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Surgical Treatment Modalities for Lymphedema

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Background

Lymphedema, an abnormal condition of lymphatic fluid accumulation, is an incurable, debilitating, and progressive condition affecting 140 million individuals worldwide. Secondary lymphedema is the most common cause in the United States, affecting over 5 million individuals, and typically results from lymphadenectomy in the treatment of solid tumors involving the axillary, groin, or genitourinary lymph node basins. Adjuvant radiation therapy adds additional injury and significantly increases the risk of developing lymphedema [1]. These secondary causes of lymphedema continue to be a growing problem that can have a significant impact on quality of life. Regardless of the location, the end result is a limb that is heavy, dysfunctional, painful, prone to infection, and at long-term risk for malignant transformation or amputation.

Despite the increasing incidence of lymphedema, the "gold standard" for treatment continues to be manual decongestive therapies and compressive bandaging. However, these conservative treatment modalities are time consuming and highly inconvenient with resultant suboptimal patient adherence [2]. Advancements in surgical reconstruction have enabled new avenues to treat chronic lymphedema that are less morbid than the traditional excisional surgeries. We will discuss the most relevant microsurgical techniques, which include Lymphaticovenular Anastomosis (LVA) and Vascularized Lymph Node Transfer (VLNT). We will also discuss Suction-Assisted Lipectomy (SAL), which has emerged as a complementary surgical option in a select group of patients.

LVA

Lymphaticovenular Anastomosis is a microsurgical technique that involves diverting the lymphatic fluid into the venous system distal to a compromised lymphatic bed, thereby bypassing the area of absent, damaged, or obstructed lymphatic channels. The concept of anastomosing a lymphatic vessel to a vein was first introduced for the treatment of lymphedema [3-6]. Since its introduction, various studies have reported on the efficacy of its practice including a recent meta-analysis that showed 89.2% of patients reporting subjective improvement, while 87.8% patients had a quantitative improvement, with 56.3% of patients being able to discontinue compression garments completely post-operatively [7]. Research also showed LVA to be especially effective in the treatment of those with early-stage lymphedema of the upper extremity, as reported in a prospective analysis of 100 Lympho-Venous bypass patients; in which 96% of those in the upper extremity group reported symptomatic improvement versus 57% of patients in lower extremity lymphedema group [8]. Other benefits from LVA include decreased rates of infection/cellulitis, which is a common complication of lymphedema often requiring recurrent antibiotic treatment [5]. For patients undergoing oncologic resections, LVA has also been investigated for its prophylactic benefits. In a group of 14 patients with subclinical lower extremity lymphedema from resection of a variety of gynecologic cancers, LVA effectively prevented symptomatic lymphedema [9]. Moreover, LVA successfully prevented lymphedema in a group of 23 women who underwent axillary lymph node dissection for breast cancer treatment [10]. The reported complication profile for this procedure also favors its use, as was seen in the meta-analysis aforementioned, showing a 3.9% incidence of infection, 4.1% incidence of lymphorrhea, and 10% requiring a subsequent operation [7]. In conclusion, good functional data and a favorable complication profile make

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LVA a viable option for the treatment of lymphedema in a subset of patients. However, the greatest disadvantages are the limited number of surgeons able to perform this demanding microsurgical technique and its unknown longer term efficacy.

VLNT

Vascularized Lymph Node Transfer (VLNT) involves the en block transfer of vascularized lymph nodes and its surrounding soft tissue to the site of lymphedema, with microsurgical anastomosis of the arteriovenous blood supply. The donor soft tissue is commonly harvested from the supraclavicular, submental, groin, axillary, or omental anatomy [6]. Although the mechanism of action has not clearly been elucidated, the theory behind this microsurgical procedure is that transplanted lymph nodes reduce lymphedema by venous shunting of lymphatic fluid and/or stimulating lymphangiogenesis [5, 11].

VLNT has been shown to be a highly effective treatment for lymphedema. In a meta-analysis that pooled 5 studies, all patients reported subjective improvement, while 90.7% of patients had quantitative improvement, and 78.0% of patients were able to discontinue compressive therapy [7, 12]. A randomized control trial also evaluated the efficacy of VLNT in treating stage II breast cancer-related lymphedema. Thirty-six patients were randomized to either VLNT with physiotherapy and compression or to conservative modalities alone. The mean limb volume was reduced by 57% in the experimental group treated with VLNT versus 18% in the non-surgical control group. Additionally, the rate of infection significantly decreased in the surgically treated group [13, 14]. Most recently, a systematic review of 18 studies and 305 patients undergoing VLNT reported improved quality of life in all patients, with 91% improvement of limb circumference, 86% with reduced limb volume, and 60% with improved lymphatic flow [15-18]. Of interest, a group from Finland reported a case series that combined VLNT with free lower abdominal breast flap reconstruction, providing favorable results through a simultaneous breast and lymphatic reconstruction. This was performed by a modification of the reconstructive flap to include the lymphatic structures and fat associated with the superficial circumflex iliac vascular pedicle [19].

One concerning complication of VLNT, however, is donor site morbidity, including seroma and lymphocele formation, delayed wound closure, and donor site lymphedema [6, 19]. To circumvent this complication, reverse lymph node mapping has helped to preserve the vital lymphatic structures at the donor site and reduce the risk of donor site lymphedema [20]. Other reported complications of VLNT include infection 7.8%, lymphorrhea 14.7%, re-exploration surgery 2.7%, and revision surgery requiring additional procedures 36% [7]. Due to the known complication profile of VLNT, many specialists offer this option to select group of patients. The current indications for LVNT include grade II to IV lymphedema, fibrosis preventing LVA, absence of functioning donor lymphatics, or grade II lymphedema with a history of multiple episodes of cellulitis [5, 6].

Despite the small volume success rates seen in various independent studies, a comparative study between the available microsurgical interventions is lacking. However, with careful patient selection and meticulous technique, it is suggested that VLNT may result in superior outcomes for the treatment of lymphedema, especially in those with lower extremity and later stage disease [7, 8, 18].

Suction-Assisted Lipectomy

In addition to the physiologic microsurgical therapies for lymphedema, Suction-Assisted Lipectomy, or liposuction, has emerged as a promising surgical treatment for patients with late stage lymphedema that have failed conservative management [6]. Liposuction was first used for the treatment of lymphedema by O'brien et al. [21]. This technique aims to remove the solid component of lymphedema after the fluid component has been drained with conservative modalities. Therefore, liposuction is especially suited for late stage lymphedema, in which tissue remodeling has produced a large solid component consisting of fibrosis and hypertrophied subcutaneous adipose tissue. In fact, most of the swelling in late stage lymphedema is from this solid component rather than fluid [22].

A prospective trial following 15 upper extremity lymphedema patients for 5 years after undergoing liposuction, showed maintained long-term efficacy when performed in conjunction with post-operative compression therapy [23]. Most recently, Green et al. has reported a mean reduction in extremity volume of 73% and improved quality of life at 3.1 years after surgery [24]. It is important to emphasize that liposuction is not a cure for lymphedema, because it does not treat the underlying cause. Hence, without the continued use of post-operative compression garments, relapse of lymphedema is inevitable [23, 25]. However, when used complementarily with conservative treatment modalities or procedures improving lymphatic drainage (i.e., LVA or VLNT), the benefit from liposuction is maintained long-term [26, 27]. Moreover, liposuction is surprisingly effective at preventing lymphedema associated cellulitis. In a series of 10 patients treated for chronic lymphedema with liposuction, incidence of cellulitis decreased from 70% to 10% [28].

Conclusion

The number of patients at risk for lymphedema continues to rise due to increasing cancer survivorship. Various attempts at preventing the development of lymphedema have led to improved clinical practices, such as sentinel lymph node biopsy and improved radiation therapy techniques. Despite these advances, lymphedema remains a significant burden for a subset of cancer survivors [17]. For patients that have reached end-stage lymphedema-characterized by extensive adipose deposition, fibrosis, and recurrent episodes of cellulitis—radical debulking surgeries such as the Charles procedure (subcutaneous tissue resection followed by skin grafting) are indicated. Unfortunately, this surgery is morbid, aesthetically displeasing, and carries a risk of amputation in the setting of skin graft failure. New hope for symptomatic improvement has emerged with microsurgical procedures such as Lymphatico-Venular bypass, Vascularized Lymph Node Transfer, and a less invasive debulking procedure, Suction-Assisted Lipectomy. Despite reported success rates on these microsurgical interventions, variability in outcome

and non-superiority of one technique leaves most experts to regard these procedures as experimental, thus warranting further investigation [13, 18]. Consequently, the mainstay of lymphedema management today largely consists of conservative modalities including manual lymphatic drainage, exercise, pneumatic pumps, and compression bandage therapy. However, these decongestive treatments are expensive, time-consuming, and disruptive to activities of daily living, leaving a poor long-term compliance rate [16]. As one can see, there is a significant need for the development of curative therapies that can prevent or retard disease progression.

Over the last decade, there have been many advances in stem cell technology. Most notably, it has been demonstrated that embryonic stem (ES) cells and mesenchymal stem cells (MSCs) undergo differentiation into Lymphatic Progenitor Cells (LPCs) and participate in post-developmental lymphangiogenesis. Moreover, certain growth factors and biologic molecules, such as VEGF-C and 9-cis Retinoic Acid (9-cis RA), have recently been shown to play in important role in lymphangiogenesis [29]. In animal models, several groups have demonstrated that exogenous treatment with VEGF-C/D stimulates post-natal lymphangiogenesis to improve lymphedema (4-7). However, reports that link VEGF-C expression with tumor metastasis [8-10] make VEGF-based therapy risky in patients with a history of cancer. To circumvent this issue, alternative classes of non-growth factor small molecules have been investigated for their potential pro-lymphangiogenic effects, most notably 9-cis RA. Through both in vitro and animal studies, 9-cis RA has been shown to effectively stimulate lymphangiogenesis and prevent lymphedema progression after combined radiation and surgical injury, as measured by clinical and standard histologic parameters [12].

The discoveries made in the last decade have opened a fascinating domain, combining stem cell technology with exogenous stimulation to discover novel therapies for lymphedema. With increasing cancer survivorship and prevalence of lymphedema, breakthrough findings of biological molecules involved in lymphangiogenesis are one of the most promising venues to cure lymphedema.

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References

1 Yamada Y (1969) The studies on lymphatic venous anastomosis in lymphedema. Nagoya J Med Sci 32: 1-21.

2 Brorson H, Ohlin K, Olsson G, Langstrom G, Wiklund I, et al. (2006) Quality of life following liposuction and conservative treatment of arm lymphedema. Lymphology 39: 8-25.

3 Jacobson JH, Suarez EL (1962) Microvascular surgery. Chest 41: 220-224

4 Sedlacek J (1969) Lymphovenous shunt as supplementary treatment of elephantiasis of lower limbs. Acta Chir Plast 11: 157-162.

5 Allen RJ, Cheng MH (2016) Lymphedema surgery: Patient selection and an overview of surgical techniques. J Surg Oncol 113: 923-931.

6 Silva AK, Chang DW (2016) Vascularized lymph node transfer and lymphovenous bypass: Novel treatment strategies for symptomatic lymphedema. J Surg Oncol 113: 932-939.

7 Basta MN, Gao LL, Wu LC (2014) Operative treatment of peripheral lymphedema: a systematic meta-analysis of the efficacy and safety of lymphovenous microsurgery and tissue transplantation. Plast Reconstr Surg 133: 905-913.

8 Chang DW, Suami H, Skoracki R (2013) A prospective analysis of 100 consecutive lymphovenous bypass cases for treatment of extremity lymphedema. Plast Reconstr Surg 132: 1305-1314.

9 Yamamoto T, Yamamoto N, Yamashita M, Furuya M, Hayashi A, et al. (2016) Efferent Lymphatic Vessel Anastomosis: Supermicrosurgical Efferent Lymphatic Vessel-to-Venous Anastomosis for the Prophylactic Treatment of Subclinical Lymphedema. Ann Plast Surg 76: 424-427.

10 Boccardo FM, Casabona F, Friedman D, Puglisi M, De Cian F, et al. (2011) Surgical prevention of arm lymphedema after breast cancer treatment. Ann Surg Oncol 18: 2500-2505.

11 Cheng MH, Huang JJ, Wu CW, Yang CY, Lin CY, et al. (2014) The mechanism of vascularized lymph node transfer for lymphedema: natural lymphaticovenous drainage. Plast Reconstr Surg 133: 192e-198e.

12 Shesol BF, Nakashima R, Alavi A, Hamilton RW (1979) Successful lymph node transplantation in rats, with restoration of lymphatic function. Plast Reconstr Surg 63: 817-823.

13 Tobbia D, Semple J, Baker A, Dumont D, Johnston M (2009) Experimental assessment of autologous lymph node transplantation as treatment of postsurgical lymphedema. Plast Reconstr Surg 124: 777-786.

14 Dionyssiou D, Demiri E, Tsimponis A, Sarafis A, Mpalaris V, et al. (2016) A randomized control study of treating secondary stage II breast cancer-related lymphoedema with free lymph node transfer. Breast Cancer Res Tr 156: 73-79.

15 Ozturk CN, Ozturk C, Glasgow M, Platek M, Ashary Z, et al. (2016) Free vascularized lymph node transfer for treatment of lymphedema: A systematic evidence based review. J Plast Reconstr Aesthet Surg pii: S1748-6815(16)30138-3.

16 De Brucker B, Zeltzer A, Seidenstuecker K, Hendrickx B, Adriaenssens N, et al. (2016) Breast Cancer-Related Lymphedema: Quality of Life after Lymph Node Transfer. Plast Reconstr Surg 137: 1673-1680.

17 Patel KM, Lin CY, Cheng MH (2015) A Prospective Evaluation of Lymphedema-Specific Quality-of-Life Outcomes Following Vascularized Lymph Node Transfer. Ann Surg Oncol 22: 2424-2430.

18 Akita S, Mitsukawa N, Kuriyama M, Kubota Y, Hasegawa M, et al. (2015) Comparison of vascularized supraclavicular lymph node transfer and lymphaticovenular anastomosis for advanced stage lower extremity lymphedema. Ann Plast Surg 74: 573-579.

19 Saaristo AM, Niemi TS, Viitanen TP, Tervala TV, Hartiala P, et al. (2012) Microvascular breast reconstruction and lymph node transfer for postmastectomy lymphedema patients. Ann Surg 255: 468-473.

20 Dayan JH, Dayan E, Smith ML (2015) Reverse lymphatic mapping: a new technique for maximizing safety in vascularized lymph node transfer. Plast Reconstr Surg135: 277-285.

21 O'Brien BM, Khazanchi RK, Kumar PA, Dvir E, Pederson WC (1989) Liposuction in the treatment of lymphoedema; a preliminary report. Brit J of Plast Surg 42: 530-533.

22 Jensen MR, Simonsen L, Karlsmark T, Bulow J (2010) Lymphoedema of the lower extremities--background, pathophysiology and diagnostic considerations. Clin Physiol Funct Imaging 30: 389-398.

23 Schaverien MV, Munro KJ, Baker PA, Munnoch DA (2012) Liposuction for chronic lymphoedema of the upper limb: 5 years of experience. J Plast Reconstr Aesthet Surg 65: 935-942.

24 Greene AK, Maclellan RA (2015) Operative Treatment of Lymphedema Using Suction-Assisted Lipectomy. Ann Plast Surg.

25 Brorson H, Svensson H (1998) Liposuction combined with controlled compression therapy reduces arm lymphedema more effectively than controlled compression therapy alone. Plast Reconstr Surg 102: 1058-1067.

26 Granzow JW, Soderberg JM, Dauphine C (2014) A novel two-stage surgical approach to treat chronic lymphedema. Breast J 20: 420-422.

27 Granzow JW, Soderberg JM, Kaji AH, Dauphine C (2014) Review of current surgical treatments for lymphedema. Ann Surg Oncol 21: 1195-1201.

28 Granzow JW, Soderberg JM, Kaji AH, Dauphine C (2014) An effective system of surgical treatment of lymphedema. Ann Surg Oncol 21: 1189-1194.

29 Brorson H, Svensson H, Norrgren K, Thorsson O (1998) Liposuction reduces arm lymphedema without significantly altering the already impaired lymph transport. Lymphology 31: 156-172.