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ORIGINAL ARTICLE
Reconstructive

Accuracy of Mirror Image Mapping of Lymphatic Tract for High-stage and Reoperative Lymphaticovenular Anastomosis: Intraoperative Analysis and Early Clinical Outcome

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Background: Indocyanine green lymphography (ICGL) generally has a nonlinear pattern in advanced-stage lymphedema. Despite the lack of a linear pattern ICGL, lymphatic vessels have been discovered in several studies. The purpose of this work was to establish lymphatic mapping utilizing information from the contralateral limb and to illustrate the symmetry of lymphatic systems.
Methods: Data were retrospectively collected from 81 patients who underwent lymphaticovenular anastomosis (LVA) using the contralateral mapping technique during 2018 to 2022. The sensitivity, specificity, accuracy, and negative and positive predictive values of this technique were calculated and analyzed.
Results: Lymphatic vessels were identified in 85.2% of the upper and 82.3% of the lower limb presumed sites using the contralateral mapping technique. The positive predictive value for successful LVA anastomosis was 93.8% for upper limb and 92.3% for lower limb cases. This mirror image technique's accuracy was 91.7% and 91.1%, for the upper limb and lower limb group, respectively. Between reoperative and new LVA cases, there was no statistically significant difference in the number, type, or diameter of lymphatic vessels or number of anastomoses.
Conclusions: LVA with contralateral mapping technique is an effective method for patients with high-stage lymphedema with a nonlinear pattern on ICGL. *(Plast Reconstr Surg Glob Open 2024; 12:e5785; doi: 10.1097/GOX.0000000000005785; Published online 13 May 2024.)*

INTRODUCTION

Lymphaticovenular anastomosis (LVA) reestablishes the drainage of obstructed lymphatic fluid directly into the venous system, thereby alleviating early-stage lymphedema.[1–7] Numerous publications in recent years have confirmed the technique's success, even in severe lymphedema cases.[8,9] As with the early stage, identifying lymphatic vessels with indocyanine green lymphography (ICGL) has been used to detect lymphatic pathways[10] and assess the severity of lymphedema.[11,12] Unfortunately, ICGL in patients with advanced-stage lymphedema frequently exhibits abnormal dermal backflow (DB). (**See figure, Supplemental Digital Content 1**, which displays illustration of ICG; linear pattern and DB in early and late-stage lymphedema, **http://links.lww.com/PRSGO/D183**.) On the other hand, some studies have reported that lymphatic vessels were discovered intraoperatively, albeit with a negative ICGL.[13–15] In this situation, many surgeons argue that lymphatic vessels can still be discovered using an anatomical approach. Some adhere to the anatomy of large veins,[16] whereas others follow the more familiar anatomical location. However, even after using these strategies, surgeons are unable to locate the lymphatic vessels in some LVA cases.

Our observations reveal a prevalent symmetrical pattern in the lymphatic system across the majority of

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cases studied. These findings are supported by qualitative research. For instance, Tzou et al[17] reported on the symmetrical nature of the right and left submental lymph nodes, whereas Blumgart et al[18] demonstrated the symmetry of the lymphatic drainage pathway of the breast. Nevertheless, there exists no direct quantitative evidence indicating that lymphatic vessels are invariably symmetrical.

Our primary aim was to demonstrate the mirror image mapping technique for the contralateral lymphatic tract in patients with advanced-stage lymphedema. This technique was particularly useful for patients who did not display a linear pattern on ICGL on the affected limb and for those who had previously undergone LVA but experienced failure due to obstructed DB. Additionally, we sought to confirm the prevalence of symmetrical lymphatic systems in our patients as it relates to the efficacy and feasibility of the mapping technique.

Takeaways

Question: How effective is the mirror image mapping technique for identifying lymphatic tracts in patients with advanced-stage lymphedema?

Findings: Among 251 lymphaticovenular anastomosis (LVA) procedures, 81 patients with nonlinear indocyanine green lymphography patterns were studied. The mirror image mapping technique yielded success rates of more than 80% for identifying lymphatic vessels. Additionally, it showed a positive predictive value of 90.9% for upper limbs and 92% for lower limbs, with an accuracy of 91.67% for upper limbs and 93.55% for lower limbs.

Meaning: The mirror image mapping technique proves highly effective in identifying lymphatic tracts during LVA surgery in patients with advanced-stage lymphedema. This approach offers a promising alternative when indocyanine green lymphography fails, potentially improving treatment outcomes.

MATERIALS AND METHODS

Patient Selection

In this study, we conducted a retrospective evaluation of our prospective patient database, which covered an entire period from May 2018 to December 2021. LVA was performed using the mirror technique on the patients included in the analysis. Inclusion criteria included individuals with at least one of the following conditions: a history of infection episodes, a lack of improvement in limb circumference after 3 months of conservative treatment, or a history of LVA surgery with persistent visibility of main lymphatic channels on lymphoscintigraphy but no linear patterns observed on ICGL. This investigation received ethical approval from the Siriraj Hospital Ethical Committee (certificate of approval no. Si 413/2021; SIRB protocol no. 385/2564).

ICGL and Mapping Technique

Patients first underwent ICGL on the affected limb at our lymphedema clinic. A near-infrared camera system (FLUOBEAM; Fluoptics Co, Grenoble, France) was used for this study. Indocyanine green (ICG; Diagnogreen; Daiichi Sankyo CO, Tokyo, Japan) was mixed with 5 mL of saline. Before the ICG, local anesthesia was injected. Then, each extremity received 0.8 mL of ICG subcutaneously divided into four sites based on a study by Suami et al.[19] Fluorescence images were taken at 15 minutes, 1 hour, and 4 hours after the injection and evaluated by a board-certified plastic surgeon (N.Y.). Patients with nonlinear ICGL were advised to undergo LVA surgery and lymphatic tract mapping utilizing contralateral limb data.

First, patients underwent ICGL on both limbs and the contralateral healthy limb (or less severe limb) was used to map the affected side for LVA surgery. The injection protocol was identical to that routinely used in our clinic, but the ICGL was evaluated using a precise coordinating reference method modified from Mihara et al[20] and Gentileschi et al.[21]

Two landmarks were chosen for the upper limb: the mid-point of the cubital fossa and the mid-point between the radial and ulnar styloid processes. For the lower limb, the mid-point of the patella's upper border and the mid-point between the medial and lateral malleoli were used. A straight line connecting the points was drawn and marked every 5 cm to serve as a reference line. Following that line, the lymphatic vessels on the normal limb were identified. Next, at each 5 cm level, the distance between the reference line and the marked lymphatic vessels on the healthy limb was measured (Fig. 1).

The augmented reality (AR) technique was then used to superimpose the lymphatic tract image from the healthy limb onto the affected limb. This enabled the creation of a reference line on the affected limb, serving as a fixed landmark for accurate mapping. It is noteworthy that our approach encompassed not only the use of the AR application Camera Lucida AR (Seattle, Wash.), but also the implementation of Hololens. (**See figure, Supplemental Digital Content 2**, which displays illustration depicting the application of AR technology, utilizing a smartphone application and Hololens, to overlay the lymphatic tract image from the healthy limb onto the affected limb, **http://links.lww.com/PRSGO/D184**.) This advanced technology facilitated the projection of the lymphatic diagram onto the patient's extremities, enhancing precision and effectiveness. (Fig. 2).

Surgical Techniques

The LVA procedures (mirror LVA) were performed under local anesthesia. First, the reference line and the proposed incision were marked on the limb surface. Then, we injected 0.2 mL of ICG subcutaneously into each of the four locations specified in each limb. ICG was visualized using a near-infrared camera. The vein visualizer mobile application (Vein Seek Pro, Los Angeles, Calif.) was used to locate subcutaneous veins around the planned incision.

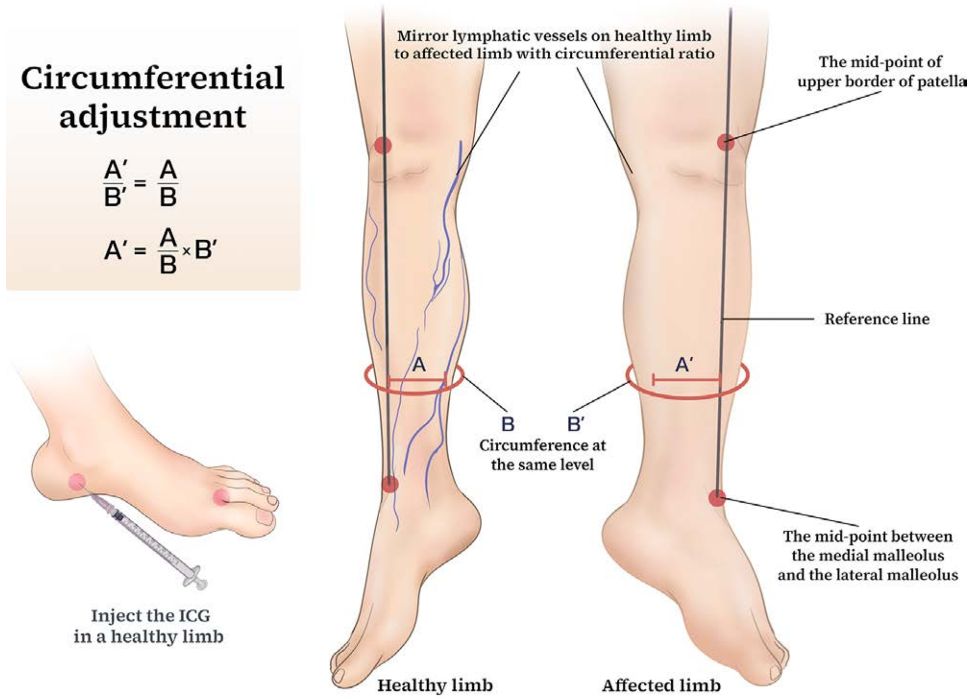

Fig. 1. Traditional manual technique for mirroring. The distance from the reference line (A) was adjusted using the circumference ratio, defined as the circumference of the affected limb divided by the circumference of the healthy limb at the same level (B′/B). The adjusted distant (A′) was used as a reference for marking the affected limb's lymphatic tract.

Fig. 2. The utilization of mirror mapping techniques. A, The manual mapping of the lymphatic tract on the unaffected arm is displayed, serving as a reference for the mapping procedure. B, The superimposition of the mapped lymphatic tract from the unaffected arm onto the affected arm is demonstrated. C, A medical professional employing Hololens, an AR device, to visualize, strategize, and draw the lymphatic tract directly onto the patient's leg is depicted, ensuring precise and accurate mapping.

The dorsum of the hand or foot, the distal forearm or leg, the proximal forearm or leg, and the superomedial region of the elbow or knee were the four levels of incision we decided to execute. Consequently, each incision was made on a distinct branch of the lymphatic system as much as possible. We made incisions where the lymphatic and venous systems meet or are near to one another.

To aid in identifying lymphatic vessels, patients were given a subcutaneous injection of 0.2 mL of 1% isosulfan blue immediately proximal to the incision. Following that, LVA was conducted using an operational microscope through a 2.0- to 3.5-cm skin incision (OPMI Pentaro 900 and OPMI Vario S88 system; Carl Zeiss Co, Jena, Germany). In cases where the lymphatic vessel could not be identified through 3.5-cm incision, the incision was extended up to

4cm (the additional length of 5mm was equally divided into 2.5mm laterally) to ensure a comprehensive exploration of the surrounding tissue. After the lymphatic vessels were visually identified, 11-0 nylon was used to connect the indicated lymphatic vessels and venules. End-to-end, end-to-side, side-to-side, and octopus techniques[22] were used for this procedure (Fig. 3). We recorded whether lymphatic vessels are present or missing in each prediction incision to assess the sensitivity and accuracy. For the intraoperative result analysis, the number of incisions, lymphatic vessels, type of lymphatic vessels,[23] outer diameter, number of anastomoses, and operative time were recorded.

Statistical Analysis

Continuous variables' descriptive statistics are presented as the mean (SD, range), whereas categorical variables' descriptive statistics are presented as frequency. The Student *t* test was used to analyze differences between two unrelated quantitative measurements. The Mann–Whitney Index U test was used to compare two nonnormally distributed quantitative groups. A *P* value of less than 0.05 was considered statistically significant. All analyses were conducted using SPSS PASW Statistics version 25.0 software (IBM Inc, Armonk, N.Y.).

RESULTS

Demographic Data

From 251 patients who underwent LVA surgery, 81 patients with a nonlinear pattern of ICGL were included. There were 45 patients (55.6%) with lower limb edema and 36 patients (44.4%) with upper limb edema. The majority of patients (81.5%) were female. The patients' average age was 57.93 ± 13.76 years. Most patients developed lymphedema following cancer treatment (61.7%). There were 73 cases classified as International Society of Lymphology stage II (late) (90.1%), and eight classified as International Society of Lymphology stage III (9.9%). Twenty-nine patients (35.7%) had a history of failed LVA operations (reoperative cases). In this group, the primary reason for failure was an inability to locate lymphatic vessels as a result of the ICGL's nonlinear pattern (82.6%) and also the poor quality of lymphatic vessels (17.4%). Among the reoperative cases, five patients were classified as stage III, whereas the remaining 24 reoperative cases were categorized as stage II. In the new LVA cases, three patients were identified as stage III, and the remaining 48 new cases were classified as stage II. The upper limb group received more radiation therapy and chemotherapy than the lower limb group.

Lymphatic Vessel Identification

In the upper limb group, lymphatic vessels were identified in 70 of 88 incisions (80.7%) as presumed sites from an incision standpoint. In the lower limb group, putative sites were found in 79 of 96 incisions (82.3%). The number of lymphatic vessels per case in the upper limb group was greater than that of the lower limb group (4.17 ± 3.38 versus 2.16 ± 1.51, *P* = 0.001). These values were linked with the number of lymphatic vessels per incision in the upper and lower limb groups (1.74 ± 1.12 and 1.12 ± 0.63, respectively, *P* = 0.019).

The lymphatic vessels were observed to have relatively large diameters. The external diameter of the lower limb group was 0.89 ± 0.43mm compared with 0.60 ± 0.22mm in the upper limb group (*P* = 0.010). This is consistent with ectasia, the most common type[23] of lymphatic pattern identified.

Success of LVA Surgery and Anastomoses

There were 70 lymphatic-identified cases (86.47%). Sixty-four patients had successful LVA operations with

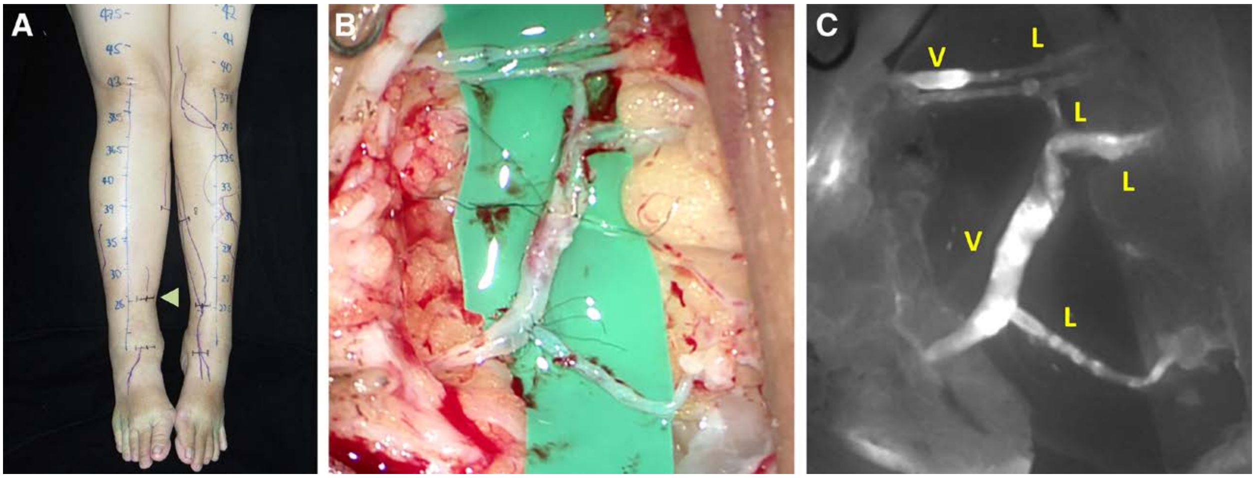

Fig. 3. A real case sample involving a 42-year-old woman with right leg lymphedema undergoing mirror LVA procedure. A, Markings for three incisions achieved through the mirror mapping technique, originating from the unaffected leg and applied to the affected site. An arrow indicates the precise incision location. B, The intraoperative scenario, showcasing the anastomosis process conducted from the marked incision site. Lymphatic vessels are visually identified, and 11-0 nylon thread is used to connect the indicated lymphatic vessels and venules. C, An immediate postoperative view of ICGL captured through a near-infrared camera. The image reveals the lymphatic flow that ensues promptly after the completion of the LVA procedure. V and L stand for venule and lymphatic vessel.

nearby veins (91.42%), and the remaining six patients had sclerosing lymphatic vessels, rendering surgery impossible. Despite expanding the incision by a maximum of 4 cm, the lymphatic vessel remained elusive in cases where it could not be identified. As the distribution of incisions performed at various extremity levels during LVA surgery, accompanied by the respective count of attained anastomoses, level 2 signified the highest number of anastomoses achieved in both upper and lower extremities (Fig. 4). Compared with the lower extremity group, the upper extremity group showed slightly more anastomoses (2.78 ± 1.55 versus 2.13 ± 1.34, $P = 0.040$).

We estimated the success rate of LVA surgery. One anastomosis of LVA was guaranteed in each lymphatic tract predicted in the upper extremity group and 98% in the lower extremity group. The positive predictive value (PPV) for one successful LVA anastomosis was 90.9% for each lymphatic vessel of the upper extremity detected by the mirror technique, with a 100% sensitivity and 50% specificity. The PPV for one successful LVA anastomosis in the lower extremity group was 92%, with a sensitivity of 100% and a specificity of 71.4%. The mirror image technique accuracy was 91.67% and 93.55% for the upper and lower extremity groups, respectively. Our study assessed the diagnostic accuracy of the mirroring technique for identifying lymphatic vessels during LVA surgery in the upper and lower extremities. The mirroring technique, using symmetry from the unaffected limb, aimed to map lymphatic pathways more accurately. Results showed a high PPV of 93.75% for the upper extremity and 92.3% for the lower extremity. This highlights the effectiveness of the mirroring technique in improving lymphatic vessel identification during LVA surgery and potentially enhancing treatment outcomes for lymphedema patients.

Reoperative LVA versus New Cases

Twenty-nine patients (35.58%) were reoperative cases whose lymphatic vessels were not detected by ICGL during a previous LVA procedure. There was no statistically significant difference in the number of detected lymphatic vessels, the type of lymphatic vessels, external diameter, or the number of anastomoses between the reoperative and new LVA cases. The mirror approach was able to raise the number of anastomoses in reoperative cases by 2.36 ± 1.50 in the upper extremity group and 1.83 ± 1.11 in the lower extremity group, but this difference did not reach statistical significance.

DISCUSSION

Recent onset of lymphedema is the primary indication for LVA,[24] but the procedure is also used in high-stage lymphedema.[25] The identification of lymphatic vessels is an important step in LVA. Unfortunately, ICGL is unable to detect lymphatic vessels that are deeper than 1–2 cm beneath the skin.[26] Mirror LVA, especially in high-stage lymphedema, can help the ICGL overcome its depth constraint. ICGL is easily visible due to the thinner subcutaneous tissue in the unaffected limb. Furthermore, the linear pattern in the healthy limb is unlikely to be obscured by DB.

The mirror mapping technique is an effective way to locate good-quality lymphatic vessels sufficient for LVA surgery as evidenced by its very high PPV. This is also an advantage in reoperative cases. ICGL is typically used to determine the stage of lymphedema and to guide surgery. However, in high-stage patients, ICGL does not show a linear pattern, making mapping impossible. Furthermore, the alternative anatomical approach reduces the total number of anastomoses because patients cannot tolerate long surgery times with local anesthesia. Because of the

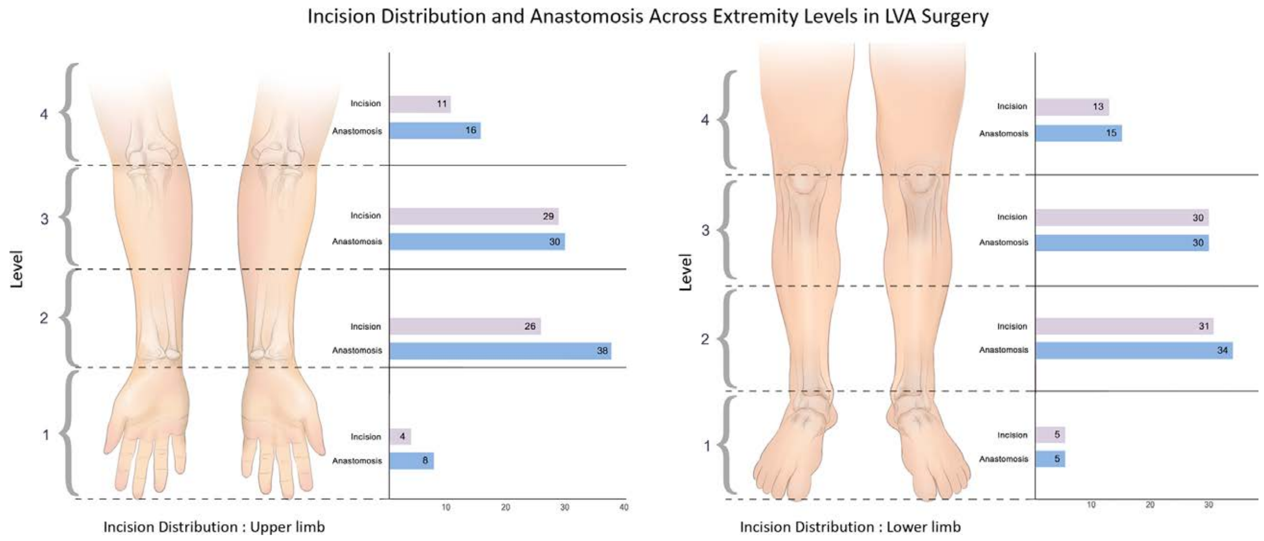

Fig. 4. Illustrates the distribution of incisions made at different extremity levels during LVA surgery, along with the corresponding number of gained anastomoses. Notably, level 2 exhibits the highest number of anastomoses achieved in both upper and lower extremities.

variation between each patient, the surgery usually ends up with a longer surgical incision, but no anastomosis can be performed.[27] Lymphatic tracking with an anatomical approach is less accurate than lymphatic mapping utilizing individualized data and the mirror technique. We hypothesized that the human body is predominantly symmetrical, and we used this to identify lymphatic vessels that were concealed.

Recent lymphedema treatment trends have highlighted the significance of early intervention and the potential efficacy of LVA in enhancing patient outcomes. However, a subset of patients still presents with advanced-stage lymphedema, which is frequently accompanied by significant functional impairment and limited treatment options. This has necessitated the investigation of alternative methods to address the unique anatomical and pathophysiological complexities of lymphedema in its advanced stages.

The choice between LVA and lymphaticovenular bypass (LVB) in the context of reoperative procedures and advanced-stage lymphedema is a nuanced decision. We carefully considered individual patient factors, opting for reoperative LVA when the extent of lymphatic damage allowed for its feasibility. Despite terminological variations, our center predominantly employs the term LVA,[28] aligning with the widely accepted practice of direct anastomosis. Garza et al[29] review indicates successful outcomes in reoperative or late-stage lymphedema cases using both LVA and LVB approaches, emphasizing the need for a diverse armamentarium to address the complexity of lymphatic pathologies. Our study contributes to this discourse by providing insights into the specific considerations and outcomes associated with LVA in our center, underscoring the broader spectrum of success reported in the literature for both techniques in advanced-stage lymphedema.

Consistent with the growing recognition of the potential benefits of LVA in late-stage lymphedema, Hara and Mihara[30] investigated the outcomes of LVA surgery in a cohort of patients with late-stage lymphedema. The researchers demonstrated significant improvements in limb volume reduction and subjective symptom scores following LVA, indicating that even in advanced cases, surgical intervention has the potential to provide meaningful benefits. The study emphasized the significance of accurately identifying viable lymphatic vessels for successful LVA and the need for innovative techniques, such as the mirror image mapping approach, to overcome the difficulties associated with late-stage lymphedema.

When comparing reoperative cases to new cases, the findings of our study made an intriguing discovery about the mirror mapping technique's accuracy in identifying the lymphatic tract. We observed that the precision in identifying lymphatic vessels in reoperative cases was almost equal to that in new cases. This suggests that even in patients who had undergone unsuccessful LVA procedures in previous years, the mirror mapping technique is still reliable and effective.

Due to the nonlinear patterns seen in advanced cases on ICGL, patients with late-stage lymphedema frequently present difficulties in terms of lymphatic vessel identification. The results of our study suggest that, regardless of prior surgical attempts, the mirror mapping technique can overcome these difficulties and provide precise lymphatic vessel mapping. Therefore, after a failed first LVA, a reoperative LVA using the mirroring approach is an option before pursuing lymph node transfer or ablative surgery. LVA using the mirror mapping approach can be done on both the upper and lower extremities. In terms of the number of lymphatic vessels detected, anastomosis, and time spent, the upper limb result is superior to the lower limb. This is because the upper limb surface area and circumference are less than the lower limb, which reduces measurement and mirroring procedure errors.

The findings of our study on the distribution of lymph nodes and its relevance to LVA surgery have unveiled a significant observation: level 2 appears as a crucial anatomical area for achieving successful anastomosis. This conclusion is consistent with previous scholarly research, exemplified by the study conducted by Czedik-Eysenberg et al[31] wherein ultrasound was only utilized for the identification of optimum LVA sites. The results indicate that anatomical characteristics at level 2, which is located between the proximal and distal extremity regions, contribute to the effective establishment of anastomosis as a result of a high concentration of lymph nodes in this area. This underscores the importance of meticulous site selection in LVA surgery to enhance outcomes in terms of restoring lymphatic flow and managing lymphedema. Nevertheless, additional research is necessary to thoroughly enhance this technique and establish tailored treatment options due to the disparities in human anatomy and the course of diseases.

Limitations

This study has several limitations that warrant consideration. First, the retrospective design introduces susceptibility to missing or insufficient data and potential biases. The small sample size may have restricted our ability to detect all statistically significant differences and correlations. Notably, the unavailability of ultrasound[32] with optimal capabilities for lymphatic system identification in our center posed a limitation in the surgical techniques used. We acknowledge the broader utility of ultrasound in identifying lymph and veins; however, the constraints in our center's ultrasound quality affected its applicability to the lymphatic system. Additionally, it is essential to recognize that the study nomenclature follows the widely accepted term LVA, rather than LVB, as the latter is not commonly utilized in our center.

Furthermore, the study's scope focused exclusively on the anterior and medial portions of the extremity, omitting the posterior portion.[16] This anatomical limitation may influence the generalizability of our findings to the entire extremity. Finally, our analysis primarily concentrated on intraoperative outcomes, and caution should be exercised in directly extrapolating these to clinical outcomes. To address these limitations and provide a more comprehensive understanding, future research endeavors should encompass a larger population size and involve a longitudinal investigation of long-term clinical outcomes.

CONCLUSIONS

Lymphedema patients with a nonlinear ICGL pattern benefited from LVA using a contralateral mirror image mapping technique. After a failed LVA, a reoperative LVA using the mirroring approach is an option before pursuing lymph node transfer or ablative surgery.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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The data that support the findings of this study are available from the corresponding author, Nutcha Yodrabum, MD, upon reasonable request.

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