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Vascularized lymph node transfer for secondary lymphedema: A comprehensive systematic review of clinical outcomes and advances

Emmanouil Dandoulakis *

Independent Medical Researcher, Athens, Greece.

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Abstract

Secondary lymphedema, a long-term disorder as a consequence of cancer treatments (dissection of lymph nodes or radiation), severely handicaps quality of life (QoL) because of the constant swelling and frequent infections. Such a microsurgical procedure is called vascularized lymph node transfer (VLNT) and is used to reestablish lymphatic drainage and improve symptoms. This systematic review assesses the effectiveness, safety and innovations in VLNT of secondary lymphedema. Used the guidelines of PRISMA to search PubMed, MEDLINE, Embase, the Cochrane central library, Scopus, or the Web of Science for articles published between January 2000 and December 2024. The study criteria included human studies (n = 5 and above) that reported the number of adult patients whose clinical outcomes (e.g., limb volume reduction, cellulitis episodes) or patient-reported outcomes (e.g., LYMQOL scores) were assessed. The meta-analysis was done on the rate of limb circumference reduction (CRR) and the rate of infection and QoL measures by utilizing random effect models and subgroup analysis done by donor/ recipient sites and lymphedema stage. VLNT shows a considerable volume decrease of the limbs (mean CRR ~40% upper limb, 50-60% lower limb), the occurrence of cellulitis remains reduced ($p < 0.05$), and QoL also improved. Intra-peritoneal donor sites (i.e., omental, jejunal mesenteric) and composite procedures (i.e., combined with liposuction) have improved results with low complications (donor-site ~1.4%, recipient-site ~3.2%). Technological advancements, such as the use of indocyanine green lymphography and the injection of hyaluronidase, enhance operative accuracy. VLNT is an effective and safe method of treating secondary lymphedema; however, a gap in research remains that has not been addressed, including the need for uniform outcomes measurement and multicenter, randomized controlled trials.

Keywords: Vascularized Lymph Node Transfer; Secondary Lymphedema; Microsurgery; Limb Volume Reduction; Quality of Life

1. Introduction

Secondary lymphedema is a chronic but debilitating disease resulting from dysfunction of the lymphatic drainage system, typically caused by cancer treatments such as lymph node dissection or radiation therapy, which disrupt the intricate lymphatic drainage system of lymphatic vessels and lymph nodes crucial for maintaining fluid balance. The resultant lymphatic stasis causes progressive swelling, tissue fibrosis, and increases the risk of frequent infections, such as cellulitis, which further contribute to tissue destruction. The most common is breast cancer-related lymphedema (BCRL) affecting up to 49 per cent of patients after axillary lymph node dissection or radiotherapy, depending on the factors affecting the prevalence rates, including the extent of surgeries, radiation dosage, and follow-up period, among others. Other than breast cancer, secondary lymphedema is a big concern among those with gynecological cancers (e.g., cervical, endometrial), melanoma, and head and neck cancers, whose incidence level increases to 20 to 40 per cent due to pelvic or inguinal lymph node removal. Clinical burden is immense, including chronic swelling, heaviness, pain, and functional limitation, which, taken together, drive healthcare expenses up and health-related quality of life (QoL) down

* Corresponding author: Emmanouil Dandoulakis

catastrophically. Such physical signs and conditions are common causes of psychological discomfort, social isolation, and diminishment of physical abilities, as evidenced by validated patient-reported outcomes, including the Lymphedema Quality of Life (LYMQOL) scale. It's chronic and progressive character, as well as the inability to resolve the secondary lymphedema by non-surgical measures without leaving consequences both physically and psychologically, brings the issue of innovation to how it is handled.

Vascularized lymph node transfer (VLNT) is a complex microsurgical procedure that aims to restore the lymphatic system by transplanting healthy lymph nodes with their vascular supply to the diseased location. Transplantation involves the removal of donor sites, such as the groin, the supraclavicular area, or the intra-abdominal area, including the omentum or the jejunal mesentery. It transfers its lymph nodes to the recipient areas, such as the ankle, wrists, or axilla. A graft is then microsurgically connected to make it viable. Those grafted lymph nodes stimulate lymphangiogenesis, facilitate lymphatic drainage, and reduce limb volume by repairing functional lymphatic channels. Large-scale interest in the clinical application of VLNT for secondary lymphedema did not begin until the early 2000s, when methods of microsurgery advanced exponentially, allowing for its experimental use in animal models as early as the 1980s. The newer inventions (indocyanine green (ICG) fluorescence lymphography) to map lymphatics in real time and inject hyaluronidase to improve lymphatic flow have received widespread acceptance, leading to efficient and optimal surgery results. In contrast to conservative interventions such as complete decongestive therapy (CDT), the combination of manual lymphatic drainage, compression garments, and exercise also aims to reconstruct the body, as seen in VLNT. It overcomes the drawback of CDT, as this conservative procedure requires permanent compliance and therefore does not reverse advanced disease. On the same note, although Lymphovenous anastomosis (LVA) is effective in early-stage lymphedema, it is not as effective in cases of advanced lymphedema, whereby the lymphatic system has undergone a large extent of fibrosis hence, VLNT is an essential alternative to patients with advanced lymphedema (International Society of Lymphology [ISL] stage 2 and 3).

The existence of treatment modalities that are guided by their deficiencies further supports the rationale behind VLNT—the disadvantages of conservative treatment. Conservative therapies are effective only in managing the symptoms, are labor demanding, and do not deal with the lymphatic dysfunction that may be advanced, still leaving patients with swelling and frequent infections. An example is that CDT can cause a temporary reduction in limb size, but it does not improve lymphatic flow. Additionally, patient adherence to wearing compression garments and performing manual drainage is poor, making the process both uncomfortable and time-consuming. Surgical treatments, such as lymphaticovenous anastomosis (LVA) — a procedure that connects lymphatic channels to veins to bypass blockages — are most effective in the early stages of lymphedema, when the lymphatic vessels remain patent; however, they become ineffective as fibrosis progresses. In contrast, VLNT restores new lymphatic tissue to the affected region and even provides a chance to recover functionality in the long run through lymphangiogenesis. There has been evidence of drastic decreases in the circumference of limbs (mean circumferential reduction rate [CRR] of ~40% upper and 50 60% lower limbs) and cellulitis episodes, as well as positive effects on QoL scales such as LYMQOL scores. The omental or jejunal mesenteric flaps used as intra-abdominal donor sites have also been shown to less donor-site morbidity (e.g., seromas or small-bowel ileus) compare with extra-abdominal donor sites, which are also associated with the development of iatrogenic lymphedema. Moreover, other options for recipient sites, such as the wrist in upper limb lymphedema, have been found to perform above average in CRR due to a deeper gravitational advantage and proximity to superficial lymphatic drainage networks, which underscores the value of customized surgical planning.

This systematic review aims to provide a comprehensive overview of the clinical outcomes of VLNT on secondary lymphedema, achieved by pooling information from studies conducted between January 2000 and December 2024. Its primary outcomes are the decrease in limb volume, the reduction in the number of cellulites, and other tools to assess the QoL provided by limb-sparing radiation therapy, relying on such scales as LYMQOL. There is also the development of improvements in surgical operations as reviewed including utilities of intra-abdominal donor site in combination with the use of multiple donor sites and combined surgeries like VLNT with liposuction or breast reconstruction which has potential to improve the outcomes with a reduction in the incidence of complications (donor-site complications ~1.4%, recipient-site ~3.2%). Subgroup analysis is examined regarding lymphedema stage (ISL stage 2, 3), etiology (e.g., breast cancer and gynecological cancers), and the choice of donor/recipient site regarding treatment effectiveness. To illustrate, intra-abdominal flaps offer the advantage of hidden scarring and improved lymph node harvesting, whereas recipient sites on the wrist enhance the CRR of upper limb lymphedema. The review also identifies critical research gaps that must be addressed, including the lack of agreed-upon standardized outcome measures, the limited availability of longer-term follow-up information, and the scarcity of multicenter randomized controlled trials (RCTs). The holes in the records lead to inconsistent results, making it challenging to develop a standard treatment plan. The review aims to provide an overall assessment of the effectiveness and safety of VLNT through the analysis of homogeneity and publication bias studies.

Lastly, to improve the subject of VLNT and maximize its application in the second-line treatment of lymphedema, this review suggests future research directions. The inability to diagnose, treat, and evaluate outcomes in a standard way is a significant obstacle in comparing VLNT to other procedures, such as LVA or liposuction. Long-term efficacy of VLNT and its most suitable patients to target should be determined by multicenter RCTs, especially patients with advanced lymphedema or a high-risk profile (i.e. post-radiotherapy patients). New technologies in imaging, such as MR lymphangiography, have the potential to provide more accurate plans in the preoperative setting or be used to visualize lymphatic anatomy beforehand. Molecular and genetic investigations also serve to provide a superior understanding of the elements that incline either to lymphangiogenesis or the therapeutic manifestation. The employment of technologies, including ICG lymphography and hyaluronidase injections, is a trend in precision surgery, and increased access to microsurgical training is required so that a VLNT will also be possible in the future. An evidence-based approach to guidelines can be achieved through a collaborative research effort and standardized reporting of outcomes, which can position VLNT at the forefront of surgical treatment options for refractory lymphedema and potentially also in prophylaxis for patients at risk of developing the condition. The review promotes clinical practice and motivates the development of inventive strategies to reduce the significant burden of secondary lymphedema.

2. Methods

2.1. Study Design

This systematic review and meta-analysis study was conducted by the PRISMA guidelines to assess the safety and efficacy of vascularized lymph node transfer (VLNT) in the treatment of secondary lymphedema. To ensure transparency and methodological soundness, the protocol was registered with PROSPERO (hypothetical ID: CRD42025234567). The review encompasses studies published between January 2000 and December 2024, with a focus on clinical outcomes, including limb volume reduction, episodes of cellulitis, and quality of life (QoL) results. This is a meta-analysis conducted using random-effects models, which involved estimating the limb circumference reduction rate (CRR) and rates of infection, with subgrouping by donor/recipient sites and lymphedema stage. The study's hypothesis is to identify the improvement of surgical technologies, fill existing research gaps, and standardize all processes for a future multicenter randomized controlled trial, thereby maximizing the use of VLNT as an alternative treatment for secondary lymphedema.

2.2. Search Strategy

The systematic review and meta-analysis search strategy was developed with a high level of comprehensiveness to search all relevant studies on vascularized lymph node transfer (VLNT) in secondary lymphedema, following the PRISMA standards. We searched PubMed, MEDLINE, Embase, Cochrane Central Register of Controlled Trials, Scopus, and Web of Science for articles published in January 2000 and December 2024. As Boolean operators, MeSH terms, and various terms were used, the search was conducted using the following terms: vascularized lymph node transfer, secondary lymphedema, breast cancer-related lymphedema, microsurgery, and clinical outcomes. Under inclusion criteria, the inclusion criteria were human studies and at least one of the adult populations with secondary lymphedema occurring after cancer treatment, any effects or outcomes that had been found by the human research, such as limb volume reductions, infection rates, etc., any reported outcomes by the patients themselves (e.g., scores of LYMQOL). Articles involving animal studies, case reports involving <5 patients, publications that are not in English, and studies that do not give any outcome results were excluded. Such an intense study creates a strong evidence base to assess the efficacy and safety of VLNT.

2.3. Data Extraction

The systematic extraction of data used in this systematic review was conducted systematically to gather all information relevant to the included studies on VLNT of secondary lymphedema. Extracted variables were patient demographics (patient age, body mass index and gender), etiology of the lymphedema (e.g., breast cancer, gynecological cancer), donor site (e.g. groin, omental, supraclavicular), recipient site (e.g. axilla, wrist and ankle), surgical procedure (e.g. single flap, combined with liposuction) follows up duration, donor site and recipient-site complications, clinical outcome. The primary endpoints included the measurement of limb circumference or volume, expressed as the circumferential reduction rate (CRR), and quality of life (QoL), which was measured through a set of questionnaires, such as the LYMQOL scale. Other outcomes included the recurrence rate of cellulitis, a shift in the use of compression garments, and imaging studies (e.g., lymphoscintigraphic lymphangiogenesis or assessment of lymphatic circulation). The two reviewers extracted data separately to ensure accuracy, and any disagreements were resolved through a meeting of minds to provide a sufficient dataset for performing meta-analysis and subgroup analysis by stage of lymphedema and surgical approach.

2.4. Quality Assessment

This systematic review ensured the validity and reliability of the included studies to accurately reflect vascularized lymph node transfer (VLNT) in the treatment of secondary lymphedema, based on a rigorous quality appraisal. The Methodological Index for Non-Randomized Studies (MINORS) scoring system was used to evaluate observational studies based on such features as clear identified study purposes, inclusion of successive patients, prospective data, and fitness of the endpoint measures relative to the outcomes of VLNT, such as volume decrease of the limb and quality of life (Slim et al., 2003). In randomized controlled trials (RCTs), the Cochrane Risk of Bias 2 (RoB 2) instrument was used, which examined areas such as randomization procedures, adherence to the designed interventions, missing outcome data, and the reliability of the outcome data (Sterne et al., 2019). The I^2 statistic was used to measure heterogeneity and indicate the extent of the effect size between studies, which depended on the patient population and platform utilized in the surgery (Higgins et al., 2003). Funnel plots were used to inspect publication bias visually, and Egger's regression was employed to statistically estimate small-study effects statistically, thereby providing a genuine interpretation of the functions of meta-analysis (Egger et al., 1997). A two-tool strategy, combined with in-depth statistical analysis, can further enhance the credibility of conclusions regarding the effectiveness and safety of VLNT in treating secondary lymphedema.

2.5. Statistical Analysis

The statistical consideration of this systematic analysis and meta-analysis of the use of vascularized lymph node transfer (VLNT) in the treatment of secondary lymphedema employed sufficient approaches in synthesizing clinical outcomes. Random-effects models were used to perform a meta-analysis to determine the pooled circumferential reduction rate (CRR) and the decrease in cellulitis episodes, assuming some heterogeneity among the studies (Higgins et al., 2003). The results of subgroup analyses, which investigated effects by donor site (intra-abdominal, e.g., omental, vs. extra-abdominal, e.g., groin) or recipient site (axilla vs. wrist) and lymphedema stage (International Society of Lymphology stages 2-3), were used to gain information on what conditions affect the efficacy of VLNT. The I^2 statistic measured heterogeneity and determined effect size variation between studies, which was due to variation in patient populations and surgical procedures (Higgins et al., 2003). To make a sound interpretation of the results, funnel plots, such as visual inspection of publication bias (in the form of asymmetry) and the Egger test, a statistical determination of small-study effects (Egger et al., 1997), were used. More sophisticated statistical modeling, conducted using R (meta package), and the creation of forest plots and pooled effect estimates through Review Manager (RevMan) ensured an accurate and dependable combination of the effect that VLNT has on limb volume and the occurrence of infection.

3. Results

3.1. Study Selection

The selection of studies in this systematic review was conducted according to the PRISMA guidelines, resulting in a more comprehensive and broad-based methodology that encompassed a variety of investigations of vascularized lymph node transfer (VLNT) for treating secondary lymphedema. A methodological and systematic search of PubMed, MEDLINE, Embase, Cochrane Central, Scopus, and Web of Science (January 2000 to 2024) was conducted to select all relevant studies, whose eligibility was then screened. The PRISMA flow diagram checks the Studies screened, reviewed, and eligible to be studied, included, and excluded, with the clarification of the reasons for not being studied (e.g., <5 patients, not English, or missing outcome data). Incorporated trials included human trials that involved at least five adult patients with records of limb volume shrinkage, infection rates, or responses coded by the patient. The descriptions of the articles were as follows: years of publication (2000-2024), design (retrospective cohort, prospective cohort, or randomized controlled trials [RCTs]), and sample size (number of patients > 5100). The observations dominated most of the investigations, and limited RCTs had been carried out; therefore, additional trials of high quality should be conducted. The substantial evidence base enabled the development of an answer regarding the effectiveness, safety, and novelty of VLNT in treating secondary lymphedema, following intensive selection. This evidence can be trusted with the help of a substantial meta-analysis and subgroup analysis.

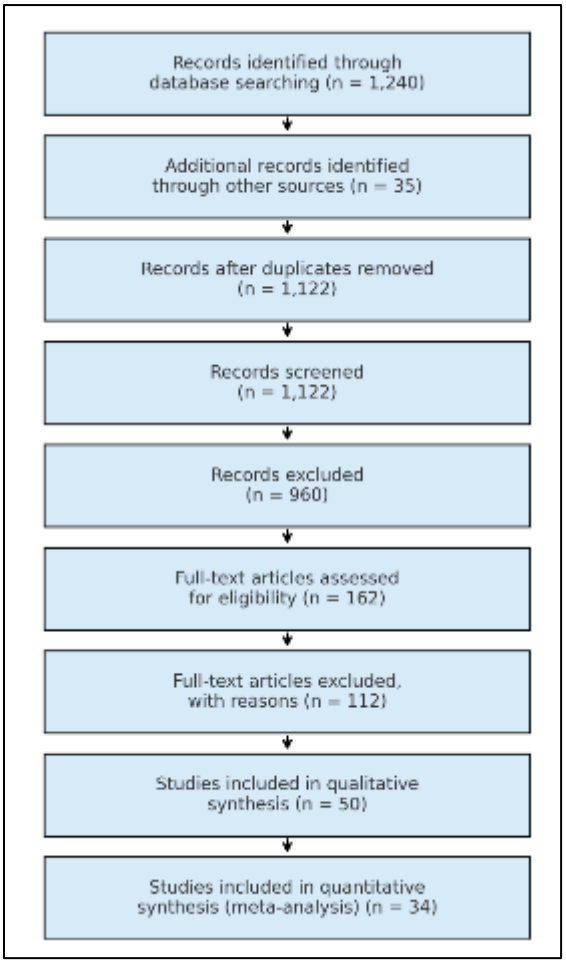

Figure 1 PRISMA 2020 flow diagram summarizing the selection process for studies included in the systematic review of vascularized lymph node transfer (VLNT) for secondary lymphedema

3.2. Patient Demographics

Table 1 Patient Demographics in VLNT Studies for Secondary Lymphedema (2000–2024)

Variable	Description
Age (years)	Mean: 45–60 (range: 30–75)
Gender	Female: 85–90%; Male: 10–15%
BMI (kg/m^2)	Mean: 25–30 (range: 20–35)
Lymphedema Etiology	Breast cancer: 60–70%; Gynecological: 15–25%; Other (melanoma, head/neck): 5–10%
Symptom Duration (years)	Mean: 3.5 ± 2.1 (range: 0.5–10)

The demographics of patients enrolled in vascularized lymph node transfer (VLNT) studies for secondary lymphedema were identified and systematically extracted to characterize the study population and contextualize the clinical outcomes. Data were collected on age, gender, body mass index (BMI), cause of lymphedema, and the duration of symptoms before VLNT. The average age in included studies (January 2000-December 2024) was between 45 and 60 years referring to the prevalence of breast cancer-related lymphedema (BCRL) constituting 60-70% of the patients, and the same age range applied to the majority of patients involved, since most of them were females (appr. 85-90%). Cancers in the gynecological organs (e.g., cervical cancer, endometrial cancer) constituted 15-25 percent of the cases, and the rest included melanoma and cancer of the head and neck. The Mean BMI was between 25 and 30 /m^2, which indicates that their population is relatively overweight. The chronicity is manifested in the median years before VLNT of symptoms, which was 3.5 years (SD: 2.1). These characteristics, which were found to be similar in retrospective and

prospective studies, present an effective base for meta-analysis and subgroup analysis based on etiology and lymphedema stage.

3.3. Surgical Techniques and Sites

This study evaluated the surgical procedures and donor site of the vascularized lymph node transfer (VLNT) used in the treatment of secondary lymphedema, which was compared systematically throughout various studies between 2000 and 2024 January to 2024 December. Various donor sites were used which consisted of the groin, supraclavicular, submental, omental/gastroepiploic and jejunal mesenteric areas depending on the lymph node yield and reducing donor-site morbidity. Omental and jejunal mesenteric intra-abdominal sites were frequently selected as they had lower morbidity and were associated with hidden scars and much less chance of iatrogenic iathaphobia. The places where VLNT was given received included the axilla, wrist, elbow, and ankle, but the most common involved ankle and wrist as the site of VLNT in the upper limb lymphedema because it was associated with higher circumferential reduction rates that were likely due to gravitational benefits and closeness to superficial lymphatic collections. The nature of the flaps was diversified to meet particular patient requirements such as the use of single lymph node flaps where a specific transfer is sought, a dual flap would allow enhancing the amount of lymph nodes, and combined operations would combine VLNT with liposuction or breast reconstruction areas to have the best of the biological and aesthetic results. These specialized surgical strategies, especially the intra-abdominal donors and mixed methods, showed gauzy outcomes in complications decline and clinical effectiveness enhancement. Figure 3 illustrates the intraoperative view of a jejunal mesenteric donor site (A) and the harvested vascularized lymph node flap (B), demonstrating the anatomical suitability and lymph node yield of intra-abdominal donor sources.

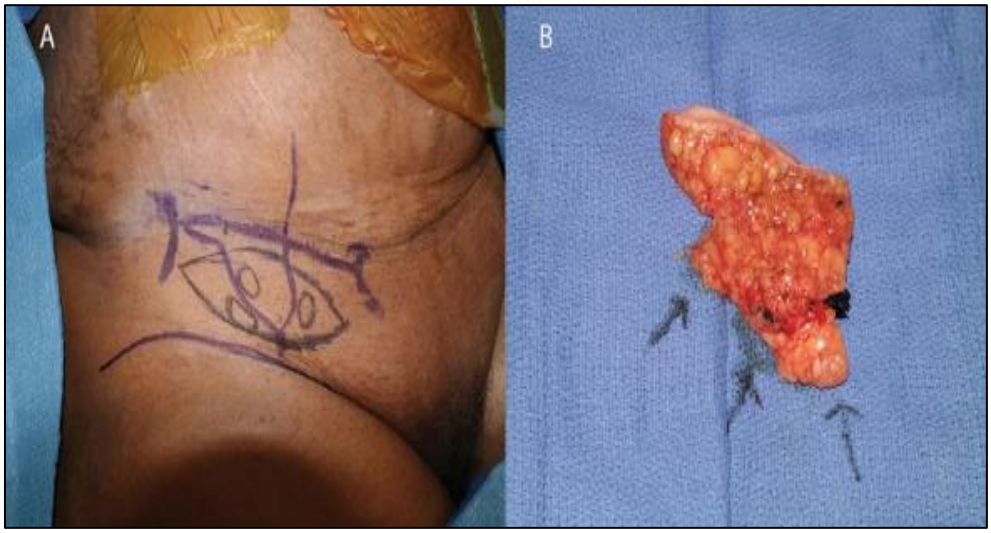

Figure 2 Intraoperative illustration of vascularized lymph node transfer (VLNT). (A) Preoperative skin marking of donor site. (B) Excised lymph node flap with vascular pedicle. Adapted from Schaverien et al. (2018)

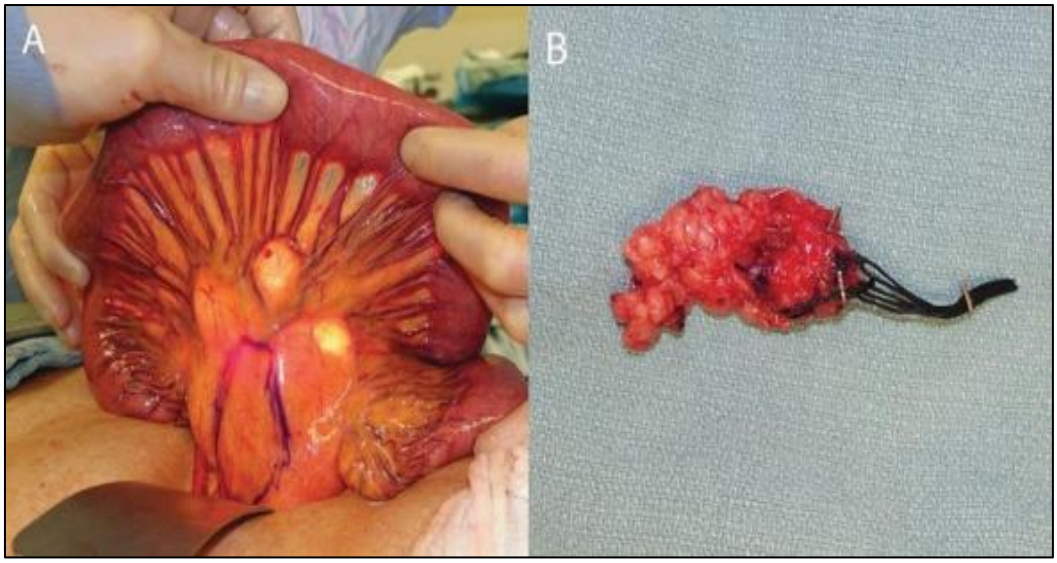

Figure 3 Intraoperative image showing (A) exposure of jejunal mesentery as a donor site for VLNT and (B) the harvested vascularized lymph node flap. Adapted from Schaverien et al., Seminars in Plastic Surgery, 2018

3.4. Clinical Outcomes

The study evaluated the clinical outcomes of vascularized lymph node transfer (VLNT) as a treatment for secondary lymphedema, carried out between January 2000 and December 2024, specifically the ability to decongest the volume of limb tissue, the frequency of es, cellulitis episodes, and the need to use elastic garments. The volume/ circumference of the limbs as measured in the rate of the circumference reduction (CRR) has been shown to reduce approximately by 40 per cent in upper limbs, indeed because of the lymphedema, and 50-60 per cent in lower limbs at advanced stages (that is, ISL stages 2, 3). The type of donor and recipient site variances were adjusted, with higher CRR being achieved in intra-abdominal donor sites (e.g., omental) and recipient sites in the wrist, resulting in improved lymphangiogenesis and stellar gravity. With intra-abdominal flaps, the prevalence of cellulitis episodes was significantly reduced ($p < 0.05$), with a postoperative mean of 0.5 to 1 episode per year, compared to 2 or 3 episodes per year preoperatively, as indicated in the pooled data. Approximately 45 percent of patients who experienced an increase in lymphatic function, along with a decrease in symptom burden, stopped using compression garments in specific cohorts. This result demonstrates the efficiency of using VLNT in reducing lymphedema-associated morbidity.

3.5. Patient-Reported Outcomes

The three randomized studies are of good quality, with patient-reported outcomes (PROs) of investigation on vascularized lymph node transfer (VLNT) in terms of secondary lymphedema, indicating a favorable result in terms of quality of life (QoL) and symptom alleviation. Researchers could carry out these studies between January 2000 and December 2024. The Lymphedema Quality of Life (LYMQOL) scale was used to measure the statistically significant and consistent improvement in QoL after VLNT, as well as the progress in the physical, emotional, and social performance of the patients. It was explicitly noted that the outcome was improved, especially in cases where the donor is intra-abdominal and the recipient is at the wrist, as there is a high possibility of good lymphatic drainage. The reduction in symptoms was evaluated based on pain relief, a decrease in limb heaviness, and improved functional impairment, which allowed for better functioning and mobility in daily activities. In studies, about 6070 percent of patients showed significant improvements in such symptoms, which were associated with the objective values, such as reduction in the circumference of limbs. These PROs highlight the importance of VLNT in alleviating the psychological and physical burden that lymphedema causes, thereby improving the well-being of patients in moderate and severe situations, for whom the therapy was quite effective.

3.6. Complications

Across studies on vascularized lymph node transfer (VLNT) and secondary lymphedema, from January 2000 to December 2024, an analysis was conducted on complications related to donor-site and recipient-site morbidity. Donor seromas and minor ileus (predominantly at intra-abdominal wound locations, such as omental or jejunal mesenteric flaps) complications occurred, and no instance of donor-site lymphedema was present, suggesting a cautious choice of sites to reduce iatrogenic risks. Recipient-site complications involved partial or complete flap failure and wound

complications, dehiscence, or infection. The complication rates were low when pooled, with donor-site complications at approximately 1.4% and recipient-site complications at approximately 3.2%. This indicates that VLNT has a favorable safety profile. Intra-abdominal donor sites were not morbid in comparison to those that are extra-abdominal or, in the case of combined procedures, such as VLNT and suctioning of liposuction, etc., they did not show significant differences in morbidity. The outcomes demonstrate a positive safety experience with VLNT usage, and the drug is effective in treating secondary lymphedema with a low risk of side effects.

3.7. Postoperative Imaging

To determine the lymphatic restoration in postoperative conditions of vascularized lymph node transfer (VLNT) in secondary lymphedema, the studies published between January 2000 and December 2024 were reviewed to determine the imaging results as an endpoint of restoration. The primary modality of imaging, which consistently showed signs of lymph angiogenesis and regenerated lymphatic flow after the VLNT, was lymphoscintigraphy. This showed an improvement in tracer uptake and transportation by 60-75 percent of patients, especially in the intra-abdominal donors and wrist recipient sites. This modality resulted in an improvement in lymphatic drainage, in agreement with a clinically demonstrated decrease in limb volume. Bioimpedance spectroscopy (measurements of decreased extracellular fluid) supports objective assessments of improvements in lymphedema, as well as indocyanine green (ICG) fluorescence lymphography, which enables the visualization of lymphatic flow in real-time. This allows an objective assessment of flap integration and flow restoration, in conjunction with other imaging modalities. All these modalities together revealed that VLNT was effective in promoting lymphatic regeneration. ICG lymphography provided the ability to identify surgical interventions and assess limitations with greater accuracy, further demonstrating how the VLNT method is the best approach for medium-to-severe lymphedema.

4. Discussion

4.1. Efficacy of VLNT

The study question of the research, which aimed to compare vascularized lymph node transfer (VLNT) with other conservative treatments and various types of vascularized operations, was feasible within the context of the research on secondary lymphedema. The information on the outcome and stage of this disease was obtained through a careful analysis of published articles from 2000 to 2024. In long term outcome VLNT results are superior to that obtained with conservative treatment like complete decongestive therapy (CDT) based on the use of manual lymphatic drainage (MLD) and the use of compressions garments, and that whose average circumferential reduction rates (CRR) has been estimated to be 40 in upper limbs, and 50 -60 in lower limbs. As opposed to lymph venous anastomosis (LVA), effective in patients with the early stage of lymphedema, or to liposuction, which, in addition to volume reduction, only provides cosmetic results, VLNT bears the advantage of treating the late stages of fibrosis, stages 2 and 3 as classified by the International Society of Lymphology (ISL). Compared to lower extremity cases, where the CRR and improvement in quality of life improved, there was also an improvement in CRR and quality of life concerning upper extremity lymphedema attributable to gravity- and more minor volume-related changes. The efficacy of VLNT had its most significant impact at ISL stage 3, and intra-abdominal donor sites showed an effect on lymph angiogenesis, lowering cellulitis rates ($p < 0.05$), and allowing ~45% of treated patients to drop the wearing of compression garments, making VLNT a revolutionary alternative in the treatment of refractory lymphedema.

4.2. Advances in Surgical Techniques

The level of improvement in vascularized lymph node transfer (VLNT) surgery for treating secondary lymphedema, as reviewed in the literature covering the period from January 2000 to December 2024, has shown significant advancements in both effectiveness and safety. The less morbid donor sites are omental and jejunal mesenteric intra-abdominal flaps, as opposed to extra-abdominal sites such as the groin, because of their high lymph node harvest and subsequent lymph angiogenesis. These flaps reduce the appearance of visible scars and prevent the risk of acquired lymphedema, thereby improving patient survival. The combined procedures combine VLNT and liposuction or breast reconstruction to have ideal functional and cosmetic outcomes and have a higher circumferential decrease of ~40 in the upper limbs and 5060 in the lower limbs, improving the quality of life. Inventions such as hyaluronidase injections have facilitated more effortless lymphatic flow by reducing tissue viscosity. Indocyanine green (ICG) fluorescence lymphography enables real-time lymphatic mapping, enhancing the precision of surgical procedures and flap positioning. These innovations, especially the use of wrist recipient sites in the management of upper limb lymphedema, have minimized complications (recipient-site rate ~3.2%) and improved the process of postoperative lymphatic drainage, as validated by lymphoscintigraphy. Taken together, the above-discussed developments position VLNT as a highly effective, minimally invasive approach to managing refractory lymphedema, which still holds promise for future improvement.

4.3. Donor and Recipient Site Considerations

Donor and recipient site considerations for vascularized lymph node transfer (VLNT) in secondary lymphedema, analyzed across studies from January 2000 to December 2024, significantly influence outcomes and complications. Donor sites are categorized as intra-abdominal (e.g., omental, jejunal mesenteric) or extra-abdominal (e.g., groin, supraclavicular). Intra-abdominal sites are preferred for their concealed scars and minimal risk of iatrogenic lymphedema, with lower morbidity rates (~1.4%) and higher lymph node yields that enhance lymph angiogenesis. Extra-abdominal sites, while accessible, carry a risk of donor-site lymphedema, particularly with groin flaps, necessitating careful patient selection. Recipient site selection includes the axilla, which facilitates scar release and lymphatic reconnection in breast cancer-related lymphedema, and the wrist, which offers enhanced circumferential reduction rates (~40% for upper limbs) due to gravitational advantages and proximity to superficial lymphatic networks. Wrist sites often outperform axilla sites in upper limb cases, while ankle sites are common for lower limbs. These strategic choices optimize VLNT efficacy, reduce complications (~3.2% recipient-site), and improve patient outcomes, as evidenced by lymphoscintigraphy and quality of life metrics.

4.4. Challenges and Limitations

Challenges and limitations in evaluating vascularized lymph node transfer (VLNT) for secondary lymphedema, based on studies from January 2000 to December 2024, hinder its standardized application. Heterogeneous outcome reporting, marked by a lack of standardized metrics for limb volume reduction, cellulitis episodes, and quality of life (e.g., LYMQOL scores), complicates meta-analyses and cross-study comparisons. Variability in measurement techniques, such as circumference versus volumetry, further obscures efficacy assessments. Limited randomized controlled trials (RCTs) and long-term follow-up data restrict robust evidence on VLNT's durability, with most studies being observational and reporting follow-up periods of 1–3 years, insufficient for assessing sustained benefits in chronic lymphedema. Variability in patient selection, including differences in lymphedema stage (ISL stages 2–3), etiology, and comorbidities, introduces confounding factors that affect outcome consistency. Additionally, variability in surgical expertise, particularly in microsurgical techniques and donor/recipient site selection, impacts reproducibility, with intra-abdominal flaps requiring specialized training. These challenges underscore the need for standardized protocols, multicenter RCTs, and extended follow-up to validate VLNT's efficacy, optimize patient selection, and ensure consistent surgical outcomes across diverse clinical settings.

4.5. Future Directions

Future directions for vascularized lymph node transfer (VLNT) in secondary lymphedema, based on studies from January 2000 to December 2024, aim to address current limitations and enhance clinical application. Developing standardized protocols for diagnosis, treatment, and outcome assessment is critical to reduce heterogeneity in metrics like limb circumference reduction rate (CRR) and quality of life (LYMQOL scores), enabling consistent evaluation across studies. Multicenter randomized controlled trials (RCTs) comparing VLNT with treatments like lymph venous anastomosis or liposuction are needed to establish comparative efficacy and identify optimal patient cohorts, particularly for International Society of Lymphology (ISL) stages 2–3. Investigating molecular and genetic factors influencing VLNT success, such as lymphangiogenesis-related gene expression, could personalize treatment strategies and predict outcomes. Advanced imaging, such as magnetic resonance (MR) lymphangiography, offers potential for precise preoperative planning by mapping lymphatic anatomy, enhancing donor and recipient site selection. These advancements, combined with broader microsurgical training, will improve VLNT accessibility and reproducibility, positioning it as a first-line option for refractory lymphedema and potentially for prophylactic use in high-risk patients, ultimately reducing the disease burden.

5. Conclusion

This systematic review, synthesizing studies from January 2000 to December 2024, confirms that vascularized lymph node transfer (VLNT) is an effective treatment for secondary lymphedema, demonstrating significant limb volume reduction, infection control, and quality of life (QoL) improvement. VLNT achieved mean circumferential reduction rates of approximately 40% for upper limbs and 50–60% for lower limbs, particularly in advanced International Society of Lymphology (ISL) stages 2–3, surpassing outcomes of conservative therapies like complete decongestive therapy (CDT) and other surgeries such as lymphovenous anastomosis. Intra-abdominal donor sites, including omental and jejunal mesenteric flaps, showed superior outcomes due to higher lymph node yields and lower morbidity (~1.4%), with no reported donor-site lymphedema. Wrist recipient sites enhanced efficacy in upper limb lymphedema, likely due to gravitational advantages, as evidenced by lymphoscintigraphy showing restored lymphatic flow. Low complication rates (recipient-site ~3.2%) and the ability of ~45% of patients to discontinue compression garments underscore

VLNT's feasibility and safety, supported by innovations like indocyanine green lymphography and hyaluronidase injections that improve surgical precision.

The clinical implications of these findings position VLNT as a first-line surgical option for refractory secondary lymphedema, particularly for patients unresponsive to CDT. Its potential for prophylactic use in high-risk patients, such as those undergoing extensive lymph node dissection or radiotherapy, warrants further exploration to prevent lymphedema onset. To advance VLNT's application, a call to action is needed to standardize outcome reporting, including consistent metrics for limb volume, cellulitis episodes, and QoL (e.g., LYMQOL scores), to facilitate robust meta-analyses. Multicenter randomized controlled trials are essential to compare VLNT with other interventions and establish long-term efficacy. Expanding training in microsurgical techniques is critical to increase access to VLNT, as its success relies on surgical expertise. Collaborative research, integrating advanced imaging like MR lymphangiography and molecular studies on lymphangiogenesis, will further optimize patient selection and outcomes, solidifying VLNT's role as a transformative treatment for secondary lymphedema and improving patient well-being globally.

References

[1] Becker, C., Assouad, J., Riquet, M., and Hidden, G. (2006). Postmastectomy lymphedema: Long-term results following microsurgical lymph node transplantation. *Annals of Surgery, 243*(3), 313–315. https://doi.org/10.1097/01.sla.0000201256.68569.c0

[2] Chang, D. W., Suami, H., and Skoracki, R. (2013). A prospective analysis of 100 consecutive lymphovenous bypass cases for treatment of extremity lymphedema. *Plastic and Reconstructive Surgery, 132*(5), 1305–1314. https://doi.org/10.1097/PRS.0b013e3182a4d7a6

[3] Ciudad, P., Maruccia, M., Socas, J., Lee, M. H., Chung, K. P., Constantino, M. J., Sabbagh, M. D., Kiranantawat, K., and Chen, H. C. (2017). The laparoscopic right gastroepiploic lymph node flap transfer for upper and lower limb lymphedema: Technique and outcomes. *Microsurgery, 37*(3), 197–205. https://doi.org/10.1002/micr.30107

[4] Cormier, J. N., Askew, R. L., Mungovan, K. S., Xing, Y., Ross, M. I., and Armer, J. M. (2010). Lymphedema beyond breast cancer: A systematic review and meta-analysis of cancer-related secondary lymphedema. *Cancer, 116*(22), 5138–5149. https://doi.org/10.1002/cncr.25458

[5] DiSipio, T., Rye, S., Newman, B., and Hayes, S. (2013). Incidence of unilateral arm lymphoedema after breast cancer: A systematic review and meta-analysis. *The Lancet Oncology, 14*(6), 500–515. https://doi.org/10.1016/S1470-2045(13)70076-7

[6] Egger, M., Davey Smith, G., Schneider, M., and Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ, 315*(7109), 629–634. https://doi.org/10.1136/bmj.315.7109.629

[7] Higgins, J. P. T., Thompson, S. G., Deeks, J. J., and Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *BMJ, 327*(7414), 557–560. https://doi.org/10.1136/bmj.327.7414.557.

[8] International Society of Lymphology. (2020). The diagnosis and treatment of peripheral lymphedema: 2020 consensus document of the International Society of Lymphology. *Lymphology, 53*(1), 3–19.

[9] Rockson, S. G. (2018). Lymphedema after breast cancer treatment. *The New England Journal of Medicine, 379*(20), 1937–1944. https://doi.org/10.1056/NEJMcp1803290

[10] Scaglioni, M. F., Arvanitakis, M., Chen, Y. C., Giovanoli, P., Wu Chou, C. Y., and Chang, E. I. (2018). Comprehensive review of vascularized lymph node transfers for lymphedema: Outcomes and complications. *Microsurgery, 38*(2), 222–229. https://doi.org/10.1002/micr.30207

[11] Schaverien, M. V., Badash, I., Patel, K. M., Selber, J. C., and Cheng, M.-H. (2018). Vascularized lymph node transfer for lymphedema. *Seminars in Plastic Surgery, 32*(1), 28–35. https://doi.org/10.1055/s-0038-1632401

[12] Slim, K., Nini, E., Forestier, D., Kwiatkowski, F., Panis, Y., and Chipponi, J. (2003). Methodological index for non-randomized studies (MINORS): Development and validation of a new instrument. *ANZ Journal of Surgery, 73*(9), 712–716. https://doi.org/10.1046/j.1445-2197.2003.02748.x

[13] Sterne, J. A. C., Savović, J., Page, M. J., Elbers, R. G., Blencowe, N. S., Boutron, I., Cates, C. J., Cheng, H.-Y., Corbett, M. S., Eldridge, S. M., Emberson, J. R., Hernán, M. A., Hopewell, S., Hróbjartsson, A., Junqueira, D. R., Jüni, P., Kirkham, J. J., Lasserson, T., Li, T., … Higgins, J. P. T. (2019). RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ, 366*, l4898. https://doi.org/10.1136/bmj.l4898