Minimally Invasive Lymphatic Supermicrosurgery

Indocyanine Green Lymphography-Guided Simultaneous Multisite Lymphaticovenular Anastomoses via Millimeter Skin Incisions

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Abstract: Among various surgical treatments, lymphaticovenular anastomosis (LVA), which bypasses congested lymph into venous circulation, is the least invasive surgical treatment. However, it usually entails skin incisions of around 3 cm, and operation time of around 4 hours. With multiple microsurgeons under guidance of indocyanine green lymphography, LVAs can be simultaneously performed under local anesthesia within approximately 2 hours via small skin incisions with length less than 1 cm, allowing minimally invasive lymphatic supermicrosurgery. We performed minimally invasive lymphatic supermicrosurgery on 11 limbs of compression-refractory peripheral lymphedema cases. Length of skin incision for LVA ranged from 1 to 9 mm. Average operation time was 1.82 hours. Of the 11 limbs, 10 showed postoperative volume reduction. Indocyanine green lymphography clearly visualizes superficial lymph flows, which helps us to decide precise skin incision sites and find lymphatic vessels in LVA surgery, shortening skin incision length and operation time. Minimally invasive lymphatic supermicrosurgery can serve as the most reasonable treatment of compression-refractory peripheral lymphedema.

Key Words: lymphedema, lymphaticovenular anastomosis (LVA), supermicrosurgery, indocyanine green (ICG) lymphography, minimally invasive lymphatic supermicrosurgery (MILS)

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PATIENTS AND METHODS
From September of 2010 to August of 2011 under the University of Tokyo Hospital institutional review board-approved protocol, we performed MILS on 11 female patients with compression-refractory peripheral lymphedema (3 arm lymphedema patients, and 8 leg lymphedema patients). All patients included in this study received compression therapy using elastic stockings or bandages, and experienced progressive lymphedema refractory to conservative therapy. Patients’ age ranged from 46 to 73 years (average, 60.6 years), and body mass index (BMI) ranged from 20.6 to 28.9 (average, 23.52). All patients gave written informed consent to this study.

Minimally invasive lymphatic supermicrosurgery, ICG lymphography-guided simultaneous multisite LVAs through millimeter skin incisions under local anesthesia, was performed as follows. Indocyanine green (Diagnogreen 0.25%; Daiichi Pharmaceutical, Tokyo, Japan) was subcutaneously injected preoperatively in arm lymphedema cases, 0.1 mL of ICG was injected at the second Web space of the hand and the ulnar border of the palmaris longus tendon at the level of the wrist, respectively, and in leg lymphedema cases, 0.2 mL of ICG was injected at the first Web space of the foot and the lateral border of the Achilles tendon, respectively.3–18 Superficial lymph flows were visualized using an infrared camera system (Photodynamic Eye [PDE]; Hamamatsu Photonics K.K., Hamamatsu, Japan) preoperatively, and using an operating microscope equipped with an integrated near-infrared illumination system (OME-9000; Olympus, Tokyo, Japan) intraoperatively. Superficial venules were also visualized as black lines using a PDE camera (Fig. 1A). After marking of lymphatic vessels and superficial venules visualized by preoperative ICG lymphography, a millimeter-long skin incision was designed as small as possible, large enough for dissection and anastomosis of the lymphatic vessel and a superficial venule (Fig. 1B). Infiltration local anesthesia was applied to the incision site by injecting 1% lidocaine with 1:100,000 epinephrine intradermally, and a skin incision was made using a fine surgical scalpel. A lymphatic vessel and a venule were dissected with guidance of intraoperative ICG lymphography (Fig. 1C). Lymphatic vessels under the superficial fascia were used for anastomoses. Anastomoses were performed using 11-0 of 12-0 interrupted suture in an end-to-end (E-E), end-to-side (E-S), and/or side-to-end (S-E) fashion (Fig. 1D, E).13 After completion of anastomosis, patency was confirmed with intraoperative ICG lymphography (Fig. 1F; see Video, Supplemental Digital Content 1, http://links.lww.com/SAP/A58 which shows ICG lymphography-guided LVA via a millimeter skin incision). Lymphaticovenular anastomoses were simultaneously performed at multiple sites by supermicrosurgeons who had experience of more than 40 LVA operations.
One week after operation, patients resumed the same compression therapy as performed preoperatively.

Pathophysiological severity stages were determined using dermal backflow (DB) stages based on preoperative ICG lymphography findings; arm DB (ADB) stage for arm lymphedema, and leg DB (LDB) stage for leg lymphedema (Tables 1 and 2; Fig. 2).

Edematous volume was evaluated using lymphedema indices; upper extremity lymphedema (UEL) index for arm lymphedema, and lower extremity lymphedema (LEL) index for leg lymphedema (Figs. 3 and 4).

Evaluation was done preoperatively, and at postoperative 6 months.

RESULTS

Preoperative ICG lymphography revealed that there were 7 legs in LDB stage II, 1 leg in LDB stage III, 1 arm in ADB stage II, and 2 arms in ADB stage III. Minimally invasive lymphatic supermicrosurgery were performed on 8 lymphedematous legs and 3 lymphedematous arms, which resulted in 40 LVA via 28 skin incisions. Lymphaticovenular anastomoses consisted of 28 E-E, 7 E-S, and 5 S-E anastomoses. All anastomosis patency were confirmed intraoperatively. Skin incision length ranged from 1 to 9 mm (average, 6.1 mm), the number of microscopes used in MILS ranged from 2 to 3 (average, 2.2), and operation time ranged from 1.0 to 3.0 hours (average, 1.82 hours). Postoperative UEL index or LEL index decreased in 10 of 11 limbs, indicating edematous volume reduction after MILS (Table 3). No postoperative complication was observed.

Pathophysiological severity stages were determined using dermal backflow (DB) stages based on preoperative ICG lymphography findings; arm DB (ADB) stage for arm lymphedema, and leg DB (LDB) stage for leg lymphedema (Tables 1 and 2; Fig. 2). Edematous volume was evaluated using lymphedema indices; upper extremity lymphedema (UEL) index for arm lymphedema, and lower extremity lymphedema (LEL) index for leg lymphedema (Figs. 3 and 4). Evaluation was done preoperatively, and at postoperative 6 months.

**TABLE 1.** LDB Stage Based on ICG Lymphography Findings

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No dermal backflow pattern</td>
</tr>
<tr>
<td>I</td>
<td>Splash pattern around the groin region</td>
</tr>
<tr>
<td>II</td>
<td>Stardust pattern extended proximal to the superior border of the patella</td>
</tr>
<tr>
<td>III</td>
<td>Stardust pattern extended distal to the superior border of the patella</td>
</tr>
<tr>
<td>IV</td>
<td>Stardust pattern extended to the whole limb</td>
</tr>
<tr>
<td>V</td>
<td>Existence of diffuse pattern with stardust pattern in the background</td>
</tr>
</tbody>
</table>

**TABLE 2.** ADB Stage Based on ICG Lymphography Findings

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No dermal backflow pattern</td>
</tr>
<tr>
<td>I</td>
<td>Splash pattern around the axilla</td>
</tr>
<tr>
<td>II</td>
<td>Stardust pattern extended proximal to the olecranon</td>
</tr>
<tr>
<td>III</td>
<td>Stardust pattern extended distal to the olecranon</td>
</tr>
<tr>
<td>IV</td>
<td>Stardust pattern extended to the whole limb</td>
</tr>
<tr>
<td>V</td>
<td>Existence of diffuse pattern with stardust pattern in the background</td>
</tr>
</tbody>
</table>

**FIGURE 1.** Indocyanine green lymphography-guided LVA via a millimeter skin incision. Preoperative ICG lymphography visualizes superficial lymph flows as white illuminated lines and superficial venules as black nonilluminated lines (A). After marking of lymphatic vessels (dotted lines) and superficial venules (lines), a 5-mm skin incision is made where a lymphatic vessel and a superficial venule cross (B). The lymphatic vessel (arrow) and the venule (arrowhead) are dissected with guidance of intraoperative ICG lymphography (C). The 0.45-mm lymphatic vessel and the 0.30-mm venule are prepared for S-E anastomosis (D). An S-E anastomosis is performed in an interrupted manner using a 12-0 nylon (E). Intraoperative ICG lymphography shows patency of the anastomosis (F).

**FIGURE 2.** Dermal backflow patterns observed in indocyanine green lymphography. As lymphedema progresses, dermal backflow patterns change from splash pattern (left), to stardust pattern (center), and finally to diffuse pattern (right).

**FIGURE 3.** Calculation of LEL index. A summation of squares of circumferences at 10 cm above the superior border of the patella, at the lateral malleolus, and at the dorsum of the foot. The LEL index less than 250 indicates mild edema, the LEL index of 250 to 300 moderate edema, and the LEL index greater than 300 severe edema.

**FIGURE 4.** Indocyanine green lymphography-guided LVA via a millimeter skin incision. Preoperative ICG lymphography visualizes superficial lymph flows as white illuminated lines and superficial venules as black nonilluminated lines (A). After marking of lymphatic vessels (dotted lines) and superficial venules (lines), a 5-mm skin incision is made where a lymphatic vessel and a superficial venule cross (B). The lymphatic vessel (arrow) and the venule (arrowhead) are dissected with guidance of intraoperative ICG lymphography (C). The 0.45-mm lymphatic vessel and the 0.30-mm venule are prepared for S-E anastomosis (D). An S-E anastomosis is performed in an interrupted manner using a 12-0 nylon (E). Intraoperative ICG lymphography shows patency of the anastomosis (F).
Case Report (Case 9)

A 46-year-old woman with 4-year history of breast cancer-related arm lymphedema was referred to our department for further treatment of LVA. She had left arm lymphedema which progressed despite 3 years of conservative treatments including skin care, elastic bandage, and manual lymph drainage, and we decided to perform MILS (Fig. 5A). Preoperative ICG lymphography revealed that her lymphedema was ADB stage III, and visualized superficial lymph flows (linear pattern) in volar aspect of the arm. The UEL index less than 130 indicates mild edema, the LEL index of 130 to 150 moderate edema, and the LEL index greater than 150 severe edema.

DISCUSSION

To maximize the treatment efficacy of LVA surgery, it is important to find vessels for anastomosis as early as possible, and to increase the number of anastomoses within limited operation time. Indocyanine green lymphography enables visualization of superficial lymphatic vessels suitable for anastomosis, which makes it an ideal tool to guide LVA surgery, and has been used in clinical cases. As our experience of ICG lymphography and LVA surgery accumulates, we are becoming able to perform multiple LVA through small skin incisions using multiple operating microscopes simultaneously in short operation time, leading to development of MILS.

**TABLE 3. MILS on Peripheral Lymphedema**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Extremity</th>
<th>DB Stage*</th>
<th>LVA Incision Length† (Type of Anastomosis)</th>
<th>No. Microscopes</th>
<th>Operation Time, h</th>
<th>Before MILS</th>
<th>After MILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63 Lower left</td>
<td>III</td>
<td>2 (S-E), 5 (E-E), 9 (E-E, E-E)</td>
<td>3</td>
<td>2.0</td>
<td>318</td>
<td>287</td>
</tr>
<tr>
<td>2</td>
<td>56 Lower left</td>
<td>II</td>
<td>8 (E-E), 8 (E-E, E-S)</td>
<td>2</td>
<td>1.5</td>
<td>266</td>
<td>254</td>
</tr>
<tr>
<td>3</td>
<td>72 Lower left</td>
<td>II</td>
<td>7 (E-E), 7 (E-S)</td>
<td>2</td>
<td>1.5</td>
<td>244</td>
<td>239</td>
</tr>
<tr>
<td>4</td>
<td>71 Lower right</td>
<td>II</td>
<td>8 (E-E), 7 (E-E, E-E)</td>
<td>2</td>
<td>1.0</td>
<td>230</td>
<td>220</td>
</tr>
<tr>
<td>5</td>
<td>53 Lower right</td>
<td>II</td>
<td>8 (E-E, E-S), 8 (E-E, E-E), 9 (E-E, E-S)</td>
<td>3</td>
<td>2.5</td>
<td>260</td>
<td>223</td>
</tr>
<tr>
<td>6</td>
<td>69 Lower right</td>
<td>II</td>
<td>5 (E-E), 8 (S-E, E-E)</td>
<td>2</td>
<td>2.0</td>
<td>278</td>
<td>262</td>
</tr>
<tr>
<td>7</td>
<td>48 Lower left</td>
<td>II</td>
<td>4 (E-E), 7 (S-E)</td>
<td>2</td>
<td>1.5</td>
<td>224</td>
<td>228</td>
</tr>
<tr>
<td>8</td>
<td>61 Lower right</td>
<td>II</td>
<td>6 (E-E, E-E), 7 (E-E, E-E)</td>
<td>2</td>
<td>1.5</td>
<td>268</td>
<td>251</td>
</tr>
<tr>
<td>9</td>
<td>46 Upper left</td>
<td>III</td>
<td>5 (E-E, E-E), 5 (E-E, E-E), 5 (E-E, E-S)</td>
<td>3</td>
<td>3.0</td>
<td>137</td>
<td>115</td>
</tr>
<tr>
<td>10</td>
<td>73 Upper right</td>
<td>III</td>
<td>3 (E-E), 5 (E-E, E-E), 9 (E-E)</td>
<td>2</td>
<td>2.0</td>
<td>151</td>
<td>136</td>
</tr>
<tr>
<td>11</td>
<td>55 Upper left</td>
<td>II</td>
<td>1 (E-E), 3 (S-E)</td>
<td>2</td>
<td>1.5</td>
<td>121</td>
<td>110</td>
</tr>
</tbody>
</table>

*ADB stage is used in arm lymphedema, and LDB stage in leg lymphedema.
†Length is in millimeters.
‡UEL index is used in arm lymphedema, and LEL index in leg lymphedema to evaluate lymphedematous volume changes 6 months after MILS.
and intraoperative ICG lymphography allows precise localization of vessels suitable for anastomosis, and facilitates secure anastomosis via a millimeter skin incision, resulting in shorter operation time. This study revealed that MILS could be performed under local anesthesia within approximately 2 hours without losing its effectiveness.

Minimally invasive lymphatic supermicrosurgery has 2 major drawbacks. First, it requires multiple microscopes and supermicrosurgeons experienced with LVA surgery. Lymphaticovenular anastomosis through a millimeter skin incision is more difficult than that through a 2- to 3-cm skin incision. Although finding a lymphatic vessel is facilitated under ICG lymphography-guidance, smaller surgical field makes it difficult to dissect and anastomose the lymphatic vessel. Therefore, LVA through a millimeter skin incision is recommended only to experienced LVA surgeons. To shorten operation time, simultaneous multisite approach using multiple microscopes is necessitated in MILS.12 Second, ICG lymphography can hardly visualize lymphatic vessels deeper than 2 cm from the skin surface, or in severe cases with extension of DB patterns.16–19 In severe lymphedema, DB patterns extend to most area of a limb; the lymphatic vessels cannot be visualized by ICG lymphography, and it would be extremely difficult to find a lymphatic vessel through a small skin incision. Minimally invasive lymphatic supermicrosurgery is applicable for lymphedema at an earlier stage, in which superficial lymphatic vessels can be visualized; ICG lymphography is helpful to guide LVA surgery in LDB/ADB stages 0 through III regardless of clinical stage.17,18,23

Although further investigations are needed to clarify efficacy and indication, MILS has a potential to be the treatment of choice for early-stage peripheral lymphedema refractory to conservative therapies.

CONCLUSIONS

When performed by multiple supermicrosurgeons with guidance of ICG lymphography, LVA can be completed under local anesthesia within 2 hours through millimeter skin incision, resulting in MILS effective to compression-refractory lymphedema.

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REFERENCES