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Lymphovenous Bypass as an Alternative Strategy for Managing Phleboedema and Venous Leg Ulcers: Preliminary Results

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Background: Chronic venous leg ulcers (VLUs) are a common manifestation of chronic venous insufficiency, accounting for up to 70% of all chronic leg ulcers. Patients sustained refractory ulcers and persistent phleboedema even with a combination of different treatment methods. Lymphovenous bypass (LVB) has shown promising results in patients with lymphedema. We hypothesize that LVB could potentially alleviate VLUs and phleboedema, given their symptom similarities with lymphedema.

Methods: From May 2021 to June 2023, we prospectively deployed LVB in patients with nonhealing stasis ulcers after 4-week traditional care, or in those with persistent phleboedema despite prior surgery for vein etiologies. Demographics, healing course and recurrence, lymphoscintigraphy, and VLU quality of life (QoL) questionnaires were collected.

Results: Thirty-one patients were treated with LVB and additional skin grafting as necessary. Their mean age was 62.6±14.7 years, with male predominance (20, 64.5%), and most patients sustained clinical, etiologic, anatomic, pathophysiologic classification C6 (25, 80.6%). Postoperatively, wound healing and phleboedema decongestion were observed mostly within 2 months. The VLU QoL questionnaire (39.3% response rate) showed improvement in QoL in activities, and psychological and symptom distress aspects.

Conclusions: Using LVB for chronic venous insufficiency showed an increase in the success rate of ulcer healing and decompression of the swollen limbs with durable results. Patient-reported outcome measures disclosed the potential benefits of LVB. Large-scale randomized controlled trials and pathophysiological studies are warranted to elucidate its efficacy. *(Plast Reconstr Surg Glob Open 2024; 12:e6064; doi: 10.1097/GOX.0000000000006064; Published online 15 August 2024.)*

INTRODUCTION

Lower extremity ulcers are wounds that result from various causes, including venous and arterial diseases, pressure-related issues, diabetic foot ulcers, posttraumatic injuries, neuropathic disorders, allergic reactions, or inflammation, leading to a breakdown of the integrity of the skin and commonly occurring on the lower leg or foot. Chronic venous leg ulcers (VLUs) are defined as nonhealing wounds on the lower leg persisting for more than 4 weeks. They are primarily caused by chronic venous insufficiency (CVI), according to the latest international classification for CVI [clinical, etiologic, anatomic, pathophysiologic (CEAP)] and are clinically categorized as C6 or C6r.[1,2]

VLUs account for approximately 70% of all chronic lower extremity ulcers and have a prevalence of 2% in Western countries, affecting millions of people worldwide. This condition leads to reduced quality of life (QoL), disability,[3] pain, worsening of the wound, increased risk of infection, psychological stress, and

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significant socioeconomic impacts, estimated at a loss of two million workdays annually. In fact, patients with lower socioeconomical status tended to have a higher CEAP class at presentation.[4] Treating VLUs in the United States alone costs approximately $1 billion annually, whereas the total expenditure in Western countries is approximately $3 billion.[5]

The lymphatic system is considered important for the removal of excessive fluid from the interstitial space, absorption of fat from the intestine, and the immune system, and is actively involved in the regulation of immune cell trafficking and inflammation. Lymphaticovenular (also known as lymphovenous bypass, LVB), diverting lymphatic drainage into the venous system in dealing with lymphedema,[6–9] not only restores TH1 and TH2 imbalance[10] but also decreases oxidative stress and increases antioxidant capacity in the serum of lymphedema patients.[11] Clinically, LVB may be an alternative treatment option for patients with lymphorrhea.[12]

Based on these facts, we hypothesized that lymphatic hypertension and lymph impregnation contribute to chronic VLU formation, and we propose a novel strategy using LVB to treat patients with refractory/recurrent chronic VLUs and phleboedema (C3).

MATERIALS AND METHODS

From May 2021 to June 2023, we prospectively deployed LVB in patients with nonhealing stasis ulcers after 4 weeks of traditional care, or in those who had lower extremity edema compromising QoL despite prior varicose vein (C2) therapy (Mueller phlembectomy or endovascular laser therapy). Patients with deep vein thrombosis and iliac vein compression were only included if they were treated for those diseases. Patients with severe peripheral arterial disease were excluded. Demographics, wound healing course, ulcer recurrence, lymphoscintigraphy, and VLU QoL questionnaires were collected under institutional review board approval (202105094RIND) and ClinicalTrials.gov registration (NCT05068258). We also demonstrate a data narrative of the questionnaires.

SURGICAL TECHNIQUE

A lymphovenous bypass procedure using a lymphangiography dye (Patent Blue V or indocyanine green), 0.2 mL was injected into the skin at the toe webspaces preoperatively.[8,13,14] The paths of lymphatic vessels were traced. On the foot dorsum of the affected limb, a horizontal incision of 2–3 cm was made close to the lymphatic vessel's pathway. Under the surgical microscope, suitable lymphatic and venous vessels were identified, usually located above the deep fascia (on the superficial side, ensuring that the extensor hallucis longus tendon remains unexposed). The coaptation between the lymphatic vessels and venules followed the same principles as those for vascular anastomosis. However, it required a higher magnification under the surgical microscope (approximately 20×), use of finer microsurgical instruments, and 11- or 12-0 nylon sutures. The evaluation included assessing the number of lymphatic vessels and venous vessels and their diameters and distances, to determine whether to use end-to-end, end-to-side, side-to-end, side-to-side, or multiple-to-one (lymphaticovenous insertion; an octopus fashion) anastomotic techniques. The success of the connection was determined by whether the lymphangiography dye flows through the anastomotic site or if there was washout of lymphatic fluid from the venous blood. For patients with C6 lesions, we performed split-thickness skin grafting for ulcer area more than 4 cm^2, and we did not use any skin substitute.

Takeaways

Question: Does lymphovenous bypass (LVB) benefit chronic venous insufficiency (CVI) in clinical symptom improvement?

Findings: Using LVB for CVI showed an increase in the success rate of skin grafting, relief of wound pain/neuralgia, decompression of swollen limbs, and improvement in the wound healing process with durable results.

Meaning: LVB may alleviate swollen limbs and problem wounds associated with both venous and lymphatic etiologies.

POSTOPERATIVE PROTOCOLS

We applied wet cotton wrap-around dressing on the patient's lower extremities and added elastic bandage for 1 day of not-strict bedrest. Then, we checked surgical wounds, changed dressing, put on an elastic bandage/pressure garment, and discharged them to resume their daily routine. We highly recommended that patients keep compression at daytime if tolerable, but this was not mandatory. We arranged lymphoscintigraphy to follow the long-term patency of LVB, corresponding to clinical improvement.

RESULTS

Thirty-one eligible patients were treated with LVB with additional skin grafting as necessary. Their mean age was 62.6±14.7 years, with male predominance (20, 64.5%), and most patients sustained CEAP classification C6 (25, 80.6%) (Table 1). Postoperatively, complete wound healing and phleboedema decongestion were observed within 2 months (Figs. 1–3). [**See figure, Supplemental Digital Content 1**, which shows a 72-year-old male patient who had chronic kidney disease and CVI (C3, C4a, and C4b) over bilateral lower extremities with antecedent trauma history. **http://links.lww.com/PRSGO/D435**.] Long-lasting results were found in patients with a single CVI etiology in at least a 1-year follow-up period. Patients were prone to recurrence (other than in previously treated areas) with comorbidities such as polio, congestive heart failure, chronic kidney disease, and antecedent trauma. VLU-QoL questionnaire (39.3% response rate) showed improvement in QoL in activities, and psychological and symptom distress dimensions. [**See figure, Supplemental Digital Content 2**, which shows patient-reported outcome measures (PROMs) disclosing the possible benefits of LVB in three dimensions, including activities and psychological and symptom distress. **http://links.lww.com/PRSGO/D436**.]

Table 1. Demographics of Patients with CVI Undergoing LVB

Characteristic	N = 31	(%)
Age, y		
Mean	62.6 (±14.7)	
Rage	24–83	
Sex		
Male	20	(64.5)
Female	11	(35.5)
CEAP classification		
C6(r)	20	(64.5)
C3 only	4	(12.9)
Varicose vein treatment	8	(25.8)
Deep vein thrombosis management	3	(9.7)
Comorbidities		
Morbid obesity*	2	(6.5)
Antecedent trauma	4	(12.9)
CHF/CKD/cirrhosis	1	(3.2)
Autoimmune disease	1	(3.2)
Polio	1	(3.2)
Deep vein thrombosis†	2	(6.5)
Skin grafting on ulcers	14	(70)
Recurrence or worsening in 6 mo		
VLUs	4	(20)
Phleboedema	0	(0)

*Both patients who underwent bariatric surgery had body mass index of 37.4 and 40.5 kg/m^2, respectively, before LVB.
†Patients with deep vein thrombosis received thrombectomy (or stenting) and on antithrombotic agents before LVB.
CHF, congestive heart failure; CKD, chronic kidney disease.

DISCUSSION

Chronic VLUs require various treatments to promote healing in addition to managing venous hypertension. These treatments included wound care, debridement, bed rest, and elevation of the affected limb. Compression therapy has also been used to facilitate healing. Despite these measures, VLUs typically take an average of 6 months to heal, and even when utilizing autologous skin grafting for extensive wounds, the success rate is only 73%,[9] with a recurrence rate of more than 58% within 5 years.[15] Consequently, various treatment methods have been developed and applied to address the pathophysiology and underlying cause of VLUs. These methods include endovenous stripping or combined high ligation for CVI or thrombosis, endovenous radiofrequency or laser ablation, and venous stent placement. Additionally, wound therapies involving negative pressure, various dressings, gels, and even autologous stem cell therapy or platelet-rich plasma preparations are used to prepare the wound bed before skin grafting surgery to achieve wound closure.

Due to the diverse range of available treatment options, multiple versions of clinical practice guidelines have been developed using systematic methods to provide medical recommendations or statements. These guidelines assist physicians and patients in making appropriate decisions regarding medical care in specific clinical situations.[16,17] We reviewed the literature on these cocktail strategies and compare them in Table 2.

Phlebolymphedema (C3) is an unavoidable outcome of the hemodynamically unique relationship between the venous and lymphatic circulation systems as one "inseparable" system. These two systems operate based on completely different hemodynamic principles, but compensated lymphatic system occurs that leads to "lymphostasis" resulting in chronic lymphatic insufficiency.[18–20] We hypothesized that lymphatic pressure

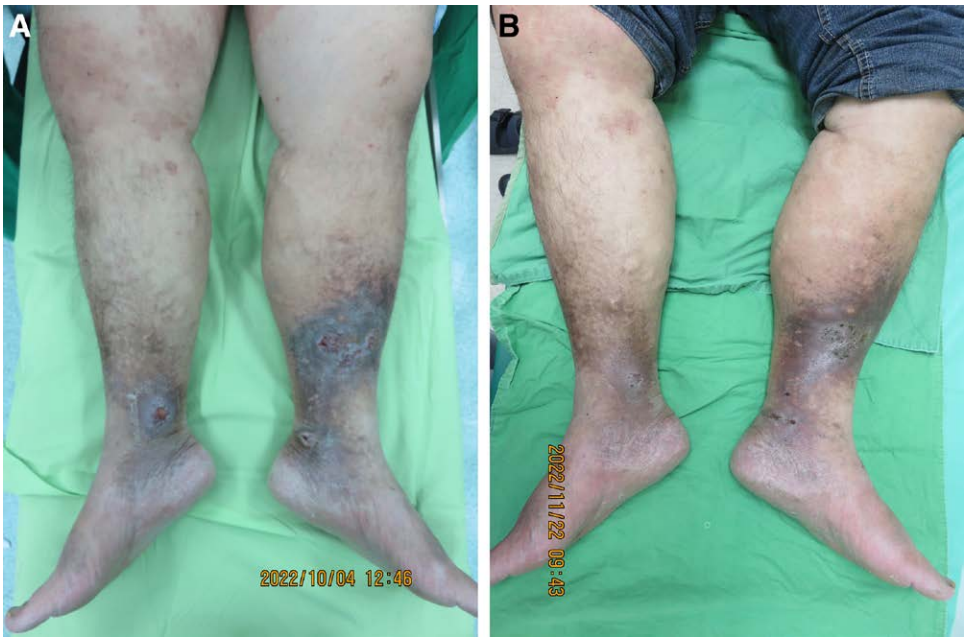

Fig. 1. This patient is a 44-year-old man who had undergone bariatric surgery for morbid obesity before sustained refractory CVI (C2, C3, C4b, and C6r) at bilateral lower extremities. LVB was done at left foot dorsum only. A, Postoperatively, wounds healed smoothly, and skin hyperpigmentation also subsided at bilateral calves without strict compression therapy (B).

Fig. 2. This patient is a 64-year-old woman who had painful VLUs for years. A, After LVB at left foot dorsum and additional split-thickness skin grafting. The wounds healed in 6 weeks without compression therapy, (B) pain was relieved, and the patient had durable results at 1.5-year follow-up (C).

Fig. 3. This patient is a 71-year-old man, who did not have any significant systemic or local diseases, who experienced swollen right feet. A, After LVB at affected foot dorsum, he was able to eliminate the compression and comfortably wear his shoes again for at least 6 months (B).

Table 2. Cocktail Strategies for CVI

Treatment	Efficacy	Cost	Side Effect	Compliance	Evidence	Comments
Compression	++++	+	+	+	++++	Basic
Dressings	++	+++	+	++	+++	Basic
Debridement	++	+	++		+++	Basic
Medications	+	+	+		+	Beneficial
Hyperbaric oxygen therapy	++	++	+	++	+	Advanced
Negative pressure wound therapy	+++	++	+	+	+++	Advanced
Surgery (phlebectomy) + skin grafting	++++	+++	+++		++++	Definite, recurrence
Cell therapy	+++	++++	++		++	Advanced

+, poor; ++, fair; +++, good; ++++, excellent.

will be higher than venous hypertension. Sometimes, lymphoscintigraphy demonstrated dermal backflow or stasis pattern in patients with CVI (not shown). During surgery, we noticed that the lymphatic vessels were nearly of normal ectasia quality. After LVB was done, even in patients with varicose veins, lymphatic fluid was diverted into the superficial vein, communicating vein and deep vein system finally, as shown in Figure 1B. Our preliminary data revealed complete wound healing and phleboedema decongestion mostly within 2 months after surgery[21,22] for those who had ulcers longer than half a year. Postoperatively, we recommend wearing pressure garments and changing lifestyle to prevent recurrence. Although not mandatory, the results of LVB seem satisfactory and durable.

PROMs, using a VLU QoL questionnaire that has been verified and authorized in the traditional Chinese version,[23,24] showed improvement in activities and psychological and symptom distress aspects after surgery in our series. This implies that LVB may restore the imbalance between the lymphatic and venous systems by exerting not only local improvement but also systemic effects.[11]

This study has several limitations. First, the number of cases was small. Second, we could not obtain specimens for the pathophysiological study due to ethical considerations. Moreover, we observed ulcer recurrence in patients with complex comorbidities. Therefore, the risk factors for VLUs recurrence and indications of aggressive resection of the lipodermatosclerotic tissue with skin grafting on muscles or free tissue transfer should be investigated in advance.

CONCLUSIONS

Our preliminary data using LVB for CVI showed an increase in the success rate of skin grafting, relief of wound pain/neuralgia, decompression of swollen limbs, and improvement in the wound healing process with durable results. PROMs also claimed the possible benefits of LVB in activities, psychological distress, and symptoms dimensions.

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DISCLOSURES

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ETHICAL APPROVAL

This study was approved by the Ethics Committee of the National Taiwan University Hospital (number 202105094RIND) and had ClinicalTrials.gov registration (number NCT05068258).

HELSINKI DECLARATION

This study was performed in accordance with the principles of the Declaration of Helsinki.

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