

Leg Ulcers In Older People: A Review Of Management

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Abstract

Leg ulcers are a common presentation in the elderly population associated with a negative impact in the quality of life. Several factors including venous and arterial insufficiency, immobility and obesity all contribute to an increased incidence in this age group. A thorough assessment including comprehensive history of ulcer development, examination of the ulcer site, size, shape, appearance and vascular assessment with Doppler ultrasound are all essential in deciding type of treatment. Various treatment modalities are available for the management of different types of leg ulcers although no clinical trials comparing the efficacy of one treatment over the other have been done. Some of them have not got strong evidence to show that they actually improve healing, still awaiting further research.

Introduction

Leg ulcers are defined as discontinuity of the epidermis and dermis in the lower limb of more than 6 weeks duration^{1, 2}. They are a common presentation in the elderly population and are associated with a negative impact on the quality of life of patients and they also cause a substantial burden on the health budget³. Pathogenesis of leg ulceration is heterogeneous⁴. Prevention strategies, early identification and proper management are paramount in improving quality of life of patients and reducing costs on an already strained health budget. In this article we review the prevalence of leg ulcers in the elderly people, its common causes and management.

Prevalence

The estimated prevalence of leg ulcers in the UK is between 1.5 and 3 per 1,000 population³. A study by Moffat et al 2004 showed a prevalence of 0.45 per 1000 which is less than the previously reported figures⁵. In the same study leg ulceration was found to be more common in females than males⁵. In a systematic review of prevalence studies for leg ulcer, the authors also reported an increase in prevalence of leg ulcers with age and in women⁶. The overall prevalence of ulcers is not affected by social class although ulcers tend to take longer to heal in lower socio economic classes⁷.

Quality of life

Several studies have shown that patients with leg ulcers have a poor quality of life compared to age matched controls^{8, 9}. A systematic review of studies measuring quality of life of patients with leg ulcers showed a negative impact on several domains of quality of life⁸. In most of the studies pain was shown to be the major complaint among leg ulcer patients compared to controls, with males experiencing greater pain intensity than female patients.^{10, 11} Restricted mobility and sleep disturbance due to pain was also reported in other studies.¹²

Leg ulcer patients often complain of itchiness, odour and leg swelling⁸. In one study, unpleasant odour was reported as causing social embarrassment leading to higher anxiety and depression scores as well as altered body image¹². Reduced mobility due to leg ulceration can restrict working capacity in younger patients¹³. A negative emotional impact on life with symptoms such as anger, depression, and social isolation was reported by 68% of patients in another study looking at impact of leg ulcers on quality of life¹⁴.

Aetiology

Several factors contribute to the development of leg ulcers. However majority of ulcers are due to venous insufficiency which accounts for about 80-85% of

all cases.^{15, 16} Frequency of venous ulcers increases with age as a result of several factors such as immobility and venous disease¹⁵. Other risk factors for venous ulceration include obesity, previous deep vein thrombosis, thrombophlebitis, previous fracture, and varicose veins¹⁷. Venous ulcers (also referred to as varicose or stasis ulcer) are commonly found between the malleoli and lower calf and are associated with a shallow base covered with granulation tissue and fibrinoid material, and have irregular margins^{16,17}. The mechanism of venous ulceration involves initial damage to valves as a result of thrombosis or valve incompetence in varicose veins leading to pooling of blood in lower limbs. Extravasation of red blood cells then follows which causes a local inflammatory reaction and collagen deposition. This impairs the healing process eventually resulting in tissue breakdown and hence ulceration¹⁶. Venous ulcers are also associated with symptoms such as oedema, eczema.

Arterial ulcers form the second largest group of leg ulcers and account for about 20% of leg ulcers. Atherosclerosis and diabetes are the commonest causes of this group of ulcers. Thrombotic episodes secondary to vasculitis, thromboangitis, and sickle cell disease can also result in arterial ulcers¹⁷. Arterial insufficiency causes hypoxia, ischaemia, tissue necrosis and consequently ulceration¹⁸. Arterial ulcers are usually found below the ankle especially on the toes. The ulcers are characteristically small, have steep edges and a dry base. Risk factors for arterial ulcers include conditions that predispose to peripheral vascular disease such as smoking, diabetes, hypertension, hyperlipidaemia and obesity¹⁷.

It is worth mentioning that diabetes causes foot ulcers via two mechanisms: ischemia and neuropathy. Neuropathic ulcers are usually found on the plantar surface of metatarsal heads or on the toes. They are a consequence of poor glycaemic control¹⁹. The risk of malignancy in chronic leg ulcers is generally believed to be small, but a study by Yang et al 1997 showed a rate of 4.4% in chronic leg ulcers.

The diagnosis should be considered in patients with non healing ulcers despite optimum management²⁰. Chronic inflammatory conditions such as rheumatoid arthritis, inflammatory bowel diseases are also associated with leg ulceration. Rare causes of leg ulceration such as ill fitting shoes have also been

reported in literature. In a study looking at complications of ill fitting footwear among 65 elderly patients, foot ulceration was reported by 15% of the patients²¹. Although small, this study showed that simple measures such as appropriate foot wear may be useful in preventing foot ulcers.

Table 1: summarises causes of ulcers and main characteristics of leg ulcers^{16, 17}

Aetiology of ulcer	Characteristics
Venous	Between malleoli and lower calf, shallow, irregular margins, granulation base. Oedema, eczema
Arterial	Painful, below ankle distal, especially toes, small, dry base Intermittent claudication
Vasculitis	Associated with Rheumatoid arthritis, Polyarthritis Nodosa(PAN)
Malignancy	Basal cell, squamous cell carcinoma, melanoma
Neuropathic	Common in diabetes, wet, deep, sharp borders on pressure points

Management

Like all medical conditions, management of leg ulcer should include a detailed history of the onset of the problem (as well as past medical history), examination of the legs and skin, investigations and modalities of treatments. The underlying causes need to be identified as this has crucial implications for management. A medical history suggestive of venous and arterial ulcers have been mentioned above but other factors to consider while assessing leg ulcer are: general health status, cigarette smoking, nutrition, limitation to self care, pedal pulses, Ankle Brachial Pressure Index (ABPI), oedema, limb size and shape, sensation and pain (Table 2).

Examination of the legs and skin identifies markers of underlying pathology. Venous disease may present with some or all of the following: brawny skin, haemosiderin staining, lipodermatosclerosis, atrophie blanche (patchy areas of ischemia), and stasis eczema, while the skin of patients with arterial disease is often shiny, hairless, pale and cool; with thickened nails and changes in foot structure. The absence of venous or arterial signs and symptoms raises the possibility of less common causes of ulceration like: Sun damaged skin, Bowen disease or a history of previous skin cancer treatment is an alert to a malignant lesion.

Table 2: Assessment of lower limb ulcers

Patient	History of ulcer development Past and current medical problems General health status Nutrition Social, occupation Mobility problems Limitation to self care Obesity Depression
Skin changes	Venous Arterial Malignant Auto immune
Vascular assessment	Pedal pulses Ankle Brachial Pressure Index
Limb factors	Oedema Circumferences Lymphoedema Orthopaedic problems Sensation and pain
Ulcer	Site Appearance Size-measure Wound base Exudate level Surrounding skin

Site & Appearance: Most venous ulcer occur in the “gaiter” area of the leg (i.e. area extending from just above the ankle to below the knee and tends to occur on both lateral and medial aspect of the leg), they are usually superficial with poorly defined margins. The base of the wound is usually red granulation tissue with moderate to high levels of exudates.

Arterial ulcers can occur anywhere on the lower leg and may appear in the gaiter region, especially with coexisting venous disease. Many arterial/ischaemic ulcers occur over bony prominences and have a history of pressure related cause. They are often deeper with a punched out appearance and may involve structures such as muscles, tendon and bone in the base. They have sloughy, devitalized tissue in the wound base and low levels of wound exudates. Ulcers occurring in atypical site with an atypical appearance require further investigation to determine the cause. Ulcers with a violaceous (purple) border, inflammation, and extreme pain, may be related to vasculitis problem or underlying connective tissue disorder.

Size: Dimensions of the ulcer should be taken at first presentation and fortnightly thereafter and recorded in the notes. This is important as it gives

an objective assessment of the effectiveness of the current treatment plan, and modify as necessary²². There are a range of techniques available such as digital photography, ruler based vertical, horizontal and depth measurements and circumferential tracings of wound margins using acetate sheets over cling film. The system chosen needs to reflect consistency, accuracy, and reduced operator error, and also provide visual feedback to the patient.

Pain: The level of pain associated with ulcer must be assessed on presentation and at each visit thereafter using a standardized pain scale (0-10). Pain may suggest infection or arterial disease, so careful assessment is required.

Surrounding skin area should be observed for the presence of eczema, hyperkeratosis skin, maceration, cellulitis, signs of irritation and scratching which are signs and symptoms associated with underlying venous disease.

Assessment should also include palpation of peripheral pulses, regular blood pressure measurement, weight (with reference to a Body Mass Index chart) as well as routine urinalysis (to screen for diabetes).

Vascular Assessment: This is mainly carried out by the use of Doppler ultrasound to measure the Ankle Brachial Pressure Index (ABPI). This is mandatory and must be repeated every 3 months. All patients with a non healing wound on the leg of greater than 4-6 weeks should have a vascular assessment to eliminate any underlying ischaemic disease²². The result of ABPI are used to determine the likelihood of arterial insufficiency and can be used to guide the management plan, especially in relation to healing potential, referral for vascular assessment and use of appropriate compression bandages.²³ The normal range for ABPI is 0.8-1.2. An ABPI of less than 0.5 or greater than 1.2 needs vascular opinion.

Treating the ulcer

Many dressing materials are available for the treatment of leg ulcers and there is no adequate evidence from clinical trials to recommend one dressing type over another, but we have to bear in mind few criteria in choosing a particular dressing. The dressing should be low adherent, cost effective and must also be comfortable as well as acceptable for the service user. The choice of product should be

determined by the level of exudate. Products which commonly cause skin sensitivity such as those containing lanolin and topical antibiotics should not be used on any service user²².

The use of white soft paraffin has been identified as a potential fire hazard risk, hence a water based emollient should be considered as an alternative to a paraffin emollients e.g aqueous cream. Please note water based emollients are not as effective in providing sustained emollient therapy as an ointment and also contain preservatives, which are known potential irritants.

Other modalities of treatments of leg ulcers are described below.

Compression Therapy

The mainstay of treatment of any venous component to ulceration is the application of sustained, graduated compression at therapeutic level²⁴. Graduated compression increases venous flow, decreases valvular reflux while walking and increases the effectiveness of the calf muscle pump resulting in a "thinning leg". The most effective level of compression to overcome venous hypertension has been determined to be around 40mmHg at the ankle²⁵. Correct application of bandages is essential to avoid pressure ulceration over the bony high points and along the anterior border of the tibia. It is acknowledged that the application of compression bandaging is a specialized skill traditionally undertaken by nurses. The combination of compression bandages used to achieve compression of 40mmHg at the ankle will depend on ankle circumference, according to Laplace's law, which states that the sub bandage pressure is inversely proportional to the circumference of the limb. A modified compression regimen is necessary when pain is present. This may be achieved by providing periods of relief until pain is controlled or removing the bandage at night when the leg is elevated. Patients with mixed arterial and venous disease may only tolerate up to 20mmHg compression to treat oedema. Bandage choices include short stretch, long stretch, multilayer systems and stockings. A Cochrane Review of compression regimens identified increased healing rates with compression compared to no compression²⁶. A high compression bandages were better than moderate compression bandages, and

that multi-layered bandages were better than single layered bandages. Comparisons between various high compression bandages systems, e.g. 4 layer and short stretch bandages, were unable to find any difference in effectiveness.

For venous ulcer with ABPI > 0.8, use 4 layer bandages as per ankle circumference below (Table 3)

Ulcers with ABPI between 0.6-0.8: Reduced compression is achieved by omitting the outer cohesive bandage (e.g. Coban)

Table 3: Multilayered bandage regime in relation to ankle circumference.

ANKLE CIRCUMFERENCE	BANDAGE REGIME
Up to 18cm	2 or more wool padding 1 light stretch bandage(Elastocrepe) 1 light elastic bandage 3a(K-plus) 1 cohesive bandage 3b(Coban)
18cm-25cm	1 wool padding 1 light stretch bandage(Elastocrepe) 1 light elastic bandage (K-plus) 1 cohesive bandage (Coban)
25cm-30cm	1 wool padding 1 high elastic bandage(Tensopress) 1 cohesive bandage (Coban)
Greater than 30cm	1 wool padding 1 light elastic bandage (K-plus) 1 high elastic bandage(Tensopress) 1 cohesive bandage (Coban)

Once the ulcer site is well healed, continue with the compression bandages for at least 4 weeks and then maintain compression at a slightly lower level indefinitely as tolerated. It must be replaced annually. Other factors to consider and deal with include:

Infection

This requires regular cleansing, more frequent changes of dressing (especially if exudates levels are high), topical antimicrobial dressings or systemic antibiotics.

Pain

Ranging from simple analgesia to potent opioid (depending on severity of pain), non steroidal anti inflammatory drugs may be beneficial. For neuropathic pain, amitriptyline can be started which can be replaced by gabapentin if no improvement. The dose can be titrated upwards.

Pressure: Requires pressure relief for the ulcer to heal especially over bony prominences.

Larval Therapy

Larval therapy has been used for debridement of wounds for many years.²⁷ Debridement is an essential component of wound care as the presence of devitalized tissue can impede the healing process. While the exact mechanism of larval therapy remains unknown, it encompasses three processes: debridement, disinfection and promotion of healing. The beneficial effects of larval therapy were first observed during the Napoleonic war by Larrey, who noted that soldiers whose wounds had become infested with maggots had an improved prognosis²⁷. During the First World War, Baer documented the successful treatment of leg ulcers and osteomyelitis using larval therapy, and paved the way for further use of it by doctors of that time. However, the development of antibiotics and improvements in surgical techniques reduced larval therapy to a “treatment of last resort”, reserved for the most intractable wounds²⁸.

The emergence of antibiotic-resistant strains of bacteria such as methicillin resistant staphylococcus aureus (MRSA) and the curiosity of researchers has prompted a resurgence of interest in larval therapy. Larval therapy has been employed effectively to treat a wide spectrum of wounds including venous and arterial leg ulcers²⁹. Some of the benefits of larval therapy include: reduction in wound pain and odour, and promoting healing process with relatively few side effects³⁰. Larval therapy is also reported as being cost-effective in comparison with conventional wound dressings. The use of larval therapy often resulted in quicker healing, and a subsequent reduction of nursing time and materials³⁰.

A further advantage of larval therapy is that, as larvae are typically applied for 3 days, wounds are disturbed less frequently than conventional dressings that require changing every 1-2 days. In addition to this, a further advantage is that treatment can usually be carried out in outpatient and community settings. A study at an outpatient wound clinic on chronic wounds, of varying aetiologies reported that using larval therapy resulted in a 62% decrease in need of amputation³¹. Larvae offer the benefit of eliminating bacteria from the wound through ingestion and subsequent degradation within their intestinal tract. They also act to reduce bacterial activity through the production of inhibitory secretions.

The most commonly mentioned disadvantage of larval therapy is the negative perception with which it is regarded by both patients and practitioners because of the unpleasant appearance. The use of “Biobags”, which completely enclose the larvae within a polyvinyl alcohol membrane, has become a popular method of improving the application of this treatment, as larvae are able to feed freely through the open cell polymer. Pain has occasionally been reported by patients, the cause may be the sharp mouth hooks and spicules with which larvae anchor themselves onto tissue. A case history has suggested larval therapy to be contraindicated with fistulae, exposed wounds connecting to vital organs³² because bloodstream infections have been reported with some larvae³³. Alteration of the disinfection process appeared to eliminate this problem, and with no further cases of sepsis occurring during the subsequent 12 months. The risk of cross-infection by escaped larvae may be greatly reduced through careful dressing.

Vacuum Assisted Closure therapy

Vacuum Assisted Closure (VAC) therapy involves the application of controlled negative pressure to wounds³⁴. Negative pressure, as a method of management for difficult to heal wounds, was initially explored in 1970, with the first wound drainage system being introduced in 1989. The use of negative pressure to heal wounds, however, is more commonly associated with the work of Argenta and Morykwas in 1997.³⁵ VAC therapy was designed with the aim of improving healing, decreasing morbidity, and decreasing the cost and length of hospital stay in patients with chronic, non-healing wounds. VAC therapy promotes healing in several ways. Firstly, the foam dressing, in combination with adhesive tape, creates an occlusive dressing. This alone prevents desiccation and increases the rate at which epithelial tissue is developed, therefore aiding healing times. Occlusive dressing prevents an increase in infection. Secondly, the suction effect and the mechanical forces generated at the interface of the foam work to decrease interstitial fluid accumulation, control wound exudates, stimulate granulation tissue formation, reverse tissue expansion, decrease bacterial colonisation and increase blood flow and dermal perfusion.

In summary, VAC therapy aids wound healing by:

- Maintaining a moist environment

- Increasing local blood flow
- Removing wound exudates
- Promoting granulation tissue formation
- Reducing infection
- Exerting mechanical pressures

VAC therapy is suitable for the following wound types/processes³⁶

- Acute (trauma, burns)
- Chronic (pressure sores, leg ulcers, diabetic ulcers)
- Surgical (skin grafts, flap surgery, wound bed preparation)
- Salvage (wound dehiscence, wound infection, post operative sternum infections)

Contraindications to the use of vacuum therapy include: wounds with untreated osteomyelitis, grossly infected wounds, when necrotic tissue is present or when there is unspecified disorder of the blood. VAC therapy should also not be used in wounds with malignancy. Dressings should not be placed over any exposed vessels or organs and VAC therapy should be used with caution in patients with active bleeding, difficult wound haemostasis and in patients taking anticoagulants.

Skin grafting

Skin grafting is the transplanting of skin, and, occasionally, other underlying tissues to another location of the body. It is the only means of reconstructing a defect in the skin, regardless of the cause of the defect³⁷.

Generally, skin grafting is used when, in the opinion of the reconstructive surgeon, other methods of reconstruction such as primary closure, secondary intention healing, or local skin flap are inappropriate, are unavailable or would produce a suboptimal result. Skin grafts are divided into 2 major categories: full thickness skin graft (FTSGs) and split thickness skin graft (STSGs). STSGs may be subdivided into thin (0.008-0.012mm), medium (0.012-0.018mm) and thick (0.018-0.030mm) grafts³⁷. STSGs are the one used in covering chronic unhealing cutaneous ulcer. Split skin grafting is technically demanding and requires hospital admission²⁵. The discharge from the surface of venous ulcers tends to dislodge continuous sheets of split skin, leaving a choice between mesh and pinch skin grafting. Pinch skin grafting provides

epithelial islands, from which epithelial growth may spread outwards as well as inwards from the ulcer margin. Pinch skin grafting has been done by district nurses in the community and has been found to be cost effective accelerating healing when used with multilayer compression bandaging.²⁵

Some contraindications to the use of skin graft generally include: vascular tissues such as exposed bone or cartilage (as this will lead to graft necrosis), uncontrolled bleeding of the recipient because of haematoma and/or seroma formation under the graft compromises graft survival.

Venous Surgery

Superficial venous surgery has been shown to improve ulcer healing in patients with only superficial venous incompetence³⁸. In patients with no deep reflux on duplex imaging, superficial venous surgery has been shown to reduce long term ulcer recurrence²⁵.

Indications for superficial venous surgery are:

- Patient fit for surgery
- Sufficient mobility to activate calf muscle pump
- Prepared to attend hospital for investigation and surgery
- Obesity controlled (BMI <30)
- Superficial venous incompetence

There are few other modalities of treatment of leg ulcers currently in use, although no strong evidence has been found to show they really improve healing.

Intermittent Pneumatic Compression

Intermittent pneumatic compression (IPC) is a mechanical method of delivering compression to swollen limbs that can be used to treat venous leg ulcers and limb swelling due to lymphoedema. It uses an air pump to inflate and deflate an airtight bag wrapped around the leg.³⁹ However, review of trials found conflicting evidence about whether it is better than compression bandages. It may increase healing compared with no compression but it is unclear whether it improves healing when added to treatment with bandages.

Electromagnetic Therapy

Electromagnetic therapy involves the use of electromagnetic, microwave, or infrared energy to diagnose or treat an illness by detecting and correcting imbalances in the body's energy fields. Electronic devices that emit some form of low-

voltage electrical current or radio frequency are often involved. It has been used in the treatment of chronic diseases like venous leg ulcers. Cochrane wound group conducted trials on several occasions comparing electromagnetic therapy with other treatments and up till now, there is no reliable evidence of benefit of electromagnetic therapy in the healing of venous leg ulcers.⁴⁰ Further research is still needed.

Oral Zinc Supplement

Leg ulcers may take long time to heal despite good wound care. This may be due to poor nutrition which reduces the ability of the body to repair itself. Minerals such as zinc are necessary for good healing and so it has been thought that taking zinc sulphate tablets might aid healing of ulcers especially if patients were found to have low baseline Zinc level. Few trials were found where zinc was used to treat leg ulcers but all were too small to pick up on any benefit, if such a benefit exists. In addition, the quality of those trials was mediocre. On the basis of the evidence available so far, it appears that taking zinc tablets does not improve leg ulcer healing, however more good quality trials are needed.⁴¹

Laser Therapy

Low level laser therapy (LLLT) refers to the use of red beam or near infrared laser with a wavelength between 600 and 1000nm power from 5-500 milliwatts. It is also referred to as cold laser therapy, low power laser therapy (LPLT), low intensity laser and low energy laser therapy. The exact effect of its mechanism is unknown; however, hypotheses have included improved cellular repair and stimulation of the immune, lymphatic and vascular system. Several randomised controlled trials involving patients with venous ulcers failed to demonstrate any significant benefits of LLLT when compared to standard treatment methods or placebos.⁴²

Hyperbaric Oxygen Therapy

Oxygen is one of the most versatile and powerful agents available to the modern medical practitioner. The therapeutic use of oxygen under pressure is known as hyperbaric oxygen therapy (HBO₂) and has been used to assist wound healing for almost 40 years. HBO₂ has several specific biological actions which can enhance wound healing processes. These include: Hyper-oxygenation of tissue, vasoconstriction, down regulation of inflammatory

cytokines, up-regulation of growth factors, antibacterial effects, potentiation of antibiotics, and leukocyte effects.⁴³ Systemic oxygen can be administered via 2 basic chambers: Type A (multiplace) and Type B (monoplace). Both types can be used for routine wound care, treatment of most dive injuries, and treatment of patients who are ventilated or in critical care. HBO₂ is a relatively safe non-invasive therapy. Side effects include middle ear and pulmonary barotraumas and myopia. Contraindications include poor cardiac output and severe obstructive pulmonary disease.

Conclusion

In this article, we have been able to show that leg ulcers are a common presentation in the elderly population and have negative impact on the quality of life of affected patients. It has been found to be more common in females. Most leg ulcers (about 80-85%) are caused by venous insufficiency, followed by arterial ulcers. A comprehensive assessment of the patient, skin, vascular status, limb and ulcer is required to determine aetiology and to formulate an appropriate management plan as described above. Several researches are still going on other modalities of treatment of leg ulcers. However, all patients should be provided with both verbal and written information to help them understand their condition and treatments they receive, as this will enable them to better understand their conditions, and will support concordance between patients and staff.

COMPETING INTERESTS

None Declared

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REFERENCES

1. Compression therapy for venous ulcers, effective health care 1997; 3(4) NHS centre for reviews and dissemination, University of New York.
2. Nelson E A and Jones J. Venous Leg Ulcers. Wounds.
3. Palfreyman S. Assessing the impact of venous ulceration on quality of life Nurs Times. 2008 Oct 14-20; 104(41):34-7.
4. Korber A, Schadendorf D, Dissemond J. Causes of leg ulcers: Analysis of data from a dermatologic wound care center. Hautarzt. 2009 Mar 22. [Epub ahead of print]
5. Moffat CJ, Franks PJ, Doherty DC et al. Prevalence of Leg ulcers in a London population. J Med 2004; 97; 431-437.
6. Graham ID, Harrison MB et al. Prevalence of Lower –limb ulceration: a systematic review of prevalence studies. Adv Skin Wound Care. 2003; 16(6):305-16.
7. Sign 1998. http://cks.library.nhs.uk/leg_ulcer/evidence/refereence#A6658.
8. Herber OR, Schnepf W, Rieger M. A systematic review on impact of leg ulceration on patients' quality of life. Health and quality of life outcomes of life outcomes. 2007; 5:44.
9. Walter SJ, Morrel CJ, Dixon S. Measuring health related quality of life in patients with venous leg ulcers. Qual Life Res. 1999; 8(4):327-36.
10. Lindholm C, Bjellerup M et al. Quality of life in chronic leg ulcers. 1993: Acta Dermatologica Venerea. 1993;73:440-444.
11. Goncalves ML, de Gouveia Santos VL et al. Pain in chronic leg ulcers. Journal of wound, Ostomy, continence nursing 2004; 31(5):275-283.
12. Cullum NRB. Leg ulcers: Nursing Management-A research based guide. Scutari Press 1995:125-134.
13. Chase S, Melloni M, Savage A: A forever healing: the lived experience of venous ulcer disease. Journal of Vascular nursing. 1997; 10(2):73-78.
14. Phillip T, Stanton B et al. A study on impact of leg ulcers on quality life: financial, social and psychological implications. Journal of the American academy of Dermatology. 1994, 31(1):49-53.
15. Simon, D.A., Dix, F.P. and McCollum, C.N. Management of venous leg ulcers. British Medical Journal. 2004; 328(7452), 1358-1362.
16. John Hickey. Management of leg ulcers. http://www.theberries.ca/ARchives/2006Winter/ulcer_management.html.
17. Grey JE, Harding KG, Enock S. Venous and arterial ulcers. BMJ. 2006; 332(7537): 347–350.
18. Sieggreen MY, Kline RA. Arterial Insufficiency and Ulceration: Diagnosis and Treatment Options. Advances in Skin & Wound care. 2004; 17:242-51.
19. Edmonds M E. Diabetic foot ulcers. BMJ. 2006; 332(7538): 407–410.
20. London NJM and Donnely R. Ulcerated Lower limb. BMJ. 2000; 320(7249): 1589–1591.
21. Burns SL, Leese GP, McMurdo M E P. Older people and ill fitting shoes. Postgrad Med J 2002; 78:344–346.
22. RCN (Royal College of Nursing) leg ulcer guidelines 2006.
23. Australian family Physician. Leg ulcers-causes and management. 2006; 35(7).
24. Nelson E. compression bandaging for venous leg ulcers Wound care 1996; 5:57-9.
25. Deborah Simon, Francis P Dix, Charles N McCollum. Management of venous leg ulcers, (clinical review). BMJ 2004; 328:1358-1362.
26. Cullum N, Nelson E, Fletcher A, Sheldon T. Compression bandages and stockings for venous ulcers. The Cochrane Library 2006, issue 4.
27. A Parnes; K.M.Lagan Int J clin Pract. 2007; 61(3): 488-493. Larval Therapy in Wound Management: A review.
28. Evans H. A treatment of last resort. Nurs times 1997; 93:62-5.
29. Donald J. Grande, David S Mezebish. Skin grafting. eMedicine Dermatology, October 2008.
30. Green T. Larval therapy in the community-challenge or opportunity? Nurse to Nurse 2004; 4:51-2
31. Sherman RA, Sherman J, Gilead L et al. Maggot debridement therapy in outpatients. Arch phys Med Rehabil 2001; 82: 1226-9
32. Thomas S, Jones M. The use of sterile maggots in wound management. Wound care Soc Educ Leaflet 1999; 6
33. Nuesch R, Rahm G, Rudin W et al. Clustering of bloodstream infections during maggot debridement therapy using contaminated larvae of *Protophormia terraenovae*. Infection 2002; 5:306-9
34. CEP 08017: June 2008. Evidence review Vacuum Assisted Therapy.
35. Argenta, Land M. Morykwas, and vacuum assisted closure: a new method for wound control and treatment: clinical experience. Annals of plastic surgery, 1997. 38: p 563-576.
36. Jones, S.M, P.E. Banwell, and P.G. Shakespeare, Advances in wound healing: topical negative pressure therapy. Postgraduate Medical Journal, 2005. 81(956): p353-357.
37. Donald J. Grande, David S Mezebish. Skin grafting. eMedicine Dermatology, October 2008.
38. Bello M, Scriven M, Hartshorne T, Bell PRF, Naylor AR, London NJM. Role of superficial venous surgery in the treatment of venous ulceration. Br J surg 1999; 86:755-9. [Medline]
39. Nelson EA, Mani R, Vowden K. Intermittent pneumatic compression for treating venous leg ulcers. Cochrane Database of Systematic Reviews 2008, Issue 2.
40. Ravaghi H, Fleming K, Cullum N, Olyaei Manesh A. Electromagnetic therapy for treating venous leg ulcers. Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD002933. DOI: 10.1002/14651858.CD002933.pub3.
41. Cochrane Database of systemic Reviews. Oral zinc for arterial and venous leg ulcers 2009.
42. Fleming K, Cullum N. Laser therapy for venous leg ulcers. The Cochrane Database of systematic Reviews 2007 issue 1.
43. James Wright. Hyperbaric Oxygen therapy for wound healing. World wide wound, May 2001