Surgical Management of Lymphedema: Past, Present, and Future

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Abstract

Recent advances in surgical management of lymphedema have provided options for patients who have failed conservative management with manual lymphatic massage and/or compression garments. The purpose of this review is to provide a historical background to the surgical treatment of lymphedema and how these options have evolved over time. In addition, we aim to delineate the various types of surgical approaches available, indications for surgery, and reported outcomes. Our goal is to increase awareness of these options and foster research to improve their outcomes.

Introduction

SECONDARY LYMPHEDEMA IS A DREADED COMPLICATION of cancer treatment and a source of significant morbidity.[1–7] The current mainstay of lymphedema management is complex decongestive therapy (CDT) and compressive garments. Although a number of different regimens have been described for CDT, most programs have an intensive primary phase (usually 5 days per week for 4–6 weeks) in which lymphatic massage and skin care are combined with continuous bandaging with short-stretch bandages, followed by a secondary phase consisting of compressive garments with or without lymphatic massage. The primary phase is usually repeated in patients with an exacerbation or progression of lymphedema. The aim of these *palliative* treatments is to prevent lymphedema progression and provide symptomatic relief. Although effective in many patients, CDT is time consuming, difficult to perform on regular basis, expensive, and often not covered by medical insurance.[8] These barriers, together with a shortage of trained lymphedema therapists, lead to high rates of noncompliance and patient dissatisfaction. As a result, numerous surgical treatments of lymphedema have been described over the past century. The purpose of this review is to highlight the previous, current, and future potential surgical treatment options for lymphedema.

Surgical Treatment of Lymphedema

There is no consensus for surgical intervention, type of procedures that are performed, or timing of intervention. However, in most cases, surgery is reserved for patients who fail conservative management with CDT and compressive garments. Surgical management of lymphedema can be broadly categorized into physiologic methods and reductive techniques (Table 1). Physiologic methods such as flap interposition, lymph node transfers, and lymphatic bypass procedures aim to decrease lymphedema by restoring lymphatic drainage. In contrast, reductive techniques such as direct excision or liposuction aim to remove fibro-fatty tissue that has been generated as a consequence of sustained lymphatic fluid stasis.

Physiological Methods

Flap interposition

A flap is a segment of tissue containing various cellular components (i.e., dermis, fat, muscle, or bone) that has an intact vascular supply. This is in contrast to a graft, a term used in most cases to refer to nonvascularized tissues (e.g., split thickness skin graft). The development of vascularized flap transfers has been a key development in reconstructive surgery, as these operations enable reliable transfer of large amounts of tissues even to extensively damaged areas.

Gilles described the first flap interposition for treatment of lower extremity lymphedema by transferring a flap of skin and subcutaneous tissues through a two-staged operation from the arm to the affected groin, thereby providing a path for lymphatic fluid to bypass the damaged lymphatics in the groin.[9] This report went largely unnoticed until 1974 when

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TABLE 1. SUMMARY OF SURGICAL TECHNIQUES FOR TREATMENT OF LYMPHEDEMA

Procedure	Technique	Highest Level of Evidence	Current Uses
Physiologic techniques			
Flap transfer	Transfer of healthy vascularized tissues to bridge obstructed area	IV[10]	Rarely used. Most commonly used in conjunction with reconstruction for other reasons such as breast reconstruction.
Lymph node transfer	Transfer of lymph nodes to damaged lymph node basin	IV[18,65]	Still considered controversial and experimental. No long-term or well controlled studies
Lymphovenous bypass	Connection of collecting lymphatics to local veins	III[27,30,39]	Used primarily in patients with early stage lymphedema (i.e., prior to onset of severe adipose tissue deposition). Supermicrosurgery procedures gaining momentum.
Lympho-lymphatic bypass	Connection of obstructed collecting lymphatics to nonobstructed lymphatics located outside the zone of injury	IV[27,33]	Used infrequently by a few centers primarily in circumstances when lymphovenous bypass is technically not feasible.
Excisional Techniques			
Skin/subcutaneous tissue excision	Direct excision of lymphedematous tissues	IV[47]	Used infrequently primarily in patients with severe lymphostatic elephantiasis
Liposuction	Circumferential suction assisted excision of lymphedematous tissues	III[50,52]	Used in patients with moderate to severe lymphedema who have failed conservative management. Level of evidence highest for upper extremity lymphedema.

Levels of evidence: Level I: randomized controlled trial; meta analysis of multiple randomized control trials; Level II: nonrandomized, controlled prospective trial; Level III: well-designed observational studies; Level IV: retrospective observational studies without controls or case-series; Level V: expert opinions or committee recommendations.

Goldsmith reported a series of 22 patients (13 with lower extremity and 9 with upper extremity) lymphedema treated by transferring the omentum transabdominally to the affected lymphatic basin.[10] Unfortunately, although some patients (38% in lower extremity and 56% in upper extremity) experienced good results, the high incidence of complications including bowel obstruction, pulmonary embolus, and hernia precluded wide acceptance of this procedure. More recently, several authors have reported small case series demonstrating decreased lymphedema and re-routed lymphatic flow from lymphedematous upper/lower extremities, genitalia, and head and neck sites after free or pedicled flap transposition of other tissues (e.g., muscle or skin).[11–14] However, despite these anecdotal results, these procedures are now rarely performed due to their unpredictable outcomes.

Lymph node transplantation

Lymph node transfers harvest healthy lymph nodes from one region (e.g., superficial inguinal nodes) and transplant them either to the original site of injury (e.g., axilla or groin) or to non-anatomic areas within the lymphedematous limb (e.g., the dorsum of the lower arm). Transplantation is performed either by simply mincing the lymph nodes and delivering them to the site as an avascular graft (i.e., without a blood supply)[15] or as a vascularized tissue flap in which the lymph nodes and surrounding fat are kept intact and transferred by repairing their arterial and venous (but not lymphatic) blood supply microsurgically.[16–18]

Isolated reports have anecdotally reported improved lymphedema after non-anatomic lymph node transfer hypothesizing the development of a "lymphatic pump" as a putative mechanism; however, these claims remain unsubstantiated.[16] Anatomic lymph node transfers are also controversial since their purported beneficial effects have been anecdotal reports with no controlled or carefully monitored trials.[17,18] Further, successful engraftment of nonvascularized lymph node grafts has not been shown definitively, and this process is probably, at best, highly variable.[19] In fact, animal studies with nonvascularized lymph node grafts have been mostly disappointing, unless the transfer is performed in the setting of augmented vascular endothelial growth factor-C (VEGF-C) expression.[20,21] The risk of lymphedema in the donor extremity is also a concern, particularly when even trivial lymphatic injury in the form of sentinel lymph node biopsy has been shown to result in lymphedema in 5%–7% of patients.[22] As a result of these limitations, lymph node transfers remain experimental and have not been widely adopted.

Lymphatic bypass

Lymphatic–lymphatic bypass.   Operations aim to connect obstructed lymphatic vessels located in the lymphedematous limb (i.e., distal to the zone of lymphatic obstruction) to healthy lymphatic vessels in another region of the body using a transplanted lymphatic or vein as an interposition graft. In a patient with upper extremity lymphedema, for example, lymphatic vessel grafts can be harvested from the thigh and

then transferred to the upper arm. The transplanted lymphatics are then microsurgically sutured to the obstructed arm lymphatics, tunneled into the neck, and connected to patent lymphatics, thereby bypassing the damaged axillary lymph node basin.[23,24] An alternative technique involves using a vein graft as the conduit and inserting several small (<0.3mm in diameter) transected lymphatic vessels into the cut distal end of the vein and connecting the proximal portion of the vein in the neck or distal to the damaged lymphatics in the groin.[25]

Lymphaticovenous bypass.   Procedures are designed to drain obstructed lymphatic vessels into the venous circulation by surgically creating lymphaticovenous shunts. Initially, these shunts were created using large superficial veins (e.g., saphenous vein) as the outlet vessels.[26] However, venous hypertension with resultant decreased lymphatic outflow led to the use of subdermal venules.[27–29] The latter technique is often referred to as "supermicrosurgery" since microsurgical anastomosis is performed in extremely small vessels (0.3–1 mm in diameter). These procedures have recently gained momentum as a preferred surgical approach, particularly in patients with early stage lymphedema, and relatively large numbers of procedures are performed in centers located in Japan, Italy, and the United States.[27–31]

There is no general consensus for indications for lymphatic bypass procedures and, in general, most studies that have been reported are retrospective in nature with variable results (Table 2). Most authors agree that lymphatic bypass procedures should be reserved for patients who have failed conservative management or suffer from recurrent cellulitis or lymphangitis.[29,30,32,33] Other authors also consider social issues such as dissatisfaction with garments or the desire to avoid garments as an indication for surgery.[25,27] Contraindications to surgery are also variable, depending on the author. However, most surgeons consider extensive tissue fibrosis or late stage lymphedema changes, venous hypertension, recurrent cancer, and patient noncompliance as contraindications to surgery.[27–30] Similarly, there is no consensus on the timing of surgery in relation to onset of lymphedema with series reporting early intervention (as early as 1–2 months after onset) or late surgery (as long as 20 years afterwards). In general, surgery is feasible as long as tissue changes in the affected limb (i.e., fibrosis, fat hypertrophy) are not severe (i.e., patients with Campisi stage I, II, or early stage III lymphedema).[27–30] Patients with more advanced lymphedema have been treated with physiologic techniques; however, the results are mixed and only limited numbers of patients are available for analysis.[27,32]

The reported results of lymphatic-bypass procedures have been highly variable with some groups describing very good/excellent results and others reporting modest or no improvement in objective measures or subjective analysis of lymphedema symptoms. This variability is likely due to a number of factors, including the retrospective nature of most studies, differences in volume or circumference measurements, length of follow-up, variable use of garments/physical therapy postoperatively, and the use of nonstandardized or validated questionnaires for subjective analysis. Measurement of volume changes in the affected limb is particularly problematic with numerous techniques used by different groups to approximate excess volume and very few studies

reporting use of complimentary techniques (e.g., volume measurements and bioimpedence or lymphoscintigraphy) as a means of corroborating their findings. In addition, many studies report mixed series of patients with either upper or lower lymphedema or lymphedema resulting from various etiologies, including cancer surgery, trauma, congenital conditions, or filiriasis. Finally, different groups have advocated variable criteria for patient selection, selection of procedures, timing of intervention, and identification of suitable lymphatic vessels for bypass surgery.

When taken as a whole, most authors describing their experience with lymphatic bypass procedures report modest improvements in limb volumes (30%–50% decreased) although a few individual patients experienced marked reductions.[24,25,27–30, 33–39] Both primary and secondary forms of lymphedema have been treated successfully with lymphatic bypass procedures, although the efficacy of these procedures in primary lymphedema has been debated.[24,35] In addition, most series have reported better outcomes for upper extremities as compared with lower extremities. Successful lymphatic bypass procedures have also been reported in retrospective studies of genital lymphedema resulting from congenital conditions or after cancer treatment.[31] The few studies that have evaluated postoperative lymphangitis have found that lymphatic bypass procedures decreased the rate of this complication in most patients.[24,26,27,33,36] A few long-term studies (follow-up >3 years) have shown that the improvements with bypass procedures are maintained even when garment use is discontinued.[27] Finally, most studies have reported improvements in subjective measures (i.e., sensation of heaviness, firmness, improved function, etc). However, very few have used validated measures for these analyses. In fact, the only study that utilized a validated measure (SF-36 questionnaire) found no improvement in subjective measures after bypass (although it could be argued that the SF-36 is not specific for lymphedema).[32]

Most reported series of lymphatic bypass surgery have reported low rates of surgical complications.[24,25,30,33,35] These complications have, in general, been minor (wound healing, lymphatic fistula, cellulitis) and improve spontaneously. Postoperative cellulitis has been reported in some studies, however, the incidence of this complication appears to be decreased by extended use of antibiotics.[33] Although it is logical that lymphedema would progress in at least some patients treated surgically, very few studies have reported worsening of lymphedema symptoms after surgery.[24,32,36]

One recent technological advance in the lymphovenous bypass procedures has been the use of fluorescence lymphangiography for intraoperative mapping of lymphatic vessels. This technique enables surgeons to evaluate the severity of lymphedema and also to identify optimal anatomic locations to perform lymphovenous shunts in real time without making skin incisions.[40] This is an important technological advance, as it enables rapid evaluation of the lymphatic system and identification of functional lymphatic vessels and as a result may improve the efficacy of these procedures.

Campisi and colleagues have recently reported the use of lymphovenous bypass procedures as a means of preventing lymphedema following axillary lymph node dissection.[41–43] In a prospective clinical study, the authors randomly divided patients into two groups (n=23 each): patients treated with axillary lymph node dissection with or without

TABLE 2. OUTCOMES AFTER LYMPHATIC BYPASS PROCEDURES

Author	Type	N	Type and stage	UE/LE	Indications	Procedure	F/U	Outcome Measures	Results	Notes
Campisi, 2010	Retro	~1800	1^0, 2^0 Stage Ib 3%; II 39%; III 52%, IV/V 6%	UE, LE	Failed conservative Rx Recurrent cellulitis Pain, dissatisfaction Volume increase >50%	LVA, LVL	Variable	Volume LS Subjective	**Volume decreased in 83% of patients (average 67%)** 87% decreased incidence of cellulitis LS improved	Some details not reported (e.g. patient follow-up details of outcomes) Subjective measures not validated
Campisi, 2006	Retro	843 (overlap with above)	$360=1^0$ $483=2^0$ Stage I/II 44%; III 49%, IV/V 7%	UE (231) LE (612)	Failed conservative management If venous hypertension then LVL	LVA, LVL	5-15yrs	Volume LS (110pts) Subjective	**"Very good" (>75% volume decrease) 73% of pts** "Good" (up to 50% decrease) 24% "Fairly good" (≤25% decrease) 3%	Some details not reported Subjective measures not validated
Campisi, 2002	Retro	133	$87=1^0$ $46=2^0$ Stage II 21%; III 47%; IV/V 15%	UE/LE	Not Discussed	LVL	Variable over 18 yrs	Volume, LS	**>75% decrease in 63 pts** 50-75% decrease in 45 pts 25-40% decrease in 20 pts <25% decrease in 5 pts Decreased lymphangitis Lymphoscintigraphy improved	Average volume reduction not given Exact f/u not reported Detailed lymphoscintigraphy results lacking
Boccardo and Campisi, 2011	Prosp	46	Prevention of BCRL	UE	ALND with or without LVA	LVA	1.5 years	Volume LS	1 patient with LVA developed lymphedema; 7 without LVA developed lymphedema (p<0.01) Improved LS after LVA	Defined lymphedema as volume increase of 100ml
Boccardo and Campisi, 2009	Prosp	55	Prevention of BCRL	UE	ALND with or without LVA	LVA	2 years	Volume LS	8% of LVA vs. 33% without LVA developed lymphedema Avg. increase arm volume LVA pts=1.3±0.7 % v.s. 8.3±10% (p<0.05)	Short-term follow-up 89% had follow-up at 2 years
Mukenge, 2010	Retro	5	2^0	Genital	Failed conservative Rx Free of disease at least 2 years and 1 yr after adjuvant therapy Recent lymphedema)	LVA	6.8±0.8 months	CT scan Lymphangiography Subjective	4/5 had "satisfactory" decrease in edema & improved subjective symptoms 3 patients with 3-5 year follow up had 90-100% resolution of edema	Subjective analysis not validated

TABLE 2. (CONTINUED)

Author	Type	N	Type and stage	UE/LE	Indications	Procedure	F/U	Outcome Measures	Results	Notes
Koshima, 2000	Retro	12	2^0	UE (most BCRL)	No improvement with conservative therapy for 6 months	LVA (supermicrosurgery)	2.2 years	Circumf.	**Mean decrease circumference = 47.3%**	First report of supermicrosurgery
Chang, 2010	Prosp	20	2^0	UE-BCRL	Stage II or III post mastectomy related lymphedema	LVA (supermicrosurgery)	1 year	Volume (perometry) Subjective	95% subjective improvement 65% had volume decrease (35% decrease volume)	Subjective analysis not a validated questionnaire
Demitras, 2010	Retro	78	$1^0, 2^0$	LE (1^0 80; 2^0 = 21)	Campisi stage II, III, IV	LVA ± LVL	13.2 months	Volume	1^0 **patients** mean decrease volume = 56.2 ± 22.8% 2^0 **patients** mean decrease volume = 60.3% ± 18.1%	Patients with stage III or IV tended to need long-term garments
Nagase, Koshhima, 2005	Retro	>80	$1^0, 2^0$	UE/LE	Failed conservative therapy × 6 months	LVA (supermicrosurgery)	4.6 years	Circumf.	62% of patients had a decrease of 4cm **Mean decrease = 4.7cm**	Best outcomes with lymphedema Some experimental details not provided
O'Brien, 1990	Retro	134	2^0	UE (102) LE (32)	Not described	LVA LVA + reduction Reduction only	3–6 years	Volume and circumf. Subjective	**LVA only:** 42% improved; 12% unchanged; 45% worse **LVA and reduction**: 60% improved; 16% no change; 24% worse 94% subjective improvement	Upper extremity had better outcomes No validated subjective analysis
Damstra, 2009	Prosp	10	2^0 (all BCRL)	UE	Failed conservative Rx Volume >800cc	LVA	1 year	Volume SF-36 LS	**No change in volume or LS** Slightly improved subjective measures in 50% of patients	All patients were Campisi stage III (i.e. later stage than most other studies)

$1^0/2^0$, primary/secondary; LE, lower extremity; LS, lymphoscintigraphy; LVA, lymphatico-venous anastomosis; LVL, lymphatico-venous-lymphatic bypass; Prosp, prospective; Retro, retrospective; UE, upper extremity.

163

lymphaticovenous anastomosis. Arm lymphatics in patients who underwent axillary dissection were visualized using lymphazurin injection and transected lymphatics (2–4 collecting lymphatics) were anastomosed to branches of the axillary vein. After 18 months of follow-up, only 1 patient (4.3%) in the bypass group developed lymphedema. In contrast, 7 patients (30.4%) in the control group developed lymphedema. This difference was statistically significant. Furthermore, patients treated with bypass were found to have increased transport of technetium-labeled colloid as compared to controls. Although these results are interesting, long-term evaluation is necessary since lymphedema can occur years after surgery (77% by 3 years). In addition, the results should be interpreted with caution since the study had relatively few patients and the authors defined lymphedema as an increase in volume of 100 ml. This figure is somewhat controversial since most previous studies consider changes in excess of 200 ml to be diagnostic for lymphedema.

Reductive Methods

Direct excision

A variety of surgical procedures has been developed for direct excision of excess tissue resulting from lymphedema. These procedures are largely of historical significance but still used occasionally in cases of severe lymphostatic elephantiasis. In 1912, Charles reported a radical debulking procedure for treatment of scrotal and lower extremity lymphedema in which skin and subcutaneous tissues were excised circumferentially to the level of the deep fascia and the resultant wound repaired using a split thickness skin graft.[44] Sistrunk (1927) and later Thompson applied similar techniques for the treatment of upper extremity lymphedema resulting from breast cancer.[45,46] In these procedures, an elliptical skin and soft tissue excision of the upper extremity is performed in the medial aspect of the arm, and dermal flaps linking the skin and underlying fascia are created in attempt to foster drainage of superficial lymph channels by the deep collecting system. No prospective or long-term studies have been performed to evaluate the outcomes of these studies, although some authors have reported favorable results.[47] However, these procedures are invasive and may result in pain, wound healing complications, infections, and lymph fistulas. Severe wound healing complications may, in some cases, even worsen lymphedema necessitating amputation.[48]

Liposuction

A number of studies have evaluated the use of liposuction for breast cancer-related upper extremity lymphedema. Brorson and colleagues reported the results of prospectively followed patients with overall favorable results.[49–52] In a study of 37 patients with unilateral nonpitting (i.e., stage II) lymphedema, the authors reported a 118% reduction in limb volumes after circumferential liposuction with continuous postoperative compression garment use.[52] These reductions were maintained when the authors reported their results for 48 patients with 4 years follow-up with an average reduction of 106% (range 66%–179%).[49] In addition, the authors reported a statistically significant decrease in the incidence of cellulitis in the affected limb (0.4 episodes per year before vs.

0.1 episodes per year after).[51] Although subjective analysis of lymphedema was not formally performed, most patients had symptomatic relief.

Qi and colleagues combined the use of liposuction and physiologic treatments (flap transfer and lymphatico–lymphatic bypass) in 11 patients with severe lymphedema of the upper extremity.[53] Although only modest decreases in arm circumference were reported (10% after 3 years), the incidence of cellulitis decreased dramatically (6.5 ± 4.3 versus 0.7 ± 0.8 episodes per year).

The indications for liposuction for the treatment of upper extremity lymphedema include nonpitting edema that has failed conservative management (>3 months); arm volume differences of at least 600 cc; no active cancers or open wounds; no family or personal history of clotting abnormalities; medical clearance for general anesthesia.[51] Symptomatic complaints including heaviness, shoulder/neck strain or pain, functional impairments, and recurrent infections are also considered indications for surgical intervention. In Brorson's study,[49] patients had lymphedema on average for 8.2 years (1–24 years) and lymphedema started a mean of 3.4 years (range 0–37 years) after axillary lymph node dissection.

The use of postoperative garments is critical for maintenance of volume reductions in the upper extremity after liposuction, as exemplified by a small number of patients in Brorson series in which compression therapy was discontinued.[49] In these patients, fluid re-accumulation occurred rapidly with only a 47% reduction in arm volume at 1 year follow-up. As a result of this, patients are usually followed closely with a lymphedema team and garments are adjusted as necessary to maintain a tight fit.

Evidence for efficacy of liposuction for lower extremity lymphedema is less convincing and comprised primarily of case reports and small series.[50,54–56] In fact, early reports of lower extremity liposuction were disappointing, resulting in only minor improvements when performed without skin excision.[56] More recent reports have demonstrated improved results using modern liposuction devices and tumescent techniques. For example, O'Brien (1989) reported an average 23% reduction in 5 patients with unilateral lower extremity lymphedema with an average follow-up of 10 months.[57] Similarly, Greene and colleagues (2006) reported a single case of a patient with bilateral stage II–III primary lymphedema treated with liposuction alone, resulting in a 75% volume reduction with 18-month follow-up.[55] Another case report demonstrated modest reductions in leg volumes in a patient with stage III bilateral primary lymphedema (40% at 14 months) with symptomatic relief and decreased episodes of cellulitis.[58]

In general, circumferential liposuction for lymphedema is safe with few reported postoperative complications. Most patients recover quickly and are discharged within 48 hours following surgery. When complications do occur, they tend to be minor and include occasional paresthesias and minor wound healing issues. The use of tourniquets and tumescent technique significantly decreases blood loss and patients rarely require transfusions. Cadaver and imaging studies have demonstrated that liposuction does not disrupt lymphatic vessels (if performed parallel to the limb) and that treatment of lymphedema with liposuction does not decrease the already impaired lymphatic transport capacity of the limb.[59–62]

Future Directions

A critical step in the evolution of surgical treatment for lymphedema is improved patient evaluation and follow-up. As noted in this review, the vast majority of studies reported to date have been case series and anecdotal reports. Very few prospective or controlled studies have been performed, making it difficult to draw conclusions about the efficacy of various treatment options. Further, few studies have compared different surgical treatments in an effort to study the relative efficacy of these procedures. Although a few studies have evaluated lymphatic function after lymphatic surgery, most studies have relied on circumference or volume measurements as a means of evaluating the outcomes of surgical treatments. The combination of these functional and anatomic studies should provide better insight and more standardized means of analyzing surgical outcomes.

Our lack of understanding about the cellular and molecular mechanisms that regulate initiation and progression of lymphedema represent significant barriers to the development of targeted measures designed specifically to decrease the incidence and morbidity of lymphedema. For instance, it remains unknown how lymphedema causes characteristic histological changes such as fibrosis or lipodystrophy. Elucidation of these mechanisms may enable us to not only predict who is at risk for lymphedema but also develop interventions that can be used in conjunction with existing measures or surgical treatments to improve outcomes. For example, recent experimental studies have evaluated the use of lymphangiogenic cytokines such as vascular endothelial growth factor-C (VEGF-C) in the treatment of lymphedema in animal models with encouraging results.[20,21,63–64]

Combination of these cytokines with vascularized tissue transfers may hold promise in some clinical scenarios.

Author Disclosure Statement

None of the authors have any disclosures or relevant conflicts of interests.

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