

Figure 1. Images of type I in a patient with left lymphedema 30 (left) and 120 (right) minutes after injection of contrast medium. There is no obvious dermal backflow. The inguinal lymph nodes are reduced in number and lymph stasis in the lymphatics or collateral lymphatics along the saphenous vein are visible (arrows). The medium remains in the lymphatics 120 minutes later.

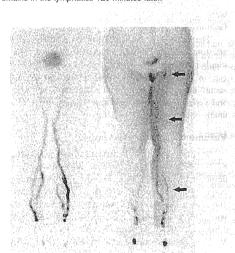


Figure 2. Images of type II in a patient with left lymphedema 30 (left) and 120 (right) minutes after injection of contrast medium. Lymph stasis in the lymphatics (arrow) and visible dermal backflow (arrow) on the left thigh can be seen. The inguinal lymph nodes are reduced in number (arrow).

#### Indications in Lymphaticovenous Anastomosis

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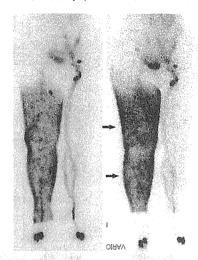


Figure 3. Images of type III in a patient with right lymphedema 30 (left) and 120 (right) minutes after injection of contrast medium. Dermal backflow (arrows) in the leg and thigh can be seen at the right.

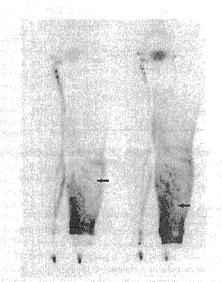


Figure 4. Images of type IV in a patient with left lymphedema 30 (left) and 120 (right) minutes after injection of contrast medium. Dermal backflow (right arrow) and lymph stasis in the lymph vessels (left arrow) in the leg can be seen and remains in the leg 120 minutes later.

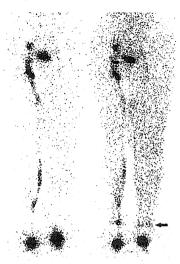


Figure 5. Images of type V in a patient with left lymphedema 30 (left) and 120 (right) minutes after injection of contrast medium. There is no obvious dermal backflow in either the leg or thigh. The medium remains in the foot (arrow) and around the ankle (arrow).

Table 2. Results of Classified Types

	Group A	Group B (/	Group B (n = 31)	
	(n=80)	Right	Left	Total
Type I	5	13	14	32
Type II	15	4	6	25
Type III	20	3	2	25
Type IV	29	3	4	36
Type V	8	8	5	21
Unclassified	3	0	0	3
Total	80	31	31	142

differences in the means of limbs in different clinical stage scales between types I and types II to V, and between type V and types II and IV by Dunn's test (Table 3).

## **Detection and Anastomosis of Lymphatics**

Lymphaticovenous anastomosis was applied to types II, III, IV, and V patients. However, in the type I patients and in some of the type II patients, combined physical therapy was indicated instead of microsurgical treatment because lymphoscintigraphy showed that they seemed to have some lymph pathways in the affected limb. In the 35 limbs of the 31 patients with lymphaticovenous anastomosis, the sites for skin incisions were chosen based on lymphoscintigraphy images. The lymphatics detected

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Table 3. Type and Clinical Stage Scale

			-	
Clinical stage scale	1	2	3	
Type I (n = 32)	19	13	0	
Type II $(n = 25)$	3	22	0	-1 J
Type III $(n = 25)$	0	22	3	
Type IV $(n = 36)$	0	31	5	ر : الساد
Type V $(n = 21)$	0	9	12	
Total $(n = 139)$	22	97	20	

n, number of limb;  $\star P <$  0.05,  $\star \star P <$  0.001 (Dunn's multiple comparison test).

Table 4. Total Number and Average Number of Anastomoses Per Limb in Each Type

	Total nur			
	Foot	Leg	Thigh	Total
Type II (n = 3)	3 (1)	5 (1.7)	2 (0.7)	10 (3.3)
Type III (n = 12)	13 (1.1)	30 (2.5)	10 (0.8)	53 (4.4)
Type IV (n = 16)	22 (1.4)	29 (1.8)	7 (0.4)	58 (3.6)*
Type V (n = 4)	6 (1.5)	4 (1)	2 (0.5)	12 (3)
Total $(n = 35)$	44 (1.3)	68 (1.9)	21 (0.6)	133 (3.8)

\*P < 0.05.

were anastomosed to suitable veins in a side to end fashion.

The total and average numbers of lymphaticovenous anastomoses per limb are shown in Table 4. The average number of anastomoses per limb in type III was the highest; in the other three types, it was approximately the same. There were significant differences between type III and type IV, and between type III and type V (One-way analysis of variance, P < 0.05).

#### Volume Change of the Limbs

Excess volume of the affected limb was reduced from 83 to 3575 ml except for four limbs in which lymphedema of the affected limb became slightly worse. The average improvement of edema in all cases was 872  $\pm$  1062 ml. The average volume reduction in each type was: 218  $\pm$  944 ml in type II, 543  $\pm$  616 ml in type III, 1335  $\pm$  1288 ml in type IV, and 615  $\pm$  817 ml in type V. There was no statistical difference among the types.

#### DISCUSSION

There are some relationships between the types based on the abnormal patterns of lymphoscintigrams in this study and the clinical staging. The abnormal patterns in

the lymphoscintigrams have been reported from the points of visualization of lymph vessels and lymph nodes, dilatation of lymphatic vessels, existence of collateral vessels, and dermal backflow.\frac{1.3}{3} These patterns vary with the progress of the lymphedema, previous treatments for edema, or the origins of the lymphedema. In cases with secondary lymphedema due to surgical intervention or irradiation therapy for oncological treatment, the lymphatic system seems to be broken from its proximal side to its distal portion. Koshima et al.\frac{8}{3} reported that occlusions of the lymphatic trunks and degeneration of the smooth muscle cells might start from the proximal ends of the extremities. This is quite indicative for our study and the types in this study indicate the progress of lymphedema. That is, the clinical staging increases its number as the number of the type increases.

The clinical stages only refer to the physical condition of the extremities. On the other hand, the location of the edema clinically varies from thigh to foot and physical conditions do not always correlate with hypo- or dysfunction in lymph transport. However, the stages don't include these factors. A more detailed classification should be proposed according to an improved understanding of the pathogenetic mechanisms of lymphedema.

Szuba et al.4 developed a system of lymphoscintigraphic scoring for grading the degree of lymphedema in the upper extremities after mastectomy. The score is based on visualization of the lymph nodes and extent of dermal backflow: There are 6 degrees in the visualization of the axillary lymph nodes and 4 degrees in the extent of dermal backflow. The score is correlated with the magnitude of the excess volume in the involved limb. Pecking et al.5 analyzed lymphoscintigrams obtained from 4,328 patients and reported the staging of lymphoscintigraphic images and grading of the severity of lymphedema in the lower limbs. There are four grades of severity according to the clinical stages<sup>6</sup> as advocated by the International Society of Lymphology and six stages of the images classified from the aspects of lymph transport, drainage route, lymph stasis, and visualization of the lymph nodes. However, their scoring or grading systems are appropriate for evaluating the conditions of lymphedema but are insufficient for assessing microsurgical indications because they are too broad to choose specific surgical applications. Therefore, we proposed another reference in lymphoscintigraphy for microsurgical treatment.

In three cases, there were three lymphoscintigraphic images that could not be classified into any type. These images showed no lymph nodes and no dermal backflow in the leg and thigh but lymphatics in the leg, which was similar to type V, but the lymph vessels were working in the leg. Long standing physiotherapy has been applied to these cases. Conservative physiotherapy might affect lymphoscintigraphic images, particularly dermal backflow.

In our study, type III is the best indication for lymphaticovenous anastomosis because we were able to apply more than four anastomoses to one limb. There are several reasons for the facility to find and anastomose the lymphatics in type III, for example, dilatation of the lymphatic lumen, moderate thickness of the lymphatic wall, and measurable lymph flow. Although it is considered that there are many factors that influence lymphedemapreoperative conditions, postoperative nonsurgical treatments, or patients' daily activities-the number of lymphaticovenous anastomoses in one limb should be one of the factors for improving lymphedema. In this study, there was no statistical difference of volume reduction in each type. This might be attributed to the small number of cases in this series. However, Huang et al.9 mentioned that the results after microlymphaticovenous anastomoses were proportional to the number of anastomoses. In addition, Campisi et al. 10,111 stressed that the earlier the treatment, the higher the edema reduction, and that it was important to select suitable patients for surgery. We presume areas suited for anastomosis vary according to type. The average number of anastomoses in one limb was almost the same in types II, IV, and V. However, that in the leg of type V was 1 and was the worst among them, meaning the area for anastomosis in type V might be more distal than those in types II and IV. Vaqueiro et al. 12 mentioned the relationship between the images of lymphoscintigraphy and lymphaticovenous anastomosis. Lymphaticovenous anastomoses were possible only in patients who had patent lymph channels visible on lymphoscintigrams. However, while this seems to be true, it is possible to find lymph vessels clinically even in areas of dermal backflow. Although these lymphatics are masked by the contrast medium in these areas, we could indeed find functional lymphatics and complete lymphaticovenous anastomosis in types II, III, IV, and V. Furthermore, MRI-lymphography sometimes provides good visualization of the lymphatic vessels<sup>13</sup> but it is difficult to obtain the best visualization because the timing required to take images varies with each patient. Development of new methods or equipment will enable the detection of masked but functional lymphatics, which may contribute to the improved treatment of lymphedema for patients with severe peripheral lymphedema.

The efficacy of the treatment for peripheral lymphedema depends on many factors, kinds of treatment, timing, and so on. Therefore, it is difficult to describe the indications clearly. A prospective study is required for a complete inquiry in the future.

#### CONCLUSION

From the images obtained in lymphoscintigraphy in this study, we were able to classify secondary lymphe-

dema into five types that suggest the progress of secondary lymphedema. Combined physical therapy should be indicated for type I because there are some pathways of lymph from the inguinal region to the center of the body. Both combined physical therapy and lymphaticovenous anastomosis could be applied for types II, III, IV, and V. However, for type V, it was difficult to find functional lymphatics in the leg for lymphaticovenous anastomosis. In conclusion, patients with type III secondary lymphedema are good candidates for lymphaticovenous anastomosis in the lower extremities. In types IV and V, some effort might be required to detect functional lymphatics for anastomosis compared with that in type III. Lymphoscintigraphy is a useful method for evaluating lymphedema and for obtaining indications of lymphaticovenous anastomosis in patients with secondary lymphedema.

#### REFERENCES

- Weissleder H, Weissleder R. Lymphedema: Evaluation of qualitative and quantitative lymphoscintigraphy in 238 patients. Radiology 1988;167:729–735.
- 1988;167:729–735.

  2. Nawaz K, Hamad M, Sadek S, Awdeh M, Higazi E, Eklof B, Abdel-Dayem HM. Lymphscintigraphy in peripheral lymphedema using technetium-labelled human serum albumin: Normal and abnormal patterns. Lymphology 1985;18:181–186.

  3. Yuan Z, Chen L, Luo Q, Zhu J, Lu H, Zhu R. The role of radionuclide lymphoscintigraphy in extremity lymphedema. Ann Nucl Med 2006;20:341–344.

- 4. Szuba A, Strauss W, Sirsikar SP, Rockson SG. Quantitative radionuclide lymphoscintigraphy predicts outcome of manual lymphatic therapy in breast cancer-related lymphedema of the upper extremity Nucl Med Commun 2002;23:1171–1175.
- Pecking AP, Albérini JL, Wartski M, Edeline V, Cluzan RV. Relationship between lymphoscintigraphy and clinical findings in lower limb lymphedema (LO): Toward a comprehensive staging. Lymphol-
- International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. Consensus document of the International Society of Lymphology. Lymphology 2003;36:84–91.
- 7. Ogata F. Narushima M. Mihara M, Azuma R, Morimoto Y, Koshima I. Intraoperative lymphography using indocyanine green dye for near-infrared fluorescence labeling in lymphedema. Ann Plast Surg 2007;59:180–184.
- 8. Koshima I, Kawada S, Moriguchi T, Kajiwara Y. Ultrastructural observations of lymphatic vessels in lymphedema in human extremities. Plast Reconstr Surg 1996;97:397-405.
- Huang GK, Hu RQ, Liu ZZ, Shen YL, Lan TD, Pan GP. Microlym-phaticovenous anastomosis in the treatment of lower limb obstructive lymphedema: Analysis of 91 cases. Plast Reconstr Surg 1985;76: 671–685.
- Campisi C, Davini D, Bellini C, Taddei G, Villa G, Fulcheri E, Zilli A, Da Rin E, Eretta C, Boccardo F. Lymphatic microsurgery for the treatment of lymphedema. Microsurgery 2006;26:65-69.
- 11. Campisi C, Boccardo F. Microsurgical techniques for lymphedema treatment: Derivative lymphatic-venous microsurgery. World J Surg 2004;22:609-613.
- Vaqueiro M, Gloviczki P, Fisher J, Hollier LH, Schirger A, Wahner HW. Lymphoscintigraphy in lymphedema: An aid to microsurgery. J Nucl Med 1986:27:1125–1130.
- 13. Lohrmann C, Foeldi E, Speck O, Langer M. High-resolution MR lymphangiography in patients with primary and secondary lymphedema. AJR Am J Roentgenol 2006;187:556-561.

## LYMPHATICOVENOUS SHUNT FOR THE TREATMENT OF CHYLOUS REFLUX BY SUBCUTANEOUS VEIN GRAFTS WITH VALVES BETWEEN MEGALYMPHATICS AND THE GREAT SAPHENOUS VEIN: A CASE REPORT

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Chylous reflux is a rare disorder in which chyle flows antidromically from its normal route to the extremities, thorax, abdominal cavity, or other parts of the body. We present a case of chylous reflux with megalymphatics in a 28-year-old boy who presented chylorhea in the foot, leg, and external genitalia, lymphedema, and hemangioma in the affected limb. Lymphaticovenous shunts using subcutaneous vein grafts with valves were applied to the patient for treatment of repeated chylorhea ther surgery, the patient has not complained of chylorhea and been freed from conservative physiotherapy such as bandaging or application of compression stockings for lymphedema for two years. A subcutaneous vein graft with valves may be considered a useful method as a shunt between incompetent and dilated lymphatics and veins instead of a saphenous vein graft in the treatment of chylous reflux in lower extremities. We discuss these treatments based on the literature about chylous disorders. © 2010 Wiley-Liss, Inc. Microsurgery 30:553–556, 2010.

Chylous reflux is a rare disorder in which the chyle flows antidromically from its normal route from the bowel through the cisterna chyli and the thoracic duct to the extremities, thorax, abdominal cavity, and/or other parts of the body. Patients with chylous reflux are relatively young and their social activities are so limited by chylorrhea, lymphedema, or cellulitis. From observations of lymphangiography, chylous reflux can be divided into two types, megalymphatics and lymphatic deficiency.

We present a case of chylous reflux with megalymphatics treated by subcutaneous vein grafts with valves between megalymphatics and the great saphenous vein in a 28-year-old boy who developed chylorrhea in the foot, leg, and external genitalia as well as lymphedema and hemangioma in the affected limb.

#### **CASE REPORT**

A 28-year-man presented with congenital edema in the lower right extremity, port-wine stain on the leg and thigh, and edema of the external genitalia. Conservative physiotherapy by using bandaging and compressive garments had been applied for treatment of lymphedema for two years. Chylous discharge from the foot, leg, and external genitalia continuously repeated for the past year (Figs. 1a and 1b). The volume of the lower extremities was 4,502 ml on the right side and 3,385 on the left side. His blood test showed no abnormalities

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Ultrasonography revealed dilated lymphatics with a diameter of about 5 mm, i.e., megalymphatics, above the ankle (see Fig. 2) and knee. Lymphoscintigraphy (Fig. 3a) and indocyanine fluorescence lymphography (see Fig. 4) also revealed dilated lymphatic vessels along the great saphenous vein and dermal backflow in the leg and external genitalia.

As the first operation to improve the chylous reflux condition in the lower right extremity, lymphaticovenous shunt operations were performed above the ankle and at the upper one third of the thigh. By harvesting a subcutaneous vein with valves from the left foot, segments of about 15 mm and 10 mm in length with valves of the vein graft were used between the megalymphatics and the saphenous vein at the thigh and at the ankle, respectively.

Each vein graft was placed with its distal end to the saphenous vein and proximal end to the megalymphatics in a fashion of end-to-side to prevent the backflow of blood (Figs. 5a and 5b). Chylorrhea disappeared soon after this operation but lymphedema of the right lower limb was not improved. Lymphoscintigraphy taken three months after the operation showed decreased dermal backflow in the lower right extremity (Fig. 3b). The patient requested additional improvement in the lymphedema of the affected limb.

Six months after the first operation, lymphaticovenous side-to-end anastomosis in the right inguinal region was then applied to reduce the edema in the external genitalia. Under general anesthesia through an incision, we could detect the subcutaneous vein and nearby lymphatics that was not similar to megalymphatics but was slightly dilated. The vein was cut and its proximal end was anastomosed to the side of the lymphatics in the manner of side to end. However, the edema of the scrotum was unchanged after surgery because the main cause of the scrotal swelling was not edema but a hydrocele that had been scheduled for treatment by urologists.



Figure 1. (a-c) Frontal view of edema and port-wine stain on the right lower extremity (a) and development of a hydrocele in the external genitalia (b) before surgery. Chylorrhea was seen in the foot, knee, and external genitalia (arrows). Frontal view of the lower extremities three months after the second operation (c). No remarkable change in volume on the affected limb between before (a) and after (c) surgery. (Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.)



Figure 2. Ultrasonography image. Above the ankle, megalymphatics (LYMP) can be seen along the great saphenous vein (SM).

For two years after these operations, the patient has not complained of chylorrhea and has avoided conservative physiotherapy such as bandaging or application of compression stockings for lymphedema. The postoperative volume

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of the affected side was 4,496 ml and unchanged from the preoperative volume even though there was a weight gain of 3 kg after surgery (Fig. 1c). The patient has not developed any respiratory problems and a chest X-ray of this patient revealed no change before and after surgery.

#### DISCUSSION

Kimmonth et al. classified chylous reflux into two types according to observations of lymphangiography. <sup>1</sup> In Syndrome I, megalymphatics exist in the abdominal cavity, pelvis, or extremities with congenital naevi present on the skin and in Syndrome II, edema was often congenital and more widespread, affecting several limbs. Lymphangiography revealed few or absent subcutaneous lymph vessels. Hypoproteinemia was noted, often with other metabolic disturbances, and the long-term prognosis was poor. These kinds of lymphatic disorders have recently been diagnosed by less invasive methods such as MRI, lymphoscintigraphy, <sup>2</sup> or fluorescence lymphography instead of conventional lymphangiography using oily material that might cause oil emboli in the lungs. <sup>3</sup> This case can be classified into Syndrome I because it has the typi-

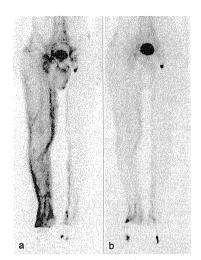


Figure 3. (a) Preoperative lymphoscintigraphy revealed lymph stasis and dermal backflow in the right leg, megalymphatics in the thigh, and decreased inguinal lymph nodes. (b) Lymphoscintigraphy taken 3 months after the first operation revealed decreased lymph stasis and diminished dermal backflow in the lea.

cal symptoms and signs: megalymphatics, simple hemangioma, and edema.

The underlying causes of congenital chylous reflux are still unknown. We built shunts not between the portal vein but between the great saphenous vein and the megalymphatics. In this case, chyle enters the systemic circulation of the body, and might cause some problems in the lung, for example. However, this specific patient has not developed any respiratory problems and a chest X-ray of this patient revealed no change before and after surgery.

In the case of congenital chylous reflux, valves of the lymphatics seem to be incompetent. Shunt plasty between the megalymphatics and the saphenous vein reduces the pressure in the lymphatic vessels, which improves chylous reflux, although lymph can flow in reverse because of a lack of valves in the vessels.

In cases of infants and children with localized lesions, conservative treatments such as a medium-chain triglyceride (MCT) diet or bowel rest with total parenteral nutrition (TPN) are effective in reducing chyle. However, in cases with widespread malformations of the lymphatic system or in cases with recurrence after conventional therapies, surgical interventions should be considered. In this case, it was difficult to apply such a diet therapy before surgery because of the patient's social situation.

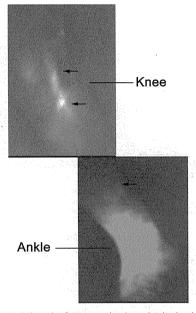


Figure 4. Indocyanine fluorescence lymphography showing dermal backflow in the leg and megalymphatics in the thigh (arrows).

Campisi et al. reported 47 cases of chylous reflux including chylous ascites, chylothorax, chyluria, and chylorrhea in the external genitalia or the lower extremities.<sup>5</sup> Of the 47 cases, 11 had chylorrhea in the leg and external genitalia. They mentioned the usefulness of lasermicrosurgical procedures as well as other surgical methods such as ligatures or excisions of incompetent dysplastic and dilated lymphatics in the treatment of several types of chylous disorders. However, details about the method used to perform the microsurgical procedures are unknown. Another report by Campisi in 2007 stated that of 12 cases with chylous ascites, 7 underwent chylo-venous and lymphovenous microsurgical shunts.<sup>6</sup> Noel et al. reported 35 cases with chylous reflux in which 14 cases had chylorrhea of the lower limbs. However, a majority clinical finding was chylothorax in 20 of the cases. Of the 35 cases, 21 had surgical treatment with 26 procedures in which two lymphaticovenous anastomoses and two grafts were performed. They also mentioned that a segment of saphenous vein with a competent valve was used for a lymphovenous shunt but it is unclear which type of graft, where, and how the graft was applied to the patients. Instead of a segment of saphenous vein, we

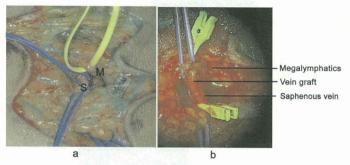


Figure 5. (a) Megalymphatics (M) and the great saphenous vein (S) with external diameters of about 3 mm and 3.5 mm, respectively, exposed through an incision in the upper one third of the right thigh. (b) Subcutaneous vein graft with valves placed between the megalymphatics and the great saphenous vein. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

used a part of the subcutaneous vein with valves in the dorsum of the nonaffected foot because a vein with an adequate diameter for use as a shunt can easily be harvested and the saphenous vein should be preserved. In our experience of lymphaticovenous anastomosis for treatment of chromic lymphedema, subcutaneous ecchymosis caused by blood backflow to the lymphatic vessels sometimes occurs, which may develop postoperative inflammation or result in occlusion of the anastomosed vessels. Therefore, the valves should be included in the grafted vein to prevent the backflow of blood from the saphenous vein. Excision, ligation, and sclerotherapy have been reported to be effective methods for chylous reflux. However, drainage methods such as a lymphaticovenous shunt seem to be essential. In a case report about chylous edema in 1966, Ketterings<sup>8</sup> stated that ligation and stripping of abnormal lymphatics were effective even if done transperitoneally or retroperitoneally. Currently, we can apply microsurgical techniques to such intractable cases without great effort. In summary, a subcutaneous vein graft with valves may be considered one useful method for a shunt between incompetent and dilated lymphatics and veins instead of the saphenous vein graft in the treatment of chylous reflux in lower extremities.

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#### REFERENCES

- 1. Kinmonth JB, Taylor GW. Chylous reflux Brit Med J 1964;1:529-
- S32.
   Berenji GR, Iker E, Glass EC, Lymphoscintigraphic findings in chylous reflux in a lower extremity. Clin Nucl Med 2007;32:725–728.
   Ketterings C, Chylous edema of the leg: a case report. Ann Surg 1967:165:647-654.
- Unger SW, Chandler JG. Chylous ascites in infants and children. Surgery 1983;93:455–461.
   Campisi C, Boccardo F, Zilli A, Borrelli V. Chylous reflux pathologies: diagnosis and microsurgical treatment. Int Angiol 1999;18: 10.13
- Campisi C, Bellini C, Eretta C, Zilli A, da Rin E, Davini D, Bonioli
- Campisi C, Bellini C, Eretta C, Zilli A, da Rin E, Davini D, Bonioli E, Boccardo F. Diagnosis and management of primary chylous ascites. J Vasc Surg 2006;43:1244–1248.
   Noel AA, Gloviczki P, Bender CE, Whitley D, Stanson AW, Deschamps C. Treatment of symptomatic primary chylous disorders. J Vasc Surg 2001;34:785–791.
   Kayikçioğlu A, Karamürsel S, Safak T, Mavili E, Erk Y. Lymphatic malformation causing intractable chylorrhagia. Plast Reconstr Surg 2000;105:1422–1425.

# Outcomes of lymphaticovenous side-to-end anastomosis in peripheral lymphedema

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Objective: Lymphaticovenous anastomosis has been used for patients with peripheral lymphedema. However, the efficacy of this procedure is controversial due to a lack of evidence regarding postoperative patency. We sought to determine midterm postoperative patency of lymphaticovenous side-to-end anastomoses (LVSEAs) using indocyanine green fluorescence lymphography.

Methods: This was a retrospective observational study set in a teaching hospital. Of 107 patients with chronic lymphedema who underwent 472 LVSEAs, 57 (223 anastomoses) consented to fluorescence lymphography and comprised the study cohort. The intervention consisted of a microsurgical LVSEA performed with a suture-stent method. Patients also had preoperative and postoperative complex decongestive physiotherapy. Anastomosis patency was assessed using indocyanine green fluorescence lymphography ≥6 months after surgery. Patency rates were calculated using Kaplan-Meier analysis. We assessed volume reduction on the operated-on limb and compared this between patients in whom anastomoses were patent and those in whom anastomoses were not obviously patent.

Results: Patency could be evaluated only at the dorsum of the foot, ankle, and lower leg because the near-infrared rays emitted by the special camera used could not penetrate the deep subcutaneous layer containing collective lymphatics in areas such as the thigh. Several patterns were observed on fluorescence lymphography: straight, radial, and L-shaped. Cumulative patency rates of LVSEAs were 75% at 12 months and 36% at 24 months after surgery. No significant difference in volume change of the affected limb was seen between the 34 patients with patent anastomosis (600 ± 969 mL) and the 24 patients without obvious evidence of patency (420 ± 874 mL).

Conclusions: Although further study is required to determine factors leading to anastomotic obstruction and to optimize the results of microlymphatic surgery, the present LVSEA technique appears promising. (J Vasc Surg 2012;55:753-60.)

Lymphaticovenous anastomosis (LVA) has been performed for patients with peripheral lymphedema since 1977. Several authors have since applied LVA in several variations of end-to-end or end-to-side, <sup>1-4</sup> or both, and have described long-term results of LVA in circumferential and volume reduction, or both, of the affected limbs. <sup>5-7</sup> However, few reports have used lymphoscintigraphy to address the postoperative patency of LVA. <sup>6,8,9</sup> In addition, patency of anastomoses can be difficult to evaluate on real-time lymphoscintigraphic images.

As an improvement over the original technique of end-to-end anastomosis, we have been performing lymphaticovenous side-to-end anastomosis (LVSEA) between the sidewall of the lymphatics and the proximal stump of the vein (Fig 1) for patients with chronic peripheral lymphedema since 1998. From the perspective of lymph flow in the anastomosed lymphatics, LV-SEA can divert the obstructed lymph flow and decompress lymphatic hypertension to the same extent as

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Competition of interest: none.

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conventional LVA, in addition to theoretically preserving the original flow even if the anastomosis becomes obstructed, a possibility that should not be ignored in patients with a limited number of functional lymphatic vessels. In addition, further operations remain applicable to other parts of the same lymphatic vessels used for anastomoses if those anastomoses become occluded in the future.

The recent development of the Photo Dynamic Eye near-infrared camera system (Hamamatsu Photonics, Hamamatsu, Japan) has enabled the detection of lymph flow in real-time through the skin as fluorescent lymphangiography using indocyanine green (ICG). 10,11 The camera activates ICG with emitted light at a wavelength of 760 nm and filters out light with wavelengths below 820 nm. ICG is injected intradermally at the web spaces of the affected limb, and lymph streams and stasis can be observed a few minutes after massage on a monitor applying the camera at 5 to 40 cm from the skin surface.

Our procedures for LVSEA have changed since May 2006, because ICG florescence lymphography and the stent method, <sup>12</sup> by which anastomoses can be performed more precisely, were introduced to our department at that time. The present study assessed midterm postoperative patency in LVSEA using ICG fluorescence lymphography in patients with peripheral lymphedema.

#### METHODS

Patients. Between May 2006 and August 2010, we performed LVSEA in 114 limbs of 107 patients with peripheral lymphedema. A total of 472 procedures were per-

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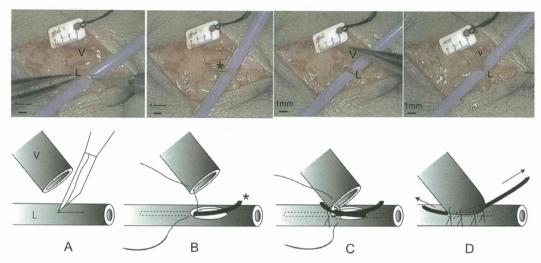


Fig 1. Operative photographs (upper row) and illustrations (lower row) show the lymphaticovenous side-to-end anastomosis technique. A, The side wall of the lymphatic vessel (L) is incised with a microknife. V, Subcutaneous vein. B, A nylon suture-stent (\*) is inserted into the lumen of the lymphatic vessel and a stitch is inserted at the edge. C, Another nylon suture-stent is inserted and stitches are inserted from edge-to-edge. D, After completion of the anastomosis, stents are removed through the anastomosis.

formed, at a mean  $\pm$  standard deviation of 4  $\pm$  1.6 procedures per limb. In 10 of these patients, 13 LVAs were performed in an end-to-end manner because of difficulties applying LVSEA.

Of the 107 patients, 85 had lymphedema of the lower extremity and the remaining 22 had lymphedema of the upper extremity. Among the 85 patients with lymphedema of the lower extremity, 57 (52 women, 5 men), who were a mean age of 55  $\pm$  15 years (range, 13-80 years), consented to postoperative fluorescence lymphography using ICG.

All patients underwent LVSEA. The total number of anastomoses in this series was 223. The 57 patients comprised 51 with secondary lymphedema after treatment for cancer and 16 with primary lymphedema. Clinical stage for the 57 patients, as proposed by the International Society of Lymphology, <sup>13</sup> was stage I in 2, stage II in 17, late stage II in 29, and stage III in 9.

All patients underwent complex decongestive physiotherapy (CDP) for 3 to 12 months preoperatively, and reduction of the affected limb was obtained in most patients. However, reductions were insufficient in some patients who had undergone CDP at other facilities for a long time. Postoperative CDP with the same contents as preoperative CDP was started 10 to 14 days after surgery and was performed for ≥6 months. Postoperative CDP lasted or decreased according to physiologic changes and complaints of the patients thereafter.

Before and at  $\sim$ 6 months after surgery, circumferential measurements of the affected limbs were performed at the following sites: 10 cm above the proximal margin of the patella, 10 cm beneath the distal margin of the patella, and

at the level of the lateral and medial malleoli of the ankle. Approximate volumes of the affected limbs were calculated using those measurements. Volume reductions were compared between patients with and without midterm postoperative patency of anastomoses at the foot and around the ankle.

We performed lymphoscintigraphy before surgery to select candidates for LVSEA.14 Patients with obvious obstruction of the lymphatic pathway with no regional lymph nodes or showing stasis of contrast medium with decrease of regional lymph nodes on lymphoscintigraphy were indicated for surgery. The operation was planned after completion of CDP for acute reduction of the affected limbs. At the beginning of surgery, a small amount of ICG (~0.1 mL each injection) for fluorescence lymphography was injected at four interdigital spaces in the affected limb and 5% patent blue dye (~0.1 mL each injection) was then injected intradermally at the same sites for detection of functional lymphatic vessels. ICG near-infrared fluorescent lymphography was then performed using the Photo Dynamic Eye. At ≥6 months after surgery, ICG fluorescence lymphography was repeated in consenting patients to determine patency of the anastomoses.

Operative technique. LVSEA was performed by one of the authors (M.J.) with the patient under general anesthesia because multiple anastomoses were required at a time. After injection of the two contrast agents, sites of anastomosis were determined between the dorsum of the foot to the thigh according to lymph stream or stasis observed by ICG fluorescence lymphography. If several lymphatic vessels were suitable for anastomoses, the one

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with the most contrast agent was selected. Even if we could detect lymphatic vessels with no fluorescence and no contrast agent in the lumen, these were not selected for anastomosis because we considered that the vessels would not work well after anastomoses were performed.

Side-to-end anastomosis was performed using a suturestent technique and 11-0 sutures. The sidewall of the lymphatic vessel was incised using a microknife according to the size of the anastomosed vein (Fig 1, A). The incision is one of the most difficult procedures in this technique, because the lumen of the lymphatic vessel can be narrow due to degeneration of the lymphatic wall in some severe cases we have encountered. In addition, care should be taken not to incise too much, otherwise adaptation of both stumps becomes difficult. Exposure of the lumen of the lymphatic vessel led to the extrusion of dyed lymph. Two 6-0 or 7-0 nylon suture stents, 3 mm in length, were inserted, one into the proximal side of the lumen and the other into the distal side (Fig 1, B and C).

If several veins were present in the incision, a vein with an appropriate size for anastomosis was selected. In our experience, a vein with a diameter of 0.5 to 1.0 mm is technically easy for anastomosis. A vein diameter <0.3 mm required insertion of a stent into the vein.

The side-to-end anastomosis began with the first stitch of the distal end of the incision on the lymphatic wall if possible, because the distal side of the lymphatics is expected to contribute a greater volume of lymph flow than the proximal side. The first stitch can be made more precisely than subsequent stitches. Clamps were used for veins with a backflow of blood from the stump, but never for lymph vessels. Side-to-end anastomoses were then completed using 11-0 nylon sutures with a tapered needle (80 µm in diameter, 4 mm in length), followed by removal of any stents (Fig 1, D).

Every anastomosis was performed using the OPMI Pentero operative microscope (Carl Zeiss Meditec AG, Oberkochen, Germany) with magnifications of ×10 to ×15. Patency of anastomoses during or at the end of surgery was always confirmed by Photo Dynamic Eye or by a patency test under microscopy (Fig 2). The number of anastomoses was decided according to the number of functional lymphatic vessels remaining and the operative time allocated for the patient. During and after the operation, no heparin or anticoagulant was used.

Statistical analysis. We calculated postoperative patency rates of LVSEA and analyzed data using the Kaplan-Meier method in the follow-up period. Differences between means of preoperative and postoperative volume were analyzed using the Student t test. Values of P < .05 were considered statistically significant. StatMate III software (ATMS, Tokyo, Japan) was used for statistical analysis. A Kaplan-Meier survival curve was generated in Graph-Pad Prism 5 software (GraphPad Software, La Jolla, Calif).

#### RESULTS

We performed 223 anastomoses in the 57 patients. Of these, 79 anastomoses in the ankle and dorsum of the foot

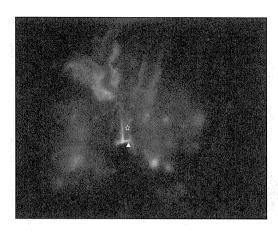
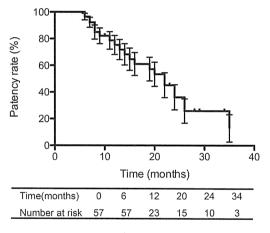


Fig 2. Patency of a lymphaticovenous anastomosis is confirmed through the surgical wound by indocyanine green fluorescence lymphography during surgery. The *star* and *triangle* indicate a cutaneous vein and a lymphatic vessel, respectively.



**Fig 3.** Kaplan-Meier survival curve is shown for patency of lymphaticovenous side-to-end anastomosis. The *error bars* show the standard error.

could be evaluated. The remaining 144 anastomoses in other areas could not be evaluated because the subcutaneous layer was too thick to allow the detection of lymph vessels by ICG fluorescence lymphography.  $^{10,11}$  Outer diameters were within the ranges of 0.2 to 0.6 mm for lymph vessels and 0.2 to 1.2 mm for veins. Mean duration of follow-up after surgery was  $14\pm9$  months (range, 6-34 months).

Postoperative patency could be observed in 48 anastomoses in the dorsum of the foot and ankle areas. Of the 57 patients, 34 had at least one patent anastomosis (group A); in the remaining 23 no anastomoses appeared patent (group B). Cumulative patency rates of LVSEAs were  $\sim$ 75%  $\pm$ 7.1% at 12 months and 36%  $\pm$ 9.4% at 24 months after surgery (Fig 3).

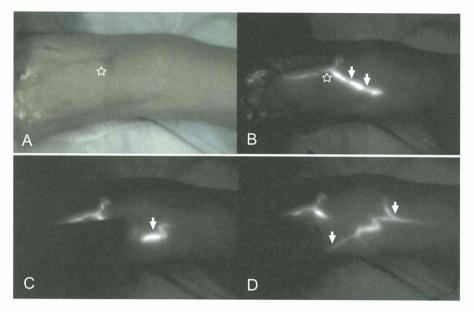


Fig 4. A, A 64-year-old patient with secondary lymphedema of the left lower extremity. The *star* indicates the site of a lymphaticovenous side-to-end anastomosis at the dorsum of the right foot. B, Indocyanine green fluorescence lymphographic images at the same site in the same patient (*star*, anastomosis site; *triangles*, lymphatic vessel; and *arrows*, subcutaneous vein). At this time, the image shows a straight pattern. C and D, When the vein is compressed, indocyanine green flows proximally through its branches, and the image shows a tree pattern.

Several ICG fluorescence lymphography patterns of the anastomosed vein could be observed at the patent anastomosis sites: straight and tree (Fig 4), radial (Fig 5), straight, and L-shaped (Fig 6).

The mean volume reductions in the leg and in the lower extremity on the affected side did not differ significantly between groups A ( $600\pm969~\text{mL}$ ) and B ( $420\pm874~\text{mL}$ ) at  $14\pm8.8~\text{months}$  after LVSEAs. No significant differences in volume reduction and number of anastomotic sites were seen between primary and secondary lymphedema.

As postoperative complications, ecchymoses expanding proximally along dermal backflow areas in the affected limb were observed on intraoperative ICG fluorescence lymphography in four patients. In all cases, this finding disappeared  $\leq 2$  weeks after surgery.

Report of a typical case. A 72-year-old woman who had undergone an extended hysterectomy with regional lymph node dissection because of uterine cancer 15 years previously developed edema of the left leg 10 years postoperatively. The patient consulted our department for surgical treatment of this edema (Fig 7, A). Lymphoscintigraphy was performed to assess whether surgery was indicated, resulting in a classification of type 4 lymphedema with a lymphoscintigraphic image of dermal backflow at the lower leg and foot and no regional lymph nodes, according to our previously described system for classifying the severity of lymphedema, <sup>13</sup> in both the right and left lower extremities. Lymphedema was severe in the left lower extremities. Lymphedema was severe in the left lower extremity (volume, 5413 mL) and mild in the right (volume, 3668 mL).

LVSEA was indicated and performed in the left lower leg because obstruction of the lymphatic pathway in the affected limb was obvious and few lymphatic vessels seemed to be able to be detected from a clinical perspective and this patient desired a reduction in CDP. We performed two LVSEAs in the dorsum of the foot, three in the leg, and one in the thigh (Fig 7, B). At 6 months, ICG fluorescence lymphography showed patency of the LVSEA on the medial side of the dorsum of the foot, whereas a tree pattern (Fig 7, C) and nonpatency were observed for the other LVSEA of the foot. The volume of the left leg was 4326 mL and that of the right was 4328 mL (Fig 7, D). Patency of the LVSEAs in the leg and thigh could not be confirmed by lymphography due to the thickness of the skin and subcutaneous tissue. Preoperative CDP with class III compression stockings was reduced to class I knee-high socks in this patient.

## DISCUSSION

An animal experiment demonstrated that the end pressure of lymphatics was higher than the venous pressure. <sup>15</sup> This suggested that LVA might be effective in peripheral lymphedema. However, postoperative patency of LVA has remained unknown in the clinical setting because of the lack of appropriate and reliable methods for postoperative detection of lymph vessels.

Several experiments assessing patency have been performed using animal models of lymphedema. Gloviczki et al<sup>16</sup> reported that four of six anastomoses were patent at 3

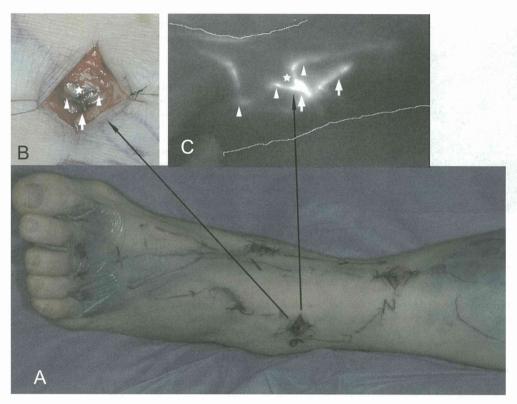


Fig 5. A 64-year-old patient with secondary lymphedema of the left lower extremity. A, Five lymphaticovenous side-to-end anastomoses were performed from the foot to the thigh on the affected limb. B, Enlargement of the anastomosis at the ankle. C, A radial pattern is seen in the indocyanine green fluorescence lymphographic imaging. The star indicates the site of anastomosis at the ankle, and the triangles indicate the lymphatic vessels. B and C, The white arrows indicate subcutaneous veins that resemble a tree with several branches.

months after LVA and that two remained patent at 8 months. In contrast, Puckett et al $^{17}$  reported that all LVAs were occluded  $\leq 3$  weeks after surgery and confirmed this by re-exposure of the wound. However, al Assal et al $^{18}$  showed long patency of a new technique of microlymphovenous anastomosis in dogs.

In clinical studies, Campisi et al<sup>8</sup> reported various changes in lymphoscintigraphy images after LVA, providing indirect proof of postoperative patency. In a study of grafting of lymph vessels, Baumeister et al<sup>9</sup> showed patency using lymphoscintigraphy, but that method differed physiologically from LVA. Anastomoses between lymphatics and veins may become obstructed more often than those between lymphatics.

Until recently, no reliable method has been available to determine the patency of LVAs. <sup>8</sup> However, ICG fluorescence lymphography evaluated using a Photo Dynamic Eye camera has recently been introduced, and this equipment has been used for detection of lymphatic vessels through the skin. <sup>10,11</sup>

The present study used ICG fluorescence lymphography to determine the competency of LVSEAs. However, because of optical limitations (the Photo Dynamic Eye camera can detect ICG no deeper than 1 cm below the skin), the areas we could evaluate were confined to the foot, ankle, and lower leg of the affected limb. In addition, the reproducibility of ICG fluorescence lymphography needs to be validated regarding the visualization of lymphatic vessels during surgery and post-operatively. Kinetics of the lymph vessels during surgery appear to differ from those at  $\geq$ 6 months after surgery. In the future, we anticipate improvements in equipment for evaluating dynamic lymph flow.

Despite these limitations, this appears to represent the first clinical report of midterm postoperative patency for LVA in patients with peripheral lymphedema assessed by ICG fluorescence lymphography. Cumulative patency rates of LVSEA were 75% at 12 months and 36% at 24 months after anastomoses, meaning that patients with anastomoses show a possibility of deterioration in lymphedema in the future. Furthermore, periodic examinations may be necessary to clarify whether additional operations are needed for patients who have received a lymphaticovenous shunt.

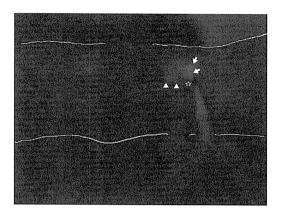


Fig 6. An L-pattern in a 32-year-old patient with primary lymphedema of the left lower extremity. The *star*, *triangles*, and *arrows* indicate the anastomosis site, lymphatic vessel, and subcutaneous vein, respectively, at the extensor side of the left lower leg.

We found no significant difference in volume change of the affected limb between patients with patent anastomoses and those without obvious evidence of patency. It is possible that the anastomoses could possibly have been patent in the areas where we could not detect by ICG fluorescence lymphography; therefore, we cannot evaluate efficacy of the patency precisely.

ICG fluorescence lymphography revealed several patterns at the patent anastomosis sites, and these patterns seemed to depend on the anastomosed vein. The radial pattern demonstrates the proximal parts of the superficial subcutaneous veins radiating like the spokes of a wheel. In the straight or straight and tree patterns, ICG seems to flow into the vein for some length and may then flow into its branches. If the proximal side of the anastomosed lymph vessel is closed, an S-shaped lymphographic pattern may be obtained. A correlation of these patterns and efficacy in edema reduction is unknown at the moment and a further examination on this issue will be performed.

Regarding the technique of LVA, the end-to-end technique joining the distal stump of the lymph vessel and the proximal stump of the vein is probably the most common worldwide. <sup>1-4</sup> If end-to-end anastomoses do not work well due to stenosis or obstruction of the anastomotic sites, edema may become worse because most patients with chronic and obstructive lymphedema are likely to have few lymphatic vessels that cannot be expected to compensate for anastomotic failure. Several reports have described good results on physiologic examination in long-term follow-up of conventional LVA, but the patency rate of conventional LVA remains unclear. <sup>5-7</sup> Further investigation is thus required to clarify optimal procedures for LVA anastomosis.

One advantage of the side-to-end technique is the potential for preservation of lymph flow if the proximal side of the anastomosis of the lymphatics remains patent.

However, incision of the sidewall of the lymphatic vessel is difficult with this technique compared with the endto-end method in some advanced cases where the lumen of the lymphatic vessel is narrow. Selection of lymph vessels is thus required and in such cases, the end-to-end method may be indicated. As a postoperative complication, ecchymosis was observed at areas proximal to the anastomotic sites. The area corresponded to the areas of dermal backflow observed on perioperative ICG fluorescence lymphography. We found no obvious leakage or breakage at the anastomotic sites during surgery; therefore, we believe that blood leaked into the interstitial space through the lymph vessels via the lymph capillary, in a similar manner to dermal backflow. 19,20 Looking back at the operative video in which we could confirm the vein selected for anastomoses, patency of the anastomotic sites tended to be observed in cases with no or little back flow from the stump of the selected vein.

In the present study, the stent method appeared useful in achieving accurate anastomosis between lymphatic vessels and small veins. Shaper et al<sup>6</sup> reported that LVAs using Teflon stents were of better quality than conventional sutured LVAs, although all anastomoses were occluded after 4 weeks. To obtain good results in microlymphatic surgery, we consider 100% patency at the time of completing the anastomosis as a requirement; otherwise, postoperative patency of the anastomosis will deteriorate. Several factors may predict postoperative anastomotic failures. One such factor may be high venous pressure due to venous disorders such as valve incompetence. Campisi et al<sup>8</sup> stressed the importance of treating venous problems before application of LVAs. Another factor may be lymph flow and pressure, because continuous inflow of lymph from the lymphatics into the vein can be expected if lymphatic pressure always overcomes venous pressure. Conversely, lymph flow is decreased in lymph vessels with very thickened walls,21 which may result in lower success rates for LVA.

In severe chronic lymphedema, lymphatic vessels lose the ability to automatically contract because of a lack of normal smooth muscle. <sup>21</sup> Even though LVA is technically successful, lymph drainage from the lymphatics to the vein tends to cease at some point after the operation, when a back flow of blood occurs once the intraluminal pressure of lymph decreases. At rest, the pressure of lymph is lower than that in the vein. <sup>8</sup> Early manual massage or CDP may thus be helpful to prevent early occlusion by fibrin or clots and to maintain long-term patency.

#### CONCLUSIONS

We demonstrated midterm postoperative patency of a LVSEA between the lymphatics and subcutaneous veins at 12 months after surgery in >70% of the present patients with peripheral lymphedema. Postoperative volume reduction in patients with anastomotic patency did not differ from that in patients without obvious patency. On the basis of these findings, development of equipment or methods to evaluate lymph flow more precisely and clearly would appear useful.

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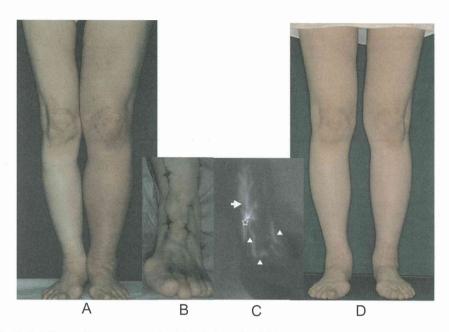


Fig 7. A, A 72-year-old woman presented with lymphedema of the left lower extremity after an extended hysterectomy with regional lymph node dissection performed 15 years previously because of uterine cancer. Severe lymphedema was evident (volume, 5413 mL). B, Two lymphaticovenous side-to-end anastomoses (LVSEAs) were performed for the dorsum of the foot, three were performed for the leg, and one for the thigh. C, Postoperative indocyanine green fluorescence lymphography shows patency of the LVSEA at the medial side of the dorsum of the foot, where a tree pattern was observed, and nonpatency at the other LVSEA of the foot (star, anastomosis site; triangles, lymphatic vessel; arrow, subcutaneous vein). D, At 6 months after LVSEA, lymphedema of the left lower extremity has improved (volume, 4326 mL).

#### **AUTHOR CONTRIBUTIONS**

Conception and design: JM
Analysis and interpretation: JM
Data collection: YY, HT, MH, KY
Writing the article: JM
Critical revision of the article: JM
Final approval of the article: JM
Statistical analysis: JM and YY
Obtained funding: Not applicable
Overall responsibility: JM

#### REFERENCES

- O'Brien BM, Sykes P, Threlfall GN, Browning FS. Microlymphaticovenous anastomoses for obstructive lymphedema. Plast Reconstr Surg 1977;60:197-211.
- Huang GK, Hu RQ, Liu ZZ, Shen YL, Lan TD, Pan GP. Microlymphaticovenous anastomosis in the treatment of lower limb obstructive lymphedema: analysis of 91 cases. Plast Reconstr Surg 1985;76: 671-85.
- 3. Campisi C. Use of autologous interposition vein graft in management of lymphedema: preliminary experimental and clinical observations. Lymphology 1991;24:71-6.
- Koshima I, Inagawa K, Urushibara K, Moriguchi T. Supermicrosurgical lymphaticovenular anastomosis for the treatment of lymphedema in the upper extremities. J Reconstr Microsurg 2000;16:437-42.
- 5. O'Brien BM, Mellow CG, Khazanchi RK, Dvir E, Kumar V, Pederson WC. Long-term results after microlymphaticovenous anastomoses for

- the treatment of obstructive lymphedema. Plast Reconstr Surg 1990;85:562-72.
- Campisi C, Boccardo F, Zilli A, Macciò A, Napoli F. Long-term results after lymphatic-venous anastomoses for the treatment of obstructive lymphedema. Microsurgery 2001;21:135-9.
- Koshima I, Nanba Y, Tsutsui T, Takahashi Y, Itoh S. Long-term follow-up after lymphaticovenular anastomosis for lymphedema in the leg. J Reconstr Microsurg 2003;19:209-15.
- Campisi C, Davini D, Bellini C, Taddei G, Villa G, Fulcheri E, et al. Lymphatic microsurgery for the treatment of lymphedema. Microsurgery 2006;26:65-9.
- Baumeister RG, Siuda S. Treatment of lymphedemas by microsurgical lymphatic grafting: what is proved? Plast Reconstr Surg 1990;85: 64.74
- Ogata F, Narushima M, Mihara M, Azuma R, Morimoto Y, Koshima I. Intraoperative lymphography using indocyanine green dye for near-infrared fluorescence labeling in lymphedema. Ann Plast Surg 2007;59: 180-4.
- 11. Unno N, Inuzuka K, Suzuki M, Yamamoto N, Sagara D, Nishiyama M, et al. Preliminary experience with a novel fluorescence lymphography using indocyanine green in patients with secondary lymphedema. J Vasc Surg 2007;45:1016-21.
- Shaper NJ, Rutt DR, Browse NL. Use of Teflon stents for lymphovenous anastomosis. Br J Surg 1992;79:633-6.
- International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. Consensus document of the International Society of Lymphology. Lymphology 2003;36:84-91.
- Society of Lymphology. Lymphology 2003;36:84-91.

  14. Maegawa J, Mikami T, Yamamoto Y, Satake T, Kobayashi S. Types of lymphoscintigraphy and indications for lymphaticovenous anastomosis. Microsurgery 2010;30:437-42.

JOURNAL OF VASCULAR SURGERY March 2012

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- Huang GK, Hsin YP. Relationship between lymphatic and venous pressure in normal and lymphedematous rabbit ears. Microsurgery 1984;5:36-9.
- Gloviczki P, Hollier LH, Nora FE, Kaye MP. The natural history of microsurgical lymphovenous anastomoses: an experimental study. J Vasc Surg 1986;4:148-56.
- Puckett CL, Jacobs GR, Hurvitz JS, Silver D. Evaluation of lymphovenous anastomoses in obstructive lymphedema. Plast Reconstr Surg 1980;66:116-20.
- al Assal F, Cordeiro AK, De Souza e Castro I. A new technique of microlympho-venous anastomoses. Experimental study. J Cardiovasc Surg (Torino) 1988;29:552-5.
- Suami H, Pan WR, Taylor GI. Changes in the lymph structure of the upper limb after axillary dissection: radiographic and anatomical study in a human cadaver. Plast Reconstr Surg 2007;15:982-91.
- Stanton AW, Mellor RH, Cook GJ, et al. Impairment of lymph drainage in subfascial compartment of forearm in breast cancer-related lymphedema. Lymph Res Biol 2003;1:121-32.
- Koshima I, Kawada S, Moriguchi T, Kajiwara Y. Ultrastructural observations of lymphatic vessels in lymphedema in human extremities. Plast Reconstr Surg 1996;97:397-405.

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#### INVITED COMMENTARY

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Chronic lymphedema continues to be an incurable and disabling condition. Microsurgical reconstructions of lymph vessels have been possible because of the pioneer work done by Julius H. Jacobson in the early 1960s; variations of techniques have been used by few microsurgical groups around the world during the past 5 decades with mixed results. Recent progress in imaging of the lymphatic system and in microsurgical techniques sparked renewed interest in microscopic lymphatic reconstructions and the article by Maegawa and colleagues (in this issue) of the Journal of Vascular Surgery is an example of what dedicated lymphatic microsurgeons can achieve in this challenging and frequently frustrating field.

One major problem of lymphatic microsurgery has been the proper patient selection for the operation. These authors have used the technique of indocyanine green fluorescence lymphography to identify patent lymph vessels during surgery. The indocyanine green dye was injected subcutaneously in the foot of the patient and the lymphatics were imaged within a few minutes through the skin using a near-infrared camera system. This imaging technique, introduced previously by Ogata et al and by Unno et al (10,11 in the article) is a new and useful tool to help during surgery and to document late patency of the anastomoses.

Supermicroscopic surgical techniques have progressed in recent years<sup>1-5</sup> and better operating microscopes with high-power magnifications (×15-20), better instruments and fine (11-0) monofilament sutures with an 80-µm needle have permitted to perform anastomosis with lymph vessels with a diameter of 0.2 to 0.6 mm. Two technical improvements these authors applied deserve to be mentioned. One is the use of 6-0 or 7-0 monofilament sutures to stent the lymph vessel or a small vein for easier and better anastomosis. The other is the side-to-end lymphovenous anastomosis technique that, in theory, may keep the lymph vessel patent even if the vein occludes after surgery. This may avoid progression of the lymphedema as a complication of surgical treatment. Both of these technical improvements were reported previously by Narshima et al.<sup>3</sup>

One of many critiques of the lymphovenous operations has been the lack of objective documentation of late patency in humans. The main value of this publication, therefore, is the attempt to confirm patency of lymphovenous anastomoses. While patency of several of the anastomoses at the level of the ankle or foot beyond 6 months could be documented using indocyanine green lymphoscintigraphy, the cumulative patency rates (75% at 12 months and 36% at 24 months) as reported by the authors, cannot be accepted without major criticism. This study originally included 472 anastomoses in 107 patients. Attempts to assess function at 6 months or later were done in only 57 patients who underwent 223 anastomoses, but only 48 of these were close to the skin and were suitable for lymphoscintigraphic evaluation. Finally, patency rates in this limited group were not reported by the number of anastomoses but by the number of patients with any patent anastomosis.

Shortcomings notwithstanding, this work by Maegawa and colleagues is an important contribution to the literature, with demonstration of exceptional microsurgical technique and a welcome documentation of late patency of lymphovenous anastomoses to improve lymphatic drainage in patients with chronic lymphedema.

#### REFERENCES

- Demirtas Y, Ozturk N, Yapici O, Topalan M. Supermicrosurgical lymphaticovenular anastomosis and lymphaticovenous implantation for treatment of unilateral lower extremity lymphedema. Microsurgery 2009;29:609-18.
- Demirtas Y, Ozturk N, Yapici O, Topalan M. Comparison of primary and secondary lower-extremity lymphedema treated with supermicrosurgical lymphaticovenous anastomosis and lymphaticovenous implantation. J Reconstr Microsurg 2010;26:137-43.
- 3. Narushima M, Mihara M, Yamamoto Y, Iida T, Koshima I, Mundinger GS. The intravascular stenting method for treatment of extremity lymphedema with multiconfiguration lymphaticovenous anastomoses. Plast Reconstr Surg 2010;125:935-43.
- Baumeister R. Lymphedema: surgical treatment. In: Cronenwett JL, Johnston KW, editors. Rutherford's Vascular Surgery. 7th ed. Philadelphia: Saunders; 2010. p. 1029-43.
- Gloviczki P. Principles and indications of reconstructive lymphatic microsurgery. In: Lee BB, Bergan J, Rockson SG, editors. Concise compendium of theory and practice. London: Springer-Verlag; 2011. p. 377-41

特集-1 形成外科手技を応用した血行再建



# 形成外科手技を応用した血行再建

# リンパ管静脈吻合術

横浜市立大学附属病院 形成外科 細野 味里、前川 二郎

#### はじめに

リンパ浮腫は発症すると難治であり、重症例ではほぼ永続的な保存療法(圧迫療法など)を行うことが多い。手術療法として、うっ滞したリンパを静脈にバイパスすることにより改善を図るリンパ管静脈吻合術が近年広く行われてきている。当科では200例近くにリンパ管静脈吻合術を施行し、保存療法が必要でなくなった症例も経験している。

今回、当科で行っているリンパ管静脈吻合術 の詳細について述べる。

#### 評価・適応について

病歴や身体所見からリンパ浮腫と思われる症例には全例でリンパシンチグラフィを施行し、リンパ機能の評価を行う。われわれはリンパシンチの画像を浮腫の程度でタイプ I から V に分類しているが Iv 2)、この中で機能的集合リンパ管(以下リンパ管)が検索しやすいのはタイプ II や II である。皮膚逆流現象 (Dermal backflow、以下 DBF) や拡張したリンパ管が認められる部位では末梢からのリンパ流がある程度保たれていると考えられ、術中に機能的なリンパ管を同定出来る確率が高い。タイプ IV や V になるとリ

ンパが中枢へ流れにくくなり、下腿の中枢側や大腿で機能的リンパ管を検索することが難しくなる。この様に、術前リンパシンチではある程度吻合部の予測が可能であり、タイプ II から V には手術適応があると考える。また、リンパ管機能が失われる前に吻合術を行うことが重要であると考えるが、手術の至適時期については今後の検討が必要である。

#### 手技内容

基礎疾患等で制限がなければ基本的に全身麻酔下で手術を施行する。

麻酔が完了したのちに、インドシアニングリーン(以下ICG)を0.1から0.2ml程度各足趾間に皮内から皮下に注入し、直ちに注入部のマッサージを施行する。蛍光赤外線カメラ(Photo Dynamic Eye、以下PDEカメラ:浜松ホトニクス社製)を使用し、経皮的に皮下のリンパ管・DBFの位置をピオクタニンでマーキングする。リンパ管が認められた部位やDBFの末梢で皮膚切開を行う。

大腿では皮下組織厚が増加するため、ICGによる蛍光赤外リンパ管造影では集合リンパ管を見つけることが困難になる症例が多い。この様な場合は、術前のリンパシンチ画像より、大腿でのリンパ管の位置を推定し、皮膚切開部分を決定する。

次に0.1から0.2ml程度の5%パテントブルーを各足趾間に皮内から皮下に注入する。

特集-1 形成外科手技を応用した血行再建

皮膚を切開して皮下を剥離する場合、パテントブルーにわずかに染まっていると、リンパ管を同定しやすくなる。

皮膚を切開し、顕微鏡下で色素を頼りに皮下 脂肪内にあるリンパ管を同定する。

切開部位に全くリンパ管が見つからない場合は、創部にPDEカメラをかざして、皮下脂肪層内のリンパ管を確認するが、これでも見つからない場合は、別の部位を切開する必要がある。 最近は顕微鏡下に蛍光を利用したリンパ管同定が可能となっている。

同定したリンパ管の周囲を剥離しベッセルループをリンパ管の下に通す。次にその近傍にある皮静脈を同定、剥離する。リンパ管と同程度(外径0.3mm)あるいはその倍程度の皮静脈が吻合に適しているが、そのような静脈が認められない場合、皮膚切開を追加して検索する。

リンパ管と静脈の吻合には、端側吻合、端々吻合、側端吻合がある。また、口径差がある場合や静脈がリンパ管まで届かない場合は静脈移植304検討する。

当科ではリンパ管本管の流れが障害されず、 上流での吻合も可能である端側吻合が最も効率 のよい吻合と考え、ほぼ全吻合で適応している。

#### 端側吻合

リンパ管の側に静脈端を吻合する。静脈はリンパ管に十分届くことを確認したのち結紮・切離し中枢端を吻合する。リンパ管はマイクロメスで静脈径に合わせて切開する。よく拡張したリンパ管であれば切開したときにパテントブルーで青く染まったリンパ液が流出することで確認出来る。拡張がないリンパ管や壁が肥厚し内腔が狭窄している症例では内腔の同定が困難なことがあるが、長さ3mmに切った6-0ナイロンをステントとして通すことにより内腔の確認が可能である。リンパ管切開部分からステントとなる6-0ナイロンを末梢側、中枢側の2方向に1本ずつ挿入する。静脈の径が細い場合は静脈端に

もステントを挿入するか。

ステントで内腔を確認しながら11-0ナイロンで吻合する。後壁を縫い合わせ、次に前壁を吻合する。ステントは残り数針となった時点で1本ずつ抜去するが、内腔が確認出来るよう、最後の1本はすべて吻合し終わったのちに抜去する。

吻合の開存はマイクロ下での青く染まったリンバ液の静脈への流入の確認、PDEカメラで ICGが静脈へ流入し、Y字あるいはT字になる ことで確認することが出来る。

#### 術後管理と後療法

術後4日間は患肢拳上とする。5~7日目までは弾性包帯による圧迫を行い、それ以降は術前に着用していた弾性着衣の着用を再開する。抗凝固療法は行っていない。用手的ドレナージは治療院と連携し、退院後早期(術後1~2週間後)より開始する。

術後1ヵ月、3ヵ月、6ヵ月で外来受診とし、 周径の測定、浮腫の変化や自覚症状の変化を確 認する。

また、術後6ヵ月以降に外来で蛍光赤外リンパ管造影を施行し、吻合部開存の確認を行っている。吻合部の開存は皮膚切開部でY字あるいはT字に造影され、静脈への流入後に流速が増すことによって確認出来る。しかし、体表から蛍光赤外リンパ管造影で開存が確認出来るのは皮下脂肪が薄い下腿遠位までに限られることが多い。

#### 結 果

リンパ管静脈吻合の効果としては体積の減少が得られる症例もあるが、皮膚が柔らかくなった、浮腫が引きやすくなった、炎症の頻度が減ったなどの自覚症状の改善を多くの症例で認めている。また、弾性着衣が不要になった例や、より軽い圧迫でも浮腫が生じにくくなるなど、理学療法の軽減が得られた症例も多い。現在の

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#### 特集-1 形成外科手技を応用した血行再建

ところ、吻合部の長期開存率は約40%である。

#### まとめ

当科でのリンパ管静脈吻合術における詳細を 報告した。

手術至適時期や、手術後の評価方法について は、今後さらなる検討を行っていく必要がある。 また、術後半年以降での長期開存に影響する因 子もいまだ十分には検討されておらず、効果的 な吻合部位や吻合数についても未だ不明な点が 多い。今後、さらに症例を重ね、より効果的な 手術法の検討を行っていく。

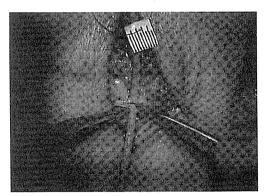


図1 リンパ管に切開を入れ、3mmに切った6-0ナイロンを両方向に挿入する

## ■文 献

- Maegawa J, Mikami T, Yamamoto Y, et al. Types of lymphoscintigraphy and indications for lymphaticovenous anastomosis. Microsurgery, 2010;30:437-442
- 前川二郎, 鮑智伸, 佐武利彦: 【四肢のリンパ浮腫の 治療】リンパシンチグラフィーによるリンパ浮腫の 評価。PEPARS.2008; 22:29-34
- Maegawa J, Mikami T, Yamamoto Y, et al. Lymphaticovenous shunt for the treatment of chylous reflux by subcutaneous vein grafts with valves between megalymphatics and the great saphenous vein: a case report. Microsurgery, 2010;30:553-556
- Shaper NJ, Rutt DR, Browse NL. Use of Teflon stents for lymphovenous anastomosis. Br J Surg 1992;79 (7):633-636.

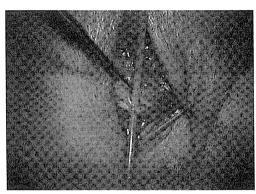


図2 吻合終了時

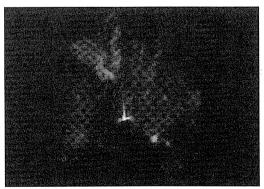


図3 PDEカメラでICGの流入を確認する

# リンパ管静脈側端吻合術におけるlate patencyの検討

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Evaluation of late patency after lymphaticovenous side-to-end anastomosis

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Key words: lymphedema, lymphaticovenous anastomosis, late patency, fluorescein angiography, indocyanine green

#### はじめに

慢性リンパ浮腫に対する外科治療として、リンパ管 静脈吻合術(lymphaticovenous anastomosis, 以下 LVA) は代表的手法の一つとして確立しつつある. し かしその一方で術後の吻合部や外科治療の臨床的効果 を評価する方法は、未だ一定したものはない。 今回リ ンパ管静脈側端吻合術術後の症例に対してインドシア ニングリーン (Indocyanine green, 以下ICG) を用い た蛍光赤外線リンパ管造影により、それらの評価を試 みた.

#### 対

対象は、2007年11月~2009年4月(1年6カ月)の 間に当院でリンパ管静脈吻合術を行った27例のうち、 術後6カ月以上経過し蛍光赤外線リンパ管造影に同意 し検査を受けた下肢リンパ浮腫症例とした, その結果, 対象症例は21例21肢で、内訳は、男性1例、女性20例、 平均57.8歳(28-80歳), 続発性18例, 原発性3例であっ た. 総吻合数は121か所であった. ただし, 上記には 両側性の症例も含まれるが、蛍光赤外線リンパ管造影 を施行しえた患肢を1肢として集計した.また、本研 究は当院倫理委員会の承認を得て行われた.

#### 方 法

光赤外線システム(浜松ホトニクス社製)を用いて観

患肢の第1,4趾間に0.25%ICGを少量皮内注射し、蛍

察した. われわれは、リンパ管の側壁に切離した静脈 の中枢側断端を吻合する側端吻合術を施行している. そのため、開存している吻合部は基本的にYあるいは T字状に造影される. また吻合脈管の方向を術中確認 しており、それも含め開存の有無の判断材料とした.

ただし、皮膚逆流現象 (dermal back flow, 以下 DBF) を伴う部位や、吻合部が深く造影が不明瞭な部 位は「評価困難」とし、開存/非開存吻合部とは分け て分類した.

検討項目は, 吻合部開存の有無, 年齢などの一般統 計的項目、および患肢の体積減少量とした。また、術 中所見のうち吻合リンパ管のリンパ流, 吻合静脈の逆 流、吻合後の吻合部を越える静脈血またはリンパ液の 有無を追跡できたものは吻合部毎に検討した.

体積の評価は円錐台への近似による計測法"を用い た. 計測ポイントは膝蓋骨上縁から10cm近位, 膝蓋骨 下縁から10cm遠位,足関節部の3点とし,それぞれに よって求められる体積をそれぞれ膝関節周囲体積、下 腿遠位部体積として算出した.

吻合部の開存が確認できた群は9例、できなかった 群は12例であった. 男女差などの一般統計的項目や重 症度、術後経過期間を比較したが、統計学的有意差は 認めなかった (表1). また、2 群間において患肢の 体積減少量を比較した (表2). 確認された群の体積

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