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Line production system for multiple lymphaticovenular anastomoses

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Summary *Background:* A drawback of multiple lymphaticovenular anastomoses (LVAs) is the need for at least two microsurgeons and the same number of microscopes. In practice, many hospitals find it difficult to access such resources. We have developed a novel line production system (LPS) to address this problem. We assessed whether or not the LPS is better than the conventional dual microscope (DM) system when performing multiple LVAs.
Methods: An LPS group, wherein a novice microsurgeon used loupes to dissect lymphatics and an expert microsurgeon used a microscope to perform the LVAs, and a DM (control) group, wherein the surgeons used microscopes to perform the LVAs. We recorded the lymphatic detection rate through the loupes and the diameter of the detected lymphatics. We also investigated the impact of using the LPS by comparing the number and quality of LVAs and improvement in lymphedema between the study groups.
Results: The mean lymphatic detection rate was 81%±15.60%, and the mean size of lymphatics was 0.44 ± 0.12 mm in the LPS. The number of LVAs/h in LPS was significantly higher than that in DM (2.15 ± 0.20 vs. 1.38 ± 0.17; $p < 0.01$). The number of successful LVAs/h in LPS was significantly higher than that in the DM (2.08 ± 0.22 vs. 0.84 ± 0.14; $P < 0.01$). Mean rate of improvement in LEL index was significantly higher than that in DM (9.36 ± 1.85 vs. 6.93 ± 1.73; $P < 0.01$).

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Discussion: The number and quality of the LVAs increase using the LPS, which leads to further improvement in lymphedema, with fewer microscopes and microsurgeons and a shorter operating time.

Introduction

A positive correlation between the number of multiple lymphaticovenular anastomoses (LVAs) performed and therapeutic efficacy in lymphedema has been reported. Therefore, it is important to create as many bypasses as possible[1]. LVAs are usually performed simultaneously at multiple sites and require use of at least two operating microscopes[2]. A drawback of this method is that it requires more than two microsurgeons and the same number of microscopes. Many hospitals find it difficult to arrange multiple expert microsurgeons and microscopes. To address this problem, we have developed a method called the line production system (LPS). In this study, we assessed whether or not the LPS is more helpful than the conventional dual microscope (DM) method when performing multiple LVAs to treat lymphedema.

Patients and methods

Patients and perioperative procedures

This cross-sectional study was conducted with approval from the institutional ethics committee, in conformance with the Helsinki Declaration and in strict adherence to the STROBE guidelines. Patients with lower limb lymphedema refractory to conventional compression therapy with elastic stockings who underwent LVA surgery between April 1, 2017, and December 31, 2017, were included in the study. Patients were included if they had Campisi clinical stage 2 or 3 lymphedema[3] and findings on lymphography compatible with stage 1–3 lymphedema by Yamamoto's classification[4]. Diagnostic lymphography was performed by injecting 0.1–0.2 mL of indocyanine green (ICG) dye (Diagnogreen® 0.5%; Daiichi Pharmaceuticals, Tokyo, Japan) subcutaneously into the first interdigital space and into the posterior lateral condylar region. The ICG images were acquired using a Photodynamic Eye system (Hamamatsu Photonics, Hamamatsu, Japan).

In all cases, the lymphedema was secondary to cervical, endometrial, ovarian, or another type of cancer. End-to-end anastomoses were performed, with the lymphatics as the peripheral vessels and the veins as the proximal vessels. All LVAs were performed under local anesthesia. LVAs were performed in 20 legs using either the LPS ($n = 10$) or the DM ($n = 10$) method. Whether to select LPS or DM was decided on the spot by the number of microscopes we were allowed to use, which were shared with other departments in the hospital. The study for each group was closed when the number of legs had reached ten. All patients resumed compression therapy at the end of the second postoperative week. The results of LVA surgery were evaluated 6 months later.

Operating surgeons

The procedures on each leg were performed by two operating surgeons, one of whom was an expert with at least 2 years of experience performing LVAs and the other a novice who had been performing LVAs for less than 6 months but had more than 2 months of experience in microsurgery before performing LVA and had successfully completed microsurgery training for LVA[5]. There was no assistant surgeon.

Line production system

The roles are divided between a novice microsurgeon and an expert microsurgeon when using the LPS to perform multiple LVAs. The novice starts at the region around the knee well away from where the expert is working to not interfere with the expert's LVA. The novice detects and dissects the lymphatics by using loupes under 4 × magnification. After the skin incision, the subcutaneous tissue is bluntly dissected with microdissection forceps. Next, 3–0 nylon sutures are placed under the identified vein and lymphatic candidates as markers. After the dissection is completed, a diluted solution of papaverine hydrochloride (1A: 40 mg=1 mL/A + 9 mL of saline) is sprayed over the dissected site. The novice repeats the same procedure on the legs toward the proximal region up to the inguinal region.

The expert microsurgeon starts the LVA procedure from the ankle area. The entire procedure is performed under an operating microscope. On completing the LVAs at the peripheral region around the ankle, the expert moves proximally to the region already dissected by the novice surgeon. The expert confirms that the target lymphatics and veins have been correctly identified and performs the LVAs. If the novice cannot identify the lymphatics or veins, the expert microsurgeon searches for these structures in the dissected tissue under a microscope. When the anastomosis is complete, the expert moves on to the next site already dissected by the novice (Figure 1).

Dual microscope method

LVAs in the DM (control) group were performed by the same surgeons who performed LVAs in the LPS, i.e., a novice microsurgeon and an expert microsurgeon, each using a microscope. Each surgeon was allocated to perform the LVAs in the lower leg or thigh. All LVA procedures including skin incision, dissection of veins and lymphatics, and anastomoses were performed under a microscope (Figure 1).

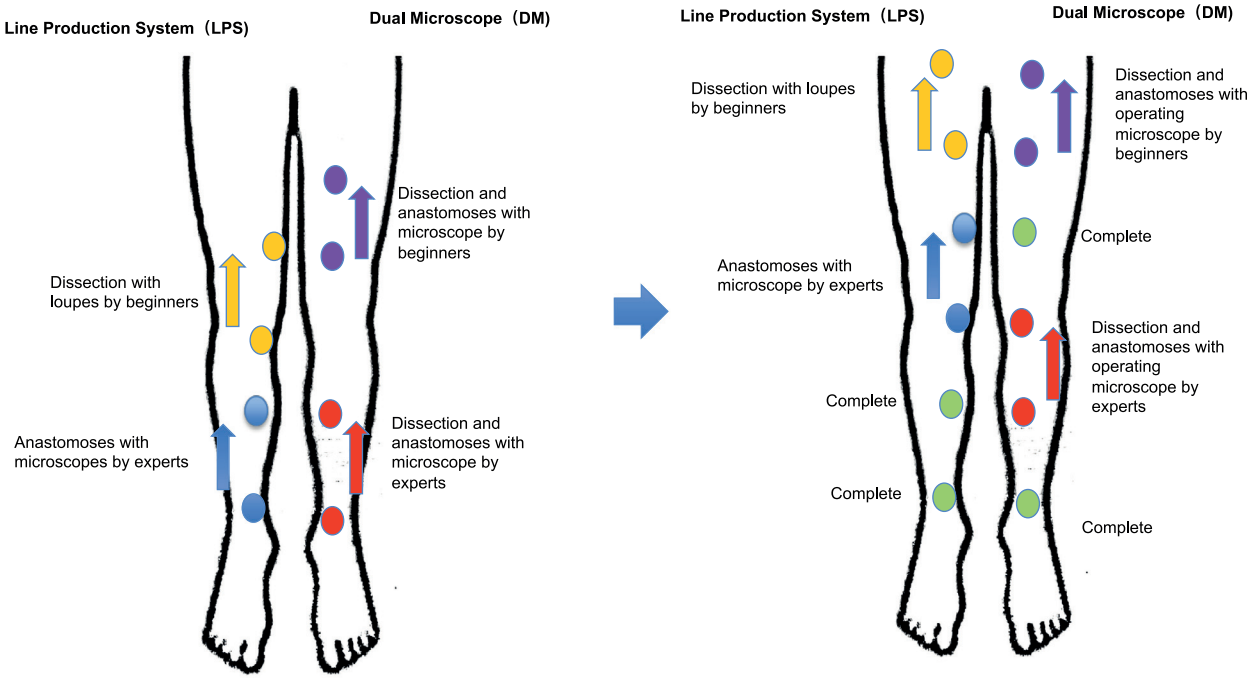

Figure 1 Schema showing the line production system and dual microscope method. Using the line production system, a novice microsurgeon uses loupes to dissect and detect veins and lymphatics while expert microsurgeons use microscopes to perform the LVAs. If necessary, the expert microsurgeon also dissects the veins and lymphatics.
Using the dual microscope method, both novices and experts use microscopes to perform the dissections and LVAs independently at separate anatomical sites.

Parameters investigated

We examined the lymphatic and vein detection rates achieved using loupes and the diameter of the lymphatics detected by the expert microsurgeons under a microscope after dissection by the novice microsurgeons in the LPS group. We also investigated the impact of LPS by comparing the number of anastomoses performed, the anastomosis success rate, the operating time, and rate of improvement in lymphedema between the study groups. The criterion for successful anastomosis was confirmation of patency by backflow of blood into the lymphatics and lymph flow into the veins in response to massage in the peripheral region. The number of LVAs performed per hour was calculated for each case to eliminate the effect of operating time. The postoperative reduction in volume was evaluated using the lower extremity lymphedema (LEL) index before and 6 months after surgery[6]. The difference between the preoperative and postoperative values was normalized by the preoperative value in each case to allow calculation of the improvement rate as follows:

$$[\{(\text{preoperative LEL}) - (\text{postoperative LEL})\}/(\text{preoperative LEL})] \times 100(\%).$$

Statistical analysis

The data are shown as the mean ± standard deviation. The total number of LVAs performed, the LVA success rate, the total number of LVAs performed per hour, and the number of successful LVAs performed per hour were compared between the LPS and DM groups using a two-sided Mann-Whitney *U* test. The operative time and rate of improvement in the LEL index were compared between the study groups using a two-sided Student's *t*-test. All statistical analyses were performed using Statcel4® software (OMS Publishing Ltd., Tokyo, Japan). A *P*-value < 0.01 was considered statistically significant.

Results

The mean detection rate using loupes was 93%±11.35% (range 75%-100%) for veins and 81% ± 15.60% (range 50%-100%) for lymphatics. The mean diameter of the lymphatics detected with loupes was 0.44 ± 0.12 (range, 0.2-0.7) mm (Table 1).

The mean number of LVAs performed per limb was significantly higher in the LPS group than in the DM group (6.5 ± 0.71 vs. 4.5 ± 0.71; $P < 0.01$). The mean number of successful LVAs per limb was significantly higher in the LPS group than in the DM group (6.3 ± 0.82 vs. 2.6 ± 0.52; $P < 0.01$). There was no significant difference in the mean operating time per limb between the LPS and DM groups (3.05 ± 0.44 vs. 3.2 ± 0.35; $P = 0.5$; Table 2).

The mean number of LVAs performed per hour was significantly higher in the LPS group than in the DM group (2.15 ± 0.20 vs. 1.38 ± 0.17; $P < 0.01$; Figure 2). The mean number of successful LVAs performed per hour was significantly higher in the LPS group than in the DM group (2.08 ± 0.22 vs. 0.84±0.14; $P < 0.01$; Figure 3).

Table 1 The mean number of areas dissected was 4.2 ± 0.63 (range 3-5), the mean number of sites where veins were detected was 3.9 ± 0.74 (range 3-5), the mean vein detection rate was 93 ± 11.35% (range 75-100), the mean number of areas where lymphatics were detected was 3.4 ± 0.84% (range 2-5), the mean rate of lymphatic detection with loupes was 81 ± 15.60% (range 50-100), and the mean diameter of the lymphatics was 0.44 ± 0.12 (range 0.2-0.7) mm.

Limb	Number of dissected areas	Vein detected sites	Lymphatic detected sites	Detection rate in vein (%)	Detection rate in lymphatics (%)	Size of main lymphatics in each area (mm)
1	4	4	3	100	75	0.3, 0.2, 0.3
2	4	4	3	100	75	0.4, 0.5, 0.4
3	5	5	4	100	80	0.3, 0.4, 0.5, 0.5
4	4	3	3	75	75	0.5, 0.4, 0.5
5	3	3	3	100	100	0.3, 0.4, 0.5
6	4	3	2	75	50	0.3, 0.3
7	5	4	5	80	100	0.5, 0.6, 0.7, 0.5, 0.4
8	4	4	3	100	75	0.3, 0.4, 0.6
9	4	4	4	100	100	0.3, 0.5, 0.7, 0.5
10	5	5	4	100	80	0.4, 0.6, 0.5, 0.5
Mean±SD				93% ± 11.35	81% ± 15.60	0.44 ± 0.12

Table 2 Number of LVAs/limb, successful LVAs/limb; Mann-Whitney *U* test Operating time; Student's *t*-test.

	Line production system (LPS)	Dual microscope (DM)	*p* value
Number of LVA/limb	6.5 ± 0.71 (Range 6-8)	4.5 ± 0.71 (Range 4-6)	0.00038
Number of successful LVA/limb	6.3 ± 0.82 (Range 5-8)	2.6 ± 0.52 (Range 2-3)	0.00016
Operative time (h)	3.05 ± 0.44 (Range 2.5-3.5)	3.2 ± 0.35 (Range 2.5-3.5)	0.5

Number of LVA/limb, Number of successful LVA/limb; Mann-Whitney *U* test.
Operative time (h); Student's *t*-test.

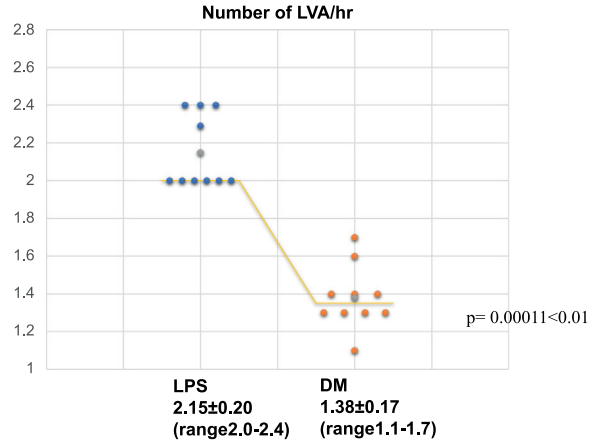

Figure 2 DM, dual microscope group; LP, line production system; LVAs, lymphaticovenular anastomoses.

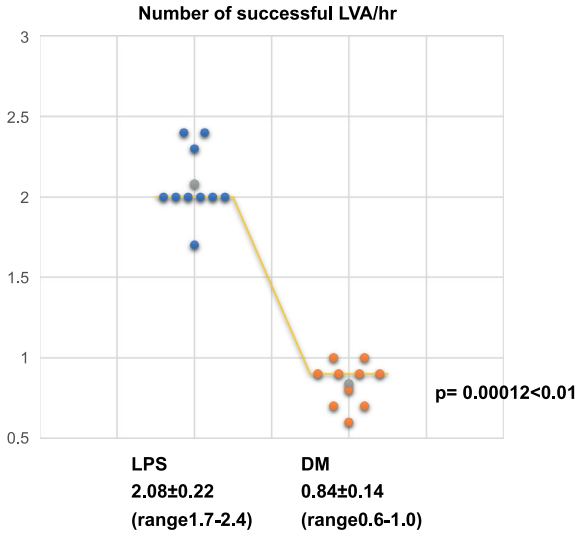

Figure 3 DM, dual microscope group; LP, line production system; LVAs, lymphaticovenular anastomoses.

The LEL index ranged from 199 to 282 in the LPS group and from 201 to 282 in the DM group preoperatively and from 178 to 259 and 188 to 264, respectively, postoperatively. The mean rate of improvement in the LEL index was significantly greater in the LPS group than in the DM group (9.36 ± 1.85 vs. 6.93 ± 1.73; $P<0.01$; Figure 4).

Discussion

This study had two important findings, i.e., that dissecting and locating lymphatics is achievable using loupes and that

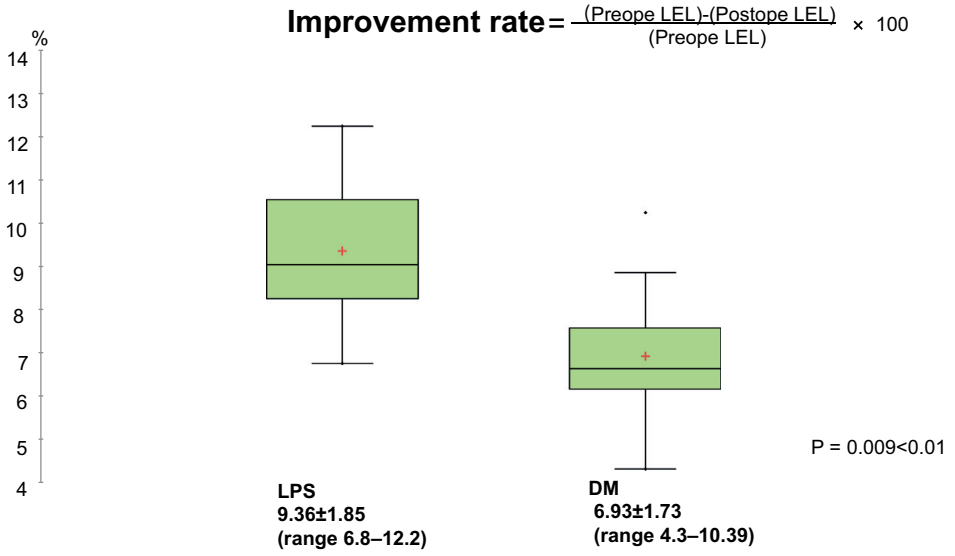

Figure 4 The mean rate of improvement in the LEL index was significantly greater in the LPS group than in the DM group (9.36 ± 1.85 (range 6.8–12.2) vs. 6.93 ± 1.73 (range 4.3–10.3); $P = 0.009 < 0.05$). DM, dual microscope group; LEL, lower extremity lymphedema; LP, line production system; LVAs, lymphaticovenular anastomoses.

use of the LPS, which requires one microscope, one expert microsurgeon, and one novice microsurgeon, increases the number and improves the quality and results of the LVAs performed.

We found that lymphatics as small as 0.3 mm in diameter could be located and dissected at a high rate under loupes. We also found that the time lag between dissection by novice microsurgeons and anastomoses performed by expert microsurgeons can be decreased by spraying papaverine to prevent lymphatic spasm, which makes it easier to anastomose and helps to increase the number and quality of LVAs performed. Moreover, there was no problem if the novices were unable to find lymphatics because the experts could dissect further to identify them under the microscope. We also believe the time lag helps to reduce spasm and makes it easier to find lymphatics. A sampling bias was avoided by selecting methods on the spot, LPS or DM, depending on the number of microscopes we were allowed to use, because microscopes are shared with other departments in our hospital.

We still believe that the most effective way to perform multiple LVAs is to prepare for multiple skilled microsurgeons and to use as many microscopes as possible. However, operating microscopes are very expensive, and it takes considerable time and effort for surgeons to master the necessary microsurgery techniques, especially to the level of being able to perform LVAs with precision. Many hospitals would have difficulty in arranging even three to four microsurgeons and microscopes.

Using the LPS, dissection is performed under loupes, which cost much less than microscopes and are much easier to prepare. Furthermore, blunt dissection is much easier than the anastomosis technique, and can be performed by novices. The microscopes used with the DM method often interfere with each other, which sometimes leads to a delay in performing LVAs. We believe that the LPS also solves this problem. A drawback of the LPS is the limited opportunities available for novice microsurgeons to perform LVAs. Therefore, it is important to create these opportunities so that novices can improve their microsurgical skills. In this study, there were considerable differences in the results achieved between the LPS and DM methods. However, it is unknown whether or not the findings would differ if the same study was performed using study groups each comprising two expert microsurgeons.

Conclusion

The LPS has the ability to increase the number and quality of LVAs, which leads to a greater rate of improvement in lymphedema with less need for microscopes and skilled microsurgeons with the same operating time.

Conflict of interest

None.

Funding

None.

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