Surgical Management of Lower Extremity Lymphedema: A Comprehensive Review

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Abstract

Lymphedema refers to the accumulation of protein-rich fluid in the interstitial spaces. This can occur secondary to congenital malformation of the lymphatic channels or nodes or as a result of an insult that damages appropriately formed channels and nodes. Stagnant, protein-rich lymph initiates an inflammatory response that leads to adipocyte proliferation, fibrous tissue deposition, and increased susceptibility to infections. The end result is permanent disfigurement and dermal changes. Early and accurate diagnosis is essential, since lymphedema is a chronic and progressive problem. When lymphedema affects the lower extremity, it is important to manage it in a way that preserves function and mobility. Early diagnosis also allows for a proactive rather than reactive approach to treatment and utilization of novel physiologic procedures, such as lymphovenous anastomosis and vascularized lymph node transfer. Such interventions slow down disease progression and reduce morbidity by allowing the surgeon to salvage the remaining functional lymphatic channels. When physiologic procedures fail or when faced with a delayed presentation, the addition of excisional procedures can provide a more comprehensive treatment of this debilitating disease. The aim of this article is to review the most current concepts in the surgical management of lower extremity lymphedema.

Keywords
► lymphedema
► vascularized lymph node transfer
► radical reduction in lymphedema with preservation of perforators
► suction-assisted lipectomy
► lower extremity lymphedema

Introduction

The term lymphedema is used to describe a chronic, progressive clinical condition characterized by edema that arises secondary to accumulation of protein-rich lymphatic fluid in the interstitial space.1,2 The main function of the lymphatic system is to remove the excess interstitial fluid from different regions of the body and return it to the blood circulation.3,4 The lymphatic system also plays an important role in regulating immune response, transportation of immune cells, in addition to self and foreign antigen processing.5 Primary lymphedema arises when the lymphatic channels or nodes are structurally or functionally impaired or underdeveloped. This can be due to obstructed, malformed, or hypoplastic lymphatic pathways. The lower extremities are more likely to be involved in cases of primary lymphedema. The exact cause remains unknown; however, gravity probably exacerbates the problem and contributes to its progression.6-9
Secondary lymphedema refers to lymphedema caused by obstruction or destruction of normally formed and developed lymphatic channels or nodes. This can occur following trauma, radiation, infection, or surgery. In the developing countries, the most common cause is parasitic infection, mostly due to Wuchereria bancrofti.

It is estimated that up to 300 million people around the world suffer from lymphedema. While the majority of these cases in developing countries are secondary to the aforementioned parasitic filarial disease, in developed countries most cases occur secondary to malignancy or malignancy-related treatment. Compared with breast cancer-related upper extremity lymphedema, the incidence of postoncologic treatment lower extremity lymphedema (LEL) is noted to be higher with gynecologic cancers. Reports vary widely due to the diverse underlying pathology, oncologic treatment protocol, and lymphedema assessment method.

Nevertheless, the following ranges have been documented in the literature: 1.2 to 47% from endometrial cancer, 0 to 55.9% from cervical cancer, 4.7 to 40.8% from ovarian cancer. The incidence of LEL is similarly high in patients undergoing inguinal lymph node dissection for melanoma and can reach up to 55%. In contrast, there is a dearth of publications on the prevalence of lymphedema in urological cancers. Even though lymphedema can develop in 50 to 100% of patients with penile carcinoma with nodal metastasis undergoing inguinal dissection, it is less common in other urological cancers. Rates from prostate cancer range from 0 to 38% depending on the extent of lymphadenectomy and adjuvant radiation. The majority of patients present with LEL within the first year after the initial insult and the disease tends to progress faster than upper extremity lymphedema.

Regardless of the underlying etiology, lymph accumulation and stasis in the interstitial space trigger an inflammatory response that leads to adipose tissue proliferation and fibrous tissue deposition. The result is mild-to-severe permanent edema of the affected body part. Edema can be further complicated by infections and wound healing problems resulting in induration and disfigurement that can cause pain, discomfort, and compromised mobility. The problem is progressive, as the accumulation of lymphatic fluids and associated inflammation leads to more destruction of the remaining functional lymphatic channels. Lymphedema results in a significant pain, morbidity, and affects the quality of life negatively. It also results in significant financial burden on both the patient and the healthcare system.

To this date, there is no definite cure for lymphedema. Lymphedema has been traditionally managed conservatively with complete decongestive therapy that encompasses manual lymphatic drainage, compression therapy, and skin/wound care. Surgical treatment was only attempted when lymphedema became refractory to conservative measures and was often complicated with recurrent infections and chronic wounds. The surgical approach was mainly excisional and aimed to remove to differing degrees the diseased skin and subcutaneous tissue. Such procedures, however, were associated with significant blood loss, morbidity, infections, as well as permanent disfigurement and recurrence of symptoms (Fig. 1).

In the recent years, advances in microsurgery and improved understanding of the lymphatic system and pathogenesis of lymphedema have allowed the introduction of novel physiologic procedures such as lymphovenous anastomosis (LVA) and vascularized lymph node transfer (VLNT). These procedures have shown significant promise in the management of lymphedema, both in animal and clinical studies. In addition, modification of procedures such as Charles’, introduction of innovative approaches such as radical reduction of lymphedema with preservation of perforators and application of suction-assisted lipectomy (SAL) has open new horizons in the surgical treatment of LEL. By strategically combining physiologic and excisional procedures, safer and more predictable outcomes can be achieved.

This article reviews the contemporary surgical management of LEL with emphasis on accurate diagnosis and algorithmic approach to selection of the appropriate treatment protocol.

Diagnosing Lower Extremity Lymphedema

A common presenting symptom in lymphedema patients is swelling of the affected limb. Thus, confirmation of lymphedema as the cause of this is of primary importance. The next step would be objective quantification of change in the limb size. Several criteria have been used to diagnose lymphedema: difference in limb circumferences more than 2 cm, limb volume differences more than 200 ml, or at least 5% limb volume change. However, all these measures merely confirm edema but do not confirm the underlying etiology. Maclellan et al reported that 25% of patients referred to a lymphedema specialist did not have true lymphedema. On the other hand, symptoms of heaviness and discomfort can be reported by the patients well before any edema becomes clinically evident. Thus, a thorough history and physical examination is still crucial in identifying the etiology, precipitating factors, disease course, relevant family history, and previous treatments. Both the involved and healthy appearing extremities should be examined to determine extent and stage of the disease. Decreased skin pliability results in a positive “Stemmer sign.” This refers to the inability of the examiner use the thumb and index finger to pinch dorsal skin of a toe. Further diagnostic imaging is then undertaken to evaluate lymphatic function and, if indicated, exclude nonlymphogenic edema (i.e., venous disease).

Objectively, several diagnostic models can be used to confirm the presence of lymphedema and follow disease progression. Radionuclide lymphoscintigraphy is one such modality that is available in many centers where the transport index of a radio nuclide from the injection site to the lymph nodes basin can be calculated to quantify the severity of the disease. Lymphoscintigraphy can also be used to visualize the lymphatic channels and evaluate for any structural abnormalities or obstruction. Magnetic resonance lymphography (MRL) is more expensive but provides superior insight into the status of the lymphatic system and the soft tissue changes associated with lymphedema. Lastly, indocyanine green (ICG) lymphangiography can be used with near-infrared
cameras that visualize the lymphatic system in real time. After injection of ICG distally (web spaces), this modality enables the visualization of the lymphatic channels and nodes. It also allows the identification of patent lymphatic channels that can be used to treat lymphedema surgically. The advantages of this technique are that it is quick, safe, can be used in patients who
cannot undergo MRL due to metal implants or contrast allergy. It can also be done immediately prior to the surgery for site marking and lymphatic channels identification.26,17,38

Despite the fact that several clinically more relevant classifications have been proposed in literature, the most widely accepted across disciplines is the International Society of Lymphology (ISL) (►Table 1).2 In ISL Stage 0 lymphedema, there is demonstrable lymphatic dysfunction with ICG lymphangiography with abnormal dermal backflow patterns. While patients may complain of subjective symptoms, edema is not clinically evident. As lymphatic function deteriorates, edema becomes evident and progresses usually in a distal to proximal fashion (ISL Stage I). On physical examination, pitting edema can be appreciated. However, at this stage edema is reversible with elevation. The transition to irreversible edema denotes ISL Stage II. Pitting, which is common in early Stage II, becomes less detectable in late Stage II as subcutaneous adipose tissue proliferation and fibrosis ensues. Finally, lymphostatic elephantiasis (ISL Stage III) is characterized by progressive edema, absence of pitting edema, visible disfigurement, and substantial skin changes such as hyperkeratosis and polypoid nodules.

**Surgical Treatment of Lower Extremity Lymphedema**

Once the diagnosis of LEL has been established and the disease severity staged, the patients are best served by a multidisciplinary healthcare team that combines their efforts to offer an optimum treatment. The treatment goals in LEL patient are to improve the functional status, reduce patient's dependence on compression devices, and to decrease the risk of recurrent infections. Furthermore, any surgical intervention should aim at allowing the patient to be able to utilize footwear.

Conservative management in the form of complete decongestive therapy is usually the first treatment the patients receive and it continues to be an integral part of any surgical treatment protocol both preoperatively and to varied degrees postoperatively (►Fig. 2). In spite of the recent surging interest in microsurgical procedures for lymphedema, there is not a universally accepted algorithm to guide decision making with regard to timing, selection, and possible combinations of the available procedures. Surgeons have reported variable results with a multitude of surgical techniques. As lymphedema progresses through the aforementioned ISL stages, the clinical deterioration reflects the histological changes that take place in the lymphedematous limb. Initially, lymphatic dysfunction leads to fluids stasis in the interstitial place and this induces inflammation. Inflammation in turn causes adipose tissue hypertrophy and progressive fibrosis. Thus, while at early stages lymphatic fluid stagnation is the main reason for the edema, later the swelling becomes irreversible due to the deposition of solid components such as fat and fibrous tissue. It is imperative that the surgical approach planned for any given stage addresses these pathophysiologic changes. Physiologic procedures promote clearance of lymphatic fluid from the interstitial space. However, since they do not directly eliminate the solid component, any surgical plan without an excisional component would fall short of fully addressing the issue at hand. This is particularly true for the more advanced stages.

**Physiologic Procedures**

As mentioned earlier, physiologic techniques improve lymphatic drainage through redirecting lymphatic drainage into the venous system or by inducing the formation of new lymphatic channels through lymphangiogenesis. Among those procedures, LVA and VLNT are among the most popular options to improve lymphatic drainage and have both shown encouraging results clinically.

**Lymphovenous Anastomosis**

LVA is a procedure where the excess lymph is directed into the venous circulation. Superficial lymphatic vessels are identified preoperatively using ICG. The procedure entails injecting 0.5 to 1.0 mL of ICG subcutaneously distally in the limb such as the web space. Near-infrared cameras are then used to identify functioning lymphatic channels. Those channels are marked and incisions are made over the areas that they are in a vicinity of a superficial vein. Isoflurane

<table>
<thead>
<tr>
<th>Stage</th>
<th>Key Features</th>
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<tbody>
<tr>
<td><strong>Stage 0</strong></td>
<td>No edema (latent/subclinical)</td>
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<tr>
<td></td>
<td>• Swelling is not yet evident despite impaired lymph transport, subtle changes in tissue fluid/composition, and changes in subjective symptoms</td>
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<tr>
<td></td>
<td>• It may exist months or years before overt edema occurs</td>
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<tr>
<td><strong>Stage I</strong></td>
<td>Reversible edema (with elevation)</td>
</tr>
<tr>
<td></td>
<td>• Fluid relatively high in protein content</td>
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<tr>
<td></td>
<td>• Pitting (+/-)</td>
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<tr>
<td></td>
<td>• Proliferating cells</td>
</tr>
<tr>
<td><strong>Stage II</strong></td>
<td>Irreversible edema (even with elevation)</td>
</tr>
<tr>
<td></td>
<td>• Pitting (+)</td>
</tr>
<tr>
<td><strong>Late</strong></td>
<td>Excess fat/fibrosis</td>
</tr>
<tr>
<td></td>
<td>• Pitting (+/-)</td>
</tr>
<tr>
<td><strong>Stage III</strong></td>
<td>Lymphostatic elephantiasis</td>
</tr>
<tr>
<td></td>
<td>• Pitting (-)</td>
</tr>
<tr>
<td></td>
<td>• Trophic skin changes: Acanthosis, severe fat deposition and fibrosis, warty overgrowths</td>
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blue dye is also injected subcutaneously just distal to the incision to allow the identification of lymphatic vessels. Once the vessels have been identified, LVA can be done in an end-to-end or end-to-side fashion using super-microsurgical techniques depending on the size discrepancy between the vein and the lymphatic vessels.\textsuperscript{4,39} (\textbf{Fig. 3}). As many LVAs as possible can be done to improve lymph flow.

Multiple studies have demonstrated the efficacy of this technique.\textsuperscript{40–42} In our experience, this procedure is effective in the management of Stage I and early Stage II lymphedema.

\textbf{Fig. 2} Patient with left lower extremity lymphedema managed conservatively with complete decongestive therapy (CDT) that encompasses manual lymphatic drainage, compression therapy, and skin/wound care. (A) Pre-CDT. (B) Three months after CDT.

\textbf{Fig. 3} Anastomotic coupler devices for lymphovenous anastomosis.
Moreover, possibly due to the dependent position of the lower extremities, LVA is much more effective for upper rather than LEL.\textsuperscript{43} The limb size reduction achieved with LVA can be variable; however, most patients report improvement in symptoms. Generally speaking, patients still need to use compression garments.

**Vascularized Lymph Node Transfer**

In patients where functional lymphatic channels or nodes are absent or dysfunctional, such as following lymphadenectomy or radiotherapy, VLNT is an alternative physiologic procedure that improves lymph drainage and flow. The exact mechanism is still unknown and several theories have been proposed. Most likely, the mechanism of action is a combination of those theories. One theory is that the lymph node absorbs the excess lymphatic fluid accumulating in the vicinity.\textsuperscript{44} Another theory is that vascularized lymph nodes induce lymphangiogenesis by releasing vascular endothelial growth factor-C.\textsuperscript{45, 46}

Various donor sites have been described for vascularized lymph node flap harvest such as the groin,\textsuperscript{45, 47} submental,\textsuperscript{48} supraclavicular,\textsuperscript{49} lateral thoracic,\textsuperscript{50} gastroepiploic,\textsuperscript{51, 52} jejunal,\textsuperscript{53} appendicular,\textsuperscript{54} and ileocecal\textsuperscript{55} lymph nodes. All of the aforementioned options offer good functional result in terms of management of lymphedema (►Fig. 4). Due to concerns about donor site morbidity and iatrogenic lymphedema in the donor site, our team has explored various options and compared outcomes following VLNTs from different donor sites.\textsuperscript{56} Our preferred donor site is the gastroepiploic lymph node flap for treatment of both upper and LEL.\textsuperscript{57} This is due to its low morbidity, reasonable length of hospital stay, and the fact that it could be harvested laparoscopically (►Figs. 5 and 6). Furthermore, no cases of instances of iatrogenic lymphedema have been seen by the time of writing this review. It is important to mention, however, that when the gastroepiploic flap is not available due to previous operations, radiation, or for any other reason, we resort to other donor sites. The choice of which is dependent on the surgeon’s experience and individualized to each case.

Once the appropriate donor site has been selected and the lymph node flap has been harvested, the choice of inset site is determined based on multiple factors. For instance, severity of lymphedema, scar tissue, and prior radiation as well as the aesthetic appearance are all factors that influence where the lymph node flap will be placed. As for the exact location on the lower limb, several reports have suggested different aspects of the limb: proximal, middle, or distal. Distal placement of the vascularized lymph node where edema is more pronounced appears to be the most effective. This is due to the fact that placing the flap in the most dependent position on the limb may facilitate the pumping and absorption function of the stagnant lymph in addition to the fact that lymph is usually pooled in the most dependent location due to the effect of gravity. Furthermore, distal locations are usually away from radiation site and when inserting the flap in the ankle, there is no need to sacrifice a large artery to use it as the recipient vessel. In the lower extremity, we prefer to use the dorsalis pedis artery as the recipient vessel. This also allows the placement of the flap on the medial aspect of the ankle where it does not affect patient’s ability to wear footwear.

Although the aforementioned procedures are effective in controlling diseases progression, it is important to keep in mind that these procedures do not have any reduction effect on the fibrosis and adipocyte hypertrophy that have occurred prior to treatment. This makes such approaches effective in
early stages of lymphedema. When limb edema is significant, excisional procedures may be necessary to reduce pain and morbidity.

**Excisional Procedures**

Excisional procedures have been described for the management of lymphedema since the early 1900. Despite the advancements made and the advent of microsurgical techniques, these procedures remain relevant and can be done to reduce morbidity, risk of infection, and improve quality of life. Excisional procedures can be done when the physiologic procedures do not offer adequate relief or satisfactory results. Excisional procedures are also done in combination with physiologic procedures to offer better volume reduction. Our first choice of excisional procedure for the LEL is SAL. While patients are advised to use compression garments after SAL, many of our patients don't follow our instructions, mainly due to the warm climate or vocational reasons. In these situations, we have performed radical reduction in lymphedema with preservation of perforators. In selected cases of advanced LEL, the modified Charles' procedure is still a reliable option.

**Suction-Assisted Lipectomy**

SAL is the least invasive procedure for lymphedema. It has minimal morbidity and high patient satisfaction when compared with other ablative procedures. Although it provides excellent results, we prefer to perform it in combination with a physiologic procedure. O’Brien et al reported using this technique for the treatment of primary and secondary lymphedema with good results and outcomes. The authors concluded that SAL is a useful and safe procedure that can be done as a primary procedure or in combination with other procedures to achieve good outcomes. At our institution, a combination of VLNT is followed by laser-assisted liposuction with promising results. Although there are no standardized guidelines on the optimal timing, we believe that best results are attained when it is performed 1 year after a physiologic procedure as

![Fig. 5](image_url) Double level inset by division in half of a single gastroepiploic vascularized lymph node flap is shown. Upper extremity (A) and lower extremity (B).
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this allows the inflammation to subside, volume reduction, and clearance of any infections. The only downside to this procedure is that patients must wear compression garments immediately following the procedure. This makes achieving good results highly dependent on patients’ compliance with postoperative recommendations. 61,62

Radical Reduction in Lymphedema with Preservation of Perforators

Improved knowledge of the vascular anatomy and perforasome theory63 has allowed the introduction of radical reduction of lymphedema procedure with preservation of perforators. This procedure combines both approaches, excisional and microsurgical principles, to manage lymphedema. Several studies have reported excellent and long-lasting outcomes, making this procedure an essential tool in the armamentarium of the reconstructive surgeon. 64,65

The advantage of this procedure is that it allows for more aggressive debulking of the lymphedematous tissue without damaging essential perforators. The disadvantages, however, lie in the fact that such procedure leaves unsightly scars, prolonged operating time, risk of infection, skin breakdown, and necrosis. This procedure also requires good microsurgical skills (► Fig. 7).

Fig. 6 A double vascularized gastroepiploic lymph node transfer had been performed in one-stage procedure from a single donor site in a patient with bilateral congenital lymphedema.

Fig. 7 (A) Preoperative and (B) postoperative appearance following radical reduction in lymphedema with preservation of perforators of the left lower extremity.
Charles’ and Modified Charles’ Procedure
The Charles’ procedure is perhaps the oldest and the most radical ablative procedure. It is usually preserved for patients with advanced stage lymphedema and elephantiasis. The main goal is to control and eradicate infection while simultaneously reducing excessive volume. The Charles’ procedure remains a valuable option in carefully selected patients with debilitating lymphedema that is not amenable to treatment using physiological procedures. The modified Charles’ procedure, on the other hand, entails the preservation of the greater saphenous vein and its superficial branches. The greater saphenous vein and its branches can be used later as a recipient drain for a transferred lymph node. Patients with severe LEL may benefit from the combination of vascularized lymph node and modified Charles’ procedure. Combining the modified Charles’ with a vascularized lymph node procedure may prevent some of the side effects of the conventional Charles’ procedure such as recurrence, infection, or worsening of the disease. Although excisional procedure could be aggressive at times, they are still valuable options for patients with advanced stages of lymphedema as they improve the quality of life and mobility through drastic reduction in limb volume. (Figs. 8 and 9).

Postoperative Management
Surgical management of lymphedema does not completely eliminate the need for compression therapy. Following physiologic procedures, compression therapy is initiated 1 month postoperatively and immediately following SAL. Patients are usually followed every 3 months postoperatively and the patient is instructed to discontinue compression therapy 2 days prior to their follow-up appointments. If the patient experiences recurrence and excessive lymph accumulation, compressive decongestive therapy is continued for another 3 months. If not, the patient can use compressive therapy during the daytime only for 3 months. Compression therapy is discontinued if maintenance of limb size for 3 months with daytime therapy was achieved.

Conclusion
Lymphedema still represents a challenge to the surgeon and the patient alike. It is manageable, however, with a myriad of surgical options that aim to reduce limb volume and restore functionality. Excellent results are within reach when the surgeon and patient are on board with a treatment plan. This
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includes, but not limited to, careful patient selection, choosing the appropriate surgical option, patient compliance with conservative management and appropriate follow-up. Thoughtful individualization and combination of multiple treatment modalities make optimal outcomes attainable in every case.

**Conflict of Interest**
None of the authors received any funds or has any financial interests to disclose.

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