



EXERCISE INTERVENTION IN THE MANAGEMENT OF VENOUS LEG ULCERS: A REVIEW

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Abstract:

Venous leg ulcers (VLUs) are the most common etiology of lower extremity ulceration, with approximately 70 to 80 percent of leg ulcers developing from venous insufficiency or disease. The financial burden of VLUs on society, increase in prevalence with age, the chronic nature of the disorder, and high recidivism rate are, in part, the driving forces behind efforts to determine the most effective management options to achieve complete wound healing in a timely and efficient manner. Thus, the purpose of this paper is to describe the etiology, diagnosis, and management of VLUs, with a particular emphasis on exercise intervention. While medical treatment of VLUs include wound debridement, infection control, and proper wound dressing, compression therapy and elevation are the most common and effective treatment option for VLUs. When combined with routine compression therapy, exercise intervention (e.g., aerobic, resistance, and flexibility exercises) significantly improves the healing of VLUs in a cost efficient manner and should be strongly considered in the routine management of patients with VLUs.

Keywords: venous leg ulcer, exercise, wound care

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1. Introduction

Venous leg ulcers (VLUs) are the most common etiology of lower extremity ulceration, with approximately 70 to 80 percent of leg ulcers developing from venous insufficiency or disease (1, 2). In 2010, the estimated annual financial burden for medical costs for VLUs was \$2 billion (3); however, in 2017, the estimated costs increased to \$9 billion (4). Approximately 1 percent of the United States population is diagnosed with a VLU, but the prevalence increases to 2 percent for people over 65 years of age in the United States (1, 5-7). Venous leg ulcers are often chronic and there is usually uncertainty in the amount of time that it will take for the ulcer to fully heal. For example, between 40 to 70 percent of VLUs heal after 6 months of treatment; however, the larger the ulcer, the decreased likelihood of complete wound healing (8-10). Additionally, if the underlying cause of the VLU is not addressed, it is likely that the ulcer will recur. The financial burden of VLUs on society, increase in prevalence with age, the chronic nature of the disorder, and high recidivism rate are, in part, the driving forces behind efforts to determine the most effective management options to achieve complete wound healing in a time efficient manner. The purpose of this paper is to describe the etiology, diagnosis, and management of VLUs, with a particular emphasis on exercise intervention.

2. Etiology and Diagnosis

Patients present with venous insufficiency when veins become incompetent in returning blood to the heart. The lower extremity has major muscle pumps located in the calf, thigh, and foot (11). The calf muscle pump, consisting of the soleus and gastrocnemius muscles, is important for its ability to generate high pressures and assist venous blood flow against the force of gravity (12, 13). Factors that may lead to venous incompetence and insufficiency include decreased mobility, decreased effectiveness of the calf muscle pump, venous valve dysfunction, venous thrombosis, or phlebitis (14, 15). Over time, venous insufficiency leads to leg veins becoming dilated and retrograde blood flow results in venous hypertension in the lower extremities. A sustained increase in venous pressure leads to extraction of fluid and proteins in the extracellular space, which results in edema, extravasation of red blood cells, and altered pigmentation of the local tissues. Persistent edema, inflammation, hypoxia, and oxidative stress causes mechanical disruption of endothelial cells and dermal tissues, which can lead to subsequent ulcer formation (16-18).

Normal ankle mobility is crucial for the activation of the calf muscle pump (19, 20). Patients diagnosed with VLUs commonly present with impaired ankle range of motion, which is associated with delayed ulcer healing. (19, 20). Other risk factors for developing VLUs include advanced age, female gender, a family history of leg ulcers, white race, previous leg injury or trauma that damages the integument, chronic leg edema, sedentary lifestyle, and prolonged standing (21, 22).

When evaluating VLUs, a thorough and careful history and physical examination are key, as these findings will be helpful for developing an accurate prognosis and an

appropriate management plan. Historical information should include whether there is a history of previous or current deep vein thrombosis, a family history of leg ulcers, varicose veins, phlebitis, chest pain, pulmonary embolism, occupations that have required prolonged standing or sitting, obesity, number of pregnancies for women, aching pain in the lower limbs, and/or surgery, trauma or fractures that could damage the venous valves or integument (23). Examination of the ulcer should include identifying the location, size, and characteristics of the ulcer, amount and type of exudates, appearance of the ulcer bed, ulcer odor, any sign of infection, and pain associated with the ulcer (24, 25). The location of a VLU is typically anterior to the medial malleolus and in the lower third of the leg. Measuring for the size of the ulcer is important to determine a prognosis for the patient. Measurements should include the length, width, and depth of the ulcer. Venous stasis ulcers typically present as shallow in depth and irregularly shaped with well-defined margins (Figure 1). Any exudates that may be present would display as yellow-white in color. Patients with VLUs present with variable pain symptoms; however, pain is typically worse at the end of the day and is typically relieved by elevation of the leg. Signs of infection need to be observed daily and are important for any health care provider to identify when treating a patient with a VLU. Signs of infection include the following: erythema, delayed healing despite appropriate treatment, increase in local skin temperature, increase in ulcer pain or changing in the nature of the pain, newly formed ulcers, discoloration, increase in exudate viscosity or volume, new-onset dusky wound hue, sudden appearance or increase in the amount of slough, and/or sudden appearance of necrotic black spots and ulcer enlargement (26).

4. Medical Management

General guidelines for medical treatment of VLUs include wound debridement, infection control, wound dressing, and compression therapy (18). Wound debridement involves removing tissue and decreasing the bacterial burden that can be accomplished by a faster, but more traumatic surgical option or through autolytic dressings that are slower, but less traumatic (27). After debridement, topical antibiotics (such as neomycin/polymyxin B/bacitracin separately or in combination, or mupirocin) and antiseptics (like acetic acid, iodine dressing, or hydrogen peroxide) may be applied to the ulcer to control for potential local infections. Topical antibiotics and antiseptics can both decrease bacterial burden in the wound; however, this may not always translate into wound healing, especially when deep tissue infection or wound etiology remains untreated.

If a deep or systemic infection is suspected, systemic antibiotics for the treatment of cellulitis or soft tissue infection should be introduced. Per guidelines from the Infectious Diseases Society of America (28), skin and soft tissue infections are divided into purulent and non-purulent. Purulent infections are usually caused by *S. aureus* (methicillin sensitive or methicillin resistant depending on situations) which is usually treated with oral doxycycline, minocycline, or trimethoprim-sulfamethoxazole in mild cases and with intravenous vancomycin, daptomycin, or linezolid in moderate to severe cases. Non-purulent infections are typically caused by streptococcus and occasionally

methicillin sensitive *S. aureus* which is treated with oral dicloxacillin, cephalexin, or clindamycin in mild cases and with intravenous nafcillin, oxacillin, cefazolin, ceftriaxone or clindamycin in moderate to severe conditions. Additionally, skin or soft tissue infection of *P. aeruginosa* (commonly noticeable for its blue-green pigmentation from pyocyanin) is not uncommon in VLUs (29), especially in patients with diabetes or other multiple comorbidities. Consequently, expanding coverage with additional oral or intravenous levofloxacin or ciprofloxacin, or intravenous piperacillin-tazobactam or carbapenems is also needed when *P. aeruginosa* infection is a concern.

Local infection, also known as, critical colonization refers to the status of wound infection without inducing an overt host response (30). Wounds and the surrounding soft tissue with critical colonization commonly lack the typical signs of redness, edema, warmth, or significant tenderness. While the use of topical antibiotics or antiseptics may be justified in critical colonization because it hinders wound healing, no evidence is present supporting the prolonged or routine use of antibiotics, especially in non-infected wounds (1). Certainly, the diagnosis of pure phlebitis does not warrant antibiotics. When considering local wound dressings for patients with VLUs, topical dressings should be utilized to create an optimal environment for wound healing, neither too dry nor too moist, while protecting the wound from further injury and shear. Potential wound dressings that are available include hydrocolloids, alginates, and foams depending on the needs of the patient and state of the wound (31). Other management strategies that have shown promise include ultrasound therapy, electrical stimulation, extra-corporeal shock-wave therapy, and aspirin therapy (18).

Compression therapy and elevation are the most common and effective medical treatment options for VLUs (18). It is imperative that medical compression therapy be prescribed accurately, to ensure that no tissue damage occurs, and the patient is compliant with the management protocol. Prior to incorporating compression therapy for a patient, it is necessary to rule out arterial insufficiency as this is an absolute contraindication (32). Elastic compression garments are preferred over non-elastic with graded pressure in a distal to proximal direction (33, 34). Additionally, four-layer bandages appear better than the short stretch bandage with respect to facilitating healing (33). The compression garment should be applied from the foot (sometimes toes depending on the need) to the knee with inclusion of the heel for maximum healing benefits (34). Typically, patients will receive compression garments that range from 30 to 40 mmHg of compression, but the amount of compression applied should be based upon several factors including the ankle-brachial pressure index, disease progression and clinical symptoms, patient body mass index, and limb shape and description (34).

5. Exercise Considerations

Up to 30 percent of chronic VLUs do not respond to compression therapy alone and remain unhealed even after a year of treatment, which suggests an alternative adjunct treatment is necessary, such as exercise (34, 35, 36). Exercise can serve as both a preventative measure and treatment option (37). Patients with VLUs have decreased

ankle range of motion and ankle plantarflexor strength, as well as impaired balance and gait in comparison to healthy individuals of equal age (38). Thus, exercise treatments should address these key impairments with a focus on activating the calf muscle pump during gait to promote improved blood circulation.

Prior to initiating an exercise program, it is recommended that clinicians thoroughly screen patients for cardiovascular risk factors. By identifying the level of cardiovascular risk for each patient, the clinician can determine whether medical clearance is necessary prior to initiating an exercise program. It is also important to assess the patient's current level of function. Submaximal exercise tests, such as the 6-minute walk test, timed-up and go test, and the 30-second chair stand test, are helpful to establish an initial exercise prescription and serve as a baseline measure to assess future progress. The 6-minute walk test assesses the distance walked over a 6-minute time period, which would assess aerobic endurance and gait capabilities, which is likely limited in patients with a VLU. The timed-up and go test assesses a patient's mobility and their static and dynamic balance. It assesses the time that a person takes to get up from a seated position in a chair, walk 3 meters, turn around, walk back to the chair, and return to the seated position. The 30-second chair stand test, which has a patient rise to a full standing position and then sit back down again as many times as they can in a 30 second period, assesses leg strength, balance, and endurance of the patient. These submaximal exercise tests along with ankle range of motion and strength of the ankle plantarflexors are important to include to assess the key impairments associated with patients with VLUs.

Since patients with VLUs may have pain and other impairments related to gait and balance that may interfere with an exercise program, and perhaps limited experience with exercise, it is prudent to begin an exercise program in-clinic under the appropriate level of clinical supervision. A study conducted by Klonizakis et al (39), evaluated the feasibility of a 12-week supervised exercise program as an adjunct to compression therapy in older patients (mean age = 64 years) with VLUs (mean ulcer duration = 8 months) (Table 1). Assessments were completed at baseline and repeated at 12 weeks, 6 months and 1 year. While all participants received standard compression therapy, the individuals in the exercise group were enrolled in a 60-minute supervised exercise program that was completed 3 times per week and incorporated a combination of aerobic, resistance, and flexibility exercises (Table 2). Patients in the exercise group demonstrated higher mean values in the physical fitness tests (6-minute walk test, chair sit and reach, chair sit and stand) and ankle range of motion at 3 months, but stabilized in all measures in relation to the non-exercise group by 12 months. When examining outcomes at 1 year, median VLU healing time was lower in the exercise group (13 versus 35 weeks) and mean costs for care were 3 times higher for those individuals in the control group. The results of this study suggest that patients who participate in an exercise program, in addition a routine compression therapy, would have improvements in physical fitness and wound healing in a shorter period of time in comparison to patients that do not exercise.

Another management option would be for patients with VLUs to be primarily managed through a home-based exercise program. In a randomized control trial, O'Brien

et al (37) assessed the impact of a home-based progressive resistance exercise program for the calf musculature in addition to routine evidence-based care on the healing rates for adults with VLUs. This study included 63 patients with VLUs (mean age = 72 years; mean ulcer duration = 16 weeks) (Table 1). Patients were randomized to receive either a 12-week progressive resistance exercise program (Table 3) with a telephone coaching component or usual care plus telephone calls. The primary outcome evaluated the effectiveness of the intervention in relation to wound healing. At 12 weeks, 77 percent of those in the intervention group healed compared to 53 percent of those in the usual care group. The authors concluded that those participants who adhered to the exercise program as an adjunctive treatment to routine evidence-based care are more likely to heal and have better functional outcomes than those who do not adhere to the exercises in conjunction with usual care. Thus, a self-management intervention that improves an individual's exercise self-efficacy and self-management capacity is a viable treatment option for patients with VLUs.

Compression therapy is the most common and effective medical treatment option for VLUs (18). In a randomized controlled trial conducted by Meagher et al (35), researchers hypothesized that adjunctive exercise therapy in combination with compression therapy might increase the rate of healing of VLUs. Thirty-five patients participated in the study; 18 patients were in the exercise group (median age = 66 years) and 17 patients were in the control group (median age = 78 years) (Table 1). All patients were treated with multilayer compression stockings during the duration of the study. The exercise group was instructed to try and increase their walking to 10,000 steps a day while the control group was instructed to not change anything out of their daily routine. Meagher et al (36) found that the more steps a patient took compared to baseline, the higher the VLU healing rate. More specifically, 67 percent of the participants in the exercise group achieved VLU healing by 8 weeks, compared with 35 percent of individuals in the control group. The results of this study emphasize the importance of exercise therapy in patients with VLUs and how exercise should be used in conjunction with other medical interventions, such as compression therapy, for treating VLUs.

It is common for patients with VLUs to have an increased incidence of medical comorbidities such as cardiac disease and diabetes (40), conditions for which exercise is indicated and beneficial. However, patients with these conditions need to be carefully monitored for the presence of symptoms that would contraindicate exercise and require medical referral (e.g., chest pain, shortness of breath with mild exertion, palpitations, syncope, etc). Health care providers also need to continue to address exercise adherence in this patient population by providing education on the positive effects of exercise on physical fitness and the healing process. Routine monitoring of wound health is also imperative to ensure proper healing is occurring.

6. Conclusions

Venous leg ulcers are the most common etiology of lower extremity ulceration. They pose a financial burden on society and increase in prevalence with age. The chronic nature of

the disorder and high recidivism rate are, in part, the driving forces behind efforts to determine the most effective management options to achieve complete wound healing in a time efficient manner. While medical treatment of VLUs include wound debridement, infection control, proper wound dressing, and therapeutic modalities, compression therapy and elevation are the most common and effective treatment option for VLUs. When combined with these treatments, exercise intervention (e.g., aerobic, resistance, and flexibility exercises) will likely improve the healing of VLUs in a cost efficient manner and should be strongly considered in the routine management of patients with VLUs.

Financial Disclosure and Conflict of Interest Statement

We affirm that we have no financial affiliation (including research funding) or involvement with any commercial organization that has a direct financial interest in any matter included in this manuscript. There are also no conflicts of interest (ie, personal associations or involvement as a director, officer, or expert witness) associated with this manuscript.

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Appendix

Table 1: Study characteristics that evaluated the effect of exercise in patients with venous leg ulcers (VLU = venous leg ulcer)

Study	Participant Characteristics	Intervention	Outcomes
Klonizakis et al (39)	<ul style="list-style-type: none"> - 39 participants with at least 1 VLU (diameter of at least 1 cm) - 23 males, 16 females - Mean age: 63.5±12.8 years 	<ul style="list-style-type: none"> - Control group (n=21): standard compression therapy for 12 weeks - Exercise group (n=18): standard compression therapy and supervised exercise for 12 weeks (3 sessions each week) 	<ul style="list-style-type: none"> - Participants in the exercise group demonstrated higher mean values in the physical fitness tests (6-minute walk test, chair sit and reach, chair sit and stand) and ankle range of motion at 3 months, but stabilized in all measures in relation to the non-exercise group by 12 months - At 1 year, median VLU healing time was lower in the exercise group (13 versus 35 weeks) and mean costs for care were 3 times higher for those individuals in the control group
Meagher et al (35)	<ul style="list-style-type: none"> - 35 participants with a newly diagnosed VLU - 17 males, 18 females - Median age: 71 years (range=32 to 91 years) 	<ul style="list-style-type: none"> - Control group (n=17): multilayer compression stockings for 12 weeks; no specific advice regarding exercise - Exercise group (n=18): multilayer compression stockings for 12 weeks and instructed to try and increase their walking to 10,000 steps a day 	<ul style="list-style-type: none"> - 33 percent of participants in the exercise group achieved an average of 10,000 steps per day - Mean daily steps at week 4: 5006 for the participants in the control group and 8161 for the participants in the exercise group - 67 percent of the participants in the exercise group achieved complete VLU healing by 8 weeks, compared with 35 percent of individuals in the control group - Participants who took more steps at both baseline and the 4-week assessment healed quicker than those who took fewer steps
O'Brien et al (37)	<ul style="list-style-type: none"> - 63 participants with VLUs - 32 males, 31 females - Mean age: 71.5±14.6 years 	<ul style="list-style-type: none"> - Control group (n=32): usual wound care plus telephone calls for 12 weeks - Exercise group (n=31): usual wound care and a 12-week home-based progressive resistance exercise program for the calf musculature with a telephone coaching component 	<ul style="list-style-type: none"> - 77 percent of those in the intervention group healed compared to 53 percent of those in the usual care group - 95 percent of those in the intervention group who adhered to the exercise protocol 75% or more of the time healed in 12 weeks

Table 2: Supervised exercise program for patients with venous leg ulcers modified from Klonizakis et al. (39)

Exercise	Dosage	Comment
Warm-up	Each session began with a 5-minute warm-up of low-intensity treadmill walking or cycling	The target for the warm-up period was for the participant to exercise at an exertion level of no higher than 11 (light) on Borg's 6-20 RPE scale.
Calf Stretch	3 repetitions for 20-seconds, held at the point of mild discomfort	
Hamstring Stretch	3 repetitions for 20-seconds, held at the point of mild discomfort	
Quadriceps Stretch	3 repetitions for 20-seconds, held at the point of mild discomfort	
*Standing Bilateral Heel Raise	2 to 3 sets of 10 to 15 repetitions to the point of moderate muscle fatigue	If the patient is unsteady, they may start in sitting; alternatively, if the patient can complete 30 bilateral heel raises without difficulty, consider progressing to a single-leg heel raise.
*Partial Squats	2 to 3 sets of 10 to 15 repetitions to the point of moderate muscle fatigue	Instruct the patient to lower into a squat as far as is comfortable for them. Place a chair behind them in case they start to fall backwards while completing the task.
*Chair Sit-to-Stand	2 to 3 sets of 10 to 15 repetitions to the point of moderate muscle fatigue	If the patient is unsteady, start with allowing them to place hands on a plinth for balance.
†Aerobic Exercise: 1. Walking 2. Cycling 3. Combination of Both	3 times per week for 30-minutes each	Patient should complete one or a combination of the two exercises for a total of 30 minutes. The intensity of exercise is guided by the use of Borg's 6-20 RPE scale, encouraging exercise at an exertion level of 12-14 (somewhat hard).

RPE = rating of perceived exertion.

*The exercises involved dynamic body-weight exercises with or without the use of dumbbells.

†Exercise mode is determined by the physical function and preference of participants, however, treadmill hill-walking was the preferred mode, since it promotes greater recruitment of the calf musculature than cycling.

Table 3: Home exercise program for patients with venous leg ulcers modified from O'Brien et al (37).

Exercise	Dosage	Comment
Ankle Active Range of Motion 1. Ankle Dorsiflexion & Plantarflexion 2. Ankle Inversion & Eversion 3. Ankle Circles (clockwise & counterclockwise)	3 to 5 sets of 10 to 20 repetitions	
*Calf Stretch	3 to 5 repetitions for 20-seconds, held at the point that elicited comfortable tension but no pain.	
*Hamstring Stretch	3 to 5 repetitions for 20-seconds, held at the point that elicited comfortable tension but no pain.	
Sitting Bilateral Heel Raise	Begin with 3 sets of 10 repetitions daily and progress to 3 sets of 25 repetitions daily	If the patient can complete 3 sets of 25 bilateral heel raises in sitting without difficulty, consider progressing to a standing bilateral heel raise, and then a standing bilateral single-leg heel raise.
†Walking	3 times per week aiming for 30-minutes each session	A target of 150 minutes (30 minutes over 5 days per week) of low to moderate intensity walking, was encouraged (as defined by a score between 9-14 on Borg's 6-20 RPE scale).

*Stretching was recommended prior to and following each exercise session.

†As most patients are relatively inactive at baseline, increases in walking are initially small and gradually increase towards the goal of 30 minutes per day of low-moderate intensity.

Figure 1: Venous leg ulcer on the lower leg. The ulcer is characteristically shallow in depth and irregularly shaped with well-defined margins (image courtesy of Dr. David Draughn and the Vein Specialists of the Carolinas, Charlotte, North Carolina)



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