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CASE REPORT

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Vascularized appendicular lymph node transfer for treatment of extremity lymphedema: A case report

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Abstract

Vascularized lymph node transfer has demonstrated promising results for the treatment of extremity lymphedema. In an attempt to find the ideal donor site, several vascularized lymph nodes have been described. Each has a common goal of decreasing morbidity and avoiding iatrogenic lymphedema while obtaining good clinical results. Herein, we present the preliminary clinical outcomes of an intra-abdominal lymph node flap option based on the appendicular artery and vein used for the treatment of extremity lymphedema. A 62 year-old woman with moderate lower extremity lymphedema, on chronic antibiotics because of recurrent infections and unsatisfactory outcomes after conservative treatment underwent a vascularized appendicular lymph node (VALN) transfer. At a follow-up of 6 months, the reduction rate of the limb circumference was 17.4%, 15.1%, 12.0% and 9% above the knee, below the knee, above the ankle and foot respectively. In addition, no further episodes of infection or other complications were reported after VALN transfer. Postoperative lymphoscintigraphy demonstrated that the VALN flap was able to improve the lymphatic drainage of the affected limb. According to our findings, the use of VALN transfer minimizes donor-site morbidity, avoids iatrogenic lymphedema and may provide a strong clearance of infection because of the strong immunologic properties of the appendiceal lymphatic tissue in selected patients. Despite these promising results, further research with larger number of patients and longer follow- up is needed.

1 | INTRODUCTION

Vascularized lymph node transfer (VLNT) has demonstrated promising results for the treatment of extremity lymphedema (Barreiro et al., 2014; Becker et al., 2012; Cheng et al., 2012; Ciudad & Kiranantawat et al., 2015; Ciudad & Maruccia et al., 2015; Coriddi, Skoracki, & Eiferman, 2016; Granzow, Soderberg, Kaji, & Dauphine, 2014; Lin et al., 2009; Raju & Chang, 2015; Sapountzis et al., 2009; Scaglioni et al., 2016). Besides the promising clinical results, in VLNT surgery, donor-site morbidity has always been a source of concern for surgeons and patients since it is always possible for the patient to develop iatrogenic lymphedema, lymphorrea, or another unexpected complication at the donor-site (Azuma, Yamamoto, & Koshima, 2013; Massey & Gupta, 2015; Pons Pons, Masia, Loschi, Nardulli, & Duch,, 2014; Scaglioni et al., 2016; Sulo et al., 2015; Vignes, Blanchard, Yannoutsos, & Arrault, 2013; Viitanen, Mäki, Seppänen, Suominen, Saaristo, 2012).

Several donor sites have been described for vascularized lymph nodes harvest, (Barreiro et al., 2014; Cheng et al., 2012; Ciudad & Kiranantawat et al., 2015; Lin et al., 2009; Sapountzis et al., 2009) focused on finding an ideal donor site that results in good clinical outcomes while avoiding iatrogenic lymphedema of the donor area. In addition, during the last years, some studies have reported the use of intra-abdominal flaps for VLNT for the treatment of extremity lymphedema (Ciudad & Kiranantawat et al., 2015; Ciudad & Maruccia et al., 2015; Coriddi et al., 2016).

Herein, we present the *preliminary* clinical outcomes of an intra-bdominal lymph node flap option based on the appendicular artery and vein (Figure 1-A). To our knowledge, this is the first report using the

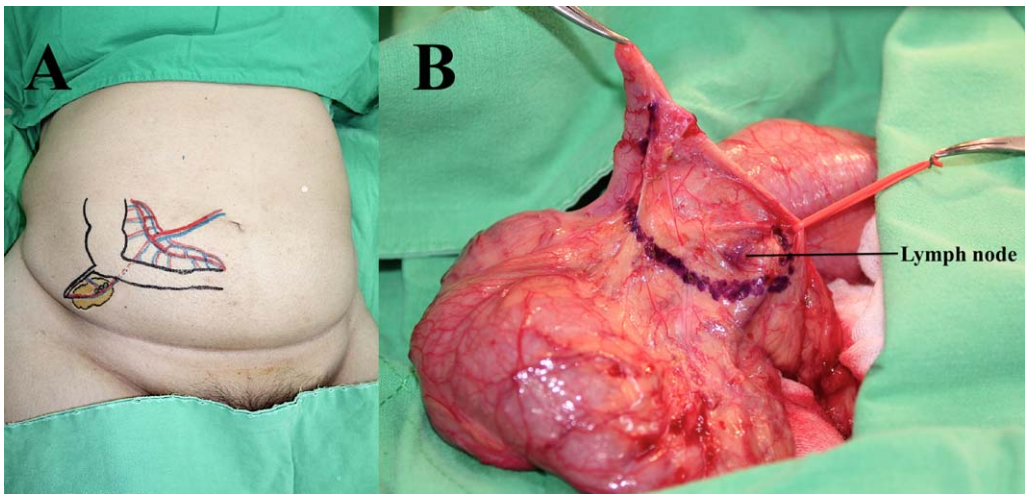

FIGURE 1 A, Anatomical landmarks of the vascularized appendicular lymph node. The flap was based on the appendicular vessels and included the surrounding lymphoid tissue and lymph nodes. B, Marking of the appendiceal lymph nodes. Dissection was performed extending to the surrounding mesenteric tissue in order to ensure preservation of the vascularity of the lymph nodes after flap harvest

vascularized appendicular lymph node (VALN) transfer for the treatment of extremity lymphedema.

2 | CASE REPORT

This is a 62-year-old female, who presented with right lower extremity lymphedema and recurrent episodes of cellulites over the affected limb after total hysterectomy, inguinal lymph node dissection, and postoperative radiotherapy. She sustained swelling of the lower limb 6 months postoperatively, which got worse over the following 3 years. Initially, the patient was treated under complex decongestive therapy, with minimal improvement. She suffered several episodes of cellulitis during this period (2–3 per year) and was treated using first generation cephalosporins, trimethoprim/sulfamethoxazole, up to requiring hospital admission for intravenous antibiotic treatment (vancomycin). Pre-operative lymphoscintigraphy revealed lymphatic obstruction with delayed uptake of contrast over the right lower limb. In addition to a total hysterectomy, she underwent percutaneous drainage of her gallbladder, followed by laparoscopic cholecystectomy secondary to acute cholecystitis. Patient was explained in detail all aspects and surgical options for VLNT procedure using intra-abdominal lymph node flaps.

A midline laparotomy was performed in order to access a vascularized lymph nodes based in the right gastroepiploic vessels However, during dissection, several adhesions were found in the right upper quadrant close to the right gastroepiploic vessels, which made an unsafe harvest of this flap for VLNT. This was most likely to secondary adhesions. At this point we decided to explore another potential intra-abdominal donor area for VLNT. After manual palpation and trans-illumination, two appendiceal lymph nodes and its sourronding tissue where found and choosen for VLNT.

The VALN is based on the appendicular artery and vein. Flap elevation starts identifying the appendicular vessels. Lymph nodes and lymphatics adjacent to the pedicle were marked and included within the flap (Figure 1-B). Indocyanine green lymphatic imaging can be performed to confirm the vascularity and the amount of the lymph nodes included within the flap. The appendicular artery and vein were carefully dissected, isolated, and ligated. Appendectomy was performed. Under the operating microscope, on a side table the mesoappendix is dissected and separated from the appendix while avoiding devascularization of the flap. The appendix was not included within the flap. A flap size of 6.0 x 5.5 cm with a pedicle of 5 cm was harvested. Total operating time for flap harvest was 50 minutes. The diameter of the appendicular artery and vein were 0.8 and 1.0 mm respectively. The flap was then exteriorized and transferred to the lymphedematous recipient site. At the recepient site, the flap was minimally trimmed at the margins, avoiding any damage to the lymphatic tissue within the flap. Microsurgical anastomoses were performed at the ankle level using the medial plantar vessels in an end-to-end fashion after adequate vessel preparation (Figure 2). No lymphatic anastomosis or other surgical procedure was performed. The total operating time was 4 hours. The procedure was uneventful and patient remained comfortable in the perioperative period.

During the period of follow-up, the affected limb became much lighter and softer 2 months after the VALN transfer in compare with the preoperative period (Figure 3-A). At 6 months of follow-up, the reduction rate of the limb circumference was 17.4%, 15.1%, 12.0% and 9% above the knee, below the knee, above the ankle and foot respectively. Most important, antibiotics were suspended and no further episodes of

FIGURE 2 Inset of the vascularized appendicular lymph node flap at ankle level and microanastomosis with medial plantar recepient vessels

infection were reported during this period. (Figure 3-B) When we compare preoperative lymphoscintigraphy (Figure 4-A), postoperative lymphoscintigraphy demonstrated that the VALN was able to improve the lymphatic drainage of the affected limb (Figure 4-B).

3 | DISCUSSION

The knowledge for the surgical treatment of lymphedema has increased in the last years and multiple different donor sites series of patients for lymph node flaps have been described including the groin, supraclavicular, submental, lateral thoracic area (Barreiro et al., 2014; Becker et al., 2012; Cheng et al., 2012; Lin et al., 2009; Sapountzis et al., 2009; Scaglioni et al., 2016) However, one of the main downsides of vascularized lymph node transfer surgery is the potential donor site morbidity and the risk of iatrogenic lymphedema after lymph node harvest (Scaglioni et al., 2016).

According to our experience, the most important aspects to have success in VLNT surgery are adequate patient selection, transfer healthy lymph nodes from any place of the body, minimize donor site morbidity and to avoid the risk of iatrogenic lymphedema.

In the last years, some of the intra-abdominal vascularized lymph nodes reported for the treatment of extremity lymphedema are the right gastroepiploic (Ciudad & Kiranantawat et al., 2015), the jejunal mesenteric (Coriddi et al., 2016) and now with this report, the appendicular lymph node flap can be part of this armamentarium. Even thought, all these studies have small series of patients with no long-term follow-up. Up to now, these flaps have avoided possible iatrogenic lymphedema and other donor site complications as seen in other fasciocutaneous vascularized lymph nodes (Scaglioni et al., 2016; Massey & Gupta, 2015; Vignes et al., 2013; Pons et al., 2014).

During the last years, our group has been using the vascularized right gastroepiploic lymph node flap for the treatment of lymphedema with very promising results (Ciudad & Kiranantawat et al., 2015; Ciudad & Maruccia et al., 2016). However, in some circumstances, such as in this case, other lymph node donor site areas may be evaluated as an alternative option for possible VLNT.

The appendix is a component of the gut-associated lymphoid tissue system and it is surrounded by lymphatic tissue and lymph nodes that play an important role in the host defense mechanism. (Corner, 1910) The appendix is an immunologic organ that actively participates

FIGURE 3 A, Pre-operative picture. B, Postoperative picture at 6 months postoperatively showed reasonable decrease of the overall limb volume. Moreover, no other episodes of infection or other complications were reported during the follow-up period

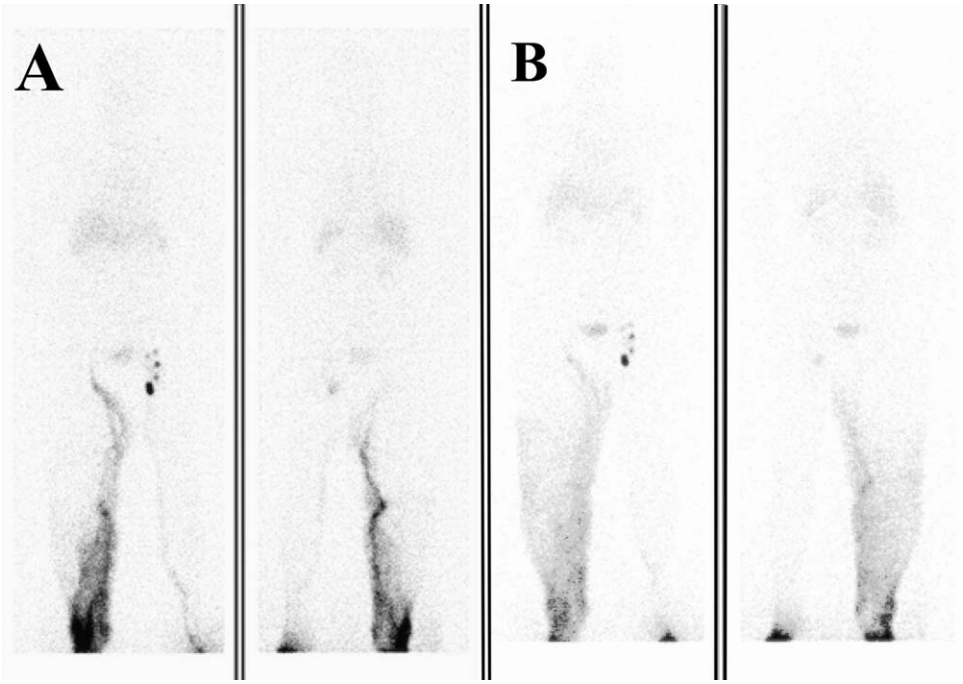

FIGURE 4 A, Pre-operative lymphoscintigraphy showed significant dermal back-flow of the radiotracer and impaired lymphatic function over the right lower limb. On the left leg, normal lymphatic function was noted. B, Post-operative lymphoscintigraphy showed improvement of the lymphatic flow of the affected limb at 6-months after VALN transfer

in the secretion of immunoglobulins, particularly Ig A (Brunicardi et al., 2005). This is an important concept since this lymphatic tissue and lymph nodes around the vascular pedicle may play an important role in the surgical management of patients with extremity lymphedema and recurrent infections. In addition, the surgical removal of the appendix causes no physiologic or functional deficiencies.

The appendix is supplied by the appendicular artery, which is the terminal branch of the ileocolic artery. Kelly et al.(Kelly & Hurdon, 1905) showed that in 66% of appendices studied, the main appendicular artery supplied the distal three quarters of the appendix, while an accessory appendicular artery supplied the proximal fourth. The appendicular artery, accompanying vein, lymphatics, and lymph nodes run through the mesoappendix (Levy, Mortele, & Yeh, 2015).

The appendix and it vascular pedicle have been used in urethral, voice, and vaginal reconstruction (Chen, Yeong, Tang, & Chen, 2012; Koshima, Inagawa, Okuyama, & Moriguchi, 1999). However, the use of an isolate VALN based on the appendicular artery and vein never have been described for the treatment of extremity lymphedema.

One of the most important properties of the appendix is to have a good lymph drainage function because of the presence of lymphoid tissue in the mucosa and submucosa (Azzali, 1998). Even thought opening the appendix along its antimesenteric border and preserving the mucosa within the flap may improve its draining function. However, in this case we did not include these bowel layers within the flap. Future studies should be done in order to confirm the function of the lymphatic mucosa in the treatment of lymphedema.

Advantages of using the vascularized appendicular lymph node are: constant vascular anatomy, dissection of this flap is relatively easy, short operating time. Harvesting the VALN, only the appendiceal vessels are sacrificed, there is minimal donor site morbidity, and most importantly there is no concern of iatrogenic lymphedema secondary to flap harvest, while allowing a two-team approach. In addition, this flap is significantly less bulky, making the inset easier and giving an overall good cosmetic result. Even though, this flap is thin, it contains visible and palpable large lymph nodes around its pedicle.

Even thought in this case we did not encounter any complication at the donor site, there are some potential complications with the use of any intra-abdominal lymph node flaps. Within the most common ones are bowel adhesions, ileus, bowel obstruction, peritonitis, incisional hernias, and potential solid and hollow viscus injury.

Regarding the surgical approach, we believe that a midline incision gives the surgeon good exposure of the intra-abdominal cavity and it is easier to perform. However, others incisions can minimize donor site morbidity but depends on surgeon expertise and preference. The use of laparoscopic or robotic techniques can help minimize the donor site morbidity for the VALN harvest. In our short experience, when using other intra-abdominal lymph node flaps, we haven't seen any of these complications(Ciudad & Kiranantawat et al., 2015; Ciudad & Maruccia et al., 2015; Corner, 1910).

In cases of lower extremity lymphedema, we prefer the use of the medial plantar artery and vein as a recipient vessel (Ciudad & Kiranantawat et al., 2015; Ciudad & Maruccia et al., 2015). The anastomosis can be performed in an end-to-end fashion, the artery is reliable and allows preservation of the dorsalis pedis and the posterior tibial vessels. In addition, the flap can be placed and hide at the medial side of the ankle with an acceptable cosmetic result.

Each of the vascularized lymph node described in the literature has advantages and disadvantages. Selection depends on surgeon's experience, surgical preference and should be tailored for each patient.

Even though we propose a new donor site option for VLNT that shows improvement of the lymphatic drainage as demonstrated in the lymphoscintigraphy, the overall volume reduction in this patient remains unpredictable, as this procedure requires a longer follow-up period, which is the main weakness of this paper.

The appendicular lymph node flap may be another option for VLNT and might become a good alternative when other more common lymph node flaps are not available. According to the results obtained, we found that the VALN contributed to the decrease of the overall limb volume, avoids iatrogenic lymphedema and may provide a faster clearance of infection because of the strong immunologic properties of the lymphoid tissue in the ileocecal region (Brunicardi et al., 2005; Ciudad et al., 2016).

Despite these promising results, further long-term studies with larger number of patients will identify the safety and efficacy of this flap for treatment of lymphedema. Currently, we are looking forward to provide further evidence based on this novel approach.

REFERENCES

Azuma, S., Yamamoto, T., & Koshima, I. (2013) Donor-site lymphatic function after microvascular lymph node transfer should be followed using indocyanine green lymphography. *Plastic and Reconstructive Surgery*, *131*, 443e–444e.

Azzali, G. (1998) Three-dimensional and ultrastructural aspects of the lymphatic vascularization of the vermiform appendix. *Journal of Submicroscopic Cytology and Pathology*, *30*, 545–553.

Barreiro, G. C., Baptista, R. R., Kasai, K. E., Dos Anjos, D. M., Busnardo, F. D., & Modolin, M., Ferreira, M. C. (2014) Lymph fasciocutaneous lateral thoracic artery flap: Anatomical study and clinical use. *Journal of Reconstructive Microsurgery*, *30*, 389–396.

Becker, C., Vasile, J. V., Levine, J. L., Batista, B. N., Studinger, R. M., Chen, C. M., & Riquet, M. (2012) Microlymphatic surgery for the treatment of iatrogenic lymphedema. *Clinics in Plastic Surgery*, *39*, 385–398.

Brunicardi, F., Andersen, D., Billiar, T., Dunn, D., Hunter, J., & Pollock, R. (2005) Schwartz's principles of surgery (The Appendix 8th ed, Chapter 29, p. 1119). New York: MC Graw-Hill.

Chen, S. H., Yeong, E. K., Tang, Y. B., & Chen, H. C. (2012) Free and pedicled appendix transfer for various reconstructive procedures. *Annals of Plastic Surgery*, *69*, 602–606.

Cheng, M. H., Huang, J. J., Nguyen, D. H., Saint-Cyr, M., Zenn, M. R., Tan, B. K., & Lee, C. L. (2012) A novel approach to the treatment of lower extremity lymphedema by transferring a vascularized submental lymph node flap to the ankle. *Gynecologic Oncology*, *126*, 93–98.

Ciudad, P., Date, S., Lee, M. H., Lo Torto, F., Nicoli, F., Araki, J., & Chen, H. C. (2016) Robotic harvest of a right gastroepiploic lymph node flap. *Archives of Plastic Surgery*, *43*, 210–212.

Ciudad, P., Kiranantawat, K., Sapountzis, S., Sze-Wei Yeo, M., Nicoli, F., & Maruccia, M., Sirimahachaiyakul, P., Chen, H. C. (2015) Right gastroepiploic lymph node flap. *Microsurgery*, *35*, 496–497.

Ciudad, P., Maruccia, M., Socas, J., Lee, M. H., Chung, K. P., Constantinescu, T., Kiranantawat, K., Nicoli, F., Sapountzis, S., Yeo, M. S., Chen, H. C. (2015) The laparoscopic right gastroepiploic lymph node flap transfer for upper and lower limb lymphedema: Technique and outcomes. *Microsurgery*, doi: 10.1002/micr.22450. [Epub ahead of print]

Coriddi, M., Skoracki, R., & Eiferman, D. (2016) Vascularized jejunal mesenteric lymph node transfer for treatment of extremity lymphedema. *Microsurgery*, doi: 10.1002/micr.30037. [Epub ahead of print]

Corner, E. M. (1910) The function of the appendix and the origin of appendicitis. *Annals of Surgery*, *52*, 512–519.

Granzow, J. W., Soderberg, J. M., Kaji, A. H., & Dauphine C. (2014) Review of current surgical treatments for lymphedema. *Annals of Surgical Oncology*, *21*, 1195–1201.

Kelly, H. A., & Hurdon, E. (1905) The vermiform appendix and its diseases. Philadelphia: W. B. Saunders., 189.

Koshima, I., Inagawa, K., Okuyama, N., & Moriguchi, T. (1999) Free vascularized appendix transfer for reconstruction of penile urethras with severe fibrosis. *Plastic and Reconstructive Surgery*, *103*, 964–969.

Levy, A., Mortele, K., & Yeh, B. M. (2015) Gastrointestinal imaging cases (Chapter 33). In: Normal Anatomy and Imaging Techniques of the Appendix (pp. 201–202). Oxford, New York: Oxford University Press.

Lin, C. H., Ali, R., Chen, S. C., Wallace, C., Chang, Y. C., Chen, H. C., & Cheng, M. H. (2009) Vascularized groin lymph node transfer using the wrist as a recipient site for management of postmastectomy upper extremity lymphedema. *Plastic and Reconstructive Surgery*, *123*, 1265–1275.

Massey, M. F., & Gupta, D. K. (2015) The incidence of donor-site morbidity after transverse cervical artery vascularized lymph node transfers: the need for a lymphatic surgery national registry. *Plastic and Reconstructive Surgery*, *135*, 939e–940e.

Pons, G., Masia, J., Loschi, P., Nardulli, M. L., & Duch, J. (2014) A case of donor-site lymphoedema after lymph node-superficial circumflex iliac artery perforator flap transfer. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, *67*, 119–123.

Raju, A., & Chang, D. W. (2015) Vascularized lymph node transfer for treatment of lymphedema: A comprehensive literature review. *Annals of Surgery*, *261*, 1013–1023.

Sapountzis, S., Singhal, D., Rashid, A., Ciudad, P., Meo, D., & Chen, H. C. (2009) Lymph node flap based on the right transverse cervical artery as a donor site for lymph node transfer. *Annals of Plastic Surgery*, *73*, 398–401.

Scaglioni, M. F., Arvanitakis, M., Chen, Y. C., Giovanoli, P., Chia-Shen Yang, J., & Chang, E. I. (2016) Comprehensive review of vascularized lymph node transfers for lymphedema: Outcomes and complications. *Microsurgery*, doi: 10.1002/micr.30079. [Epub ahead of print]

Sulo, E., Hartiala, P., Viitanen, T., Mäki, M., Seppänen, M., & Saarikko, A. (2015) Risk of donor-site lymphatic vessel dysfunction after microvascular lymph node transfer. *Journal of Plastic, Reconstructive & Aesthetic Surgery 68*, 551–558.

Vignes, S., Blanchard, M., Yannoutsos, A., & Arrault, M. (2013) Complications of autologous lymph-node transplantation for limb lymphoedema. *European Journal of Vascular & Endovascular Surgery*, *45*, 516–520.

Viitanen, T. P., Mäki, M. T., Seppänen, M. P., Suominen, E. A., & Saaristo, A. M. (2012) Donor-site lymphatic function after microvascular lymph node transfer. *Plastic and Reconstructive Surgery*, *130*, 1246–1253.