Surgical Intervention for Lymphedema

Kristalyn Gallagher, DO*, Kathleen Marulanda, MD, MS, Stephanie Gray, MD

INTRODUCTION

Lymphedema is a chronic, progressive disease that affects approximately 140 to 200 million people worldwide.1,2 There is no curative treatment and palliation is challenging. The incidence is difficult to quantify as early stage lymphedema is often underreported until it necessitates intervention. The etiology includes congenital malformations (primary) and direct injury to the lymphatic channels (secondary). Oncologic treatment for solid tumors is the leading cause of secondary lymphedema in the developed world. In the upper extremity, it is most often associated with breast cancer treatment. Patients with breast cancer who have undergone axillary lymph node dissection and/or radiotherapy are a particularly susceptible group, with reported lymphedema rates as high as 65% to 70%.3,4 Other causes of secondary lymphedema include trauma, neoplastic obstruction, or inflammatory destruction of the lymphatics. Obesity-induced lymphedema occurs in super obese patients with body mass indexes of greater than 50 to 60 kg/m² stemming from overwhelmed or damaged lymphatics secondary to increased adipose tissue and fibrosis.5,6

Lymphedema can manifest as mild to severe arm swelling, pain, dysfunction, disfigurement, lipodermatosclerosis, skin ulceration, cellulitis, and rarely lymphangiosarcoma. Treatment of lymphedema includes both nonsurgical and surgical strategies.

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KEYWORDS
- Lymphedema • Surgery • Lymph node transfer • Axillary reverse mapping
- LYMPHA • Lymphovenous anastomosis • Vascularized lymph node transfer
- Liposuction

KEY POINTS
- Lymphedema is a chronic, progressive disease with no curative treatment.
- Surgical treatment options are effective at managing early and late stage lymphedema.
- Standardized methods for quantifying lymphedema, universal reporting standards, and an increased amount of high-quality evidence are necessary to advance understanding and management of lymphedema.
Nonsurgical management involves meticulous skin care, limb elevation, lifelong external compression therapy (both static and pneumatic), and physical therapy with manual lymph drainage and massage to minimize symptoms. Surgical options have been reserved for failure of conservative management historically, but recent data suggest early intervention with surgical techniques may reduce incidence of symptom progression.7–9 Preventative surgical techniques have been described to reduce the initial disruption of the lymphatics and maintain function. Microsurgical techniques, including lymphaticovenous anastomosis (LVA), vascularized lymph node transfer (VLNT), and lymphaticolymphatic bypass aim to restore the underlying physiologic impairment. Additional surgical interventions such as liposuction and surgical excision remove affected tissues to effectively decrease the drainage load. The successful selection of surgical therapy depends on the stage of lymphedema with LVA and VLNT more suitable for fluid-predominant disease and suction-assisted protein lipectomy (SAPL) for solid disease. Open debulking and reductive procedures are used for management of late-stage solid lymphedematous disease.

ANATOMY AND PATHOPHYSIOLOGY

Lymphedema is an abnormal accumulation of protein-rich interstitial fluid within the interstitial space. It can occur anywhere in the body, most commonly in the lower extremity, followed by the upper extremity and genitalia. Disruptions in the interstitial pressures lead to an imbalance between the arterial capillary inflow, an increased demand for lymphatic outflow, and the decreased capacity of the lymphatic circulation.10–12 Secondary lymphedema occurs because of surgical, inflammatory, neoplastic, or traumatic destruction of the dermal lymphatics and their outflow tracts. During early stage lymphedema, compensatory mechanisms including lymphatic regeneration make up for the initial insult. At later stages, the lymphatic capillaries become overwhelmed and damaged leading to fibrosis, thickened basement membranes, and loss of permeability of the lymphatic capillaries.11 This breakdown allows protein to leak into the interstitial tissues, which increases the tissue colloid osmotic pressure. Water then accumulates in the interstitial space. The edematous tissues signal increased numbers of fibroblasts, adipocytes, keratinocytes, and inflammatory cells. These cell types cause increased collagen deposition, adipose accumulation, chronic inflammation, and fibrosis of the skin and subcutaneous tissues.11,13 Clinical manifestations include nonpitting edema with overlying skin changes. Stasis of the protein-rich fluid makes the subcutaneous tissues prone to recurrent bacterial and fungal infections, which ultimately leads to progressive damage of the lymphatics.14

The enlarged and edematous limb can subsequently cause debilitating and chronic pain, decreased quality of life (QoL), psychosocial issues, increased infection risk, higher medical costs, and loss in productive days for those afflicted with the disease.15,16 Although the incidence, onset, and progression of lymphedema differ greatly among patients, there are several associated risk factors that have been identified. These risk factors include obesity (body mass index \( \geq 30 \text{ kg/m}^2 \)), number of nodes resected during oncologic surgery, radiation therapy, high rates of paclitaxel use, infection, and underlying genetic makeup.16,17

CLINICAL PRESENTATION

Patients who have undergone breast cancer treatment with surgery, radiation, and/or chemotherapy have a lifetime risk of lymphedema occurrence17,18 and should be monitored with a low threshold of suspicion. Most patients become symptomatic within 8 months of surgery and 75% will present in the first 3 years.17
The two most commonly used staging systems for lymphedema are the International Society of Lymphology and Campisi systems (Table 1). Both systems agree that lymphedema can be classified as subclinical, mild (early), moderate (intermediate), or severe (advanced). The symptoms of lymphedema by stage are listed in Table 2. Early lymphedema typically presents with subjective symptoms, most commonly heaviness in the affected limb without any appreciable swelling or edema. These symptoms may be present for months or years before any detectable physical change occurs. As interstitial fluid accumulates, patients experience increased extremity circumference followed by pitting edema that usually worsens at the end of the day (Fig. 1). A 2 cm or greater difference in arm circumference or a 200 mL limb volume difference between affected and nonaffected arms is considered to meet diagnostic criteria for lymphedema, although no universal criteria exist. Early symptoms are initially alleviated with compressive garments, limb elevation, and physical therapy with manual lymph drainage and massage to minimize symptoms. As the disease progresses, irreversible, nonpitting edema develops. Patients report increased firmness, decreased functionality, and disfigurement. Significant swelling and increased limb volume severely impair limb mobility and cause chronic debilitating pain that impedes activities of daily living. This disease

<table>
<thead>
<tr>
<th>ISL Staging and Description</th>
<th>Campisi Staging and Description</th>
<th>Proposed Surgical Treatment</th>
</tr>
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<tbody>
<tr>
<td>Subclinical 0</td>
<td>No overt swelling despite impaired lymph drainage</td>
<td>None</td>
</tr>
<tr>
<td>Mild I</td>
<td>Accumulation of fluid with high protein content, which subsides with limb elevation. Usually lasts ≤24 h.</td>
<td>Ia Reversible swelling with limb elevation</td>
</tr>
<tr>
<td>mild II</td>
<td>Rarely resolves with limb elevation alone.</td>
<td>II Persistent swelling with elevation</td>
</tr>
<tr>
<td>Moderate IIa</td>
<td>Loss of pitting owing to progression of dermal fibrosis. Sometimes called spontaneously irreversible lymphedema.</td>
<td>II Persistent swelling with recurrent lymphangitis</td>
</tr>
<tr>
<td>Moderate IIb</td>
<td>Lymphostatic elephantiasis. No pitting; develop trophic skin changes (fat deposits, acanthosis, and warty overgrowths).</td>
<td>III Persistent swelling with elevation</td>
</tr>
<tr>
<td>Severe III</td>
<td>Fibrotic changes with columnlike limb Elephantiasis with limb deformation including widespread lymphostatic warts</td>
<td>IV Persistent swelling with elevation</td>
</tr>
</tbody>
</table>

Abbreviations: CDT, complex decongestive therapy; ISL, International Society of Lymphology; LVA, lymphaticovenous anastomosis; SAPL, suction-assisted protein lipectomy; VLNT, vascularized lymph node transfer.

Data from Refs. 19,24,27
Table 2
Symptoms of lymphedema by stage

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
</tr>
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<tbody>
<tr>
<td>Subclinical</td>
<td>0  • Heaviness</td>
</tr>
<tr>
<td></td>
<td>• Tightness</td>
</tr>
<tr>
<td></td>
<td>• Firmness</td>
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<tr>
<td></td>
<td>• Pain</td>
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<tr>
<td></td>
<td>• Aching</td>
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<tr>
<td></td>
<td>• Soreness</td>
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<tr>
<td></td>
<td>• Numbness</td>
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<tr>
<td></td>
<td>• Limb fatigue</td>
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<tr>
<td></td>
<td>• Limb weakness</td>
</tr>
<tr>
<td></td>
<td>• Impaired limb mobility</td>
</tr>
<tr>
<td></td>
<td>• Absence of swelling</td>
</tr>
<tr>
<td>Early (mild)</td>
<td>I  • Above symptoms</td>
</tr>
<tr>
<td></td>
<td>• Presence of swelling that decreases with compression or elevation</td>
</tr>
<tr>
<td>Moderate (Intermediate)</td>
<td>II • Above symptoms</td>
</tr>
<tr>
<td></td>
<td>• Disfigurement</td>
</tr>
<tr>
<td></td>
<td>• Early skin changes</td>
</tr>
<tr>
<td></td>
<td>• With or without cellulitis or infections</td>
</tr>
<tr>
<td></td>
<td>• Presence of swelling that does not decrease with compression or elevation</td>
</tr>
<tr>
<td>Severe (Advanced)</td>
<td>III • Above symptoms</td>
</tr>
<tr>
<td></td>
<td>• Disability</td>
</tr>
<tr>
<td></td>
<td>• Recurrent cellulitis or infections</td>
</tr>
<tr>
<td></td>
<td>• Late skin changes (hyperkeratosis, hyperpigmentation, papillomas, induration)</td>
</tr>
</tbody>
</table>

Data from Refs. 10,19–21,23–26

Fig. 1. Clinical presentation of lymphedema.
progression results in an undeniable decline in QoL. Disfiguring skin changes including hyperpigmentation and skin infections also arise secondary to chronic venostasis in the affected limb.\textsuperscript{10,19,20,24–26} Very rarely, this results in Stewart-Treves syndrome or angiosarcoma. Conservative palliation for advanced disease is exceedingly difficult.

The severity of disease is closely mirrored to a multifactorial decline in both objective and subjective symptoms, thereby making it difficult to accurately stage or define lymphedema. As such, no standardized staging system exists; the two predominantly used systems, the International Society of Lymphology and the Campisi (see Table 1), are limited owing to their heavy reliance on physical examination findings. Supplemental imaging studies and QoL evaluations are necessary to provide a more comprehensive assessment.\textsuperscript{19,24,27} This step is crucial, because the outcome, effectiveness of treatment, and risk of recurrence greatly depend on the stage of lymphedema at presentation.\textsuperscript{28}

**CLINICAL MONITORING**

Early detection and intervention lead to increased effectiveness of management therapies, fewer invasive procedures, and a decreased financial burden.\textsuperscript{7,29,30} Prospective surveillance is recommended for at least 1 year postoperatively. For improved diagnostic accuracy, preoperative baseline assessments are established and monitored serially to determine disease progression and therapeutic response. Early detection and treatment can lead to reversal and prevention of progression.\textsuperscript{7–9}

Limb size and volume measurements are typically used to quantitatively characterize the disease. The most commonly used criteria define lymphedema as a 10% change in limb volume measured by perometry or a 2-cm change in arm circumference.\textsuperscript{31}

The ideal measuring tool should be simple and easily reproducible for serial measurements. Water displacement is considered the gold standard owing to its high sensitivity and specificity for quantifying overall limb volume, but owing to its burdensome technique it is rarely performed.\textsuperscript{31} Tape measurements of arm circumference at 10 cm intervals along the limb are most frequently used owing to low cost and simplicity. Preferably, serial measurements are performed by the same operator to minimize variability. An increase in size between measurements (>10 cm or >10%) is found to correlate with subclinical lymphedema. Additional techniques available include perometry, a noninvasive optoelectronic device that uses infrared light to quantify limb volume, and bioelectrical impedance, which measures the flow of electrical currents to indirectly determine the limb volume. Notably, a recent study by Deltombe and colleagues\textsuperscript{32} found that perometry is superior to both water displacement and arm circumference tests, but applicability remains limited owing to its high cost.\textsuperscript{33}

Symptoms are frequently reported before any measurable physical changes, and continue to worsen in parallel with increasing volume.\textsuperscript{34} The Functional Assessment of Cancer Therapy questionnaire including breast cancer and arm function subscales (FACT B+4), the Lymphedema and Breast Cancer Questionnaire, and the Morbidity Screening Tool\textsuperscript{35} are used to assess QoL. These questionnaires evaluate symptoms including swelling and heaviness within the past year, which are the 2 most predictive factors associated with objective measurements.\textsuperscript{31} High-quality evidence regarding lymphedema-specific symptoms remains scarce and most questionnaires are not specific to breast cancer-related lymphedema.

**DIAGNOSTIC IMAGING**

Lymphography was historically used, but is seldom used currently owing to technical difficulties with cannulization of the lymphatic vessels and morbidity associated with
administration of oil-based contrast agents. Current guidelines recommend lymphoscintigraphy as the gold standard to assess the caliber and anatomic location of lymphatic vessels, functional status, and disease severity. Radionuclide dye is injected intradermally via the interdigital space and taken up by the lymphatic system to visualize dynamic flow, areas of blockage, and dermal backflow. Disadvantages of this technique include prolonged radionuclide uptake, poor image quality, and limited visibility of small vessels owing to relatively poor spatial resolution. Additional adjunct imaging modalities have been described including duplex ultrasound, which identifies tissue spaces and fluid accumulation, and computed tomography scan/MRI, which can delineate lymphatic abnormalities at multiple tissue levels.

In recent years, the development of near-infrared fluorescence (NIRF) imaging has significantly enhanced noninvasive in vivo imaging capabilities. NIRF imaging is a highly sensitive, quick and reproducible technique, which typically uses indocyanine green (ICG) as an optical contrast agent. In contrast with lymphoscintigraphy, NIRF imaging provides immediate, high-resolution images that assess contractile lymphatic flow volume and velocity, as well as finely detailed images of the lymphatic anatomy, including lymph nodes and surrounding collateral lymphatic network. Mihara and colleagues found that, unlike lymphoscintigraphy, NIRF imaging can definitively diagnose early stage lymphedema. NIRF imaging is equally beneficial intraoperatively when performing microsurgical procedures, and postoperatively to evaluate posttherapeutic response. Further research may support the potential use of NIRF imaging as a screening diagnostic tool.

**NONSURGICAL MANAGEMENT OF LYMPHEDEMA**

Lymphedema has traditionally been managed with nonoperative methods, primarily complex decongestive therapy, which consists of manual lymph drainage with massage, compression garments, meticulous hygiene, and physical therapy to decrease swelling and improve mobility. Patients are required to be active lifelong participants in their care and, therefore, the success of complex decongestive therapy is highly dependent on patient compliance and engagement.

Surgical options have emerged to avoid a lifetime commitment to compressive therapy and the potential to achieve a definitive cure. Currently, there is no widely accepted consensus for the role for surgical management, optimal timing of surgery, which surgical procedure to perform, or which surgical technique is preferred. Nevertheless, it is generally recognized that earlier initiation of treatment is preferred, given the progressive nature of the disease, which will only continue to deteriorate the lymphovascular system over time.

**PREVENTATIVE SURGICAL TECHNIQUES**

Surgical techniques such as sentinel lymph node biopsy (SLNB), axillary reverse mapping (ARM), and Lymphovascular anastomosis (“LYMPHA”) have been developed to prevent or minimize the disruption of lymphatic flow from the upper extremity during breast cancer surgery.

**Sentinel Lymph Node Biopsy**

SLNB is a technique by which the tumor’s most proximal draining lymph node(s) are identified with radioactive dye and/or isosulfan blue and excised. Reported rates of lymphedema range from 1% to 7% after SLNB. Recent data from ACOSOG (American College of Surgeons Oncology Group) Z0011, ACOSOG Z1071, SENTINA (Sentinel-Lymph-Node Biopsy in Patients With Breast Cancer Before and After
Neoadjuvant Chemotherapy), AMAROS (Comparison of Complete Axillary Lymph Node Dissection With Axillary Radiation Therapy in Treating Women With Invasive Breast Cancer), and OTOSAR (Optimal Treatment of the Axilla - Surgery or Radiotherapy) clinical trials show the usefulness of minimizing axillary surgery even in the setting of selective patients with node-positive disease in the axilla.46–52

Axillary Reverse Mapping

ARM is a procedure where isosulfan blue is injected into the proximal arm, identifying and sparing the lymphatic drainage of the arm in patients with breast cancer who undergo axillary lymph node dissection or SLNB.23,44,53,54 If ARM is used during SLNB, the radioisotope (Tc-99m) is injected into the breast and the blue dye is injected into the arm.

The ARM technique was initially described by Klimberg and colleagues53,54,55 in 2007 as a way to directly visualize arm lymphatics and preserve them to minimize injury. A volume of 2 to 5 mL of isosulfan blue is injected subcutaneously into the volar aspect of the upper arm in the medial bicpital sulcus (Fig. 2) before incision. The blue dye travels through the arm lymphatics highlighting them for visualization during axillary surgery (Fig. 3). Multiple studies have demonstrated statistically significant improvement in lymphedema rates when the ARM technique is used (33% vs a range of 4%–9% in ARM groups).55–59 Tausch and colleagues60 reported identification of arm nodes, but did not show a statistically significant difference in prevention of lymphedema at 19 months of follow-up. In 2015, Yue and colleagues61 performed a prospective feasibility study on 265 patients and showed reduction in lymphedema (33.7% in the control group and 5.93% in the ARM group; \( P < .001 \)). They used both blue dye and radioisotope (Tc-99m-Nano-coll). Most studies have reported the feasibility of the procedure without long-term outcomes. Currently there is no large, multicenter trial assessing the effectiveness of this technique.

The ARM technique was developed with the hypothesis that the arm and breast lymphatic drainage systems are separate. Metastatic disease has been reported in 8.7% to 25% of ARM nodes. The involvement of the ARM node increases with the increased axillary burden of disease (more common in N2 and N3 disease). The possibility of crossover nodes should be discussed with patients preoperatively. If a lymph node is dyed blue and there is strong clinical suspicion for involvement, the node

Fig. 2. Injection site for axillary reverse mapping procedure: 3 to 5 mL of isosulfan blue is injected subcutaneously in the volar surface of the upper extremity.
should be removed along with the remaining axillary nodes. The oncologic resection should not be compromised to minimize the risk of lymphedema (Fig. 4).

**Lymphovascular Anastomosis Technique**

The lymphovascular anastomosis ("LYMPHA") technique performed at the time of initial axillary dissection has shown a statistically significant reduction in the development of lymphedema at 18 months (30% vs 4.05%; \( P < .01 \)).\(^4\) This technique was originally described by Boccardo in 2009. Isosulfan blue is injected into the volar aspect of the ipsilateral upper arm before incision (see Fig. 2). During axillary dissection, the blue lymphatics are identified and the afferent lymphatics are clipped near insertion into the node. After dissection, the afferent lymphatics are directly anastomosed into a collateral branch of the axillary vein with microsurgical technique.\(^4\)

**Surgical Techniques**

Surgical treatment options are divided into two general categories, reductive versus physiologic procedures. In this section, we focus on the physiologic procedures, which aim to assuage the physiologic disturbances that result from increased adipose volume and fibrosis in the affected limb. Microsurgical procedures, including LVA and VLNT, target the fluid component that predominates at earlier stages of the disease (Fig. 4).

**Lymphaticovenous Anastomosis**

LVA, first described in 1969, is a microsurgical procedure that effectively bypasses diseased lymphatics and restores adequate lymphatic drainage via direct drainage into the venous system.\(^1\)\(^9\),\(^6\)\(^2\) Serial anastomoses are typically created between small lymphatics and subdermal venules, preferably less than 1 cm in diameter, along the entirety of the upper extremity. The minimally invasive approach allows multiple anastomoses to be created via a single 1- to 2-cm incision. The procedure is typically performed under locoregional anesthetic, which may be better suited for candidates with extensive comorbidities.

**Indications**

LVA is indicated after failed management of conservative therapy, and early International Society of Lymphology stage II disease with evidence of partial lymphatic obstruction.\(^2\)\(^7\) Functional lymphatic vessels, albeit partially functional, are required
to create an effective anastomosis with durable patency; complete occlusion of the
lymphatics is an absolute contraindication to LVA. Studies have shown that the earlier
LVA is introduced, the greater the success of the procedure, likely owing to the
decreased presence of irreversibly damaged vessels. Guided by a similar premise,
it was previously absolutely contraindicated to perform LVA on patients with primary
lymphedema given the concern for hypoplastic vessels. However, studies have shown
that certain types of primary lymphedema are adequately treated with LVA.

**Lymphoscintigraphy**
Superior results have been reported when perioperative lymphatic mapping is used to identify lymphatic vessels and determine functionality. ICG lymphoscintigraphy is a simple tool, frequently used to locate functional lymphatics, determine severity of disease, and identify optimal placement for surgical incisions. Intraoperatively, the
dye illuminates functional lymphatics as it travels through the surgical field, which has been shown to increase the number of anastomoses created\textsuperscript{70} despite an overall shorter length of operation.

Postoperative anastomotic patency is subsequently monitored with lymphoscintigraphy; the rate of radiotracer clearance provides an indirect measure of lymphatic flow.

**Technique**
There is no consensus in the literature regarding timing, location, number, or configuration of anastomoses when performing a LVA; these decisions are primarily dictated by surgeon preference. However, the likelihood of successful outcomes is determined primarily on the surgeon’s ability to identify suitable venules and lymphatic vessels within the affected limb. Ideally, both vessels should be of similar diameter, preferably less than 0.8 mm, in close proximity to one another, and with minimal to no venous backflow after division.\textsuperscript{24,71} Smaller veins are preferred because of the greater risk of increased intraluminal pressure, and subsequent risk of venous reflux associated with larger veins.

The number and location of anastomoses varies and is highly dependent on the presence of functional and accessible vessels; both proximal and distal placements have been widely reported. Stepped anastomosis creates multiple bypasses at various levels of the affected extremity (ie, wrist, forearm, and arm in the upper extremity),\textsuperscript{72} which aims to improve success rates by providing additional routes for lymphatic drainage. Previously, Huang and colleagues\textsuperscript{73} demonstrated that increased number of anastomoses provided better results. However, that has been refuted in a large study by O’Brien and colleagues, as well as a large prospective trial\textsuperscript{63} which showed no difference in results based on number of anastomoses.\textsuperscript{64,70} A variety of configurations may similarly be used including end-to-end, end-to-side, or side-to-end anastomoses without significant difference in outcomes. If anatomy permits, it is always preferred to create multiple lymphaticovenous anastomoses via a single incision.

**Results**
LVA has been proven to be an efficacious treatment option for patients that have failed nonoperative management. It is associated with a decrease in the overall incidence of severe cellulitis, compression garment discontinuation, and a subjective improvement in symptoms and QoL, compared with women who received conservative management alone.\textsuperscript{19,74,75} In a systematic review of high-quality studies, 5 studies reported QoL outcomes, and found 91.7% symptom improvement, 94.5% average satisfaction rate, 90% improved QoL, and 50% subjective improvement in patients who underwent LVA.\textsuperscript{42,63,76–78}

However, studies have shown that the success of LVA is primarily restricted to early stage disease; this is presumably owing to the ongoing presence of functional lymphatics that are subsequently irreversibly damaged in advanced disease. Chang and colleagues\textsuperscript{63} found that, after LVA, stage I and II patients experienced a 61% volumetric reduction compared with 17% volumetric reduction in stage III patients after 1 year of follow-up. In another study, no limb volume reduction was seen in stage III patients.\textsuperscript{72} Rates of recurrence are also closely associated with clinical staging. Poumellec and colleagues\textsuperscript{72} reported 19.3% recurrence rates; however, all recurrences were isolated to patients with stages III and IV lymphedema. This finding further supports the notion that LVA is better suited for patients with early stage lymphedema.

**Complications**
Complications are uncommon after lymphaticovenous bypass, with rates reported at 5.9%.\textsuperscript{27} Although the incidence is rare, known complications are infection, lymphatic
fistula, partial skin ulceration, and wound dehiscence. Given the low incidence of complications, LVA seems to be a safe and feasible procedure.

**Vascularized Lymph Node Transfer**

VLNT is a microsurgical procedure, in which a soft tissue flap containing lymphatic tissue and its associated arteriovenous supply is relocated from a donor site to the affected axilla. The reintroduction of healthy lymphatic tissue aims to restore function in the impaired limb, but the exact mechanism remains unclear. One theory hypothesizes that the transferred lymph nodes serve as a “sponge” that absorbs lymphatic fluid that is, then redistributed back into the lymphovenous circulatory system. A second theory suggests that lymphangiogenesis, primarily driven by vascular endothelial growth factor, leads to increased lymphatic vessel formation.

**Indications**

Indications for VLNT include stages II to V lymphedema (Capisi staging system), absolute occlusion of lymphatic pathways verified on imaging (MRI or lymphoscintigraphy), fibrosis preventing lymphaticovenous bypass, brachial plexus neuropathy, chronic infections in the affected limb (ie, repeated episodes of cellulitis), and failed conservative management. Conversely, some studies support the use of VLNT in early-stage lymphedema owing to the progressive course of the disease. Although lymph node transfer is not curative, early intervention may reduce the accumulation of excess lymphatic fluid and thereby, inhibit the positive feedback cycle that drives the progression of lymphedema.

**Technique**

The recipient site may be selected as the axilla, elbow, or wrist of the affected limb. Axillary dissection may prove to be more challenging in patients who have undergone prior radiation therapy owing to significant scar tissue formation. However, wrist placement is less cosmetically pleasing owing to protrusion of the tissue and the possible need for skin grafting. Cheng and colleagues suggests that wrist placement is more suitable for functionality, but the elbow provides improved aesthetic results. Ultimately, selection depends on surgeon preference, because recipient site selection has not been shown to impact outcomes. The most crucial part of axillary dissection is to ensure wide removal of all scar tissue; it is necessary to remove the obstruction to allow for good flow through the underlying lymphatics and to have sufficient space for placement of harvested lymph nodes. An external neurolysis should also be performed if a neuroma is identified during dissection to avoid development of postoperative pain. After careful identification of the thoracodorsal vessels, attention can be turned to the lymph node flap.

Lymphodynamic evaluation is conducted preoperatively with the aid of multiple imaging modalities. ICG assesses the severity of dermal backflow, and locates any viable and functional lymphatic vessels in the region. If an adequate amount of adequately functioning vessels is identified preoperatively, then a lymphovenous shunt may be considered, and the more invasive VLNT procedure can be avoided. Additionally, the presence of lymphatic drainage obstruction can be confirmed on Tc99 lymphoscintigraphy. Lymphoscintigraphy does not provide good information about the spatial and temporal resolution of the lymphatic system and involves exposure to radiation. If available, MRI and dynamic magnetic lymphangiography are preferred owing to the increased sensitivity and specificity to identify anatomic and functional variations.

The optimal donor site remains unclear, but the most common location is the inguinal region; it is based off the branches of the superficial circumflex iliac or
superficial inferior epigastric vessels. Groin flaps are chosen owing to their abundance of lymph nodes in a well-understood anatomic region, an easily hidden scar, and a dual role in total breast reconstruction. Dissection is delineated by 3 borders: the inguinal ligament (caudal), the muscular aponeurosis (deep), and the cribriform fascia (superficial). It is recommended that the surgeon not dissect lymph nodes beyond the caudal and deep borders to avoid inadvertent removal of deeper lymph nodes to minimize the risk of donor site lymphedema. Less commonly, the submental, supraclavicular, thoracic, and omental tissues are used as donor sites. The submental and supraclavicular nodes require tedious dissection owing to nearby lymphatic ducts and branches of the marginal mandibular nerve. Although the omental nodes are the least likely to develop donor site iatrogenic lymphedema, the need for abdominal surgery poses additional risks.

Anastomosis selection varies depending on the flap of choice; the superficial circumflex iliac vessels are typically used in isolated VLNT, versus combined VLNT with microvascular breast reconstruction, in which the deep inferior epigastric vessels are preferred. Currently, no strict guidelines exist to determine which vessels should be used for optimal results. A recent study by Nguyen and colleagues created an algorithm for transferring vascularized inguinal lymph nodes during autologous abdominal free flaps (AFP), specifically deep inferior epigastric perforator or transverse rectus abdominis myocutaneous flaps; the goal was to provide an alternative vasculature selection to the commonly used thoracodorsal vessels, which may be crucial later if the initial flap fails. Nguyen and colleagues address 3 different scenarios: (1) hemiabdominal flap for bilateral mastectomy or prior midline incision—ipsilateral VLNT, ipsilateral AFP, thoracodorsal pedicle; (2) unilateral reconstruction without prior violation of the midline—contralateral VLNT, ipsilateral AFP, internal mammary artery pedicle; and (3) a history of prior surgery with subsequent division of superficial vessels—VLNT ipsilateral, AFP contralateral, and internal mammary artery pedicle. Their study demonstrated promising results with 79% of patients reporting improved symptoms, and reduction of excess limb volume from 21% preoperatively down to 10% at 1 year of follow-up.

Results
VLNT has been shown to have successful outcomes with decreases in limb circumference and limb volume, as well as improvement in patient function and QoL. A large systematic review by Carl and colleagues found a 33% excess volume reduction and 16.1% absolute circumference reduction after lymph node transfer. Notably, patients report a substantial improvement in limb functionality before any self-perceived changes in limb appearance, suggesting that even a slight decrease in size may prove beneficial with regard to limb mobility, and inevitably, better QoL. These functional improvements were reported as early as 1 month postoperatively, and continued throughout the first year of follow-up. Similarly, psychosocial issues including appearance, symptoms and mood also improved. Studies have shown that patients who undergo lymph node transfer report 91.7% symptom improvement, 94.5% average satisfaction rate, 90% improved QoL, and 50% subjective improvement. Despite the promising results, particularly in late-stage disease, VLNT is not a curative therapy. Patients are recommended to continue conservative therapies, including compressive bandages, elastic garments, and manual lymph drainage postoperatively.

Complications
The success rates for volume reduction, compression therapy discontinuation, and improved QoL are similar to those reported for LVA; however, the complication rates
of donor site seroma, lymphocele, infection, delayed wound closure, and donor site lymphedema make VNLT a higher risk surgery. VLNT is also associated with longer durations of hospital stay, longer duration of operation, and greater anesthetic requirements (general vs local) when compared with LVA. A large, retrospective review of all high-quality studies demonstrated a 30.1% complication rate after lymph node transfer. This finding is further supported by Vignes and colleagues, who found an equally high complication rate at 38%. Similar findings are reported after combined VLNT and microvascular breast reconstruction with 25% recipient site complications (delayed wound healing, partial mastectomy flap necrosis, and abdominal flap venous thrombosis) and 20% donor site complications (abdominal wound healing or dehiscence, abdominal hernia, and groin seroma).

The most dreaded complication after lymph node transfer is iatrogenic lymphedema at the donor site. Despite low rates reported in the literature, it remains a significant concern among clinicians. Studies have shown that, even with modified conservative surgical techniques, lymphoscintigraphy findings demonstrate subclinical disruptions in lymphatic flow postoperatively. Given these findings, studies recommend supportive modalities including reverse mapping, ICG, and lymphoscintigraphy to maximally mitigate the risk of iatrogenic lymphedema. It should be noted, however, that complications are reported inconsistently across the literature, even among high-quality studies.

COMBINATION PROCEDURES

The combination of physiologic procedures with reductive surgery, which allows for removal of the chronic adipose and fibrotic tissue disrupting the lymphatic system, is the most effective treatment for severe lymphedema. Multiple combinations of excisional and physiologic procedures have been used, including VLNT with suction-assisted lipectomy, VLNT with microvascular breast reconstruction, and some surgeons have also attempted LVA with VLNT. Limb volume reduction was reported to be as high as 91% after liposuction with VLNT. Owing to its low risk profile, liposuction is an appealing adjunct treatment option, particularly in patients with nonpitting edema. Studies have shown that, after LVA, 16.0% of patients benefit from additional liposuction postoperatively. Likewise, when VLNT is used as the primary approach, additional reductive procedures are needed in 31.6% of patients. The promising outcomes after combination therapy may represent an opportunity to minimize the need for serial invasive surgical interventions and simultaneously yield better outcomes. Nevertheless, similar to lymph node transfer, high rates of complications are associated with excisional procedures, as high as 39.3%, and therefore, careful patient selection is required with the procedure reserved for those with severe disease.

LIPECTOMY

SAPL involves the removal of fat and fibrosis with suction technique. Lipectomy addresses the solid component (fibrosis and hypertrophied subcutaneous adipose tissue) that typically presents later as chronic, nonpitting lymphedema of an extremity after the fluid component has been conservatively drained. Patients often complain of discomfort and dysfunction in the affected arm despite conservative management. Indications for lipectomy include stage II and III disease that has failed conservative management. Contraindications include active cancer, infection, wounds, or insufficient conservative management. If there is more than 4 to 5 mm of pitting edema in the affected extremity, the patient should attempt conservative measures rather than undergo liposuction, because liposuction is a method to remove fibrotic adipose tissue, not fluid.
During suction-assisted protein lipectomy, a tourniquet is first applied to the affected extremity to minimize the amount of fluid present in the operative field. Liposuction is performed with suction cannulas through multiple incisions that are 3 mm long. Starting distal to the tourniquet, liposuction is performed circumferentially and in a longitudinal direction to the extremity to minimize damage to the remaining lymphatics. This process is continued until liposuction is performed past the point of the tourniquet and the maximal amount of adipose tissue is removed. The incisions are left open to drain externally. A sterilized compression sleeve and glove are applied for hemostasis and minimization of edema. Perioperative antibiotics are generally given for 5 to 10 days. The patient is instructed to wear their compression sleeve and glove at all times.

Studies have found that, in patients with lymphedema from breast cancer therapy, a statistically significant volume reduction of almost 1 L on average was achieved and maintained at 12 months. Additionally, there is a significant improvement in QoL and decrease in infection rates. However, lipectomy does not treat the underlying cause of lymphedema, namely lymphatic stasis and obstruction. Lifelong compression therapy, lymphedema therapist treatment, and/or lymphovascular anastomosis or VLNT must be used as adjuncts to prevent the reaccumulation of lymphedema. Lifelong compression therapy involves continuous use of a sleeve and glove on the affected arm, which requires strict patient compliance. Lymphedema therapy generally involves a combination of manual reduction, physical therapy, and yoga, which is also heavily reliant on patient compliance and motivation. LVA and VLNT are microsurgical procedures that may be performed after the volume reductions from SAPL have stabilized and the patient has sufficiently healed from the first surgery. LVA and VLNT help to prevent fluid reaccumulation and reduce compression garment use after SAPL has removed the solid component of the lymphedema.

SURGICAL EXCISION

Surgical excision or radical debulking for severe lymphedema was first described in 1912 as the Charles procedure. Several modifications of the Charles procedure have also been reported. Indications for this procedure include advanced (end-stage) fibrosclerotic lymphedema not amenable to other procedures, recurrent episodes of cellulitis, and severe disfigurement or dysfunction, and an inability to exclude sarcoma on the affected extremity. The major disadvantage is that superficial skin lymphatic collaterals are removed or further obliterated. Additionally, there is significant morbidity, scarring, and risk of skin graft failure with these operations. When lymphedema recurs at the hand or foot, regrafting and finger or toe amputations may prove necessary.

During the Charles procedure, longitudinal skin incisions are made along the length of lymphedema. The excess skin and subcutaneous tissue of the lymphedematous limb are excised circumferentially down to the level of the deep fascia. Care is taken not to injure the deep fascia. Split thickness skin grafts are then harvested from the excised skin and are implanted onto the deep fascial layer. Sterile dressings are applied and the skin flaps are monitored postoperatively for adequate blood supply and infection.

Given the risks and morbidities listed, several versions of the modified Charles procedure were developed for severe lymphedema treatment. In the first modified Charles procedure, the initial debulking procedure is performed. A portion of the split thickness skin graft is deepithelialized and is buried into the deep subcutaneous tissues. The goal of this modification is to connect the deep subfascial lymphatics...
with the superficial dermal lymphatics, thereby facilitating lymph drainage. Other modifications include use of negative pressure dressings, perpendicular cross-incisions, and combination procedures with liposuction and VLNT to decrease the amount of skin removed and allow primary closure.

**SUMMARY**

Breast cancer–related lymphedema is a lifelong disease that is difficult to treat and requires multimodal therapy. A systematic review by Carl and colleagues using MINORS criteria to distinguish high-quality studies attempted to create an algorithm for management of lymphedema. The microsurgical technique LVA at the time of axillary lymph node dissection has been proposed as a primary preventative treatment for arm lymphedema. The after treatments are suggested according to the International Society of Lymphedema Staging System. Conservative measures such as physiotherapy and compression garments are appropriate for stage 0 (subclinical) lymphedema. LVA or VLNT procedures are best suited for early stage I lymphedema (soft, pitting edema with little to no fibrosis). Suction-assisted protein liposuction should be considered for moderate stage II (nonpitting edema with fibrosis) and severe stage III lymphedema (nonpitting edema with severe fibrosis and hypertrophic skin changes). Surgical excision (the Charles procedure and its modifications) should be reserved for severe stage III lymphedema with severe disfigurement or disuse. Most patients do report decreased edema and improved QoL after surgical intervention; however, compression garments or physiotherapy are still recommended postoperatively to maintain or further reduce limb volume.

Further research must be conducted in establishing best practices in lymphedema prevention and treatment. A standardized staging system for lymphedema would allow for accurate comparison of outcomes based on intervention type. There are also inconsistent methods of recording surgical outcomes and reporting outcomes and QoL indicators. At this time, there are limited large, randomized, controlled trials in the lymphedema literature that focus specifically on breast cancer related lymphedema. Much of the data come from observational studies that combine data from both upper extremity and lower extremity lymphedema. Lack of consistent quantitative reporting prevents comprehensive conclusions regarding which surgical approaches are associated with the greatest subjective improvements. Even the studies that did include QoL outcomes and reported overall improvement in function, symptom severity, and aesthetics after surgery, these data cannot be reliably used because they are inconsistently documented among the studies.

**REFERENCES**


