LUMEN ET VIRTUS
ISSN: 2177-2789

IMMEDIATE LYMPHATIC RECONSTRUCTION DURING AXILLARY DISSECTION FOR LYMPHEDEMA PREVENTION AFTER BREAST CANCER TREATMENT

RECONSTRUÇÃO LINFÁTICA IMEDIATA DURANTE DISSECÇÃO AXILAR PARA PREVENÇÃO DE LINFEDEMA APÓS TRATAMENTO DO CÂNCER DE MAMA

RECONSTRUCCIÓN LINFÁTICA INMEDIATA DURANTE DISECCIÓN AXILAR PARA PREVENCIÓN DE LINFEDEMA DESPUÉS DEL TRATAMIENTO DEL CÁNCER DE MAMA

https://doi.org/10.56238/levv17n63-039

Data de submissão: 30/06/2026 **Data de publicação:** 14/08/2026

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ABSTRACT

Introduction: Breast cancer-related lymphedema (BCRL) is a chronic complication of axillary lymph node dissection (ALND) that can impair upper-limb function, psychosocial well-being, and quality of life. Immediate lymphatic reconstruction (ILR) uses microsurgical lymphaticovenous bypass (LVB) during ALND to restore lymphatic drainage before clinical lymphedema develops. Objective: To evaluate the effectiveness, safety, technical feasibility, and methodological certainty of ILR for preventing BCRL after breast cancer treatment. Methods: A systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses principles. PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform were searched for recent human studies. Randomized and nonrandomized comparative studies, prospective cohorts, and clinically informative case series were eligible. Risk of bias was assessed with RoB 2 and ROBINS-I, and certainty of evidence was evaluated using GRADE. Results and Discussion: Twenty studies were included. Most observational studies reported lower BCRL incidence after

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technically successful ILR, commonly between 4% and 12%, compared with approximately 20%–50% in contemporaneous or historical ALND controls. Preliminary randomized evidence also favored ILR, but another prospective pragmatic study found no significant adjusted difference. Technical success depended on lymphatic visualization, recipient-vein availability, microsurgical expertise, body mass index, and operative anatomy. Oncologic recurrence patterns did not indicate an evident axillary safety signal, although follow-up was insufficient for definitive oncologic conclusions. Heterogeneous diagnostic thresholds, variable surveillance duration, selection bias, incomplete blinding, and attrition reduced confidence in pooled estimates. Conclusion: ILR is a promising preventive microsurgical strategy that may substantially reduce BCRL after ALND. Its use is best supported in experienced multidisciplinary centers with standardized surveillance, while adequately powered multicenter randomized trials establish long-term effectiveness, oncologic safety, cost-effectiveness, and patient-selection criteria.

Keywords: Breast Neoplasms. Lymphedema. Lymphatic System. Anastomosis. Surgical.

RESUMO

Introdução: O linfedema relacionado ao câncer de mama (LRCM) é uma complicação crônica da dissecação de linfonodos axilares (DLNA) que pode prejudicar a função do membro superior, o bem-estar psicossocial e a qualidade de vida. A reconstrução linfática imediata (RLI) utiliza derivação linfaticovenosa microcirúrgica (DLV) durante a DLNA para restaurar a drenagem linfática antes do desenvolvimento do linfedema clínico. Objetivo: Avaliar a efetividade, segurança, viabilidade técnica e certeza metodológica da RLI para prevenir o LRCM após tratamento do câncer de mama. Métodos: Uma revisão sistemática foi conduzida de acordo com os princípios do Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Foram pesquisados PubMed, Scopus, Web of Science, a Biblioteca Cochrane, LILACS, ClinicalTrials.gov e a Plataforma de Registro de Ensaios Clínicos Internacionais da Organização Mundial da Saúde em busca de estudos recentes em humanos. Estudos comparativos randomizados e não randomizados, coortes prospectivas e séries de casos clinicamente informativas foram elegíveis. O risco de viés foi avaliado com RoB 2 e ROBINS-I, e a certeza da evidência foi avaliada usando GRADE. Resultados e Discussão: Vinte estudos foram incluídos. A maioria dos estudos observacionais relatou menor incidência de LRCM após RLI tecnicamente bem-sucedida, comumente entre 4% e 12%, em comparação com aproximadamente 20%–50% em controles DLNA contemporâneos ou históricos. Evidência randomizada preliminar também favoreceu a RLI, mas outro estudo prospectivo pragmático não encontrou diferença significativa ajustada. O sucesso técnico dependeu da visualização linfática, disponibilidade de veia receptora, experiência microcirúrgica, índice de massa corporal e anatomia operatória. Os padrões de recorrência oncológica não indicaram um sinal de segurança axilar evidente, embora o seguimento tenha sido insuficiente para conclusões oncológicas definitivas. Limiares diagnósticos heterogêneos, duração variável de vigilância, viés de seleção, mascaramento incompleto e atrito reduziram a confiança nas estimativas agrupadas. Conclusão: A RLI é uma estratégia microcirúrgica preventiva promissora que pode reduzir substancialmente o LRCM após DLNA. Seu uso é melhor apoiado em centros multidisciplinares experientes com vigilância padronizada, enquanto ensaios clínicos randomizados multicêntricos adequadamente alimentados estabeleçam a efetividade a longo prazo, a segurança oncológica, a custo-efetividade e os critérios de seleção de pacientes.

Palavras-chave: Neoplasias da Mama. Linfedema. Sistema Linfático. Anastomose Cirúrgica.

RESUMEN

Introducción: El linfedema relacionado con el cáncer de mama (LRCM) es una complicación crónica de la disección de ganglios linfáticos axilares (DGLA) que puede afectar la función del miembro superior, el bienestar psicosocial y la calidad de vida. La reconstrucción linfática inmediata (RLI) utiliza un bypass linfaticovenoso microquirúrgico (BLV) durante la DGLA para restaurar el drenaje linfático antes del desarrollo del linfedema clínico. Objetivo: Evaluar la efectividad, seguridad, viabilidad técnica y certeza metodológica de la RLI para prevenir el LRCM después del tratamiento del cáncer de mama. Métodos: Se realizó una revisión sistemática de acuerdo con los principios de Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Se buscaron en PubMed, Scopus, Web of Science, la Biblioteca Cochrane, LILACS, ClinicalTrials.gov y la Plataforma de Registro Internacional de Ensayos Clínicos de la Organización Mundial de la Salud estudios recientes en humanos. Fueron elegibles estudios comparativos aleatorizados y no aleatorizados, cohortes prospectivas y series de casos clínicamente informativas. El riesgo de sesgo se evaluó con RoB 2 y ROBINS-I, y la certeza de la evidencia se evaluó utilizando GRADE. Resultados y Discusión: Se incluyeron veinte estudios. La mayoría de los estudios observacionales reportaron menor incidencia de LRCM después de RLI técnicamente exitosa, comúnmente entre 4% y 12%, en comparación con aproximadamente 20%–50% en controles DGLA contemporáneos o históricos. La evidencia aleatoria preliminar también favoreció la RLI, pero otro estudio prospectivo pragmático no encontró diferencia significativa ajustada. El éxito técnico dependió de la visualización linfática, la disponibilidad de vena receptora, la experiencia microquirúrgica, el índice de masa corporal y la anatomía operatoria. Los patrones de recurrencia oncológica no indicaron una señal de seguridad axilar evidente, aunque el seguimiento fue insuficiente para conclusiones oncológicas definitivas. Los umbrales diagnósticos heterogéneos, la duración variable de la vigilancia, el sesgo de selección, el enmascaramiento incompleto y la deserción redujeron la confianza en las estimaciones agrupadas. Conclusión: La RLI es una estrategia microquirúrgica preventiva prometedora que puede reducir sustancialmente el LRCM después de la DGLA. Su uso está mejor respaldado en centros multidisciplinarios experimentados con vigilancia estandarizada, mientras que ensayos clínicos aleatorizados multicéntricos adecuadamente diseñados establezcan la efectividad a largo plazo, la seguridad oncológica, la rentabilidad y los criterios de selección de pacientes.

Palabras clave: Neoplasias de la Mama. Linfedema. Sistema Linfático. Anastomosis Quirúrgica.

1 INTRODUCTION

BCRL is a chronic accumulation of protein-rich interstitial fluid resulting from disruption or functional insufficiency of upper-extremity lymphatic drainage after breast cancer treatment.[1] It can cause swelling, heaviness, discomfort, recurrent infection, restricted movement, and clinically meaningful deterioration in daily functioning.[1] Population-level evidence confirms that its incidence remains substantial despite contemporary reductions in axillary surgical morbidity.[1] ALND is the most important treatment-related risk factor because it interrupts multiple collecting lymphatics and removes nodal drainage pathways.[2] Regional nodal irradiation, greater numbers of excised or positive nodes, obesity, postoperative complications, and systemic treatment may increase this risk further.[2] These interacting factors produce marked clinical heterogeneity and complicate individual prediction of BCRL.[2]

Recent predictive models have attempted to integrate treatment variables with patient characteristics to support personalized surveillance.[3] External validation has nevertheless shown that discrimination and calibration can vary among populations, institutions, and outcome definitions.[3] Risk prediction therefore complements but does not replace prospective limb measurement and symptom assessment.[3] Current preventive care relies largely on education, exercise, weight management, skin protection, prospective surveillance, and early compression-based intervention.[4] These strategies can reduce progression when subclinical disease is detected but do not directly restore lymphatic channels transected during ALND.[4] Interest has consequently shifted toward preventive surgery performed at the time of axillary treatment.[4]

Axillary reverse mapping, selective lymphatic preservation, ILR, and preventive lymphatic microsurgery represent related approaches intended to reduce treatment-related lymphatic injury.[5] Among these, ILR is distinctive because it creates a new drainage route rather than relying solely on preservation of potentially vulnerable lymphatic structures.[5] The approach is biologically attractive for patients who require ALND and cannot avoid substantial axillary disruption.[5] During ILR, arm-draining lymphatics are identified and connected to one or more nearby venous branches under microscopic magnification.[6] LVB may be constructed with intussusception, end-to-end, end-to-side, or other supermicrosurgical configurations according to vessel caliber and anatomy.[6] Patency is generally evaluated intraoperatively by observing passage of a lymphatic tracer into the recipient vein.[6]

Successful implementation requires coordination between breast and reconstructive surgeons so that suitable lymphatics and recipient veins are preserved during oncologic dissection.[7] Program development also requires microsurgical equipment, trained personnel, appropriate tracer protocols, and longitudinal lymphedema surveillance.[7] Consequently,

feasibility and outcomes may differ considerably between high-volume specialist centers and institutions beginning their learning curve.[7] Early systematic evidence suggested a lower frequency of BCRL after ILR than after ALND alone.[8] However, much of that evidence consisted of small observational studies with variable follow-up and nonuniform diagnostic criteria.[8] These limitations made causal interpretation and generalization difficult.[8]

A subsequent systematic review and meta-analysis found a strong preventive signal but emphasized the limited number of controlled studies.[9] Differences in baseline risk, radiotherapy exposure, successful bypass construction, and loss to follow-up were important sources of uncertainty.[9] The apparent magnitude of benefit therefore could not be separated completely from selection and ascertainment effects.[9] Another meta-analysis similarly associated ILR with reduced secondary lymphedema while identifying important methodological weaknesses.[10] Few studies used randomized allocation, blinded outcome assessment, prespecified objective thresholds, or sufficiently long follow-up to capture delayed BCRL.[10] These weaknesses remain important because treatment-associated lymphedema may emerge several years after ALND.[10]

Contemporary clinical discussion has increasingly focused on standardization, durability, and the patients most likely to benefit.[11] Proposed priorities include uniform definitions of technical success, objective preoperative baselines, standardized postoperative time points, and reporting of unsuccessful or aborted procedures.[11] Long-term evaluation of bypass patency and oncologic outcomes is also necessary before ILR can be considered routine care.[11] Updated systematic evidence continues to show generally favorable outcomes while revealing wide variation in measured incidence and follow-up completeness.[12] The literature also contains reports of higher late BCRL frequencies and studies without statistically significant adjusted benefits.[12] These discordant findings require interpretation alongside the more favorable institutional series.[12]

Recent pooled analyses have strengthened the estimated association between ILR and reduced BCRL after ALND.[13] Nevertheless, statistical heterogeneity and reliance on nonrandomized data constrain the certainty and transportability of the estimates.[13] The clinical meaning of pooled relative effects also depends on each center's underlying ALND-associated risk.[13] Meta-analytic evidence published in 2025 further supports a preventive effect but identifies inconsistent diagnostic thresholds and follow-up intervals.[14] The studies also differ in lymphatic mapping methods, anastomotic techniques, surgeon experience, radiotherapy, and use of compression.[14] Such variability prevents designation of a single optimal protocol.[14]

A broader synthesis of preventive lymphatic surgery indicates that favorable pooled findings remain sensitive to study design and comparator selection.[15] Concurrent controls generally provide more credible estimates than historical cohorts, particularly when surveillance protocols change over time.[15] Randomization is preferable because successful completion of ILR may itself select patients with more favorable anatomy or operative circumstances.[15] Randomized evidence has begun to address these concerns but remains limited by sample size and interim follow-up.[16] Observational evidence therefore remains clinically informative but requires structured risk-of-bias appraisal and cautious grading of certainty.[16] A contemporary systematic review must integrate these complementary forms of evidence while distinguishing statistical association from proven causality.[16]

2 OBJECTIVES

2.1 MAIN OBJECTIVE

To systematically evaluate the effectiveness and safety of ILR performed during ALND for the prevention of BCRL after breast cancer treatment.

2.1 SECONDARY OBJECTIVES

1. To compare the incidence and severity of BCRL after ILR with those observed after ALND without lymphatic reconstruction.
2. To examine technical feasibility, procedural success, operative considerations, and factors associated with unsuccessful ILR.
3. To evaluate functional, quality-of-life, bioimpedance, limb-volume, and patient-reported outcomes.
4. To assess postoperative complications, oncologic recurrence patterns, and the available evidence concerning oncologic safety.
5. To appraise risk of bias, heterogeneity, evidence certainty, research limitations, and priorities for future clinical practice and investigation.

3 METHODOLOGY

This systematic review was structured according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses principles. The review question was defined using population, intervention, comparison, outcome, and study-design criteria: patients undergoing ALND for breast cancer; ILR performed during the same operation; ALND without ILR or an appropriate historical comparator; subsequent BCRL and related outcomes; and

randomized, nonrandomized, cohort, or clinically informative case-series designs. A systematic-review design was selected because the rapidly expanding literature includes heterogeneous surgical techniques and both randomized and observational evidence.

PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform were searched from January 1, 2021, through July 31, 2026. Search concepts combined breast neoplasms, axillary dissection, lymphedema, immediate lymphatic reconstruction, preventive lymphatic surgery, lymphaticovenous anastomosis, and LVB, with spelling and terminology variants. No language restriction was applied. The protocol allowed extension to January 2016 if fewer than 10 eligible studies were identified, but this extension was unnecessary.

Eligible studies enrolled patients undergoing ALND for breast malignancy and reported clinical outcomes after attempted or completed ILR. Studies were retained despite small samples when they supplied clinically relevant effectiveness, feasibility, safety, or patient-reported information; small sample size was recorded as a limitation rather than used as an automatic exclusion criterion. Studies treating established lymphedema, reports without separable breast cancer data, commentaries, and purely technical publications without eligible outcomes were excluded. Human evidence was prioritized, and animal or in vitro studies were to be reported in separate tables; none met the eligibility criteria. Overlapping cohorts were reconciled by retaining the most informative nonduplicative report, although publications from the same program could remain eligible when they evaluated clearly distinct primary outcomes or follow-up periods.

Two reviewers independently screened titles, abstracts, and full texts, with disagreements resolved by consensus and third-reviewer adjudication when necessary. They independently extracted study design, setting, enrollment period, population, body mass index (BMI), cancer treatment, mapping technique, ILR configuration, technical-success rate, comparator characteristics, follow-up, BCRL definition, limb measurements, bioimpedance spectroscopy (BIS), quality of life (QoL), complications, recurrence, and adjusted effect estimates. Duplicate records were removed before screening, and the selection process was documented in a PRISMA flow structure.

Randomized controlled trials (RCTs) were evaluated with the revised Cochrane risk-of-bias tool, RoB 2, and nonrandomized intervention studies with ROBINS-I. QUADAS-2 was prespecified for diagnostic-accuracy studies, but no included study required its application. Certainty of evidence was evaluated with GRADE across risk of bias, inconsistency, indirectness, imprecision, and publication bias. Because definitions, time points, and comparator structures were heterogeneous, findings were synthesized narratively with

emphasis on absolute event rates, adjusted estimates, and concordance between objective and patient-reported outcomes.

4 RESULTS

The search identified 1,622 records. After removal of 428 duplicates, 1,194 titles and abstracts were screened, and 1,071 records were excluded. Full texts were assessed for 123 reports, of which 103 were excluded because of an overlapping cohort without a distinct outcome (n=29), absence of ILR (n=24), treatment of established lymphedema (n=19), technical or descriptive content without eligible clinical outcomes (n=18), or inadequate outcome data (n=13). Twenty studies were included in the qualitative synthesis.

Table 1

Characteristics and principal findings of the included studies

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Herremans et al. (2021)	The study evaluated 132 patients undergoing ALND, including 76 treated with ILR and 56 managed without reconstruction.	BCRL occurrence, procedural feasibility, and changes across a five-year institutional learning period were evaluated.	ILR was feasible and associated with fewer BCRL events, although selection effects and the surgical learning curve influenced interpretation.
Johnson et al. (2021)	The cohort comprised patients in whom ILR was attempted during ALND, with 32 technically successful reconstructions available for outcome analysis.	Transient and persistent BCRL, complications, and short-term clinical follow-up were reported.	Technically successful ILR was associated with a low persistent BCRL frequency, but the small cohort and short follow-up limited certainty.
Cook et al. (2021)	Thirty-three patients underwent ALND with ILR in a prospective institutional series without a concurrent untreated control group.	Persistent BCRL, transient edema, BMI, nodal yield, and treatment-related factors were assessed.	Persistent BCRL occurred in approximately 9%, and higher BMI and greater nodal disruption appeared clinically relevant.
Ozmen et al. (2022)	Patients undergoing ALND with or without simplified lymphatic microsurgical preventive healing approach reconstruction were compared.	BCRL was monitored through clinical assessment and lymphedema index measurements derived from BIS.	Preventive reconstruction was associated with lower biometrically detected BCRL, although the nonrandomized design remained vulnerable to confounding.
Weinstein et al. (2022)	Sixty-six patients with completed ILR were compared with a retrospective ALND control cohort	Clinical BCRL, adjuvant-treatment	BCRL was reported in 6% after ILR versus 44% in controls, suggesting

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	under an institutional surveillance protocol.	exposure, and postoperative follow-up outcomes were analyzed.	substantial benefit but possible historical-control bias.
Guzzo et al. (2022)	The study followed 137 breast cancer patients after ALND and ILR to evaluate recurrence patterns.	Local, regional, axillary, and distant cancer recurrence were recorded during follow-up.	No axillary recurrences were observed, providing preliminary reassurance without establishing long-term oncologic noninferiority.
Le et al. (2023)	Outcomes were compared between 252 patients with completed ILR and 29 patients in whom reconstruction was attempted but could not be performed.	BCRL incidence and adjusted associations between reconstruction status and subsequent disease were examined.	BCRL occurred in 4.8% after completed ILR versus 24.1% after unsuccessful reconstruction, although anatomical selection was an important concern.
Levy et al. (2023)	A longitudinal ILR cohort was evaluated for approximately four years after ALND and reconstruction.	Late BCRL, clinical surveillance findings, and durability of prevention were examined.	A comparatively high late BCRL incidence demonstrated that early favorable outcomes may not persist uniformly during extended follow-up.
Granoff et al. (2023)	The study included 186 patients undergoing unilateral ALND with ILR in a high-volume microsurgical program.	BCRL incidence, anatomical characteristics, treatment factors, and four-year clinical outcomes were evaluated.	The overall BCRL frequency was approximately 9%, supporting durable benefit while identifying anatomical and treatment-related residual risk.
Chung et al. (2023)	Twenty-six patients with successful ILR were compared with 183 patients receiving ALND without reconstruction.	BCRL incidence, time-to-event outcomes, and adjusted hazard estimates were reported.	ILR showed a lower numerical BCRL frequency, but the adjusted association did not reach conventional statistical significance.
Deldar et al. (2023)	Patients undergoing ALND with prophylactic LVB were compared with patients managed without preventive reconstruction.	BCRL development, limb findings, and comparative postoperative outcomes were assessed.	Prophylactic LVB was associated with a marked absolute reduction in BCRL, although nonrandom treatment allocation created serious confounding potential.
Coriddi et al. (2023)	Participants undergoing ALND were randomized to ILR or no lymphatic	Cumulative BCRL, BIS,	ILR reduced cumulative BCRL and improved several objective and

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	reconstruction in a preliminary RCT analysis.	compression use, indocyanine green (ICG) lymphography, and QoL were evaluated.	patient-centered outcomes, but longer complete follow-up was required.
Haravu et al. (2024)	Patients with successful ILR were compared with patients whose planned reconstruction was aborted and with historical controls.	Technical success, BCRL, anatomical feasibility, smoking, age, and BMI were analyzed.	Successful ILR produced favorable outcomes, while aborted procedures identified an anatomically and clinically higher-risk subgroup.
Le et al. (2024)	Seventy-seven consecutive ILR recipients were compared with 94 matched patients who underwent ALND without reconstruction.	Two-year BCRL incidence and adjusted associations with radiotherapy and other treatments were assessed.	ILR was associated with substantially lower BCRL, while regional irradiation remained an important residual risk factor.
Médor et al. (2024)	Patients received ILR with LVB during completion ALND and underwent structured postoperative surveillance.	BCRL incidence, clinical measurements, symptoms, and QoL outcomes were reported.	The study found a low BCRL incidence and generally favorable patient-reported outcomes, although no randomized comparator was available.
Jakub et al. (2024)	A prospective pragmatic cohort compared 131 patients scheduled for ILR with 99 patients undergoing ALND alone, with 115 completed reconstructions.	Relative arm-volume change, graded BCRL, binary thresholds, and propensity-adjusted outcomes were examined.	No statistically significant adjusted benefit was identified, challenging the magnitude and consistency of effects reported by earlier cohorts.
Cho et al. (2025)	A nine-year institutional cohort compared approximately one-quarter of 370 ALND patients receiving prophylactic LVB with patients receiving ALND alone.	BCRL, limb circumference, symptoms, subsequent therapeutic LVB, and clinical predictors were evaluated.	Prophylactic LVB was associated with lower BCRL and fewer subsequent interventions, but temporal and selection biases remained possible.
Yakaback et al. (2025)	Seventeen women underwent prospective ILR and long-term clinical and patient-reported follow-up.	BCRL-free survival, limb findings, and lymphedema-specific QoL were assessed.	Most participants remained free of BCRL at 42 months, but the sample was too small to provide precise comparative estimates.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Hassan et al. (2025)	A multicenter cohort included 172 patients receiving ILR across six hospitals in a regional health system.	Cumulative BCRL, compression use, complications, and demographic differences were evaluated.	The overall incidence was 7%, but substantially higher risk among Black patients revealed unresolved disparities despite ILR.
Kim et al. (2025)	Sixteen patients receiving ILR were compared with 57 patients undergoing ALND without ILR during a median follow-up of approximately 37 months.	BCRL incidence and adjusted time-to-event estimates were analyzed.	ILR was associated with 6.3% BCRL versus 24.6% without reconstruction and retained an adjusted protective association.

Source: Prepared by the authors.

5 RESULTS AND DISCUSSION

Herremans *et al.* provided an early comparative institutional experience in which ILR was associated with fewer BCRL events than ALND alone.[17] The study was clinically valuable because it documented program evolution over five years and showed that preventive microsurgery can be incorporated into oncologic workflows.[17] Its nonrandomized allocation, changing expertise, and potential temporal differences between groups nevertheless produced moderate-to-serious confounding risk.[17] Johnson *et al.* reported low persistent BCRL after technically successful ILR and demonstrated that the procedure could be completed without an obvious increase in short-term complications.[18] Only a subset of attempted reconstructions was technically successful, making feasibility an important component of the apparent treatment effect.[18] Short follow-up and the absence of a robust concurrent comparator prevented strong conclusions regarding delayed BCRL.[18]

Cook *et al.* observed persistent BCRL in approximately 9% of 33 ILR recipients and identified BMI and axillary treatment burden as relevant residual-risk considerations.[19] Their findings support the concept that bypass construction mitigates but does not eliminate the biological effects of extensive lymphatic injury.[19] The small sample and single-arm design generated imprecision and prevented separation of ILR effects from institutional surveillance and early treatment.[19] Ozmen *et al.* used BIS-derived measurements to detect subclinical as well as clinically evident changes after preventive reconstruction.[20] The favorable comparison supports objective longitudinal surveillance rather than dependence on symptoms or circumference alone.[20] However, nonrandom allocation and incomplete uniformity in treatment exposures limited causal inference.[20]

Weinstein *et al.* reported BCRL in 6% of ILR recipients compared with 44% in a retrospective control group.[21] This large absolute difference is clinically compelling and

remained directionally consistent with several other institutional reports.[21] The magnitude may have been inflated by historical-control differences in surveillance, radiotherapy, supportive care, and referral patterns.[21] Guzzo *et al.* addressed oncologic safety by monitoring recurrence after ILR and reported no axillary recurrences during the available follow-up.[22] The occurrence of distant and other recurrences without an axillary concentration provides preliminary reassurance that bypass construction did not create an evident regional failure pattern.[22] The study was not designed or powered as a noninferiority trial, so rare or delayed oncologic effects cannot be excluded.[22]

Le *et al.* compared successful ILR with attempted but unsuccessful reconstruction and found BCRL incidences of 4.8% and 24.1%, respectively.[23] The unsuccessful group offers a clinically proximate comparator because all patients were considered for the same procedure at the same institution.[23] Nevertheless, inability to identify usable lymphatics or veins may mark more extensive disruption, adverse anatomy, or higher baseline risk, creating confounding by technical feasibility.[23] Levy *et al.* reported a substantially higher late BCRL burden than many short-duration studies.[24] That finding indicates that preventive efficacy should not be judged exclusively at 6 or 12 months, particularly when radiotherapy-associated fibrosis and progressive lymphatic dysfunction may emerge later.[24] Attrition and the characteristics of patients remaining under long-term observation may also influence late incidence estimates.[24]

Granoff *et al.* reported an overall BCRL incidence near 9% across extended follow-up in a large unilateral ILR cohort.[25] The study suggested that durable risk reduction is possible while emphasizing persistent variation related to anatomical and treatment characteristics.[25] Its detailed institutional experience improved clinical interpretability, but the lack of randomized controls preserved residual confounding.[25] Chung *et al.* found a lower numerical BCRL frequency after ILR, although the adjusted time-to-event estimate was not statistically significant.[26] This result illustrates how favorable absolute differences can become uncertain when event numbers are small and confidence intervals are wide.[26] The study therefore contributes to the preventive signal without establishing an independent effect.[26]

Deldar *et al.* reported a marked reduction in BCRL among patients undergoing prophylactic LVB compared with patients receiving ALND alone.[27] The magnitude suggests that maintenance of a lymphatic outflow route may provide clinically meaningful protection in high-risk axillary surgery.[27] Nonrandom allocation, potential baseline imbalance, and a relatively small treated group placed the result at serious risk of confounding.[27] Coriddi *et al.* supplied the most influential randomized evidence and found cumulative BCRL of approximately 9.5% after ILR versus 32% without reconstruction in the preliminary analysis.[28]

Concordant improvements in BIS, compression use, ICG lymphography, and selected QoL measures strengthened the biological coherence of the finding.[28] Incomplete long-term follow-up and declining numbers at later assessment points produced imprecision and justified continued trial surveillance.[28]

Haravu *et al.* showed that successful ILR was associated with substantially less BCRL than aborted reconstruction and historical management.[29] The study also identified smoking, BMI, age, and the number or quality of visualized lymphatics as possible influences on technical completion and outcomes.[29] Comparisons based on successful versus aborted surgery require caution because anatomical feasibility is a post-allocation factor closely related to prognosis.[29] Le *et al.* subsequently reported two-year BCRL in approximately 10% of ILR recipients compared with 38% of matched controls.[30] Matching and adjusted analysis improved comparability, and the persistent association after accounting for major treatment factors supported an independent preventive effect.[30] Regional irradiation remained clinically important, indicating that a patent bypass may not fully compensate for postoperative tissue injury.[30]

Médor *et al.* found a BCRL incidence of approximately 7.7% following ILR during completion ALND.[31] The inclusion of symptoms and QoL complemented objective measurements and reflected outcomes that matter directly to patients.[31] Without randomized controls, however, improvement could partly reflect structured follow-up, early intervention, or favorable selection.[31] Jakub *et al.* provided a necessary counterpoint through a prospective pragmatic comparison that found no significant difference in arm-volume or categorical BCRL outcomes after adjusted analysis.[32] Its real-world design and prespecified surveillance increased applicability beyond highly selected microsurgical series.[32] Nonrandomized treatment selection and crossover between planned and completed ILR remained limitations, but the neutral result substantially reduces confidence in uniformly large benefits.[32]

Cho *et al.* evaluated a nine-year institutional experience and observed BCRL in 8.7% after prophylactic LVB versus 20.1% without it.[33] Better circumference and symptom outcomes and fewer later therapeutic bypass procedures supported clinical relevance beyond a single diagnostic threshold.[33] The long enrollment interval created possible temporal bias because oncologic treatment, surgical experience, and surveillance practices may have changed.[33] Yakaback *et al.* prospectively followed 17 women and estimated 88% BCRL-free survival at 42 months.[34] The prospective design and long observation period were strengths, but only two events produced extremely imprecise estimates.[34] Nonsignificant QoL differences should therefore be interpreted as inconclusive rather than evidence of equivalence.[34]

Hassan *et al.* reported a cumulative BCRL incidence of 7% across six hospitals, demonstrating that ILR can be disseminated beyond a single specialist center.[35] Black patients experienced a substantially higher incidence than White patients despite reconstruction, suggesting that access, comorbidities, treatment intensity, biology, surveillance, or structural inequities require investigation.[35] Frequent compression use and postoperative breast complications also showed that ILR does not remove the need for comprehensive survivorship care.[35] Kim *et al.* reported BCRL in 6.3% after ILR versus 24.6% after ALND alone at a median follow-up of approximately three years.[36] The adjusted hazard estimate remained protective, supporting benefit after accounting for measured covariates.[36] The small ILR group generated wide confidence intervals and limited assessment of uncommon complications or effect modification.[36]

Across studies, most estimates favored ILR, but their magnitude varied according to comparator selection, surveillance duration, diagnostic threshold, radiotherapy exposure, and technical success.[37] Historical-control comparisons generally produced larger effects than pragmatic concurrent comparisons, consistent with inflation from secular and selection biases.[37] Small-study effects and preferential publication of favorable specialist-center experiences also remain plausible.[37] Evidence-based risk-reduction recommendations support prospective surveillance, patient education, physical activity, and early intervention regardless of whether preventive microsurgery is performed.[38] ILR should therefore be considered an additional risk-reduction component rather than a substitute for established multidisciplinary care.[38] Standardized baseline and follow-up measurement is particularly important because early subclinical abnormalities may occur without symptoms.[38]

Contemporary axillary-surgery guidance emphasizes de-escalation whenever oncologically appropriate, since avoiding ALND prevents lymphatic injury more reliably than reconstructing it.[39] ILR is most relevant when ALND remains indicated because of nodal burden, treatment context, or inability to use a less extensive axillary approach.[39] Routine adoption should be linked to surgeon competency, prospective outcome auditing, reporting of aborted procedures, and oncologic governance.[39] International consensus recommendations likewise support integrated prevention involving surgeons, rehabilitation professionals, nurses, physiotherapists, and lymphedema specialists.[40] Under GRADE, certainty was judged moderate for short-term efficacy from preliminary randomized evidence, low for overall comparative effectiveness, and very low for long-term oncologic safety and subgroup effects.[40] Future multicenter RCTs should use standardized diagnostic criteria, blinded outcome assessment, complete follow-up beyond five years, economic evaluation, and equitable recruitment.[40]

6 CONCLUSION

ILR performed during ALND is a biologically plausible and increasingly studied strategy for preventing BCRL. Most included studies reported lower BCRL incidence after technically successful reconstruction, and preliminary randomized evidence supports a clinically important preventive effect.

The certainty of this conclusion remains limited by the predominance of nonrandomized studies, small samples, historical controls, heterogeneous definitions, and incomplete long-term surveillance. A well-conducted pragmatic cohort with adjusted analysis found no significant benefit, demonstrating that effects may be smaller or less consistent than early institutional reports suggest.

Technical success depends on the availability of suitable arm-draining lymphatics and recipient veins, appropriate preservation during ALND, microsurgical expertise, and multidisciplinary coordination. Patients should be informed that reconstruction may be aborted and that successful ILR reduces risk rather than guaranteeing prevention.

Available recurrence data have not demonstrated an evident axillary oncologic safety signal. These observations remain preliminary because existing studies were not adequately powered or followed long enough to establish oncologic noninferiority or exclude rare harms.

ILR may reasonably be offered to selected high-risk patients in experienced centers with standardized measurement, rehabilitation, and prospective auditing. Definitive implementation requires multicenter randomized evidence addressing long-term BCRL, bypass durability, patient-reported outcomes, disparities, oncologic safety, and cost-effectiveness.

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