

Cumulative Experience in Lymphovenous Anastomosis for Lymphedema Treatment: The Learning Curve Effect on the Overall Outcome

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Abstract

Background The lymphovenous anastomosis (LVA) has become one of the treatment options for lymphedema. However, it is regarded as a difficult surgery that many young microsurgeons are reluctant to try. This report investigates the learning curve in regard to symptom improvement.

Methods This is a retrospective analysis performed in 33 consecutive lymphedema patients (38 extremities) who underwent only LVAs from August 2010 to February 2016. Surgical outcomes in regard to surgeon's experience were evaluated. The surgeons experience was divided into three groups: early group with less than 2 years, moderate with 2 to 4 years, and mature group with more than 4 years of experience.

Results A total of 31 limbs (8/8 in upper extremity and 23/30 in lower extremity) showed improvement. When we compare volume change and recurrence of cellulitis with regard to surgeon's experience, there were no statistically significant differences. However, the mean time per LVA was significantly decreased as the experience increased over time ($p = 0.017$).

Conclusion LVA is an effective treatment option to reduce the volume in the affected limb and to improve symptoms involved. Regardless of the number and experience of the surgeons, cellulitis improves significantly after LVA. The experience of the surgeon does not significantly impact the positive outcome while proficiency increases with experience.

Keywords

- ▶ lymphedema
- ▶ lymphovenous microanastomosis
- ▶ learning curve

Lymphedema is a chronic and debilitating condition that has traditionally been seen as refractory or incurable. The clinical presentation is characterized by pain, limitation of daily activities, and difficulties in wearing normal clothes. Furthermore, lymphedema increases the risks of developing recurrent episodes of cellulitis in the affected extremity which frequently requires admission.¹ In rare cases, chronic lymphedema is

associated with increased incidence of malignancies such as lymphangiosarcoma (Stewart–Treves' syndrome), Kaposi sarcoma, and lymphoma.² The disease may be primary, caused by agenesis or dysplasia of any component of the lymphatic network, or secondary, most commonly after trauma, surgical disruption, or recurrent infection.³ Most patients in developed countries present with lymphedema resulting from treatment

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of malignancy. Lymphedema is reported to occur in up to 49% of breast, 20% of gynecologic, 16% of melanoma, 10% of genitourinary, and 6% head and neck cancer patients after lymph node dissection with or without radiotherapy.⁴ Lymphedema after gynecologic surgery in ovarian cancer is present in 11.1%⁵ and in 12.6% after cervical cancer radical surgery.⁶

In our center, all patients with lymphedema began with combined decongestive therapy (CDT). After a trained lymphedema therapist performs CDT, therapist or patients themselves should follow maintenance treatment. CDT consists in multiple components: manual lymph drainage/massage, compression bandaging, therapeutic exercise, and careful skin care.⁷⁻⁹ These approaches are frequently satisfactory enough but some patients' refractory to the CDT will require some form of surgical intervention to ultimately reduce the lymphatic burden on their extremities.

The surgical approaches are based on an algorithm where physiological approach such as lymphovenous anastomosis (LVA) and vascularized lymph-node transfer (VLNT) are considered first. With the aid of new diagnostic tools, such as magnetic resonance lymphangiography (MRL), indocyanine green lymphography (ICG-L), Doppler venous flowmetry and manometry, and phleboscintigraphy and phlebography (in cases of phlebolymphedema angiodysplasia), it is now possible to consider the patient for LVA, VLNT, or combination of both.¹⁰⁻¹² The LVA redirects excessive lymph fluid from the lymphedematous limb into the venous system by anastomosing lymphatic vessels to subdermal venules thus improves the symptom, while VLNT acts as a sponge to absorb the lymphatic fluid and stimulate neolymphangiogenesis improving the drainage from the extremity.¹³⁻¹⁸ When these physiological approaches are not indicated or have little effect, then symptomatic approaches are considered such as circumferential suction-assisted lipectomy or excisional surgical procedures.¹⁹⁻²²

The LVA, VLNT, or combination of both is now becoming the primary approach for many patients with lymphedema. However, LVA is a relatively new microsurgical approach (super-microsurgery) that needs special skills and tools, may be very challenging, and still has many questions to be answered. This study focused on authors' experience in LVA and to evaluate the LVA effect on symptom improvement especially cellulitis. Another question was to address the outcome of surgery based on surgeon's experience to provide an insight on whether accumulating experience impacts the overall outcome.

Patients and Methods

A retrospective analysis was performed in 33 consecutive lymphedema patients (38 extremities) with primary and secondary lymphedemas who underwent only LVAs from August 2010 to February 2016. This study was approved by the Institutional Review Board at the Asan Medical Center.

Relevant information was collected such as age, body mass index (BMI), lymphedema etiology, lymphedema duration, clinical stage, symptoms and their improvements, surgical data (operative time, number of LVAs, complications, etc.), follow-up time, and pre- and postoperative cellulitis episodes. To see the impact of experience on outcome, we

divided the results based on years of surgeon's LVA super-microsurgery experience: early experience—surgeons with less than 2 years of experience, moderate experience—surgeons with less than 4 years of experience, and mature experience—surgeons with more than 4 years of experience.

Measurements

All patients underwent to preoperative and postoperative measurements of both upper and lower limbs to serve as a baseline and as a control for response to therapy. Circumference measurements were taken with a tape measure at 5, 10, and 15 cm above and below the elbow/knee; before surgery; and after 1, 3, 6, and 12 months postoperative. Each volume segment was measured according to the formula of a truncated cone (**Fig. 1**).²³

$$V = \pi \times h \times (R^2 + r^2 + R \times r)/3$$

where π is a constant; h is the height; R is the radius on base; and r is the radius on top.

Using this formula, we were able to estimate the volume of part of the limb. These estimations were analyzed to evaluate lymphedema improvement after surgical treatment. In patients with unilateral lymphedema, measurements of the nonaffected limb allowed to compare with the lymphedematous limb and determination of the percentage of excess volume (PEV) of the affected limb (PEV = volume of affected limb – volume of unaffected contralateral limb/volume of unaffected contralateral limb). The reduction excess volume (REV) between preoperative and postoperative was calculated in unilateral cases (REV = [preoperative PEV – postoperative PEV]/preoperative PEV). In bilateral cases, difference of preoperative and postoperative volume and volume percentage change was calculated (VPC = [postoperative volume – preoperative volume]/preoperative volume).

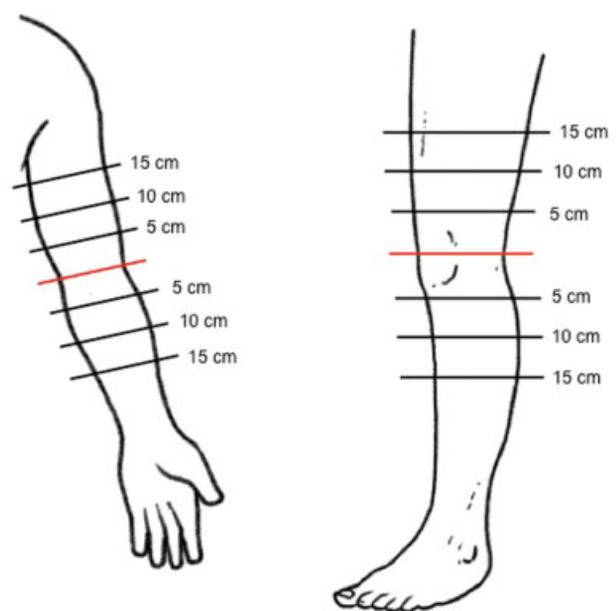


Fig. 1 Circumference measurements sites in upper extremities and lower extremities.

Surgical Technique

Approaches were based on preoperative MRL and ICG-L. Then, a 3-cm incision was made to obtain subdermal/subcutaneous venules as the proximal recipient of lymphatic vessels. The LVA technique was not indicated in cases where lymphostatic disease was associated with venous flow impairment (varices, venous hypertension, and valvular incontinence). LVA was performed with 10-0 or 11-0 suture. Usually, a three-level approach was used in the lower extremity, which involves the ankle, knee, and groin region. The upper extremity involves two levels at wrist and elbow in addition with scar release on the axilla region. After the procedure, the skin is closed and minimal pressure dressing was applied.

Postoperative Care

After the operation, splints were applied for immobilization of operated sites. Patients stayed hospitalized for 3 to 5 days after operation. Absolute circumference of operated limbs was measured daily on postoperative days 1 to 5. Postoperative rehabilitation protocol was followed where the patients started their CDT 2 weeks after surgery.

Statistical Analysis

Wilcoxon's signed-rank test was performed to compare preoperative and postoperative volume and percentage of excess of volume. Kruskal-Wallis' test was performed to compare these results in the three periods of time. SAS software version 9.4 (SAS Institute, Cary, NC) was used for statistical analysis.

Results

A total of four surgeons were evaluated. LVA was performed in 8 upper extremities (6 left and 2 right) and 30 lower extremities (8 left, 12 right, and 5 bilateral). The upper extremity lymphedema was secondary to breast cancer

treatment in 100% of the cases. Lower extremity lymphedema was primary in 13 extremities (43.3%), secondary to gynecologic cancer treatment in 14 extremities (46.6%), and trauma in 3 extremities (9.9%). All patients were selected with the same criteria among the surgeons.

Upper Extremity

The mean age of the patients was 48.9 years (range: 35–59). The mean lymphedema duration was 4.61 years (range: 2–9.25). The mean BMI was 23.34 kg/m² (range: 19.91–29.95). The mean preoperative volume of the affected upper limb was 1,204.6 mL (range: 900.8–1,535.2) and the mean preoperative PEV between the affected and the healthy limb was 26.73% (range: 8.28–47.4%). Patient's mean follow-up time was 27.4 months (range: 3–84).

Symptoms improved in 100% of the patients (eight cases). Postoperative mean volume measurement was 1,054.5 mL (range: 771–1,217) and postoperative mean PEV was 11.55% (range: –11.75 to 39.02) demonstrating a statistically significant quantitative improvement in both parameters ($p = 0.012$). The reduction of excess volume after LVA was 64.97 (→ Fig. 2).

Mean operative time was 257.5 minutes (range: 163–354). Mean number of LVA per upper extremity was 3.75 (range: 1–6), so mean time per LVA was 96.1 (range: 27.1–261) minutes. Preoperative mean number of cellulitis episodes per year was 1.3 (range: 0–3). It decreased dramatically to 0 episode after LVA (→ Table 1).

When we compared volume change with regard to surgeon's experience, there were no statistically significant differences. However, the mean time per LVA significantly decreased as the experience increased for surgeons.

Lower Extremity

The mean age of the patients was 44.1 years (range: 6–72). The mean lymphedema duration was 11.025 years (range: 1–45). The mean BMI was 25.18 kg/m² (range: 16.41–37.99). In



Fig. 2 (A, B) Preoperative and 7 years follow-up postoperative pictures of a 59-year-old female patient with left unilateral upper extremity lymphedema secondary to breast cancer treatment. Preoperatively she had 1,535.25 mL and postoperatively 1,109.05 mL on her left arm, with an absolute volume decrease of 426.2 mL.

Table 1 Results of upper extremity lymphedema patients

Characteristics	No.	Range or %
Mean age at surgery (y)	48.9	(35–59)
Mean BMI (kg/m ²)	23.34	(19.91–29.95)
Mean lymphedema duration (y)	4.61	(2–9.25)
Lymphedema stage	I	2 25%
	II	5 62.5%
	III	1 12.5%
Side	Left	6 75%
	Right	2 25%
Mean operative time (min)	257.5	(163–354)
Mean number of LVA	3.75	(1–6)
Mean follow up (mo)	27.4	(3–84)
Symptoms improvement	8	100%
Volume	Mean	
Mean preoperative volume (mL)	1,204.66	(900.84–1,535.25)
Mean postoperative volume (mL)	1,054.52	(771–1,217.04)
Percentage of volume excess	Mean	
Mean preoperative volume excess (%)	26.73	(8.28–47.4)
Mean postoperative volume excess (%)	11.55	(–11.75–39.02)
Reduction of excess volume (%)	64.97	(5.02–153.02)
Cellulitis	Mean	
Number of episodes per year preoperative	1.3	(0–3)
Number of episodes per year postoperative	0	0

Abbreviations: BMI, body mass index; LVA, lymphovenous anastomosis.

unilateral cases, the mean preoperative volume of the affected lower limb was 2,795.2 mL (range: 1,485.1–4,935.2 mL) and the mean preoperative PEV between the affected and the healthy limb was 33.58% (range: –22.63–92.98%). In bilateral cases, the mean preoperative volume of the affected lower limb was 2,876.3 mL (range: 2,226.2–4,263.1 mL). Patient's mean follow-up time was 16.6 months (range: 3–48).

Symptoms improved in 77% of the cases (23 extremities). In unilateral cases, postoperative mean volume measurement was 2,605.2 mL (range: 1,212–4,145.9 mL) and postoperative mean PEV was 25.23% (range: –12.1–104.08%) demonstrating a statistically significant quantitative improvement in the first parameter ($p = 0.03$ and $p = 0.061$, respectively). In bilateral cases, postoperative mean volume measurement was 2,600.4 mL (range: 2,059.8–3,125.8 mL) demonstrating a statistically significant quantitative improvement ($p = 0.013$). The reduction of excess volume after LVA was 39.81% (►Fig. 3).

Mean operative time was 213.7 minutes (range: 81–543). Mean number of LVA per lower extremity was 2.3 (range: 1–7); therefore, mean time per LVA was 116.8 (range: 38.7–274) minutes. Preoperative mean number of cellulitis episodes per year was 2.6 (range: 0–10). It decreased dramatically to a mean number of episodes of 0.12 after LVA (range: 0–1) (►Table 2).

When we compare volume change with regard to surgeon's experience, there were no statistically significant differences. However, the mean time per LVA significantly decreased as the surgeon's experience increased over time ($p = 0.017$) (►Fig. 4).

Discussion

Lymphedema is a progressive and debilitating condition associated with dysfunction of the lymphatic system.²⁴ The performance of LVA in patients affected by upper or lower limb lymphedema achieved a significant reduction in the volume of the treated limb with reported improvement of symptoms such as less effort in lifting extremity, less discomfort, increased range of motion, and decreased episodes of cellulitis. Episodes of cellulitis are especially severe as it frequently needs admission despite the use of prophylactic antibiotics which has been the mainstream treatment.^{25–27} Definitive prevention of cellulitis from lymphedema remains to be seen. Among the expected outcomes of LVA, decrease in frequency of cellulitis episodes and its severity is very important since it can be even a life-threatening condition. In a cohort of 95 patients, Mihara et al evaluated cellulitis episodes and found a statistically significant decrease in frequency in patients with upper or lower limb lymphedema comparing before and after LVAs.²⁸ Our patients experienced a dramatic decrease in number of episodes of cellulitis after LVA from 1.3 (range: 0–3) episodes per year to 0 episode in the upper extremity and 2.6 (range: 0–10) episodes per year to 0.12 episodes in lower extremity reducing the need for prophylactic antibiotics and improving the quality of life and possibly preventing a vicious cycle of aggravation caused by recurrent cellulitis. This was an interesting finding as most of the LVA despite the number of anastomosis or experience of the surgeon did not play a role in overall outcome of cellulitis. Furthermore, improvement in cellulitis recurrence was noted even in some patients who did not have a significant improvement in volume reduction. Thus, a minimal number of LVA may limit the formation of cellulitis from lymphedema or even may be able to prevent it from recurring.

Outcome evaluation methods following LVA may vary depending on the institution. Objective analysis using limb volume differences between normal and affected limbs in unilateral cases appear to be the most adequate. We performed preoperative and postoperative measurements of both limbs to serve as a baseline and as a control for response to therapy. We calculated the volume using the truncated cone formula and the PEV as previously reported.²³ When lymphedema is bilateral, there is a limitation because we can just compare the improvements within the same limb without having a reference unaffected limb; therefore, body weight changes can interfere in the proper follow-up assessment.



Fig. 3 (A, B) Preoperative and 4 years follow-up postoperative pictures of a 72-year-old female patient with right unilateral lower extremity primary lymphedema. Preoperatively she had 4,074.25 mL and postoperatively 2,789.6 mL on her left lower limb, with an absolute volume decrease of 1,284.65 mL. Number of episodes of cellulitis decreased dramatically from 3 to 4 per year to 0 episode after LVA. LVA, lymphovenous anastomosis.

Koshima et al reported their experience with 18 patients (aged: 38–73 years) with upper extremity lymphedema who underwent supermicrosurgical LVA.²⁹ The average duration of upper extremity lymphedema was 7.2 years (range: 11 months–22 years). The patients were followed up for an average of 2.6 years (range: 1–10 years), and a decrease in the circumference in average 4.5 cm (0–8.5 cm) was obtained. The average decrease rate in the circumference was 45.2% of the preoperative excess length. Chang et al found in a prospective study in 100 consecutive patients that LVA can be effective in reducing lymphedema severity.³⁰ In patients with early-stage lymphedema, a mean volume differential reduction of 61% at 12 months after LVA was noted. In patients with late-stage lymphedema with few functioning lymphatic vessels and significant tissue fibrosis, the results were not as impressive with only a 17% mean volume differential reduction at 12 months after LVA. We also considered it necessary to perform a different analysis for upper and lower extremity lymphedema. The behavior can be different over time as lower limb lymphedema treatment may be more complicated due to the dependent position of the leg, the larger volume of the lower limb, and the effects of ambulation. In our series, lower extremity lymphedema stages were more severe compared with the upper extremity lymphedema stages. Our upper limb improvements were better than lower limb, but in both cases, the decrease of postoperative volume was statistically significant. Although the results showed significant reduction, large portion of the patients did not reach the normal appearance compared with the unaffected arm. This was due to the fact that the patients reviewed in this study, with the exception of two upper limbs and one lower limb, were all advanced stages of lymphedema. The approach has now moved to detect nonresponders to CDT who are still in the early stages of lymphedema to increase their chance for full recovery.^{31,32}

It has been reported that the higher number of LVA sites performed during surgery correlates to better volume reduction.³² We agree with this approach but the time and effort consumed to find the lymphatic vessels cannot be overlooked. Report suggesting that only one functional LVA could be enough to obtain satisfactory outcomes has nudged us to move to a simpler approach.³³ The authors have simplified the approach to identify relatively constant lymphatic vessels that are easier to find. These lymphatic vessels are usually easily identifiable at wrist and elbow for the arm and foot/ankle, knee, and groin for the lower extremity. Frequently, the scar formed after dissection of lymph nodes on the axilla region requires scar removal to improve the continuity of the lymphatic flow located in the fat. The strategy to have a three-level approach has allowed us to have reasonable results even for beginners as shown in this study.

The fear to start a lymphedema practice using LVA can be challenging and daunting for beginners. An interesting finding in this study was the consistent positive result regardless of the years of experience implying that although supermicrosurgical skills are needed, beginners can perform LVA achieving good results. The approach to anatomically constant and relatively large lymphatic vessels allows increased chance for successful outcome. As the surgeon gains experience, operating time per LVA decreased significantly. This finding was evident in our review as one surgeon's experience passed through all the phase of early, moderate, and mature experience. However, if one questions the quality of the outcome, it was very difficult to determine it as each patient progress differs due to various factors and may remain as a limitation of this study. We also realize that individual's given innate hand skills may play a role. Nevertheless, most patients showed reduction of volume despite

Table 2 Results of lower extremity lymphedema patients

Characteristics	No.	Range or %
Mean age at surgery (y)	44.1	(6–72)
Mean BMI (kg/m ²)	25.18	(16.41–37.99)
Mean lymphedema duration (y)	11.025	(1–45)
Lymphedema stage	I	1 3.3%
	II	19 63.3%
	III	10 33.3%
Side	Left	8 26.6%
	Right	12 40%
	Bilateral	5 33.3%
Mean operative time (min)	213.7	(81–543)
Mean number of LVA	2.3	(1–7)
Mean follow up (mo)	16.6	(3–48)
Symptoms improvement	23	92%
Volume	Mean	
Unilateral		
Mean preoperative volume (mL)	2,795.23	(1,485.15–4,935.25)
Mean postoperative volume (mL)	2,605.28	(1,212.07–4,145.97)
Bilateral		
Mean preoperative volume (mL)	2,876.31	(2,226.25–4,263.11)
Mean postoperative volume (mL)	2,600.41	(2,059.87–3,125.82)
Percentage of volume excess	Mean	
Mean preoperative volume excess (%)	33.57	(22.63–92.98)
Mean postoperative volume excess (%)	25.23	(–12.10 to 104.08)
Reduction of excess volume (%)	39.81	(–85.93 to 208.79)
Cellulitis	Mean	
Number of episodes per year preoperative	2.6	(0–10)
Number of episodes per year postoperative	0.12	(0–1)

Abbreviations: BMI, body mass index; LVA, lymphovenous anastomosis.

the experience of the surgeon. The authors encourage microsurgeons who do not perform lymphatic surgery to dare to perform LVA because it is a reliable technique with good results, which allows the treatment of many patients affected by this disease.

Conclusion

Lymphovenous anastomosis is an effective treatment option to reduce the volume in the affected limb and to improve symptoms involved. Regardless of the number and experi-

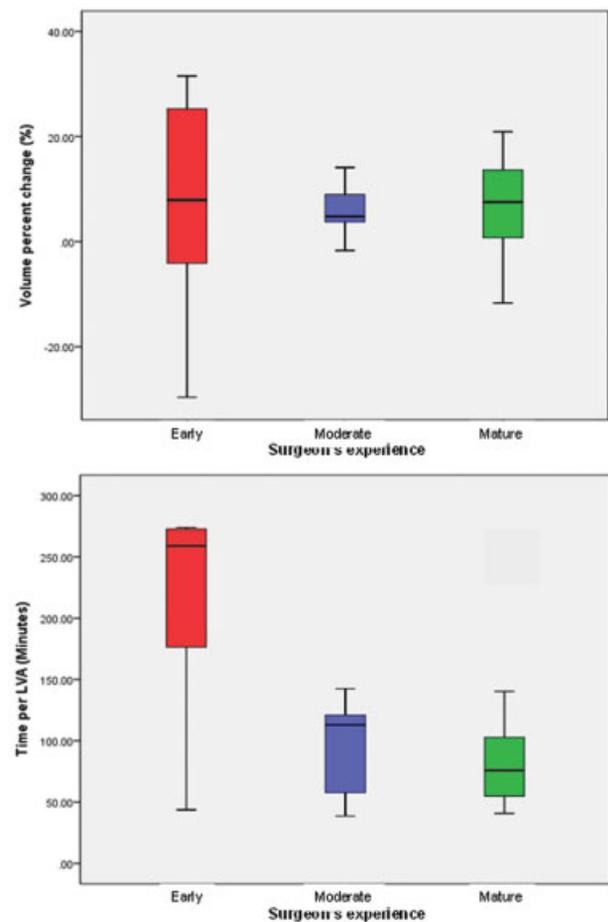


Fig. 4 Lower extremity lymphedema with regard to surgeon's experience: early experience (< 2 years), moderate experience (< 4 years), and mature experience (> 4 years). (Above) Volume percentage change with regard to surgeon's experience, with no statistically significant difference showing consistent results. (Below), Mean time per LVA decreases as surgeon's experience increases, with statistically significant difference ($p = 0.017$). LVA, lymphovenous anastomosis.

ence of the surgeons, cellulitis improves significantly after LVA. The experience of the surgeon does not significantly impact the positive outcome, while proficiency increases with experience.

Conflict of Interest

None.

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