Modern approaches to lymphatic surgery: a narrative review

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Background and Objective: Lymphedema is a chronic, progressive disease secondary to damage to the lymphatic system that results in interstitial fluid accumulation, fat deposition and inflammation. Lymphatic surgery includes a spectrum of procedures aimed to treat these sequelae of lymphedema as well as decrease the risk of lymphedema if performed as prophylactic surgery. We reviewed the literature regarding current surgical treatment options for lymphedema, imaging approaches, and directions the field may head towards both in treatment access and techniques.

Methods: We systematically reviewed PubMed, Embase, and Cochrane Library databases to identify approaches to surgical management of lymphedema, including physiologic and reductive methods, as well as challenges that lymphedema patients face for adequate access and insurance coverage to surgical treatment options.

Key Content and Findings: Lymphatic surgery can be broadly categorized as physiologic or reductive. Physiologic lymphatic surgery functions to decrease the fluid burden associated with lymphedema and includes lymphovenous bypass as well as vascularized lymph node transplant procedures. Reductive lymphatic surgery reduces the fibroadipose component of lymphedema and include suction lipectomy and excisional procedures. Advances in imaging technology as well as supermicrosurgical techniques have allowed for reproducible, positive clinical outcomes after lymphatic procedures. Access to care and coverage of procedures are persistent challenges in the field, though increasing adoption and research have led to important strides forward to providing patients with this care.

Conclusions: Lymphatic surgery can improve symptoms and quality of life for lymphedema patients. A clear understanding of the predominant pathology in a patient (i.e., fluid dominant vs. fat dominant) can help guide counseling and surgical management options for patients. Despite the established benefits for patients, equitable access and insurance coverage for lymphedema surgery are still required.

Keywords: Lymphedema; lymphatic surgery; supermicrosurgery; lymphovenous bypass (LVB)

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Introduction

Lymphedema is characterized by increased lymphatic fluid in the interstitial spaces due to damage of the lymphatic system. Through a chronic inflammatory process of lymphosclerosis and fat deposition, clinical characteristics of pitting edema secondary to excess fluid progress to non-pitting edema, excess fibroadipose tissue and skin changes (1,2). Primary, or idiopathic, lymphedema refers to the malformation of the lymphatic system and can be present at birth (i.e., congenital lymphedema) or develop later in life (3). Secondary lymphedema refers to the acquired factors impacting the function of a normally developed lymphatic system. Oncologic extirpation, notably axillary lymph node dissection (ALND), is the most common cause of secondary lymphedema in developed countries, but other causes include trauma, infection and radiation (4,5). The overall incidence of lymphedema is complex as it is often underrecognized and undertreated, but estimates indicate primary lymphedema affects 1 in 100,000 people, and secondary lymphedema afflicts 1 in 1,000 Americans (6).

Lymphedema symptoms including chronic swelling and enlargement of an extremity impair activities of daily life, quality of life, and can result in recalcitrant wounds and infections when severe. Non-surgical treatment of lymphedema is known as complete decongestive therapy (CDT), a multimodal staged treatment regimen involving compression garments, bandaging, manual lymphatic drainage, physical therapy exercises, and hygiene care.

Surgical options can be categorized as physiologic or reductive procedures. While neither approach is curative, both aim to provide patients with symptom relief. Physiologic procedures target the fluid-dominant portion of the disease while reductive procedures address the late-stage, fibroadipose pathology of lymphedema. Physiologic approaches include lymphovenous bypass (LVB) and vascularized lymph node transplant (VLNT), and reductive techniques include liposuction and excisional surgery. LVB is a supermicrosurgical technique that effectively shunts lymphatic drainage into the systemic circulation distally by connecting lymphatic vessels to subdermal venules. VLNT is another physiologic approach wherein an autologous free flap containing a cluster of lymph nodes on a vascularized pedicle is relocated to the lymphedematous extremity. For patients with an additional fibroadipose component of disease, debulking surgery as part of their overall treatment plan should be considered for optimal outcomes (7). These encompass liposuction as well as excisional surgeries such as the Charles and Homan's procedures which aim to remove excess fibroadipose tissue (8-10).

Given this knowledge in the literature, this review focuses on current approaches to lymphedema treatment including modern imaging technologies, contemporary surgical approaches, and future directions for the field of lymphatic surgery. We present this article in accordance with the Narrative Review reporting checklist (available at https://tbcr.amegroups.com/article/view/10.21037/tbcr-24-49/rc).

Methods

A systematic review of PubMed, Embase, and Cochrane Library databases was used to identify approaches to surgical management of lymphedema from January 2000 to February 2024. MeSH terms and keywords included "lymphovenous bypass surgery", "lymphovenous bypass", "lymphovenous anastomosis", "lymphovenous anastomosis surgery", "lymphatic surgery", "lymphedema surgery", "vascularized lymph node transfer", "vascularized lymph node transplant", "physiologic lymphedema surgery", "excisional or reductive lymphedema surgery", "vascularized lymphatic vessel transplant", "vascularized lymphatic vessel transfer", "VLVT", and/or "imaging for lymphedema". Inclusion criteria included observational articles including retrospective and prospective studies, experimental original articles, systematic reviews, and meta-analyses. Non-English manuscripts and abstracts were excluded from the review (*Table 1*).

Discussion

Immediate lymphatic reconstruction (ILR)

ILR is a prophylactic surgery considered for populations at increased risk of developing secondary lymphedema, and is performed at the time of lymphadenectomy. In 2009, Boccardo *et al.* described their findings in the Lymphedema Microsurgical Preventative Healing Approach (LyMPHA) study which involved performing an axillary LVB immediately following ALND in 19 patients (11). They found that LVB prevented secondary lymphedema in all cases at both follow-up periods of 6 and 12 months. Variations of this technique have become the mainstay for ILR which typically utilize telescoping or intussusception anastomosis of cut lymphatic channels draining the upper extremity to branches of the axillary vein (*Figure 1*). A follow-up study over four years later demonstrated a 4% rate of lymphedema (11). Subsequent similar studies of prophylactic ILR following ALND have described a lowered rate of lymphedema ranging from 4% to 12% (12-15). More recently, the preliminary results of a randomized controlled trial comparing ILR to no lymphatic reconstruction following ALND for breast cancer demonstrated an incidence of breast cancer related lymphedema (BCRL) in 9.5% of the ILR group compared to 32% in the control group at 24 months (16). Secondary outcomes additionally supported this finding with lower bioimpedance values, less dermal backflow, and improved quality of life in the ILR group.

In cases where there is considerable distance between the afferent lymphatic and the target vein, a vein graft may

Table 1 The search strategy summary

Items	Specification
Date of search	February 29, 2024
Databases and other sources searched	PubMed, Embase, Cochrane Library
Search terms used	"Lymphovenous bypass surgery", "lymphovenous bypass", "lymphovenous anastomosis", "lymphovenous anastomosis surgery", "lymphatic surgery", "lymphedema surgery", "vascularized lymph node transfer", "vascularized lymph node transplant", "physiologic lymphedema surgery," "excisional or reductive lymphedema surgery", "vascularized lymphatic vessel transplant", "vascularized lymphatic vessel transfer", "VLVT", and/or "imaging for lymphedema"
Timeframe	1/1/2000–2/29/2024
Inclusion and exclusion criteria	Inclusion: all studies including case reports, case series, randomized control trials, literature reviews
	Exclusion: studies not written in English
Selection process	E.Z., N.Y. conducted the study independently and consensus was obtained with review from all authors

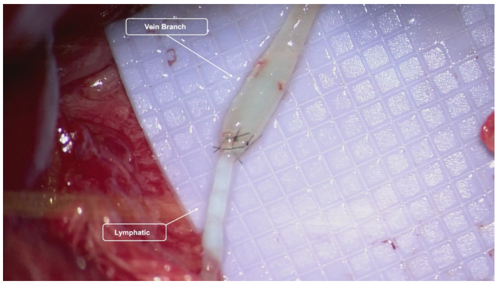

Figure 1 Lymphovenous bypass for immediate lymphatic reconstruction using an intussusception technique. Blue dye visualized in the vein branch confirms a patent anastomosis.

be utilized (17,18). The use of vein grafts allows for more flexibility in choosing the final recipient vein, incorporation of valves to minimize backflow, improved size matches, and facilitation of multiple independent anastomoses with different branching patterns. The more routine use of vein grafts has led certain authors to decrease abortion rates from 14% to 0% in ILR (17). Venous couplers have also been described for LVB during ILR (19,20). Spoer *et al.* described a coupler-assisted technique anastomosing multiple lymphatics to a single vein (19). Other authors have also utilized couplers in an end-to-end fashion during immediate LVB with good short-term reported outcomes (20). Prophylactic VLNT for ILR has also been described though is less commonly utilized (21). These procedures are typically reserved for patients with severe anticipated soft tissue loss after extirpative nodal surgery and subsequent radiation.

Intraoperative mapping of lymphatic channels is a critical component of ILR. The use of blue dye and indocyanine green (ICG) are commonly utilized through intradermal injection in the ipsilateral extremity to identify lymphatics cut during ALND that are draining the upper extremity. More recently, fluorescein isothiocyanate (FITC) has been described to aid in identification of lymphatics during active dissection (22). As FITC is excitable in the visible spectrum, it is possible to view the fluorescence using a fluorescent-capable microscope amongst the surrounding tissues in one visual surgical field (22).

ILR has also been described in the lower extremity. Alarcón *et al.* utilized both LVB and VLNT for lower extremity ILR with a lymphedema rate of 10.5% in the prophylactic cohort compared to 37% in the retrospective control group without lymphatic reconstruction (23). Cakmakoglu *et al.* employed ILR for patients undergoing ilioinguinal lymphadenectomy, and amongst the 12 patients, none developed lymphedema (24). Promising results have also been demonstrated in gynecological neoplasms. In seven patients with uterine neoplasms underdoing hystero-oophorectomy and intrapelvic lymph node dissection, Takeishi *et al.* performed prophylactic intrapelvic LVB and found 1 of 7 patients to have mild lymphedema in a follow-up period of 18 months (25). Comparative studies on LVB at the time of inguinal lymph node dissection identified an incidence of lymphedema at 8.3% with ILR compared to 25.0% for the historical control (26). While ILR has been described at the time of melanoma resection (27), general consensus guidelines have advised against prophylactic ILR at

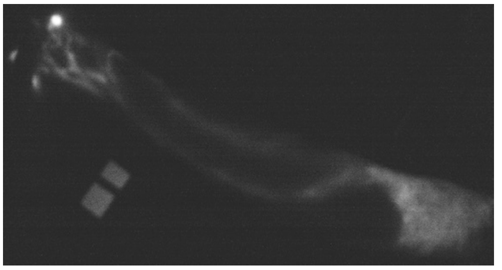

Figure 2 Indocyanine green lymphography demonstrating linear channels ending in dermal backflow.

the time of resection of cutaneous extremity neoplasms (28).

While immediate, proximally-based LVB is the leading surgical technique for lymphedema prophylaxis, technical concerns with vessel mismatch, pressure gradients and radiation of anastomoses have led some authors to consider a delayed or distally located LVB (29-31). Pierazzi *et al.* investigated the outcomes of delayed LVB performed at a location distal to the lymphadenectomy site and after the completion of radiation therapy (29). A total of six patients underwent distal prophylactic LVB between 85 to 130 days after lymphadenectomy with no increased in limb circumference after 12 months of follow-up. Although the number of patients in this study is small, it introduces important considerations of optimal timing and location of distal LVB for lymphedema prophylaxis. In a retrospective review of distal LVB following ALND, Wong *et al.* reported a 3.8% incidence of lymphedema in the experimental group compared to 17.2% in controls (31). The authors describe benefits of distal LVB to include an improved vessel size match and avoidance of theoretical damage from radiotherapy. Conversely, the bypass of distal lymphatic channels with potentially intact proximal drainage and the implications of delayed LVB thrombosis in prophylactic distal LVB must also be considered. While distal lymphatic reconstruction following lymphadenectomy has been shown to decrease the incidence of lymphedema, refinements to the site, timing, and indication need to be further studied to identify the best outcomes for patients.

Delayed physiologic lymphatic reconstruction

Delayed lymphatic reconstruction is performed to treat established lymphedema. A multidisciplinary care team is critical for these patients, particularly with the involvement of certified lymphedema therapists. Prior to considering lymphatic surgery, patients should have completed CDT, a collection of non-surgical modalities including lymphatic drainage, muscle pumping exercises to promote lymphatic flow, proper skin care, compressive bandaging/garments, and education (32,33). This therapeutic approach, along with a clear assessment of a patient's baseline measurements, quality of life, and patient compliance to treatment, are important to establish prior to surgical care. Physiologic surgery including LVB, VLNT, and vascularized lymphatic vessel transplant (or transfer) (VLVT) is aimed at treating the fluid burden associated with lymphedema whereas reductive surgery, primarily suction lipectomy, is utilized to reduce the excess fibroadipose tissue. Decision-making between different procedures is complex and involves principally determining the dominant fat to fluid ratio as well as the severity of disease based on symptoms, physical exam and imaging findings.

LVB

LVB involves the anastomosis of lymphatic vessels to nearby venules to distally reroute lymphatic flow into the systemic circulation. LVB is indicated to treat fluid-dominant lymphatic disease, typically in earlier-stage patients. Successful outcomes of LVB are closely linked to the quality of lymphatic channels, namely, the ability to identify functional lymphatic vessels for anastomosis as well as an appropriate recipient venule with significant venous backflow. The MD Anderson (MDA) staging criteria is one of several classification systems based on ICG lymphography patterns (*Figure 2*) that evaluates the presence of functional linear channels appropriate for LVB in relation to dermal backflow (34). It defines six progressive stages based on the ICG patterns of linear channels in relation to dermal backflow. LVB is typically indicated for MDA stage I or II (34), where functional linear lymphatic channels can be identified on ICG lymphography. In addition to providing diagnostic and staging information, ICG lymphography is commonly employed intraoperatively as it provides real-time mapping of intact linear channels which guide surgical planning. More recently, the utilization of newer adjunctive imaging technologies including magnetic resonance (MR) lymphography and ultra-high frequency ultrasound (UHFUS) have allowed for successful outcomes with LVB in later stages cases as well (35,36).

Multiple anastomotic techniques for LVB have been described, the most common being end-to-end and end-to-side anastomoses (*Figure 3*) (37). Additional techniques reported in the literature include the side-to-end (38), sleeve-in anastomosis (39,40), "octopus" approach (41),

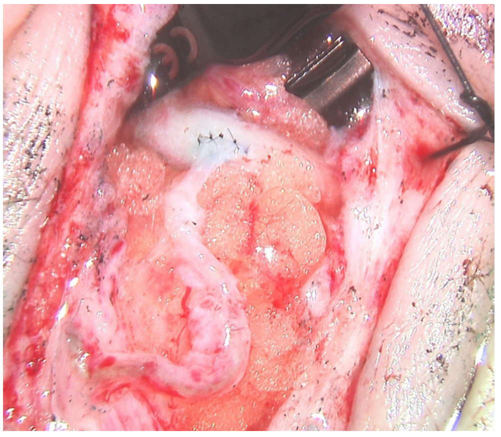

Figure 3 End-to-side lymphovenous bypass.

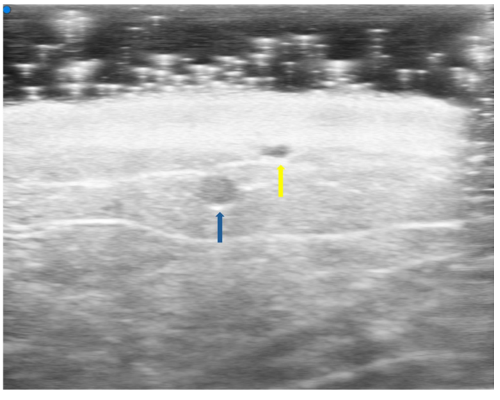

Figure 4 Ultra-high frequency ultrasound allows for preoperative planning to identify the location and size of lymphatic channels (yellow arrow) and nearby venules (blue arrow).

lambda-shaped with intravascular stenting (42,43), pi-shaped (44), modified lambda-shaped anastomosis (43), buffalo-skull (45), and Y-shaped venoplasty (46). These inventive approaches all aim to accomplish maximal drainage of excess lymph fluid and have demonstrated success as independent techniques. However, there is no consensus on the ideal anastomotic approach. AlJindan *et al.* showed that side-to-end anastomosis conferred greater reduction in limb circumference compared to the end-to-end cohort (38). Other reports have proposed that the quantity of anastomoses correlates to better outcomes (41), while some have contended that better outcomes can be accomplished with LVB in deep lymphatics rather than superficial (47). While multiple techniques can be utilized successfully, the superiority of one over another remains to be determined.

Identification of functional lymphatic vessels as well as nearby venules are a critical component of successfully LVB surgery. UHFUS has emerged as an invaluable preoperative planning tool given its ability to scan at resolutions down to 30 µm (36,48,49). This modality has demonstrated superior visualization of lymph vessel and function compared to conventional high frequency ultrasound (CHFUS) and strong association with lymphatic vessel histology patterns in patients with secondary lymphedema undergoing LVB (36,50). UHFUS (*Figure 4*) allows for precise localization of lymphatics even in cases of severe dermal backflow (51), selection of larger, ectatic lymphatics and identification of nearby venule branches thereby increasing efficiency in LVB surgery.

Photoacoustic lymphangiography (PAL) has also recently been evaluated as a pre-operative visualization tool for operative planning for LVB (52,53). This technique utilizes a glucose and ICG mixture injected into digit webspaces, followed by near-infrared fluorescent imaging to capture both lymphatic and venous vessel anatomy on a static image. Suzuki *et al.* found that when compared to mainstay ICG lymphography, the PAL offered better definition of lymphatic vessels, particularly in areas where there is dermal backflow superficial to healthy lymphatic vessels (52).

Venule quality is another critical factor in LVB planning. Venules with backflow can result in venous reflux across the anastomosis and unfavorable pressure gradients increase the risk of anastomotic thrombosis. Visconti *et al.* investigated the quality of recipient venules and found vessels with increased backflow had poorer postoperative outcomes after LVB (54). Multiple techniques can be utilized to optimize venule selection. Ligating of feeding branches or transcommissural valvuloplasty have been reported (55) as well as other types of venoplasty to minimize LVB backflow (46).

Outcomes after LVB have demonstrated a positive impact both microscopically and clinically in the short and long term. At the cellular level, decreased oxidative stress markers have been reported one month after LVB (56). Patients with a follow-up period of more than three years have demonstrated decreased cellulitis episodes and sustained improvement in quality of life metrics (57). Several studies have shown that compression garment therapy can be reduced or even discontinued after LVB for patients with earlier stage lymphedema (47,58,59). A randomized clinical trial of over 300 cases by Mihara *et al.* demonstrated that LVB with conservative decongestive therapy reduced lower extremity cellulitis and firmness of tissue compared to non-operative decongestive therapy alone (60). Consensus guidelines based on systematic review by Chang *et al.* reported that LVB can reduce the severity of lymphedema, particularly for those with early-stage disease (grade 1C) (28).

More recently, robotic-assisted techniques have emerged as a promising advancement in the field of LVB and supermicrosurgery (61-63). In a pilot study by van Mulken *et al.*, anastomosis completion was accomplished in less than half the time with robotic-assisted LVB compared to manual LVB (63). In a 1-year follow-up study, the authors found that those who underwent robot-assisted LVB had slightly increased episodes of postoperative lymphedema maintenance including manual lymphatic drainage and daily compressive garment use (62). Despite this, the two groups were not significantly different in the lymphedema functioning, disability, and health questionnaire that assessed quality of life. As this technology continues to be adopted, additional studies will further define its clinical utility in LVB.

New frontiers have explored the impact of lymphatics on the central nervous system. Impaired meningeal lymphatic flow has been correlated with amyloid beta accumulation, significant in the pathogenesis of dementia and Alzheimer's disease. Da Mesquita *et al.* found delivering vascular endothelial growth factor (VEGF)-C, critical to lymphangiogenesis, improved lymphatic function and amyloid beta drainage in murine models (64). Preliminary outcomes following brain lymphatic reconstruction in 50 patients with Alzheimer's disease demonstrate notable improvements in memory, cognitive function, and behavior after 9-month follow-up; however, this study is ongoing and more objective evidence is needed to support these observations towards the treatment of Alzheimer's disease (65).

VLNT

VLNTs are another form of physiologic delayed lymphatic reconstruction. VLNTs are typically indicated for patients with fluid-dominant disease. They are utilized in more advanced ICG lymphography patterns without functional linear channels amenable to LVB (66), though simultaneous LVB and VLNT for earlier stage lymphedema has also been advocated given the different physiologic mechanisms of these surgeries (67). Multiple mechanisms have been proposed to explain how VLNT clinically improves lymphedema. Transplanted nodes promote VEGF-C expression, increasing lymphangiogenesis, and creating new lymphatics to further establish intact lymphatic flow (66,68-70). Lymph node flaps can also function as a "pump", drawing in the fluid from the surrounding tissue and rerouting into the vascular system (69,71). Multiple lymph node donor sites have been described including the omentum, submental, groin, thoracic, supraclavicular and mesenteric sites (72).

The omentum is a common donor site given the minimal risk of donor-site lymphedema (72,73). The omentum has a dual blood supply from the right and left gastroepiploic arteries, permitting a segmental harvest of the omentum. In the context of omental VLNT, generally the entire omentum is not needed, and harvest is usually limited to the right gastroepiploic artery and the associated segment of omentum. Anatomical studies demonstrate and average of 2.6–3.1 number of lymph nodes in this described harvest (73,74), but can be up to 7.3 (75,76). Historically an open laparotomy approach was utilized for omental harvest; however, advances in minimally invasive abdominal surgery and training has increased the use of laparoscopic harvest (77).

Given its native bi-directional venous flow based on the right and left gastroepiploic veins and lack of a capillary bed, a single venous anastomosis can result in venous hypertension of the flap which can ultimately threaten flap viability (78). Different techniques have been described to overcome this venous hypertension including anastomosing both the right gastroepiploic vein and the left gastroepiploic veins in order to restore the native bi-directional venous (76,78,79) as well as additionally creating an arterial flow through flap by anastomosing both right and left gastroepiploic arteries (76). Post-omental VLNT outcomes include lymphedematous extremity circumference reduction ranging from 37.8% to 74.5% (80-83), no recurrence of cellulitis post-operatively (80), and significant improvement in quality of life and patient satisfaction (82-84).

The submental VLNT harvests level Ia and Ib lymph nodes of the neck (66) based on the submental artery (85,86). A platysma-sparing technique aims to minimize the potential negative cosmetic outcome of lower lip motion that can be observed in partial platysma resection as part of the flap (87). Advantages of this flap include the low risk of donor-site lymphedema and an inconspicuous scar of the donor site. The variability of number of lymph nodes in the submental region may warrant preoperative imaging to select the side with the higher number of lymph nodes within the submental flap as some studies suggest the number of lymph nodes transferred may correlate with limb circumference reduction (88,89).

The groin offers a rich superficial lymphatic basin that

Figure 5 The sentinel lymph node(s) draining the lower extremity is marked during groin VLNT and avoided to prevent iatrogenic lymphedema. This node typically resides below the groin crease and can be localized using technetium injection in the distal extremity and an intraoperative gamma probe. VLNT, vascularized lymph node transplant. Written informed consent was obtained from the patient.

drains the abdomen and flanks based on the superficial circumflex iliac vessels along with a concealed donor site that makes it a favorable VLNT option (90). Of note, the deep lymphatics of the groin drain the lower extremity, typically residing below the groin crease, and must be avoided. Reverse lymphatic mapping is now routinely employed to minimize the risk of iatrogenic lymphedema. This technique involves the injection of radioisotope in the ipsilateral lower extremity of the groin VLNT as well as ICG in the abdomen/flanks, allowing the surgeon to avoid the sentinel nodes draining the leg while identifying the desired superficial nodes for the flap (*Figure 5*) (91). More recently, single-photon emission computed tomography-computed tomography (SPECT-CT) has been described for preoperative reverse mapping to identify aberrant drainage of the lower extremity into the superficial lymphatic system (92). Groin VLNT in conjunction with physiotherapy and compression was found to have a 57% limb volume reduction compared to the non-surgical cohort treated with physiotherapy and compression alone who experienced 18% limb volume reduction in one randomized control study (93). A prospective study found similar results with a 40.4% circumferential reduction rate in the groin VLNT group compared to 8.3% in the physical therapy alone group after an average follow-up period of 3.3 years (94).

The superficial circumflex iliac artery perforator (SCIP) flap can be combined with the associated groin lymph nodes, otherwise known as a composite SCIP (69,95). In cases where patients are at risk of developing post-oncologic or post-traumatic lymphedema along with a soft tissue defect, a prophylactic VLNT may also be performed at the time of soft tissue coverage (96,97). The lymphatic system transfer (LYST) builds upon the composite SCIP VLNT to include afferent lymph vessels as a means of potentially reducing the time needed for lymphangiogenesis (98).

The combination of a groin VLNT and an abdominal-based autologous flap can also be used for breast reconstruction and for treatment of lymphedema simultaneously (99-101). Multiple studies have demonstrated improved lymphedema-related quality of life for patients following this combined reconstruction (102,103). While it is possible to harvest both flaps as a unit (104), they may also be harvested separately with possible orthotopic inset of the VLNT more distally on the affected extremity (105).

The lateral thoracic VLNT utilizes the level 1 axillary lymph nodes with a pedicle from the lateral thoracic artery or the thoracodorsal artery (69,71,106). As with groin lymph nodes, harvesting the thoracic lymph nodes poses a risk of donor site lymphedema, and reverse lymphatic mapping is critical (91). A benefit of this flap includes a long vascular pedicle, the ability to include a skin paddle and a relatively high number of lymph nodes within the transfer (106), though anatomic variability in perfusion often requires isolating both the thoracodorsal and lateral thoracic system, with a potential need to anastomose both pedicles. The thoracic VLNT may also be harvested in a pedicled fashion with a partial latissimus flap for ipsilateral lymphedema after ALND, also providing soft tissue bulk if needed for the axilla (107).

The supraclavicular lymph node flap is comprised of the level Vb nodes of the neck and is supplied by the transverse cervical artery (108,109). It offers straightforward anatomical landmarks with low risk of donor site lymphedema. However, care must be taken to avoid injury to surrounding critical structures including the carotid arteries, internal jugular vein, phrenic nerve, and right lymphatic and left thoracic ducts (108). Safety has been demonstrated in large series, included a prospective trial of 100 cases, with two reported infections and three cases of chyle leak (110). In this series, the chyle leak was treated conservatively with medium chain fatty acid diet and drainage; however, high volume chyle leak following supraclavicular VLNT can be significantly more difficult to manage (111).

Recipient site location for VLNT is also an important consideration. Orthotopic transplants are placed anatomically and proximally such as in the axilla or groin, whereas heterotopic VLNTs are transplanted non-anatomical and distally such as near the ankle or wrist (66,108). The advantages of an orthotopic recipient site include cosmetic scar location and restoring lymph nodes at the site of removal, though fibrosis effects from previous surgery or radiation can increase difficulty. Heterotopic VLNTs have more visible scars and can be bulky depending on the flap choice, though gravitational forces and pathophysiologic retrograde lymphatic flow may shift impaired lymph movement towards the flap (66,69,94,112).

Although the exact mechanism of VLNT continues to be elucidated, improved outcomes for patients are widely reported. VLNT has a high level of evidence (grade 1B) as an effective surgical treatment for reducing the severity of lymphedema (28). A recent meta-analysis identified 31 studies (581 patients) and reviewed outcomes in limb volume, cellulitis episodes, and quality of life scores, all of which improved following VLNT (113). A prospective study by Brown *et al.* demonstrated significant improvement of average limb reduction and reduction in cellulitis after two years in 89 patients who underwent either omentum, lateral thoracic, supraclavicular or groin VLNT, with 34% of patients no longer requiring compression therapy (79). VLNT have been demonstrated to be more effective in reducing limb circumference and incidence of cellulitis compared to compression and decongestive therapies alone (28).

Combined lymphatic surgery approaches

The multiple presentations of lymphedema with regards to fluid and fat ratios as well as severity have led to the utilization of combined surgical approaches to address different components of the disease. This can include combination physiologic and reductive procedures as well as different physiologic procedures at one time. In a cohort of 21 patients, Brazio *et al.* demonstrated that LVB or VLNT with simultaneous liposuction confers benefits related to decreased lymphedematous volume and episodes of cellulitis, and a meaningful reduction in the duration of post-operative compression garment application (114). A single stage combination procedure may be prudent when there is both fluid and fibroadipose presentation and it is unclear which is the dominating pathology, which has been consistent with other reports that have additionally shown patient reports of improved clinical symptoms (115) and quality of life (116).

Combined physiologic approaches have demonstrated success in a diverse group inclusive of early and late-stage lymphedema, primary and secondary etiologies, and lymphedema localized to different anatomic regions (67,117-120). Chang *et al.* was able to demonstrate a volume reduction rate of 20–36% and improved quality of life scores over 4 years post-operatively in patients with primary, early-stage secondary, and late-stage secondary lymphedema who underwent combined LVB and VLNT procedures (67). As LVB and VLNT have different mechanisms to treat fluid burden, these procedures may be flexibly utilized for patients regardless of their staging. Institutions have proposed different algorithms to determine which patients may be suitable candidates for a combined approach (114,117,118), and while there is no consensus, it is increasingly evident that this mixed approach may yield improved results than standalone procedures for specific patients.

VLVT

VLVT is a technique that isolates lymphatic vessels within a soft tissue flap that is transferred to an affected area without lymphatic vessel anastomosis or node transplant (121-125). Mechanisms of action are attributed to lymphangiogenesis conferred by the perfused lymphatics within the flap (124). The technique has been advocated for patients who wish to avoid donor site lymphedema (121) and can be combined with VLNT other lymphatic reconstruction techniques to optimize patient outcomes (122).

Chen *et al.* demonstrated improvement in lymphedema symptoms in six patients who underwent SCIP-based VLVT for fluid dominant lymphedema (124). The superficial lymphatics within the region of the SCIP flap were identified using ICG lymphography, and the flap was raised in a non-anatomic superficial plane to capture lymphatic vessels but spare the superficial inguinal lymph nodes. At 1-year follow-up, all six patients showed decreased limb circumference measurements, and the emergence of new linear patterns on post-operative lymphography. While early results are promising, larger studies with longer follow-up are needed to further elucidate efficacy and indications.

While VLVT is described mainly for the treatment of chronic lymphedema, it may have a role in the prophylactic management of acute extremity wounds. Yamamoto *et al.* investigated the importance of aligning the axis of lymphatics within a flap to the axis of the extremity requiring soft tissue coverage (126). In coverage of acute traumatic wounds or oncologic defects of the extremities, lymph-interpositional-flap transfer or LIFT, which used lymphography to help design and guide inset of the flap to align the axis of lymphatic flow within the flap parallel to the axis of the affected extremity, had lower rates of lymphedema and a higher rate of restored lymphatic flow compared to traditional soft tissue flaps. Additionally, a subset of LIFT flaps where the lymphatic stumps in the flap were approximated within 2 cm to the lymphatic stumps of the recipient site (LIFT+) had higher rates of restored lymphatic flow and lower rates of lymphedema compared to the group where the lymphatics stumps were farther than 2 cm apart (LIFT−). This study indicates the importance of considering lymphatic directionality of a flap during VLVT as well as possible distance limitations of lymphangiogenesis.

Reductive surgery

Suction-assisted lipectomy (SAL)

The progression of lymphedema results in the transition from a fluid to a fibroadipose dominant state. In patients with more advanced disease, reductive procedures including both SAL as well as excisional techniques are effective means of removing this excess fibroadipose tissue. SAL involves liposuction of affected lymphedematous extremities to remove excess adipose deposition and is indicated for patients with fat-dominant or mixed fluid and fatty disease. These procedures are typically performed using tourniquet control and tumescent infiltration to minimize blood loss.

SAL has shown up to 94% reduction in lower extremity volume, decreased cellulitis recurrence, enhanced range of motion, and improved quality of life. For cases of upper extremity lymphedema, Brorson *et al.* showed up to 104% reduction amongst patients treated with SAL and controlled compression versus those on compression alone (127). Meta-analysis of 6 case studies (294 patients) showed an average limb volume reduction of 1,702 mL in those treated with liposuction combined with compression therapy (28). SAL has furthermore been shown to improve lymphedema symptoms (128), patient quality-of-life based on validated questionnaires (129), and long-term volume reduction up to over 20 years in appropriately managed patients (9). Consensus guidelines conclude there is a role for SAL in the treatment of moderate to severe lymphedema as it targets the non-fluid component of the advanced disease; however, timing and staging with physiologic procedures have yet to be determined (grade 1C) (28).

Compression garments are a critical component of postoperative management after SAL to minimize fluid accumulation in the affected extremity. While case reports have suggested that liposuction may actually improve lymph fluid transport based on postoperative lymphoscintigraphy (10), these procedures remain targeted at addressing the fibroadipose and not fluid component of lymphedema. In patients with mixed disease, staged approaches have been recommended combining both physiologic and reductive procedures to address these different components (130).

Excisional reductive techniques

Excisional reductive techniques can be considered for volume reduction and symptomatic relief in chronic severe lymphedema where there is extensive tissue fibrosis and hypertrophy. One of the oldest approaches to debulking advanced cases of lymphedema, the Charles procedure, excises tissue to the level of fascia and covers the wounds with skin grafts. The Charles procedure is effective in reducing limb size and removing lymphedematous tissue but can carry significant complication risks including infection, significant blood loss requiring transfusion, skin graft failure, chronic wounds and even amputation (131-134).

The invasive nature of the Charles procedure has led to the evolution of modified approaches. Staging debulking the debulking and grafting procedures aims to offset the physiologic burden placed on the body (8). The Homans procedure is another variation that utilizes longitudinal incisions along the extremity, subdermal debulking and preservation of the skin (135-137). These excisional approaches have found relevance in modern lymphedema treatment as part of an integrated approach of excision and physiologic restoration for cases of severe or end stage lymphedema. Ciudad *et al.* describe a combined, single-stage protocol of the Charles procedure, Homan's procedures, and VLNT on 68 patients with stage III lower extremity lymphedema with no major complications (138). Sapountzis *et al.* modified the Charles procedure to spare the superficial venous system and lesser saphenous vein as outflow options for VLNT (139). A similar, combined excisional and VLNT approach in 29 patients with bilateral lower extremity demonstrated a significant decrease in cellulitis and increase in quality of life (133).

Additional considerations

Insurance coverage

Despite the burden of lymphedema on over a million Americans, legislation and policy to mandate insurance coverage for lymphedema therapy has been slow to become reality and many limitations remain. Conservative therapeutic regimens such as compression garments, manual lymphatic drainage, and physical therapy have historically been covered on a case-by-case basis with wide variance based on a patient's insurance plan or state (140,141). Given the routine cadence needed to manage lymphedema including regular garment changes and therapeutic appointments, costs can easily exceed 3,000 USD annually (142). Tenuous coverage for conservative measures may not only impose a cost burden on patients but can also influence treatment compliance and ultimately lead to increased medical costs, hospitalizations, and complications. While the spectrum of nonoperative lymphedema therapies has yet to be fully covered, the Lymphedema Treatment Act (LTA), effective 2024, reflects a monumental stride forward (143). This legislation mandates insurance companies to cover medically necessary compression garments for lymphedema treatment, affording access to a mainstay of decongestive therapy. Notably, the LTA is actualized over a decade after its initial conception, signaling that the expansion of medically necessary treatments for lymphedema requires vigilance for success.

Despite the safety profile and successful outcomes of lymphedema surgery, countless obstacles have been faced by providers and patients alike as most insurance companies do not formally acknowledge surgical intervention for lymphedema as standard of care (144-146). ILR remains an elective procedure not covered by more than 50% of insurance companies and LVB and VLNT are also commonly denied by insurance providers (145,146). Part of this dilemma may be due to the variable coding taxonomy which lends to inconsistent pricing rates for surgical treatment not only between physiologic and reductive procedures, but within each type as well (147). While federal policy has yet to materialize, a major accomplishment involves the collaboration between the Boston Lymphatic Center, Lymphatic Education and Research Network, and Blue Cross Blue Shield Massachusetts (148). This work highlighted the disconnect that can exist amongst disciplines and reinforced the necessity of multidisciplinary efforts to bridge knowledge gaps pertaining to evidence-based practices, fiscal plans, and operative outcomes for lymphedema. Together, a policy was formulated for lymphatic procedures by standardization of the lexicon and measurements involved in the approach for evaluation, diagnostic workup, treatment, and outcomes.

Conclusions

Lymphedema is a burdensome disease for patients that impacts daily quality of life and carries significant morbidity in advanced stages. The advent of surgical treatment modalities for lymphedema and recent advancements in supermicrosurgery and imaging technologies offer patients and providers an expanded toolkit to treat lymphedema. This review demonstrates the utility of modern physiologic and reductive surgical techniques as both treatment and preventative tools. Additionally, these approaches do not have to exist in silos; rather, techniques are versatile and should be combined as well as individualized to fit each patient's specific needs. As surgical treatment options continue to demonstrate their utility, it is important for policy and insurance to align in coding nomenclature and fiscal rates to ensure equitable access.

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Footnote

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