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Supermicrosurgical lymphaticovenous anastomosis for breast cancer related lymphedema in low resources settings



Tarek Hashem¹ and Takumi Yamamoto^{2*}

Abstract

Background Supermicrosurgical lymphaticovenous anastomosis (LVA) is becoming popular for the management of breast cancer-related lymphedema (BCRL), but mainly provided in well-developed countries. Little is known on possibility of LVA with limited resources. This study aimed to evaluate feasibility of LVA in Egypt, where latest devices are not available.

Methods Medical records of patients who underwent LVA for progressive BCRL were reviewed. All patients were refractory to conservative treatment for 6 months or longer. As devices for near-infrared fluorescent lymphography was not available, a conventional high-frequency (18-MHz) ultrasound was used to localize the lymph vessels and veins for LVA. LVA was done using conventional microsurgery sets and 10–0 nylon sutures under an operating microscope with 40 times magnification. One-year postoperative results were evaluated based on upper extremity lymphedema index (UEL index), cellulitis frequency, and subjective symptoms.

Results Twenty-three patients were included. The number of LVAs per limb ranged from 2 to 3 (average, 2). Lymph vessel detection rate was 92.6% (50/54). Ten (43.5%) patients with dermal backflow (DB) showed 19.2% postoperative volume reduction based on UEL index after one year. Thirteen (56.5%) patients without dermal backflow showed only 2% reduction. Postoperative UEL index was significantly lower than preoperative UEL index (123.5 \pm 7.3 ml vs. 136.4 \pm 9.4 ml, *P*=0.017). Postoperative cellulitis frequency was decreased compared to preoperative one (2.15 \pm 0.85 vs. 0.09 \pm 0.18 attack/year, *P* [<] 0.001). 13(56.5%) patients reported improvement in all subjective symptoms; limb tension improvement in 18 (78.3%) patients, limb heaviness in 15 (65.2%), and overall limb mobility in 13 (56.5%).

Conclusions LVA could be safely and effectively performed in limited resources settings without latest device for lymphatic mapping nor supermicrosurgery instruments. A conventional high-frequency ultrasound allows lymphatic and venous mapping useful for LVA. LVA should not be given up even with limited resources.

Keywords Supermicrosurgery, Lymphaticovenous anastomosis, Lymphedema, LVA, BCRL

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Introduction

Lymphedema is the progressive accumulation of protein rich fluid in the subcutaneous tissues. It is a debilitating condition that affects a certain percentage of breast cancer patients. The main causing factor is the surgical removal of axillary lymph nodes during axillary dissection. Other contributing factors have been identified as radiation therapy, a high body mass index (BMI) and post operative seroma. The incidence of breast cancerrelated lymphedema (BCRL) is somewhat not standardized. Some reports mention an incidence as high as 40% post axillary dissection. Even the introduction of sentinel lymph node biopsy leaves the incidence of BCRL as high as 10% [1]. The common pathophysiology in these cases is the loss of the natural direction of lymphatic flow due to obstruction. After lymph flow obstruction, retrograde lymph flows take place, which is shown as dermal backflow (DB) on lymph flow imaging. The lymphatic fluid, loaded with remnants of cellular metabolism is trapped in the subcutaneous tissues. This leads not only to a progressive increase in the limb circumference, size and weight, but also predisposes to repeated attacks of cellulitis and inflammation. These attacks in turn lead to aggravation of lymphatic obstruction.

The management of BCRL has traditionally comprised of two options: either compressive decongestive therapy or surgery. Surgical management which once had a limited role in lymphedema treatment is now gaining more grounds. Historical ablative procedures such as Charles or Sistrunk operations have now been replaced by physiologic techniques [2]. Using microvascular approach these operations aim at restoring a physiologic lymphatic flow. One of the options is to bypass the lymphatic obstruction by directly connecting superficial lymphatic vessels to the venous system. The created lympho-venous shunt will thus help drain the trapped lymphatic fluid. As old-style lympho-venous shunts of lymphaticovenous implantation and lymph node-to-vein coaptation have very high risk of thrombosis, it is essential to create the lympho-venous bypass with an intima-to-intima coaptation technique which is supermicrosurgical lymphaticovenous anastomosis (LVA). In order for this procedure to be successful the lymphatic vessels should preferably retain their functionality and be positioned in the vicinity of a vein with comparable diameter. Therefore, preoperative lymphatic mapping plays a critical role in LVA surgery.

Lymphoscintigraphy is a gold standard for lymph flow imaging, and has been used in most institutions where lymphedema management and researches are conducted. However, lymphoscintigraphy's images are obscure, and not good at precise visualization especially in a small region. The advent of indocyanine green (ICG) fluorescent lymphography has changed lymphedema management, as it can clearly visualize superficial lymph flows in real-time without ionized radiation exposure. [3–9] Unlike other lymph flow imaging modalities such as lymphoscintigraphy and magnetic resonance lymphography, ICG lymphography localizes lymph flows directly on the skin surface, which is ideal for lymphatic mapping before LVA. However, ICG lymphography requires a dye of ICG and a near-infrared camera system for fluorescent visualization, which is not available in all hospitals. Unavailability of ICG lymphography leads to limited dissemination of LVA surgery, especially outside well-developed countries.

To address the challenging conditions in Upper Egypt where ICG lymphography nor supermicrosurgery instruments are not available, we employed a conventional high-frequency ultrasound (HFUS) with 18-MHz which was possessed and used by radiologists, internists, or anesthesiologists, in preoperative mapping for LVA. This study aimed to evaluated the feasibility of LVA in limited resource settings.

Methods

Medical records of patients who underwent LVA for progressive BCRL from April 2023 to December 2024 were reviewed at Shefaa Al Orman Cancer Hospital in Luxor, Upper Egypt. BCRL patients with lymphedema-specific symptoms who have been treated with complete decongestive therapy for at least 6 months were included. Patients followed for shorter than 1 year were excluded from the study. This retrospective observational study was approved by an institutional review board (IRB; approval number: IRB-SOH-2023-015), and written informed consent was waived by the IRB as only anonymous data was used in this study. Diagnosis of BCRL was determined based on lymphedema-specific symptoms and lymphoscintigraphy findings of dermal backflow. All patients underwent conservative treatment of complete decongestive therapy for at least 6 months. Patients who had shown progressive course refractory to the conservative management were selected for LVA surgery. On the day of LVA surgery, a HFUS (18-MHz, Logic S7, General Electric, Wisconsin) was performed to map vessels for anastomosis. The superficial anatomy of the main superficial lymphatic trunks of the affected upper limb were first drawn using a colored marker. This was done according to previous lymphography studies describing the anatomy of superficial upper limb lymphatics [10, 11]. The ultrasound probe was positioned perpendicular to the course of lymphatic channels. Mapping started from the most proximal point of the lymphatic trunks anticipating the vessels with largest caliber. Lymphatic vessels were identified just below the superficial fascia and were uncollapsible. LVA sites were designed on lymphedematous lesions where HFUS showed a patent lymph vessel

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Fig. 1 High frequency ultrasound mapping of superficial lymphatics (yellow) and venules (blue)



Fig. 2 Lympho-venous anastomosis

and a nearby vein with similar caliber (Fig. 1). Two or 3 sites were designed according to visibility of the vessels on HFUS. The whole procedure took an average of 25 min.

Under magnification of the surgical microscope the skin of the most proximal location was incised in a transverse manner. Inter-lobular dissection was performed to dissect the adiposal layer to the superficial fascia; a recipient vein was usually found during this procedure before reaching the superficial fascia. The Skin margins were sutured to make the surgical field open. Then incision of the superficial fascia was carefully done, searching for the lymph vessel. Dissection was done in an inter-lobular plane respecting the integrity of the subcutaneous fat lobules until the lymph vessel was identified and dissected. No dyes were used to identify lymphatic vessels. Localization of lymphatic channels relied on anticipating their anatomical course just below the superficial fascia. The lymph vessel was transected at the most proximal point in the field, and the vein at the most distal point for end-to-end anastomosis; if vessels' length were redundant with a risk of kinking, the vessels were trimmed as needed to prevent kinking. Using a 10-0 nylon suture, the vessels were anastomosed in an intima-to-intima coaptation manner (Fig. 2).

When there was a significant size discrepancy between the of the lymph vessel and the vein, the smaller vessel was anastomosed to the larger one in an end-to-side fashion. The anastomosis site was loosely covered with the surrounding fat lobules. The skin was carefully closed under the microscope, not to affect the vessels or the anastomosis site. The same procedures were repeated in the remaining sites according to preoperative mapping; the second proximal site for the second, and if there was, the most distal site for the last.

Immediately after the last LVA, the whole arm was bandaged starting from the palm of the hand to above the elbow joint. The patient was discharged the same day and was instructed to stay in bandage till one day before the first post operative outpatient appointment which was in two weeks. At this appointment the wounds were inspected for signs of inflammation or infection and a circumference measurement was taken at the same fixed points of the upper limb. Patients were advised to keep the limb in a compressive garment for at least a year postoperatively. Compression garments covering the hand to above elbow of at least Class II, generating a pressure of 23-32 mmHg, were recommended. The wounds were checked with the same measurements one month after the operation and regular visits were arranged every three months thereafter.

Collected data included age, BMI, past history, history of breast cancer, history of lymphedema, intraoperative findings, and perioperative lymphedematous conditions. Lymphedematous volume was evaluated based on upper extremity lymphedema (UEL) index [12, 13]. UEL index is calculated using BMI and circumferences measured at five points as follows; 5 cm above the olecranon (C_1), the olecranon (C_2), 5 cm below the olecranon (C_3), the wrist (C_4), and the hand (C_5).

UELindex =
$$(C_1^2 + C_2^2 + C_3^2 + C_4^2 + C_5^2)$$
 /BMI

lymphoscintigraphy findings were classified into DB group and control group; DB and uptake of the tracer in the proximal regions were found in DB group, whereas not in control (Fig. 3).



Fig. 3 Lymphoscintigraphy of control (left) and DB (right)

Demographics of the patient characteristics and the operative findings were described with ranges (averages) or counts (percentages). UEL index, cellulitis frequency, and subjective symptoms were compared before and 1 year after LVA. The outcomes were compared between DB and control groups. Plus-minus values represented means and standard deviations. Mann-Whitney U test and chi-square test were used for statistical analyses. A *P*-value < 0.05 was set as a statistical significance [14].

Results

Twenty-three patients were included. Patient's age ranged from 34 to 76 years (was average, 43.3 years), BMI from 28.1 to 38.4 kg/m² (average, 31.21 kg/m²). There were 3 (13%) patients who had type II diabetes mellitus and 3 (13%) other patients who had both diabetes and essential hypertension. Two (8.7%) patients suffered from ischemic heart disease and 3 (13%) patients of hypothyroidism. Seventeen (73.9%) patients had previously undergone modified radical mastectomy with axillary lymph node dissection, and 6 (26.1%) patients had breast conserving surgery with axillary dissection. All patients had positive node metastasis and received postoperative radiation. The least lymph node harvest was 9 nodes and the greatest was 32 lymph nodes with an average of 16 nodes. Laterality of BCRL was right in 12 (52.2%) patients, and left in 11 (47.8%). Duration of BCRL ranged from 13 to 228 months (average, 38.2 months). Seven (30.4%) patients had cellulitis history; cellulitis frequency ranged from 1 to 4 attack/year (average,2 attacks/year). Severity of lymphedema, according to international society of lymphology (ISL) stage, included ISL stage I in 5 (21.7%), ISL stage II early in 17 (73.9%), and ISL stage II late in 1 (4.4%). UEL index ranged from 119.6 to 148.2 (average, 136.4).

In total, 54 LVAs were performed on 23 limbs; the number of LVAs ranged from 2 to 3 (average, 2.4 anas-tomoses/limb). 42(77.8%) lymph vessels were anastomosed in an end-to-end fashion, and 12 (22.2%) in an

end-to-side fashion. Lymph vessel detection rate was 92.6% (50/54); the lymph vessel was not found in 4 (7.4%) sites, and anastomosis was not performed there. Anastomosis patency was confirmed in all anastomosis sites, which was evaluated by observing expansion of the recipient vein with lymph fluid after compressing the distal limb intraoperatively. Operation time per site ranged from 52 to 78 min (average, 65.3 min), and total operation time from 110 to 134 min (average, 123.3 min). Two (8.7%) patients suffered from superficial wound infection which was managed conservatively only with dressing changes. Seven (30.4%) patients were compliant regarding the use of compressive garments for one year after the operation; 16 (69.6%) patients could not continue compression therapy for one year (Table 1).

Postoperative UEL index ranged from 104.4 to 145.2 (average, 123.5), and there was a statistically significant difference between pre- and post-operative UEL indices (136.4 ± 9.4 vs. 123.5 ± 7.3 , P = 0.017). (Fig. 4)

Postoperative volume reduction rate ranged from 2 to 19.2% (average, 9.5%). Postoperative cellulitis frequency from 0 to 1 attack/year (average, 0.1 attack/year), and there was a statistically significant difference between pre- and post-operative cellulitis frequency (2 ± 0.9 vs. 0.1 ± 0.2 attack/year, $P \leq 0.001$). Twenty-one (91.3%) patients had no cellulitis attack after LVA surgery. Regarding postoperative improvement of subjective symptoms, limb tension was improved in 18 (78.3%) patients, limb heaviness in 15 (65.2%), and overall limb mobility in 13 (56.5%) (Table 2).

There were statistically significant differences between DB and control groups, in postoperative volume reduction rate (19.2% \pm 2.3% vs. 2% \pm 1.3%, *P* [<] 0.001), cellulitis frequency reduction rate (0.0% \pm 0.0% vs. 0.21% \pm 0.127%, *P*=0.049), limb tension improvement (100.0% vs. 61.5%, *P*=0.003), limb heaviness improvement (90.0% vs. 46.2%, *P*=0.0022), and in overall limb mobility improvement (90.0% vs. 30.1%, *P* [<] 0.001) (Table 3).

Table 1 23 Patient's characteristics

Age (years)*	43-76 (43.3)
BMI (kg/m ²)*	28.1-38.4 (31.2)
Breast Cancer Management	
MRM	17 (73.9%)
BCS	6 (26.1%)
RTH	23 (100%)
N°. Of dissected LNs *	9-32 (16)
Laterality of BCRL (right/left)	12/11 (52.2%/47.8%)
Duration of BCRL (months) *	13-228 (38.2)
ISL stage I	5 (21.7%)
ISL stage II	17 (73.9%)
ISL stage II (late)	1 (4.4%)
h/o cellulitis	7 (30.4%)
UEL index *	119.6-148.2 (136.4)

Data are counts (percentage) otherwise indicated

*Data are ranges (average)



Fig. 4 Preoperative (left) and 12 months post-operative result (right)



Discussion

This retrospective study revealed that it was possible to conduct surgical management of BCRL with LVA in limited resources settings. Unlike conventional LVA performed in well-developed countries, lymphoscintigraphy and conventional HFUS were used for selection of LVA cases and preoperative mapping, and 10-0 nylon suture for anastomosis without supermicrosurgery instruments in this study cohort. As shown in the results of better outcomes in DB group, lymphoscintigraphy findings were useful to predict prognosis or therapeutic efficacy after LVA surgery. Although further improvements are required in clinical management of patients showing unfavorable findings on lymphoscintigraphy, our protocol of LVA using lymphoscintigraphy and HFUS seems feasible for surgical management of BCRL even in limited resource settings.

Heterogeneity of patient characteristic with different stages of lymphedema is considered a major factor affecting the overall limited improvement in some patients. This would suggest the limitation of lymphoscintigraphy to consider indication of LVA. ICG lymphography would have clearly shown differences between good and poor indications of LVA; overlapping regions where linear

results
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Post-op UEL*	104.4 -145.2 (123.5)		
Volume reduction *	2%-19.2% (9.5%)		
Post-op cellulitis rate *	0 -1 (0.1)		
Limb tension improvement	18/23 (78.3%)		
Heaviness improvement	15/23 (65.2%)		
Mobility improvement	13/23 (56.5%)		

Data are counts (percentages) otherwise indicated.

* Data are ranges (averages).

 Table 3
 Results of DB group and control group

	DB group (10)	Control group (13)	p-value	
Volume reduction	136.4/110 (19.2%)	136.4/134 (2%)	< 0.001	
Cellulitis frequency	0.0%	0.21%	0.049	
Limb tension	10/10 (100.0%)	8/13 (61.5%)	0.003	
Limb heaviness	9/10 (90.0%)	6/13 (46.2%)	0.002	
Limb mobility	9/10 (90.0%)	4/13 (30.8%)	< 0.001	

pattern is shown at an early transient phase, and DB pattern at a late plateau phase of ICG lymphography. [3–9, 15–1715–17] Nonetheless, lymphoscintigraphy still has a role in lymphedema evaluation and patient selection for LVA, as this study showed the feasible results and better postoperative conditions than preoperative ones. To improve postoperative outcomes, it would be better to perform LVA only on patients showing DB and tracer uptake in the proximal lymph pathways on lymphoscintigraphy, as previously reported [18].

Interestingly, subjective improvements were noted in most patients, even in ones who did not show significant postoperative volume reduction, as previously reported [18–20]. Despite the fact that 56.5% of the study group had only 2% volume reduction after one year, more than half of patients reported at least one subjective improvement in their limb condition. Improvements of limb tension and heaviness are considered to be related to reduced lymphatic pressure after LVA even without postoperative volume reduction. To observe postoperative volume reduction, a significant amount of lymph fluid should be drained, but some patients would have not shown such a significant drainage but felt improvements of subjective symptoms [21-26]. Therefore, LVA seems to be of positive effects even on patients without significant volume reduction. Another possible explanation for cases that did not show significant volume reductions lies maybe in the composition of their lymphedema. In some cases, while the lymphedematous lesion is mainly composed of retained lymph, a considerable portion of increased limb volume is due to adipose tissue deposition. These patients can benefit from liposuction to achieve a significant volume reduction.

This study has several limitations, including retrospective observational nature of this study. The lack of ICG lymphography could be considered both a point of strength and a drawback. It was difficult to assess the condition of lymphatic vessels preoperatively without subjecting patients to some degree of radioactivity during lymphoscintigraphy. However, this study proved the feasibility of LVA even without ICG lymphography. Due to economic restraints, ICG and a near-infrared cameras might not be available in many cancer centers in developing countries. This study results showed usefulness of LVA even without such latest technologies, indicating that our protocol would make BCRL patients benefit from the latest surgical advances of LVA even in limited resource settings. Another study limitation is the reliability of circumference measurements to assess volume reductions. Since volume is a three-dimensional, it seems ideal to measure volume in a three-dimensional way such as using a gold standard of water displacement method. However, UEL index has been developed for better volumetry taking body-physique-correction into consideration, this study results would be feasible for lymphedematous volume comparisons between cases, as previously reported [12, 13, 22, 24, 26]. As this study included a relatively small number of patients in a single institution, further prospective studies are warranted with a larger cohort involving multiple institutions.

Conclusions

LVA surgery was still feasible under conditions where ICG lymphography or supermicrosurgery instruments were not available. Lymphoscinticraphy and HFUS could be effectively used for preoperative evaluation before LVA. More strict patient selection based on lymphoscintigraphy and HFUS findings would further improve the overall outcomes of LVA.

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Author contributions

TH arranged for data collection and statistical analysis. TY and TH both arranged for manuscript writing. the cases were accomplished by TY and TH.

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No datasets were generated or analysed during the current study.

Data availability

Declarations

Ethics approval and consent to participate

This study was performed after approval of the ethical committee of Shefaa Al Orman Hospital, Luxor -Egypt. All patients provided an informed consent before participation.

Consent for publication

All patients were consented for publication of their relevant data and pictures.

Competing interests

The authors declare no competing interests.

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