Summary of recommendations for leg ulcers

Sunil Dogra, Rishu Sarangal

Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Access this article online
Website: www.idoj.in
DOI: 10.4103/2229-5178.137829
Quick Response Code:

Address for correspondence:
Dr. Sunil Dogra, DNB FRCPB, Department of Dermatology, Venereology and Leprology, Post Graduate Institute of Medical Education and Research, Chandigarh - 160 012, India.
E-mail: sundogra@hotmail.com

INTRODUCTION

Leg ulcers are debilitating and painful, greatly reducing patient's quality of life. These ulcers are often difficult to treat and the successful treatment of leg ulcers depends upon the accurate diagnosis and treatment of the underlying cause. According to most of the Western and European studies, the most common type of leg ulcer is venous ulcer the others being neuropathic ulcer and arterial ulcers. These three kinds of ulcers account for almost 90% of cases of lower leg ulceration.[1] In tropical countries like India, there is a paucity of epidemiological studies regarding prevalence and etiology of leg ulcers. A study from one center in India suggests leprosy (40%), diabetes (23%), venous disease (11%), and trauma (13%) causes of lower extremity wounds.[2] The following evidence-based recommendations are in general to lower leg ulcers without referring to any specific cause of ulcerations and adherence to these will lead to speedy healing of lower leg ulcerations.

RECOMMENDATIONS

Clinical assessment

Clinical history and examination of leg and ulcer (Level B)

Clinical assessment includes full clinical history and physical examination of the patient of leg ulcer presenting either first time or with recurrent leg ulcer. In history, the duration/recurrence of an ulcer, pain, trauma, comorbid factors, and associated medical causes should be considered. The comorbid factors such as old age, malnutrition, poor hygiene, intravenous drug abuse, obesity, varicose veins, deep vein thrombosis, and coexisting medical causes such as diabetes mellitus, peripheral arterial diseases, rheumatoid arthritis, systemic vasculitis adversely affect both prognosis, and outcome of the treatment.

Examination of both legs should be done, which includes palpation of peripheral pulses, edema if present whether it is pitting or nonpitting type, signs of venous hypertension such as varicose veins, hemosiderin pigmentation, varicose eczema, atrophie blanche, and lipodermatosclerosis should be noted. The range of hip, knee, and ankle movement should be determined, and sensation should be tested to exclude peripheral neuropathy (evidence Level B).[1-6]

Clinical assessment of ulcer includes the assessment of site, size, depth, edge, margins, floor, base, and condition of the surrounding skin. The site of the ulcer medial, lateral, anterior, posterior, or combination should be noticed, this give clue to the underlying etiology of the ulcer. The size and surface area of the ulcer is determined by measuring the two maximum perpendicular axis, tracing the margins, and clinical photography. The surface area of the ulcer should be serially measured over time (evidence Level C).[7,8] A study compared the accuracy of ulcer measurement from digital images with contact tracing, and it was found that the two methods were equally accurate and reproducible, but that the digital image measurement was significantly quicker and offered a number advantages (evidence Level C).[9]

Vascular assessment

In patients with lower extremity ulcers, the accurate assessment of the arterial and venous systems is necessary to establish the diagnosis and essential for adequate treatment selection (Level B).[10-19]

Doppler measurement of ankle/brachial pressure index

All patients presenting with an ulcer should be screened for arterial disease by Doppler measurement of ankle/brachial pressure index (ABPI) (evidence Level B).[10-15]

Ankle/brachial pressure index: Is an objective evidence to substantiate the presence or absence of significant peripheral arterial

disease (except in heavily calcified vessels) is the ratio of the ankle to brachial systolic pressure and can be measured using a sphygmomanometer and hand held Doppler device. The significance of its assessment is highlighted by the fact that compression therapy can be safely applied to patients with ABPI >0.8 (evidence Level C).[10,12] Compression applied to legs with arterial insufficiency could result in pressure damage, limb ischemia, and even amputation. Doppler ultrasound to measure ABPI should also be conducted when the ulcer is deteriorating, ulcer not healed fully by 12 weeks, sudden increase in size of ulcer, sudden increase in pain, foot color or temperature change, or there is recurrence of ulcer (evidence Level B).[13-15]

Role of color flow Doppler imaging in arterial disease

Color flow Doppler imaging is advantageous over ABPI measurements in cases in which wounds and ulcers prevent the use of a cuff for measuring ABPI (evidence Level D).[16]

Color flow Doppler imaging quantifies any proximal arterial disease (aortoiliac) and the degree of involvement of distal vessels. And in addition, may detect nonflow limiting lesions to nonaxial arteries such as the deep femoral artery or lesions limited to a single tibial artery.[16]

Role of venous color flow Doppler imaging

It is a gold standard investigation for the assessment of the venous system of lower limb (evidence Level B).[15-19]

This noninvasive modality has revolutionized the diagnostic approach to venous disorders. It assesses the superficial, deep or perforating veins separately for the presence of obstruction and reflux. Absence of flow is considered as obstruction and reflux is defined as the retrograde flow lasting more than 0.5 s, which is the time required for valve closure. It is highly recommended in the setting of venous ulcers.

Biopsy

Referral to a specialist unit for biopsy should be considered if the appearance of the ulcer is atypical or if there is deterioration or failure to progress after 12 weeks of active treatment (evidence Level C).[18,20-22]

Bacteriological evaluation

- Bacteriological swabbing is unnecessary unless there is evidence of clinical infections such as inflammation, redness, cellulitis, increased pain, purulent exudates, rapid deterioration of the ulcer, pyrexia, and foul odor (evidence Level B).[21-23]

Bacteriological swabs have certain limitations the swab cultures typically show the presence of numerous organisms, which have little or no clinical relevance, there is no standard technique for obtaining a swab culture, which shows reproducible results, inappropriate technique for taking swabs like from necrotic or nonviable tissue and they lack the ability to differentiate between bacteria resting on the wound surface versus infecting organisms. There are no reports in the literature that validate the use of swab cultures in chronic wounds.[22]

- However, a quantitative tissue biopsy should be obtained if there is no progression of the wound after 2 weeks of standard treatment (evidence Level B).[22,24,25]

The gold standard for the treatment of infection is $>10^5$ colony-forming units of bacteria per gram of tissue on quantitative biopsy.[24] The exception to this rule is β-hemolytic streptococcus, which is harmful at any level in the wound tissue.[25]

Patch-testing

Leg ulcer patients with dermatitis/eczema should be considered for patch-testing (evidence Level C).[26-29]

The incidence of contact allergy increases with the duration of ulceration.[26] Two studies in which patients with venous leg ulcer were patch-tested for a range of allergens contained in current ulcer dressings found that in one, 46% and in the other 61% of reactions were to these additional allergens.[27,28] Several large patch-test studies have demonstrated that the principal sensitizers are ingredients of applications, dressings, and bandages, with common sensitizers being lanolin, antibiotics, antiseptics, preservatives, emulsifiers, resins, and latex.[26-29]

Cleaning

- Cleaning of an ulcer is recommended using simple irrigation with either normal saline compresses or plain tap water (evidence Level E).[30,31]
- Dressing technique should be clean and aimed at preventing cross-infection (evidence Level E).[30]

Wounds and skin are colonized by bacteria and currently there is a lack of evidence that the presence of colonizing bacteria impedes wound healing. In a systematic review of the effects of antimicrobials including topical antiseptics on chronic wounds identified no randomized controlled trials (RCT's) to support the cleansing by antiseptic solutions.[30] In another systematic review that looked for effects of using tap water in comparison to distilled water or boiled water or normal saline for cleansing of wound found no difference in infection or healing rates while using any of them.[31]

Debridement

When slough and wound debris obscure the base of the ulcer, debridement becomes essential. Removal of necrotic and devitalized tissue can be achieved through mechanical, autolytic, chemical, or enzymatic debridement. Mechanical debridement should be undertaken by the expert with the

surgical skills (evidence Level C).[32-37] Necrotic tissue left in the ulcer contributes to reduced host resistance to infection because it acts like a foreign body. In this area, there is usually a high concentration of harmful proteases and bacteria that can inhibit wound healing. Skin debridement consists of removing nonviable, nonbleeding skin. A chronic wound has to be converted by debridement to an acute wound, so that it can proceed through the normal healing phases.[32,33] However, debridement is contraindicated in ulcers when healing is complicated by severe arterial insufficiency.[32] There are several methods of wound debridement available to the clinician. These include autolytic, chemical, mechanical, surgical and biological modalities. In general, autolytic debridement (i.e. breakdown and removal of dead tissues by body's own cells and enzymes) is recommended for wounds with minimal debris and without clinical signs of infection. This is facilitated through the maintenance of the moist wound environment by simple nonadherent wound dressing. Surgical debridement is most appropriate in wounds with large amounts of necrosis and eschar, but must be undertaken by specialist.[37]

Dressing

- Chronic ulcer management requires the use of the wound dressings that provide the optimal "moist" environment. Dressing should be simple, low or nonadherent, low cost and acceptable to the patient (evidence Level A).[32,38-40]
- No single dressing material is favored (evidence Level C).[32,38]

In the two systematic reviews, many RCT's are identified comparing various dressings and topical agents in patients of venous ulcers, but no single consensus can be drawn in favor of any particular dressing material.[32,38] The different types of wound dressings available are occlusive plastic films, hydrocolloid dressing, absorbent dressings, calcium alginate, hydrogels, and biological dressings.[32] In a recent *in vitro* study of effects of different dressing on keratinocyte cell viability and proliferation has highlighted few important points, which can be used as a guide to decide the dressing material. The study results showed that silver-based dressings are cytotoxic and should not be used in the absence of infection. Alginate dressings with high calcium content affect keratinocyte proliferation probably by triggering terminal differentiation of keratinocytes. Such dressings should be used with caution in cases in which keratinocyte proliferation is essential. All dressings should be tested *in vitro* before clinical application.[39]

- Biological wound dressings are effective when used along with compression therapy in venous ulcers as compared with compression therapy alone (evidence Level A).[40]

Regarding the role of biological wound dressings containing cultured, allogenic, bilayered human skin equivalents a randomized multicentered prospective study of 275 patients of venous ulcer, have shown it more effective than compression therapy alone. The researchers found that treatment with human skin equivalent was more effective than compression therapy alone in the percentage of patients healed at 6 months (63% vs. 49%). Furthermore, the median time to complete wound closure was 61 days for the human skin equivalent group compared to 181 days for those receiving compression therapy alone. Both results were considered statistically significant. Although, this dressing is expensive, but human skin equivalent may provide an alternative treatment for nonhealing wounds.[40]

Topical antimicrobials and antiseptics

- Antibiotics are indicated in cases of overt wound infection where the classical signs of infection are evident (evidence Level C).[41,42]

In chronic wounds, reduction of certain microbial species, such as anaerobic bacteria in order to limit undesirable odors or perhaps mixed communities of four or more bacterial species that impede healing use of topical antibiotics may be justified (evidence Level C).[41,42]

Various studies on dressings incorporating antibiotics and antiseptics are reviewed, but no single consensus for any particular topical agent could be made. This is partly due to the different mechanism and spectrum of action of the antimicrobials. The most frequently used topical antimicrobials in wound care practice are chlorhexidine, iodine, silver containing products, and mupriocin, fucidic acid. In the past acetic acid, honey, hydrogen peroxide, sodium hypochlorite, potassium permanganate, and proflavine have been used.

Chlorhexidine-impregnated dressings

- Effective in reducing vascular and epidural catheter bacterial colonization (evidence Level A).[43]
- Use is associated with fewer adverse effects on wound healing (evidence Level C).[44]

In a systematic review, which assessed the effect of chlorhexidine-impregnated dressing on the risk of vascular and epidural catheter bacterial colonization and infection, around eight randomized controlled clinical trials comparing chlorhexidine-impregnated dressing with placebo or povidine-iodine dressing were identified. It concluded that chlorhexidine-impregnated dressing is effective in reducing vascular and epidural catheter bacterial colonization and is also associated with a trend toward reduction in the catheter-related bloodstream or central nervous system infections.[43] In a recent evaluation of human studies has demonstrated that it is associated with few adverse effects on healing.[44] Despite reports of decreased bacterial counts, increased healing rates, and lack of toxicity, it is concluded that at present, there is insufficient data to assess safety and efficacy, and that further

clinical trials are required before the use of chlorhexidine on open wounds is either recommended or condemned.

Iodine: Available as povidine-iodine and second generation dextranomer and cadexomer

- Reduces bacterial load, decreases infection rates and promotes healing (evidence Level C).[44-46]

In one study, healing rates of chronic venous leg ulcers, each treated with one of three topical agents were compared to untreated control ulcers in each respective patient. All agents were seen to reduce bacterial load, silver sulfadiazine, and chlorhexidine digluconate caused slight improvements in healing rates and times, but povidine-iodine yielded statistically significant increases. Furthermore, histological assessment indicated a lack of cytotoxicity because povidine-iodine induced less change in microvessels and dendrocytes.[45] In addition, a report of the ability of iodine released from a dressing to modulate the secretion of cytokines by human macrophages *in vitro* has provided another justification of its role in promoting healing.[46]

- Cadexomer iodine: Leads to reduction of methicillin resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* with evidence from clinical reports of efficacy in stimulating healing (evidence Level C).[44,47,48] Its lack of toxicity for human fibroblasts *in vitro* suggests a lack of toxicity for chronic wounds *in vivo* (evidence Level D).[49]

Silver (evidence Level C)

At present, human studies with silver containing dressings are rather limited, yet many trials provide encouraging results.[50-53] In an uncontrolled, prospective study of a series of chronic wounds treated with an ionized nanocrystalline silver dressing demonstrated improved clinical parameters together with decreased surface wound bioburden, but unchanged deep tissue loads. The implication was that surface flora contributed more significantly to delayed healing than deeper flora (evidence Level D).[54]

Mupirocin

A systematic review identified one small RCT (n = 30) of patients with leg ulcer, which compared topical mupirocin with placebo, in addition to standard compression for all. There was no significant difference between groups in rates of complete healing, or eradication of Gram-positive bacteria.[55] There is insufficient evidence on which to base a recommendation for mupirocin.

Systemic antibiotics

- According to recommendations systemic antibiotic should only be used in cases of clinical infection and not for bacterial colonization (evidence Level C).[55,56]

A systematic review included five small RCTs of variable quality examining healing rates of ulcers with a range of systemic antibiotics given for a variable period of time (10 days to 20 weeks). Studies did not differentiate between infected and colonized ulcers. There was insufficient evidence to support the routine use of antibiotics.[55] One randomized, controlled trial compared the use of elastic support bandages to the same treatment plus systemic antibiotics. No significant differences were noted in terms of healing rates or changes in bacterial flora.[56] The routine use of systemic antibiotics is ineffective, costly, and will only facilitate the emergence of yet more drug-resistant bacteria.

Compression therapy

- Recommendations are for graduated, multi-layered high compression system with adequate padding should be the first line of treatment for uncomplicated venous leg ulcers with ABPI ≥0.8 in all settings (evidence Level A).[57-60]

Three systematic reviews of the literature identifying many randomised controlled trials[57-60] concluded that compression systems improve the healing of venous leg ulcers and should be used routinely in uncomplicated venous ulcers.

Compression systems may be classified into three groups: Short-stretch bandages (SSB), long-stretch bandages, and stockings. If the limb affected by the ulcer is edematous, most experts recommend using an SSB system (evidence Level C).[61-63] Compression pressures of at least 30-40 mm Hg at the ankle should be utilized in the management of venous leg ulcers. All compression bandage systems must create a pressure gradient from ankle to knee.

Pain relief

Regular monitoring of patients for pain associated with leg ulcers is required. It is important to formulate individual management plan, which may consist of simple physical methods such as leg elevation and exercise, compression therapy, and analgesia (evidence Level C).[64-66]

The assessment of pain should include the severity, type, timing of pain and establishing the exacerbating and relieving factors. Simple physical methods considered such as raising the foot end of the bed in venous ulceration or lowering the foot end of the bed in arterial disease. Leg elevation is important in venous ulcers since it aids venous return and reduces swelling and pain in leg. Opioids like morphine are extremely useful for very severe pain uncontrolled by weaker agents and particularly for severe exacerbations. For neuropathic pain, antidepressants (e.g. amitryptiline) or anticonvulsants (e.g. gabapentin) are alternative agents of proven efficacy (evidence Level D).[64] Compression therapy counteracts the harmful effects of venous hypertension and may relieve pain (evidence Level B).[65]

Role of eutectic mixture of local anesthetic (EMLA) is highlighted by a systematic review which identified six RCTs comparing EMLA with placebo in pain during debridement. The meta-analysis showed that EMLA cream was associated with pain reduction (evidence Level A).[66]

Other supportive treatment

Drugs: Pentoxifylline

Systematic review identifying nine RCT's recommend the use of pentoxifylline (1200-2400 mg) along with compression therapy, enhances healing of venous ulcer (evidence Level A).[67]

Use of granulocyte macrophage colony-stimulating factor

The topical and peri-lesional injections of granulocyte macrophage colony-stimulating factor (GM-CSF) promotes healing of leg ulcers and is safe (evidence Level B).[68-72]

The GM-CSF promotes wound healing through many mechanisms, affecting one or all of the wound healing phases, such as homeostasis, inflammation, proliferation, and maturation. Several case series and pilot studies have demonstrated that topical and peri-lesional injection of GM-CSF promotes healing of leg ulcer wounds.[68-72] Two randomized, double-blind, placebo-controlled studies showed increased healing of chronic leg ulcers treated with GM-CSF compared with controls.[68,69] In first RCT authors found that half of the patients treated with a single intradermal, peri-lesional injection of 400 μg of GM-CSF led to complete healing of the ulcers at 8 weeks as compared with 11% of patients in the placebo group.[68] The second randomized trial aimed at dose-finding, it was a double-blind trial of weekly dosages of either 200 μg or 400 μg of GM-CSF given peri-lesional in patients with chronic venous leg ulcers. The two conclusions drawn out of the study were higher rate of healing in patients receiving peri-lesional injected GM-CSF as compared with the placebo group and 57% versus 61% patients showed healing of leg ulcers at week 13 of study in 200 μg and 400 μg groups respectively.[69] Case reports and case series have shown that GM-CSF is useful for treating leg ulcers due to various other causes as well.[70-72] Because of the pain associated with injections of GM-CSF, use of topical GM-CSF in a series of 52 venous ulcers was studied and about 90% of ulcers healed, with an average healing time of 19 weeks.[72]

Though the use of GM-CSF in chronic leg ulcer is shown beneficial for healing in all above mentioned studies, but further studies are necessary to confirm the efficacy of this agent in healing venous ulcers and to define the optimal dose and dosing schedule.

Care of surrounding skin

General care of the skin surrounding an ulcer is essential to maintain skin integrity and minimize the risk of further ulceration. Gentle washing and emollients have been shown to be effective in all forms of eczema/dermatitis. They help to restore the barrier function and reduce the role of infective organisms as a cause of damage. Washing for about 10 min twice a day is optimal. Water just above body temperature is most desirable, and more natural the emollient soap, more supportive it is of the epidermis (evidence Level E).[73]

Exercise

Calf muscle exercises are recommended (evidence Level B).

Role of supervised calf muscle exercises in increasing the calf muscle pump function and improving the hemodynamics in venous leg ulcers had been highlighted in one prospective study and another pilot RCT.[74,75]

Nutrition

Patient of leg ulcer with suspected malnourishment should be assessed by a nutritionist and dietician (evidence Level D).[76-78]

Impaired/poor wound healing is associated with many factors one of which is malnutrition. Studies have shown that changes in energy, carbohydrates, proteins, fats, vitamin, and mineral metabolism affect the wound healing process.[76] No significant benefit on wound healing is seen with nutritional supplements such as vitamins C, A, E, and zinc in a nondeficient individuals.[77,78]

Psychological support

- Large ulcers (>10 cm^2) and long duration of ulcer leads to poorer health-related quality of life (HRQoL) index (evidence Level D).[79]

A cross-sectional study done to determine the association between clinical and social variables and HRQoL in patients suffering from chronic leg ulcers showed that bodily pain, emotional and social isolation was associated with patients of large ulceration for longer duration. Such patients do well with adequate treatment in specialist units and when provided with adequate psychological support along with.[79]

Indications for surgery

- Patient with chronic venous leg ulcer and superficial venous reflux should be considered for surgery to promote ulcer healing and to prevent recurrence of the ulcer (evidence Level B).[32,80]

Surgical ablation of incompetent superficial veins is done if an ulcer shows no sign of healing after 3 months of best management of wound. Perforator incompetence and disease of the superficial venous system can be managed using new surgical techniques that are associated with only mild

morbidity.[32] After ulcer healing, if significant superficial and/or perforator vein incompetence exists, surgical ablation/ligation should be considered as part of overall preventive care to prevent ulcer recurrence.[32,80]

Indications for sclerotherapy

Sclerotherapy is indicated for the superficial varicosities and incompetent perforators surrounding the ulcer this also helps in fast healing of ulcers (evidence Level D).[81]

Indications for laser therapy

- No benefit of low-level laser therapy on leg ulcer healing (evidence Level A).[82]

In the previous Cochrane systematic review, the four RCTs were identified studying the local application of energy from low-level lasers to accelerate the healing of venous leg ulcers. According to the review, there was no evidence of benefit associated with low-level laser therapy on venous leg ulcer healing.[82]

- Endovascular laser therapy (EVLT) enhances leg ulcers healing (evidence Level C).[83-86]

In recent studies on the effectiveness of EVLT have shown enhanced healing in venous leg ulcers.[83-86] Data from a small RCT showed that 22 (81%) of patients in the EVLT group had healed ulcers at 12 months compared with 6 (24%) in the control group - elastic or inelastic compression therapy ($P = 0.0001$).[84] The present data is minimal to support laser therapy treatment. In conclusion, more studies are required to establish the role of local laser therapies or EVLT in the treatment of leg ulcers.

Prevention of ulcer recurrence

Factors that are associated with ulcer nonhealing and recurrence: Overweight body mass index, history of deep venous thrombosis, large ulcer area, noncompliance with compression therapy, and triple-system venous disease involving superficial, perforating, and deep veins (evidence Level D).[87] The strategies to prevent the ulcer recurrence should target these factors. These could be implemented as regular clinical evaluations, patient education and life-long compression therapies. Patient's education should be regarding skin care, elevation of the affected limb when immobile, compliance to compression therapy, encourage mobility, and exercise. To encourage, early self-referral at signs of possible skin breach.

Compression therapy

Use of compression stockings reduces ulcer recurrence and is thus highly recommended in patients of venous leg ulcers. Patients are encouraged to wear the strongest compression they can tolerate for life-long, if not contraindicated otherwise (evidence Level A).[88,89]

Indication for referral

The patients with chronic leg ulcer which are complicated by following conditions requires specialist referral to medicine and surgery units (evidence Level E).[5,87,90]

- Patients with significant occlusive arterial disease require specialist assessment of the severity[5]
- For treatment of underlying medical problems such as rheumatoid arthritis, peripheral vascular disease, diabetes mellitus, etc.
- Ulcers with mixed etiologies, diabetic ulcers
- Suspected malignant ulcers
- Nonhealing ulcers (a minimum of at least 6 months of compression and local wound care followed by reassessment of venous function should be done before operative plastic surgical intervention is considered)[87]
- Rapid deterioration of the ulcer
- Recurrent ulcers
- Reduced ABPI <0.8 or increased ABPI >1.0
- Infected foot
- Ischemic foot.

REFERENCES

1. London NJ, Donnelly R. ABC of arterial and venous disease. Ulcerated lower limb. BMJ 2000;320:1589-91.
2. Saraf SK, Shukla VK, Kaur P, Pandey SS. A clinico-epidemiological profile of non-healing wounds in an Indian hospital. J Wound Care 2000;9:247-50.
3. Stevens J, Franks PJ, Harrington M. A community/hospital leg ulcer service. J Wound Care 1997;6:62-8.
4. Scottish Leg Ulcer Trial Participants. Effect of a national community intervention programme on healing rates of chronic leg ulcer: Randomised controlled trial. Phlebology 2002;17:47-53.
5. Dodds SR. Shared community-hospital care of leg ulcer using an electronic record and telemedicine. Int J Low Extrem Wounds 2002;1:260-70.
6. Nelzén O, Bergqvist D, Lindhagen A. Venous and non-venous leg ulcers: Clinical history and appearance in a population study. Br J Surg 1994;81:182-7.
7. Stacey MC, Burnand KG, Layer GT, Pattison M, Browse NL. Measurement of the healing of venous ulcers. Aust N Z J Surg 1991;61:844-8.
8. Yang D, Morrison BD, Vandongen YK, Singh A, Stacey MC. Malignancy in chronic leg ulcers. Med J Aust 1996;164:718-20.
9. Samad A, Hayes S, French L, Dodds S. A comparative study of computerised digital image tracing versus contact tracing for objective measurement of leg ulcers. J Wound Care 2002;11:137-40.
10. Moffatt CJ, Oldroyd MI, Greenhalgh RM, Franks PJ. Palpating ankle pulses is insufficient in detecting arterial insufficiency in patients with leg ulceration. Phlebology 1994;9:170-2.
11. Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. Br J Surg 1969;56:676-9.
12. Male S, Coull A, Murphy-Black T. Preliminary study to investigate the normal range of Ankle Brachial Pressure Index in young adults. J Clin Nurs 2007;16:1878-85.
13. Stubbing NJ, Bailey P, Poole M. Protocol for accurate assessment of ABPI in patients with leg ulcers. J Wound Care 1997;6: 417-8.
14. Simon DA, Freak L, Williams IM, McCollon CN. Progression of arterial disease in patient with healed venous ulcers. J Wound Care

1994;3:179-80.
15. Scriven JM, Hartshorne T, Bell PR, Naylor AR, London NJ. Single-visit venous ulcer assessment clinic: The first year. Br J Surg 1997;84:334-6.
16. Lazarides MK, Giannoukas AD. The role of hemodynamic measurements in the management of venous and ischemic ulcers. Int J Low Extrem Wounds 2007;6:254-61.
17. Grabs AJ, Wakely MC, Nyamekye I, Ghauri AS, Poskitt KR. Colour duplex ultrasonography in the rational management of chronic venous leg ulcers. Br J Surg 1996;83:1380-2.
18. Androulakis AE, Giannoukas AD, Labropoulos N, Katsamouris A, Nicolaides AN. The impact of duplex scanning on vascular practice. Int Angiol 1996;15:283-90.
19. van Bemmelen PS, Bedford G, Beach K, Strandness DE. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg 1989;10:425-31.
20. Senet P, Combemale P, Debure C, Baudot N, Machet L, Aout M, *et al*. Malignancy and chronic leg ulcers: The value of systematic wound biopsies: A prospective, multicenter, cross-sectional study. Arch Dermatol 2012;148:704-8.
21. Serena TE, Robson MC, Cooper DM, Ignatius J. Lack of reliability of clinical/visual assessment of chronic wound infection: The incidence of biopsy-proven infection in venous leg ulcers. Wounds 2006;18:197-202.
22. Serena TE, Hanft JR, Snyder R. The lack of reliability of clinical examination in the diagnosis of wound infection: Preliminary communication. Int J Low Extrem Wounds 2008;7:32-5.
23. Gardner SE, Frantz RA, Hillis HL, Park H, Scherubel M. Diagnostic validity of semiquantitative swab cultures. Wounds-a Compendium of Clinical Research and Practice 2007;19:31-8.
24. Robson MC, Heggers JP. Bacterial quantification of open wounds. Mil Med 1969;134:19-24.
25. Schraibman IG. The significance of beta-haemolytic streptococci in chronic leg ulcers. Ann R Coll Surg Engl 1990;72:123-4.
26. Paramsothy Y, Collins M, Smith AG. Contact dermatitis in patients with leg ulcers. The prevalence of late positive reactions and evidence against systemic ampliative allergy. Contact Dermatitis 1988;18:30-6.
27. Wilson CL, Cameron J, Powell SM, Cherry G, Ryan TJ. High incidence of contact dermatitis in leg-ulcer patients: Implications for management. Clin Exp Dermatol 1991;16:250-3.
28. Zaki I, Shall L, Dalziel KL. Bacitracin: A significant sensitizer in leg ulcer patients? Contact Dermatitis 1994;31:92-4.
29. Kulozik M, Powell SM, Cherry G, Ryan TJ. Contact sensitivity in community-based leg ulcer patients. Clin Exp Dermatol 1988;13:82-4.
30. O'Meara S, Cullum N, Majid M, Sheldon T. Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration. Health Technol Assess 2000;4:1-237.
31. Fernandez R, Griffiths R, Ussia C. Water for Wound Cleansing. The Cochrane Library. Chichester: John Wiley and Sons Ltd.; 2003.
32. Kunimoto BT. Management and prevention of venous leg ulcers: A literature-guided approach. Ostomy Wound Manage 2001;47:36-42, 44-9.
33. Fowler E, van Rijswijk L. Using wound debridement to help achieve the goals of care. Ostomy Wound Manage 1995;41:23S-35.
34. Berger MM. Enzymatic debriding preparations. Ostomy Wound Manage 1993;39:61-2, 66-9.
35. Fowler E. Instrument/sharp debridement of non-viable tissue in wounds. Ostomy Wound Manage 1992;38:26, 28-3032.
36. Attinger CE, Janis JE, Steinberg J, Schwartz J, Al-Attar A, Couch K. Clinical approach to wounds: Débridement and wound bed preparation including the use of dressings and wound-healing adjuvants. Plast Reconstr Surg 2006;117:72S-109.
37. Falabella AF. Debridement and management of exudative wounds. Dermatol Ther 1999;9:36-43.
38. Bradley M, Cullum N, Sheldon T. The debridement of chronic wounds: A systematic review. Health Technol Assess 1999;3:iii-iv, 1-78.
39. Paddle-Ledinek JE, Nasa Z, Cleland HJ. Effect of different wound dressings on cell viability and proliferation. Plast Reconstr Surg 2006;117:110S-8.
40. Falanga V, Margolis D, Alvarez O, Auletta M, Maggiacomo F, Altman M, *et al*. Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. Human Skin Equivalent Investigators Group. Arch Dermatol 1998;134:293-300.
41. Bowler PG, Davies BJ. The microbiology of acute and chronic wounds. Wounds 1999;11:72-8.
42. Trengove NJ, Stacey MC, McGechie DF, Mata S. Qualitative bacteriology and leg ulcer healing. J Wound Care 1996;5:277-80.
43. Ho KM, Litton E. Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: A meta-analysis. J Antimicrob Chemother 2006;58:281-7.
44. Drosou A, Falabella A, Kirsner RS. Antiseptics on wounds: An area of controversy. Wounds 2003;15:149-66.
45. Fumal I, Braham C, Paquet P, Piérard-Franchimont C, Piérard GE. The beneficial toxicity paradox of antimicrobials in leg ulcer healing impaired by a polymicrobial flora: A proof-of-concept study. Dermatology 2002;204 Suppl 1:70-4.
46. Moore K, Thomas A, Harding KG. Iodine released from the wound dressing Iodosorb modulates the secretion of cytokines by human macrophages responding to bacterial lipopolysaccharide. Int J Biochem Cell Biol 1997;29:163-71.
47. Mertz PM, Oliveira-Gandia MF, Davis SC. The evaluation of a cadexomer iodine wound dressing on methicillin resistant *Staphylococcus aureus* (MRSA) in acute wounds. Dermatol Surg 1999;25:89-93.
48. Danielsen L, Cherry GW, Harding K, Rollman O. Cadexomer iodine in ulcers colonised by *Pseudomonas aeruginosa*. J Wound Care 1997;6:169-72.
49. Zhou LH, Nahm WK, Badiavas E, Yufit T, Falanga V. Slow release iodine preparation and wound healing: *In vitro* effects consistent with lack of *in vivo* toxicity in human chronic wounds. Br J Dermatol 2002;146:365-74.
50. Wunderlich U, Orfanos CE. Treatment of venous ulcera cruris with dry wound dressings. Phase overlapping use of silver impregnated activated charcoal xerodressing. Hautarzt 1991;42:446-50.
51. Tebbe B, Orfanos CE. Therapy of leg ulcers and decubitus ulcers with a xero-dressing: Modern wound dressings with antibacterial activity. H + G Brand (Special Edition) 1996;71:11-3.
52. Bornier C, Jeannin C. Clinical trials with ACTISORB: Carried out on 20 cases of complex wounds. Soins Chir 1989;99:39-41.
53. Cassino R, Ricci E, Carousone A. Management of infected wounds: A review of antibiotic and antiseptic treatments (Poster Presentation). In: 10th European Wound Management Association Conference, Dublin; 2001.
54. Sibbald RG, Browne AC, Coutts P, Queen D. Screening evaluation of an ionized nanocrystalline silver dressing in chronic wound care. Ostomy Wound Manage 2001;47:38-43.
55. O'Meara S, Al-Kurdi D, Ovington LG. Antibiotics and antiseptics for venous leg ulcers. The Cochrane Library. No. 1. Chichester: John Wiley and Sons Ltd.; 2010.
56. Alinovi A, Bassissi P, Pini M. Systemic administration of antibiotics in the management of venous ulcers. A randomized clinical trial. J Am Acad Dermatol 1986;15:186-91.
57. Fletcher A, Cullum N, Sheldon TA. A systematic review of compression treatment for venous leg ulcers. BMJ 1997;315:576-80.
58. Cullum N, Nelson EA, Fletcher AW, Sheldon TA. Compression for venous leg ulcers. The Cochrane Library. No. 2. Chichester: John Wiley and Sons Ltd.; 2001.
59. O'Meara S, Cullum NA, Nelson EA. Compression for venous leg ulcers (Review). The Cochrane Library. No. 1. Chichester: John Wiley and Sons Ltd.; 2009.
60. O'Brien JF, Grace PA, Perry IJ, Hannigan A, Clarke Moloney M, Burke PE. Randomized clinical trial and economic analysis of four-layer compression bandaging for venous ulcers. Br J Surg 2003;90:794-8.

61. Gaylarde PM, Sarkany I, Dodd HJ. The effect of compression on venous stasis. Br J Dermatol 1993;128:255-8.
62. Zimmet SE. Venous leg ulcers: Modern evaluation and management. Dermatol Surg 1999;25:236-41.
63. Hampton S. Venous leg ulcers: Short-stretch bandage compression therapy. Br J Nurs 1997;6:990-2, 994, 996-8.
64. Cooper SM, Hofman D, Burge SM. Leg ulcers and pain: A review. Int J Low Extrem Wounds 2003;2:189-97.
65. Franks PJ, Oldroyd MI, Dickson D, Sharp EJ, Moffatt CJ. Risk factors for leg ulcer recurrence: A randomized trial of two types of compression stocking. Age Ageing 1995;24:490-4.
66. Briggs M, Nelson EA. Topical agents or dressings for pain in venous ulcers. The Cochrane Library. No. 1. Chichester: John Wiley and Sons Ltd.; 2003.
67. Jull AB, Waters J, Arroll B. Pentoxifylline for treatment of venous leg ulcers. The Cochrane Library. No. 1. Chichester: John Wiley and Sons Ltd.; 2002.
68. Marques da Costa R, Jesus FM, Aniceto C, Mendes M. Double-blind randomized placebo-controlled trial of the use of granulocyte-macrophage colony-stimulating factor in chronic leg ulcers. Am J Surg 1997;173:165-8.
69. Da Costa RM, Ribeiro Jesus FM, Aniceto C, Mendes M. Randomized, double-blind, placebo-controlled, dose- ranging study of granulocyte-macrophage colony stimulating factor in patients with chronic venous leg ulcers. Wound Repair Regen 1999;7:17-25.
70. Halabe A, Ingber A, Hodak E, David M. Granulocyte-macrophage colonystimulating factor: A novel therapy in the healing of chronic ulcerative lesions. Med Sci Res 1995;23:65-6.
71. Pojda Z, Struzyna J. Treatment of non-healing ulcers with rhGM-CSF and skin grafts. Lancet 1994;343:1100.
72. Jaschke E, Zabernigg A, Gattringer C. Recombinant human granulocyte-macrophage colony-stimulating factor applied locally in low doses enhances healing and prevents recurrence of chronic venous ulcers. Int J Dermatol 1999;38:380-6.
73. Ryan TJ. Common denominators for the low-cost management of leg conditions. Int J Low Extrem Wounds 2002;1:62-7.
74. Kan YM, Delis KT. Hemodynamic effects of supervised calf muscle exercise in patients with venous leg ulceration: A prospective controlled study. Arch Surg 2001;136:1364-9.
75. Jull A, Parag V, Walker N, Maddison R, Kerse N, Johns T. The prepare pilot RCT of home-based progressive resistance exercises for venous leg ulcers. J Wound Care 2009;18:497-503.
76. Arnold M, Barbul A. Nutrition and wound healing. Plast Reconstr Surg 2006;117:42S-58.
77. Telfer NR, Moy RL. Drug and nutrient aspects of wound healing. Dermatol Clin 1993;11:729-37.
78. ter Riet G, Kessels AG, Knipschild PG. Randomized clinical trial of ascorbic acid in the treatment of pressure ulcers. J Clin Epidemiol 1995;48:1453-60.
79. Franks PJ, Moffatt CJ. Do clinical and social factors predict quality of life in leg ulceration? Int J Low Extrem Wounds 2006;5:236-43.
80. Barwell JR, Davies CE, Deacon J, Harvey K, Minor J, Sassano A, *et al*. Comparison of surgery and compression with compression alone in chronic venous ulceration (ESCHAR study): Randomised controlled trial. Lancet 2004;363:1854-9.
81. de Waard MM, der Kinderen DJ. Duplex ultrasonography-guided foam sclerotherapy of incompetent perforator veins in a patient with bilateral venous leg ulcers. Dermatol Surg 2005;31:580-3.
82. Flemming K, Cullum N. Laser therapy for venous leg ulcers. The Cochrane Library. No. 2. Chichester: John Wiley and Sons Ltd.; 2000.
83. Howard DP, Howard A, Kothari A, Wales L, Guest M, Davies AH. The role of superficial venous surgery in the management of venous ulcers: A systematic review. Eur J Vasc Endovasc Surg 2008;36:458-65.
84. Viarengo LM, Potério-Filho J, Potério GM, Menezes FH, Meirelles GV. Endovenous laser treatment for varicose veins in patients with active ulcers: Measurement of intravenous and perivenous temperatures during the procedure. Dermatol Surg 2007;33:1234-42.
85. Huang Y, Jiang M, Li W, Lu X, Huang X, Lu M. Endovenous laser treatment combined with a surgical strategy for treatment of venous insufficiency in lower extremity: A report of 208 cases. J Vasc Surg 2005;42:494-501.
86. Sharif MA, Lau LL, Lee B, Hannon RJ, Soong CV. Role of endovenous laser treatment in the management of chronic venous insufficiency. Ann Vasc Surg 2007;21:551-5.
87. Labropoulos N, Wang ED, Lanier ST, Khan SU. Factors associated with poor healing and recurrence of venous ulceration. Plast Reconstr Surg 2012;129:179-86.
88. Nelson EA, Bell-Syer SE, Cullum NA. Compression for preventing recurrence of venous ulcers. The Cochrane Library. No. 1. Chichester: John Wiley and Sons Ltd.; 2000.
89. Vandongen YK, Stacey MC. Graduated compression elastic compression stockings reduce lipodermatosclerosis and ulcer recurrence. Phlebology 2000;15:33-7.
90. Clinical Practice Guidelines. The Nursing Management of Patients with Venous Leg Ulcers: recommendations. London: Royal College of Nursing; September 2006. Available from: http://www.rcn.org.uk/_data/assets/pdf_file/0003/107940/003020.pdf. Last accessed on 2012 May 07.

Cite this article as: Dogra S, Sarangal R. Summary of recommendations for leg ulcers. Indian Dermatol Online J 2014;5:400-7.

Source of Support: Nil, **Conflict of Interest:** None declared.