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The Dynamic Lymphaticovenular Anastomosis for Breast Cancer–related Lymphedema without Compression: Salvaging Lymphedema Patients Who Lost Conservative Treatment Opportunity

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Background: In conservative treatment for breast cancer–related lymphedema (BCRL), compression therapy has a crucial role. However, some BCRL patients are unable to use compression, and then their lymphedema continues to worsen as they miss treatment opportunity. Although lymphaticovenular anastomosis (LVA) is an effective and minimally invasive surgical treatment for BCRL, compression therapy is still important to enhance lymphatic fluid flow in LVA. The authors previously reported the dynamic LVA method for BCRL, in which patient's natural hand movements theoretically propel lymph to the anastomosed vein. This study is conducted to clarify whether dynamic LVA can salvage BCRL patients without pre- and postoperative compression therapy.

Methods: The study involved 17 BCRL patients, 18 limbs. All patients had International Society of Lymphology stage-2 lymphedema, but they had no compression: six patients had difficulty by other diseases to undergo compression, and other 11 patients refused any compression usage because of the burden of the treatment itself. Three dynamic LVAs were performed in each patient.

Results: Patients' mean age was 60.4±10.1, and mean body mass index was 24.0±3.3. The mean follow-up period was 25.5±9.2 months. The volume of the lymphedematous limb, according to the upper extremity lymphedema (UEL) index, was reduced in all 18 limbs postoperatively (postoperative UEL index 101.8±9.4 versus preoperative UEL index 116.0±20.1; $P < 0.01$). Twelve of the 18 limbs were cured without edema.

Conclusion: Even without compression therapy, International Society of Lymphology stage-2 BCRL patients can be treated by the dynamic LVA method.
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INTRODUCTION

Lymphaticovenular anastomosis (LVA) is an effective, minimally invasive surgical treatment for upper and lower extremity lymphedema.[1–10] In a majority of cases, surgical improvements are supported by continuous compression therapy both before and after LVA.

Preoperative usage of compression can control edema, lymphedematous stiffness, and inflammation; it improves LVA treatment outcome. In addition, preoperative complete decongestive therapy for severe lymphedema makes LVA procedures easy because lymphatic fluid emerging from the surgical wound can be decreased in the less edematous limb by the therapy. Postoperative usage of compression is also important in LVA. Physiologically, lymphatic flow power, which is mainly created by the smooth

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muscle of the lymphatic vessels, has an important role in propeling lymphatic fluid into the anastomosed vein in LVA.[11–14] However, patients with progressive lymphedema, including those with breast cancer–related lymphedema (BCRL), have sclerosis of the lymphatic vessels.[12–14] Because lymphatic vessels with degenerated smooth muscle have difficulty working as an adequate power source in producing lymphatic flow, postoperative compression therapy is generally recommended for patients who taken LVA to increase lymphatic flow by pushing lymphatic fluid to the anastomosed vein.[15–17] Therefore, compression therapy has a key role in surgical treatment for lymphedema.

However, in treating lymphedema, we should not overlook the fact that there are lymphedema patients who cannot undergo compression therapy; some patients have difficulty to use compression because of their diseases, including contact dermatitis or muscle atrophy, and other patients refuse any compression because of the burden of compression therapy itself for their daily life. Although compression therapy is highly recommended for all BCRL patients, patients' compliance for conservative therapy has limitations.[18–20] Compression-unable BCRL patients gradually reveal uncontrollable progressive lymphedema because they lose important treatment opportunities.

The authors previously reported a reliable method, the dynamic lymphaticovenular anastomosis (dynamic LVA) method, in which preoperative dynamic ultrasonography is used to find the best incision point where patient's natural hand movements work as an additional power source to propel lymphatic fluid to the anastomosed vein.[21–24] Most BCRL patients treated by the dynamic LVA revealed immediate improvements of lymphedema even before they restarted postoperative compression therapy. Some of these patients had finished postoperative compression therapy by their own decisions because they felt some release from lymphedema. Dynamic LVA seems to have the possibility to treat BCRL with high clinical efficacy, without compression.

To resolve problems in BCRL patients who cannot undergo compression therapy, we conducted this retrospective study to evaluate feasibility of dynamic LVA in treating compression-unable BCRL patients. The study was conducted under approval from the St. Marianna University School of Medicine ethics committee (approval no. 4768). This study is the first trial of LVA salvage for compression-unable BCRL patients who lost treatment opportunity.

Takeaways

Question: There are many breast cancer–related lymphedema (BCRL) patients who are dropouts from conservative treatment. These patients' lymphedema usually continues to worsen as they miss treatment opportunities. However, it is apparent that they need to be enlightened and salvaged. Can lymphaticovenular anastomosis effectively treat these patients?

Findings: The dynamic lymphaticovenular anastomosis could salvage BCRL patients who cannot use any compression therapy with high volume reduction of edema.

Meaning: Surgical treatment of lymphedema can treat more BCRL patients, including patients who are dropouts from conservative treatment.

METHODS

Study Patients

In the study period between October 2017 and December 2019, most BCRL patients treated in our institutions were under compression therapy, and only 17 patients (18 limbs) were unable to use any compression therapy. The study patients revealed International Society of Lymphology (ISL) stage 2a and 2b BCRL,[25] and their lymphedema continued to worsen without adequate conservative treatment. All 17 patients did not undergo any compression therapy before or after dynamic LVA: six patients (seven limbs) had difficulty using compression by other diseases, and the other 11 patients refused any compression because compression therapy itself was a burden for their work and daily lives. Characteristics of patients are shown in Table 1. Five patients had too severe contact dermatitis to undergo compression, and one bilateral BCRL patient had too much muscle weakness of both hands from myopathy to undergo compression. All 18 upper limbs were treated by three LVAs from three incisions using dynamic LVA, in which preoperative dynamic ultrasonographic findings were used to determine the incision sites with the maximum muscle pumping by patients' natural hand movements (we reported the detail of the method as the dynamic LVA method as follows). The LVAs in all 18 limbs were created by one of the authors of this study (Y.S.). No pre- or postoperative compression therapy was used, and patients were only recommended to perform five-time voluntary hand grasping and opening exercises when they felt some form of edema at the arm.

Preoperative Lymph Mapping on the Lymphedematous Arm (Fig. 1)

As preparation of the method, the lymphatic vessel pathways (lymph lines) were identified first. Any modalities to visualize the lymphatic vessels can be used to identify lymph lines in performing the dynamic LVA method. In this study, we used bilateral indocyanine green (ICG) lymphography findings at affected and nonaffected arms, as we previously reported.[21–24] ICG lymphography was performed to map the lymph lines in the patients' arms (Fig. 2). We divide the lymphedematous forearm conceptually into three regions (anterior, posterior, and ulnar) because LVAs work on each major lymphatic pathway in the arm independently.[26] LVAs were created on each major lymphatic pathway to reduce edema at three different regions.

In ICG lymphography, each 0.1 mL ICG (Diagnogreen 0.25%; Daiichi Pharmaceutical, Tokyo, Japan) was injected intradermally at the second and third 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

Table 1. Characteristics of Patients in the ISL Stage 2a Group and ISL Stage 2b Group

Characteristic	Total, n = 18 Limbs	ISL Stage 2a, n = 5 Limbs	ISL Stage 2b, n = 13 Limbs	*P*
Age (y)	44–81 (mean, 60.4)	48–67 (mean, 58.2)	44–81 (mean, 63.8)	0.256*
Gender				
Feminine	18 (100%)	5 (100%)	13 (100%)	1.000†
Masculine	0 (0%)	0 (0%)	0 (0%)	
Duration of edema (mo)	3–132 (mean, 39.7)	7–132 (mean, 63.2)	3–96 (mean, 30.6)	0.138*
BMI	18.7–29.6 (mean, 24.0)	19.0–24.9 (mean, 22.0)	18.7–29.6 (mean, 24.8)	0.104*
Etiology of edema				
Breast cancer	18 (100%)	5 (100%)	13 (100%)	1.000†
No compression reason				
Other diseases	7 (38.9%)	1 (20.0%)	6 (46.2%)	0.322†
Contact dermatitis	5	0	5	
Myopathy	2	1	1	
Burden of life	11 (61.1%)	4 (80.0%)	7 (53.8%)	

Number and percentage of limbs are shown, unless otherwise indicated.
*By Mann-Whitney *U* test.
†By χ^2 test.

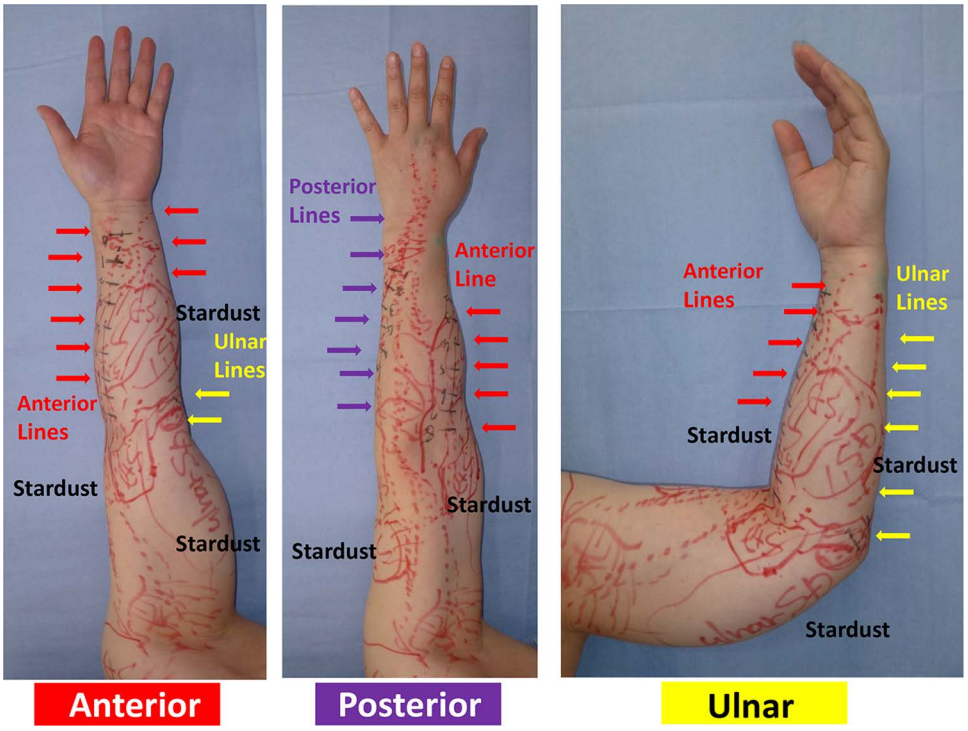

Fig. 1. Preoperative lymph mapping on the lymphedematous arm. Lymph lines were traced on the patient's arm using linear patterns of ICG lymphography. The lymphedematous arm was conceptually divided into three regions (anterior, posterior, and ulnar) because LVA works on each major lymphatic pathway at the arm independently. LVAs were created on each major lymphatic pathway to reduce edema in the whole arm.

both ulnae. ICG lymphography was performed in two different phases: early phase (5–15 minutes after ICG injection) and plateau phase (2 hours after ICG injection).[23]

In performing LVA, mapping of linear patterns is important to visualize lymphatic vessels; however, some linear patterns are visualized only in the early phase and are concealed by stardust patterns in the late phase. On the other hand, other linear patterns are emerging only in the late phase. Also, the plateau phase is important to evaluate lymphedema severity by mapping stardust and diffuse pattern areas.

All linear patterns and stardust patterns were traced and mapped on both of the patient's arms for the following dynamic ultrasonography. If the patient's lymphedematous limb showed no or partial linear patterns, a mirror image of the linear pattern seen in the nonaffected limb was used in predictive lymph mapping on the lymphedematous limb.[21–23,27,28]

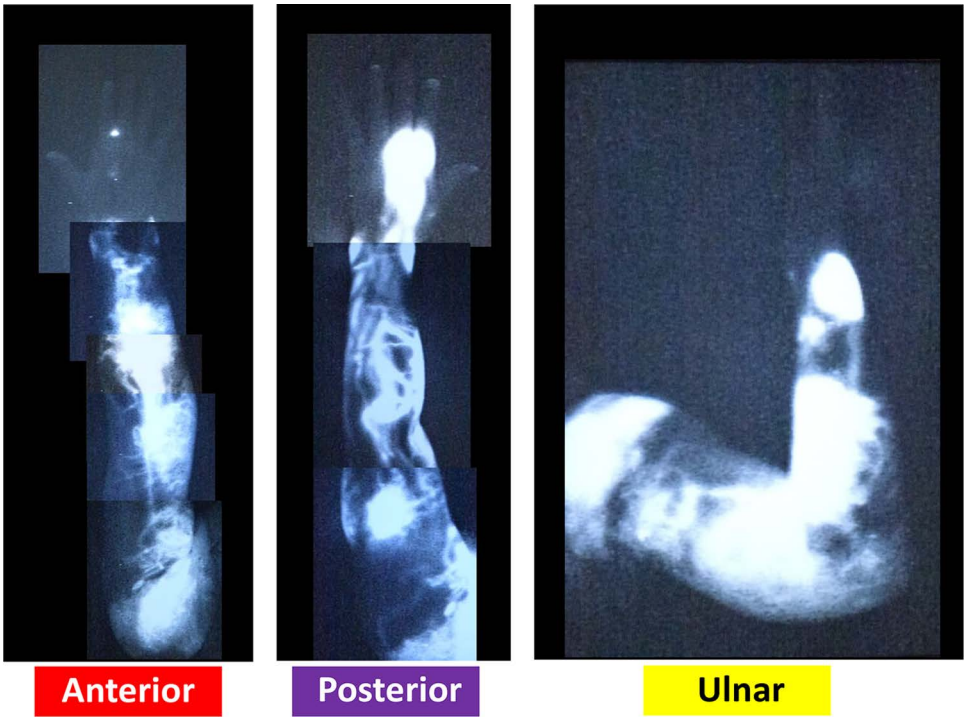

Fig. 2. Two-hour plateau phase of ICG lymphography after injection in the Figure 1 patient. In ICG lymphography, each 0.1 mL ICG (Diagnogreen 0.25%) was injected intradermally at the second and third web space of both hands, at the anterior border of the styloid process of both radii, and at the anterior border of the styloid process of both ulnae. Lymph lines were traced on the patient's arm using linear patterns of ICG lymphography. In the early phase (5–15 minutes after ICG injections), emerging linear patterns were traced at the arm before stardust patterns would conceal linear patterns. In the plateau phase (over 2 hours after ICG injection), other linear patterns that were only visualized in late phase were traced on the arm with stardust areas. When linear patterns were not identified, lymph lines were assumed using mirror images of the linear patterns at the nonaffected arm.

Dynamic LVA Method Using Dynamic Ultrasonography to Determine Incision Point

As noted above, 18 limbs of 17 patients had been treated by means of dynamic LVA. Because the patients' dominant hand, lifestyle, work, and other activities affect muscle development and tissue structure in the arm, anatomical and physiological function of lymphatic and venous systems are not uniform in upper extremity lymphedema (UEL) patients. By these reasons, the best incision sites for LVA in patients with UEL must be determined individually.

The dynamic LVA method is a new LVA technique for UEL patients, in which preoperative dynamic ultrasonography (US) is performed to determine the best incision point on each lymphatic vessel.[21–24] Throughout dynamic US examination, patients are instructed to move the lymphedematous hand continuously to evaluate muscle and venous pumping in the subcutaneous tissue. (**See Video [online]**, which depicts incision decision method in the dynamic LVA.) 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). In the dynamic LVA method, US is used not to detect lymphatic vessels, but to evaluate pumping of muscles and subcutaneous veins around 1.00 mm in diameter.[21–23]

From the distal end of the mapped lymph line, dynamic US was performed, and the incision site for LVA was determined as below. The most important finding in the dynamic US was the existence of pumping veins in conjunction with muscle movements in dynamic US. If there was only one point with the pumping vein, the point was chosen for the incision. If there were more than two points with pumping veins, the difference between soft tissue thicknesses in the diastolic and systolic phases was measured at the points. The incision was defined at the point with greater changes in the soft tissue thickness (Fig. 3). If there was no point with pumping veins, the incision was defined at the point with greatest changes in the soft tissue thickness on the lymph line, where muscle pumping maximally affects the soft tissues and the recipient vein.

In this study, we defined the size of pumping vein as over 0.70 mm in diameter. Also, small pumping veins were utilized as recipient veins when the diameter of lymphatic vessels were suitable for anastomoses.

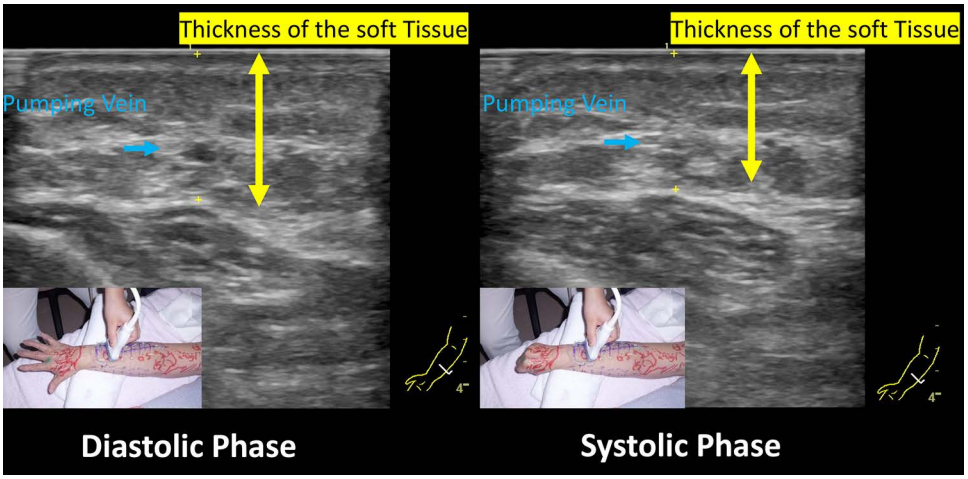

Fig. 3. Incision point selection in the dynamic lymphaticovenular anastomosis. On the lymph line, dynamic ultrasonography was performed from distally to proximally during the patient's continuous hand movements. With a grasping motion (right: systolic phase), the soft tissue that included lymphatic vessels and veins for LVA was compressed between the skin surface and the deep fascia, and with a hand-opening motion (left: diastolic phase), the soft tissue was released. Effective venous pumping was found on the subcutaneous vein larger than 0.70 mm in diameter. Marked between-phase difference in the thickness of the soft tissue was measured.

Statistical Analysis

All values are reported as mean ± SD. Lymphatic vessel sclerosis was defined as thickened lymphatic vessel wall with white appearance under intraoperative microscopic observation.[14]

The UEL index was used to evaluate the volume of the lymphedematous arm. This involved taking measurements of the patient's arm circumference at five points (the olecranon, 5 cm above and below the olecranon, the wrist, and the dorsum of the hand) and their body mass index (BMI). The UEL index is calculated by squaring each measurement, adding them together, and then dividing by the BMI.[29] The UEL index was determined preoperatively and then postoperatively, and for the study, the reduction in volume was compared between the two groups. Frequency of cellulitis was evaluated preoperatively and then postoperatively in the patients who demonstrated cellulitis preoperatively. All *P* values were two-sided, and statistical significance was accepted at a *P* value less than 0.05. All statistical analyses were performed with JMP Pro16 software (SAS Institute, Cary, N.C.).

RESULTS

The mean age of the patients was 60.4±10.1 years (range, 44–81 years). The mean duration of lymphedema was 39.7 months (range, 0–11 years). All patients were treated by dynamic LVA and used no pre- or postoperative compression therapy.

Three dynamic LVAs were created in all 17 patients (18 limbs) by end-to-end anastomosis using 12-0 nylon suture. Each of the three lymph lines identified were used for dynamic LVA. Lymphatic vessels were detected in all incisions in all 18 limbs.

The mean diameter of the lymphatic vessels was 0.52±0.21 mm. Thirty-eight of 54 lymphatic vessels used in LVA were sclerotic lymphatic vessels. Diameters of the lymphatic vessels were significantly larger by the thickened wall of the vessels in ISL stage 2b versus stage 2a (0.38±0.10 mm vs. 0.57±0.22 mm; $P < 0.01$). Sclerotic lymphatic vessels were encountered at a greater frequency in ISL stage 2b incisions versus stage 2a incisions [53.3% (8/15 incisions) versus 77.0% (30/39 incisions); $P = 0.096$] (Table 2). The frequency of encountering sclerotic lymphatic vessels was significantly high in incisions with stardust patterns of ICG lymphography than that in linear patterns [97.2% (35/36 incisions) versus 16.7% (3/18 incisions); $P < 0.01$] (Table 3).

Preoperative and postoperative lymphedema severity between ISL stage 2a and 2b is shown in Table 4. Lymphedema symptoms were improved from just after the surgery in all patients. The mean follow-up period was 25.5±9.2 months. Preoperative volume of the lymphedematous limb, according to the UEL index, was more severe in ISL stage 2b patients than in stage 2a patients [preoperative UEL index in stage 2a 103.8±6.7 (n = 5) versus preoperative UEL index in stage 2b 120.6±21.7 (n = 13); $P < 0.05$].

The circumferences and the volume of lymphedematous limbs were both reduced in all 18 limbs. The amount of volume reduction calculated by UEL index (Figs. 4 and 5) was 4.2–45.0 (mean 14.1±17.5; postoperative UEL index 101.8±9.4 versus preoperative UEL index 116.0±20.1; $P < 0.01$). Twelve of the 18 limbs were clinically cured without edema ($P < 0.01$).

Six of the 17 patients demonstrated cellulitis in their lymphedematous limbs, with a preoperative incidence of cellulitis averaging 2.17 per year. After the operation, the average number of episodes of cellulitis decreased to 0.17 per year ($P < 0.01$).

Table 2. Intraoperative Findings of Lymphatic Vessels in the ISL Stage 2a and ISL Stage 2b Group

	Total	ISL Stage 2a	ISL Stage 2b	*P*
Number of vessels for LVA	n = 54	n = 15	n = 39	
Diameter of lymphatic vessels (mm)	0.52±0.21	0.38±0.10	0.57±0.22	<0.01*
Degeneration of lymphatic vessels	38/54 (70.4%)	8/15 (53.3%)	30/39 (77.0%)	0.096†

Number (and percentage) and diameter of lymphatic vessels are shown.
*By Mann-Whitney *U* test.
†By χ^2 test.

Table 3. Intraoperative Findings of Lymphatic Vessels in the Linear and Stardust Pattern Incisions

	ICG Patterns at the Incisions			
	Total	Linear Pattern	Stardust Pattern	*P*
No. vessels for LVA	n = 54	n = 18	n = 36	
Diameter of lymphatic vessels (mm)	0.56±0.21	0.38±0.10	0.42±0.20	<0.01*
Degeneration of lymphatic vessels	38/54 (70.4%)	3/18 (16.7%)	35/36 (97.2%)	<0.01†

Number (and percentage) and diameter of lymphatic vessels are shown.
*By Mann-Whitney *U* test.
†By χ^2 test.
"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.

DISCUSSION

LVA is an effective minimally invasive surgical treatment for lymphedema in bypassing lymphatic blockage and providing alternate routing of lymphatic fluid into the venous system.[1–10,15–17] However, the clinical effect of traditional LVA performed for BCRL varies between patients: some BCRL patients are totally released from lymphedema symptoms, whereas others experience partial improvements of lymphedema.

Varieties in surgical outcome of LVA could be explained by the different status of capacity of each patient's lymphatic dynamics, if the procedure of LVA and physical therapies are performed in the same ways. The most important difference in lymphatic dynamics is degree of lymphatic vessel degeneration. Once degeneration of smooth muscle cells of the lymphatic vessels sets in,[12–14] the edema worsens progressively as the function of the smooth muscle weakens. Lymphatic vessels with degenerated smooth muscle are sometimes inadequate even as a power source in producing lymphatic flow to LVA. In our study patients, 38 of 54 (70.4%) lymphatic vessels used in LVA revealed sclerosis of the vessels. However, optimal results in this study suggest that the muscle pumping of dynamic LVA can compensate degeneration of the lymphatic vessels.

Compression therapy is a highly recommended conservative treatment for peripheral lymphedema.[30,31] The purpose of conservative compression is reducing symptoms of swelling and preventing lymphedema progression. These effects of compression are also important as preoperative managements for LVA in controlling lymphedematous stiffness and inflammation. In less edematous limbs, compression allows LVA procedures to be performed more easily and precisely because lymphatic fluid emerging from the surgical wound must be decreased. Postoperative usage of compression is also important in LVA. Compression at the affected limb increases lymphatic pressure to push lymphatic fluid to the anastomosed vein in the LVA.[15–17] In addition, continuous lymphatic flow at the anastomosis by compression can reduce lymphatic and blood stagnation around the anastomosis, and it can also reduce the risk of postoperative occlusions of LVA. Compression therapy is widely considered necessary not only for treating progressive lymphedema but also for perioperative management for LVA.

However, we should not overlook the fact that there are BCRL patients who cannot undergo compression. Because our institution highly recommended compression therapy for BCRL, we had only 18 limbs with BCRL without any compression use in this study period. Although it is often assumed that there are not many such patients, there are potentially many more because these patients likely do not seek medical care. Even if medical professionals strongly emphasize the importance of treatment, patients' compliance for conservative therapy has limitations.[18–20] These patients gradually develop uncontrollable progressive lymphedema because they lose accesses to important treatment opportunity. It is apparent that they need to be enlightened and salvaged by new treatment methods.

In upper extremity, the diameter of lymphatic vessels is relatively smaller in size than lymphatic vessels in lower extremity. In LVA for upper extremity, 12-0 nylon suture is usually selected in performing LVA, because a majority of lymphatic vessels are between 0.25 mm and 0.50 mm in

Table 4. Pre- and Postoperative Lymphedema Severity in ISL Stages 2a versus 2b Group

	Total	ISL Stage 2a	ISL Stage 2b	*P* (Stage 2a versus 2b)
No. limbs	(n = 18 limbs)	(n = 5 limbs)	(n = 13 limbs)	
Limb volume reduction	18/18 (100%)	5/5 (100%)	13/13 (100%)	1.000*
Preoperative UEL index	116.0±20.1	103.8±6.7	120.6±21.7	0.043†
Postoperative UEL index (mean 25.5±9.2 months)	101.8±9.4	97.2±5.6	103.6±10.2	0.152†
Change in UEL index	14.1±17.4	6.7±1.6	17.0±20.0	0.257†
P (volume reduction)	0.009*	0.174*	0.013*	

Number and percentage of patients are shown.
*By χ^2 test.
†By Mann-Whitney *U* test.

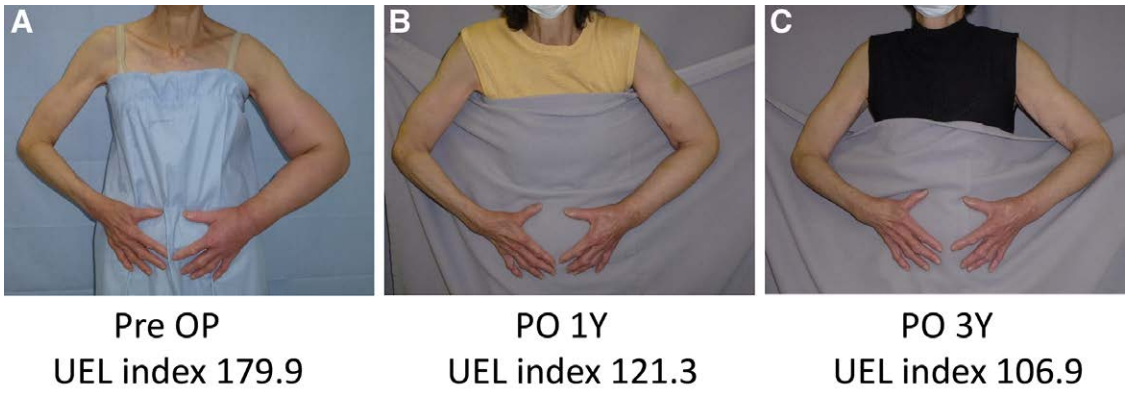

Fig. 4. Left UEL treated by the dynamic LVA method without any compression therapy. A, A 71-year-old woman had left ISL stage 2b UEL after undergoing breast cancer treatment 12 months previously. The preoperative left UEL index was 179.9. Lymphedema-associated reddened skin was observed on her right arm with skin hardness. The patient could not use any compression because of contact dermatitis, and her lymphedema continued to worsen. B, Three lymphaticovenular anastomoses were created via the dynamic LVA method. Soon after the surgery, the reddening disappeared, and at 1 year, the right UEL index was reduced to 121.3. C, At 3 years, the right UEL index was reduced to 106.9, and the patient felt no edema at her left arm without any compression use. Pre OP, preoperative; PO, postoperative; Y, years.

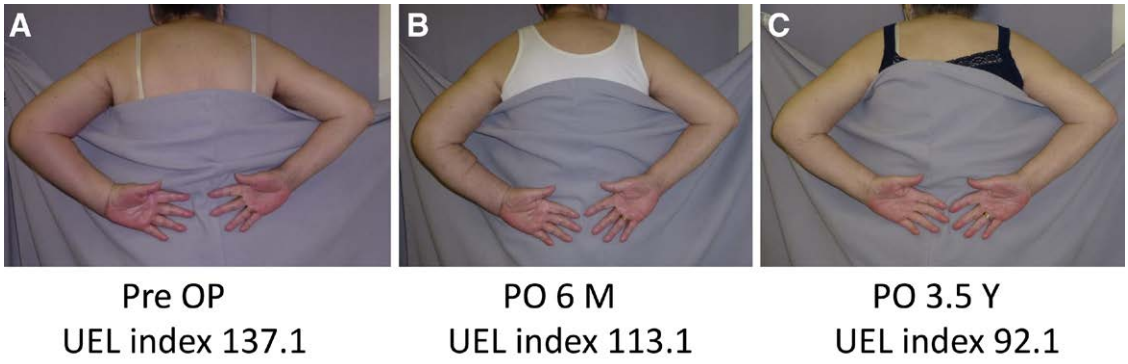

Fig. 5. Left UEL treated by the dynamic LVA method without any compression therapy. A, A 70-year-old woman had left ISL stage 2b UEL after undergoing breast cancer treatment 6 months previously. The preoperative left UEL index was 137.1. Lymphedema-associated reddened skin was observed on her left arm with skin hardness. The patient refused to undergo any compression therapy because of the burden of compression itself for her daily life, and her lymphedema continued to worsen. B, Three lymphaticovenular anastomoses were created via the dynamic LVA method. Soon after the surgery, the reddening disappeared, and at postoperative 6 months, the left UEL index was reduced to 113.1. C, At 3.5 years, the right UEL index was reduced to 92.1, and the patient felt little edema at her left arm without any compression use. Pre OP, preoperative; PO, postoperative; Y, years.

diameter in the upper extremity. If the lymphatic vessel's size is under 0.20 mm in diameter, 12-0 s nylon (approximately one-fourth the size of 12-0 nylon suture) is selected for LVA. However, the smallest lymphatic vessel was 0.25 mm in diameter in this study, and we only used 12-0 nylon suture for LVA.

In this study, the dynamic LVA significantly improved all BCRL patients without any compression therapy. The reason for no statistically significant volume reduction in ISL stage 2a patients in this study was considered to be due to less severity of preoperative lymphedematous volume in ISL stage 2a group and the small number of ISL stage 2a patients. However, all five ISL stage 2a patients revealed improvement of lymphedema, and four of the five ISL stage 2a patients were clinically cured from lymphedema without any symptoms. This study result can relieve lymphedema patients who are not receiving compression therapy. However, our study results never underestimate the importance of compression therapy. It might be possible that further improvements of lymphedema were obtained in severe lymphedema patients in our study group if they underwent compression.

On the other hand, one of the goals of surgical treatment for lymphedema is releasing the lymphedema patients from their lifelong burdens by daily compression therapy.[31] No patients use compression voluntarily and willingly. Cheng et al reported their trails for no compression usage just after LVA with high clinical outcomes.[32,33] If

lymphedema was released without compression, patients would be glad to finish their compression totally. However, treating BCRL without pre- and postoperative compression therapy is more challenging. In this study, all 17 patients were free from any compression from the first. We think that "clinical cure" of lymphedema can be determined only by the status of no symptoms of lymphedema without compression therapy. Twelve of the 18 limbs in our study showed clinical cure of lymphedema without pre- and postoperative compression.

The optimal clinical results in this study were achieved by the dynamic LVA method. The dynamic LVA method is a reliable LVA method, which we developed in 2016.[21] In this method, LVAs were created at the points where patient's natural hand movements made maximum muscle pumping power to propel lymphatic fluid to the site of anastomosed vein. Although utility of muscle pumping is the nature of this method's effectivity, the selection of an appropriate incision site with a pumping vein is critical to enhance the efficacy of LVA in promoting lymphatic fluid flow. The pumping action of the vein generates a negative pressure during the diastolic phase, which facilitates the drawing in of more lymphatic fluid through the LVA. That is why we only recommended BCRL patients to perform five-time voluntary hand grasping and opening exercises when they feel some form of edema at the arm. Patients treated by the dynamic LVA perform the exercise mostly in the morning because patients do not use hand motions when they sleep, and patients tend not to feel edema at noon and in the evening after the treatment. This phenomenon is distinct from the typical presentation of BCRL, wherein patients report worsening of lymphedema in the evenings after the use of their affected limb. If BCRL patients wish to undergo treatment using the dynamic LVA method combined with compression therapy, we believe that nighttime-only soft type compression therapy is more feasible for a majority of patients with this phenomenon of the dynamic LVA effect.

This study was conducted according to the fact that the dynamic LVA released many BCRL patients from the burden of compression therapy. In fact, 80% of our previous study patients in the dynamic LVA group could finish their compression at postoperative 2 years.[22,23] This high rate of compression release after dynamic LVA raises the clinical question of whether dynamic LVA can salvage compression-unable BCRL patients with sclerotic lymphatic vessels. In this study, even 38 of the 54 sclerotic lymphatic vessels shown in Tables 2 and 3 in severe BCRL patients or stardust area in ICG lymphography could propel lymphatic fluid to the venous system. Also, high clinical efficacy indicated that the dynamic LVA could prevent LVA occlusions in the mid- or late postoperative period by continuous lymphatic flow made by daily hand movements even without compression therapy.

Selection of incision points with pumping subcutaneous veins for LVA is the most important point in performing the dynamic LVA. In previous studies, we used branches of the pumping subcutaneous vein over 1.00 mm as the pumping recipient vein of lymph-to-venous anastomosis. However, in this study, we expanded the definition of pumping veins. Depending on the diameter of the lymphatic vessels, branches of the pumping subcutaneous vein over 0.70 mm and the pumping subcutaneous veins over 0.70 mm were used for the recipient veins of LVA. We confirmed that this modification on the definition of pumping vein resulted in optimal clinical results for BCRL patients in this study because more pumping veins could be utilized in LVA creation.

A limitation of the study is the small number of compression-unable BCRL patients included. There were only 18 limbs (17 patients) without any compression in this 26-month study period because most of the BCRL patients were under compression before consultation with our surgical team. In this study period, we salvaged all compression-unable BCRL patients who visited us. Further studies are required to confirm differences in using compression or not in large study groups.

CONCLUSION

The dynamic LVA method is clinically beneficial for BCRL patients who cannot use compression therapy.

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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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REFERENCES

1. Yamada Y. The studies on lymphatic venous anastomosis in lymphedema. *Nagoya J Med Sci.* 1969;32:1–21.
2. O'Brien BM, Sykes P, Threlfall GN, et al. Microlymphaticovenous anastomoses for obstructive lymphedema. *Plast Reconstr Surg.* 1977;60:197–211.
3. Koshima I, Inagawa K, Urushibara K, et al. Supermicrosurgical lymphaticovenular anastomosis for the treatment of lymphedema in the upper extremities. *J Reconstr Microsurg.* 2000;16:437–442.
4. Chang DW. Lymphaticovenular bypass for lymphedema management in breast cancer patients: a prospective study. *Plast Reconstr Surg.* 2010;126:752–758.
5. Chang DW, Suami H, Skoracki R. A prospective analysis of 100 consecutive lymphovenous bypass cases for treatment of extremity lymphedema. *Plast Reconstr Surg.* 2013;132:1305–1314.
6. Yamamoto T, Narushima M, Yoshimatsu H, et al. Minimally invasive lymphatic supermicrosurgery (MILS): indocyanine green

lymphography-guided simultaneous multisite lymphaticovenular anastomoses via millimeter skin incisions. *Ann Plast Surg.* 2014;72:67–70.
7. Garza RM, Chang DW. Lymphovenous bypass for the treatment of lymphedema. *J Surg Oncol.* 2018;118:743–749.
8. Pons G, Clavero JA, Alomar X, et al. Preoperative planning of lymphaticovenous anastomosis: the use of magnetic resonance lymphangiography as a complement to indocyanine green lymphography. *J Plast Reconstr Aesthet Surg.* 2019;72:884–891.
9. Visconti G, Yamamoto T, Hayashi N, et al. Ultrasound-assisted lymphaticovenular anastomosis for the treatment of peripheral lymphedema. *Plast Reconstr Surg.* 2017;139:1380e–1381e.
10. Hayashi A, Hayashi N, Yoshimatsu H, et al. Effective and efficient lymphaticovenular anastomosis using preoperative ultrasound detection technique of lymphatic vessels in lower extremity lymphedema. *J Surg Oncol.* 2018;117:290–298.
11. Breslin JW. Mechanical forces and lymphatic transport. *Microvasc Res.* 2014;96:46–54.
12. Koshima I, Kawada S, Moriguchi T, et al. Ultrastructural observations of lymphatic vessels in lymphedema in human extremities. *Plast Reconstr Surg.* 1996;97:397–405; discussion 406–407.
13. Mihara M, Hara H, Hayashi Y, et al. Pathological steps of cancer-related lymphedema: histological changes in the collecting lymphatic vessels after lymphadenectomy. *PLoS One.* 2012;7:e41126.
14. Yamamoto T, Yamamoto N, Yoshimatsu H, et al. Factors associated with lymphosclerosis: an analysis on 962 lymphatic vessels. *Plast Reconstr Surg.* 2017;140:734–741.
15. Yoshida S, Koshima I, Imai H, et al. Modified intraoperative distal compression method for lymphaticovenous anastomosis with high success and a low venous reflux rates. *J Plast Reconstr Aesthet Surg.* 2021;74:2050–2058.
16. Onishi F, Tsugu W, Okuda N, et al. Integration of perioperative reduction treatment with lymphaticovenular anastomosis for the management of lower extremity lymphedema. *Plast Aesthet Res.* 2021;8:50.
17. Yamamoto T, Yamamoto N, Kageyama T, et al. Technical pearls in lymphatic supermicrosurgery. *Glob Health Med.* 2020;29:29–32.
18. Ridner SH, Dietrich MS, Kidd N. Breast cancer treatment-related lymphedema self-care: education, practices, symptoms, and quality of life. *Support Care Cancer.* 2011;19:631–637.
19. Johnstone PA, Hawkins K, Hood S. Role of patient adherence in maintenance of results after manipulative therapy for lymphedema. *J Soc Integr Oncol.* 2006;4:125–129.
20. Sneddon M, Lewis M. Lymphoedema: a female health issue with implications for self care. *Br J Nurs.* 2007;16:76–81.
21. Seki Y, Kajikawa A, Yamamoto T, et al. The dynamic lymphaticovenular anastomosis method for breast cancer treatment-related lymphedema: creation of functional lymphaticovenular anastomoses with use of preoperative dynamic ultrasonography. *J Plast Reconstr Aesthet Surg.* 2019;72:62–70.
22. Seki Y, Kajikawa A, Asai R, et al. Functional lymphaticovenular anastomosis for peripheral lymphedema: incision selection methods with muscle pumping. *Plast Aesthet Res.* 2021;8:58.
23. Seki Y. The dynamic LVAs. In: Hayash A, Visconti G, eds. *Supermicrosurgical Lymphaticovenular Anastomosis: A Practical Textbook.* 1st ed. Rome, Italy: HV Projects; 2020:119–136.
24. Seki Y, Kajikawa A, Yamamoto T, et al. Real-time indocyanine green videolymphography navigation for lymphaticovenular anastomosis. *Plast Reconstr Surg Glob Open.* 2019;24;7:e2253.
25. International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. 2009 Consensus document of the International Society of Lymphology. *Lymphology.* 2009;42:51–60.
26. Seki Y, Yamamoto T, Kajikawa A. Lymphaticovenular anastomosis for breast cancer treatment-related lymphedema: three-line strategy for an optimal outcome. *J Plast Reconstr Aesthet Surg.* 2018;71:e13–e14.
27. Mihara M, Seki Y, Hara H, et al. Predictive lymphatic mapping: a method for mapping lymphatic channels in patients with advanced unilateral lymphedema using indocyanine green lymphography. *Ann Plast Surg.* 2014;72:706–710.
28. Gentileschi S, Servillo M, Albanese R, et al. Lymphatic mapping of the upper limb with lymphedema before lymphatic supermicrosurgery by mirroring of the healthy limb. *Microsurgery.* 2017;37:881–889.
29. Yamamoto N, Yamamoto T, Hayashi N, et al. Arm volumetry versus upper extremity lymphedema index: validity of upper extremity lymphedema index for body-type corrected arm volume evaluation. *Ann Plast Surg.* 2016;76:697–699.
30. Jung C, Kim J, Seo YJ, et al. Who will continuously depend on compression to control persistent or progressive breast cancer-related lymphedema despite 2 years of conservative care? *J Clin Med.* 2020;9:3640.
31. Rangon FB, da Silva J, Dibai-Filho AV, et al. Effects of complex physical therapy and multimodal approaches on lymphedema secondary to breast cancer: a systematic review and meta-analysis of randomized controlled trials. *Arch Phys Med Rehabil.* 2022;103:353–363.
32. Cheng MH, Liu TT. Lymphedema microsurgery improved outcomes of pediatric primary extremity lymphedema. *Microsurgery.* 2020;40:766–775.
33. AlJindan FK, Lin CY, Cheng MH. Comparison of outcomes between side-to-end and end-to-end lymphovenous anastomoses for early-grade extremity lymphedema. *Plast Reconstr Surg.* 2019;144:486–496.