Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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Title: Lymphedema-Surgical Treatments

Description/Background

LYMPHEDEMA

Lymphedema is an accumulation of fluid due to disruption of lymphatic drainage. Lymphedema can be caused by congenital or inherited abnormalities in the lymphatic system (primary lymphedema) but is most often caused by acquired damage to the lymphatic system (secondary lymphedema). The goal of treatment is to control limb swelling, since the underlying disease usually cannot be corrected.

Diagnosis and Staging

A diagnosis of secondary lymphedema is based on history (e.g., cancer treatment, trauma) and physical examination (localized, progressive edema and asymmetric limb measurements) when other causes of edema can be excluded. Imaging, such as magnetic resonance imaging (MRI), computed tomography (CT), ultrasound, or lymphoscintigraphy, may be used to differentiate lymphedema from others causes of edema in diagnostically challenging cases.

Table 1 lists International Society of Lymphology (ISL) guidance for staging lymphedema based on "softness" or "firmness" of the limb and the changes with elevation of the limb.[1]

***Table 1. Recommendations for Staging Lymphedema**

Stage	Description
Stage 0 (subclinical)	Swelling is not evident and most patients are asymptomatic despite impaired lymphatic transport
Stage I (mild)	Accumulation of fluid that subsides (usually within 24 hours) with limb elevation; soft edema that may pit, without evidence of dermal fibrosis
Stage II (moderate)	Does not resolve with limb elevation alone; limb may no longer pit on examination
Stage III (severe)	Lymphostatic elephantiasis; pitting can be absent; skin has trophic changes

Management and Treatment

Early and ongoing treatment of lymphedema is necessary. Conservative therapy may consist of several features depending on the severity of the lymphedema. Patients are educated on the importance of self-care including hygiene practices to prevent infection, maintaining ideal body weight through diet and exercise, and limb elevation. Compression therapy consists of repeatedly applying padding and bandages or compression garments. Manual lymphatic drainage (MLD) is a light pressure massage performed by trained physical therapists or by patients designed to move fluid from obstructed areas into functioning lymph vessels and lymph nodes. Complete decongestive therapy is a multiphase treatment program involving all of previously mentioned conservative treatment components at different intensities. Pneumatic compression pumps may also be considered as an adjunct to conservative therapy or as an alternative to self-MLD in patients who have difficulty performing self-MLD.

Microsurgical Options

Microsurgical operations have been explored as possible treatments for lymphedema which is refractory to non-operative methods. These surgical options consist of various methods for restoration of obstructed or obliterated lymphatic channels.

Table A. Physiologic Microsurgical Interventions for Lymphedema

Surgery	Description	Key Features
Lymphatic-lymphatic bypass	Connects functioning lymphatic vessels directly to affected lymphatic vessels; healthy vessels come from donor site	• Lymphedema can develop in donor extremity • Scarring at donor site
Lymphovenous bypass and lymphaticovenular anastomosis	Lymphatic vessels in an affected limb are connected to the venous system	• Outpatient procedure or usually discharged within a day • Quick return to daily activities
Autologous lymph node transplantation and vascularized lymph node transfer (autologous or vascularized)	Healthy lymph nodes are transferred to the affected limb	• Inpatient procedure; requires 2-3 days of hospitalization • Lymphedema can develop in donor extremity
Greater omental lymph node flap (GOLF)	The right, middle and left omental arteries are harvested based on this blood supply for free tissue transfer	• Inpatient procedure • Laparoscopic technique • For individuals who have failed other treatment options or have limited node transfer donor sites
Lymphatic microsurgical preventing healing approach (Lympha)	After complete nodal dissection, during breast cancer surgery, lymphatics are identified and anastomosed with a tributary to the axillary vein	• Preventative technique • No extra scarring

Liposuction for Debulking of Limb

Liposuction for lymphedema is usually performed under general anesthesia. Small incisions in the affected extremity(ies) are made and excess tissue is removed by vacuum aspiration. Liposuction is generally performed around the entire circumference of the limb and compression bandaging is applied postoperatively to control bleeding and limit post-operative swelling. Antibiotics are commonly prescribed. To achieve ultimate volume reduction, patients

must wear a garment, which often is custom-fitted to the extremity. Patients may need to return for new garment fitting throughout the first year until a stable limb volume is achieved.

Regulatory Status

Physiologic microsurgery for lymphedema and/or debulking are surgical procedures and, as such, is not subject to regulation by the U.S. Food and Drug Administration.

Medical Policy Statement

Lymphovenous bypass and vascularized lymph node transplant for lymphedema may be considered established as a therapeutic option when indicated.

Surgical treatment of massive localized lymphedema and late stage lymphedema by liposuction and/or excision is considered established.

Inclusionary and Exclusionary Guidelines

LYMPHOVENOUS BYPASS AND VASCULARIZED LYMPH NODE TRANSPLANT

Inclusions:

Lymphovenous bypass and vascularized lymph node transplant may be considered as a surgical options when the following criteria are met:

A. Signs and symptoms consistent with lymphedema as determined by a certified lymphedema therapist
B. AND a diagnosis of stage ≥ I lymphedema by the International Society of Lymphology (ISL) standards.

AND

C. For lymphovenous bypass for unilateral disease, at least one of the following positive quantitative measurements:
    1. MR lymphangiogram demonstrating residual lymphatic channels
    OR
    2. Lymphoscintigraphy findings showing a minimum of a one-hour delayed transit time to first-level lymph nodes, axillary lymph nodes (upper extremity lymphedema) or inguinal lymph nodes (lower extremity lymphedema), or a dermal back flow pattern
    OR
    3. Volumetry differential (circumferential measurements and/or perometry differential) >10% (if affected extremity dominant extremity) or >7% (affected extremity is non-dominant extremity),
    OR
    4. Bioimpedance abnormality differential consistent with lymphedema,

D. Patients with bilateral disease should meet A, B, and C-1or C-2, above.

E. For vascularized lymph node transfer, at least one of the following:

1. MR lymphangiogram showing absence of lymphatic channels

OR

2. Lymphoscintigraphy findings showing a minimum of a one-hour delayed transit time to first-level lymph nodes, axillary lymph nodes (upper extremity lymphedema) or inguinal lymph nodes (lower extremity lymphedema), OR a dermal back flow pattern

OR

3. Volumetry differential (circumferential measurements and/or perometry differential >10% (if affected extremity dominant extremity) or >7% (affected extremity is non-dominant extremity),

OR

4. Bioimpedance abnormality differential consistent with lymphedema.

F. Patient also meets all of the following eligibility criteria:

1. Patient has BMI ≤ 35-40kg/m2
2. Patient has undergone a course of conservative treatment under the supervision of a lymphedema therapist
3. Patient has demonstrated the ability to tolerate post-surgical compression therapy and physical therapy sessions per treating lymphedema provider.

G. NONE of the following are present:

1. Chronic venous disease (e.g., chronic venous insufficiency, superior vena cava syndrome)
2 Congestive heart failure (CHF)
3. Medication-induced swelling
4. Liver disease including but not limited to cirrhosis, hypoproteinemia v. nephropathy including end-stage renal disease
5. Active infection of the affected extremity (cellulitis/erysipelas).
6. History of dye anaphylaxis

H. Microsurgery for lymphedema is performed by surgeons with specialized training in lymphedema surgery and lymphology.

Exclusions:

- Lymph node transplant and/or lymphovenous bypass is considered experimental/investigational if the above criteria are not met.
- Debulking of a limb not impacted by lymphedema or lipedema is considered experimental/investigational if the above criteria are not met.
- Greater omental lymph node flap (GOLF) is considered experimental/investigational.
- Lymphatic microsurgical preventing healing approach (Lympha) is considered experimental/investigational.

*Refer to Table 1 for staging of lymphedema.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

15833	15836	15878	15879	38589	38999

Note: The above codes are established only when patients meet criteria for coverage and the procedure is an established procedure.

Other codes (investigational, not medically necessary, etc.):

49329	49999

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

PHYSIOLOGIC MICROSURGERY TO TREAT LYMPHEDEMA

Clinical Context and Therapy Purpose

The purpose of microsurgery treatments for lymphedema in individuals who have primary or secondary lymphedema is to provide a treatment option when conservative therapy with compression garments or bandages, manual lymph drainage or pneumatic pumps, and decongestive therapy has failed.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals who have been treated for primary or secondary lymphedema, and who have insufficient symptom reduction with conservative therapy Lymphedema in its late chronic phase is irreversible. The surgical techniques of interest in this review are those performed in individuals who have not reached the irreversible stage, i.e., those who have functioning lymphatic channels (stage I, II or early stage III) (see Table 1).

Interventions
Microsurgical interventions include several techniques and can be broadly grouped into procedures that (1) reconstruct or bypass the obstructed lymphatic vessels to improve lymphatic drainage and (2) transfer lymph tissue into an obstructed area to reestablish lymphatic flow (see Table A).

Comparators
Physiological microsurgery may be used as an adjunct to conservative therapy. Conservative therapy is multimodal. It involves meticulous skin hygiene and care, exercise, compression therapy, and physical therapy (manual lymphatic drainage). Complete decongestive therapy and pneumatic compression pumps are also used as adjuncts to conservative therapy.

Outcomes
Objective outcomes of interest include reduction in limb circumference and/or volume and reduction in the rates of infections (e.g., cellulitis, lymphangitis). Volume is measured using different methods; e.g., tape measurements with geometry formulas, perometry, and water displacement. Bioimpedance spectroscopy may be used to detect changes in tissue fluid accumulation.

Patient-reported outcomes (PROs) of interest include symptoms, quality of life, and functional measures.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with preference for prospective studies.
c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded.

Because multiple systematic reviews of studies were available for both classes of microsurgery, focus is on systematic reviews published in 2015 or later.

Review of Evidence

Surgeries That Reconstruct or Bypass Using Donor Lymph Vessels

Leung et al (2015) reported on a systematic review of surgical management breast cancer−related lymphemdema.[4] The search included studies reporting on the efficacy of surgical techniques used for the prevention or treatment of breast cancer−related lymphedema published between 2000 and 2014. Only 1 study on lymphatico-lymphatic bypass (LLB) was identified and published since 2000. The study included 7 patients followed for 2.6 years. One patient had “complete recovery” as measured by circumference of the affected limb and the remaining 6 patients had a “reasonable outcome”. Post-surgery complications were cellulitis, donor-site lymphorrhea, and transient edema of donor leg.

Surgeries That Reconstruct or Bypass Using the Venous System

Systematic Reviews

Three systematic reviews specifically evaluating microsurgical procedures using the venous system (lymphaticovenular anastomosis [LVA], lymphovenous bypass) have been reported.[5,6] Two broader systematic reviews of treatments for lymphedema including several microsurgical procedures have also been reported.[4,7] Corneilissen et al (2018) and Leung et al (2015) were limited to studies of breast cancer−related lymphedema but the remaining reviews were not. Fourty publications on LVA were included across the 4 systematic reviews. Characteristics of the reviews are shown in Table 3.

Chang et al (2021) reported on a systematic review and meta-analysis of LVA, liposuction, and vascularized lymph node transfer (VLNT) for treatment of lymphedema.[29] The results of liposuction will not be reviewed. Overall, 66 total studies were included, with 16 studies included on LVA. Follow-up ranged from approximately 6 to 68 months. The number of patients with breast cancer-related lymphedema was not described. In addition, studies evaluating use of these procedures for both upper and lower extremity lymphedema were included. The study reported findings for limb circumference and incidence of cellulitis. Results for patients treated with lymphovenous bypass are presented in Table 4.

Coriddi et al (2020) reported on a systematic review of PROs following surgical treatment of lymphedema, including lymphovenous bypass and VLNT.[30] Overall, 32 studies were identified (details regarding study design were not reported) with follow-up ranging from approximately 4 months to 43 months. The number of patients with breast cancer-related lymphedema was not described. The study reported findings for both validated and non-validated instruments assessing quality of life; however, only 18 studies (n=717 patients) reported individual patient data to permit quantitative assessment of the proportion of patients experiencing quality of life improvements. Results for patients treated with lymphovenous bypass are presented in Table 4.

Cornelissen et al (2018) reported on a systematic review assessing the effect of LVA in breast cancer−related lymphedema.[5] Fifteen observational studies were identified (11 prospective, 4 retrospective) with follow-up times ranging from 2 months to 8 years. Although LVA surgery was performed in the included studies, the technical procedure differed among studies: 6 studies used only end-to-end anastomoses; 4 studies used both end-to-end and end-to-side anastomoses; 1 study used the ‘‘Octopus technique’’; and 4 studies did not report the LVA technique used. Only 2 studies included a control group (bandaging, decongestive therapy).

Scaglioni et al (2017) reported on a systematic review of LVA for the treatment of lymphedema.[6] Reviewers noted significant variations in surgical techniques, numbers of anastomoses, and supplementary interventions (i.e., compressive therapy, additional

debulking surgery). Nine studies included secondary lymphedema alone, while 8 studies included patients with both primary and secondary lymphedemas. The number of patients with breast cancer−related lymphedema was not described. As mentioned, the Carl (2017) and Leung (2015) reviews included multiple surgical techniques. Leung (2015) was limited to breast cancer−related lymphedema while Carl (2017) was not.

Table 3. Characteristics of Systematic Reviews Assessing Lymphedema Surgeries Using the Venous System

Study	Dates	Studies	Participants	N (Range)	Design	Duration (Range)
Chang et al (2021)	Up to 2019	Overall: 66 LVA: 16	With secondary lymphedema undergoing lymphovenous bypass (n=16 studies), VLNT (n=17 studies), liposuction (n=43), or combination therapy (n=3)	NR (4 to 124)	• Randomized controlled trials, prospective and retrospective cohort and case-control studies	LVA: 6 to 68 mo
Coriddi et al (2020)	Up to 2019	32	With lymphedema undergoing lymphovenous bypass (n=18 studies) or VLNT (n=14 studies)	954 (6 to 100)	• Studies reporting QOL outcomes after physiologic proceduresb	Weighted average, 9.2 mo (range, 4.2 to 43.1 mo)
Cornelissen et al (2018)	1999-2017	15	With breast cancer-related lymphedema	268 (3-39)	• Observational or single-arm: 11	Cornelissen et al (2018)5
Scaglioni et al (2017)	Up to 2016	18	With lymphedema of any cause except filariasis-related	939 (5-154) (no. with breast cancer-related lymphedema NR	• Observational or single arm: 8 • Prospective: 10	24 mo (5-55 mo)
Carl et al (2017)	2000-2016	Overall: 69 LVA: 27[a]	With extremity lymphedema of any cause	NR	• Observational or single-arm	LVA: 6-120 mo
Leung et al (2015)	2000-2014	Overall: 13 LVA: 6	With breast cancer-related lymphedema	146 (6-89)	• Observational or single-arm	LVA: 17 mo to 8 y

LVA: lymphaticovenular anastomosis; NR: not reported.
[a] Only 12 “high-quality” LVA studies were discussed.

Results of the systematic reviews are shown in Table 4. In 4 of the reviews, given the variability in the procedures, metrics for measuring the outcomes, and the time periods of reporting, meta-analyses were not possible and only a narrative synthesis provided. In the Carl (2017) review, meta-analyses were performed for the outcome measure of percent excess circumference reduction, although only a small subset of studies reported this outcome and could be combined.

Table 4. Results of Systematic Reviews Assessing Lymphedema Surgeries Using the Venous System

Study	Reduction in Circumstance or Volume of Affected Limb	Reduction in Symptoms	Infection Frequency	Postoperative Complications
Corneilissen et al (2018)				
n	255	NR	NR	205
Narrative	Overall reduction in either circumference or volume reported in 13/15 studies	• Reduction in symptoms reported in 12/15 studies • Percent patients with improvements varied from 50% to 100%		• 1 study reported 2 complications (skin irritation on the contrast injection site) • 10 studies reported no complications • 4 studies did not report whether complications occurred
Scaglioni et al (2017)				
Total n	939	NR	NR	NR
Narrative	All studies reported reductions in circumference measurements	Vast majority reported subjective symptom relief on basis of patient opinion and feeling	Reduction in no. of cellulitis episodes present in all cases	
	Excess Circumference Reduction (%)			
Carl et al (2017)				
n	474 (3 LVA studies)	NR (5 studies)	NR	NR (2 studies)
PE (95% CI) or narrative	16.1 (2.6 to 29.6)	• 1 study reported 92% symptom improvement • 2 studies reported average satisfaction rate of 94.5% • 2 studies reported improved QOL in 90% of patients and subjective improvement in 50%		• Partial skin ulceration (n=1) • Wound dehiscence (n=1)
I^2 (p)	0% (0.17)			
Leung et al (2015)				
Total n	146	NR	NR	109
Narrative	• Mean percent reduction in volume at 1 y was 2%, 35%, and			• No complications in 2 studies • Remaining studies did not report on

	42% in 3 studies • Mean absolute circumference reduction was 4.1 cm and 0.85 cm in 2 studies				complications
Chang et al (2021)					
Total N	134 (10 studies)	NR	37 (3 studies)	NR	
PE (95% CI) or narrative	LVA plus compression reduced circumference by a mean of 3.8 cm (2.93 to 4.67 cm)		Reduction in number of cellulitis infections before vs. after surgery (mean difference, 2.57; 95% CI, 1.75 to 3.38)		
I^2 (p)	NR (<.00001)		NR		
Coriddi et al (2020)					
Total N	NR	596	NR	NR	
Narrative		• All studies showed an improvement in QOL (range, 50% to 100%) • Validated instruments: QOL improvement, 50% (1 study) • Non-validated instruments: QOL improvement, 57% to 100% (11 studies)			

CI: confidence interval; LVA: lymphaticovenular anastomosis; NR: not reported; PE: pooled effect; QOL: quality of life

Randomized Controlled Trials

No RCTs were identified.

Nonrandomized or Observational Studies

Winters et al (2017) reported on the results using LVA to treat breast cancer-related lymphedema (BCRL). Patients were eligible for inclusion if they suffered from unilateral BCRL, if functional lymphatics were available, if compression therapy was used for at least 6 months, and if the follow-up was 12 months at minimum. Twenty-nine consecutive female patients with unilateral BCRL were included. The preoperative mean difference in arm volumes was 701 ± 435 ml (36.9%). This was reduced to 496 ± 302 ml (24.7%) at 6-month follow-up (p = 0.00). At 12-month follow-up, the mean difference in arm volume was 467 ± 303 ml (23.5%) (p = 0.02). The overall perceived QoL was increased from 5.8 ± 1.1 to 7.4 ± 0.7 (p = 0.00). The functionality score decreased from 2.2 to 1.8 (p = 0.00), the appearance score decreased from 2.6 to 1.9 (p = 0.00), the symptoms score decreased from 2.8 to 1.8 (p = 0.00), and the mood score decreased from 2.7 to 1.5 (p = 0.00). Fifteen patients (53.6%) were able to discontinue the use of compression garment.

Additional single-arm studies have been published since the systematic reviews. Salgarello et al (2018) reported the outcomes of patients' health-related quality of life (HRQoL) after LVA for lower and upper extremity lymphedema.[8] After a mean follow-up of 8.5 months (range: 2-21 months), the authors observed an increase of 2.3 points in the overall QoL average for upper limb and 2.6 points for lower limb ($p < 0.001$). A statistically significant improvement in all four domains ($p < 0.01$) was reported after surgery, being present from the first postoperative months for both upper and lower extremities. In addition both a reduction of episodes of lymphangitis and a decrease in the need of conservative therapy were observed in this cohort of patients.

In another study, Phillips et al (2019) assessed the effects of LVA on patients' limb volume and quality of life. Pre- and postoperative limb volumes and QOL scores were collected for patients undergoing LVA for lymphedema secondary to breast cancer. Thirty-seven patients underwent LVA. A significant reduction was seen in median excess limb volume postoperatively (13.3%-6.6%, $P < 0.005$), with volumetric improvement seen in 78% of patients. Thirteen patients were able to discontinue compression garment use. Eighty-six percent of patients reported improved quality of life postoperatively with median QOL score increasing from 90 to 104 points ($P < 0.005$).

Surgeries That Transfer Lymph Tissue

Systematic Reviews

Systematic reviews evaluating microsurgical procedures that transfer lymph tissue (autologous lymph node transfer [ALNT], vascularized lymph node transfer [VLNT]) have been reported. Characteristics of systematic reviews of surgeries for lymphedema are shown in Table 5. Ozturk et al (2016) reported on a systematic review of VLNT for treatment of lymphedema.[9] They included treatment for both primary and secondary lymphedema and as such comprised a heterogeneous population. However, 191 of 305 of the surgeries were for breast cancer−related lymphedema. Eighteen studies were identified (3 prospective, 15 retrospective). For breast cancer−related lymphedema, VLNT with a skin island or VLNT with an autologous flap was used. There was inconsistent reporting of staging of lymphedema. Reviewers did not state whether any of the studies included a control group. Two systematic reviews of various surgical methods previously described also included a review of lymph node transfer.[4,7]

Table 5. Characteristics of Systematic Reviews Assessing Lymphedema Surgeries Using Lymph Tissue Transfer

Study	Dates	Studies	Participants	N (Range)	Design	Duration
Demiri et al (2018)	NR	11	With breast cancer-related lymphedema treated with VLNT	189 (8-42)	RCT, observational, or single-arm	Mean, 38 mo (range, 6-132 mo)
Carl et al (2017)	2000-2016	Overall: 69 VLNT: 17[a]	With extremely lymphedema of any cause	NR	Observational or single-arm	NR
Ozturk et al (2016)	1980 to 2015	18	With primary or secondary upper- or lower-limb lymphedema (63% breast cancer-related)	305 (6-52)	• Observational or single-arm: 3 • Prospective: 15	2-132 mo
Leung et al (2015)	2000-2014	Overall: 13 LNT: 6	With breast cancer-related lymphedema	80 (3-24)	Observational or single-arm	LNT: 6 mo to 8 y

NR: not reported; RCT: randomized controlled trial; VLNT: vascularized lymph node transfer.
[a] Only 10 “high-quality” VLNT studies were discussed.

Results of the systematic reviews are shown in Table 6. In Ozturk (2016) and Carl (2017), results for the subgroup of breast cancer−related lymphedema were not presented so the table includes all available participants. Due to differences in outcomes metrics and timing of measurements, meta-analyses were not possible and narrative summaries were provided by Ozturk (2016), Demiri (2018), and Leung (2015). Carl (2017) performed meta-analyses for the excess volume outcome but only a few studies could be pooled in the combined estimate.

Table 6. Results of Systematic Reviews Assessing Lymphedema Surgeries Using Lymph Tissue Transfer

Study	Reduction in Circumference or Volume	Reductions in Symptoms	Infection Frequency	Post-operative Complications
Demiri et al (2018)				
Total n	NR	NR	NR	189
Narrative				Donor limb lymphedema: • 3 (1.6%) cases • 8 studies reported donor-site complications: ○ Seroma (n=8) ○ Lymphocele (n=3) ○ Lymphorrhea (n=2) ○ Wound infection (n=2) ○ Delayed wound healing (n=3)

				○ Donor-site pain, numbness, or discomfort (n=9) ○ Transient edema of donor site (n=1) ○ Lymphedema of lower limb (n=3)
	Excess Circumference Reduction (%)			
Carl et al (2017)				
Total n	NR (4 studies)[a]	NR	NR (4 studies)[a]	NR (7 studies)[a]
PE (95% CI) or narrative	39.5% (36 to 43)		• Quantitative summaries not given • Improved function, appearance, and mood • Decreased pain	• Quantitative summaries not given • Cellulitis, lymphocele, donor-site pain, seroma, lymphedema hematoma, wound dehiscence, wound infection, hydrocele, partial skin graft loss, venous congestion
I^2 (p)	0% (0.85)			
Ozturk et al (2016)				
Total n	305[a]	105[a]	106[a]	198[a]
Narrative	• Overall reduction in either circumference or volume reported in all studies • 17/182 patients evaluated by limb circumference showed no improvement • 16/114 patients evaluated by volume showed no improvement	• Various PROs reported in 7 studies • 98/105 reported high level of patient satisfaction	• Decrease reported in 7 publications using various metrics • Remaining publications did not quantify decrease	• Delayed wound healing: 4% • Seroma/hematom: 3% • Infection: 2% • Abdominal bulge: 0.5% • Persistent donor lymphedema: 0%
Leung et al (2015)				
Total n	80	NR	NR	52
Narrative	• Mean percent reduction in circumference was 40% and 51% in 2 studies • “Reduction” in circumferenc			• Donor-site edema (n=1) • Wound infection (n=1) • Venous congestion (n=1) • Seroma (n=3) • Delayed wound closure (n=2) • 2 studies did not report on complications

	e reported in 10/21 (47%), 22/24 (92%), and 7/9 (78%) in 3 studies			

CI: confidence interval; NR: not reported; PE: pooled effect; PRO: patient-reported outcome.
[a] All eitiologies included; results not provided for subgroup of patients with breast cancer-related lymphedema.

Randomized Controlled Trials

Dionyssiou et al (2016) reported on an RCT that evaluated VLNT plus physical therapy vs. physical therapy alone for lymphedema in 36 women with stage II breast cancer−related lymphedema.[11] Trial characteristics are shown in Table 7.

Table 7. Characteristics of RCTs of Lymphedema Surgeries Using Lymph Tissue Transfer

Study	Countries	Sites	Dates	Participants	Interventions	
					Surgery	**Control**
Dionyssiou et al (2016)	Greece	1	2011-2014	Women with stage II, unilateral, upper-limb lymphedema related to breast cancer treatment and 1+ infections during last year	18 received VLNT followed by physical therapy[a] for 6 mo	18 received physical therapy[a] for 6 mo

RCT: randomized controlled trial.
[a] Physical therapy included manual lymphatic drainage for 1 month and pressure garments for 5 months.

RCT results of reported in Dionyssiou (2016) are shown in Table 8. At 18 months, the reduction in excess volume of the affected limb as a percentage of the intact limb was 57% in the VLNT group and 18% in the physical therapy group (treatment effect not reported, p<0.001). The mean number of lymphedema-related infections per patient per year was lower in the VLNT group (0.28 vs. 1.16; treatment effect not reported, p=0.001). The trial had several limitations described in Tables 9 and 10. Notably, there was no description of allocation concealment and the trial was not blinded, possibly introducing both selection and ascertainment bias.

Table 8. Results of RCTs of Lymphedema Surgeries Using Lymph Tissue Transfer

Study	Reduction in Circumference of Affected Limb	Reduction in Volume of Affected Limb	Infections	Function or Quality of Life	Post-operative Complications
		Reductions in Excess volume of Affected Limb as % of Intact Limb at 18 mo (%)	**Mean Episodes per Patient per Year**	**VAS for Functional Impairment at 18 Months**	
Dionyssiou et al (2016)					
n	NR	36	36	36	18

Surgery	NR	57%	0.28	1.22	4[a]
Control	NR	18%	1.16	4.61	N/A
TE (95% CI); p	NR	NR (NR); <0.001	NR (NR); 0.001	NR (NR); 0.001	

CI: confidence interval; N/A: not XXX; NR: not reported; RCT: randomized controlled trial; TE: treatment effect; VAS: visual analog scale
[a] Two with mild discomfort at donor side lower limb; 2 with prolonged lymphorrhea at donor area.

Nonrandomized or Observational Studies

Additional single-arm studies have been published since the systematic reviews. Ciudad et al (2017) evaluated the long-term clinical outcomes among different VLNT used at one institution. Between July 2010 and July 2016, all patients with International Society of Lymphology (ISL) stages II-III who underwent VLNT were evaluated.[13] Demographic and clinical data (limb circumference, infectious episodes, lymphoscintigraphic studies) were recorded pre-operatively. Clinical outcomes, complications, and additional excisional procedures were analyzed post-operatively. At least 2-year follow-up was required for inclusion. Overall, 83 patients (Stage II:47, Stage III:36) met the inclusion criterion. Mean follow-up was 32.8 months (range, 24-49). Lymph node flaps used were groin (n = 13), supraclavicular (n = 25), gastroepiploic (n = 42), ileocecal (n = 2), and appendicular (n = 1). Total mean circumference reduction rate was 29.1% (Stage II) and 17.9% (Stage III) ($P < 0.05$). A paired t-test showed that VLNT significantly decreased the number of infections ($P < 0.05$). Three patients reported no improvement of the symptoms. Major complications included one flap loss and one donor site hematoma. After the period of follow-up, 18 patients (21.7%) underwent additional excisional procedures.

Gennaro et al (2017) reported on the reduction of the frequency of cellulitis before and after microsurgical LVA in lymphedema patients.[14] Thirty-seven patients affected by lymphoedema were enrolled. All patients received preoperative indocyanine green lymphography. Under local anesthesia s-LVA was performed on all patients. All patients were followed for 1 year. Lymphoedema was staged using the lymphoedema staging classification recommended by the International Society of Lymphology. Cellulitis rate was recorded for all patients the year before and after the s-LVA. A t-test was used to evaluate differences in the frequency of cellulitis the year before surgery and the year following surgery. Cellulitis incidence decreased in all patients, with a mean 1.7 cases the year before s-LVA and 0.1 the year after s-LVA. A significant difference between preoperative and postoperative cellulitis rate was found ($p = 0.0012$).

PHYSIOLOGIC MICROSURGERY TO PREVENT LYMPHEDEMA (LYMPHA)

Clinical Context and Therapy Purpose

The purpose of lymphatic physiologic microsurgery simultaneous to lymphadenectomy for breast cancer (i.e., the Lymphatic Microsurgical Preventing Healing Approach [LYMPHA]) is to prevent lymphedema in individuals who are being treated for breast cancer. While recommendations on preventive measures for lymphedema exist, such as avoiding needle sticks, limb constriction, and air travel, most recommendations are based on clinical opinion. A systematic review of preventive measures for lymphedema by Cemal et al (2011) found strong scientific evidence only for the recommendations to maintain a normal body weight or avoid weight gain and to participate in a supervised exercise regimen.[15]

LYMPHA is a preventive LVA procedure performed during nodal dissection or reconstructive surgery that involves anastomosing arm lymphatics to a collateral branch of an axillary vein.

The following **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest is individuals who are undergoing a lymphadenectomy or breast reconstruction procedure for breast cancer.

Interventions
This review focuses on physiologic microsurgical intervention called LYMPHA.

Comparators
LYMPHA could be used as an adjunct to standard care. Standard care may involve education regarding lymphedema and recommendations for hygiene, avoidance of blocking flow of fluids in the body, maintaining a normal body weight and exercise, as well as surveillance for lymphedema during follow-up with referral as needed.

Outcomes
Outcomes of interest include diagnosis of lymphedema, lymphedema symptoms, quality of life, and operative and postoperative complications. As discussed, the diagnosis of lymphedema is based on history and physical examination (localized, progressive edema, asymmetric limb measurements). There is no universal agreement on measurement criteria for asymmetric limbs. It may be quantified by a 2 or more centimeters difference in limb girth, a 200 mL difference in limb volume, or a 10% limb volume change from baseline.[16,17] Patient report of heaviness or swelling, either "now" or "in the past year" may also be used to suggest lymphedema. The estimated incidence of lymphedema varies by the measurement criteria used.[17]

Systematic Reviews
Ciudad et al (2022) and Jorgensen et al (2017) reported on a systematic review of prophylactic LVA and shunts for preventing cancer−related lymphedema, not limited to breast cancer.[31] Systematic review characteristics are shown in Table 11. Twelve articles were included in the qualitative analysis (5 specific to breast cancer) and four of those studies (2 specific to breast cancer) were included in a meta-analysis.

Table 11. Characteristics of Systematic Reviews of LYMPHA to Prevent Lymphedema

Study	Dates	Studies	Participants	N (Range)	Design	Duration, mo
Jorgensen et al (2017)	1980-2016	12 (5 specific to breast cancer)	Underwent lymphadenectomy for cancer treatment and prophylactic LVA for prevention of extremity lymphedema	364 (8-74)	RCT, observational, single-arm	6-69
Ciudad et al (2022)	1980-2016	12 (5 specific to breast cancer)	Underwent lymphadenectomy for cancer treatment and prophylactic LVA for	364 (8 to 74)	RCT and observational	6 to 69

			prevention of extremity lymphedema			

LVA: lymphaticovenular anastomosis; LYMPHA: Lymphatic Microsurgical Preventing Healing Approach; RCT: randomized controlled trial.

Results of the systematic review are shown in Table 12. Jorgensen et al (2017) performed a meta-analysis of the incidence of lymphedema that included 4 studies (2 specific to breast cancer) with a control group consisting of patients without prophylactic LVA. The relative risk for incident lymphedema was 0.33 (95% CI, 0.19 to 0.56) favoring prophylactic LVA vs. control; however, because the incidence of lymphedema varies over time and the follow-up times varied across studies, it is not clear whether it would be appropriate to pool the risk including all time points. Ciudad et al (2022) reported that the pooled cumulative rate of upper and lower extremity lymphedema after oncological surgical treatment and LVA was 5.15% (95% CI, 2.9 to 7.5) and 6.66% (95% CI, <1 to 13.4), respectively. When compared to no intervention, the LVA reduced the incidence of upper and lower limb lymphedema by -18.7% (95% CI, -29.5 to -7.9) and -30.3% (95% CI, -46.5% to -14%), respectively.

Table 12. Results of Systematic Reviews of LYMPHA to Prevent Lymphedema

Study	Incidence of Lymphedema	Lymphedema Symptoms	Quality of Life	Complications
Jorgensen et al (2017)				
Meta-analysis				
n	176	NR	NR	NR
RR (95% CI)	0.33 (0.19 to 0.56)			
I^2 (p)	0% (0.74)			
Qualitative synthesis				
n range	8-74	NR	NR	Not clear
Range estimates	0%-30% with varying follow-up times			• 1 study reported lymphorrhea in 1 patient • Unclear if other studies reported no events or did not report on complications
Ciudad et al (2022)				
N	1547			
TE (95% CI); p-value	Upper extremity: 5.15% (2.9 to 7.5); <.01			
Risk difference (95% CI); p-value	Upper extremity: -18.7% (-29.5 to -7.9); <.001			

CI: confidence interval; LYMPHA: Lymphatic Microsurgical Preventing Healing Approach; NR: not reported; RR: relative risk.

Randomized Controlled Trials

Boccardo et al (2011) reported on results of an RCT including 46 women referred for axillary dissection for breast cancer treatment between 2008 and 2009 who were randomized to LYMPHA or no preventive surgery (control).[20] All LVA procedures were performed by the same surgeon, reported to be skilled in lymphatic microsurgery. The LVA surgeon was not the same surgeon who performed lymph node dissection. The same axillary dissection treatment was

performed in the 2 treatment groups. Lymphedema was diagnosed as a difference in excess volume of at least 100 mL compared with preoperative volume measurements. Trial characteristics are shown in Table 13.

Table 13. Characteristics of RCTs of LYMPHA to Prevent Lymphedema

Study	Countries	Sites	Dates	Participants	Diagnosis of Lymphedema	Interventions	
						Active	**Comparator**
Boccardo et al (2011)	Italy	1	2008-2009	Women referred for complete axillary dissection for breast cancer treatment	Difference in excess volume of ≥100 mL vs. preoperative volume	23 LYMPHA	23 no preventive surgery for lymphedema

LYMPHA: lymphatic microsurgical preventing healing approach; RCT: randomized controlled trial.

Results of the Boccardo (2011) RCT are shown in Table 14. Lymphedema was diagnosed in 1 (4%) woman in the LYMPHA group and 7 women (30%) in the control group by 18 months of follow-up. The change in volume with respect to baseline was reportedly higher in the control group than in the LYMPHA group at 1, 3, 6, 12, and 18 months (all $p<0.01$). The trial had several limitations described in Tables 15 and 16. Notably, the follow-up duration was only 18 months. Methods of randomization and allocation concealment were not described and there was no justification of the sample size. The patients and investigators were not blinded (i.e., no sham procedure was performed) and there was no discussion of whether outcome assessors were blinded. There is no indication that the trial was registered.

Table 14. Results of RCTs of LYMPHA to Prevent Lymphedema

Study	Incidence of Lymphedema	Change in Volume of Associated Limb, mL	Symptoms of Lymphedema	Quality of Life	Complications
	Cumulative at 18 Months	**At 18 Months**			
Boccardo et al (2011)					
n	46	46	NR	NR	NR
LYMPHA	4%	10^{th} percentile:≈ -60 mL[a] 90^{th} percentile:≈ +40 mL[a]			
Control	30%	10^{Th} percentile:≈ +50 mL[a] 90^{th} percentile:≈ +130 mL[a]			
TE (95% CI); p	NR (NR); 0.05				

CI: confidence interval; LYMPHA: Lymphatic Microsurgical Preventing Healing Approach; NR: not reported; RCT: randomized controlled trial; TE: treatment effect.
[a] Estimated based visual inspection of figure.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Nonrandomized or Observational Studies

Additional single-arm studies have been published since the systematic reviews.[21] However, these studies suffer from the same limitations as the studies included in the systematic reviews and do not capture longer periods of follow up and/or larger populations than the existing studies.

Greater Omental Lymph Node Flap

Attash and Al-Sheikh (2013) reported on four cases of long-standing unilateral, secondary lymphedema of the lower extremity, for which conservative treatment had failed.[22] These four patients underwent a pedicled omental flap procedure and were followed for a period of one year after the procedure. Frequency measurements of the affected limb revealed a reduction in the circumference ranging between 50% in the first patient to 75% in the fourth patient. Although this procedure showed some improvement in terms of walking, daily activities, sports and work, the authors concluded that larger studies are required to confirm these results.

In another study, Nguyen et al (2017), looked at some long-term outcomes of the minimally invasive free vascularized omental lymphatic flap for the treatment of lymphedema.[12] Overall, 42 patients underwent a free omental lymphatic flap and had a mean follow-up of 14 (3-32) months. Subjective improvements were noted in 83% of patients. Mean volumetric improvement was 22%. Postsurgical complications occurred in 16% (n = 7) of patients; this included one episode of pancreatitis and one flap loss.

In a 2019 systematic review by Forte et al, hypothesized that the analyzed studies would show vascularized omentum lymph node transfer (VOLT) would show positive outcomes.[23] The author's search yielded 35 potential papers in the literature, but only six studies fulfilled the study eligibility criteria. The total number of patients was 137. Three studies described single VOLT, two studies described double VOLT and one study described two cohort patients, one that was treated with single VOLT and another one that was treated with double VOLT. Postoperative reduction of arm circumference, arm volume, and symptoms of the upper extremity were reported in all patients. Nonetheless, in one study, seven patients did not notice any extremity circumference reduction during the follow-up period and four patients noticed an increase in arm volume. Flap loss was reported by two authors in a total of two patients.

Debulking of Limb Impacted by Lymphedema

For patients with lymphedema who undergo debulking procedures, the evidence includes one systematic review and meta-analysis, one prospective cohort study, one retrospective review, and two case series.[7] Three studies involve a BCRL patient-population. The systematic review and meta-analysis by Carl et al. include 105 patients with both upper extremity (n=99) and lower extremity (n=9) lymphedema. Liposuction is the technique used in three studies and suction-assisted lipectomy is used in one study. All four studies report on volume reduction (using circumferential measurements and water displacement) compared to the contralateral side. On meta-analysis, the weighted excess volume reduction in the study by Carl et al. was 96.6% (95%CI: 86.2-107). Patients were told to adhere to a post-operative compression regimen. ISL staging was used in two studies and patients undergoing debulking procedures were at least stage II. Three studies reported on quality of life measures and showed improvement in the personally important activities index, reduced anxiety and improved sense

of wellbeing. The SF-36 was also used to evaluate physical function improvement in one study. Follow up time ranged from a minimum of 12 months to 38.4 months. In a study by Lee et al. in an exclusive breast cancer patient population (122/130 receiving adjuvant radiation), a 97% decrease was found in upper extremity girth.[25] Although there was an overall decreased incidence of infection (erysipelas) observed in this cohort, de novo infection did occur in 6 of 56 patients who had never had a prior occurrence. Decrease in infection was observed across all studies assessing this outcome. In the study by Lamprou et al, cellulitis incidence decreased from a mean of 6 attacks/year to 0.3 attacks/year after surgical intervention.[25] The overall incidence of complications was low. In one study by Brorson et al, patients who underwent liposuction and used post-operative compression were compared to patients receiving compression only (control).[26] Patients receiving compression had decreased volume changes compared to the intervention group and scored comparatively worse on all quality of life and functional indices used (VAS, HAD, NHP, PSG)

SUMMARY OF EVIDENCE

Surgeries That Reconstruct or Bypass Using the Venous System

For patients with lymphedema who undergo reconstruction or bypass using the venous system, the evidence includes largely systematic reviews. No controlled trials were identified evaluating the physiologic microsurgeries using techniques such as lymphovenous bypass or LVA that reconstruct or bypass the obstructed lymphatic vessels using the venous system in patients with cancer−related lymphedema. Systematic reviews have indicated that most of the available evidence for these procedures comes from uncontrolled studies including fewer than 40 participants each, most of which lack adequate descriptions of how patients were selected for inclusion. Surgical technique, severity of lymphedema, outcomes metrics, and follow-up times varied across studies making it difficult to draw conclusions. Surgical complications have been inconsistently reported but appear to be rare. In addition, these single-arm studies reported on significant reduction in limb volume along with an increase in perceived QoL scores. The evidence is sufficient to determine that the procedure results in a meaningful improvement in net health outcomes.

Surgeries That Transfer Lymph Tissue

For patients with lymphedema who undergo lymph tissue transfer, the evidence includes one RCT and systematic reviews. The RCT (36 participants) evaluated VLNT that uses lymph tissue transfer in patients with breast cancer−related lymphedema. The trial reported reductions in excess volume of the affected limb and rates of lymphedema-related infections for VLNT plus physical therapy compared with physical therapy alone. Systematic reviews have indicated that most of the remaining available evidence for these procedures comes from uncontrolled studies including fewer than 50 participants each, most of which lacked adequate descriptions of how patients were selected for inclusion. Surgical techniques, severity of lymphedema, outcomes metrics, and follow-up times varied across studies. Although surgical complications were inconsistently reported, a systematic review of complications estimated that donor-site lymphedema occurs in approximately 2% of surgeries and seroma occurs in approximately 4%. The evidence is sufficient to determine that the procedure results in a meaningful improvement in net health outcomes.

Prevention of Secondary Lymphedema in Breast Cancer Patients (LYMPHA)

For patients with lymphedema who undergo the LYMPHA procedure, the evidence includes a RCT and systematic reviews. One RCT with was identified evaluating LYMPHA to prevent

lymphedema in 49 patients referred for axillary dissection for breast cancer. The trial reported that lymphedema developed in 4% of women in the LYMPHA group and 30% in the control group by 18 months of follow-up. Longer follow-up is needed to observe incident lymphedema occurring after 18 months and assessed the durability of the procedure. The trial had limitations that could have introduced bias: methods of randomization and allocation concealment were not described, and there was no sham procedure or blinding. Systematic reviews have indicated that most of the remaining available evidence for LYMPHA comes from uncontrolled studies, although 2 controlled observational studies in women with breast cancer have been performed. Selection of the control group was identified as a potential source of bias in both controlled studies. Outcomes metrics and follow-up times varied across studies. Additional RCTs of LYMPHA are needed and 1 such trial is underway (see NCT03428581). The evidence is insufficient to determine the effects of the procedure on health outcomes.

Greater Omental Lymph Node Flap

For patients with lymphedema who undergo greater omental lymph node flap the evidence includes a report of four cases of long-standing unilateral, secondary lymphedema of the lower extremity, one study that reviewed long term outcomes and a systematic review analyzing outcomes of vascularized omentum lymph node transfer. Additional evidence to support the safety and effectiveness of greater omental lymph node flaps for the treatment of lymphedema are required. The evidence is insufficient to determine the effects of the procedure on health outcomes.

Debulking of Limb Impacted by Lymphedema

For patients with lymphedema who undergo debulking procedures, the evidence includes one systematic review and meta-analysis, one prospective cohort study, one retrospective review, and two case series. Three studies involve a BCRL patient-population. Three studies reported on quality of life measures and showed improvement in the personally important activities index, reduced anxiety and improved sense of wellbeing. The SF-36 was also used to evaluate physical function improvement in one study. A decrease in infection (erysipelas) was observed across all studies assessing this outcome. The overall incidence of complications was low. The evidence is sufficient to determine that the procedure results in a meaningful improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

National Lymphedema Network

The National Lymphedema Network published a position paper on the diagnosis and treatment of lymphedema in 2011.[27] The paper stated the following on microsurgical procedures:

> "Microsurgical and supramicrosurgical (much smaller vessels) techniques have been developed to move lymph vessels to congested areas to try to improve lymphatic drainage. Surgeries involve connecting lymph vessels and veins, lymph nodes and veins, or lymph vessels to lymph vessels. Reductions in limb volume have been reported and a number of preliminary studies have been done, but there are no long-term studies of the effectiveness of these techniques."

An update of this position paper is in development as of July 2023.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network Guidelines on Breast Cancer and Breast Cancer Survivorship (Version 4.2023) does not specifically mention surgical treatments for lymphedema. The guideline recommends educating patients on lymphedema, monitoring for lymphedema, and referring for lymphedema management as needed.

National Cancer Institute

National Cancer Institute (NCI): The NCI Health Professional Version [Physician Data Query (PDQ®)] on lymphedema states that "Surgery is rarely performed on patients who have cancer-related lymphedema. The primary surgical method for treating lymphedema consists of removing the subcutaneous fat and fibrous tissue with or without creation of a dermal flap within the muscle to encourage superficial-to-deep lymphatic anastomoses. These methods have not been evaluated in prospective trials, with adequate results for only 30% of patients in one retrospective review. In addition, many patients face complications such as skin necrosis, infection, and sensory abnormalities. The oncology patient is usually not a candidate for these procedures. Other surgical options include the following: Microsurgical lymphaticovenous anastomoses in which the lymph is drained into the venous circulation or the lymphatic collectors above the area of lymphatic obstruction; liposuction; superficial lymphangiectomy; fasciotomy" (2019).

International Society of Lymphology

International Society of Lymphology published a consensus document on the diagnosis and treatment of peripheral lymphedema in 2020.[1] The document stated the following on lymphaticovenous (or lymphovenous) anastomoses (LVA):

> "LVA are currently in use at multiple centers around the world. These procedures have undergone confirmation of long-term patency (in some cases more than 20 years) and some demonstration of improved lymphatic transport (by objective physiologic measurements of long-term efficacy)."

ONGOING AND UNPUBLISHED CLINICAL TRIALS

Some currently unpublished trials that might influence this review are listed in Table 17.

Table 17. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04579029	PRELUDE study of lymphatic surgery to treat breast cancer related lymphedema.	64	Dec 2023
NCT03683095	Efficacy of lymphovenous bypass in the treatment of extremity lymphedema	20	Oct 2022
NCT02790021	Microsurgical treatment of breast cancer-related lymphedema by lymphaticovenous anastomosis	120	Aug 2022
NCT03428581	Preventing lymphedema in patients undergoing axillary lymph node dissection via axillary reverse mapping and lympho-venous bypass.	264	Feb 2023
NCT04328610	To assess the efficacy of the LYMPHA in the prevention of lymphedema following axillary dissection for breast cancer.	34	Feb 2021

Unpublished			
NCT03073096	LYMPHA: eliminating the burden of lymphedema in patients requiring nodal dissection.	20	Sep 2019
NCT03941756	Lymphovenous bypass procedure before underarm lymph node surgery in preventing lymphedema in patients with inflammatory or locally advanced non-inflammatory breast cancer	50	Dec 2020

NCT: national clinical trial

Government Regulations

National:

There is no national coverage determination (NCD) for this service.

Local:

There is no local coverage determination (LCD) for this service.

Medicare does show facility as well as non-facility fees assigned to codes 15835, 15836, 15878 and 15879.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Pneumatic Compression Pumps for Lymphedema

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through November 2023, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
11/01/18	9/7/18	8/28/18	Joint E/I policy established.
11/1/19	8/20/19		Routine policy maintenance, no change in policy status.
3/1/21	2/19/21		Policy status changed to established with criteria for surgery. The rationale section has also been revised.
3/1/22	12/14/21		Routine policy maintenance, no change in policy status.
3/1/23	12/20/22		Routine policy maintenance, no change in policy status.
3/1/24	12/19/23		Routine policy maintenance, added references 29-31. No change in policy status. Vendor managed: N/A (ds)

Next Review Date: 4th Qtr. 2024

Pre-Consolidation Medical Policy History

Original Policy Date	Comments
BCN:	Revised:
BCBSM:	Revised:

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: LYMPHEDEMA-SURGICAL TREATMENTS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	See policy criteria
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.