

Comparison of patency rates of lymphaticovenous anastomoses at different sites for lower extremity lymphedema



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ABSTRACT

Objective: Lymphaticovenous anastomosis (LVA) is one of the surgical treatments of lymphedema. However, only a few reports have evaluated LVA directly. This study aimed to evaluate the patency of LVA using indocyanine green fluorescence lymphography and to determine the optimal anastomosis site in patients with lower extremity lymphedema.

Methods: Thirty-six patients, with a total of 123 anastomoses for lower extremity lymphedema including 3 cases of idiopathic lymphedema, who underwent LVA for the first time between March 2014 and March 2017 were selected for enrollment in this study. The patency of the anastomoses was evaluated using PDE-neo (Hamamatsu Photonics, Hamakita, Japan) by injecting indocyanine green into the subcutaneous tissue at 6 months postoperatively. The site of anastomosis was the intersection point of the lymphatic vessel and vein, which was identified preoperatively. To determine the best surgical location, the anastomosis site was classified into the joint area (ankle and knee) and nonjoint area (dorsum and lower leg). The anastomosis was evaluated as either patent or nonpatent.

Results: Patency was confirmed in 37 of the 76 (49%) anastomoses at the joint area and 12 of the 47 (26%) at nonjoint areas ($P = .01$).

Conclusions: The patency rate was significantly higher around the joint area than at the nonjoint areas. LVA around the joint area is recommended to ensure favorable technical and surgical outcomes for patients with lower extremity lymphedema. (*J Vasc Surg: Venous and Lym Dis* 2019;7:222-7.)

Keywords: Lymphaticovenous anastomosis; Indocyanine green; Lower extremity lymphedema; Patency

Lymphaticovenous anastomosis (LVA), one of the treatment modalities for lymphedema, is aimed at symptom relief by creation of an anastomosis between the congested lymphatic vessel, secondary to lymphedema, and a vein. LVA reconstructs the physiologic lymphatic flow with minimal invasiveness and contributes to improving patients' lives. However, it requires a sophisticated supermicrosurgical technique as the diameter of the lymphatic vessel is usually smaller than 0.8 mm.¹ Thus, evaluating the patency of the anastomosis in patients who have undergone LVA surgery yields information on the technical outcomes. Indocyanine green (ICG) fluorescence lymphography can be used for real-time evaluation of the lymphatic flow. A few published reports have evaluated the postoperative anastomosis

patency.^{2,3} However, no reports investigating the optimal anastomosis site have been published so far.

LVA essentially connects the lymphatic vessel to the vein to relieve congestion in the lymphatic flow. Hence, the patency rate is one of the most important factors by which the surgical results can be judged. Thus, this study aimed to evaluate the patency of LVA using ICG fluorescence lymphography in patients with lower extremity lymphedema and to determine the optimal anastomosis site to obtain the best technical and surgical outcomes.

METHODS

Thirty-six female patients with lower extremity lymphedema who underwent LVA between March 2014 and March 2017 were included in this study. The LVA patency was evaluated using ICG fluorescence lymphography at 6 months after the first LVA operation. We simultaneously collected subjective data by asking the patients about the symptoms they noticed, without telling the patients patency results. When the patient was aware of improvement in the edema, the LVA outcome was considered to be positive. When the edema was static or aggravated, the outcome was considered negative.

All patients underwent complex decongestive physiotherapy at least 6 months before surgery. Patients wore compression garments during the day, and lymphatic drainage was performed at night using a wearable low-pressure compression wrap originally made of urethane foam. Surgery was performed in patients who

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exhibited a linear lymphatic pattern, as detected by ICG. This linear pattern reflected adequate functioning of the lymphatic vessel, and favorable results were expected.⁴ The anastomosis site was to this linear pattern (Fig 1). During the operation, the lymphatic vessel was identified by injection of patent blue (Wako Junyaku Kogyo Co, Ltd, Osaka, Japan),⁵ and it was anastomosed to the vein using 11-0 or 12-0 nylon. The patients underwent either lymphaticovenous side-to-end anastomosis (LVSEA) or lymphaticovenous end-to-end anastomosis (LVEEA). We mainly performed LVSEAs to preserve the remaining lymphatic vessels, whereas LVEEAs were performed only in regions in which the main lymphatic flow was less crucial, such as before dermal backflow (Fig 1), or where two functioning lymphatic vessels were found near the anastomosis site.³ The patency of the anastomosis was evaluated using an infrared camera system (PDE-neo; Hamamatsu Photonics, Hamakita, Japan) after injection of ICG into the subcutaneous tissue. PDE-neo emits light at a wavelength of 760 nm and activates ICG, thus enabling detection of the lymphatic flow in subcutaneous tissue.⁶ The anastomosis was classified as either patent or nonpatent (Fig 2; Video, online only). The lymphatic flow was mapped for all patients using ICG and PDE-neo 1 day before LVA surgery. The vein for anastomosis was identified by ultrasound. We assessed the adjacent lymphatic vessels to identify the vein, including where the vein originated, its diameter, and its flow direction. In this study, the site of the anastomosis was decided on the basis of the following protocol. First, the linear pattern in the ICG was checked. Second, the linear pattern through the dermal backflow was detected. Third, the appropriate vein for anastomosis that was closest to the lymphatic vessel and had a diameter of around 1 mm was identified. Finally, the anastomosis site, which was the intersection point or the site adjacent to the lymphatic vessel and vein, was classified into four locations: dorsum of the foot, around the ankle, in the middle of the lower leg, and around the knee. The middle portion of the lower leg is considered a site where the skin is not extended by joint motion. It spans from approximately 5 cm above the malleolus to approximately 5 cm beneath the patella. In addition, ankle and

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center retrospective study
- **Key Findings:** Using indocyanine green fluorescence lymphography to evaluate patency of 123 lower extremity lymphaticovenous anastomoses in 36 patients with lower extremity lymphedema, patency was >49% (37/76) in joint areas (knee and ankle) vs 26% (12/47) in nonjoint areas ($P = .01$).
- **Take Home Message:** Lymphaticovenous anastomoses performed around the knee or the ankle rather than in the mid lower leg or dorsum of the foot have the best patency for treatment of lower extremity lymphedema.

knee areas were grouped as joint areas and the other areas (dorsum and middle of the lower leg) as the nonjoint areas. Potential anastomotic sites are not always limited to these locations. Anastomosis can also be performed in the thigh or in the groin level. However, because of the thick subcutaneous tissue in these areas, assessing lymphatic flow by ICG is difficult; thus, the patency of the anastomosis around the thigh and groin cannot be accurately assessed. Therefore, we excluded these two areas from our analysis.

Retrospective evaluation was conducted by reviewing the patients' medical records, intraoperative pictures, and motion videos. Fisher exact test was used to compare the objective patency result and patients' subjective results, and the χ^2 test was used to compare the patency rates of each anastomosis site. A P value < .05 was considered statistically significant.

All study participants provided written informed consent. This study was approved by our institution's Institutional Review Board.

RESULTS

Among the 36 patients enrolled in this study, a total of 123 anastomoses were performed (47 LVEEAs and 76 LVSEAs). All 36 patients were female, with an average age of 57 years (range, 34-80 years). The cause of lymphedema was cervical cancer in 15 patients, uterine cancer in

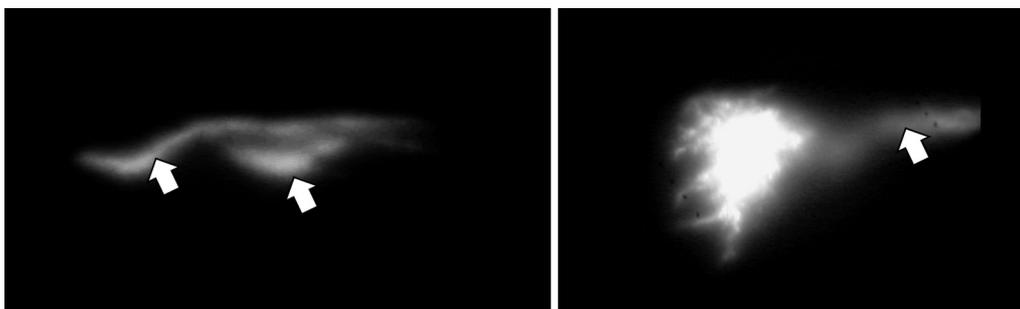


Fig 1. The arrow shows the linear pattern that reflects good lymphatic function (left and right). Linear pattern just before dermal backflow (right). We chose to conduct lymphaticovenous end-to-end anastomosis (LVEEA) in this area.

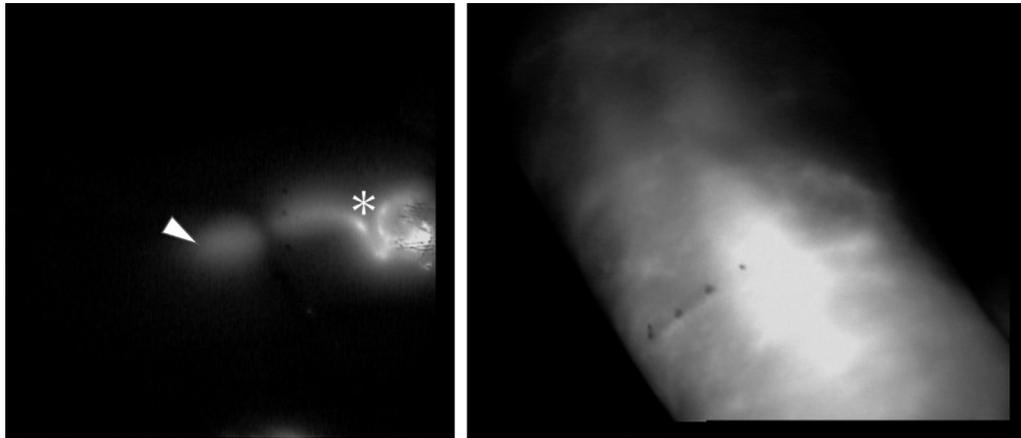


Fig 2. *Left.* Patency is suggested by the flow of indocyanine green (ICG). *Right.* Patency cannot be evaluated because of dermal backflow. This anastomosis was considered nonpatent. *, Lymphatic vessel; ▽, vein.

13, ovarian cancer in 3, surgery of nonmalignant origin in 1, and trauma in 1; there were 3 patients with primary lymphedema. The patients' demographic data are listed in Table I. The relationship between ICG patency and the patients' postoperative subjective data is shown in Table II. Thirty patients had at least one patent anastomosis, and all of them experienced an improvement in edema. Six patients had no patent vessels despite multiple anastomoses; four of them had unfavorable outcomes. The differences between these groups were statistically significant (Fisher exact test, $P < .01$).

The following anastomoses were patent: 3 of the 12 (25%) anastomoses at the dorsum of the foot, 18 of the 33 (55%) around the ankle, 9 of the 35 (26%) in the middle of the lower extremity, and 19 of the 43 (44%) around the knee. In summary, 37 of 76 anastomoses were patent in the joint area, and 12 of 47 were patent in the nonjoint area. A significant difference in the patency rate was found between the anastomoses in the joint area and those in the nonjoint area ($P < .05$; Fig 3). In addition, we focused on the LVSEA result. A total of 26 of 54 anastomoses were patent in the joint area, and 7 of 30 were patent in the nonjoint area. A significant difference in the LVSEA patency rate was also found between the anastomoses in the joint area and those in the nonjoint area ($P < .01$; Fig 4).

DISCUSSION

Surgical treatments such as LVA and lymph node transfers are currently used for lymphedema in addition to conservative compression therapy.^{3,4,7,8} LVA effectively reconstructs the physiologic lymph flow by connecting the congested lymphatic vessel to a vein; it is minimally invasive surgery as the skin incision measures only 2 to 3 cm. Favorable outcomes have been reported for lymphedema treatment^{2,8-10}; however, LVA was sometimes found to be ineffective for advanced lymphedema.

Circumference, water volumetry^{8,9,11} and lymphoscintigraphy^{8,9} are well-known postoperative evaluation modalities after LVA. However, evaluation according to the extremity volume, such as the circumference, is easily affected by compression therapy. Thus, it is difficult to obtain true technical results. Lymphoscintigraphy can

Table I. Demographic data of the patients

Age, years	
Average	57
Range	34-80
Duration of lymphedema, years	
Average	4.3
Range	0.5-19
Sex	
Female	36
Male	0
Causative disease	
Cervical cancer	15
Uterine cancer	13
Ovarian cancer	3
Primary	3
Others	2
Lymphadenectomy ^a	
Positive	23
Negative	1
Unknown	8
Radiation therapy ^a	
Positive	6
Negative	20
Unknown	6
History of cellulitis	
Positive	13
Negative	23

^aThree primary lymphedemas and one lymphedema caused by trauma were excluded.

Table II. Relationship between indocyanine green (ICG) patency and patients' postoperative subjective data

	Patent anastomosis	
	Positive	Negative
Subjective result		
Good	30	2
Poor	0	4

Significant difference was found between these groups (Fisher exact test, $P < .01$).

evaluate lymphatic function by assessing the postoperative lymphatic flow and dermal backflow. However, evaluation of the local anastomosis site is difficult, especially if many anastomoses are performed in one operation. Therefore, ICG was used for postoperative evaluation. A few previous studies have used ICG fluorescence lymphography to evaluate the patency of anastomosis.^{2,3} ICG can evaluate each anastomosis in real time. However, it is difficult to penetrate areas deeper than 2 cm using ICG,^{6,12,13} including the area under dermal backflow. As a result, some anastomoses may be mistakenly evaluated as nonpatent. This is a disadvantage of this procedure that would make the test inaccurate. However, in our study, the knee area showed a higher patency rate despite its being deeper than the calf area. Thus, we believe the accuracy of this test is supported to some extent. In addition, Table II shows that the patency rate and postoperative subjective symptoms were strongly correlated. This means that the technical result and the

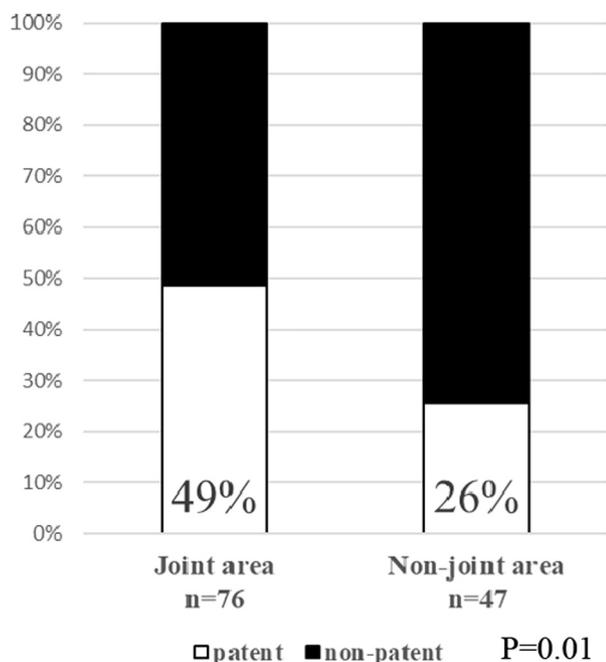


Fig 3. Patent vs nonpatent lymphaticovenous anastomoses (LVAs) between the joint and nonjoint areas.

surgical result are correlated. Evaluating the subjective symptom was a blinded test because we asked patients for their assessment without telling them the actual patency.

We found that there was a significant difference between the joint area and the nonjoint area (Fig 3). In addition, we analyzed these data in depth. First, we used the two strategies of LVEEA and LVSEA. This may cause a bias in that LVEEA showed relatively low patency rates compared with LVSEA because the lymphatic vessel was possibly damaged. Thus, we focused only on LVSEA. Even if we used only LVSEA to compare patency around the joint area and nonjoint area, there were significant differences ($P < .01$). The fact that the patency rate is higher around the joint area than in the nonjoint area is strongly supported by segmental data.

The reason for this high patency rate was hypothesized according to the following reasons. First, the knee area is well known to be a good anastomosis site, and it is the site used for the superior-edge-of-the-knee incision (SEKI) method.¹⁴ It is hypothesized that anastomosis around the knee, a highly movable periarticular area, leads to accelerated lymphatic flow by muscle compression, thereby leading to favorable results. The ankle area is also a joint area, wherein the surrounding skeletal muscle helps in accelerating lymphatic flow, thereby leading to favorable outcomes. The patency rate of the

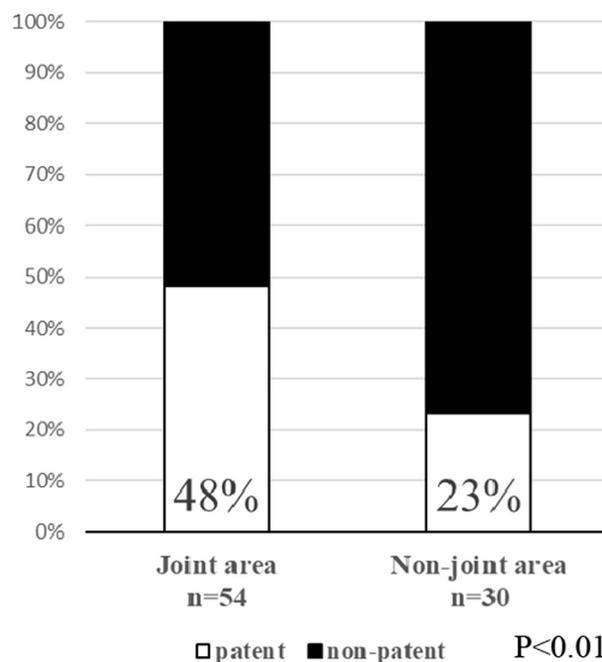


Fig 4. Patent vs nonpatent lymphaticovenous anastomoses (LVAs) between the joint and nonjoint areas focused on side-to-end anastomoses only, representing more segmental data. Significant differences can be observed in segmental data, implying that the differences are more reliable.

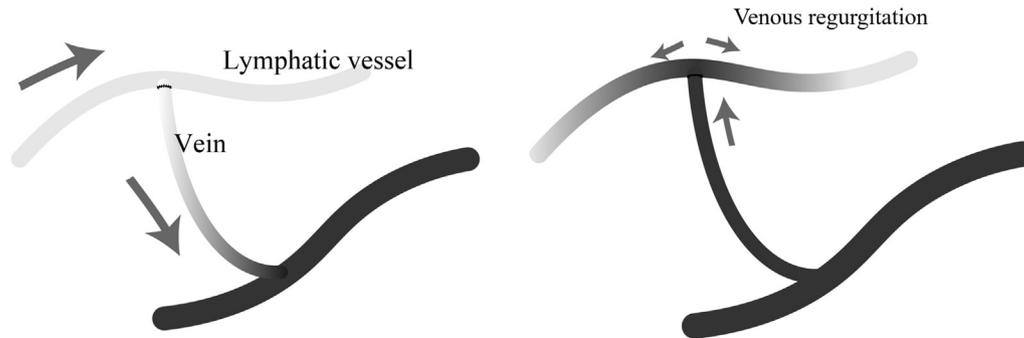


Fig 5. Venous regurgitation sometimes occurs after lymphaticovenous anastomosis (LVA). Thus, to evaluate LVA, it is imperative to evaluate both lymphatic and venous functions.

anastomosis around the ankle area was relatively high in this study.

Furthermore, venous factors in addition to lymphatic factors may contribute to favorable surgical outcomes. We often encounter poor runoff of the lymphatic flow because of regurgitation from the vein (Fig 5). Lymphatic pressure is higher than the venous pressure in animal models¹⁵; however, regurgitation often occurs after LVA. It has been proved that venous factors are among the non-negligible factors for this procedure. A venous diameter of approximately 1 mm is suitable for anastomosis. Studies have shown that such veins with a diameter of at least 1 mm have valves.^{16,17} Valves in veins, especially those 2 mm in diameter, are called microvenous valves (MVVs). MVVs are more frequently encountered in regions over hard structures, such as tendons.¹⁸ Tendons are clearly abundant around joint areas. It is possible that the abundant MVVs may reduce regurgitation. Moreover, muscle pumping may reduce the venous pressure, which can reach up to >100 mm Hg when a patient is standing. Lymphatic and venous systems interact in complicated ways to achieve good and patent anastomosis.

Based on our findings, we believe that LVA around the joint areas will lead to favorable outcomes. Multiple LVAs are reported to have favorable outcomes,¹⁹ but it is difficult to conduct multiple operations in some hospitals. We believe that less invasive and more effective “minimized LVA” can be performed around joint areas. This study is limited in that an anastomosis that was patent in 6 months sometimes presented with occlusion when we assessed the same area after a year. This is only a midterm result. Thus, future studies should be conducted assessing the long-term outcome.

CONCLUSIONS

The anastomosis patency rates around the joint areas were significantly higher than those around the other areas. This suggests that anastomosis around these areas will lead to improved surgical outcomes.

AUTHOR CONTRIBUTIONS

Conception and design: YS, HS

Analysis and interpretation: YS, HS

Data collection: YS, HS, SY

Writing the article: YS

Critical revision of the article: YS, HS, SY

Final approval of the article: YS, HS, SY

Statistical analysis: YS

Obtained funding: Not applicable

Overall responsibility: YS

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