Omental Lymph Node Transfer for Lymphedema Patients: A Systematic Review

Antonio J. Forte 1, Gabriela Cinotto 1, Daniel Boczar 1, Maria T. Huayllani 1, Sarah A. McLaughlin 2


Abstract

Lymph node transfer is a surgical treatment that is becoming more prevalent. The lymph nodes from the groin and neck are most frequently used. Iatrogenic lymphedema can be a consequence of the dissection of the groin nodes; thus, some surgeons prefer to use the neck as a donor site. Literature reporting surgical algorithms for the treatment of lymphedema is scarce. Thus, we conducted a systematic review of vascularized omentum lymph node transfer (VOLT) in patients with lymphedema to provide more information about this increasingly common procedure. We hypothesize that the analyzed studies will show that VOLT has positive outcomes. Two reviewers (G.J.C., D.B.) performed independent searches using the PubMed database without timeframe limitations initially through title and abstract descriptions and then by full-text review. The search was done using the following keywords: Breast cancer lymphedema OR lymphedema AND lymph node transfer OR lymph node flap OR lymph node graft AND omental OR omentum OR gastroepiploic. Eligibility criteria included publications evaluating patients with lymphedema in the upper extremity and lower extremity, who underwent VOLT. Our search yielded 35 potential papers in the literature, but only six studies fulfilled the study eligibility criteria. The total number of patients was 137. Three studies described single VOLT, two studies described double VOLT and one study described two cohort patients, one that was treated with single VOLT and another one that was treated with double VOLT. Postoperative reduction of arm circumference, arm volume, and symptoms of the upper extremity were reported in all patients. Nonetheless, in one study, seven patients did not notice any extremity circumference reduction during the follow-up period and four patients noticed an increase in arm volume. Flap loss was reported by two authors in a total of two patients. Overall, patients experienced successful lymphedema treatment with VOLT. All authors presented results with reduced circumferential size of the affected upper and lower limbs, as well as reduction of the infectious intercurrences, such as cellulitis, with a small incidence of associated complications.

Introduction And Background

Lymphedema is a chronic and progressive disease caused by the impairment of the lymphatic system with the accumulation of proteins in the interstitial fluid, adipose tissue hypertrophy, and fibrosis. Lymphedema is classified as primary (congenital or idiopathic) or secondary [1-2]. Early diagnosis and treatment reduces morbidity and mortality and may help prevent irreversible chronic changes in the limb [3]. Identifying risk factors aids in the prevention of disease onset.
Physiologic and excisional procedures to treat lymphedema refractory to conservative therapy have been described [4-5]. The physiologic procedures are lymphovenous anastomosis and lymph node transfer (LNT). The excisional procedures are the radical reduction and preservation of perforators (RRPPs) and suction-assisted lipectomy (SAL).

Lymph node transfer is a surgical treatment that is gaining more popularity [6-7]. The lymph nodes from the groin and neck are most frequently used. Iatrogenic lymphedema can be a consequence of the dissection of the groin nodes; thus, some surgeons prefer to use the neck as a donor site [8]. The vascularized omentum lymph node transfer (VOLT) flap is another resource that provides lymph nodes for lymphedema treatment. Because of the immunogenic and angiogenic properties, the omentum is a better choice for patients with lymphedema associated with cellulitis [9]. The intra-abdominal donor site is also a good option for patients who have limited donor sites or have not responded to other treatments [10]. The vascular endothelial growth factor C, produced by the omental lymph nodes flap, promotes lymphangiogenesis inducing the recanalization of the lymphatic vessels inside the recipient set and the LNT transferred [5,11-13].

Literature reporting surgical algorithms for the treatment of lymphedema is scarce. Thus, we conducted a systematic review of VOLT in patients with lymphedema to provide more information about this increasingly common procedure. We hypothesize that the analyzed studies will show that VOLT has positive outcomes.

Review

Materials and methods

Two reviewers (G.C., D.B.) performed independent searches using the PubMed database without timeframe limitations. Initially, through title and abstract descriptions and then by a full-text review. Disagreements regarding article identification and final selection for study inclusion were resolved by another reviewer (A.J.F.). The search was done using the following keywords: breast cancer lymphedema OR lymphedema AND lymph node transfer OR lymph node flap OR lymph node graft AND omental OR omentum OR gastroepiploic. The bibliographic reference list of the studies that fulfilled the study eligibility criteria was also examined in order to include articles not present in our initial search. This study followed the guidelines outlined in the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA flowchart).

Selection criteria

Eligibility criteria included publications evaluating patients with lymphedema in the upper extremity and lower extremity, who underwent VOLT, including all subtypes. Therefore, we excluded papers that did not report VOLT as a lymphedema treatment. Abstracts, presentations, reviews, meta-analyses, case reports, nonclinical studies, and studies without descriptive outcomes were also excluded.

Data extraction and processing

Extracted data included the year of study, country, population, intervention, circumference/volume-reduction/symptoms, lymphoscintigraphy, and complications. Data extraction from articles, tables, and figures was performed by two reviewers (G.C., D.B.), with the accuracy of data entry confirmed by an additional reviewer (A.J.F.).

Results
The search yielded 35 potential papers (Figure 1) but only six studies fulfilled the study eligibility criteria (Table 1) [4,6-7,14-16]. All included studies were published from 2017 to 2019, in various countries: two studies from China, two studies from the United States, one from Peru, and one from Iran. The total number of patients was 137. The patients’ ages ranged from 18 to 73 years and the follow-up period ranged from 0.5 to 48 months. The population included 88 patients with upper extremity lymphedema, 78 of which had lymphedema after breast cancer treatment, 48 patients had lower extremity lymphedema, and two patients had breast lymphedema.

![PRISMA flowchart](image)

**FIGURE 1: PRISMA flowchart**

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

<table>
<thead>
<tr>
<th>Author</th>
<th>Demographic Data</th>
<th>Follow-up Period Mean (Range)</th>
<th>Age, Mean (Range)</th>
<th>Population</th>
<th>Intervention</th>
<th>Circumference/Symptomatic/Volume Reduction</th>
<th>Lymphoscintigraphy</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Country</td>
<td>Number</td>
<td>Age</td>
<td>Percentage</td>
<td>Location</td>
<td>Vascularization</td>
<td>Procedure</td>
<td>Results</td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------</td>
<td>--------</td>
<td>-----</td>
<td>------------</td>
<td>----------</td>
<td>----------------</td>
<td>------------</td>
<td>---------</td>
</tr>
<tr>
<td>Ciudad et al. [4]</td>
<td>China</td>
<td>10</td>
<td>14.7 (range, 9–42)</td>
<td>*Female: 37</td>
<td>*Stage II: 2</td>
<td>*Upper extremities: 19</td>
<td>*Gynecological cancer-related: 5 patients</td>
<td>*Laparoscopically harvested right gastroepiploic lymph node flap</td>
</tr>
<tr>
<td>Ciudad et al. [7]</td>
<td>China</td>
<td>7</td>
<td>9.7 (range, 9–42)</td>
<td>*Female: 37</td>
<td>*Stage II: 2</td>
<td>*Upper extremities: 19</td>
<td>*Gynecological cancer-related: 5 patients</td>
<td>*Double gastroepiploic vascularized lymph node transfer</td>
</tr>
<tr>
<td>Ciudad et al. [6]</td>
<td>Peru</td>
<td>16</td>
<td>14.2 (range, 12-19)</td>
<td>*Female: 37</td>
<td>*Lower extremities: 19</td>
<td>*Upper extremities: 19</td>
<td>*Gynecological cancer-related: 5 patients</td>
<td>*Primary lymphedema: 1</td>
</tr>
<tr>
<td>Mousavi et al. [16]</td>
<td>Iran</td>
<td>24</td>
<td>1 to 4</td>
<td>*Female: 37</td>
<td>*Lower extremities: 19</td>
<td>*Upper extremities: 19</td>
<td>*Gynecological cancer-related: 5 patients</td>
<td>*Vascularized lymph nodes were transferred from the gastroepiploic lymph nodes to the volar forearm</td>
</tr>
</tbody>
</table>
Three studies described single VOLT \cite{4,14,16}, two studies described double VOLT \cite{6-7}, and one study described two cohort patients, one that was treated with single VOLT and another one that was treated with double VOLT \cite{15}. The recipient site was variable according to the lymphedema area. Postoperative reduction of arm circumference, arm volume, and symptoms of the upper extremity were reported in all patients. Nonetheless, in one study, seven patients did not notice any extremity circumference reduction during the follow-up period, and four patients noticed an increase in arm volume \cite{14}. Flap loss was reported by two authors in a total of two patients \cite{14-15}. Nguyen et al. reported venous hypertension \cite{14}, and Kenworthy et al. reported a soft-tissue infection after a single VOLT procedure as a cause of flap failure \cite{15}. Moreover, arteriovenous fistula \cite{14}, seroma \cite{6,14}, hematoma \cite{14-15}, nasogastric tube for additional 24-48 hours \cite{14-15}, pancreatitis \cite{14-15}, partial skin graft loss \cite{4}, paresthesia \cite{6}, and hyperesthesia were reported as complications by five authors \cite{6}. Lymphoscintigraphy was described as a diagnostic method used during the follow-up period to evaluate the patients by five authors \cite{4,6-7,14-15}. The quality of life scores were also evaluated in some of the studies \cite{4,6-7}.

**Discussion**

The literature described different lymph node donor sites: the supraclavicular fossa, groin, intra-abdominal, submandibular region, lateral thoracic area, and axilla donor sites \cite{4,17}. There is no evidence indicating one site’s superiority over the others. The first authors that described the lymphedema treatment in animals with intra-abdominal-omentum tissue were Goldsmith and De Los Santos \cite{18} while the omental transposition to the axilla was reported for the first time by Nakajima et al. \cite{19}.

In this systematic literature review, we found that lymphedema improved considerably after VOLT, which suggests it as a promising technique. The understanding of lymphedema and the evolution of laparoscopic and microsurgery techniques have made VOLT a safe alternative to treat lymphedema, mainly because some patients had refractory lymphedema, did not have a successful lymph node transfer, or had limited donor sites \cite{10}. The objective is to use the lymph nodes from donor sites that have a larger number of lymph nodes with multiple drainage sources or use flaps that only remove the lymph nodes that are not crucial to the drainage functions of the donor region. The plentitude of lymph nodes at the omentum and the morphology of the blood vessels make this flap amenable to division \cite{6}. The disadvantages of VOLT include the risk of incisional hernia, hypertrophic scars, adhesions, bowel obstruction, and pancreatitis, which is a rare complication associated with VOLT. The gastroepiploic vessels are thinner compared to vascularized lymph node Transfer (VLNT) from other sites; therefore, they are more prone to kinking. The flap could be performed by laparoscopy or by open laparotomy \cite{6,16}.

From this literature review, we noticed differences between the techniques that were used to perform VOLT. In one direction, the authors performed single VOLT, which showed good results and with a reduced surgical time \cite{4,14-16}. In the other direction, the authors performed double VOLT, which is a double-level inset from a single lymph node flap transfer (LNFT) \cite{6-7,15}. The advantage of this procedure is the opportunity to split the flap into two levels, avoiding the
possible morbidity associated with a second harvest site. Moreover, this allows the surgeon to
choose two different recipient sites.

The choice of the recipient site in lymph node transfer is controversial [20]. Patients with
previous inguinal or axillary lymph node dissection can be favored with the re-establishment
of the lymphatic network with an orthotopic VLNT [6]. Moreover, it allows for scar release or
removal through the same incision. Decompression of the axillary vein can also be achieved
and these patients will not require a skin flap. However, the stagnation of fluid is more
prominent at the distal extremity and increases the risks of degenerative lesions caused by
lymphedema, which is why some surgeons prefer distal placement. According to Ciudad et al.,
the placement of the second LNT at the center of the extremity combined with a distal lymph
node transfer (LNT) improves the pump-absorbing lymphatic fluid in two sites and gives the
extremity a double site for lymphangiogenesis. The midlevel inset site, such as the proximal
recipient site, avoids the need for a skin graft [6-7].

Ciudad et al. published in 2019 the first study that associated double VOLT with RRPPs in
patients with advanced lymphedema [6]. One flap was placed at the midlevel at the cubital
fossa and the other inset was placed at the wrist where the RRPPs cannot be performed
improving the lymphatic drainage of the extremity. The preservation of the superficial vein
system and the scar release undertaken in patients with secondary lymphedema are the major
modifications that the author showed on the review. The mean circumference reduction was
70.8%±5.9% (range, 62%-84%), being the higher reduction between the reviews from this author
[6]. Ciudad et al. performed two more studies: one with a single VOLT and the other with
double VOLT [4,7].

The patients with dense fibrosis and excess adipocutaneous tissue benefit from the additional
treatment with an excisional procedure such as RRPPs and SAL [6]. The SAL procedure is
preferred over the RRPPs; however, the compression garments made the SAL a selective
method that requires a periodic follow-up to achieve good results. The advantages of the RRPPs
as compared to SAL are the removal of fibrotic tissue, the reduction of redundant skin, and the
preservation of perforators, which is essential to maintain the nutrition of the skin [6].

Venous hypertension at the flap is commonly associated with conventional microanastomoses.
To avoid it, Kenworthy et al. suggested anastomosis of the distal gastroepiploic vein to a second
recipient vein [15]. The symptom is clinically evident, with pulsation at the end of the distal
gastroepiploic vein [15].

Our systematic review reports PubMed-based manuscripts to date that evaluated VOLT
procedures in the English-language literature. We recognize the presence of several limitations
to our study. First, the small number of studies and, consequently, a small cohort. Second, the
lack of prospective randomized studies and the nonstandardization of the obtained results
make it difficult to establish protocols. Last, the absence of objective measurement of arm
circumference and volume, as well as cellulitis rate reduction, impeded a quantitative
evaluation of outcomes. In addition, the follow-up duration in the studies is too little to
evaluate the persistent benefit of these procedures. However, despite these limitations, we
believe that VOLT is a promising technique with good results. We suggest future retrospective
and prospective studies enrich the evidence to support this practice.

Conclusions
Overall, patients experienced successful lymphedema treatment with VOLT during the follow-
up period (ranging from 0.5 to 48 months). All authors present the results with the reduced
circumferential size of the affected upper and lower limbs, as well as the reduction of infectious
intercurrences, such as cellulitis, with a small incidence of associated complications.
Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

This study was supported in part by the Plastic Surgery Foundation, Mayo Clinic Center for Individualized Medicine, and Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery.

References


