

Outcomes of Lymphovenous Anastomosis for Upper Extremity Lymphedema: A Systematic Review

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Background: Lymphovenous anastomosis (LVA) is an accepted microsurgical treatment for lymphedema of the upper extremity (UE). This study summarizes and analyzes recent data on the outcomes associated with LVA for UE lymphedema at varying degrees of severity.

Methods: A literature search was conducted in the PubMed database to extract articles published through June 19, 2020. Studies reporting data on postoperative improvement in limb circumference/volume or subjective improvement in quality of life for patients with primary or secondary lymphedema of the UE were included. Extracted data consisted of demographic data, number of patients and upper limbs, duration of symptoms before LVA, surgical technique, follow-up, and objective and subjective outcomes.

Results: A total of 92 articles were identified, of which 16 studies were eligible for final inclusion comprising a total of 349 patients and 244 upper limbs. The average age of patients ranged from 38.4 to 64 years. The duration of lymphedema before LVA ranged from 9 months to 7 years. The mean length of follow-up ranged from 6 months to 8 years. Fourteen studies reported an objective improvement in limb circumference or volume measurements following LVA, ranging from 0% to 100%. Patients included had varying severity of lymphedema, ranging from Campisi stage I to IV. The maximal improvement in objective measurements was found in patients with lower stage lymphedema.

Conclusion: LVA is a safe, effective technique for the treatment of UE lymphedema refractory to decompressive treatment. Results of LVA indicate greater efficacy in earlier stages of lymphedema before advanced lymphatic sclerosis. (*Plast Reconstr Surg Glob Open* 2021;9:e3770; doi: [10.1097/GOX.0000000000003770](https://doi.org/10.1097/GOX.0000000000003770); Published online 25 August 2021.)

INTRODUCTION

Lymphedema is a chronic pathological state of impaired drainage of lymphatic fluid, leading to excess regional tissue fluid accumulation most commonly in the extremities.^{1,2} Lymphedema can occur as a primary process due to incompetent lymphatic valves or obliterated lymphatics.³ More commonly, however, lymphedema occurs secondary to surgical, traumatic, inflammatory, or

neoplastic obstruction of lymph drainage.⁴ In the United States, most cases of lymphedema afflict the upper extremity (UE), following mastectomy, axillary lymph node dissection (ALND), and adjuvant radiation in breast cancer patients.^{5,6} Studies report varying incidences of UE lymphedema,⁷ but pooled estimates from prospective cohort studies demonstrate an approximately 21% incidence in breast cancer patients.⁸

The treatment of lymphedema is primarily conservative, utilizing physiotherapeutic techniques such as manual massage to stimulate lymph drainage and compression bandages or garments.⁹ For patients who fail conservative management, surgical treatment may be considered. Traditionally, surgical treatment involved direct resection of the affected interstitial tissue or liposuction of the hypertrophic interstitial adipose tissue.² More recently, microsurgical techniques have been introduced, aimed at preserving the native tissue and bypassing damaged lymphatic pathways. These techniques include lymphovenous anastomosis (LVA), lympholymphatic bypass, and vascularized lymph node transfer (VLNT)^{9,10} (Fig. 1).

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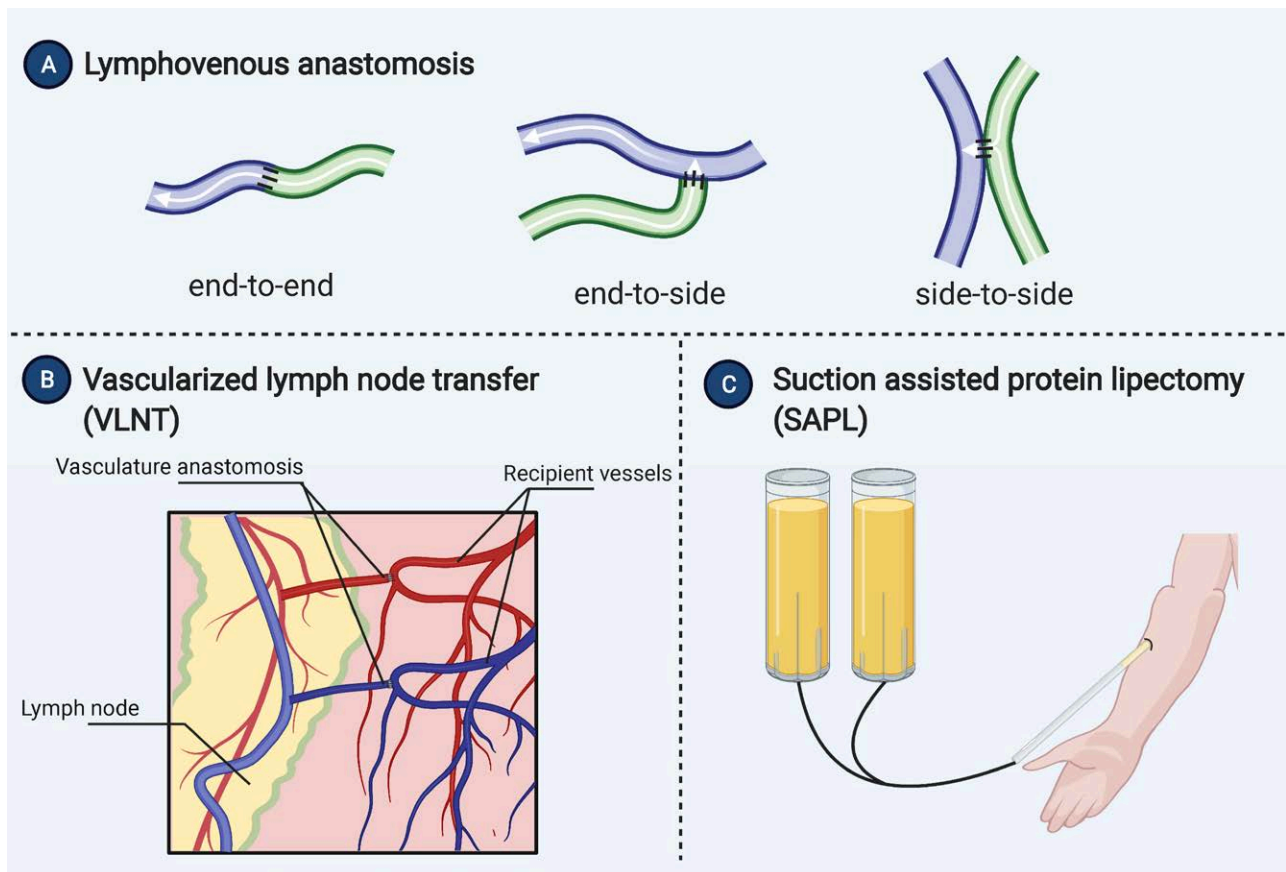


Fig. 1. Surgical techniques for lymphedema. A, LVA is a microsurgical technique to anastomose subdermal distal lymphatics with the adjacent venues. B, VLNT has its primary objective to transfer healthy lymph nodes to the affected site. C, SAPL is a reductive technique that seeks to remove the fibrofatty tissue by liposuction, generated secondary to a long period of lymph stasis in the limb. Created with BioRender.com.

LVA was first described in the 1960s,¹¹ but has gained traction in recent years as a gold standard microsurgical technique for lymphedema treatment. LVA allows obstructed lymphatic pathways to be bypassed by connecting superficial lymphatic vessels to nearby venules.¹² Increasing studies and reviews have shown the promise of LVA for extremity lymphedema,¹³ but the literature remains new on systematic measures of both objective and subjective improvement following LVA for UE. Furthermore, little data exist on an optimal preoperative and perioperative treatment plan [eg, use of compression and/or splinting; use of indocyanine green (ICG)] to achieve satisfactory outcomes.¹⁴ The purpose of this systematic review is to quantify the treatment plan and measures of objective and subjective clinical improvement associated with LVA for varying stages of UE lymphedema.

METHODS

Literature Review and Search Criteria

A literature search was conducted in the PubMed database to extract articles published up until June 19 2020. The search strategy used was as follows: {[lymphovenous anastomosis] OR [lymphovenous bypass] OR ["Anastomosis, Surgical"(Mesh)] AND ["Lymphatic Vessels"(Mesh)] OR

["Lymphatic Vessels/surgery"(Mesh)] OR ["lymphatic surgery"] AND ["Lymphedema"(Mesh)] AND ["Upper Extremity"(Mesh)] OR [arm (tiab) OR arms (tiab) OR elbow (tiab) OR elbows (tiab) OR forearm (tiab) OR forearms (tiab) OR hand (tiab) OR hands (tiab) OR finger (tiab) OR fingers (tiab) OR shoulder (tiab) OR shoulders (tiab) OR wrist (tiab) OR wrists (tiab)]].

Inclusion and Exclusion Criteria

Inclusion criteria comprised all studies in which LVA was performed for primary or secondary upper extremity lymphedema, and the authors reported data on post-operative objective improvement in limb circumference/volume or subjective improvement in quality of life and/or symptoms. Only human studies written in English were eligible for data extraction. Exclusion criteria included review articles, studies reporting on primary prevention of lymphedema, single patient case reports, and studies examining filariasis-related lymphedema.

Data Extraction and Outcome Measures

Article screening and data extraction were performed manually by two independent reviewers (N.G. and E.M.V.) as per eligibility criteria. In the case of disagreement, a third reviewer (C.M.T.) adjudicated the study. For all

studies included, extracted data consisted of demographic data, study type, year of publication, number of patients, number of upper limbs, duration of lymphedema before LVA, surgical technique including number and type of anastomoses, follow-up, and objective and subjective outcomes. If a study reported data on both lower and upper extremity lymphedema, efforts were made to extract only data relevant to UE lymphedema.

RESULTS

A total of 92 articles were identified and screened, of which 16 studies were deemed eligible for final inclusion in this study (Fig. 2). Eligible studies are outlined in Table 1 and comprised a total of 349 patients and 244 upper limbs.¹⁵⁻³⁰ Of note, the number of upper limbs included is less than the total number of patients because three studies did not report the exact number of

upper limbs affected in their cohort.^{16,18,24} As reported in Table 2, the average age of patients ranged from 38.4¹⁵ to 64 years,¹⁸ although four studies were not included in this as they did not stratify age by upper versus lower extremity.^{16,21,28,29} Only five studies reported the average BMI specifically in UE patients,^{15,18-20,24} which ranged from 21.1¹⁵ to 26.¹⁹

Of the included studies, 13 were performed in prospective fashion^{15-19,21,23-28,30} and three were retrospective in nature.^{20,22,29} No randomized control trials were eligible for inclusion in this review. The mean length of follow-up across studies ranged from 6 months²¹ to 8 years.²⁵ The duration of lymphedema before LVA ranged from 9 months¹⁹ to 7 years,^{22,28} though three studies did not report this.^{18,21,29} Six studies included patients with primary lymphedema (PL) or secondary lymphedema (SL),^{15-17,23,27,29} and 10 studies exclusively evaluated patients with SL.^{18-22,24-26,28,30}

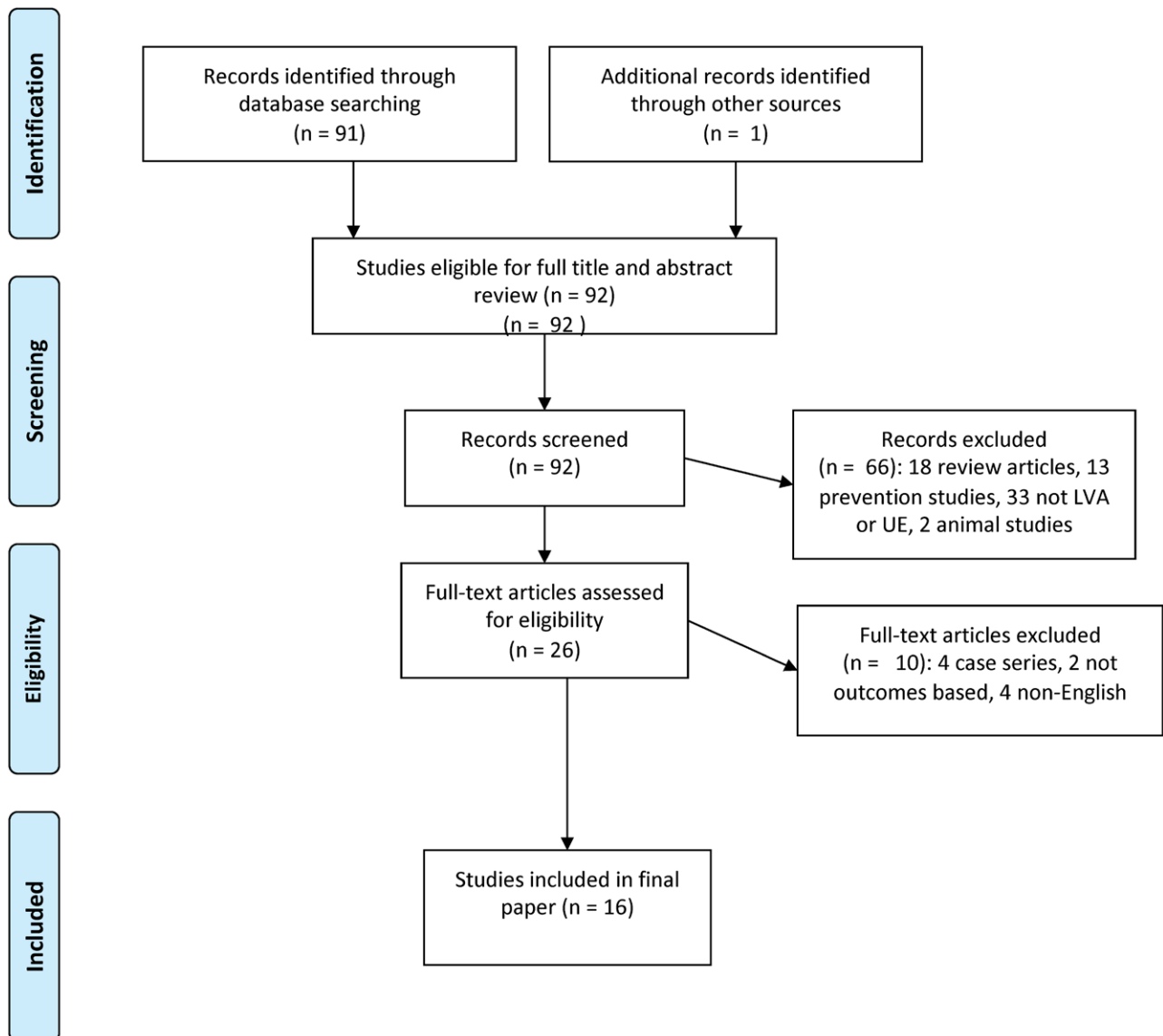


Fig. 2. PRISMA flow diagram.

Table 1. Study Details, Lymphedema Status, and Outcome Measures¹⁵⁻³⁰

Authors (y)	Study Type	No. Patients	No. Upper Limbs	Lymphedema Type (PL vs SL)	Duration of Lymphedema before LVA	Intervention	Anastomoses (Mean #)	Measurement Method	Follow-up Time (Mean)	Objective Improvement in % Patients	Subjective Improvement in % Patients
Aljindan et al (2019) ¹⁵	Prospective	20	20	PL and SL	54.1 mo	LVA (8 end to end, 12 side to end) + ICG	3.7	Limb circumference	16.5 mo	100	
Salgarello et al (2018) ¹⁶	Prospective	44		PL and SL	56 mo	LVA + ICG	3.38	LYMQoL questionnaire	8.5 mo		61
Gentileschi et al (2017) ¹⁷	Prospective	16	16	PL and SL	5.7 y	LVA + ICG	1.8	Circumference measurements, LYMQoL questionnaire	12.1 mo	88	94
Poumellec et al (2017) ¹⁸	Prospective	31		SL		LVA	3.75	Circumference measurements, QoL questionnaire	12.7 mo	93.5	84
Winters et al (2017) ¹⁹	Prospective	29	29	SL	9 mo	LVA (end to end, end to side, and invagination)	1.67	Volume measurements, QoL questionnaire	12 mo	97	53
Pereira et al (2018) ²⁰	Retrospective	8	8	SL	4.61 y	LVA + ICG	2.67	Circumference measurements, volumetric estimation	27.4 mo	100	100
Yamamoto et al (2014) ²¹	Prospective	3	3	SL		LVA + ICG	1.6	Circumference measurements	6 mo	100	
Lee et al (2017) ²²	Retrospective	3	3	SL	7 y	End to end LVA	2.7	Volume measurements	41.8 mo	100% at 12 mo, 67% at 24 mo	Did not separate by UE vs LE
Ayestray et al (2013) ²³	Prospective	20	20	PL and SL	3.2 y	LVA + patent blue		Circumference measurements and volumetric estimation	12 mo	85	90
Cornelissen et al (2017) ²⁴	Prospective	20		SL	6 y	LVA + ICG	1.5	Lymph-ICF QoL questionnaire	7.8 mo		85
Damstra et al (2009) ²⁵	Prospective	10	11	SL	5.3 y	LVA (end to end) + lymphoscintigraphy		Volume measurements, SF-36 QoL questionnaire	8 y	0	50
Chang (2010) ²⁶	Prospective	20	20	SL	4.8 y	LVA	3.5	Volumetric measurement	12 mos	65	85
Ayestray and Bekara (2014) ²⁷	Prospective	12	12	PL and SL	4.6 y	Pt-shaped LVA with patent blue	5.4	Circumference measurements, QoL questionnaire	Did not separate by UE vs LE	100	
Narushima et al (2010) ²⁸	Prospective	2	2	SL	7 y	LVA + ICG with intravascular stenting	5	Girth measurements	8.9 mo	Did not separate by UE vs LE	
Mihara et al (2014) ²⁹	Retrospective	11	11	PL and SL		LVA + ICG	3	Frequency of cellulitis	At least 1 y	Did not separate by UE vs LE	
Chang et al (2013) ³⁰	Prospective	100	89	SL	3.5 y	LVA + ICG		Volume differential (excess limb volume compared to the unaffected limb)	30.4 mo	74	96

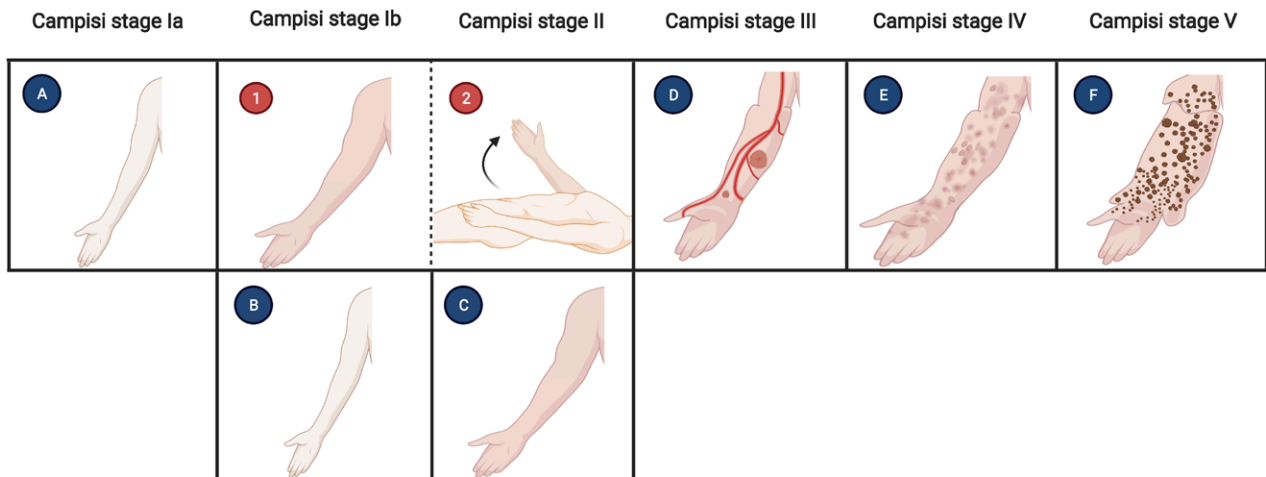
Table 2. Patient Details^{15–30}

Authors (Year)	No. Patients	No. Upper Limbs	Average Age (y)	Average BMI
Aljindan et al (2019) ¹⁵	20	20	42.1 in end-to-end group 38.4 in side-to-end group	21.1 in end-to-end group 24.2 in side-to-end group
Salgarello et al (2018) ¹⁶	44		Not stratified by UE vs LE	Not stratified by UE vs LE
Gentileschi et al (2017) ¹⁷	16	16	58.1	Not reported
Poumellec et al (2017) ¹⁸	31		64	25.3
Winters et al (2017) ¹⁹	29	29	59	26
Pereira et al (2018) ²⁰	8	8	48.9	23.34
Yamamoto et al (2014) ²¹	3	3	Not stratified by UE vs LE	Not reported
Lee et al (2017) ²²	3	3	41.3	Not reported
Ayestaray et al (2013) ²³	20	20	60.1	Not reported
Cornelissen et al (2017) ²⁴	20		55.9	25.1
Damstra et al (2009) ²⁵	10	11	58.7	Not reported
Chang (2010) ²⁶	20	20	54	Not reported
Ayestaray and Bekara (2014) ²⁷	12	12	59.2	Not reported
Narushima et al (2010) ²⁸	2	2	Not stratified by UE vs LE	Not reported
Mihara et al (2014) ²⁹	11	11	Not stratified by UE vs LE	Not stratified by UE vs LE
Chang et al (2013) ³⁰	100	89	54	Not reported

Objective measures of lymphedema included limb circumference measurements, volume measurements, and volume differential (the excess volume of the edematous limb compared to the unaffected limb). Of the 14 studies that reported on objective improvement in UE lymphedema following LVA, three studies did not separate outcome measures by UE versus LE.^{27–29} Objective improvements were seen in 0%–100% of patients across the remaining 11 studies, with six studies reporting an improvement in >90% of patients.^{15,18–22} Only one study reported no significant improvement in volumetric measurements of the affected limbs following LVA.²⁵ No surgically related complications were reported, barring one episode of skin irritation at the site of contrast injection²⁴ and one episode of hypertrophic scarring.²⁷ Three studies reported a significant decrease in episodes of cellulitis following LVA.^{16,20,29} Salgarello et al¹⁶ found that the incidence of greater than three cellulitis episodes per year decreased from approximately 20% to 6% postoperatively. Pereira et al²⁰ reported a decrease in the mean number

of yearly cellulitis episodes from 1.3 to 0, while Mihara et al²⁹ reported a similar decrease from 0.82 to 0.09 episodes. Aljindan et al¹⁵ also reported a decrease in episodes of cellulitis, but did not stratify this decrease by patients with upper versus lower extremity lymphedema.

Few studies stratified outcomes by surgical method or stage of lymphedema. Aljindan et al¹⁵ compared objective outcomes in patients who underwent end-to-end versus side-to-end anastomoses and found a statistically significant improvement in the circumferential difference in the side-to-end group versus the end-to-end group (3.4% versus 2.5%), despite similar demographics and stages of lymphedema in both groups.¹⁵ Seven studies reported on the Campisi stage of lymphedema in their patients^{18,21,22,24–26,30} (Fig. 3). Poumellec et al¹⁸ reported 42% of their cohort was patients with stage III or IV lymphedema. Yamamoto et al²¹ reported two stage III patients and one stage V. Lee et al²² reported two stage II patients and one stage III. Cornelissen et al²⁴ reported one stage I patient and 19 stage II patients.



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Fig. 3. Campisi staging. A, No swelling or skin changes are present even though there is impaired lymphatic circulation. The distinctive characteristic between stage Ib and II is the persistence of edema (1) after elevation of the extremity (2). B, Stage Ib has partial improvement with the extremity’s elevation; (C) stage II has persistent edema even with the maneuver. D, Persistent edema with lymphangitis. E, Fibrotic lymphedema and column-like extremity with the presence of warts. F, Elephantiasis with deformity of the extremity is present.

Damstra et al²⁵ reported 10 stage III patients. Chang²⁶ reported 10 stage II patients and 10 stage III patients, and found no difference in outcomes between the two groups. Poumellec et al¹⁸ and Chang et al³⁰ both reported a greater improvement in volume or circumference measurements in patients with lower stage lymphedema. Specifically, Poumellec et al¹⁸ found a 29.5% decrease in lymphedema in stage II patients, a 13.07% decrease in stage III patients, and a 0% decrease in stage IV patients. Chang et al³⁰ reported a greater volume differential reduction in stage I or II (61% at 12 mo) versus stage III or IV (17% at 12 mo).

Studies reported a varying number of mean anastomoses per patient, ranging from 1.6 to 5.4.²⁷ Nine studies reported utilizing ICG for preoperative visualization of the lymphatic system.^{15–17,20,21,24,28–30} Two studies utilized patent blue for this purpose,^{23,27} and one utilized lymphoscintigraphy.²⁵ Four studies did not report on preoperative lymphatic visualization. No study reported the use of preoperative MRA for visualization. Studies reported varying perioperative care, with one utilizing no compressive bandages after postoperative day 1¹⁵ to others resuming usual compressive treatment on postoperative day 7,²¹ day 21,²⁸ or day 28.³⁰

Eleven studies reported on subjective symptom relief and/or validated quality of life measures.^{16–20,23–27,30} Five of these studies used validated quality of life tools, namely the lymQOL, lymph-ICF, and SF-36 tools.^{17–19,24,25} The remaining six studies relied on subjective patient reports.^{16,20,23,26,27,30} Fifty-three percent¹⁹ to 100%^{20,27} of patients across all studies reported an improvement in their quality of life. Damstra et al²⁵ reported an improvement in the quality of life for 50% of patients, despite no objective improvement in UE lymphedema. AlJindan et al¹⁵ reported that 100% of patients were able to stop compressive stockings definitively postoperatively, whereas Ayestaray et al,²³ Winters et al,¹⁹ and Cornelissen et al²⁴ reported that 30%, 53%, and 85% of patients were able to discontinue compressive therapy, respectively. One study also reported a significant decrease in complex decongestive physical therapy sessions postoperatively from 1.7 to 0.77 sessions per patient per year ($P = 0.01$), though they did not separate this finding by UE versus LE.²²

DISCUSSION

This study systematically reviewed the findings of 16 articles that utilized LVA for primary or secondary UE lymphedema. Data were comprehensively analyzed on the duration and severity or staging of symptoms before surgical intervention, preoperative and perioperative protocol, as well as both the objective measures of lymphedema improvement and subjective measures of symptom relief and quality of life improvement. Objective improvements in limb circumference or volume were seen in 0%–100% of patients across the 11 studies which stratified outcomes by upper extremity, with six studies reporting an improvement in more than 90% of patients.^{15,18–22}

Recent advances in lymphoscintigraphy, MR angiography, and contrast agents such as ICG have allowed

microsurgeons to preoperatively identify lymph vessels that would be optimal sites for anastomoses.³¹ Twelve of the 16 studies reviewed used some form of preoperative visualization, with ICG being the most common. This has not only allowed for the expansion of patient selection, but also decreased the number of anastomoses that need to be made to achieve optimal outcomes.²⁶

Of the 16 studies included, various anastomosis techniques and perioperative protocols were described. One study reported improved outcomes in side-to-end anastomoses relative to end-to-end, but other studies did not compare techniques.¹⁵ Some authors have raised concerns about the pressure in the venous system when performing end-to-end anastomoses. Theoretically, this may be considered less physiologic than end-to-side or side-to-end. However, valves in the venules used for anastomosis would likely ameliorate pressure-related flow issues from the lymphatic system to the venous system. A practical way that surgeons ensure avoidance of an unfavorable pressure gradient is to ensure that a vein does not “back bleed” before performing end-to-end anastomosis. Interestingly, two studies reported that the mean numbers of anastomoses per patient were not associated with objective outcome measurements.^{19,20} Consensus remains elusive regarding the need for additional anastomoses. Although some authors have suggested that the more anastomoses the better, others believe that the quality of the anastomosis is more important than the absolute number. Additionally, it is plausible that larger anastomoses are similarly superior to the number of anastomoses. As seen in the current report, data regarding quantity, quality, and other factors are mixed. Perioperatively, authors also reported differing protocols regarding prophylactic antibiotic use, splinting, and when to reinstate use of compressive bandages. No uniform guidelines can be readily ascertained from the available data. Moving forward, to effectively compare long-term outcomes and develop perioperative guidelines, it would be useful for future studies to provide perioperative protocols in addition to surgical technique.¹⁹

Of the seven studies that reported on the Campisi stage of lymphedema,³² two reported an increased benefit of LVA for UE lymphedema at earlier stages.^{18,30} The remaining studies did not stratify outcomes by the stage of lymphedema. Interestingly, the one study that found no objective improvement in lymphedema following LVA included only Campisi stage three patients.²⁵ Chang²⁶ also commented on how the stage of lymphedema did not necessarily align with the mean duration of symptoms before surgery. Given that a successful LVA relies on an intact lymphatic system, these findings suggest that patients with severe lymphedema may be poor candidates for LVA due to sclerotic lymph vessels (Fig. 4). Alternatively, different anastomosis techniques may be preferred in this patient population, as one study found that side-to-end anastomosis lends itself better to more sclerotic vessels.³³ It is unclear whether outcomes vary by Campisi staging for other microsurgical techniques such as VLNT or suction-assisted protein lipectomy. It is

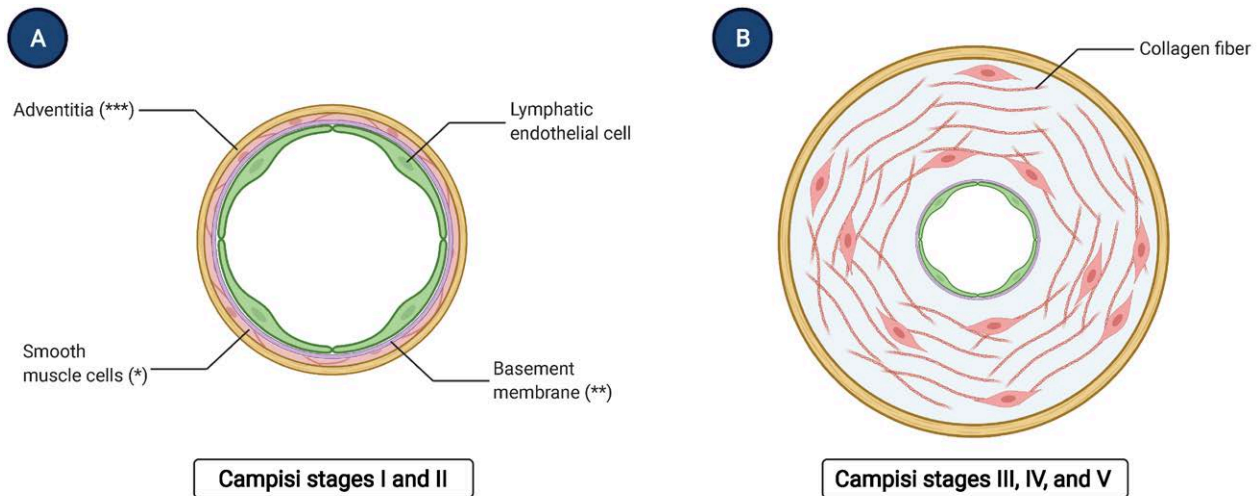


Fig. 4. Lymphatic vessels in patients with different Campisi stages. Patients with higher Campisi stages might not be candidates for LVA due to sclerosed lymphatic vessels. Since LVA relies on a healthy lymphatic vessel architecture, patients with lower Campisi stages might be better candidates for this procedure. A, Cross-section of a healthy lymphatic vessel (valves are not displayed). B, Cross-section of a sclerotic lymphatic vessel, with an increased collagen deposition between the endothelium basement membrane and the adventitia and a reduced vessel lumen. *Collecting lymphatics have a thin layer of smooth muscle cells, whereas initial lymphatics lack one completely. **Collecting lymphatics have a basement membrane, whereas initial lymphatics do not, or have a scarce amount. ***Collecting lymphatics have an adventitia, whereas the endothelium of initial lymphatics is in direct contact with connective tissue. Created with BioRender.com.

possible that suction-assisted protein lipectomy may be more appropriate than LVA or VLNT for more advanced stages of lymphedema.³⁴ Future studies should examine outcomes of LVA for the varying microsurgical techniques stratified by the severity of symptoms in addition to duration of symptoms.

Another microsurgical technique used for UE lymphedema is VLNT. VLNT transplants healthy lymph nodes and vascularized tissue into areas affected by lymphedema to promote lymphatic regeneration and bridging. The most utilized donor site is the inguinal region, although nodes from the submental, supraclavicular, and thoracic can also be successfully transplanted,³⁵ especially in UE lymphedema. Recent literature has also examined the indications of LVA versus VLNT for extremity lymphedema. Cheng et al³⁶ demonstrated improved outcomes for advanced lymphedema treated with VLNT over LVA, suggesting that appropriate microsurgical technique may hinge on the severity of symptoms (Fig. 5). This supports the notion that LVA may be less efficacious in patients with advanced stages of lymphedema as the lymphatic channels may be too sclerosed to salvage.³⁷ Further studies will better identify patients appropriate for LVA, VLNT, and a combination of the two.

Given the possible decreased efficacy of LVA for higher stages of UE lymphedema, recent studies have discussed immediate lymphatic reconstruction (ILR) for primary prevention of lymphedema in breast cancer patients undergoing ALND.³⁸ With ILR, LVA is performed at the time of axillary surgery in an effort to improve lymphatic drainage.³⁹ Often, one or more lymphatic vessels are secured in an end-to-end fashion

to a branch of the axillary vein or other nearby venous branch.³⁹ One recent study of 380 patients found a 16% reduction in the incidence of UE lymphedema following ILR compared to similar patients who did not undergo ILR protocol,⁴⁰ with several smaller studies also showing similar promise.^{41–43} A recent review of 19 studies also found a significant decrease of over 20% in the pooled cumulative incidence of UE lymphedema in patients who underwent ALND with ILR.⁴⁴ In addition to improved outcomes, a recent analysis by Johnson et al⁴⁵ demonstrated that ILR is cost-effective when used after ALND with and without adjuvant radiotherapy. Indeed, ILR is extremely promising and ongoing studies with long-term follow-up will help to identify long-term risk reduction associated with its use.

As LVA increases in popularity, the economics of this microsurgical procedure must be considered. One Canadian study quantified the upfront costs of LVA and found that the total upfront cost of LVA is offset by the possible discontinuation of postoperative decompressive therapy.⁴⁶ In our results, Aljindan et al¹⁵ reported that all patients were able to discontinue decompressive therapy postoperatively, whereas Ayestaray et al²³ found this was only true in 30% of patients. Similarly, one study found that ILR results in a greater than 40% cost saving in patients undergoing mastectomy with ALND,⁴⁷ as the lifetime cost of lymphedema treatment surpasses the upfront cost of ILR.

This review has several strengths. First, it is the most recent systematic review of the literature comprehensively examining subjective and objective outcomes of LVA for UE lymphedema at varying stages of lymphedema. Efforts were made to stratify all demographic, perioperative, and

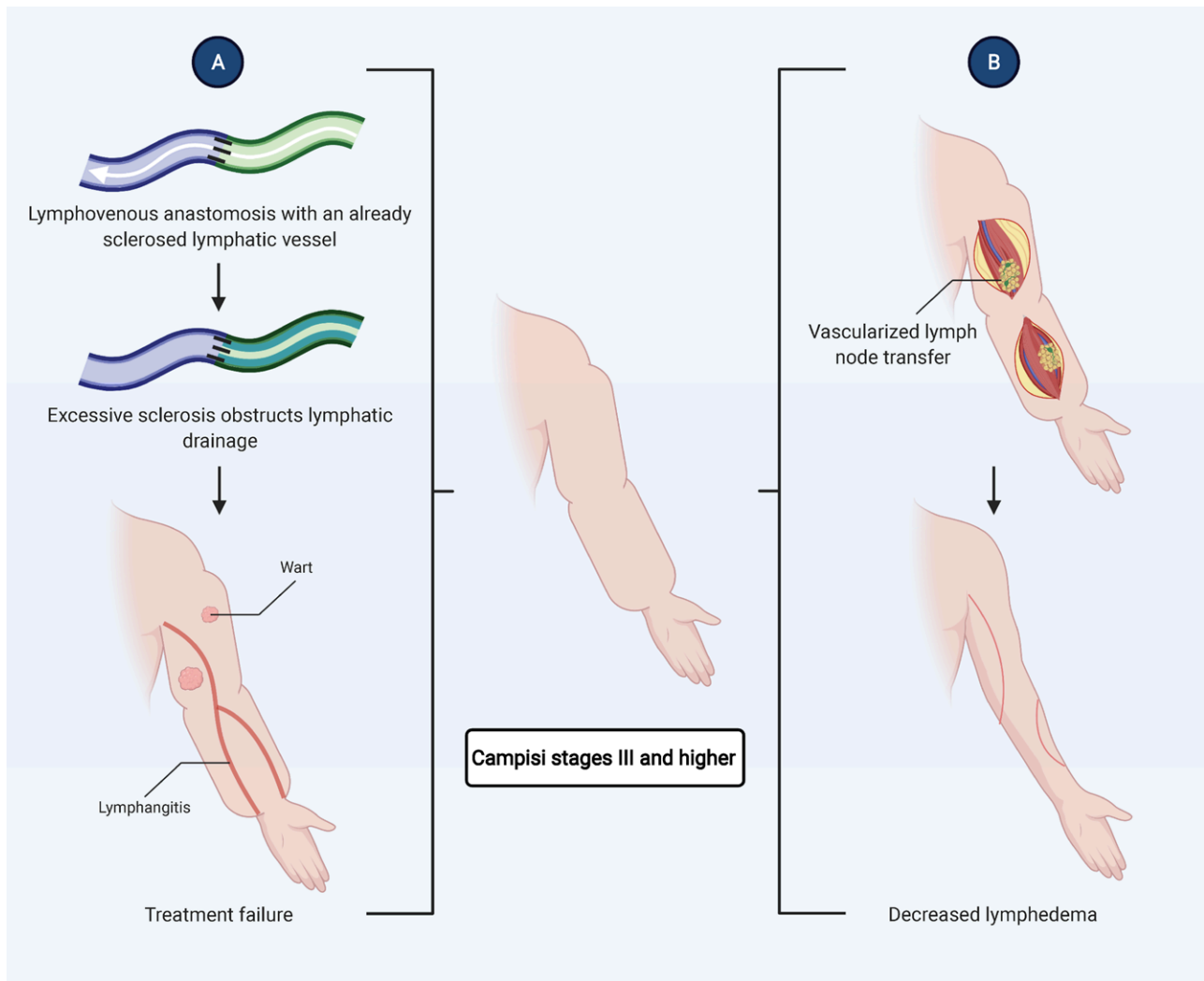


Fig. 5. Cheng et al³⁶ improved outcomes using VLNT over LVA for patients with advanced lymphedema. According to Cheng et al³⁶ results, patients with higher Campisi stages showed a better treatment response to VLNT than to LVA. A, Choosing an LVA to treat patients with high Campisi stages might lead to suboptimal long-term vessel patency. The progressive increase in lymphatic sclerosis decreases the vessel's lumen diameter, increasing the lymphatic system's pressure. The low numbers of healthy lymphatic vessels cannot compensate, leading to treatment failure or worsening of lymphedema. B, VLNT might be a better option for these patients since it does not rely on the existing local lymphatic vessels. Created with BioRender.com.

outcome data specifically by UE, in the case of studies that included patients with lower and UE lymphedema. Furthermore, outcomes were stratified by the stage of lymphedema where possible to explore how LVA fits into an evolving microsurgical toolbox including other procedures such as VLNT. Finally, inferences that have been made are evidence-based. Nevertheless, many questions still remain.

In addition to strengths, several limitations must be noted. First, inherent limitations of the studies examined are important to note, including nonuniform patient staging, outcome analyses, perioperative protocols, and operative techniques. Many studies did not stratify outcomes and results by type of extremity, surgical technique, or stage of lymphedema, making broad generalizations difficult. Duration of follow-up was also limited, preventing the ability to draw reliable conclusions. When considerable

heterogeneity exists, there is risk for interpretation bias of the data as well as the inability to perform robust statistical analyses. Additionally, as LVA remains an emerging technique, there is a relative paucity of literature that directly compares various procedures and techniques. Finally, the possibility for selective reporting bias is important to recognize when data regarding subjective patient symptoms are included. The results of this review are consistent with previous reports of LVA⁴⁸; however, large, controlled studies performed prospectively are key for validation of the results herein as well as for ongoing investigation of LVA effectiveness in UE lymphedema.

CONCLUSION

The results of the current systematic review indicate that LVA is a safe, effective, and versatile technique for the

treatment of UE lymphedema refractory to decompressive treatment. It is likely that operations performed on patients with less advanced lymphedema (ie, before the lymphatic system has become too fibrotic and/or damaged for effective anastomoses) will yield more durable and longer-lasting positive results.

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