Journal of Plastic, Reconstructive & Aesthetic Surgery (2019) 72, 62–70

JPRAS
An International Journal of Surgical Reconstruction
www.JPRASurg.com

The dynamic-lymphaticovenular anastomosis method for breast cancer treatment-related lymphedema: Creation of functional lymphaticovenular anastomoses with use of preoperative dynamic ultrasonography☆

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Received 7 April 2018; accepted 7 September 2018

KEYWORDS
Lymphaticovenular anastomosis;
Lymphedema;
Dynamic ultrasonography;
Supermicrosurgery

Abstract *Background:* Lymphaticovenular anastomosis (LVA) is generally an effective procedure for breast cancer treatment-related upper extremity lymphedema (UEL). Clinical improvement is, however, limited by the degree of sclerosis of the lymphatic vessels. We have developed a method by which we use dynamic ultrasonography to depict vessels through which lymph can be propelled into the LVA under the power of the patient's natural hand movements.
Methods: We assessed the dynamic-LVA method by comparing clinical details of 15 cases of breast cancer treatment-related lymphedema treated by dynamic LVA and 15 corresponding cases treated by conventional LVA.

☆ This paper was presented in part at the 9th Congress of the World Society for Reconstructive Microsurgery (WSRM 2017) held at Seoul, Korea, June 15–17, 2017, and Lymphology 2017, the 26th World Congress of Lymphology, held at Barcelona, Spain, September 27–30, 2017.

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https://doi.org/10.1016/j.bjps.2018.09.005

Results: Placement of incisions at a total of 90 forearm sites (three per patient) yielded 90 LVAs (32 in "linear ICG lymphography pattern incisions" and 58 in "stardust pattern incisions"). Sclerotic lymphatic vessels were encountered at greater frequency in "linear pattern incisions" in the dynamic LVA group than in the conventional LVA group (7.1% vs. 38.9%, $P = 0.030$). Postoperative volume reduction was significantly greater in the dynamic LVA group than in the conventional LVA group; the UEL index at 1 month was 8.12 ± 3.08 vs. 3.74 ± 5.82, respectively ($P = 0.018$), and at 1 year was 10.23 ± 6.16 vs. 2.03 ± 9.36, respectively ($P = 0.014$).
Conclusions: Dynamic LVA is clinically beneficial because the imaging guides decisions over the locations where the incisions should be placed so that a patient's natural hand motions can be used to propel lymph into the anastomosis despite the presence of sclerosis and because even early improvements are obtained.

Introduction

Lymphaticovenular anastomosis (LVA) is a generally effective, minimally invasive surgical treatment for lymphedema.[1-10] Although LVA reliably reduces the severity of the disorder in the early stage, its effect is often limited when the disorder has reached the late stage. In addition, therapeutic efficacy of LVA is difficult to ascertain during the early postoperative period because the reduction in symptoms occurs gradually.

One main factor hindering therapeutic efficacy in patients with progressive upper extremity lymphedema (UEL), including those with progressive UEL related to breast cancer treatment, is sclerosis of the lymphatic vessels.[11-13] Lymphatic vessels with degenerated smooth muscle are inadequate to propel lymph into the anastomosed vein.

Indocyanine green (ICG) lymphography is useful as a minimally invasive imaging modality for the detection of lymphatic vessels,[14-15] which can be easily detected by the appearance of linear patterns upon ICG lymphography of the affected limb. Lymphatic vessels in the affected limb that are totally concealed by the presence of stardust patterns can be mapped as mirror images of the linear patterns observed in the non- or less affected limb.[16,17] Furthermore, recent advancements in ultrasonography (US) currently allow detection not only of the adequacy of a subcutaneous vein as recipient for LVA but also of the lymphatic vessel itself.[18-21] Methodological advances in imaging studies, including application of the mirror image concept, have made finding lymphatic vessels for LVA in patients with UEL fairly easy. However, decisions regarding where to place the incisions on the identified or predicted lymph lines to obtain the maximum benefit from LVA are made somewhat arbitrarily.

We reported taking advantage of knee joint movement to propel lymph into the vein incorporated into the LVA when LVA is performed for lower extremity lymphedema (LEL).[22,23] Muscle movement is enlisted to assist the sclerotic lymphatic vessels in propelling lymphatic fluid to the LVA site. The procedure ensures good LVA outcomes; early improvement is seen even in patients with severe lymphedema who only have sclerotic lymphatic vessels. The advantage of having recipient vessels at the incision point also ensures clinical efficacy: subcutaneous veins there usually have good valves that result in continuous lymph flow with less venous reflux. Visconti et al. reported the importance of the recipient venule in LVA for good surgical outcomes and suggested classification of flow dynamics for recipient vessels.[21]

We have since developed a new procedure for LVA in patients with UEL with the goal of ensuring effective outcomes in all patients with UEL, including those whose relevant lymphatic vessels are severely sclerosed. The findings from dynamic US performed preoperatively are used to determine placement of the incisions so that natural hand motions can be used to propel lymph through the LVA even when the lymphatic vessel is sclerotic. We began applying our new procedure, which we refer to as dynamic LVA, in November 2016. We describe a retrospective observational study that we conducted to evaluate the efficacy of the new procedure. The study was conducted under approval from the St. Marianna University School of Medicine Ethics Committee.

Methods

Study patients

The study included 30 patients in whom three LVAs had been created for International Society of Lymphology (ISL) stage 2a and 2b UEL.[24] Each of the three LVAs was created through one of three incisions placed in the arm. Fifteen of the patients had been treated between July 2014 and October 2016 by conventional LVA (conventional LVA group), and 15 had been treated between November 2016 and May 2017 by dynamic LVA (dynamic LVA group). All included patients had undergone compression therapy with an elastic sleeve. The LVAs in all 30 patients were created by one study author (Y.S.).

Identifying relevant lymph lines in the lymphedematous arm

To identify and predictively map the relevant lymphatic vessels, ICG lymphography was performed preoperatively for each patient as follows: 0.1 mL of ICG (Diagnogreen 0.25%; Daiichi Pharmaceutical, Tokyo, Japan) was injected intradermally at the second web space of both hands, at the anterior border of the styloid process of both radii, and at the anterior border of the styloid process of both ulna.

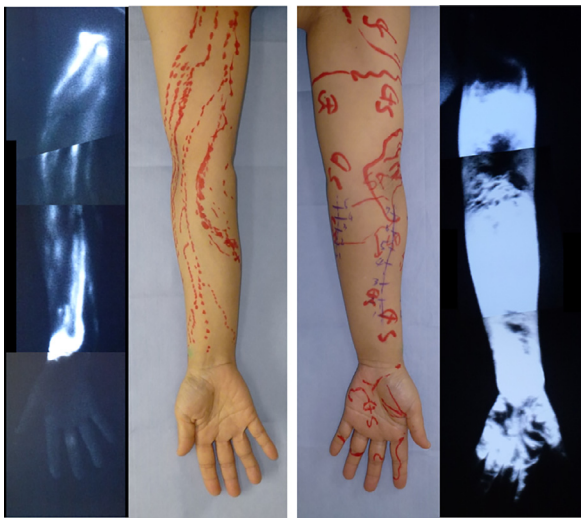

Figure 1 Identification of the lymph lines in a lymphedematous arm when a lymphography stardust pattern is seen. (Right) Preoperative indocyanine green (ICG) lymphogram showing normal linear patterns in a patient's right arm. (Left) Preoperative ICG lymphogram showing dermal backflow in the same patient's lymphedematous left arm. The stardust pattern fully concealed the possible "linear pattern" lymph lines. In situations like this, the lymph lines in the left arm are assumed to be mirror images of the linear patterns in the nonaffected right arm.

ICG fluorescence imaging was performed after 2 h of administering the injections. The lymphedematous forearm was divided conceptually into three regions—anterior, posterior, and ulnar—because three major lymphatic pathways are considered to work independently at the forearm.[25] To allow creation of an LVA within each region, we looked for a lymph line, identified as a linear ICG lymphography pattern, in each of the three regions.[14] When a linear pattern was partially concealed by a stardust pattern, the concealed part of the lymph line was mapped as a mirror image of the linear pattern seen in the non- or less affected limb. When a stardust pattern involved the entire forearm, the entire lymph line was mapped as a mirror image of the linear pattern seen in the non- or less affected limb (Figure 1).

Dynamic-LVA method

As noted above, 15 of the study patients had been treated by means of dynamic LVA, meaning that we used preoperative dynamic US of the forearm to determine the incision points. Dynamic LVA is performed as follows: Each of the three lymph lines in the lymphedematous arm is traced on the patient's arm, and each tracing is then marked at 1.5 cm increments. Dynamic US is performed at each mark starting at the distal end. The patient is instructed to move the corresponding hand continuously throughout the US examination. With a grasping motion (systolic phase), the soft tissue that includes lymphatic vessels and veins for LVA is compressed between the skin surface and the deep fascia, and with a hand-opening motion, soft tissue compression is released (diastolic phase) (Figure 2). Flexion and extension of the wrist have the same effects.

US is used to ascertain the existence of effective muscle pumping at each mark, which is evaluated by the presence of a pumped subcutaneous vein and/or difference in thickness of the soft tissue that is compressed by muscle movement. If a subcutaneous vein larger than 1.0 mm in diameter at the site of a mark is compressed by muscle movement in the systolic phase, that mark is selected for placement of an incision. If there are more than two marks that correspond to such a subcutaneous vein, the thickness of the soft tissue at each mark is measured in the diastolic and systolic phases on the dynamic US images, and the incision is placed at the mark with the greater difference in soft tissue thickness (Figure 2) (**See Video, Supplemental Digital Content 1**, which depicts application of dynamic US for choosing the incision sites). When we cannot visualize contraction of such a subcutaneous vein, we place an incision at the mark with the greatest difference in soft tissue thickness (this method is in contrast with that used for conventional LVA in which each incision is made at the most edematous point along the lymph line). LVA is performed through each incision at the time of the incision.

LVA in the study patients

LVA was performed under local anesthesia in all 30 patients.[8,22,23] At each incision site, the largest lymphatic vessel was identified from among lymphatic vessels that were detected over or under the superficial fascia in the subcutaneous tissue, and this vessel was cut. After detection of a vein, the distal end of the lymphatic vessel was anastomosed to the vein with a 12-0 nylon suture. An operating microscope was used to confirm patency of the LVA, i.e., observation of lymph-blood border movement across the anastomosis. One week later, the conservative therapy that patients had been undergoing preoperatively was reinstated.

Statistical analysis

All values are reported as mean ± SD. Patients' clinical characteristics and intraoperative findings in lymphatic vessels were compared between the two patient groups. Lymphatic vessel sclerosis was defined as a thickened lymphatic vessel wall with white appearance under intraoperative microscopic observation.[13] The UEL index was determined preoperatively and then postoperatively at 1 month, 6 months, and 1 year, and for the study, reduction in volume was compared between the two groups.[26] All P values were two sided, and statistical significance was accepted at $P < 0.05$. All statistical analyses were performed with JMP Pro 12 software (SAS Institute, Cary, NC, USA).

Results

Patient's clinical characteristics for each group are shown in Table 1. None of the characteristics we assessed differed significantly.

Three LVAs were created in all 30 patients. Each of the three lymph lines identified was used for an LVA. Thus, 90

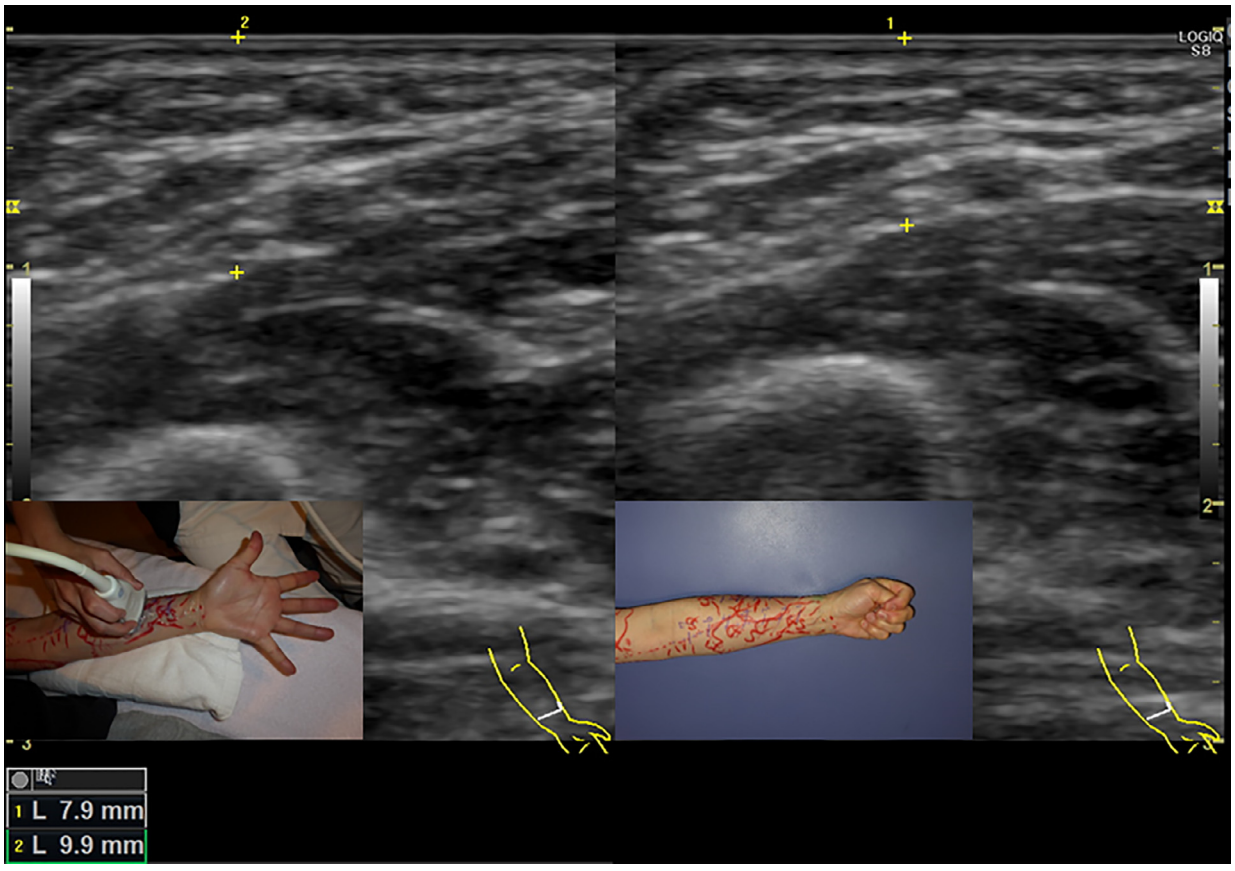

Figure 2 Determining the incision point in the dynamic-lymphaticovenular anastomosis (dynamic-LVA) method. On the lymph line, transverse marks are made at 1.5 cm increments starting at the distal end of the line. Dynamic ultrasonography is performed at all marks along the lymph line tracing. With a grasping motion (systolic phase), the soft tissue that includes lymphatic vessels and veins for LVA is compressed between the skin surface and the deep fascia, and with a hand-opening motion (diastolic phase), the soft tissue is released. Effective venous pumping is evaluated on the basis of the existence of a blood-filled subcutaneous vein larger than 1.0 mm in diameter and/or a marked between-phase difference in the thickness of the soft tissue. (Right) In the case depicted, because no pumped subcutaneous vein larger than 1.0 mm in diameter was seen at any of the marks in the systolic phase, the thickness of the soft tissue was measured at each mark in the systolic and diastolic phases. In the systolic phase, the soft tissue was 7.9 mm thick at the third mark. (Left) In the diastolic phase, the soft tissue was 9.9 mm thick at this mark. Thus, the third mark was selected as the incision site because 2.0 mm was the greatest between-phase difference found in the thickness of the soft tissue at the lymph line.

anastomoses were created through 90 incisions. Lymphatic vessels were detected in all incisions in all 30 patients.

Diameters of the lymphatic vessels did not differ significantly between the conventional LVA group versus the dynamic LVA group (0.43 ± 0.25 mm vs. 0.47 ± 0.14 mm; $P = 0.332$) or in the prevalence of dynamic flow of lymph to veins without venous reflux (64.4% vs. 73.3%; $P = 0.362$) (Table 2). Sclerotic lymphatic vessels were encountered at a significantly greater frequency in "linear pattern incisions" (incisions made for lymph lines with a distinct linear pattern) in the dynamic LVA group versus the conventional LVA group (7.1% [1/14 incisions] vs. 38.9% [7/18 incisions]; $P = 0.030$). The frequency of encountering sclerotic lymphatic vessels in "stardust pattern incisions" did not differ significantly between the groups (80.1% [25/31 incisions] vs. 74.1% [20/27 incisions]; $P = 0.550$).

Diameters of the lymphatic vessels were significantly larger by the thickened wall of the vessels in ISL stage2b versus stage 2a (0.40 ± 0.13 mm vs. 0.52 ± 0.27 mm; $P = 0.013$) (Table 3). Sclerotic lymphatic vessels were encountered at significantly greater frequency in ISL stage 2b versus stage 2a (42.6% [23/54 incisions] vs. 83.3% [30/33 incisions]; $P < 0.001$).

Postoperative change in lymphedema severity for each patient group is shown in Table 4. Affected limb circumference was reduced at 1 and 6 months in all 15 patients in the dynamic LVA group, but by 6 months, lymphedema had recurred in four patients in the conventional LVA group ($P = 0.013$). Volume reduction was significantly greater in the dynamic LVA group than in the conventional LVA group. Mean reduction in the UEL index was 8.12 ± 3.06 ($n = 15$) vs. 3.74 ± 5.82 ($n = 15$) ($P = 0.018$) at 1 month, 8.74 ± 3.58 ($n = 15$) vs. 2.62 ± 10.39 ($n = 15$) ($P = 0.046$) at 6 months, and 10.23 ± 6.16 ($n = 15$) vs. 2.03 ± 9.36 ($n = 13$) ($P = 0.014$) at 1 year (Figure 3). Volume reduction did not differ significantly between ISL stage 2a and stage 2b (Table 5).

Table 1 Characteristics of patients in the conventional LVA group and dynamic LVA group.

	Conventional LVA ($n=15$)	Dynamic LVA ($n=15$)	*P* value
Age (years)	37–69 (mean, 53.3)	48–74 (mean, 59.1)	0.076†
Sex			
Female	15 (100%)	15 (100%)	1.000‡
Male	0 (0%)	0 (0%)	
Duration of edema (months)	3–53 (mean, 19.1)	3–124 (mean, 36.9)	0.128†
BMI	17.4–31.8 (mean, 22.7)	16.5–31.1 (mean, 23.2)	0.750†
Etiology of lymphedema			1.000‡
Breast cancer treatment	15 (100%)	15 (100%)	
ISL Stage			
2a	9 (60.0%)	9 (60.0%)	1.000‡
2b	6 (40.0%)	6 (40.0%)	

Number and percentage of patients are shown unless otherwise indicated.
LVA, lymphaticovenular anastomosis; BMI, body mass index; ISL, International Society of Lymphology.
† by Mann–Whitney *U* test.
‡ by χ^2 test.

Table 2 Intraoperative findings in the conventional LVA group and dynamic LVA group.

	Conventional LVA ($n=45$ vessels)	Dynamic LVA ($n=45$ vessels)	*P* value
Diameter of lymphatic vessels (mm)	0.43 ± 0.25	0.47 ± 0.14	0.332†
Degeneration of lymphatic vessels			
Total	26/45 (57.8%)	27/45 (60.0%)	0.830‡
In "linear pattern" incisions	1/14 (7.1%)	7/18 (38.9%)	0.030‡
In "stardust pattern" incisions	25/31 (80.1%)	20/27 (74.1%)	0.550‡
Lymph-to-venous flow			
Total	29/45 (64.4%)	34/45 (75.6%)	0.249‡
In "linear pattern" incisions	9/14 (64.3%)	12/18 (66.7%)	0.888‡
In "stardust pattern" incisions	19/31 (61.3%)	22/27 (81.5%)	0.088‡

Number (and percentage) of lymphatic vessels are shown.
LVA, lymphaticovenular anastomosis; "linear pattern" incisions, incisions made at sites where the ICG lymphography pattern was linear; "stardust pattern" incisions, incisions made at sites where a stardust ICG lymphography pattern was seen.
† by Mann–Whitney *U* test.
‡ by χ^2 test.

Table 3 Intraoperative findings in ISL stages 2a and 2b upper extremity lymphedema.

	ISL stage 2a ($n=54$ vessels)	ISL stage 2b ($n=36$ vessels)	*P* value
Diameter of lymphatic vessels (mm)	0.40 ± 0.13	0.52 ± 0.27	0.013†
Degeneration of lymphatic vessels			
Total	23/54 (42.6%)	30/36 (83.3%)	<0.001‡
In "linear pattern" incisions	4/27 (14.8%)	4/5 (80.0%)	0.004‡
In "stardust pattern" incisions	19/27 (70.4%)	20/31 (64.5%)	0.635‡
Lymph-to-venous flow			
Total	39/54 (64.4%)	22/36 (61.1%)	0.271‡
In "linear pattern" incisions	19/27 (70.4%)	2/5 (40.0%)	0.201‡
In "stardust pattern" incisions	20/27 (74.1%)	20/31 (64.5%)	0.431‡

Number (and percentage) of lymphatic vessels are shown.
ISL, International Society of Lymphology; "linear pattern" incisions, incisions made at sites where the ICG lymphography pattern was linear; "stardust pattern" incisions, incisions made at sites where a stardust ICG lymphography pattern was seen.
† by Mann–Whitney *U* test.
‡ by χ^2 test.

Table 4 Postoperative improvement in the conventional LVA group and dynamic LVA group.

	Conventional LVA	Dynamic LVA	*P* value
1 month after surgery	(*n* = 15 limbs)	(*n* = 15 limbs)	
Limb volume reduction	13/15 (86.7%)	15/15 (100%)	0.0877†
Change in UEL index	3.74 ± 5.82 (−7.68-12.18)	8.12 ± 3.08 (3.22-14.52)	0.0176‡
6 months after surgery	(*n* = 15 limbs)	(*n* = 15 limbs)	
Limb volume reduction	11/15 (73.3%)	15/15 (100%)	0.0130†
Change in UEL index	2.62 ± 10.39 (−29.33-10.97)	8.74 ± 3.58 (4.41-18.52)	0.0458‡
1 year after surgery	(*n* = 13 limbs)	(*n* = 15 limbs)	
Limb volume reduction	9/13 (69.2%)	15/15 (100%)	0.0085†
Change in UEL index	2.03 ± 9.36 (−15.51-16.53)	10.23 ± 6.16 (3.83-26.17)	0.0140‡

Number and percentage of patients are shown unless otherwise indicated.
LVA, lymphaticovenular anastomosis; UEL, upper extremity lymphedema.
† by χ^2 test.
‡ by Mann-Whitney *U* test.

Table 5 Postoperative improvement in ISL stages 2a and 2b upper extremity lymphedema.

	ISL stage 2a	ISL stage 2b	*P* value
1 month after surgery	(*n* = 18 limbs)	(*n* = 12 limbs)	
Limb volume reduction	16/18 (88.9%)	12/12 (100%)	0.1437†
Change in UEL index	5.13 ± 5.31 (−7.68-10.97)	7.13 ± 4.69 (0.45-14.52)	0.2872‡
6 months after surgery	(*n* = 18 limbs)	(*n* = 12 limbs)	
Limb volume reduction	15/18 (83.3%)	11/12 (91.7%)	0.4994†
Change in UEL index	5.45 ± 5.22 (−8.99-13.59)	6.02 ± 11.70 (−29.33-18.52)	0.8770‡
1 year after surgery	(*n* = 17 limbs)	(*n* = 11 limbs)	
Limb volume reduction	14/17 (82.4%)	10/11 (90.9%)	0.5167†
Change in UEL index	5.02 ± 6.97 (−13.89-15.21)	8.59 ± 10.90 (−15.51-26.17)	0.3481‡

Number and percentage of patients are shown unless otherwise indicated.
ISL, International Society of Lymphology; UEL, upper extremity lymphedema.
† by χ^2 test.
‡ by Mann-Whitney *U* test.

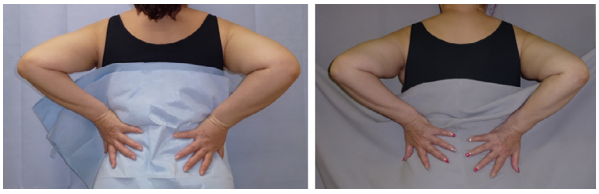

Figure 3 Right upper extremity lymphedema (UEL) treated by the dynamic-lymphaticovenular anastomosis (dynamic-LVA) method. (Left) A 61-year-old woman suffered right International Society of Lymphology stage 2b UEL after undergoing breast cancer treatment 19 months ago. The preoperative right UEL index was 107.4. Lymphedema-associated reddened skin was observed on her right arm. (Right) Three lymphaticovenular anastomoses were created by the dynamic-LVA method. Soon after the surgery, the reddening disappeared, and at 1 year, the right UEL index was reduced to 95.7.

Discussion

LVA is undertaken to bypass lymphatic blockage and provide alternate routing of drainage into the venous system. Clinical effects of LVA performed for peripheral lymphedema vary between patients: some patients with severe lymphedema show marked clinical improvement whereas others show only limited improvement.

Degeneration of lymphatic vessel smooth muscle cells is thought to explain the varied surgical outcomes; lymphatic vessels in some patients are inefficient in pushing lymph into the vein incorporating the LVA.[11-13] Using our reported superior-edge-of-the-knee incision method to identify suitable lymphatic vessels, we could achieve reliable flow in patients treated for LEL despite degeneration of smooth muscle cells in some of these patients.[22,23] Natural knee joint movement results in upward propulsion of lymph into the anastomosed vein. As with the superior-edge-of-the-knee

incision method, the dynamic LVA method described herein allows appropriate incision points to be found for LVA in the arm so that natural joint movement can be used to overcome the limitations of even sclerotic lymphatic vessels (**See Video, Supplemental Digital Content 2**, which depicts increased lymph flow at the LVA during hand movement, facilitated by the dynamic-LVA method).

Technically advanced US performed preoperatively to detect lymphatic vessels and veins can facilitate LVA.[18-20] Although such a nondynamic study is useful for detecting suitable lymphatic vessels and veins, it cannot always ensure optimum clinical results. Before developing the dynamic-LVA method, we tried to establish specific points where LVA should be performed in all patients with UEL. Dynamic US was first applied for LEL by the authors in 2016 to evaluate muscle movements at the superior-edge-of the-knee incision point. Because the gracilis muscle works as a pump there, we thought that dynamic US would allow discovery of specific and best locations for LVA in UEL. Despite our efforts to find workable locations for all patients, we could not establish incision points suitable for LVA in all types of UEL. As our surgical group members reported trials using a prototype method of dynamic LVA, best sites for UEL seemed to be at the specific points above the specific muscles.[27] However, sites very effective for LVA in some patients were not suitable for LVA in others. We concluded that the best sites for LVA in patients with UEL are not uniform because muscle development and the structure of muscle tissues can vary. The gracilis muscle works as the power source in all patients with LEL to push lymph because knee joint movement is simple,[22,23] but hand movements differ radically from knee joint movements. The best incision sites in patients with UEL must be determined individually because the patient's dominant hand, lifestyle, work, and other activities affect muscle development and tissue structure in the arm. The dynamic-LVA method resolves the difficulty in achieving effective LVA for UEL by visualizing how lymph is propelled through the anastomosis in each patient.

Recent developments in imaging have facilitated intraoperative detection of lymphatic vessels for LVA.[18-21,28] ICG lymphography is particularly useful in detecting lymphatic vessels,[4-10,14-17,25] but its ability to detect lymphatic vessels in patients with progressive lymphedema is limited because the stardust or diffuse pattern conceals the existing linear patterns. To overcome this limitation, we apply predictive lymph mapping by using an image of the non- or less affected limb to map lymphatic vessels in patients with severe LEL or UEL.[16,17] Because mirror images have potential limitations in preciseness, further developments are expected in identifying lymph lines in more detail. Hayashi et al. recently reported a novel method to accurately detect lymphatic vessels by US.[18] Such technological advancements will complement the preciseness of mirror images. Thus, the main challenge in LVA has shifted from the detection of lymphatic vessels to how best to use the detected lymph line.

In ICG-navigated LVA, regions in which linear patterns are observed are generally recommended for LVA because incisions in these areas tend to reveal suitable, typically nonsclerotic, lymphatic vessels, especially in patients with early-stage UEL (Table 3).[13,29] We found remarkable clinical

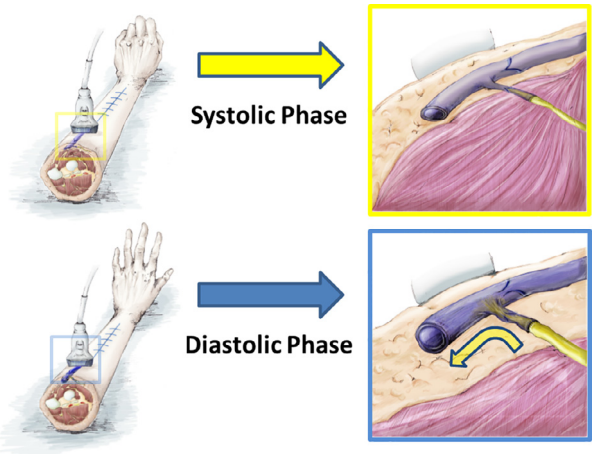

Figure 4 Pumping system used in the dynamic-LVA method. On the mark at which an LVA is created, subcutaneous soft tissues including lymphatic vessels and veins are gently compressed between the skin surface and the deep fascia during hand grasping (systolic phase, above) and then released during hand opening (diastolic phase, below). The muscles in the arm act as a pump to efficiently propel lymph into the anastomosed vein at the point where the subcutaneous vein larger than 1.0 mm in diameter is compressed in the systolic phase. Continuous pumping of blood through a subcutaneous vein between the systolic and diastolic phases means that negative pressure exists in the vein during the early diastolic phase, and hence, lymph will be propelled into the anastomosed vein; the negative pressure in the relatively large subcutaneous vein influences nearby veins, including the anastomosed vein.

improvement in our dynamic LVA group patients, notwithstanding the high number of sclerotic lymphatic vessels found in "linear patterns incisions" in this group. Even when we applied the dynamic-LVA method, a stardust area was sometimes selected as an incision point regardless of the presence of a linear pattern along the lymph line. Nevertheless, our results indicate that there is a better chance of obtaining effective lymphatic flow when the incision is placed appropriately, even when the lymphatic vessel is sclerotic.

Dynamic US is a direct, definite way to evaluate motion of the soft tissues and muscles.[30,31] After identifying the relevant lymph lines, dynamic US can be applied to effectively utilize the lymph line by detecting specific points on the line where subcutaneous soft tissues including lymphatic vessels and veins are gently compressed during hand grasping (systolic phase) and then released during hand opening (diastolic phase) (Figure 4). The arm muscles act as a pump to efficiently propel lymph into the anastomosed vein at the point where the subcutaneous veins are compressed between phases and the difference in soft tissue thickness is greatest.

Our rationale for determining incision points with the dynamic-LVA method lies in its ability to depict the potential for lymph propulsion into the anastomosed vein. Although propulsion depends in part on the surrounding soft tissue thickness, continuous pumping of blood through subcutaneous veins with a diameter larger than 1.0 mm in the diastolic phase is a more important feature suggestive of

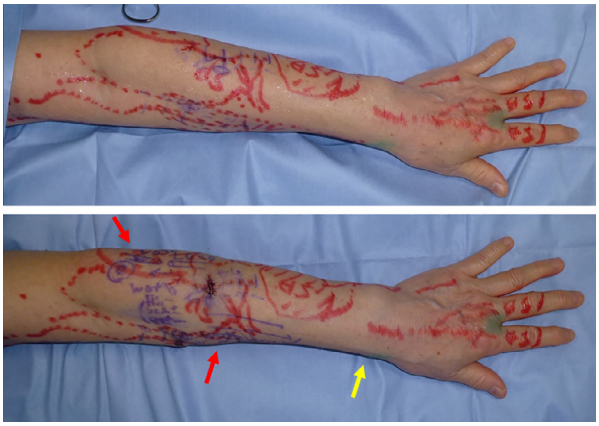

Figure 5 Early improvement of edema. In this case, LVAs were created within three incisions by the dynamic-LVA method. Upon completion of the surgery, the stiffness and the size of the patient's left arm were significantly reduced around the site of the LVAs (red arrows). The subcutaneous vein (yellow arrow) at the left wrist, which the patient had not been able to see since the lymphedema set in, was apparent upon completion of the surgery.

powerful propulsion of lymph at the incision point. Continuous pumping of blood through a subcutaneous vein between the two phases means that negative pressure exists in the vein during the diastolic phase, and thus, lymph will be propelled by muscle movement into the anastomosed vein; the negative pressure in the relatively large (> 1.0 mm diameter) subcutaneous vein influences nearby veins, including the anastomosed vein.

The recurrence of UEL within 6 months after the surgery in four of 15 conventional LVA group patients likely resulted from occlusion of the anastomosed vessel or weak lymph-to-venous flow. A major difficulty in some LVA cases is subsequent occlusion of the anastomosed vessel(s).[32] The risk of occlusion is increased when the lymphatic vessel is sclerotic and thus yields poor lymph flow.[9,12,13] Failure in recipient vessel selection can also increase the risk of occlusion.[21] The resulting stagnation of fluid caused by both the status of the lymphatic vessel and the vein selected for anastomosis leads to LVA occlusion. We speculate that the dynamic-LVA method will substantially reduce the incidence of LVA occlusion because normal hand movements result in continuous lymph flow through the pumped anastomosed vessels.

The clinical significance of the dynamic-LVA method is very early improvement of the edema seen intraoperatively in our patients as decreased stiffness and volume reduction around the LVAs (Figure 5). Such improvement might also signal LVA patency and prove useful in post-treatment patient monitoring.

Potential advantages of the dynamic-LVA method are as follows: degenerated lymphatic vessels can also be used for anastomosis because the therapeutic effect originates, theoretically, from exploitation of natural hand movements to propel the lymph; veins are easily detected by US because dynamic hand movements enhance venous flow; the likelihood of early recurrence of lymphedema is lessened; and clinical improvement in edema is readily identifiable, thereby manifesting immediately after the surgery.

Conclusions

The dynamic-LVA method is clinically beneficial because imaging guides the placement of incisions so that a patient's natural hand motions are used to propel lymph through the anastomosis, and early improvements are obtained. The results of this new method are promising, but will require further confirmation through longer follow-up in a greater number of patients.

Disclaimers and conflicts of interest

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

Acknowledgments

The authors thank Miyuki, Hanano, Mayoko, and all members of our department for their kind support during manuscript preparation. We also thank Kei Ono, Nozomi Oba, and Maiko Toguchi for their contributions in performing dynamic ultrasonography; Makiko Haragi for her clear anatomical illustrations; and Tina Tajima for her meticulous English editing. We specially thank Isao Koshima for naming our dynamic-LVA method "*Kinouteki*-LVA" in Japanese or "functional LVA" in English. This work was supported by JSPS KAKENHI, Grant no. JP17K17038.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2018.09.005.

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