JPRS Journal of Plastic and Reconstructive Surgery
https://doi.org/10.53045/jprs.2023-0017
https://j-prs.jp/index.html

Review Article

Fundamentals for Supermicrosurgical Lymphaticovenular Anastomosis: Part 1 Comprehensive Review of Anastomosis Techniques and Proposal for a Flowchart Algorithm

Guido Gabriele, Simone Benedetti, Flavia Cascino, Antonino Ungaro and Paolo Gennaro

Department of Maxillo-Facial Surgery, S. Maria alle Scotte University Hospital of Siena, Siena, Italy

Abstract

Supermicrosurgical lymphaticovenular anastomosis represents an established procedure for lymphedema treatment, the effectiveness of which has been well documented in international literature.

Nevertheless, currently, no standards for supermicrosurgical lymphaticovenular anastomosis have been established regarding the type, location, and number of anastomoses so that the approach to surgical scenarios still depends on the surgeons' preference and ability.

A comprehensive literature search for articles involving supermicrosurgical lymphaticovenular anastomosis techniques was performed on the PubMed/Medline/SCOPUS databases. Results, including the names of the technique and their characteristics, such as indications, surgical time, and configuration of the vessels, are reported.

Each technique included was then performed five times, and for each of them, patency was tested intraoperatively and 30 days after surgery. Moreover, an efficacy score was assigned, taking into consideration the number of lymphatic vessels anastomosed, the average time for anastomosis, and the difficulty of each technique.

A total of 148 articles resulted from the literature search. In total, 16 papers met the criteria for inclusion as defined in the methods and were included in the review as a "supermicrosurgical lymphaticovenular anastomosis technique." Efficacy scores ranged from 0.21 to 1, intraoperative patency ranged from 80% to 100%, and the 30-days patency test ranged from 60% to 100%.

To perform effective anastomoses and aim to maximize the results of supermicrosurgical lymphaticovenular anastomosis, a modern microsurgeon should be trained to recognize and manage the most common vessel configurations, performing the most adequate one of the several techniques described. Further studies are required to validate and compare the use of the supermicrosurgical lymphaticovenular anastomosis techniques reviewed.

Keywords

LVA, supermicrosurgery, supramicrosurgery, LVA technique, Flowchart algorithm

J Plast Recontr Surg 2024; 3(2): 43-52
https://doi.org/10.53045/jprs.2023-0017

Introduction

Since its introduction in 2000, supramicrosurgery has demonstrated high specificity for lymphaticovenular anastomosis (LVA) for the treatment of lymphedema[1].

Furthermore, in the last two decades, the consensus regarding the efficacy of supramicrosurgical LVA for both primary and secondary lymphedemas has grown internationally and the number of surgeons managing this technique has increased significantly[2].

Although the popularity of the technique has grown exponentially and is spreading internationally, still no standards for LVA have been established regarding the type, location, number of anastomoses to perform, and methods to identify lymphatic vessels[3].

In the present paper, the authors aim to offer a review of the supermicrosurgical lymphaticovenular anastomosis techniques and their indications depending on the intraoperative vessel configuration and propose an efficacy score to evaluate every supermicrosurgical lymphaticovenular anastomosis (sLVA) technique and a flowchart for choosing between the right techniques depending on the vessel configuration en-

Corresponding author: Simone Benedetti, simone.benedetti1992@gmail.com
Received: May 9, 2023, Accepted: August 9, 2023, Advance Publication by J-STAGE: October 12, 2023

Table 1. Parameters for the Calculation of Efficacy Score (E).

Parameter	Meaning	Parameter Variability	Parameter Ranges
E	Efficacy	Deriving from the formula results	From 0 to X as per formula output
N	Number of lymphatics involved	1 ÷ 10	1 ÷ 10
Time for anastomosis	Basic Minimum Time	T_1 = 0 ÷ 30 min	1
T = (T_1 + $\Sigma\Delta T_i$)	First Time incremental	ΔT_2 = 15 min	+0.5
	Second Time Incremental	ΔT_3 = 15 min	+0.5
	N^{th} Time incremental	ΔT_N = 15 min	+0.5
Difficulty Coefficient D = (D_0 + $\Sigma\Delta D_i$)	Basic Difficulty: close vessels, same diameter	D_0 = first level difficulty	1
	Additional difficulty for different diameter vessels	ΔD_1 = Vessel diameter ratio > (2:1)	0.2
	Additional difficulty for distant vessels	ΔD_2 = Distant vessels	0.2
	Additional difficulty for shaping vessels	ΔD_3 = Need to shape the vessels before anastomosis	0.4

countered.

Materials and Methods

A comprehensive literature search was performed on the PubMed/Medline/SCOPUS databases. Papers published in English between 2000 and March 2021 were considered.

The search terms included "lymphaticovenous" OR "lymphovenous" OR "lymphaticovenular" AND "supermicrosurgical" OR "supramicrosurgical" OR "supermicrosurgery" OR "supramicrosurgery" AND "anastomosis" OR "technique."

The reference list of articles included in the review was examined for potentially eligible studies.

Papers were classified according to the following criteria: (1) articles describing an sLVA technique.

Extracted data included the name of the technique and its characteristics, such as indications, surgical time, number, and characteristics of the vessels involved. Both advantages and disadvantages highlighted by the author were reviewed.

Each anastomosis technique that resulted from the literature search was performed at least five times by a senior surgeon. The study was performed in accordance with the Declaration of Helsinki and was approved by the ethics committee of the authors' institution.

All patients included were informed regarding the purposes of the study and were invited to give their written informed consent to participate.

For every anastomosis, a score from 1 to 3 on average time (T) required to complete the anastomosis was assigned. Time was calculated from the visualization of all vessels to the completion of the anastomosis. In addition, a difficulty score (D) was assigned, the calculation of which was based on factors such as the number of vessels involved, their characteristics and differences, and the need to shape the vessels participating in the anastomosis. To each of these factors, a difficulty coefficient was arbitrarily assigned by the two senior authors. Moreover, an efficacy score (E) for each technique was assigned, taking into consideration the number of lymphatic vessels anastomosed and the aforementioned parameters T and D as follows:

$$E = \frac{N}{T \cdot D}, (1)$$

where

E = efficacy score

N = number of lymphatic vessels involved in the anastomosis technique

T = time score

D = difficulty score.

Table 1 defines all parameters involved in the assessment of the efficacy score. The rationale behind the formula for the efficacy score is explained as follows:

A. Mathematical structure of the formula

The formula that defines the efficacy score is based on two assumptions:

1. The relation between the efficacy score and the various parameters involved (N, T, and D) is simple direct or inverse proportionality. This is what emerges in the operational context. Thus, each of these variables is placed to the first power in both the numerator and denominator.

2. The three parameters N, T, and D are independent of each other. Therefore, they interact with each other through simple multiplication relations. This setting allows the extraction and visualization of the dependence of the quantity E on each single parameter via a simple mathematical analysis. Furthermore, this simple setting allows the customization of the formula in the future by easily introducing, if necessary, additional parameters by other authors.

B. Choice of incremental parameters

The purpose of the development of the formula was to give a different setting to the incremental values of the three parameters N, T, and D based on the experience gained and the intended use of the instrument:

1. For the N parameter, it was decided to adopt a simply and exclusively proportional approach: for example, with other conditions being equal (T, D), the doubling of N of treated vessels corresponds to the doubling of the efficacy score.

2. An incremental approach was adopted for parameter T, identifying a weighting of 50% for each additional quarter of an hour of activity. Time slot and weighting percentage were derived from daily experience and could possibly be

Table 2. Vessel Configuration and Scores for LVA Techniques.

LVA Technique	N. veins	N. lymphatics	Antegrade + Retrograde Flow	Time Score (T)	Difficulty Score (D)	P0 Patency	P1 Patency	Efficacy Score
End-to-End (E-E) LVA[1]	1	1	−	1	1	5/5	5/5	1
Side-to-End (S-E) LVA[4]	1	1	+	1.5	1.2	5/5	5/5	0.55
End-to-Side (E-S) LVA[5]	1	1	−	1.5	1.2	5/5	5/5	0.55
Side-to-Side (S-S) LVA[6]	1	1	+	1.5	1	4/5	4/5	0.66
Lambda LVA[7]	1	1	+	2	1	5/5	5/5	0.50
Modified Lambda LVA[8]	1	2	+	2.5	1.6	5/5	4/5	0.50
Funnel Technique LVA[9]	1	1	−	2	1.6	5/5	4/5	0.31
Buffalo Skull LVA[10]	1	2	−	2.5	1.6	5/5	4/5	0.50
Fusion Lymphoplasty LVA[11]	1	2	−	2.5	1.6	4/5	3/5	0.50
Modif. Fusion Lymphoplasty LVA[12]	1	2	−	2.5	1.6	4/5	4/5	0.50
Venous Branch-Plasty LVA[13]	1	1	−	3	1.6	4/5	3/5	0.21
Sequential LVA[14]	1	2	+	2.5	1	4/5	3/5	0.80
Diamond LVA[15]	1	1	−	1.5	1	5/5	5/5	0.66
Ladder LVA[16]	1	3	+	3	1.2	4/5	3/5	0.83
Pi LVA[17]	1	1	+	2	1	5/5	5/5	0.50
Octopus LVA[18]	1	>1	−	1.5	1.2	5/5	4/5	$L÷1.8$*

Surgical Time: 1 = < 30 min; 1.5 = 30 < t < 45 min; 2 = 45 < t < 60 min; 2.5 = 60 < t < 75 min; 3 = 75 < t < 90 min. Difficulty: the sum of all the difficulty coefficients present in the technique (see Table 1). P0 Patency: patency evaluated intraoperatively, expressed as the number of patent anastomoses out of the total of 5 for every technique. P1 Patency: patency evaluated 30 days after surgery. Efficacy score: result of Equation 1 (see text).
*For the octopus LVA technique, the efficacy score depends on the number of lymphatics (L) used for anastomosis, which can be variable.

redefined if necessary.

3. For parameter D, weighting has been proposed with respect to the basic condition, which is a function of the particular technique used: the operator may apply the necessary correction, taking into account the large library of cases attached to this paper. As in the previous case, this approach allows further customizations with the future extension of other possible techniques and/or the redefinition of the contributions of the techniques already present due, for example, to the evolution of the state-of-the-art technique.

During surgery, in case of any anastomosis leakage or doubts over patency, revision of the anastomosis was performed. For each anastomosis, patency was evaluated intraoperatively at the end of the definitive anastomosis (P0) and 30 days postoperatively (P1), and the patency test consisted of injecting intradermally 0.1 mL of a solution obtained by mixing 10 mL of normal saline solution with 25 mg of indocyanine green (ICG) (Verdye, Diagnostic Green, Aschheim-Dornach, Germany) at the second and third interdigital spaces of the operated limb. After injection, dynamic fluorescence images were obtained and recorded using an infrared camera system (Fluobeam, Fluoptics, Grenoble, France). Anastomoses were considered patent when clear flow of ICG could be appreciated through the anastomosed vessels. When the flow could not be clearly identified or when a clear absence of the ICG flow was appreciated, the anastomoses were considered nonpatent.

Results

A total of 148 articles resulted from the literature search. Of these, 40 full-text articles were selected and reviewed. In total, 16 papers were found to meet the inclusion criteria as defined in the methods and were included in our review as an “LVA technique” (**Table 2**). **Figure 1** depicts the search flow diagram. All studies were then analyzed by two senior surgeons with more than 10 years of experience in lymphedema supramicrosurgery (GG and PG). To evaluate the 16 techniques included in the study, each one of them was performed at least five times in total between March 2021 and March 2023, and numerical scores for difficulty, time, and efficacy for each LVA technique were assigned. Each anastomosis was tested for patency using ICG lymphography at P0 and P1 as described in the methods. All data retrieved from the study are summarized in **Table 2**.

End-to-end (E-E) LVA

The proximal extremity of the lymphatic vessel and the distal extremity of the venule are both cut, and end-to-end (E-E) (**Figure 2A**) anastomosis is performed. It is considered the standard anastomosis when the number of vessels is equal, their diameters are similar, and the vessels lie in proximity and have a parallel course. This technique was first described by Koshima in 2000, and it is still part of the fundamentals because of its feasibility and low risk of occlusion[1].

Side-to-end (S-E) LVA

A window is created on a lymphatic vessel, and a side-to-end (S-E) (**Figure 2B**) fashion to the venule anastomosis is performed. It is a useful technique when the lymphatic vessel diameter is bigger than the venule diameter. Both anterograde and retrograde lymph flows are preserved[4].

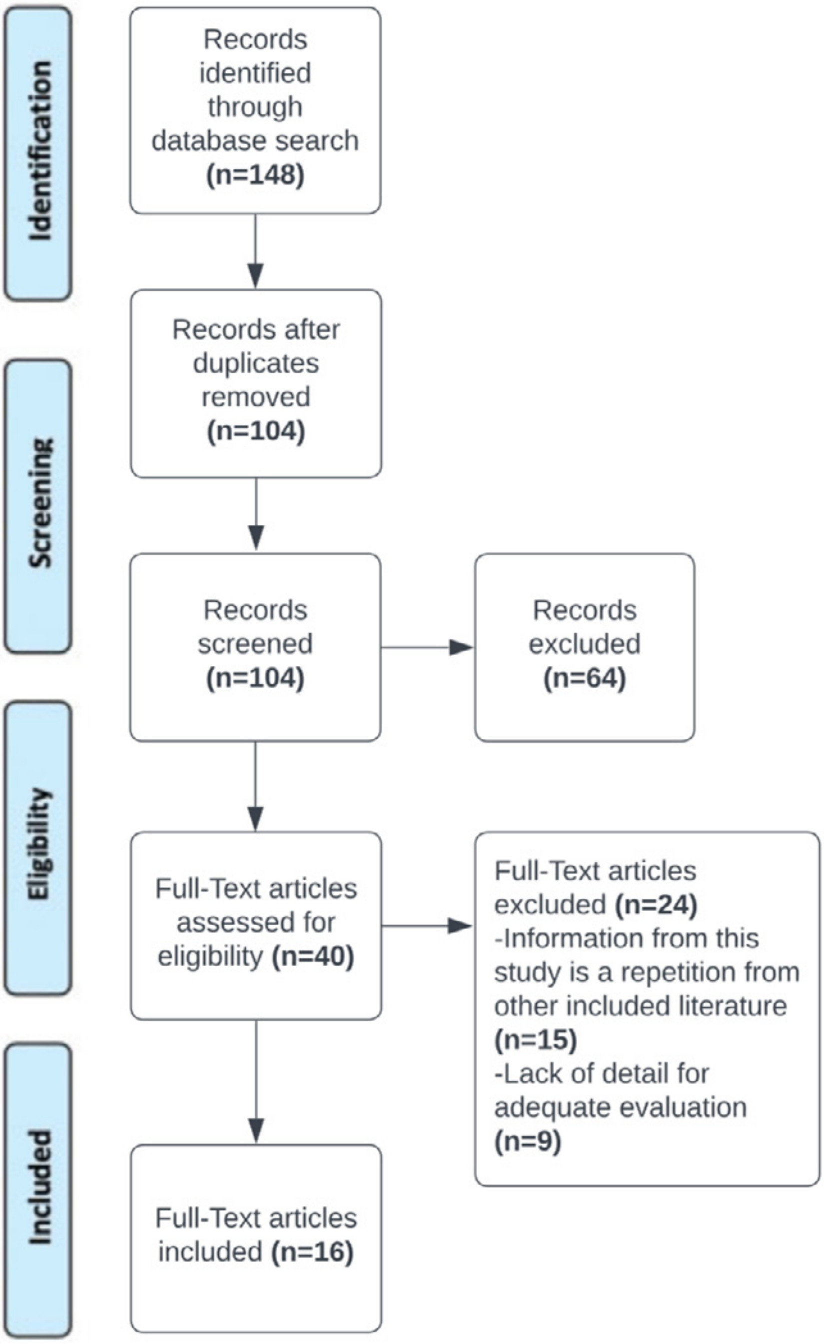

Figure 1. PRISMA diagram showing the status of the searched articles for review. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses

End-to-side (E-S) LVA

For end-to-side (E-S) (**Figure 2C**) anastomosis, an incision on the venule sidewall is required. The lymphatic vessel is transected and anastomosed to the venule window in an end-to-side fashion[5].

Side-to-side (S-S) LVA

In side-to-side (S-S) (**Figure 2D**) LVA, a window is performed on both the lymphatic vessel and venule sidewalls. The two orifices are then sutured one over the other. In this way, normal flow for both vessels is preserved[6].

Lambda LVA

The lambda-shaped LVA (**Figure 3A**) technique is performed between the two ends of a transected lymphatic vessel and a vein in an end-to-end and end-to-side fashion, respectively, for each extremity, draining both normograde and retrograde lymph flows into one vein[7].

Modified lambda LVA

Modified lambda-shaped LVA (**Figure 3B**) allows the channeling of the lymph flow from two lymphatic vessels to one vein using the distal ends and proximal ends of two cut lymphatic vessels anastomosed to one vein. Both distal and

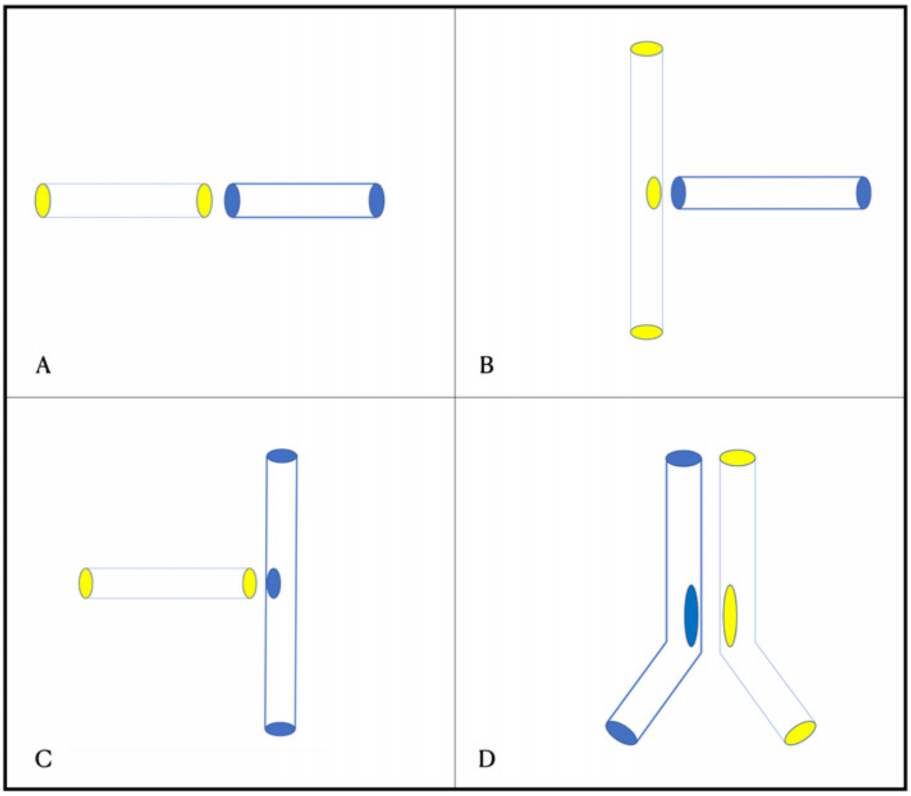

Figure 2. Schematics of four supermicrosurgical lymphaticovenular anastomosis (sLVA) techniques: A) end-to-end LVA, B) side-to-end LVA, C) end-to-side LVA, and D) side-to-side LVA.

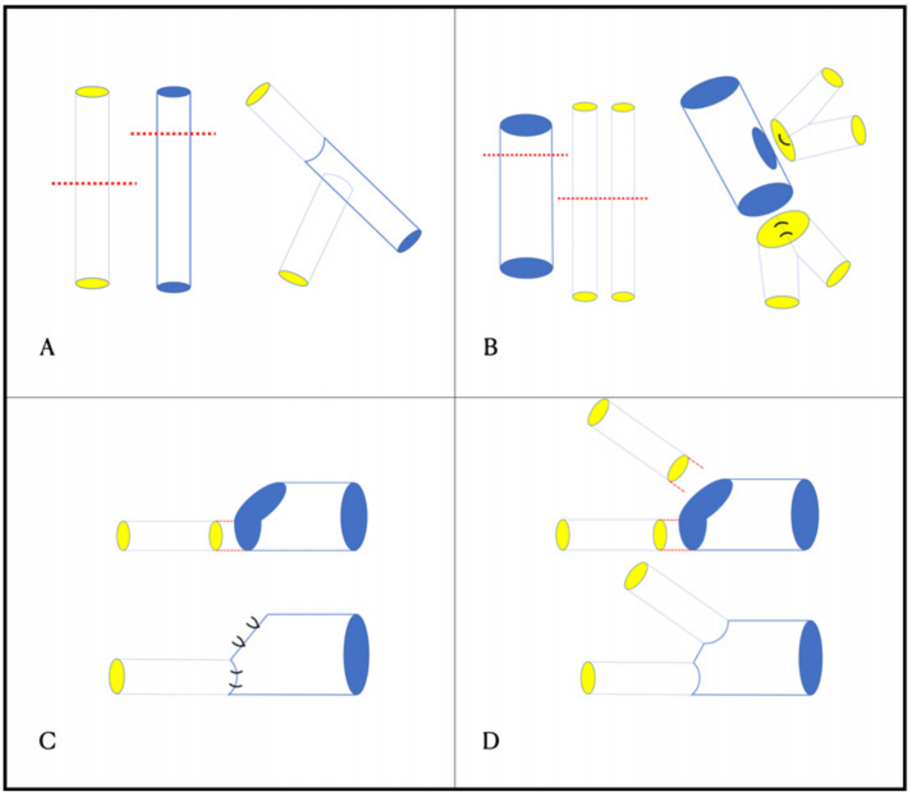

Figure 3. Schematics of four supermicrosurgical lymphaticovenular anastomosis (sLVA) techniques: A) lambda LVA, B) modified lambda LVA, C) funnel technique LVA, and D) buffalo skull LVA.

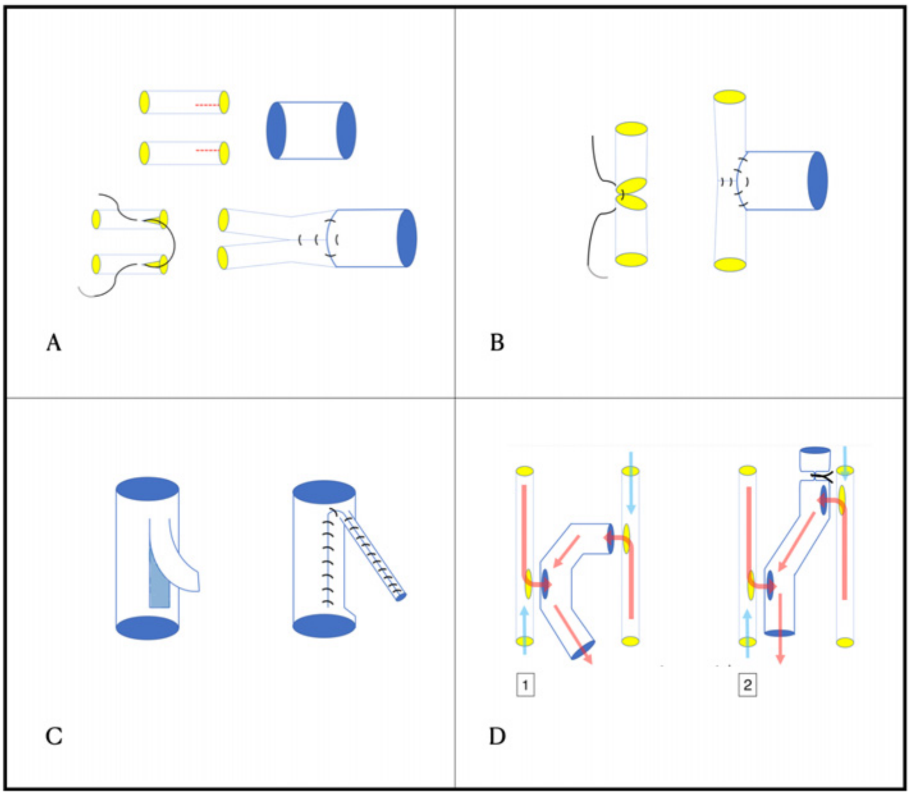

Figure 4. Schematics of four supermicrosurgical lymphaticovenular anastomosis (sLVA) techniques: A) fusion lymphoplasty, B) modified fusion lymphoplasty, C) venous branch-plasty, and D) sequential.

proximal lymphatic ends are tied, resulting in two large caliber ends (lymphoplasty). Subsequently, the larger caliber extremity is anastomosed to the vein in an end-to-end fashion and the other in end-to-side anastomosis. The present technique is recommended when there are two lymphatic vessels and one vein in a surgical field. Lymphoplasty reduces the difference in caliber between lymphatic vessels and veins[8].

Funnel technique E-E

This is an E-E anastomosis performed when a small lymphatic vessel is sutured to the edge of a bigger venule, which is cut in an oblique fashion. The remaining part of the venule edge is sutured using a conventional technique (**Figure 3C**). This is useful when there is a relevant mismatch between vessels of equal number[9].

Buffalo skull E-E

This is an E-E anastomosis where two small lymphatic vessels are anastomosed to a single bigger vein (**Figure 3D**). The venous stump is cut obliquely and is sutured in an E-E fashion to both lymphatic vessels. The remaining part of the venous stump is closed with conventional sutures. The technique is useful in case of a large distance between vessels[10].

Fusion lymphoplasty E-E

The fusion lymphoplasty technique (**Figure 4A**) consists of the longitudinal fusion of two lymphatic vessels, creating a neo-orifice, which is then anastomosed to a bigger vein in an E-E fashion. This technique has similar indications to the buffalo skull technique, being useful when there is a discrepancy in number and diameter between vessels[10,11].

Modified fusion lymphoplasty E-E

Modified fusion lymphoplasty (**Figure 4B**) is a modified technique, which is useful when there are two distant lymphatic vessels with similar diameters in a surgical field. The lymphatics are approximated and transected to create a neo-lymphatic channel, which is anastomosed to the vein in an S-E fashion[12].

Venous branch-plasty E-E

In the venous branch-plasty (**Figure 4C**) procedure, the venous wall is incised and a flap is raised. The flap edges are sutured to create a neo-branch with a diameter similar to that of the lymphatic, to which it is anastomosed in an E-E fashion[13].

Sequential S-S + S-E

This technical procedure is represented by a double LVA, which can be performed in two different configurations (**Figure 4D**). In the first option, two lymphatic vessels are anastomosed to one vein. One lymphatic vessel is connected in a side-to-side manner and the other lymphatic vessel in a side-to-end manner (**Figure 4D-1**). The second option is represented by a double side-to-side LVA in which two lymphatic vessels are anastomosed both in a side-to-side style to the vein. This one is then ligated distal to the anastomosis site to avoid venous backflow (**Figure 4D-2**). This technique

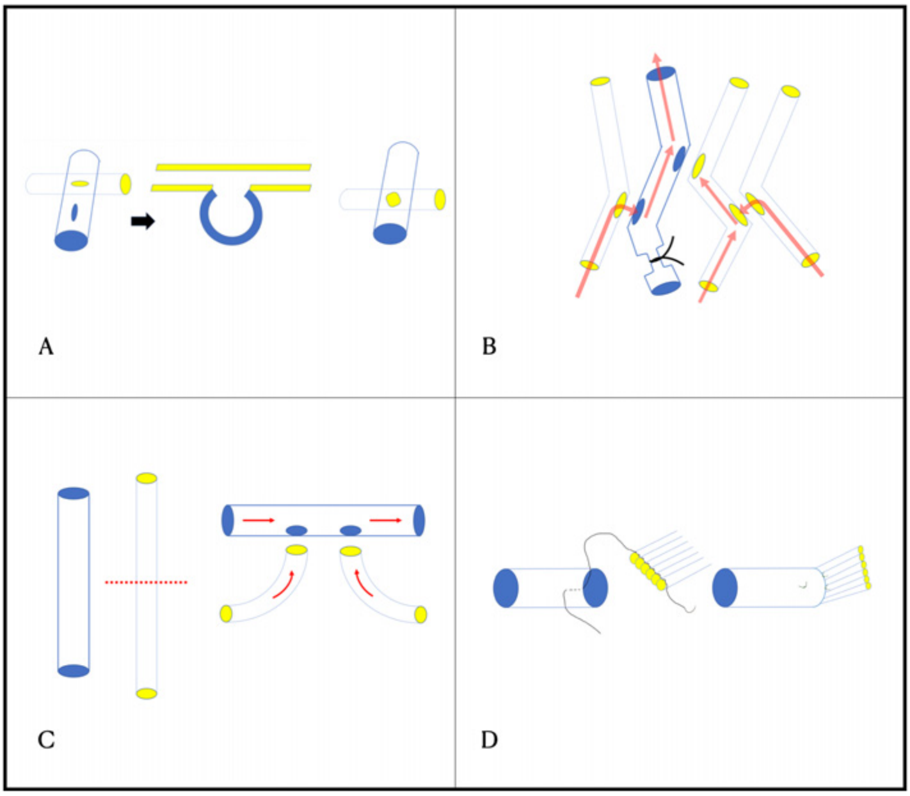

Figure 5. Schematics of four supermicrosurgical lymphaticovenular anastomosis (sLVA) techniques: A) diamond LVA, B) ladder LVA, C) pi LVA, and D) octopus LVA.

should be preferred when there are multiple lymphatic vessels and only one vein is found in a surgical field[14].

Diamond S-S

This is a modified S-S anastomosis for vertically crossing vessels (**Figure 5A**), where the incisions are performed longitudinally on both vessels to keep the orifice open[15].

Ladder S-S

This technique is represented by a triple side-to-side lymphatic anastomosis (**Figure 5B**) that allows us to converge the lymph flow of three lymphatic vessels into one vein. This is useful when there are three lymphatic vessels and one vein and one of the three lymphatics is distant from the vein in a surgical field. Two lymphatic vessels that lie next to a vein are anastomosed to it in a side-to-side style. The other lymphatic vessel is anastomosed to the next lymphatic vessel in a side-to-side style. In summary, two S-S LVA and one lymphatico-lymphatic S-S anastomoses are performed, tying the vein distal to the LVA site to avoid venous backflow[16].

Pi E-S

This is a double end-to-side LVA. The two ends of a transected lymphatic vessel are anastomosed to a vein in an end-to-side manner, draining both antegrade and retrograde flows from the lymph vessel. This double end-to-side LVA describes the shape of a pi (**Figure 5C**)[17].

Octopus

Before performing the octopus technique, all lymphatic vessels in a surgical field must be skeletonized. The suture of the anastomosis is performed by grasping transversely the adventitia of each lymphatic vessel and then by suturing the complex of lymphatic vessels to a vein of an adequate caliber. The completed LVA resembles the aspect of an octopus due to the multiple lymphatics (**Figure 5D**). This technique allows the surgeon to obtain a high number of LVA with only a single anastomosis[18].

Discussion

Supermicrosurgical lymphaticovenular anastomosis and its precursor, microsurgical lymphovenous bypass, have been developed as a physiological approach to lymphedema treatment, with the aim to recreate an anterograde lymphatic flow in the affected extremity[19,20].

First described by Koshima in 1997, *supermicrosurgery technique* is defined as the microsurgical anastomosis of vessels with a diameter smaller than 0.8 mm. This evolution appeared like the natural progress of microsurgery, the first steps of which were made in the 1960s, due to new surgical techniques, intraoperative magnification, finer instruments, and microsutures[2]. With supermicrosurgery, this field was brought to a whole new dimensional level. Nowadays, operative microscopes can reach a magnification of over 60× and 12-0 microsutures with 30 μm needles are available[21].

In the last 10 years, LVA has grown in popularity. The

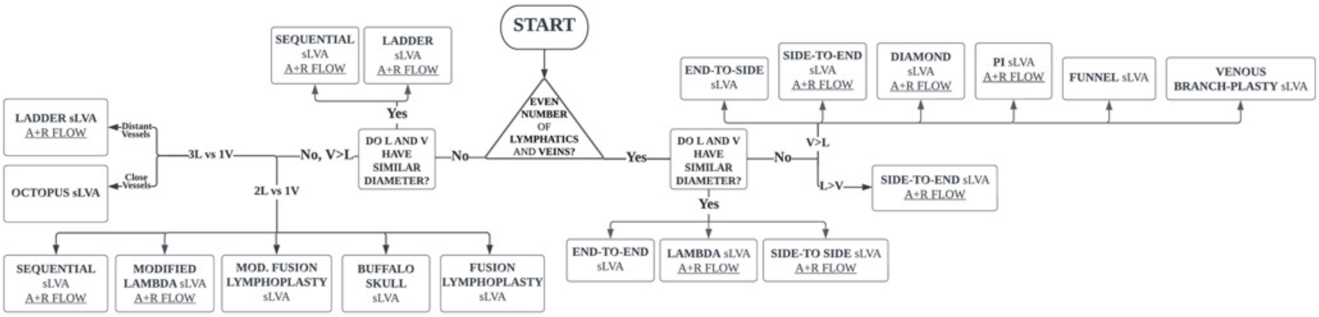

Figure 6. Flowchart guiding the choice of the sLVA technique.

number of surgeons, and consequently also scientific production on lymphatic supermicrosurgery, has incredibly increased[2]. Despite the intrinsic difficulty of performing LVA, the need for specific training and instrumentation, and the growing interest for the newly introduced techniques for lymphedema treatment, such as the vascularized lymph node transfer (VLNT)[22], the lymphatic vessel transfer, and liposuction[23], LVA remains one of the best procedures in terms of cost-effectiveness, especially for moderate severity lymphedema. Among its advantages, LVA has demonstrated high efficacy in treating some of the most severe complications of lymphedema, such as cellulitis[24] and genital lymphedema[25].

On the field, supermicrosurgical LVA remains technically challenging: a variety of surgical scenarios can be encountered during the procedure, such as vessel number and size mismatch, and unfavorable pressure gradients and vessel position, so that different anastomotic configurations have been proposed. As suggested by Narushima et al., the ultimate goal of the microsurgeon approaching this type of surgery should be to prefer anastomotic configurations that decompress both anterograde and retrograde lymphatic flows, maximizing the lymphatic flow in a markedly altered lymphedematous disease state, thus relegating the use of the E-E anastomosis as the last resort[26].

Regarding this topic, recently, some controversies have been raised regarding the effects of retrograde anastomoses, as highlighted by the work of Yang et al.[27] and by the work of Mackie et al.[28], although larger studies will be needed to assess the impact of retrograde anastomoses on LVA outcome.

However, despite the fact that new interesting preoperative lymphatic imaging modalities are under development[29,30], the ultimate decision as to which type of anastomosis to perform can only be made intraoperatively. This leads to the need to have experience with as many anastomotic configurations as possible and to choose the technique that should theoretically have the best efficacy, maximizing the number of lymphatics involved while avoiding venous backflow.

The standard LVA technique is represented by the end-to-end (E-E) anastomosis, but this configuration requires contiguous vessels and similar diameters. In all other cases, when caliber and/or number mismatches between the vein and lymphatic vessel are present or when the lymphatic and vein are distant, other anastomosis strategies must be found.

As a general rule, the choice of the technique to address each configuration should aim to maximize the number of lymphatics anastomosed while considering surgical time, technical difficulty, and the patency of the anastomosis.

To this regard, in this paper, we aimed to summarize and evaluate all supermicrosurgical LVA configurations described in literature while offering a proposal of an efficacy score based on the intrinsic characteristics of each technique. From the results of our study, end-to-end sLVA, owing to the very short time of anastomosis and basic difficulty, still represents the workhorse for sLVA with a high-efficacy score. However, despite the choice of which anastomosis technique to use should follow the aforementioned principles, it can ultimately be made only intraoperatively and should be as effective as possible. Some techniques require more experience than others to be effectively performed because of their intrinsic characteristics (i.e., the need to shape the vessel end before anastomosis), and this factor, which we included in the difficulty parameter, lowers their efficacy and should be considered when choosing what technique to perform.

Figure 6 represents the proposal of a flowchart algorithm to aid in the choice of the technique based on the vessel configuration encountered.

In case of equal numbers and diameters of lymphatics and veins, E-E and lambda-shaped LVA can be performed. This last technique allows us to direct both normograde and retrograde lymph flows inside the venule.

When encountering a bigger diameter in the lymphatic vessel compared to the vein, a side-to-end (S-E) anastomosis can be carried out.

In case of a configuration with a bigger venule and a smaller lymphatic, techniques such as the end-to-side (E-S), side-to-side (S-S), funnel, diamond, or venous branch-plasty can be performed.

When a larger venule is present but there are two lymphatics, anastomosis techniques such as modified lambda, octopus, sequential, buffalo skull, pi, fusion lymphoplasty, or modified fusion lymphoplasty can be chosen, also depending on the distance between the vessels.

Instead, in cases of multiple lymphatic vessels and a single larger vein, techniques such as the ladder or octopus should be chosen. The first one, despite being an advanced technique, is useful when one of the lymphatics is distant from the vein.

Despite the vast majority of the studies included in this comprehensive review not including clear data over the patency of the described sLVA techniques, our patency tests performed for every technique showed a good to excellent mid-term patency rate (**Table 2**).

To the best of our knowledge, this study is the first to review all supermicrosurgical techniques described in literature, aiming to give the microsurgeon who treats lymphedema a global view of all technical opportunities available and proposing a score to evaluate both the current techniques and those that will be described in the future.

Between the limitations of the experimental part of the study in which patency and the efficacy score are assessed, there is the limited number of times in which each technique was performed. Further comparative studies are warranted to support our findings.

Moreover, because of the recent increase in doubts regarding the beneficial effects of retrograde flow anastomosis in lymphedema reduction[27,28)], further studies are required to assess the impact of retrograde flow bypass on the results of sLVA.

Conclusion

LVA represents the first line approach in lymphatic dysfunction due to its efficacy and less invasive surgical strategy. A variety of surgical scenarios has led to the development of different anastomosis techniques that should be used according to local vessel conditions to ensure the efficacy of the anastomoses. A modern microsurgeon who wants to engage lymphatic supramicrosurgery at its best should be trained to recognize and manage the most frequent anastomotic configurations to choose a high-efficacy technique that should optimize the clinical results. In this regard, very few works statistically determine the superiority of a technique over the others[4,5,26,31)]. For this reason, long-term prospective comparison studies with large numbers of patients are required.

Acknowledgments: We deeply thank Engr. Giulio Benedetti for the support in creating, analyzing, and testing the efficacy score.

Author Contributions: SB and PG proposed the research idea and composed the Introduction, Materials and Methods, Results, and Discussion.

SB, FC, and AU supported the literature review, helped in revising the manuscript, and provided clinical suggestions.

SB, GG, and PG performed the data analysis, composed the conclusions, and prepared the manuscript for submission.

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest: There are no conflicts of interest.

Compliance with Ethical Standards: The study was performed in accordance to the Declaration of Helsinki, and it was approved by the medical ethics committee (S. Maria alle Scotte University Hospital, decision no. 540, 2021).

Disclaimer: Author Paolo Gennaro, MD, PhD, is one of the Editorial Committee members of Journal of Plastic and Reconstructive Surgery. This author was not involved in the peer-review or decision-making process for this paper.

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