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ORIGINAL ARTICLE

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Lymphaticovenular anastomosis improves quality of life and limb volume in patients with secondary lymphedema after breast cancer treatment

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Abstract

Secondary lymphedema is a common side effect of breast cancer treatment, with significant impact on patients' physical and psychological well-being. Conservative therapies are the gold standard treatment, however surgical options are becoming more popular. Lymphaticovenular anastomosis (LVA) is a supermicrosurgical procedure that aims to restore lymphatic flow by anastomosing damaged lymphatics to subcutaneous venules. We aimed to assess the effects of LVA on patients' limb volume and quality of life. Pre- and postoperative limb volumes and LYMQOL scores were collected for patients undergoing LVA for lymphedema secondary to breast cancer. Thirty-seven patients underwent LVA. A significant reduction was seen in median excess limb volume postoperatively (13.3%-6.6%, $P < 0.005$), with volumetric improvement seen in 78% of patients. Thirteen patients were able to discontinue compression garment use. Eighty-six percent of patients reported improved quality of life postoperatively with median LYMQOL score increasing from 90 to 104 points ($P < 0.005$). LVA is a minimally invasive surgical option for patients with early stage lymphedema. It can lead to significant volumetric improvements and in select patients, freedom from compression therapy. LVA can also lead to significant improvements in quality of life, in particular patients' mood and perception of their appearance.

KEYWORDS

breast cancer, LVA, lymhaticovenular anastomosis, LYMQOL, quality of life, secondary lymphedema

1 | INTRODUCTION

Breast cancer is the most common cancer in the UK, with 50 000 new cases diagnosed every year.[1] The mainstay of treatment involves surgical removal of the tumour with lymph node biopsy or excision. This is frequently followed by adjuvant chemotherapy, radiotherapy, or hormonal treatment.[2] Five-year survival is now over 85%,[1] resulting in an increasing number of women living with long-term side effects of treatment and an increased emphasis being placed on quality of life after cancer.[3]

Surgery and radiotherapy can damage the lymphatics,[4] and one in five women develop lymphedema after breast cancer treatment.[5] Lymphedema is a disabling condition whereby damage to lymphatic channels causes accumulation of protein-rich lymphatic fluid within the subcutaneous tissues of the arm.[4] It affects patients' psychosocial well-being, causes swelling and discomfort of the limb, and increases the risk of recurrent cellulitis.[4,6]

Although there is no cure for lymphedema, several conservative and surgical therapies exist, aiming to alleviate symptoms by limiting fluid accumulation. Lymphedema has traditionally been

managed conservatively, using labor-intensive, time-consuming methods such as complex decongestive physiotherapy, skin care, and compression sleeves.[4,7,8] When conservative treatment fails, surgical options include reductive methods or physiological treatments, such as lymph node transfer and lymphatico-lymphatic bypass[7,9] these are significant operations requiring general anesthetic.

Lymphaticovenular anastomosis (LVA) is a minimally invasive supermicrosurgical procedure that aims to restore lymphatic flow by anastomosing lymphatic channels to subcutaneous venules with a diameter <0.8 mm, in order to bypass areas of lymphatic damage. It is a viable treatment option for selected patients with proximal lymphatic obstruction but patent distal vessels. It is performed under local anesthetic, making it a good option for a wide range of patients, including the elderly and those with significant co-morbidities.[10] LVA has also been performed prophylactically at the time of axillary dissection,[3] when subclinical lymphedema is detected,[11] or when conservative methods have failed.

We aimed to assess the effects of LVA on volumetric measurements and quality of life in a cohort of women with secondary lymphedema after breast cancer treatment.

2 | METHODS

Data were collected prospectively for all patients undergoing LVA to treat lymphedema secondary to breast cancer treatment between September 2013 and December 2016.

2.1 | Patient selection

Patients with upper limb lymphedema self-referred or were referred for consideration of LVA by their general practitioner, surgeon, or lymphedema practitioner. Indocyanine Green (ICG) lymphography was performed on all patients. Patients were selected for LVA surgery if Indocyanine Green (ICG) lymphography confirmed the presence of lymphedema, or demonstrated patterns of dermal backflow considered high risk for the development of clinically apparent lymphedema.[11] Additionally, patients were required to have adequate functional lymphatic channels, as evidenced by passage of ICG dye from a subcutaneous injection point at the wrist to at least the level of the elbow within 45 minutes.

2.2 | Procedure

All patients underwent repeat preoperative ICG lymphography on the day of surgery to determine the location of functioning lymphatics.[12,13] All procedures were performed under local anesthetic by two consultant microsurgeons operating simultaneously. An average of four transverse incisions between 2 and 5 cm was made in the arm, typically one in the upper medial arm and three in the forearm. Suitable lymphatic vessels were anastomosed to subdermal venules using 11/0 Ethilon (Figure 1). An average operation lasted 4 hours. Postoperatively patients were advised to elevate the limb and massage from distal to proximal toward the scars. Patients were followed up at 3, 6, and 12 months.

2.3 | Quality of life

Quality of life was measured preoperatively and at every appointment postoperatively using the Lymphoedema Quality of Life Questionaire (LYMQOL). This is a validated quality of life assessment tool for patients with lymphedema. Patients are asked 24 questions falling into the following domains; symptoms, body image/appearance, function, and mood.[14] The highest total score is 118, with a higher score indicating better quality of life.

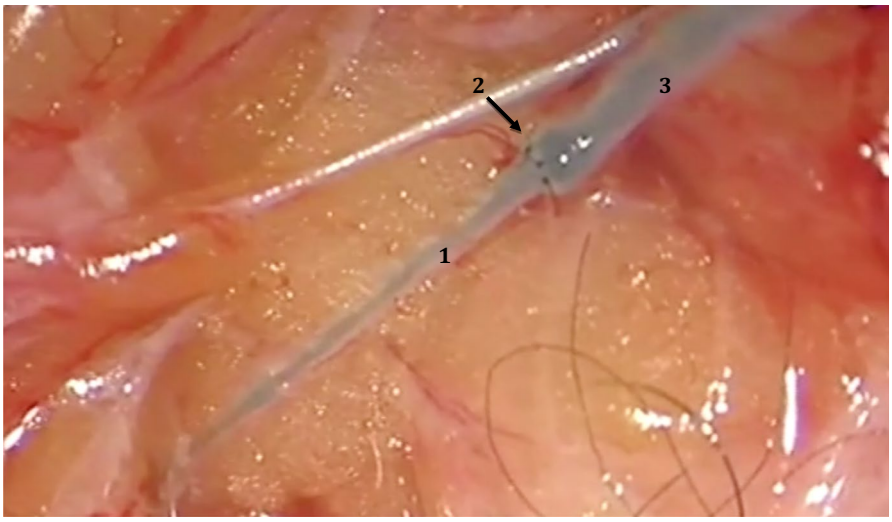

FIGURE 1 Lymphaticovenular anastomosis involves anastomosing multiple functioning distal lymphatics to small subcutaneous venules in order to restore lymphatic flow. (1) Lymphatic vessel containing patent blue dye, (2) Anastomosis with 11/0 Ethilon, (3) Venule containing patent blue stained lymphatic fluid [Color figure can be viewed at wileyonlinelibrary.com]

2.4 | Volumetric measurements

Volumetric measurements were recorded from both limbs preoperatively and at all postoperative appointments. Measurements were taken using a perometer. Excess limb volume is a measure of the volume difference between the affected and unaffected limb.

2.5 | Statistics

Descriptive statistics were used to calculate change in quality of life and limb volumetric measurements. The paired *t*-test was used to evaluate statistical significance.

3 | RESULTS

3.1 | Demographics

Thirty-seven patients with unilateral lymphedema secondary to breast cancer treatment underwent LVA surgery. Median follow-up was 6.5 months (range 3-33 months).

3.2 | Volume reduction

The median preoperative excess volume was 13.3% (range -0.8%-59.5%). Twenty-eight out of 37 patients (78%) showed a reduced limb volume postoperatively (Figure 2). The median postoperative excess was 6.6% (range 3.5%-36.4%, $P < 0.005$). The median relative volume reduction across all patients was 23%.

There was a clear difference in change in volume between groups depending on the starting volume difference between arms. Volumetric improvement was seen in three of the nine patients with a starting excess volume <5%, whereas in patients with an initial excess of 5%-20%, 12 out of 17 patients (71%) achieved improvement. In patients with a starting excess of over 20%, seven out of eight (88%) showed a volumetric improvement. Patients with an initial excess volume of 5%-20% and greater than 20% achieved a median 47% and 29% reduction respectively in excess volume (Figure 3).

3.3 | Quality of life

The median preop LYMQOL was 90 points (range 46-116), which improved to 104 points (range 45-113) postoperatively ($P < 0.005$; Figure 4A). The median improvement in quality of life was 9% with 32 of 37 patients (86%) reporting improved quality of life postoperatively. Improvement in quality of life was greatest in patients with the smallest differential volume between arms lymphedema (Figure 4A). When analyzing the LYMQOL domains separately, the greatest improvements were in patients' perception of mood and appearance (Table 1). Improvements were seen in all LYMQOL domains irrespective of initial excess volume except limb function in patients with greater than 20% excess volume (Figure 4B).

3.4 | Compression therapy

Of the 37 patients in this study, 13 have been able to discontinue wearing a compression sleeve. Six of nine patients with an initial excess volume less than 5% were able to discontinue wearing a compression sleeve, compared to seven of the 17 with a preoperative excess volume between 5% and 20%. All patients with an initial excess volume greater than 20% have required ongoing compression therapy.

3.5 | Complications

There were no complications in this cohort of patients. In particular we did not observe persistent lymphatic leak, wound infection, or cellulitis following surgery.

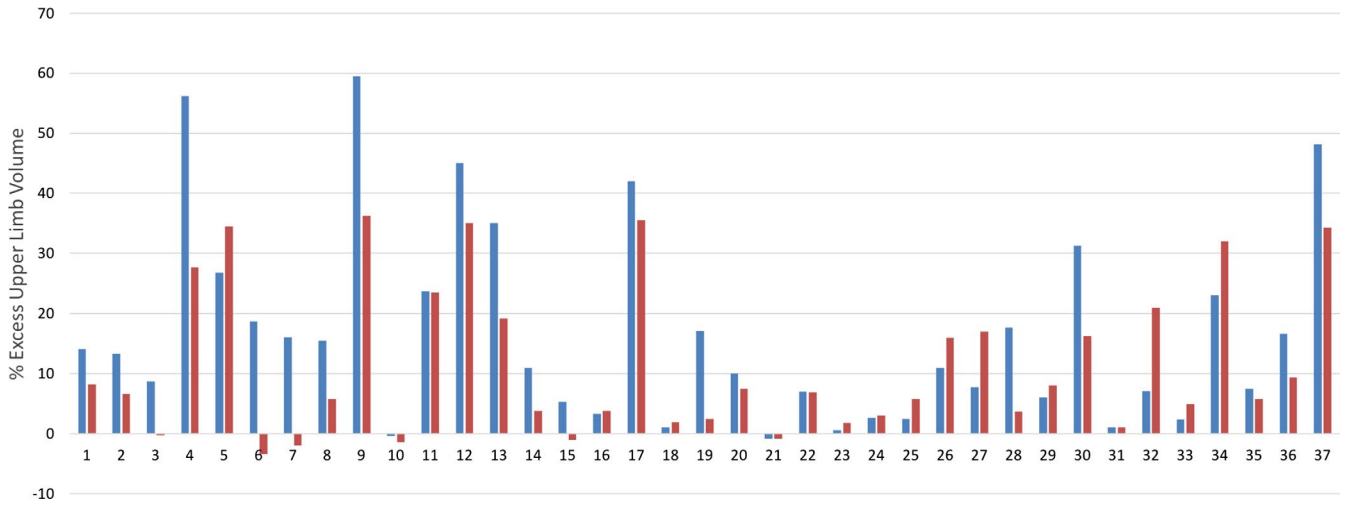

FIGURE 2 Pre- and postoperative percentage excess limb volume of each patient undergoing LVA. Each bar represents one arm: preop (blue) and postop (red). Postop excess volume was measured at the most recent clinic follow-up appointment [Color figure can be viewed at wileyonlinelibrary.com]

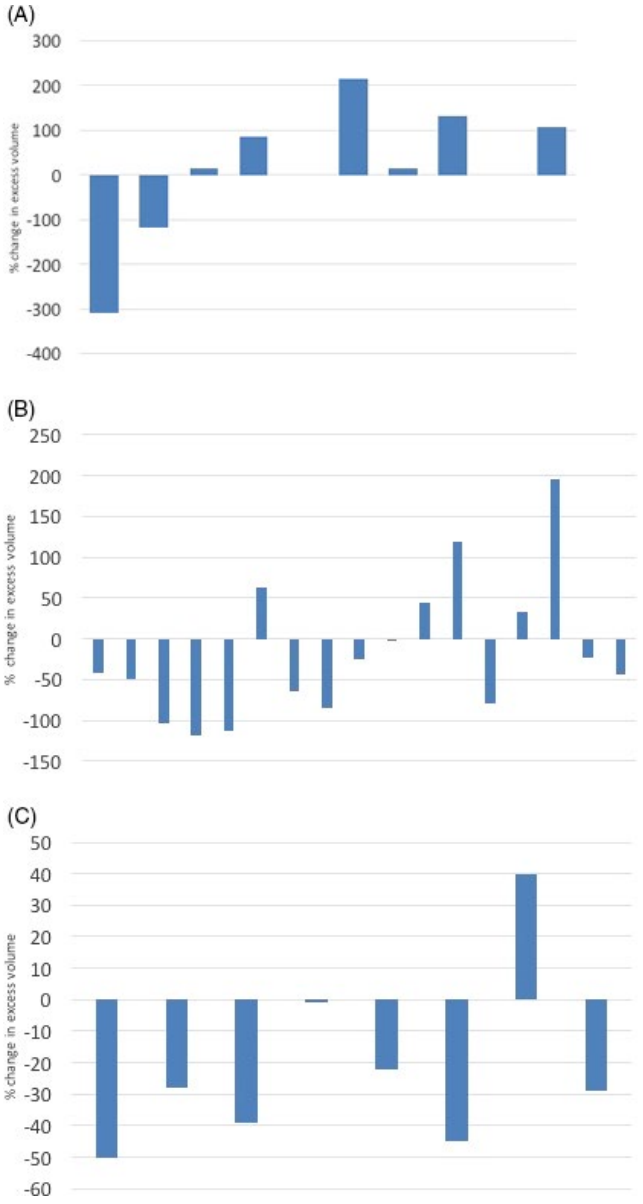

FIGURE 3 Percentage change in excess volume for each patient dependent on patient's initial (preoperative) percentage excess volume. A, Initial excess volume less than 5%. B, Initial excess volume between 5% and 20%. C, Initial excess volume greater than 20%. Each bar represents one arm [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

Here we have demonstrated that minimally invasive LVA surgery improved both quality of life and volumetric measurements in patients with stable lymphedema. Overall, the median reduction in excess volume was 23%, but results varied depending on the volumetric discrepancy preoperatively. Results have been variable in the literature,[15] however surgeons experienced in the procedure achieve similar degrees of volume reduction, dependent on the lymphedema stage.[7]

Although more substantial volumetric improvements are achieved with reductive techniques,[16,17] they require a greater degree of conservative management postoperatively, often with compression garments being worn for 23 hours per day. LVA has the benefit of being minimally invasive and performed under local anesthetic. In addition, LVA reduced the need for compression therapy in a significant number of patients: 34% of patients were able to discontinue compression therapy. When analyzed by starting volume discrepancy 70% of those with <5% initial excess volume, and 38% of those with between 5% and 20% excess volume were able to stop compression. The majority of other patients achieved improved limb volumes and were able to reduce the frequency or strength of compression garments without adverse effects. The decision to taper use of compression therapy is based on clinical assessment and discussion with the patient. Our aim is for patients with up to 15% excess volume preoperatively to no longer be reliant on compression garments postoperatively. In comparison, following liposuction, patients must continue lifelong compression therapy.[16] Furthermore, unlike LVA, reductive procedures can damage and further compromise the remaining functional lymphatics.[17] Improving lymphatic drainage and reducing lymphatic stasis has also been shown to significantly reduce the incidence of cellulitis in patients with lymphedema, though our study was not designed to test this outcome.[6,18]

Our results are skewed by the apparent increase in limb volume in patients with low grade lymphedema and an initial excess volume of <5%. It should be highlighted that in this cohort an apparent 200% increase in excess volume seen in one patient (Figure 3A) actually represents a change from 10ml excess volume to 32 mL excess volume from preop to 11 months follow-up. This is a tiny absolute volume increase, and within the measurement error of the perometer.[19] Furthermore, the LYMQOL for this patient increased from 94 to 111, mainly because she felt the arm was less tight, and she no longer wore a compression sleeve or undertook any other forms of conservative therapy. In our experience, the improvement in quality of life reported by patients with early lymphedema and minimal preoperative excess limb volume is explained by the reduced need for compression wear and an improvement in the heaviness and discomfort associated with poorly functioning lymphatics.

It should also be noted that all patients in this study have stable or worsening lymphedema despite conservative therapy and so without surgical treatment limb volume would be expected to worsen or at best, remain static.

There are difficulties in measuring successful outcomes in patients presenting with very early stage lymphedema. These patients may already have a high quality of life and minimal excess limb volume and little improvement in these values may be achieved postoperatively. However, a successful outcome is prevention of the development of clinically significant lymphedema and removing the reliance on compression sleeves. Interestingly, the greatest improvements in quality of life are seen in patients within this group. This is likely due to the fact that a large number of these women are able to maintain low excess volumes without use of compression therapy postoperatively.

Independent of their initial excess volume, the majority of patients reported improved quality of life postoperatively. Lymphedema is known to have significant impact on patients'

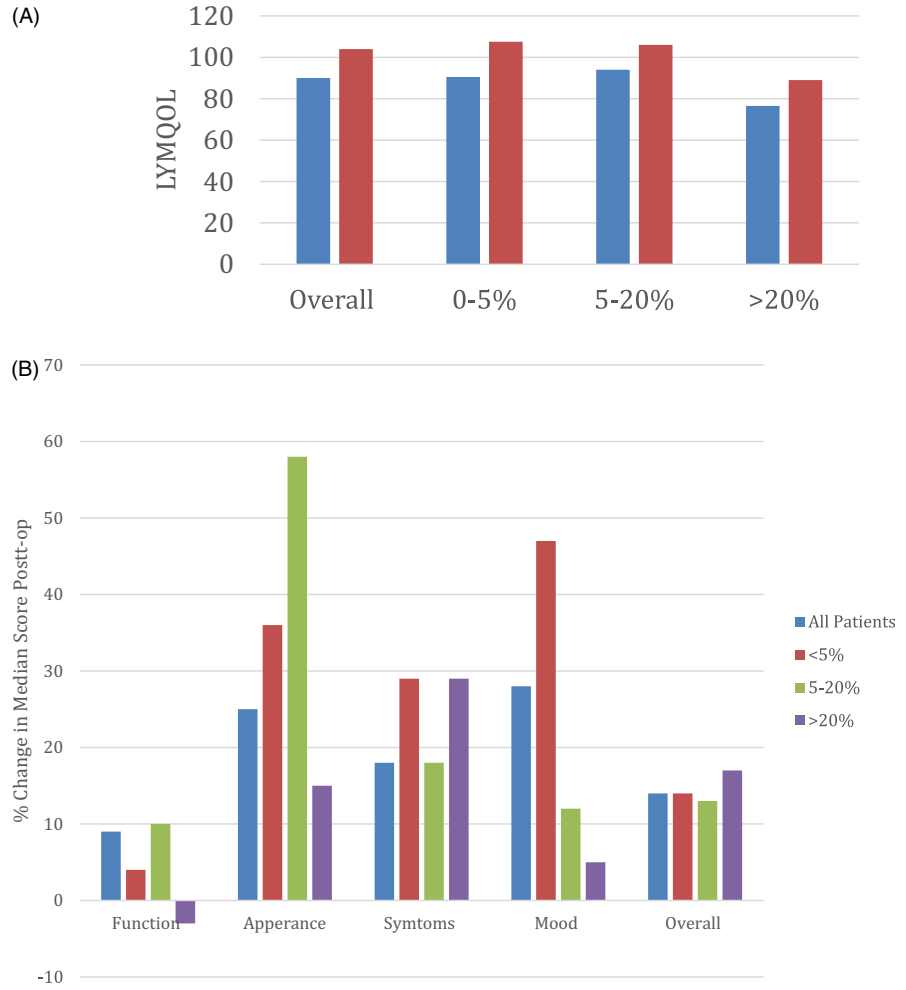

FIGURE 4 Median pre- and postoperative LYMQOL. A, Median score shown for all patients and dependent on initial excess volume. Blue bar is preoperative LYMQOL and red is postoperative LYMQOL. B, Median percentage improvement in LYMQOL domains postoperatively dependent on preoperative excess volume [Color figure can be viewed at wileyonlinelibrary.com]

psychosocial well-being.[20] The greatest improvements we observed were in patients' mood and perception of their appearance.

Lymphaticovenular anastomosis is a technically demanding operation requiring specialist training but can be performed safely under local anesthetic as a day case, making it a treatment option for patients with multiple co-morbidities.[21] Supermicrosurgical LVA was preceded by microsurgical LVA which anastomosed the lymphatics to venules greater than 2 mm rather than the smaller subdermal venules. The use of smaller venules with a lower pressure reduces the risk of anastomosis site thrombosis and improves patency.[17] LVA is a safe procedure. In this cohort, we report no complications, though we have observed minor complications such as wound healing problems and wound infection in other patients in our practice whose lymphedema was secondary to gynecological malignancy, or primary lymphedema.

Due to the latent onset of lymphedema there is wide variation in when the procedure is performed. Some groups have used LVA as an effective preventative measure at the time of axillary dissection for breast cancer,[3] whilst others detect subclinical lymphedema using ICG lymphography and intervene to prevent lymphedema development.[11]

TABLE 1 Median percentage improvement in LYMQOL score for each domain in all patients postoperatively

Domain	% Improvement in LYMQOL score	*P*-value
Function	9	0.01
Appearance	25	0.02
Symptoms	18	<0.005
Mood	28	0.001
Overall	14	0.02

Other groups use LVA in those who have tried but failed conservative treatment.[22] In patients with established lymphedema, LVA is a treatment option for patients with stage I-II, after which fibrosclerotic changes to lymphatic vessels prevent successful functioning of a LVA. As a result, our group offers LVA to patients with ICG-proven subclinical and clinical lymphedema up to and including stage II. Disease stage rather than duration of lymphedema is the determining factor in patient selection as the distal lymphatic channels must be patent and free of fibrosclerotic changes.

5 | CONCLUSION

Lymphaticovenular anastomosis is a minimally invasive technique providing significant volumetric reduction and improvement in quality of life for lymphedema after breast cancer treatment and should be considered as a first surgical intervention in patients with lymphedema not responding to conservative management.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

ETHICAL APPROVAL

Study carried out in accordance with the Declaration of Helsinki.

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