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Review Article

Immediate and delayed lymphatic reconstruction of breast-cancer related lymphedema: A systematic review and network meta-analysis

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ABSTRACT

Background: Breast cancer-related lymphedema (BCRL) is a significant morbidity due to its negative impact on physical, social, and psychological well-being. The objective of this work was to systematically evaluate the evidence for the efficacy of these surgical techniques in the preventive and curative treatment of BCRL by comparing the techniques with each other in an updated review and network meta-analysis of the literature.
Methods: PubMed, Cochrane Central Register of Controlled Trials, Web of Science, Embase, and Google Scholar databases were queried from January 2010 to March 2025.
Results: In the preventive setting, the pooled random-effects model showed a significant reduction in BCRL compared to the control for both axillary reverse mapping (odds ratio [OR] = 0.28; 95% confidence interval [CI] = 0.19–0.41) and lymphovascular anastomoses (OR = 0.25; 95% CI = 0.15–0.41), without difference between those technique (OR = 1.06; 95% CI = 0.60–1.87). In the curative setting, both LVA and vascularized lymph node transfer showed a benefit toward surgery for the upper extremity lymphedema index (UEL) and changes in excess volume/circumference. There was no difference between those techniques in terms of efficacy. Quality of life improved after curative surgery (standardized mean difference = 2.60; 95% CI = 1.17–4.02).
Conclusions: The literature data suggest that preventive and curative surgery techniques are safe and effective, with a real impact on improving the lives of breast cancer survivors.

Contents

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Introduction

Breast cancer is the most common cancer in women worldwide, with an estimated 2.3 million new cases per year in 2022 (23.8% of all cancers), and is the leading cause of cancer-related death in women (15.4% of cancer mortality) [1]. In the United States (US), women have a one-in-eight lifetime risk of developing breast cancer [2], while in Europe this risk is approximately one-in-twelve at 75 years-old [3]. Improved treatment and increased screening have reduced breast cancer mortality in recent decades, while incidence is increasing steadily [2]. It is estimated that by 2020 in Europe, 5% of the population was alive after a cancer diagnosis [4], and breast cancer was the most common cancer among female cancer survivors [4]. In the US, it is estimated that in 2019 there were more than 3.8 million breast cancer survivors, representing 44% of all female cancer survivors [5]. Although most survivors report good quality of life, some experience treatment-related complications. Breast cancer-related lymphedema (BCRL) is a significant problem due to its negative impact on physical, social, and psychological well-being [6], and represents a current public health issue due to its frequency and its consequences.

BCRL is caused by an impairment of the lymphatic system, resulting in abnormal accumulation of lymph in interstitial spaces and persistent swelling of the arm, neck, shoulder, breast or thoracic region [7]. It can occur at any time after breast cancer treatment [8], but usually peaks 18 months after surgical treatment [9]. The main risk factors for the development of BCRL are axillary surgeries – particularly axillary lymph node dissection (ALND), but also sentinel lymph node biopsy (SLNB) – and radiotherapy [10,11]. The incidence is variable, depending in particular on the surgical technique used for axillary staging, and varies from 6 to 60% across studies. Estimates based on prospective cohort studies show an incidence of around 21% in patients with breast cancer [12].

BCRL is currently considered a chronic disease and can cause numerous symptoms such as heaviness, pain, impaired limb function, cosmetic appearance, and recurrent infections. In addition, BCRL can be the cause of significant disability and financial burden for patients and society. Its conservative treatment is multimodal and consists of comprehensive decongestive therapy, including daily compression and, in some cases, long-term physical therapy [13]. In recent decades, preventive strategies have been progressively integrated into surgical oncology practice, notably through axillary surgical de-escalation, sentinel lymph node biopsy, and refinement of adjuvant radiotherapy fields. These measures have contributed to reducing the incidence of BCRL but have not eliminated the risk, particularly in patients receiving multimodal treatment.

Beyond these general measures, microsurgical preventive strategies have been proposed for high-risk patients. The axillary reverse mapping (ARM) aims to identify and preserve the lymphatic pathways that drain the upper limb during axillary surgery, thus minimizing disruption of lymphatic drainage [14]. Similarly, immediate lymphatic reconstruction with prophylactic lymphatic–venous anastomosis (LVA) performed during axillary dissection seeks to reestablish lymphatic continuity by directly anastomosing transected lymphatic channels to nearby venules [15]. Early clinical series suggest a potential reduction in postoperative lymphedema rates without compromising oncologic safety, although the current evidence remains limited and heterogeneous. In parallel, for patients with established and often chronic BCRL, secondary lymphatic reconstruction has emerged as a therapeutic option. Two main approaches are currently used: lymphovenous anastomosis, which diverts lymphatic flow into the venous system to bypass proximal obstruction, and vascularized lymph node transfer (VLNT), which transplants healthy lymph nodes with their vascular supply from a donor site, sometimes combined with free flap breast reconstruction [16,17].

The rationale of immediate and delayed lymphatic reconstruction is based on preserving or restoring lymphatic continuity before irreversible structural and inflammatory changes occur. Experimental and clinical data suggest that early lymphatic injury leads to lymphatic hypertension, chronic interstitial inflammation, and progressive lymphatic vessel sclerosis and fibrosis, which are key mechanisms in the transition from subclinical lymphatic dysfunction to established lymphedema [18,19]. By intervening at the time of axillary surgery, immediate or delayed reconstruction aims to maintain or restore physiological lymphatic drainage and reduce the risk of chronic lymphatic remodeling.

In the last decade, several studies have examined the feasibility, efficacy, and safety of these techniques. Although the results support the benefits of performing this type of surgery, it is not currently standard practice. There is no generally accepted curative surgical treatment or consensus on surgical procedures in general or specific techniques. Although systematic reviews and meta-analyses have evaluated surgical approaches for BCRL, most have focused on either preventive or curative strategies in isolation, or have assessed individual techniques without comparative integration. Direct comparisons between ARM, LVA, and VLNT remain scarce, and no prior synthesis has simultaneously evaluated these techniques across both preventive and curative settings. In addition, comparative data on quality-of-life outcomes and indirect treatment effects remain limited. Consequently, the objective of this work was to systematically evaluate the evidence for the efficacy of these surgical techniques in the preventive and curative treatment of BCRL by comparing the techniques with each other in an updated review and meta-analysis of the literature.

Methods

A review of the literature published in PubMed from January 2010 to March 2025 was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines [20] and the GRADE methodology (Grading of Recommendations Assessment, Development and Evaluation) [21].

Eligibility criteria

For the preventive setting, in all stages of the selection process, the articles were evaluated according to the following criteria:

- Population: patients with breast cancer undergoing surgical treatment including axillary surgery
- Intervention: surgical technique for BCRL prevention (*i.e.*, ARM or LVA)
- Control: no surgical technique for BCRL prevention
- Outcome: efficacy as the main outcome; and quality of life as the secondary outcome

For the curative setting, the criteria were the following:

- Population: patients with BCRL
- Intervention: surgical technique for BCRL treatment (*i.e.*, LVA or VLNT)
- Control: no surgical technique for BCRL treatment, or patients before surgery (baseline)
- Outcome: efficacy as the main outcome; and quality of life as the secondary outcome

Additional eligibility criteria were as follows:

- Original studies (including retrospective cohort studies) only were included; animal and cadaveric studies were excluded; literature reviews and meta-analyses were excluded
- Surgical procedure described
- Language: at least English title and abstract

Outcomes

The main objective was to evaluate the efficacy of surgical treatment or prevention of BCRL. Therefore, the main outcome was defined according to the curative or preventive setting and was composite. Secondary outcomes included quality of life and safety (both surgical complications and oncological outcomes).

In the preventive setting, the main outcome was the incidence of BCRL. In the curative setting, the main outcome was composite and defined as a change in the affected limb depending on the different available measurements:

- Modification of the UEL (Upper Extremity Lymphedema) index, an index based on perimetric measurements adjusted for body mass index, allowing for a diagnosis of the severity of lymphedema regardless of morphotype [22]. The higher the index, the greater the lymphedema. UEL index changes can be expressed in pre- and post-operative values, as well as in change ratios (same approach as for volume and circumference)
- Change in volume (V) and circumference (C): unlike the UEL index, volume and perimeter measurements are not standardized between studies: the formulas used for calculations vary, the locations and number of measurements are different, etc. Consequently, to allow comparison between studies, the change in excess volume/circumference (CEV/CEC) was calculated, reported as a percentage, and defined by the formula: $CEV = (V postoperative - V preoperative)/V preoperative$ or $CEC = (C postopoerative{-}C preopoerative)/C preopoerative$. Negative values reflect a reduction in excess volume/circumference and therefore treatment efficacy.

BCRL was staged according to the International Society of Lymphology (ISL) classification [23]: stages 0 (subclinical), I (early, reversible edema), II (persistent edema with tissue fibrosis), or III (advanced lymphedema with skin changes).

Bibliographic selection

The following databases were queried: PubMed, Cochrane Central Register of Controlled Trials, Web of Science, Embase, and Google Scholar (20 first pages). The research was conducted with the following index terms: (((lymphoedema)OR (lymphedema)) AND ((breast cancer) OR (breast neoplasm) OR (upper extremity))) AND ((surgery) OR (microsurgery) OR (supermicrosurgery) OR (reconstruction) OR (lymphovenous anastomosis) OR (axillary reverse mapping) OR (vascularized lymph node transfer) OR (bypass)). These searches were supplemented with a manual review of references from included articles, review articles, and other related articles identified during the search. A total of 4139 articles were identified through the initial search. Other sources were included after a manual review of references.

Identified articles were screened in two steps: (1) titles and abstracts, and (2) full-text articles. After initial screening, 438 full-text papers were assessed for eligibility and 108 articles were included in the qualitative analysis. We separated the articles into two groups, depending on whether it was a preventive or curative approach of BCRL. Preventive management consisted of LVA or ARM techniques and included 41 articles. The curative techniques regrouped VLNT and LVA, and included 67 articles. For quantitative analysis (network and pooled meta-analysis), 49 articles were included, 17 for preventive surgery and 32 for curative surgeries, respectively. Bibliographic selection is described in Fig. 1.

The following data were extracted if available: type of surgery, number of patients included, inclusion criteria (including type of axillary surgery), duration of follow-up, BCRL incidence, measures of arm volume or circumference reduction (including UEL index), and quality of life on any standardized scale.

Description of surgical techniques

Axillary reverse mapping

Axillary Reverse Mapping (ARM) is a surgical technique that aims to identify and preserve upper extremity lymphatic drainage during axillary surgery in breast cancer patients, thus minimizing the risk of iatrogenic lymphedema. The procedure involves subcutaneous injection 1–3 ml of a tracer dye (*e.g.* methylene blue and more recently indocyanine green) into the ipsilateral medial upper arm, antecubital fossa, finger web spaces, preoperatively or intraoperatively (15–30 min before dissection). Using fluorescence or direct visualization, surgeons can delineate lymphatic channels and lymph nodes specific to arm drainage. During sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND), ARM nodes and channels are distinguished from those draining the breast and preserved when oncologically appropriate [14, 24].

Lymphovenous anastomoses

Lymphovenous anastomosis (LVA) is a lymphatic reconstruction technique that does not require autologous tissue grafting. It was first described in the 1960s [25]. This supermicrosurgical technique involves suturing superficial lymphatic vessels to subcutaneous venules to create peripheral bypasses in the lymphedematous limb, thereby circumventing obstructed or low-flow lymphatic zones. These anastomoses allow excess lymph to drain directly into the venous system [26]. Patients must have functional lymphatic vessels, confirmed preoperatively by lymphography (such as indocyanine green fluorescence or magnetic resonance lymphangiography). Consequently, LVA is indicated primarily for subclinical and early-stage lymphedema; In more

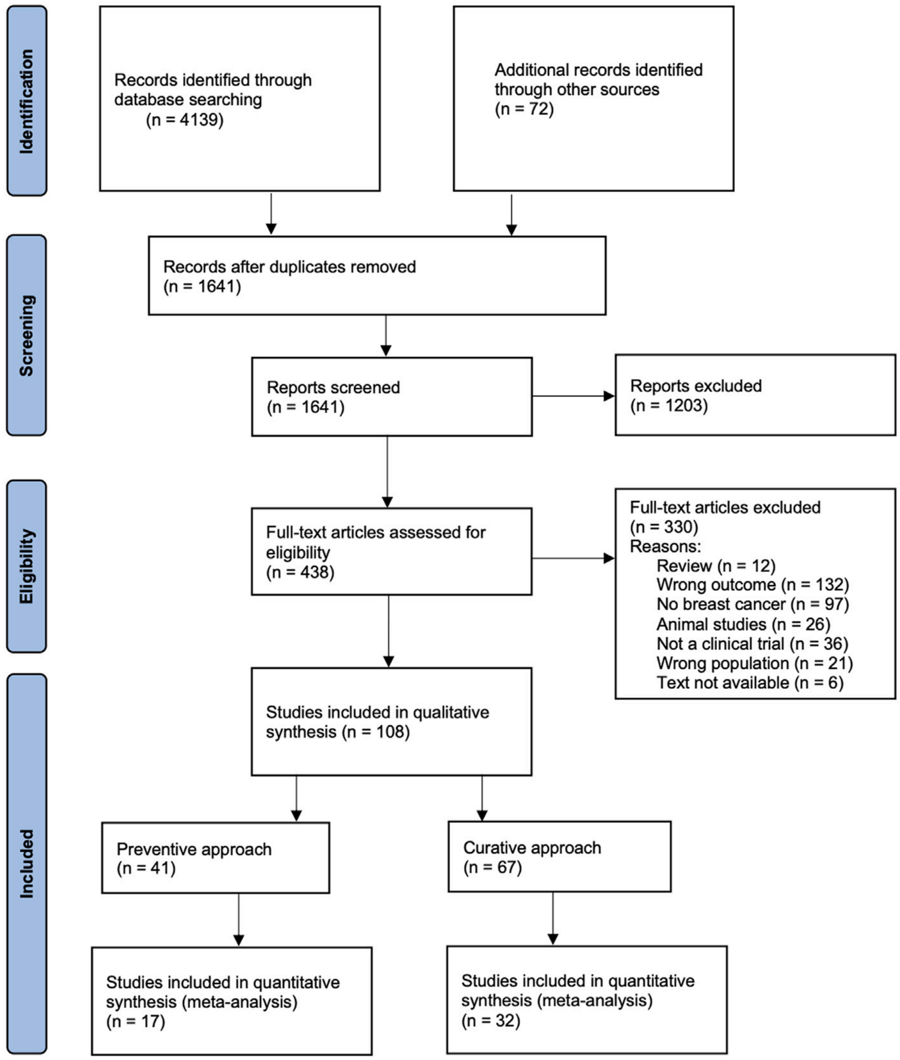


Fig. 1. Bibliography flowchart.

advanced stages, the absence of viable superficial lymphatics limits its effectiveness.

The procedure is performed under general or local anesthesia in the outpatient setting, using supermicrosurgical instruments and a microscope for vessels smaller than 0.5 mm. Intraoperative identification of suitable lymphatic vessels is facilitated by Patent Blue dye injection (15 cm distal to the surgical incision) or indocyanine green lymphography, allowing visualization of patent lymphatic channels under microscopic magnification (25–50×). Suitable recipient venules are identified by their location in the subcutaneous plane, appropriate diameter (typically 1–3 mm), and intact valve function confirmed by gentle probing. Both lymphatic vessels and venules should be of similar caliber to optimize anastomotic patency. [27,28] Anastomoses are performed using 11-0 or 12-0 nylon sutures. A minimum of three anastomoses per limb/procedure is generally regarded as standard practice; however, the exact number should be determined by the prevailing anatomical constraints, and the emphasis should be placed on the quality of the anastomoses rather than their quantity.

Compression therapy is conducted directly after surgery, and some patients reach compression discontinuation or reduction after a few months.

Vascularized lymph node transfer

The other principal microsurgical approach for lymphedema management is vascularized lymph node transfer (VLNT). This technique involves transplanting healthy lymph nodes along with their vascularized tissue to the affected area, promoting lymphatic regeneration [29]. This allows for the formation of a functional neolymphatic network over the long term [30], while providing a short-term lymphatic pumping effect. The most common donor site is the inguinal region, harvesting superficial lymph nodes based on either the superficial circumflex iliac artery or the superficial inferior epigastric artery [31]. Other donor sites include the lateral thoracic, submental, and supraclavicular lymph nodes, as well as intra-abdominal sites such as the omentum [32,33]. Preoperative imaging guides selection of 1–5 lymph nodes with intact vascular pedicles and surrounding adipose tissue (flap dimensions 8–15 cm). The flap is positioned in the subcutaneous plane at the site of maximal lymphedema and secured with sutures. Postoperative flap viability is monitored clinically and with ultrasound assessment of vascular pedicle patency. [34,35]

Some patients may benefit from combined breast reconstruction and VLNT, known as lympho-DIEP (deep inferior epigastric perforator flap), in which the lymph node graft is anastomosed to axillary vessels [34]. VLNT can be performed in patients with stage 0 to 2 lymphedema (subclinical, early, and advanced), regardless of the presence of functional superficial lymphatics. It can also be combined with LVA, breast reconstruction, and other reparative surgeries [36]. However, there remains a risk of secondary lymphedema at the donor site.

Conversely to LVA, compression therapy is applied after the flap viability is confirmed and therefore not directly after surgery. For all techniques, postoperative physiotherapy protocols are rarely described and not standardized, they may be conducted after complete wound healing.

Statistical analysis

We conducted both a conventional meta-analysis and a network meta-analysis, the latter allowing indirect comparisons between the two surgical techniques (LVA and VLNT). All statistical analyses were performed using R version 4.3.2 (2023-10-31) [37] with the following packages: *metafor*, *meta*, *tidyverse*, *readxl*, *ggpubr*, *metagear*, *netmeta*, and *broom*.

For the primary outcomes, separate random-effects meta-analyses were conducted for the UEL index, CEC and CEV. Quality of life data were standardized between studies by transforming all scores to a scale of 0 to 100, with 100 representing the best possible quality of life.

Given the expected heterogeneity between study populations, differences in outcome definitions (*e.g.*, criteria for lymphedema volume), various quality of life scales, and follow-up durations, random effects models were selected. The heterogeneity between studies was quantified using the maximum likelihood estimator for τ^2, and the Higgins statistic I^2 was calculated. For the heterogeneity test, the *p*-value of Cochran's Q was obtained using a Wald-type test.

For each included study, we extracted effect sizes as standardized mean differences (SMDs) with their associated variances. Each study was weighted according to the standard error of the population, which was determined by the size and homogeneity of the cohort.

To indirectly compare the two surgical interventions, we conducted a network meta-analysis using the *netmeta* package. Based on effect sizes and standard errors as previously described, each intervention was compared with a common reference group (preoperative status), allowing the construction of a treatment network. Random effects models were applied to estimate indirect and mixed treatment comparisons. Multiple comparisons were addressed by ensuring coherence of the data, distinguishing between direct and indirect effects. For quality of life analysis, duplicate data from the same cohort were excluded to avoid redundancy.

The results were presented as forest plots annotated with heterogeneity statistics, mean effect sizes with 95% confidence intervals, and study-specific weights.

Results

Preventive surgery

Among the 41 articles included, 20 studies performed ARM procedures [38–56], and 21 studies performed LVA procedures [57–77]. The studies were primarily prospectively designed. The characteristics of the included studies are shown in Appendix Tables .6 and .7. According to GRADE, the certainty of evidence was overall low to moderate, mainly limited by observational study designs, small cohorts, and lack of blinding. The findings were consistent and most of the studies reported a reduction in BCRL incidence when surgical treatment was performed. Imprecision and indirectness came from heterogeneous techniques, patient populations, and follow-up durations. There was no statistical difference between groups regarding follow-up durations. No study directly compared ARM *versus* LVA. The evidence from randomized trials was in favor of surgical treatment which showed better outcomes versus control: two studies for LVA [58,62]; and six studies for ARM [38,39,42,43,54,55].

Axillary reverse mapping

Twenty studies reported the incidence of BCRL during follow-up [38–56]. The sample sizes ranged from 60 to 1354 patients, with an average follow-up period of 6 to 44 months (mean 23.6 months). In the subgroup analysis restricted to prospective studies that evaluated ARM, 11 articles [38–40,42–44,47,51,54–56] were included (Fig. 2(a)). The pooled random-effects model demonstrated a significant reduction in the risk of BCRL compared to the control, with a odds ratio (OR) = 0.28 (95% confidence interval [CI] = 0.19 – 0.40). Individual study estimates ranged from OR = 0.11 (95% CI = 0.05 – 0.25) [56] to OR = 0.62 (95% CI = 0.21 – 1.85) [39]. Complications were reported for 3 patients. One developed skin necrosis at the blue dye (methylene blue) injection site [40]. Two patients developed metastasis in the arm lymph nodes [78]. There were no other reported complications.

Lymphovascular anastomoses

The qualitative analysis included 21 studies [57–77]. The duration of follow-up ranged from 6 months to 4 years (mean 16.6 months). The incidence of BCRL in LVA-treated cohorts ranged from 3% to 31.1%, compared to 7.7% to 50% in control groups. Most studies reported low complication rates associated with LVA, with only minor adverse events such as seroma or superficial infections. A total of six prospective studies [58,62,66,71,75,76] were included in the meta-analysis (Fig. 2(b)). The pooled random-effects model showed a significant reduction in the risk of breast cancer-related lymphedema, with an OR = 0.25 (95% CI = 0.15–0.41). Individual study estimates ranged from OR = 0.10 (95% CI = 0.01 – 0.93) [58] to OR = 0.41 (95% CI = 0.21 – 0.82) [76]. No study was in favor of the control group or did not show significant benefit.

Network meta-analysis

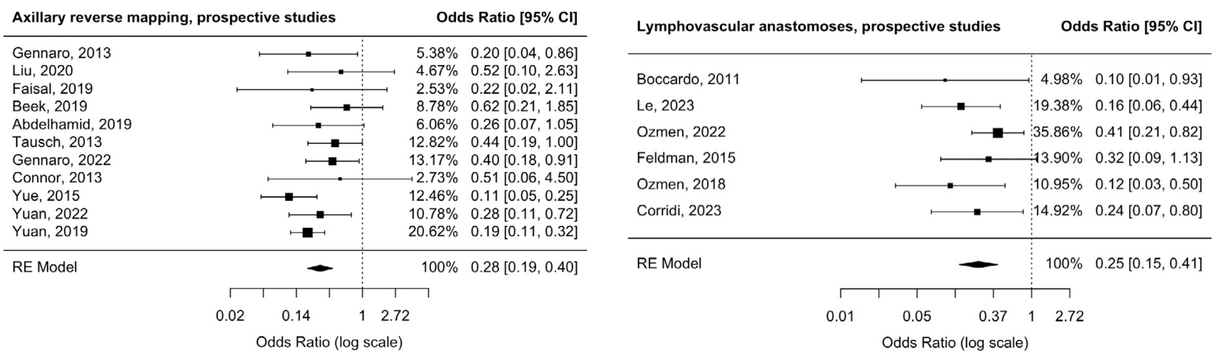
In the network meta-analysis (see Fig. 3), both ARM and LVA demonstrated a statistically significant reduction in the risk of breast cancer-related lymphedema compared to standard care. Direct evidence from 11 studies showed that ARM was associated with an OR = 0.27 (95% CI, 0.20–0.37; I^2 = 16.2%), indicating a 73% relative reduction in incidence compared to the control. Similarly, direct evidence from six studies demonstrated that LVA reduced the risk of lymphedema *versus* control with an OR of 0.25 (95% CI, 0.16–0.41; I^2 = 0%). In contrast, no significant differences were found between ARM and LVA (network estimate OR = 1.06; 95% CI, 0.60–1.87), suggesting a comparable preventive efficacy between the two approaches.

Quality of life

No eligible study reported quality-of-life outcomes in a manner suitable for quantitative synthesis. As a result, the planned secondary analysis could not be performed. However, qualitative descriptions available in several studies suggested a trend toward improved patient-reported quality of life after both ARM and LVA, although these findings were heterogeneous and derived from nonstandardized assessments.

Curative surgery

In total, 32 articles were included in the quantitative literature synthesis, with 13 articles on LVA [27,28,79–89], and 24 articles on VLNT [31,32,34,35,90–105]. The Appendix Tables .8 and .9 summarize the characteristics of each study. Twelve studies [33,36,106–115] were excluded from the meta-analysis due to non-extractable outcome data. In general, these studies suggested that both techniques provided a symptomatic or objective improvement in BCRL, often combined with breast reconstruction. The vast majority (29 of 32, 91%) reported the use of preoperative imaging for patients undergoing surgical treatment for breast cancer-related lymphedema. Indocyanine green lymphography was the most frequently employed imaging modality across both cohorts, often used in combination with other techniques such as lymphoscintigraphy, computed tomography angiography, magnetic resonance lymphangiography, and Doppler ultrasound. The benefits reported included reduced volume, fewer infections and improved quality of life, although some studies did not find a measurable effect [115]. The follow-up ranged between 2 and 41.8 months for LVA (mean 16.3 months), and between 6 and 70 months for VLNT (mean 22.7 months).



(a) Axillary reverse mapping (b) Lymphovascular anastomoses

Fig. 2. Quantitative meta-analysis of preventive surgeries, divided by technique.

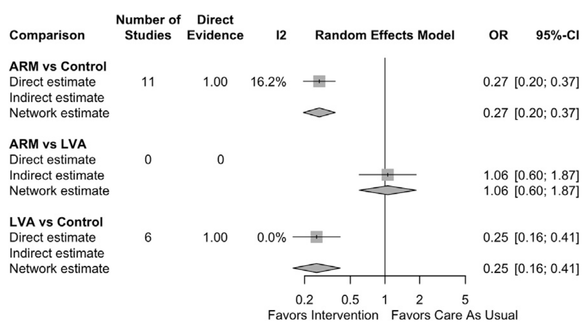


Fig. 3. Network meta-analysis of preventive surgical techniques.

There was no statistical difference between groups regarding follow-up durations. The only comparative analysis showed a greater reduction in circumference with VLNT than with LVA [109]. No crossover between preventive and curative groups was reported in the included studies.

Efficacy on measures reduction

Twenty-six studies detailed the evolution of the measures before and after the intervention, with a total of 922 patients. Among the various included studies, 6 evaluated the UEL index [35,79,82,86,88,104], 14 assessed changes in excess volume (CEV) [27,28,32,34,80,81,83,84,95–97,100,103,105] and 9 assessed changes in excess circumference (CEC) [27,30,80,85,92,99,101–103].

The Fig. 4 summarizes the different outcomes in terms of efficacy on measurement changes. The combined effect estimate of the UEL index and changes in excess volume/circumference favored a significant reduction of BCRL when using a microsurgical technique in this curative context: the standardized mean difference (SMD) for the UEL index was −0.33 [95%CI −0.64 – −0.02; P = 0.039, Fig. 4(a)], and the SMDs of the percentages of changes in excess volume/circumference were −0.30 [95%CI −0.53 – −0.07; P = 0.012, Fig. 4(c)] and −0.33 [95%CI −0.57 – −0.09; P = 0.008, Fig. 4(e)], respectively. The analysis of the indirect effect, *i.e.*, the comparison between LVA and VLNT (network meta-analysis), does not reveal a significant difference between the two techniques (Figs. 4(b), 4(d) and 4(f)), with P-values ranging from 0.67 to 0.78.

Quality of life changes

Fourteen studies evaluated the quality of life: 5 addressed LVA and 9 examined VLNT. In total, the meta-analysis was conducted on 487 patients from the various studies. Fig. 5 summarizes the different results in terms of impact on the quality of life for each study, ranked according to the type of quality-of-life scale used. Five different scales were used, and the LYMQOL scale was the most common (7 studies). Among the different scales, 3 showed a statistically significant improvement in quality of life after lymphatic reconstructive microsurgery of BCRL, with combined effect estimates (standardized mean differences) of 4.39 [95% CI 2.27 – 6.52; P = < 0.001] for LYMQOL, 0.33 [95% CI 0.05 – 1.61; P = 0.022] for Lymph-ICF, and 0.95 [95% CI 0.66 – 1.25; P = < 0.001] for LLIS (Fig. 5(a)). One study evaluated the quality of life according to 2 scales in the same patients, and found no benefit with ULL-27 and a benefit with LLIS. The analysis of the indirect effect, *i.e.*, the comparison between LVA and VLNT (network meta-analysis), conducted only on the LYMQOL scale, did not find a significant difference between the two techniques (Fig. 5(b)).

Safety

Postoperative complications related to microsurgical techniques for the treatment of lymphedema were rare. Regarding LVA, Jonis et al. report four moderate adverse events in the LVA group: erysipelas, skin infection, pneumonia, and an allergic reaction [82]. Khan et al. mention two cases of postoperative cellulitis, which may compromise the patency of the anastomoses [83]. Brahma et al. note several cases of recurrence of lymphedema with repeated cellulitis related to premature cessation of compression therapy [79]. Ayestaray et al. report no infectious or allergic complications related to the use of patent blue, but mention persistent skin staining in 20% of cases [27]. Finally, Phillips et al. report no per- or postoperative complications, particularly no lymphatic leakage or wound infection [28]. Complications associated with VLNT vary according to the techniques and donor or recipient sites used, but remain rare. Several studies report complications at the donor site, especially iatrogenic lymphedemas of the corresponding limb [115], as well as seromas [115,116] and chronic pain [115]. In a series of 100 VLNT (upper and lower limb), the authors describe a 3% flap loss rate [116]. Complications such as delayed healing or hernias have also been described [113]. On the recipient site side, hematomas, redo anastomoses, and partial flap necrosis have been reported [103]. Other studies have observed superficial infections, transient chyle leaks, and paresthesias [116]. Some teams have observed no major complications, either at the donor or recipient site, especially when perioperative lymphatic mapping was performed [99,105]. Finally, in no study – for both techniques – an increased risk of local, regional recurrence or a deleterious progression of cancer has been described.

The main quantitative outcomes of preventive and curative lymphatic reconstruction are summarized in Table 1 to facilitate comparison across settings and techniques.

Discussion

This study shows the effectiveness of immediate and delayed lymphatic reconstruction techniques in breast cancer-related lymphedema

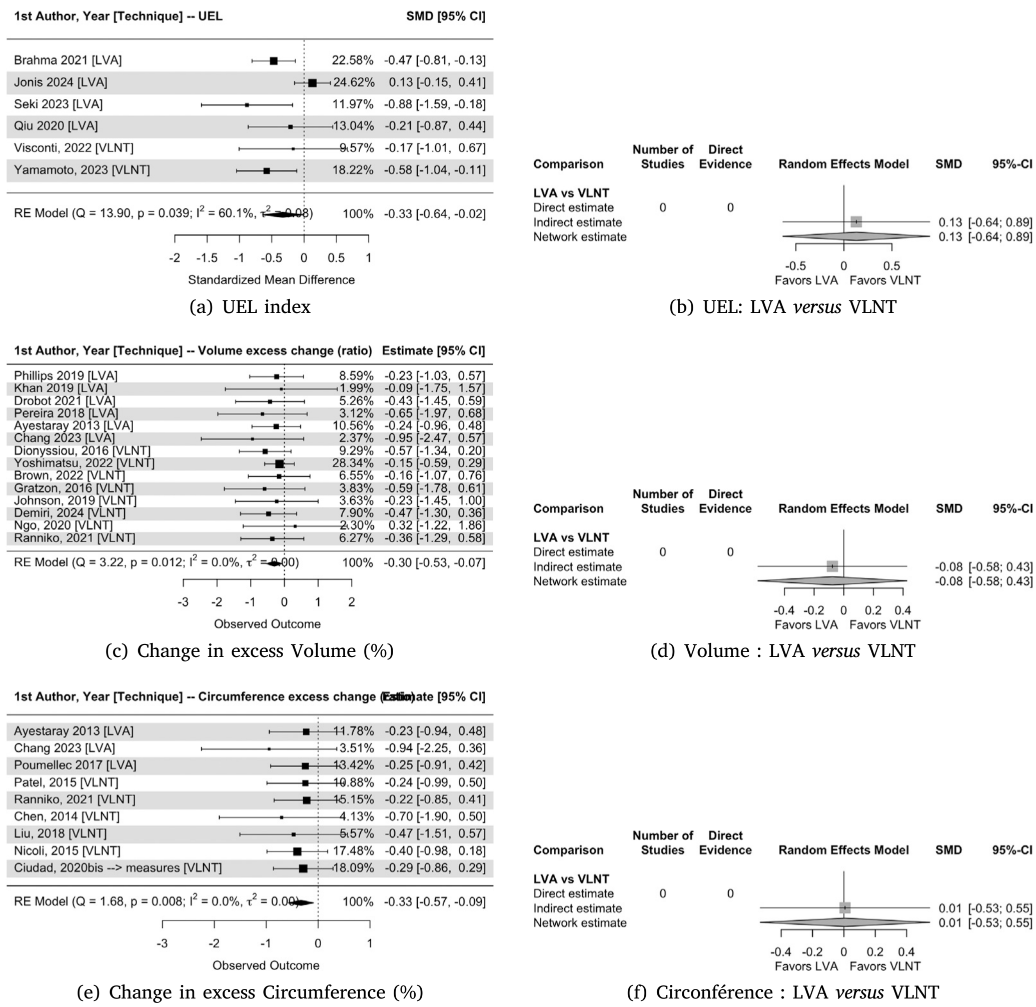


Fig. 4. Quantitative and network meta-analysis of curative surgery techniques. Panels 4(a), 4(c) and 4(e) show individual and pooled effects of both techniques together. Panels 4(b), 4(d) and 4(f) show the indirect effect, which is the comparison between the two techniques.

Table 1
Summary of pooled quantitative outcomes of preventive and curative surgical techniques for breast cancer-related lymphedema.

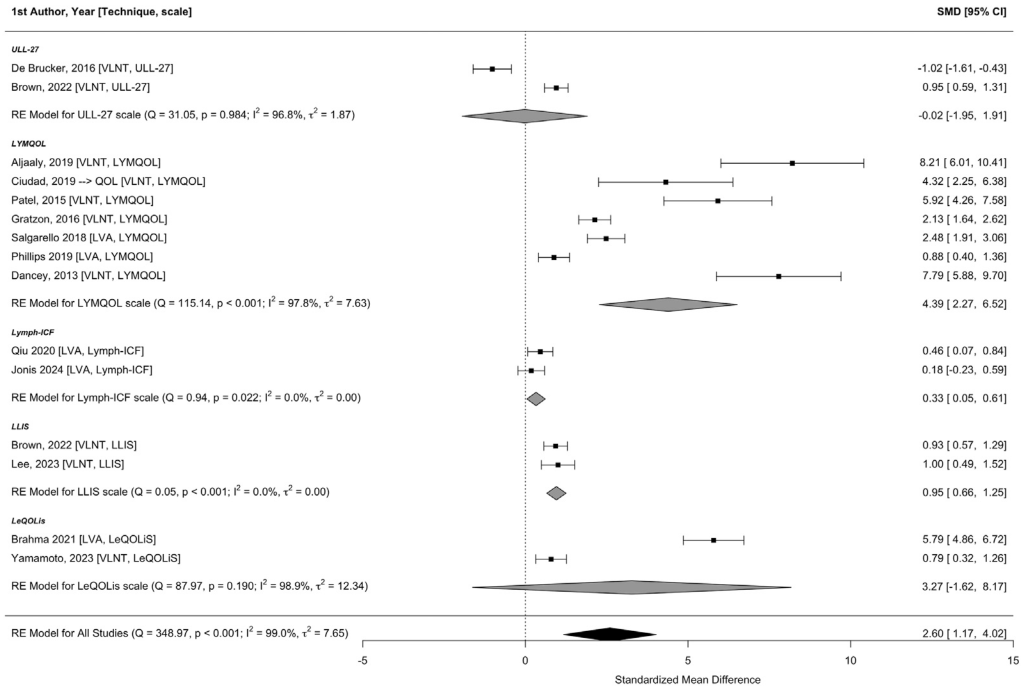
Setting	Technique	No. of studies	No. of patients	Main outcome	Pooled effect estimate (95% CI)
Preventive	ARM	20	3616	BCRL incidence	OR 0.28 (0.19–0.40)
Preventive	LVA	21	2083	BCRL incidence	OR 0.25 (0.15–0.41)
Curative	LVA or VLNT	6	253	UEL index	SMD −0.33 (−0.64 to −0.02)
Curative	LVA or VLNT	14	481	CEV	SMD −0.30 (−0.53 to −0.07)
Curative	LVA or VLNT	9	378	CEC	SMD −0.33 (−0.57 to −0.09)
Curative	LVA or VLNT	14	487	Quality of life	SMD 2.60 (1.17–4.02)

ARM, axillary reverse mapping; LVA, lymphovenous anastomosis; VLNT, vascularized lymph node transfer; BCRL, breast cancer–related lymphedema; UEL, upper extremity lymphedema index; CEV, circumferential excess volume; CEC, circumferential excess circumference; OR, odds ratio; SMD, standardized mean difference; CI, confidence interval.

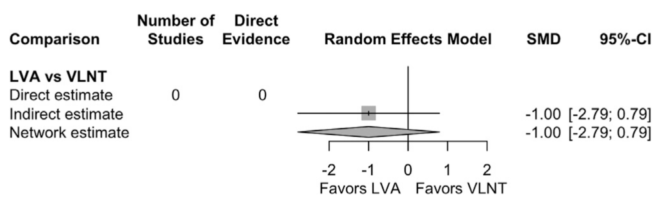
and shows a significant benefit in terms of prevention, treatment, and improvement of quality of life. These results are consistent with the results of individual studies published on the subject, as well as other meta-analyses or systematic reviews of the literature [117–121]. All these elements therefore favor the development of these techniques in routine practice, in order to offer the treatment of this major side effect of locoregional breast cancer treatment on a larger scale. The curative approach presents itself as an alternative to conservative treatment, which currently combines decongestive therapy and compression. The choice of indication and surgical technique depends on many factors and determines the functional outcome of this treatment.

The curative surgery as an alternative to conservative treatment

Unlike the conservative approach to lymphedema management, microsurgical interventions do not involve the same long-term costs or time-consuming process as decongestive physiotherapy or compression therapy. Conservative treatment requires good patient adherence to be effective, but long-term adherence to these treatments is often difficult, potentially compromising treatment effectiveness and leading to worsening of symptoms [122,123]. An American study published in 2021 compared the cost-effectiveness balance of the two microsurgical techniques and showed that VLNT is more advantageous in terms of



(a) Quality of life meta-analysis



(b) Quality of life : LVA versus VLNT

Fig. 5. Quantitative and network meta-analysis of the impact of curative techniques on quality of life. Panel 5(a) shows the individual data from each study and the overall effect of the two techniques combined according to scale. Panel 5(b) shows the indirect effect, *i.e.*, the comparison between the two techniques based on the LYMQOL scale, the one mostly reported.

cost and effectiveness than LVA in 97% of the simulations [124]. The authors also demonstrated that VLNT becomes unprofitable when its failure rate exceeds 43.8%, and that LVA becomes more cost effective than VLNT when its failure rate is below 21.4% [124]. Furthermore, a recent German study analyzed the cost–benefit balance of conservative approaches versus microsurgical interventions, and showed that the annual cost per patient is already lower in the case of microsurgical intervention from the 2nd year, suggesting an interest in terms of public health as well [125]. Similarly, another cost-effectiveness analysis showed that LVA had similar costs compared to the conservative therapy, but reduced the costs of ongoing conservative therapy and was therefore beneficial [126]. In addition to the benefit of stopping conservative treatment, it is important to note that the use of these techniques and the restoration of physiological function of the lymphatic system also reduce the incidence of infections (subcutaneous dermal hypodermitis) in the affected upper limb in both techniques [27,36,80,86,100,102,104,111]. As reported above, the risks of curative microsurgical techniques appear to be low, therefore favoring the development of those techniques in clinical practice.

Limits of the secondary lymphatic reconstruction

However, secondary lymphatic reconstruction has its limits. First, there are limitations due to the use of the curative microsurgical approach to BCRL, namely the availability of technical support with an appropriate microscope to suture vessels smaller than 0.5 mm, the dedicated operative time, and operators trained in this surgery. Furthermore, the treatment of BCRL (and lymphdema in general) is multidisciplinary and this type of approach must be integrated into a structure that already includes a quality care pathway for this pathology. On the other hand, there are also limits because these are currently non-standardized techniques. For LVA, there is no consensus on the timing, location, and number of anastomoses, and these parameters vary between different studies evaluating this type of technique. This variability in surgical procedures is even more prominent for VLNT, where the donor site, recipient site, number of lymph nodes, association with immediate breast reconstruction, and other parameters differ significantly between published studies.

The role of surgical prevention

Although secondary lymphatic reconstruction can sometimes reduce and/or successfully treat BCRL, it is not the only approach to reduce BCRL burden in breast cancer survivors. In fact, in recent decades, initial breast cancer management strategies have evolved significantly. The goal of achieving an optimal oncological outcome while minimizing short- and long-term functional impact has led to the evaluation and validation of therapeutic de-escalation in axillary surgery. In the context of surgical de-escalation, the replacement of ALND with SLNB has reduced, though not eliminated, the risk of BCRL, with an incidence approximately four times lower after SLNB (5.6%; 6.1%–7.9%) than ALND (19.9%; 13.5%–28.2%) [12]. SLNB has, in the last decades, replaced ALND in many cases, both in upfront surgeries and after neoadjuvant systemic treatments [127]. In addition, complementary ANLD after positive SLNB is also decreasing, and the development of the targeted axillary dissection technique – which consists of a marked initially positive lymph node excision and SLNB – after neoadjuvant treatment is also accumulating evidence and is becoming established as standard practice. [128]. In fact, evidence suggests that axillary surgery has essentially a staging benefit and not a therapeutic one [129], especially for low axillary involvement pN0 and pN1, which represent 86%–96.5% of all non-metastatic breast cancers [130]. Finally, a growing body of published trials investigated the omission of axillary surgical staging in early invasive "low-risk" breast cancer, and showed that no axillary surgery was non-inferior to SLNB [131,132]

When ALND cannot be avoided, the micro- or macro-surgical preventive techniques described in this study can be used to further reduce the risk of BCRL. The findings presented in this study favor the use of preventive techniques to reduce BCRL risk without compromising oncological safety, and align with other reviews of the literature [133,134]. Furthermore, from an economic perspective, microsurgical preventive surgery has similar outcomes to curative approaches. Studies showed that LVA was cost-effective when performed during mastectomy and ALND, with or without adjuvant radiotherapy [135]. Similarly, the LyMPHA (LVA of disrupted lymphatic channels to the branches of the axillary vein, during ALND [15]) procedure was cost-effective in immediate lymphatic reconstruction [136]. Despite those favorable analyses, a United States health policy study by Rochlin et al. [137] highlighted that surgeon reimbursement remains insufficiently aligned with operative effort, thus partly explaining the limited dissemination of preventive microsurgery despite its favorable economic profile.

Overall, the complication profile identified in this analysis aligns with previously published data, with lymphatic reconstructive procedures generally associated with low morbidity. Adverse events were infrequent and predominantly minor in severity, with donor-site morbidity in vascularized lymph node transfer (VLNT) constituting the principal procedure-specific concern. Notably, no evidence of an increased risk of locoregional or distant oncologic recurrence attributable to lymphatic reconstruction was observed. These considerations should be integrated into preoperative planning and patient counseling regarding the anticipated benefits and potential risks of lymphatic reconstructive surgery.

Finally, it should be highlighted that other nonsurgical techniques have shown significant efficacy in reducing BCRL risk after ALND and should be considered as an alternative or complementary approach. For example, the wearing of a compression sleeve for 3 months after ALND surgery showed a reduction in BCRL with a hazard ratio of 0.61 in a randomized controlled trial [138].

Surgical technique choice and indication

Based on the available evidence, early integration of lymphatic reconstruction strategies should be considered a key component of breast cancer care in patients at high risk of BCRL. The authors of this article advocate for breast units to consider and integrate BCRL prevention and treatment strategies according to the available resources. In the preventive setting, non-surgical measures should be considered, such as compression sleeve and axillary surgery de-escalation when safely possible. Both preventive surgical techniques can be offered when axillary surgery is at risk of post-operative BCRL. To evaluate this risk, the type of axillary surgery is the primary consideration; however, other risk factors for BCRL may also be considered in the surgical planning process. The choice of technique also depends on the possibilities of the breast center and the availability of microsurgery. It is important to note that secondary lymphatic reconstruction utilizing microsurgical techniques can be performed in a specialized facility, while immediate lymphatic reconstruction with preventive LVA requires collaboration between breast and lymphatic surgeons or, alternatively, requires dual expertise. In the curative setting, although LVA and VLNT have demonstrated their effectiveness in the treatment of BCRL, the optimal implementation strategy for these procedures has not yet been established. The effectiveness of LVA depends on the presence of functional lymphatic channels and is therefore generally applicable to patients in the early stages of lymphedema [139]. In contrast, VLNT does not require fully functional lymphatic vessels, making it more suitable for patients with advanced BCRL [139]. As a result, the distribution of BCRL stages is unlikely to be comparable across LVA and VLNT cohorts in the underlying literature. Therefore, an accurate assessment of the stage of lymphedema is crucial. The diagnosis of lymphedema is based primarily on clinical examination and history, and the use of the ISL classification is recommended [13]. During preoperative evaluation, imaging tests, such as lymphoscintigraphy, can be performed to confirm or specify lymphatic involvement [13]. Finally, it is essential to exclude other causes of edema before initiating specific treatment [13]. Furthermore, secondary lymphatic reconstruction is sometimes performed simultaneously with secondary breast reconstruction using a free flap [31,34,93,105,113], and this element should be considered during surgical planning. The combination of the two techniques is possible and aims to immediately reduce the excess circumference/volume with LVA, while achieving long-term restoration of physiological function through VLNT [117]. A sequential approach has also been reported: in fact, some studies have evaluated the use of VLNT only after the failure of LVA [104,106], reflecting treatment escalation rather than crossover between immediate and delayed reconstruction strategies. Finally, taking into account the patient's preferences and their individual assessment of the benefit-risk balance is essential since to date no approach has shown its superiority.

Perspectives

The use of lymphatic reconstructive microsurgery is on the rise and is likely to see significant development in the coming years. As an example, the protocol for the prospective randomized controlled trial LYMPH [140] was published in 2025. This multicenter study compares the effectiveness of microsurgery (LVA and/or VLNT, potentially combined with liposuction) combined with complete decongestive therapy versus complete decongestive therapy alone in patients with BCRL. The primary objective is to evaluate the lymphedema-specific quality of life at 15 months. Secondary criteria include arm volume measurements, economic evaluations, and imaging at different times. Long-term follow-up is planned for up to 10 years after randomization. The study plans to recruit 280 patients across more than 20 sites worldwide [140]. There is also published data on the use of newly developed microsurgical robots, which could help reduce some limitations in the use of this surgery, such as operator fatigue and tremor. A recent study reports the use of these robots in lymphatic reconstruction in 204 LVAs, the vast majority of which involved BCRL, and highlighted the possible interest of this technology for this indication [141].

Beyond clinical efficacy and from an organizational standpoint, preventive surgical interventions may, in the future, be implemented in the majority of oncologic breast surgery centers, provided that the requisite technical expertise and training are established. In contrast, curative procedures, particularly VLNT, may be more appropriately referred to specialized centers. Such a tiered service model has significant implications for the structuring of healthcare networks but appears feasible when integrated into well-defined, multidisciplinary care pathways. Importantly, centers capable of performing LVA may provide both preventive and curative treatment strategies.

Strengths and limitations of this study

The work presented above represents a comprehensive and up-to-date review of the literature and a meta-analysis following a rigorous methodology. To our knowledge, this is the only meta-analysis that evaluates the impact of primary and secondary lymphatic reconstruction surgery on quality of life, as well as the only one that compares the LVA and VLNT techniques with each other through a network meta-analysis estimating the indirect effect. Given the absence of direct comparisons between the surgical techniques, this analysis does not support claims of superiority for any specific intervention. Instead, it demonstrates that the evaluated procedures are effective when compared with non-surgical approaches or standard-of-care management. However, this work has limitations, particularly the significant heterogeneity of the included studies. Indeed, the studies do not necessarily have the same inclusion criteria (severity and duration of BCRL evolution, sometimes even patients without BCRL), the same definition of BCRL, the techniques are heterogeneous, the follow-up durations are different, and the measures varied in terms of incidence, effectiveness (volume excess, perimeter, UEL index, but also other non-analyzable measures) or quality of life (several scales used). Moreover, in the curative setting, a possible bias is that some studies evaluated the use of VLNT only after LVA [104], which may reduce the interpretability of the estimated indirect effect. Some secondary lymphatic reconstructions are accompanied by a preliminary liposuction of the affected upper limb, and this is done in both techniques [80,101], which can bias the measurement of the therapeutic effect of the microsurgical technique itself. In addition, selection bias is also possible, as most included studies were observational and treatment allocation was not randomized. Indeed, in the curative setting, BCRL stage may have impacted the choice of the technique, as LVA is preferred when functional lymphatic channels were present and VLNT may be the only option considered for advanced lymphedema.

For LVA, the number of anastomosis differed between studies, as well as the modality of anastomosis (end-to-end, end-to-side, etc.). For VLNT, there may be a difference between the donor site and the number of lymph nodes transplanted. There are also a variety of subjective and objective measures in place to assess efficacy, such as subjective quality of life questionnaires, objective limb measurements, imaging such as lymphoscintigraphy, and clinical outcomes such as number of cellulitis episodes. Although helpful in summarizing the results, these results should be interpreted with scrutiny given the great amount of heterogeneity between the studies. Each of these diagnostic modalities has a different diagnostic focus and availability. There may be confounding bias on our results, from the impact of other treatments used than surgery, as radiotherapy that may have an impact on the evolution of lymphedema, or the use of medical treatment (it was not always described whether patients continued or discontinued the use of compression).

Conclusion

Despite advances in breast cancer treatment and management, lymphedema affects approximately one in five breast cancer survivors. Secondary lymphedema is a chronic complication of breast cancer treatment that remains difficult to successfully treat, although there are different ways and scientific evidence is growing in favor of implementation. On the one hand, surgical prevention is one way to reduce the incidence of BCRL when extensive axillary surgery is still needed, while microsurgical techniques are a very promising avenue to help control lymphedema and reduce the need for intensive compression therapy. As shown in this work, the data in the literature suggest that these are safe and effective techniques with a real impact on improving the lives of patients with this sequellary side effect. Therefore, the development and implementation of these techniques in routine practice should be an integral part of the surgical management of breast cancer. Since immediate and delayed lymphatic reconstruction involves microsurgical reconstruction of the smallest human vessels – with very low tolerance for error – it is necessary to train breast surgeons in these techniques and to develop multidisciplinary pathways, particularly with surgical specialties already mastering microsurgery of this caliber. In centers where microsurgery is not performed, the integration of axillary reverse mapping and other preventive non-surgical approaches could be an alternative to reducing the burden of BCRL in breast cancer survivors. Immediate lymphatic reconstruction or axillary reverse mapping may be most beneficial for high-risk patients undergoing axillary surgery, whereas delayed reconstruction should be tailored according to disease severity, residual lymphatic function, concomitant breast reconstruction, and donor-site risks.

Although this analysis does not identify a single superior technique, it provides high-level evidence that surgery in both preventive and curative settings is an effective and validated component of contemporary breast cancer care. These findings support the integration of surgical lymphatic interventions into standard practice and provide a benchmark to guide patient selection, technique choice, and future standardization of outcome reporting.

CRediT authorship contribution statement

Claire Zhang: Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft. **Massimo Lodi:** Conceptualization, Methodology, Software, Formal analysis, Resources, Writing – review & editing, Visualization, Supervision, Project administration, Funding acquisition.

Institutional review board statement

This study used publicly available data and was exempt from IRB review in accord with federal guidance and institutional policy.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the author(s) used Writefull (Netherlands, version 2025.31.0, writefull.com) for the purposes of language editing, as they are non-native English speakers. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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Declaration of competing interest

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Supplementary data

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