

Supramicrosurgical lymphatico-venular anastomosis (LVA) in treating lymphoedema: 36-months preliminary report

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Abstract. – **OBJECTIVE:** Lymphoedema of the extremities is a widespread pathological condition that mostly occurs as a complication of cancer resections, especially in women. Conventional therapy refers to conservative and physiotherapeutic approaches. Surgical strategies have been widely reported in the literature and are still challenging. Part of this literature focuses on the supra microsurgical lymphaticovenular anastomosis (LVA) technique. LVA is characterized by a high success rate, minimal invasivity and broad indications. Furthermore, this procedure can be performed under local anesthesia.

PATIENTS AND METHODS: From October 2011 through October 2014, 69 patients affected by lymphoedema underwent LVA surgery in Siena University Hospital, Italy. Preoperative and postoperative evaluations were taken.

RESULTS: Totally, 366 anastomosis have been performed. The average rate was 5.3 anastomosis per patient. All patients registered a decrease in the size of the affected side. The average volume reduction was 50%. Patients also showed a reduction of lymphangitis episodes and reduction of compression garments class. Moreover, a satisfaction index was evaluated. The majority of patients (72.5%) was extremely satisfied of the surgery.

CONCLUSIONS: LVA has demonstrated to be an effective surgical strategy to treat lymphoedema, especially in secondary cases in early stages. Although LVA is widely discussed in the literature, the majority of works relates to Japanese authors and few reports exist outside Japan. This paper represents the very first retrospective analysis of the adoption of LVA technique in Italy and one of the few outside Japan.

Key Words

Lymphoedema, Surgical treatment, Supramicrosurgery, Lymphaticovenular anastomosis, Indocyanine green, Lymphography, ICG, LVA.

Introduction

Lymphoedema of the extremities is a chronic pathological condition determined by an output failure in lymphatic flow with subsequent progressive persistent edema. It mainly occurs as a complication of radical resections of various cancers, especially, but not only, in women. Current treatment of lymphoedema is based on conservative therapies and consists of manual lymphatic drainage, intermittent pneumatic therapy, multilayered bandages and compression garments. Also, surgical approaches have been described. Surgical strategies include liposuction, excisional procedures and microvascular surgery.

Thanks to the advancements in microsurgery and the introduction of supra microsurgery, a novel technique has been developed. This procedure, known as lymphaticovenular anastomosis (LVA), offers a high rate of positive outcomes with a minimally invasive surgical approach. In this paper, the authors offer a retrospective analysis of 69 patients affected by monolateral upper or lower extremities lymphoedema, treated adopting LVA. A 36 months follow-up is presented. Although LVA has been well documented in the literature, the majority of works relates to Japanese experience and few reports exist outside Japan, especially in Europe. In this paper, the authors present the first Italian report.

Patients and Methods

Retrospective analysis of 36 months follow-up in 69 patients is presented. From October 2011 through October 2014, 69 patients affected by monolateral upper or lower extremities lymphoedema under-

went LVA surgery in our department. All patients were operated at Siena University Hospital by one of the authors. The nature and possible risks of the study had been described in details to each patient and written informed consent was obtained. Of the 69 patients, 64 were females (93%) and 5 were male. Mean patient age was 55 years old (range: 16 to 76). 60 patients (87%) suffered from secondary lymphoedema after cancer resection, 1 was a secondary case after a traumatic injury, while 9 were primary cases. 42 patients (61%) have been treated for upper extremities lymphoedema whereas 27 patients presented the pathology in the lower extremities. The majority, 40 patients (58%), reported a history of breast cancer; 9 patients (13%) showed endometrial cancer; 3 (4%) patients were affected by melanoma and underwent lymphadenectomy; 2 (3%) patients were treated for ovarian cancer; 2 (3%) patient was treated for cervical cancer; 1 (1.5%) patient presented a history of sarcoma; 1 (1.5%) patients was treated for bladder cancer and underwent lymphadenectomy; 1 (1.5%) patient was treated for prostate cancer; 9 patients (13%) were primary case and 1 (1.5%) patient presented lymphoedema arisen after a traumatic injury.

39 patients (57%) underwent radiotherapy.

The average lymphoedema duration was 5.8 years (range 1-23).

Each patient was evaluated according to the guidelines established by the International Society of Lymphology. In particular, 39 patients (57%) presented stage III, 27 patients (39%) presented stage IV and 3 patients (4%) stage.

Also, we analyzed cellulitis episodes: 34 patients (49%) suffered from cellulitis episodes in the previous years.

Each patient was evaluated before and after surgery: preoperatively ultrasonography, echo-color-Doppler of the venous system and bilateral multiple circumferential measurements of the extremities were taken. The measurements of the upper extremities were taken at the palm of the hand, at wrist, 5 cm below the elbow, at the elbow and 5 cm above the elbow. As for the lower extremities measurement were taken at foot dorsum, at the ankle, 10 cm below the inferior margin of the patella, at the patella and 10 cm above. Additionally, the same measures of the specular healthy limb were recorded.

The difference in size between the affected and the contralateral healthy side was also taken. 1 year after surgery and at each subsequent visit multiple circumferential measurements were taken every time.

Then, the preoperative and postoperative sum of measures were confronted.

Body weight was evaluated before surgery and at every visit after surgery in order to consider variation in volume due to adipose tissue: none of the patients had an increase or reduction in weight (> 3 kg) which would have resulted in the exclusion from the study.

Preoperatively, the patients underwent to indocyanine green dye (ICG) lymphography. For upper extremities, 0.1 ml indocyanine green was injected subcutaneously at the second web space of the hand and the ulnar border of the palmaris longus tendon at the level of the wrist. For lower extremities, 0.2 ml of indocyanine green dye were injected at the first web space of the foot and the tibial aspect of the ankle.

After injection lymphatic drainage was studied using an infrared camera system (Photodynamic Eye (PDE); Hamamatsu Photonics, Hamamatsu City, Shiznoka, Japan). Results were evaluated according to the classification described by Yamamoto¹. In particular, 30 patients (44%) presented stardust pattern, 25 patients (36%) diffuse pattern, 14 patients (20%) splash pattern².

Postoperatively patients have been asked to evaluate their feelings after LVA. The satisfaction index consisted of questions regarding the patient's clinical conditions and quality of life before and after LVA and was established as a 1 to 4 scale (1= not satisfied; 4= extremely satisfied).

Anesthesiologic consideration

Local anesthetics were performed adopting a mixture of 2% lidocaine and epinephrine at a dilution of 1:200,000. Since the intervention requires immobility, deep sedation was adopted to increase patient's comfort. Propofol (2 mg/kg/h) and Remifentanyl (0.015 mcg/kg/min) were used while maintaining spontaneous breathing. Oxygen was administered at 4l/min via nasal cannula or Venturi's mask. Patients were premedicated with Midazolam (0.02 mg/kg). Antibiotic prophylaxis, gastric protection as well as antiemetic were used. Patients were monitored during the surgical procedure. Adequate postoperative analgesia was obtained with acetaminophen 1 g every 8 hours for the first 24 hours.

Operative technique

LVA was performed under local anesthesia. According to the patient's conditions and compliance. Patients undergoing LVA under local anesthesia were allowed to move the limb and have some rest

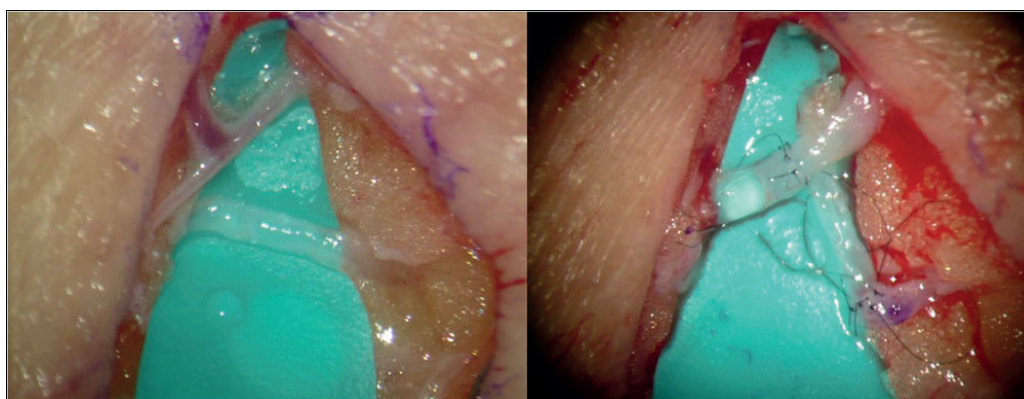


Figure 1. Intraoperative view. Lymphatic and vein can be seen before (*left side*) and after (*right side*) double anastomosis. Mean diameter of these vessels were 0.5 mm; 11-0 suture was adopted.

between the incisions. Multiple (range 3-5) 2 cm linear skin incisions were performed. Sites of incisions were chosen according to ICG lymphography findings. Microscopic dissection was carried out in order to identify lymphatic vessels and venules. Lymphatic vessels were prepared and sutured to veins using 11-0 or 12-0 sutures. (Figure 1).

For the lower extremities, incisions were performed on thin adipose portions such as the medial aspect of the pretibial areas of the proximal and middle lower leg and ankle. Lymphatics were detached between adipose particles in the superficial or deep adipose layer and sometimes in the subdermal layer. As for the upper extremities, the lateral and medial aspects of the forearm and snuff box were suitable for incisions. The subdermal venules, which exist anywhere underneath the dermis, were found in the proximity of lymphatics. These venules presented low blood pressure which is demonstrated by the absence of backflow. After anastomoses have been completed, lymphatic flow was observed into the venules.

Patients were dismissed the day after surgery and received oral antibiotic therapy for 6 days.

Patients were evaluated at 2 weeks, 1 month, and every 6 months after surgery. Two weeks after surgery stitches were removed.

Results

The authors evaluated results in patients with at least one-year follow-up (Table I).

Totally, 366 anastomoses have been performed with an average rate of 5.3 anastomoses for patient.

The average duration of the procedure was 180 minutes. Surgeries were performed by two

operators using one or two microscopes. No complications were observed postoperatively. After surgery, patients received the same physiotherapy they adopted before. In particular, they were encouraged to undergo lymphatic drainage and to wear a compression stocking for 12 months.

Every patient registered a decrease in the size of the affected side.

No patient incurred in worsening of the disease after surgery. The average size reduction was 50% (range 11-98%). The average reduction in the secondary lymphoedema was 49% (range 11-98%), while the average in the primary was 61% (range 41-87%) (Table II) (Figures 2, 3, 4).

The average reduction in patients presenting “splash” pattern at ICG lymphography was 63%, in “stardust” pattern 56% and 36% in “diffuse” pattern.

The average reduction in patients who never had lymphangitis was 55%, while was 49% in patients who had 1 or 2 episodes of cellulitis, and 33% in patients with a history of more than 2 episodes.

The average reduction in patients who have had lymphoedema for less than 2 years was 58%, and was 49% in the others.

Every patient (100%) who suffered from cellulitis before surgery reported no episodes after surgery during the follow-up period.

Also, post-operative ICG lymphography was taken. Patency of anastomosis was observed in 337 anastomoses of 366 (92%) (Figure 4).

67 patients (97%) were satisfied of their clinical improvement after LVA. 2 patients were not fully satisfied. The average satisfaction level was 3.7 point on a 4-point scale. Also, they reported a reduction in heaviness, hardness, functional impairment and pain of the affected limb.

Table 1. Retrospective analysis of results in 69 patients with at least a 1 year follow-up is offered. Every patients registered a decrease in size of the affected side. The mean volume reduction was 50%. LVA has demonstrated to be more effective in patients affected by early stages lymphoedema, in patients who have splash pattern at ICG lymphography and in patients who never had cellulitis.

| Patient LVA | Age | Gender | Affected limb | Etiology | Radio-therapy | Grade Icg pattern | Affected Period (Years) | Number of Anastomosis | Sum of diameters before LVA | Sum of diameters after LVA | Sum of unaffected limb diameters | Size reduction | Operation times | N. Microscopes | Lymph-angitis before surgery | Lymph-angitis after surgery | Compression class | Satisfaction |
|-------------|-----|--------|---------------|-------------------|---------------|-------------------|-------------------------|-----------------------|-----------------------------|----------------------------|----------------------------------|----------------|-----------------|----------------|------------------------------|-----------------------------|-------------------|--------------|
| 1 | 61 | F | Upper limb | Breast CA. | Y | IV Diffuse | 3 | 4 | 155 | 152 | 122 | 38% | 135 | 1 | 1 | 0 | Y | 4 |
| 2 | 46 | F | Upper limb | Breast CA | Y | III Stardust | 1 | 6 | 122,5 | 119,5 | 115 | 40% | 170 | 2 | 0 | 0 | Y | 4 |
| 3 | 60 | F | Upper limb | Breast CA. | Y | III Diffuse | 4 | 6 | 127 | 115 | 106 | 57% | 205 | 1 | 2 | 0 | Y | 4 |
| 4 | 63 | F | Upper limb | Breast CA. | Y | III Splash | 4 | 6 | 146 | 135,5 | 121,5 | 43% | 155 | 2 | 0 | 0 | Y | 4 |
| 5 | 76 | F | Lower limb | Melanoma | N | IV Diffuse | 23 | 5 | 192,5 | 184,5 | 168 | 33% | 160 | 2 | 1 | 0 | Y | 4 |
| 6 | 49 | F | Lower limb | Endometrial CA. | N | IV Diffuse | 19 | 6 | 169 | 160,5 | 150,5 | 46% | 210 | 2 | 0 | 0 | Y | 4 |
| 7 | 54 | F | Lower limb | Endometrial CA. | N | IV Diffuse | 3 | 5 | 227 | 195 | 161 | 48% | 190 | 2 | 0 | 0 | Y | 4 |
| 8 | 52 | F | Upper limb | Breast CA. | Y | III Stardust | 2 | 5 | 123 | 113 | 107 | 63% | 195 | 1 | 0 | 0 | Y | 4 |
| 9 | 47 | F | Upper limb | Breast CA. | Y | IV Diffuse | 5 | 4 | 141 | 134,5 | 111 | 22% | 140 | 1 | 0 | 0 | N | 3 |
| 10 | 48 | F | Upper limb | Primary | N | III Stardust | 4 | 5 | 181 | 168 | 149,5 | 41% | 175 | 2 | 0 | 0 | Y | 4 |
| 11 | 48 | F | Upper limb | Breast CA. | Y | III Stardust | 1 | 5 | 126 | 117 | 109,5 | 55% | 165 | 2 | 2 | 0 | Y | 4 |
| 12 | 74 | F | Upper limb | Breast CA. | Y | III Stardust | 4 | 6 | 142 | 123 | 108,5 | 57% | 150 | 2 | 1 | 0 | Y | 4 |
| 13 | 16 | F | Lower limb | Primary | N | III Diffuse | 15 | 7 | 149 | 146,5 | 144,5 | 56% | 190 | 2 | 0 | 0 | Y | 4 |
| 14 | 34 | F | Lower limb | Primary | N | III Stardust | 8 | 5 | 174,5 | 165 | 159 | 61% | 200 | 2 | 0 | 0 | Y | 3 |
| 15 | 58 | M | Upper limb | Breast CA. | Y | III Stardust | 2 | 6 | 160 | 144 | 130,5 | 54% | 185 | 1 | 1 | 0 | Y | 4 |
| 16 | 49 | F | Upper limb | Thoracic Melanoma | N | IV Stardust | 18 | 4 | 151 | 137,5 | 123,5 | 58% | 165 | 2 | 0 | 0 | Y | 4 |
| 17 | 56 | F | Lower limb | Primary | N | III Diffuse | 3 | 5 | 154 | 149 | 146 | 63% | 205 | 2 | 0 | 0 | Y | 4 |
| 18 | 54 | F | Upper limb | Breast CA. | Y | IV Stardust | 1 | 6 | 150 | 142,5 | 128 | 34% | 185 | 1 | 1 | 0 | N | 3 |

Continued

Table I. Retrospective analysis of results in 69 patients with at least a 1 year follow-up is offered. Every patients registered a decrease in size of the affected side. The mean volume reduction was 50%. LVA has demonstrated to be more effective in patients affected by early stages lymphoedema, in patients who have splash pattern at ICG lymphography and in patients who never had cellulitis.

| Patient LVA | Age | Gender | Affected limb | Etiology | Radiotherapy | Grade Icg pattern | Affected Period (Years) | Number of Anastomosis | Sum of diameters before LVA | Sum of diameters after LVA | Sum of unaffacted limb diameters | Size reduction | Operation times | N. Microscopes | Lymph-angitis before surgery | Lymph-angitis after surgery | Compression class | Satisfaction |
|-------------|-----|--------|---------------|-----------------|--------------|-------------------|-------------------------|-----------------------|-----------------------------|----------------------------|----------------------------------|----------------|-----------------|----------------|------------------------------|-----------------------------|-------------------|--------------|
| 19 | 46 | F | Upper limb | Breast CA. | Y | III Stardust | 1 | 6 | 108 | 103,5 | 100,5 | 60% | 145 | 2 | 0 | 0 | Y | 4 |
| 20 | 43 | F | Upper limb | Breast CA. | Y | IV Stardust | 1 | 5 | 126 | 115 | 108,5 | 63% | 170 | 2 | 1 | 0 | Y | 4 |
| 21 | 57 | F | Lower limb | Endometrial CA. | N | III Diffuse | 7 | 4 | 171 | 168,5 | 149 | 11% | 135 | 2 | 3 | 0 | Y | 3 |
| 22 | 45 | F | Lower limb | Primary | N | IV Stardust | 10 | 5 | 144 | 140 | 138 | 67% | 190 | 2 | 0 | 0 | Y | 4 |
| 23 | 37 | F | Upper limb | Breast CA. | Y | IV Stardust | 3 | 6 | 124,5 | 110,5 | 108 | 85% | 160 | 2 | 1 | 0 | Y | 4 |
| 24 | 34 | F | Upper limb | Breast CA. | N | III Splash | 1 | 5 | 118,5 | 108 | 104,5 | 75% | 185 | 1 | 0 | 0 | Y | 4 |
| 25 | 58 | F | Lower limb | Endometrial CA. | N | IV Stardust | 6 | 6 | 162 | 156 | 154 | 75% | 190 | 2 | 2 | 0 | Y | 4 |
| 26 | 46 | F | Lower limb | Primary | N | III Diffuse | 2 | 7 | 191 | 177,5 | 167 | 56% | 220 | 2 | 0 | 0 | Y | 4 |
| 27 | 74 | M | Lower limb | Bladder CA. | N | IV Diffuse | 8 | 7 | 196 | 192 | 162,5 | 12% | 160 | 2 | 1 | 0 | N | 3 |
| 28 | 52 | F | Lower limb | Primary | N | II Splash | 11 | 6 | 166 | 159 | 156,5 | 74% | 175 | 2 | 0 | 0 | Y | 4 |
| 29 | 53 | F | Lower limb | Cervical CA. | Y | III Stardust | 4 | 7 | 174 | 164 | 161 | 77% | 210 | 2 | 2 | 0 | Y | 4 |
| 30 | 55 | F | Upper limb | Breast CA. | Y | IV Diffuse | 4 | 4 | 129,5 | 125,5 | 109,5 | 20% | 185 | 2 | 6 | 0 | N | 3 |
| 31 | 61 | F | Upper limb | Breast CA. | Y | III Splash | 6 | 4 | 140,5 | 136,5 | 112 | 40% | 220 | 1 | 1 | 0 | Y | 4 |
| 32 | 48 | F | Upper limb | Breast CA. | N | III Splash | 2 | 5 | 119 | 112 | 108 | 64% | 180 | 2 | 1 | 0 | Y | 4 |
| 33 | 74 | F | Upper limb | Breast CA. | Y | III Diffuse | 18 | 4 | 152 | 145 | 117,5 | 41% | 165 | 2 | 1 | 0 | Y | 4 |
| 34 | 64 | F | Upper limb | Breast CA. | Y | III Splash | 1 | 5 | 122 | 117 | 112,5 | 53% | 205 | 1 | 1 | 0 | Y | 4 |
| 35 | 70 | F | Upper limb | Breast CA. | Y | IV Stardust | 4 | 5 | 158 | 138,5 | 116 | 46% | 180 | 2 | 14 | 0 | Y | 4 |
| 36 | 58 | F | Lower limb | Endometrial CA. | Y | III Splash | 1 | 8 | 231 | 215,5 | 203,5 | 60% | 220 | 2 | 1 | 0 | Y | 4 |

Continued

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| Patient LVA | Age | Gender | Affected limb | Etiology | Radio-therapy | Grade Icg pattern | Affected Period (Years) | Number of Anastomosis | Sum of diameters before LVA | Sum of diameters after LVA | Sum of unaffected limb diameters | Size reduction | Operation times | N. Microscopes | Lymph-angitis before surgery | Lymph-angitis after surgery | Compression class | Satisfaction |
|-------------|-----|--------|---------------|-----------------|---------------|-------------------|-------------------------|-----------------------|-----------------------------|----------------------------|----------------------------------|----------------|-----------------|----------------|------------------------------|-----------------------------|-------------------|--------------|
| 37 | 56 | F | Upper limb | Breast CA. | Y | III Stardust | 2 | 6 | 134 | 118,5 | 107,5 | 58% | 215 | 1 | 2 | 0 | Y | 4 |
| 38 | 55 | F | Lower limb | Endometrial-CA. | N | IV Diffuse | 4 | 6 | 193,5 | 187 | 169 | 27% | 175 | 2 | 0 | 0 | N | 3 |
| 39 | 61 | F | Upper limb | Breast CA. | Y | III Stardust | 9 | 5 | 148 | 133,5 | 115,5 | 45% | 190 | 1 | 7 | 0 | Y | 4 |
| 40 | 67 | M | Lower limb | Prostate CA. | N | IV Diffuse | 8 | 5 | 201 | 182 | 170 | 61% | 165 | 2 | 0 | 0 | Y | 3 |
| 41 | 57 | F | Upper limb | Breast CA. | N | IV Diffuse | 2 | 4 | 131 | 123 | 109,5 | 37% | 140 | 2 | 0 | 0 | Y | 3 |
| 42 | 33 | F | Lower limb | Primary | N | III Stardust | 7 | 5 | 162 | 152 | 150,5 | 87% | 170 | 2 | 0 | 0 | Y | 4 |
| 43 | 72 | F | Lower limb | Ovarian CA. | N | III Stardust | 6 | 4 | 194 | 179 | 174 | 75% | 175 | 2 | 0 | 0 | Y | 4 |
| 44 | 52 | F | Upper limb | Breast CA. | Y | IV Diffuse | 11 | 4 | 137 | 128,5 | 113 | 35% | 185 | 1 | 11 | 0 | N | 3 |
| 45 | 73 | F | Upper limb | Breast CA. | Y | IV Diffuse | 9 | 4 | 145,5 | 135,5 | 123 | 44% | 200 | 1 | 2 | 0 | Y | 3 |
| 46 | 72 | F | Upper limb | Breast CA. | Y | III Splash | 2 | 5 | 138 | 135 | 129 | 89% | 190 | 2 | 0 | 0 | Y | 4 |
| 47 | 63 | F | Upper limb | Breast CA. | Y | IV Diffuse | 8 | 5 | 122 | 120,5 | 110 | 13% | 230 | 1 | 0 | 0 | N | 3 |
| 48 | 44 | F | Lower limb | Endometrial CA. | N | III Stardust | 6 | 5 | 178 | 168 | 151,5 | 38% | 150 | 2 | 0 | 0 | N | 3 |
| 49 | 61 | F | Upper limb | Breast CA. | Y | IV Stardust | 13 | 6 | 131 | 126,5 | 114 | 26% | 140 | 2 | 2 | 0 | N | 2 |
| 50 | 65 | M | Upper limb | Breast CA. | Y | III Splash | 1 | 4 | 133 | 129,5 | 125,5 | 47% | 145 | 2 | 1 | 0 | Y | 4 |
| 51 | 71 | F | Lower limb | Endometrial CA. | N | IV Diffuse | 4 | 5 | 239 | 221 | 182 | 32% | 170 | 2 | 3 | 0 | N | 3 |
| 52 | 49 | F | Upper limb | Breast CA. | N | III Stardust | 2 | 6 | 125,5 | 108,5 | 106,5 | 81% | 165 | 2 | 2 | 0 | Y | 4 |
| 53 | 46 | F | Upper limb | Breast CA. | Y | III Stardust | 3 | 4 | 115 | 106,5 | 101 | 61% | 180 | 2 | 0 | 0 | Y | 4 |

Continued

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| Patient LVA | Age | Gender | Affected limb | Etiology | Radiotherapy | Grade | ICg pattern | Affected Period (Years) | Number of Anastomosis | Sum of diameters before LVA | Sum of diameters after LVA | Sum of unaffected limb diameters | Size reduction | Operation times | N. Microscopies | Lymph-angitis before surgery | Lymph-angitis after surgery | Compression class | Satisfaction |
|-------------|-----|--------|---------------|-----------------|--------------|-------|-------------|-------------------------|-----------------------|-----------------------------|----------------------------|----------------------------------|----------------|-----------------|-----------------|------------------------------|-----------------------------|-------------------|--------------|
| 54 | 56 | F | Upper limb | Breast CA. | Y | III | Splash | 4 | 6 | 152 | 140,5 | 110 | 27% | 165 | 2 | 0 | 0 | Y | 3 |
| 55 | 68 | F | Upper limb | Breast CA. | Y | III | Splash | 1 | 5 | 119 | 116 | 114,5 | 67% | 180 | 2 | 0 | 0 | Y | 4 |
| 56 | 62 | F | Lower limb | Cervical CA. | Y | IV | Diffuse | 4 | 4 | 249,5 | 230,5 | 178 | 27% | 145 | 2 | 2 | 0 | N | 3 |
| 57 | 43 | F | Upper limb | Breast CA. | N | III | Stardust | 1 | 4 | 141 | 132 | 121 | 45% | 140 | 2 | 0 | 0 | Y | 4 |
| 58 | 58 | F | Upper limb | Breast CA. | Y | IV | Stardust | 10 | 5 | 152 | 134,5 | 108,5 | 40% | 205 | 1 | 4 | 0 | Y | 4 |
| 59 | 59 | F | Upper limb | Breast CA. | Y | III | Stardust | 3 | 4 | 149 | 138,5 | 118 | 34% | 150 | 2 | 2 | 0 | Y | 3 |
| 60 | 54 | F | Lower limb | Primary | N | III | Diffuse | 7 | 6 | 171,5 | 163,5 | 155 | 48% | 190 | 2 | 2 | 0 | Y | 4 |
| 61 | 39 | F | Lower limb | Traumatic | N | IV | Splash | 1 | 8 | 161 | 142 | 133,5 | 69% | 220 | 2 | 0 | 0 | Y | 4 |
| 62 | 57 | F | Upper limb | Breast CA. | Y | III | Diffuse | 9 | 6 | 120 | 118 | 110,5 | 21% | 195 | 2 | 0 | 0 | N | 2 |
| 63 | 58 | F | Lower limb | Endometrial CA. | N | IV | Diffuse | 14 | 5 | 194 | 184,5 | 160,5 | 25% | 235 | 1 | 1 | 0 | Y | 4 |
| 64 | 52 | F | Upper limb | Breast CA. | Y | IV | Diffuse | 12 | 5 | 135 | 127,5 | 111 | 31% | 170 | 1 | 0 | 0 | Y | 4 |
| 65 | 46 | F | Upper limb | Breast CA. | Y | II | Splash | 3 | 6 | 145 | 125,5 | 125 | 98% | 215 | 1 | 0 | 0 | Y | 4 |
| 66 | 71 | M | Lower limb | Sarcoma | Y | III | Stardust | 9 | 7 | 136 | 116,5 | 113 | 76% | 190 | 1 | 0 | 0 | Y | 4 |
| 67 | 62 | F | Lower limb | Ovarian CA. | N | III | Stardust | 8 | 6 | 169 | 161,5 | 151 | 42% | 210 | 2 | 0 | 0 | N | 4 |
| 68 | 61 | F | Lower limb | Melanoma | Y | III | Stardust | 6 | 6 | 193 | 184 | 169 | 38% | 165 | 2 | 1 | 0 | Y | 4 |
| 69 | 54 | F | Upper limb | Breast CA. | N | II | Splash | 3 | 5 | 118 | 106,5 | 103 | 77% | 150 | 1 | 0 | 0 | Y | 4 |

COMPARISON BETWEEN THE DIFFERENCES IN MEASUREMENTS BETWEEN THE AFFECTED AND HEALTHY LIMB

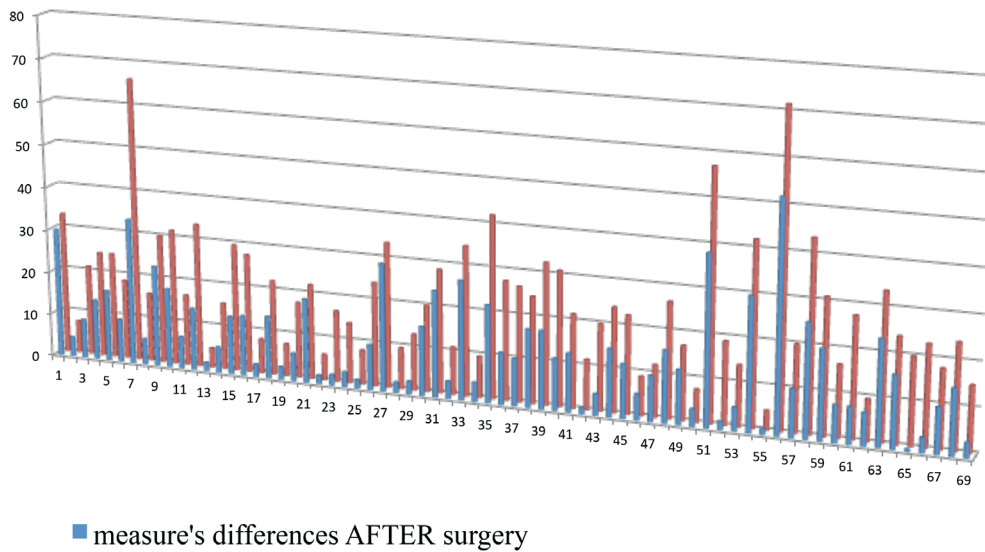


Table II. The figure shows the comparison between the differences in measurements between the affected and healthy limb: the blue lines show the difference in measurements between the sick and the healthy limb before surgery, the red lines show the difference during follow-up. We can see that the surgery has reduced the size of the limb in all patients.



Figure 2. A patient preoperative and postoperative view. An important reduction in size of the affected extremities can be seen. This patient experienced an early treatment which is the best indication for LVA surgery with successful result.



Figure 3. A patient preoperative and postoperative view. Reduction of edema is visible especially on the hand.

Patients also reported an increased efficacy of physiotherapy after LVA. In particular, 56 patients (81%) reported a reduction of compression class of garments.

We also applied a significance test to the results we have obtained. Assuming a normal distribution of our population, we performed a test to check for equality between the average of

our two samples using two-sided t -tests. The test rejects the null hypothesis of equality between the means and, with a p -value of 0.027, provides statistical evidence that there is a significant difference between the size of the limbs before and after the surgery. Therefore, it can be concluded that the LVA surgery has led to a significant reduction in limb size.



Figure 4. A patient preoperative and postoperative evaluation: a slight reduction of edema can be appreciated. Red lines show lymphatic vessels after ICG-lymphography. Also the sites of injection can be seen.

Discussion

Lymphoedema of the extremities is a chronic pathological condition determined by an output failure in lymphatic flow with subsequent progressive edema. Lymphoedema could appear as a primary or secondary disease. Secondary lymphoedema mostly occurs as a consequence of the surgical treatment of various cancers, especially in women. Lymphoedema due to filariasis is seen as endemic in tropical regions of Africa, South Asia, and South America. Other types of secondary lymphoedema include obstruction of lymphatics due to traumas or secondary compression³.

Notably, current treatment of lymphoedema is based on conservative therapies consisting in manual lymphatic drainage, intermittent pneumatic therapy, multilayered bandages and compression garments. Földi introduced the methodology of combined physiotherapy, intermittent pneumatic compression, and skin care. However, such approaches, not addressing the physiopathology of the disease, are time-consuming and lack satisfactory results⁴.

Surgical management of lymphoedema has been described. Surgical approaches include liposuction, excisional procedures, and microvascular surgery. Also, Kinmonth et al⁵ described island ileum transfer to the inguinal lymph region, aimed to the drainage via mesenteric lymph systems. However, although these strategies were worldwide accepted and success was reported in some patients, their effectiveness has never been consistent. Lymphaticovenular anastomosis was firstly reported in 1969 by Yamada⁶; according to this method, the proximal end of the transected lymph vessel is sutured to the main trunk of a large cutaneous vein in end-to-side fashion.

Subsequently, Koshima et al⁷ standardized the technique introducing minimally invasive supra microsurgical approach for lymphaticovenular anastomosis.

LVA is designed as a bypass procedure aiming to restore lymph drainage and to treat edema on a long-term basis^{8,9}. Recent super- (or supra) microsurgical techniques made possible the precise anastomosis of vessels of 0.8 to less than 0.2 mm caliber using 11-0 or 12-0 nylon with 50 to 70 μm needle¹⁰.

Supra microsurgical LVA differs from traditional lymph-venous bypass surgery because it requires microvascular anastomosis while according to the traditional technique a lymphatic tissue is inserted in a larger vein. The venules adopted for supra microsurgical LVA are subdermal veins

whit a caliber of few millimeters: these venules, because of their low pressure, do not show backflow; therefore, after the anastomosis is completed, the wash-out of lymph into the venule can be appreciated.

Furthermore, although satisfactory results have been described adopting traditional LVA technique, surgically approaching the axillary or groin area can result in a difficult identification of lymphatics because of retracted or irradiated tissue. In this district surgical complications may produce a worsening of lymphoedema.

Moreover, as described by Yamamoto et al¹¹, in lymphoedema patients the degeneration of lymphatic system runs from proximal to distal side: lymphatics adopted for supra microsurgical LVA are peripheral vessels which present a major functional reserve. In addition, this kind of vessels can be easily detached around distal joints and at ICG lymphography show linear pattern. Furthermore, supra microsurgical LVA is characterized by a minimal invasivity and can be performed under local anesthesia.

Preoperative indocyanine green (ICG) lymphography has demonstrated its clinical effectiveness in clinical staging and in detaching appropriate lymphatics vessels¹².

However, although it is easier for surgeons to find good lymphatic vessels in patients showing "linear" pattern, the authors agree that lymphatics can be found even if ICG-lymphography show "splash" or "stardust" dermal backflow pattern. However, lymphatics can rarely be spotted in "diffuse" dermal backflow pattern. Moreover, performing ICG-lymphography in the contralateral healthy extremity helps to select the site of the incision on the affected side¹³.

Also, ICG-lymphography is a noninvasive, non-radioactive test that allows real-time evaluation of superficial lymphatic system¹⁴. Moreover, in lymphoedema patients, a fibrotic involution of lymphatic vessels could be seen¹⁵. The LVA technique also aims to stop the progression of fibrogenesis affecting lymphatic vessels which stand remarkable point in a progressive pathology. The timing of the occlusion and degeneration of the smooth muscle cells may not directly correspond to the edema duration. This means that can be worth trying a lymphaticovenular anastomosis even in patients with a duration of lymphoedema of more than 20 years¹⁶.

Furthermore, the use of LVA, on bypasses performed at different sites on the affected extremity, is likely to give benefits also in seriously compromised areas¹⁷.

LVA has shown a high success rate and broad indications. Best results can be achieved in patients presenting mild lymphoedema in early stages, and outcomes can be analyzed objectively and subjectively. As for objective outcomes, LVA has demonstrated a decrease in the circumference of the affected extremities and a severe contraction of cellulitis episodes¹⁸.

Postoperative ICG lymphography was taken to demonstrate the patency of anastomosis. 92% of anastomosis was working 1 years after surgery.

As far as subjective outcomes are concerned, patients feel their extremities lighter and softer. Physiotherapy is considered much more effective after LVA. Additionally, strength class of garment has been reduced¹⁹. Therefore, every patient can benefit from this technique. Moreover, remission of lymphoedema can be achieved at an early stage. Indeed, future perspectives should be focused on preventive intervention in patients at risk for the development of a lymphoedema.

Conclusions

Surgical treatment of lymphoedema is still challenging and an unanimous consensus on principles, indications and outcomes are still far to be achieved. Lymphaticovenular anastomosis (LVA) is characterized by broad indications and high success rate. LVA has also the unquestionable advantage of the extremely minimal invasivity which allows to perform the procedure under local anesthesia and in patients whose conditions would advise against general anesthesia. LVA has demonstrated to be an effective surgical strategy to treat lymphoedema, especially in patients affected by secondary lymphoedema in early stages. Although LVA has been well documented in the literature, the majority of works relates to Japanese experience and few reports exists outside Japan, especially in Europe. The present paper represents the first Italian report about supra microsurgical LVA.

Conflict of Interests

The Authors declare that they have no conflict of interests.

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