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Free vascularized lymph node transfer for treatment of lymphedema: A systematic evidence based review

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KEYWORDS

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Summary *Background:* Free vascularized lymph node transfer (VLNT) is a relatively novel technique for treatment of lymphedema. The purpose of this systematic review was to evaluate the current evidence on VLNT and to determine if there is objective data concerning improved outcomes.

Methods: A literature search of PubMed, EMBASE and CENTRAL electronic databases was conducted to identify articles written in the English language on VLNT for treatment of lymphedema. Publications were selected according to inclusion criteria. Papers reporting adjunct techniques and those that did not describe outcomes were excluded. Data including patient demographics, surgical technique, complications and outcomes were extracted. A quality score was calculated for each article.

Results: Eighteen studies were included with an overall study population of 305 patients. Mean quality score of articles was 5.3 with levels of evidence range from II to IV. Among 182 patients who underwent limb circumference assessment, 165 (91%) showed postoperative improvement. Reduction of limb volume was noted in 98 of 114 (86%) patients. Ninety two patients underwent lymphoscintigraphy/lymphangiography and 55 (60%) demonstrated moderate or significant improvement of flow. Patient satisfaction was questioned in 105 patients and with exception of 7 patients, all reported a high satisfaction level with significant relief in symptoms and improved quality of life. Publications also reported a reduction in infectious episodes.

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Conclusion: VLNT appears to provide improvement in lymphedema. More studies with standardized methods for reporting outcomes and uniform patient selection are needed to evaluate this technique thoroughly.

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Introduction

Lymphedema is caused by disruption of lymphatic drainage systems that subsequently result in enlargement of the affected site. In the early stages, the swelling is due to accumulation of fluid in the interstitial space, however as the condition progresses, the amount of fat and fibrotic tissue also increase. Acquired etiology is more prevalent and is commonly due to iatrogenic removal of lymph nodes, and radiation treatment.¹ The patients usually present with swelling, heaviness and enlargement of the affected limb, skin atrophy and recurrent episodes of cellulitis.²

Lymphedema is initially managed by decongestive physiotherapy that consists of compression garments, exercise, mechanical measures and manual drainage.^{3,4} Late phase, chronic lymphatic dysfunction is difficult to cure and does not respond well to conservative management. For such cases, debulking procedures and physiologic operations to increase lymphatic outflow have been advocated.^{5–10} Excisional procedures are beneficial, however they may result in the destruction of remaining lymphatics and poor cosmetic results.¹¹ Physiologic operations like lymphovenous anastomoses are technically challenging due to requirement of supermicrosurgery as lymphatic vessels are usually less than 1 mm in diameter. Free vascularized lymph node transfer (VLNT) is a relatively novel technique which aims to bring functional lymph nodes into the affected site to promote lymphangiogenesis via growth factors and acting as a pump.^{12,13} The lymph nodes are usually transferred en-block with surrounding soft tissue and microsurgical anastomoses are performed at the recipient site. The lymphatic tissue transfer could also be incorporated into major reconstructive surgery such as autologous breast reconstruction.^{14,15}

There is emerging evidence that VLNT could potentially improve lymphedema, however more evidence is needed to provide a rationale for harvesting lymph nodes from a distant site. The primary goals of this review are to evaluate the published evidence on VLNT and determine if there is objective data on improvement. Existing literature reviews on VLNT are mostly narrative and are broad including a mixture of techniques. The objective of this systematic review was to evaluate recent literature reporting solely on VLNT.

Materials and methods

Literature search

A literature search of PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) electronic databases

was conducted to identify all articles involving microsurgical lymphatic surgery techniques, specifically VLNT, to treat lymphedema. The following search strings were used: (1) Pubmed: (lymphedema) AND (flap) OR (grafting) OR grafts) OR graft) OR transplantation) OR transplant) OR transfers) OR transfer)) AND (“lymph vessel”) OR lymphatic) OR “lymph node”) OR (“lymphatic vessels/transplantation”[MeSH Terms]) OR “lymphatic vessels/surgery”[MeSH Terms]) OR “lymph nodes/transplantation”[MeSH Terms]) OR “lymph nodes/surgery”[MeSH Terms]) Filters: Publication date from 1980/01/01; English, (2) EMBASE: ('lymph nodes'/exp OR 'lymph nodes') OR ('lymph vessel'/exp OR 'lymph vessel') OR ('lymphatic'/exp OR lymphatic) AND (transfer OR transfers OR transplant OR transplantation OR graft OR grafts OR grafting)) OR ('surgical flaps'/exp OR 'tissue flap'/exp OR flap) AND ('lymphedema'/exp OR lymphedema) AND [english]/lim AND [1980–2015]/py, (3) CENTRAL: vascularized lymph node transfer.

PubMed and EMBASE searches were limited to English language articles published between 1980 and May 1, 2015, the date the searches were last run. Titles and abstracts were examined and articles were selected for full text review based on the inclusion and exclusion criteria as follows: 1. The surgical technique was free VLNT (without adjunct modalities), 2. The VLNT was utilized to treat upper or lower limb lymphedema, 3. The study reported more than 5 cases, 4. The study reported outcomes data, specifically improvement of lymphedema, and 5. The article had patient based clinical data (not data from cadaver or animal studies). Additionally, a manual search of study references was performed to include any articles that were missed during the initial search. A flow chart of the selection process is presented in [Figure 1](#).

Data extraction

Data obtained from papers included age, anatomic location, etiology, stage, duration of lymphedema, surgical technique, postoperative care, surgical complications, follow-up and outcomes. Details of reduction in circumference, reduction in volume, patient satisfaction, ability to discontinue conservative therapy, decrease in infection episodes, and flow assessment with lymphoscintigraphy or lymphangiography were recorded. Studies reporting on a mixed patient population (i.e. employing adjunct techniques in several of their patients) were analyzed to exclude data pertaining to combined procedures.

Quality assessment

The final 18 papers were reviewed independently by 4 co-authors for methodological quality of the original studies. A

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