as an adjunct treatment for chronic, nonhealing wounds, especially those that are deep and complicated.

SURGERY

Surgical treatment to correct venous hypertension or treating the ulcer itself by skin grafting is one treatment of many that could be used. Other surgical procedures include superficial stripping and excision of varices, subfascial perforating vein interruption, excision and skin grafting, excision and free flap coverage.

OTHER TREATMENT OPTIONS

There are many types of grafts and skin substitutes available; a summary of the most common types is included in Table 5.

Figure 4

Table 5: Selected grafts and skin substitutes and some of their characteristics.

Type	Characteristics
• **Autologous Split-Thickness Grafts (STSG)**	Immediately available for use on chronic ulcers. Need for donor site.
• **Cadaveric allograft**	Immediately available. Risk of rejection or disease transmission.
• **Epidermal skin substitutes**	Fragile, no dermal substitutes. Help relieve the pain upon application to the ulcer.
1. Cultured Keratinocyte Autografts (Epicel)	Need biopsy from patient.
2. Cultured Keratinocyte Allografts	Not commercially available. May be cryopreserved and stored.
• **Dermal Skin substitutes**	Immediately available.
1. Human Cryopreserved allograft skin	Temporary coverage of the wound.
2. Human allograft skin treated (Alloderm)	Allows ultrathin split-thickness skin graft.
3. Bovine collagen and chondroitin sulfate (Integra)	Susceptible to infection. Require wound excision before application.
• **Composite (epidermal and dermal) skin substitutes**	
1. Apligraf (bilayered skin equivalent)	Limited shelf life (5 days) Expensive.
2. Collagen-glycosaminoglycan substrate with fibroblasts and keratinocyte layer	Easily handled. Limited quantity.

SKIN GRAFTS

Pinch grafts may be performed as an outpatient procedure in patients with small ulcers. Small punch biopsies are taken from the patient's thigh and placed dermal side down on the ulcer bed. Split thickness graft is used for large ulcers. The graft may be meshed to avoid build-up of exudate underneath it. This procedure requires anesthesia and has the disadvantage of creating a new donor site ulcer.

APLIGRAF (GRAFTSKIN)

Apligraf is a bi-layered viable skin construct manufactured using neonatal foreskin keratinocytes and fibroblasts with bovine type I collagen. It was approved by the FDA for treatment of hard to heal leg venous ulcers, and for diabetic foot ulcers. ([33]) In a multicenter, randomized, controlled clinical trial, Apligraf has been shown to be safe and effective. It achieved more cases of complete venous ulcer closure faster than standard compression therapy alone. In a recent prospective randomized multicenter trial involving 208 patients with diabetic foot ulcers Veves et al. ([34]) concluded that application of Apligraf for a maximum of 4 weeks resulted in a higher healing rate compared to saline moistened gauzes (standard of care). Prior to Apligraf

application to a wound, the ulcer bed preparation should be performed. This involves debridement and control of infection.

OASIS

Oasis, an FDA approved product, is used for wound management. It is a small submucosal derivate of pig intestine biomaterial, with an intact extracellular matrix; it provides a three-dimensional scaffold for remodeling to enable host cells to incorporate. It is biocompatible, acellular, has an extended shelf life, and does not require refrigeration.

OTHER METHODS USED IN WOUND CLOSURE

Cultured keratinocyte allografts could be grown in advance, cryopreserved, and stored. They provide rapid coverage of wounds. Keratinocyte allografts represent “off-the-shelf” skin replacements which avoid both the need for a patient donor site and the delay required for autologous keratinocyte culture. The chief action of keratinocyte allografts is probably cytokine-mediated. Keratinocyte allografts were used for donor sites, and partial-thickness burns. These allografts are being used as adjunct treatment for selected chronic leg ulcers, but they are not yet commercially available.([35])

Other methods of wound closure include infrared UV, low energy and laser irradiation, ultrasonography, electrical stimulation, and hydrotherapy. Constant tension approximation (a technique that applies constant-tension traction to wounds), and warming therapy with heat bandages, as well as many other growth factors have been used.

CONCLUSION

Leg ulcers are very common and physicians should be familiar with the common methods used for their diagnosis and management. Some laboratory investigations may be helpful and can be ordered as part of the baseline work up. Unusual leg ulcers need more specific tests. An extensive armamentarium of wound care products is available. Surgical repair techniques and a number of skin-substitutes are available for optimum management. A wound-healing specialist should be consulted for atypical and difficult to heal leg ulcers. More information about chronic leg ulcers can be found at: Diagnosis of Leg Ulcer, The Internet Journal of Dermatology, Volume 1 Number 2, 2002.

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