



Immediate lymphatic reconstruction for breast cancer-related lymphedema: current status and challenges

Yuki Otsuki, Takashi Nuri, Koichi Ueda

Department of Plastic and Reconstructive Surgery, Osaka Medical and Pharmaceutical University, Takatsuki City, Osaka, Japan

Correspondence to: Yuki Otsuki, MD, PhD. Department of Plastic and Reconstructive Surgery, Osaka Medical and Pharmaceutical University, 2-7 Daigakucho, Takatsuki City, Osaka 569-8686, Japan. Email: yuuki.otsuki@ompu.ac.jp.

Comment on: Coriddi M, Dayan J, Bloomfield E, *et al.* Efficacy of Immediate Lymphatic Reconstruction to Decrease Incidence of Breast Cancer-related Lymphedema: Preliminary Results of Randomized Controlled Trial. *Ann Surg* 2023;278:630-7.

Keywords: Immediate lymphatic reconstruction (ILR); lymphedema; lymphaticovenous anastomosis; lymphedema microsurgical prevention healing approach (LYMPHA); breast cancer

Submitted Dec 21, 2023. Accepted for publication Feb 21, 2024. Published online Mar 20, 2024.

doi: 10.21037/gs-23-527

View this article at: <https://dx.doi.org/10.21037/gs-23-527>

Breast cancer-related lymphedema (BCRL) after axillary lymph node dissection (ALND) has reportedly reduced patients' quality of life (1,2). In recent years, immediate lymphatic reconstruction (ILR) has been reported as a prophylactic surgical treatment for BCRL, in which lymphatic vessels are identified immediately after ALND and anastomosed to a nearby vein. In 2009, Boccardo *et al.* reported the concept of ILR as the lymphedema microsurgical prevention healing approach (LYMPHA) and showed positive results with postoperative lymphoscintigraphy (3). Some retrospective studies of the effectiveness of ILR have recently been published (4,5). In a recent report with a relatively large number of cases, Le *et al.* reported that in 252 patients treated with ILR, BCRL occurred in 4.8% of patients, compared with 24.1% in 29 patients not treated with ILR, indicating that ILR was effective in preventing BCRL (6). Hill *et al.* also conducted a systematic review and meta-analysis of the efficacy of ILR for BCRL. The systematic review analyzed 11 articles and found that 24 of 417 patients (5.7%) who underwent ILR developed BCRL. Furthermore, a meta-analysis showed that 6 of 90 patients (6.7%) in the ILR group developed BCRL, whereas 17 of 50 patients (34%) in the control group developed it, for a risk ratio of 0.22 in the ILR group (7). However, Levy *et al.* found that, in a retrospective study of 90 patients with more than 4 years of follow-up after ILR, the incidence of BCRL was 31.1% in

the ILR group and 33.3% in the non-ILR group, with no significant difference (8). In their discussion, they noted that the definition and diagnosis of lymphedema varied greatly among studies, and no consensus has been reached on the diagnostic criteria for lymphedema.

In addition, for ILR to develop into a widely used treatment throughout the world, one must not only ensure its efficacy and safety, but also solve the issue of insurance coverage for ILR. La-Anyane *et al.* reported that more than half of the main insurance companies in the United States that have a public coverage statement deny ILR coverage (9). Furthermore, Rochlin *et al.* indicated that the current relative value unit (RVU) allocation undervalues ILR, introducing inefficiency into breast cancer operations when combined with ILR. The RVUs assigned to ILR should be re-evaluated to protect patient access to this procedure (10). Thus, from these perspectives, more studies with high-quality evidence, such as randomized controlled trials (RCTs) of the efficacy and safety of ILR are desirable.

Coriddi *et al.* conducted an RCT to evaluate the efficacy of ILR (11). They randomized 152 breast cancer patients who had undergone ALND 1:1 to two groups: ILR or non-ILR. They calculated the relative volume change (RVC) by measuring arm circumference from the wrist to axilla at 4-cm intervals in patients enrolled in this RCT, and they defined BCRL as a case in which the value changed by 10% or more between preoperative and postoperative periods of

12, 18, and 24 months. Bioimpedance, indocyanine green (ICG) lymphangiography, and 4 patient-reported outcome measures (PROMs) were also used as secondary outcomes. They used the Lymphedema Quality of Life (LYMQOL) and the Upper Limb Lymphedema-27 (ULL-27) to quantify subjective symptoms of BCRL, and the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R) and the Beck Anxiety Inventory (BAI) to measure depression and anxiety. The cumulative incidence of BCRL was significantly lower in the ILR group than in the control group. In the ILR group, the cumulative incidence of BCRL was 2.0% [95% confidence interval (CI): 0.16–9.3%] at 12 months, 9.5% (95% CI: 3.0–21%) at 18 months, and 9.5% (95% CI: 3.0–21%) at 24 months, compared to 18% (95% CI: 9.0–30%) at 12 months, 24% (95% CI: 12–37%) at 18 months, and 32% (95% CI: 17–47%) at 24 months in the control group. In the secondary outcomes, the average change in bioimpedance values from baseline was also smaller in the ILR group than in the control group, but this difference was not statistically significant. ICG lymphangiography-based lymphedema stage at 12 and 24 months was compared between the ILR and control groups using the Fisher exact test. It showed substantially and significantly fewer cases of dermal back flow in the ILR group at 12 months postoperatively. Patient-reported lymphedema symptoms assessed using lymphedema-specific PROMs did not differ significantly between the ILR and control groups over time, but there was a trend toward a better function score in the ILR group. ULL-27 physical domain scores and LYMQOL function domain scores worsened in both groups over time, although the ILR group showed less changes from baseline scores than the control group. This report is beneficial by providing meaningful objective and subjective data, however it is limited in that it is not blinded, as the operative details were recorded in the operative report and made available to the patients.

Another issue that was not discussed in this RCT was whether ILR increases lymph node metastasis and distant metastasis. Although a few publications regarding the oncological safety of ILR have been published (12,13), they were all retrospective studies, and obtaining high-level evidence about not only the efficacy of ILR, but also its oncological safety is required.

In conclusion, the study undertaken by Coriddi *et al.* (11) is a rare randomized controlled study in this field and makes a substantial contribution to evaluating the efficacy of ILR. Further high-quality studies are expected in the near future to determine whether ILR is an effective intervention.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Gland Surgery*. The article has undergone external peer review.

Peer Review File: Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-527/prf>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-527/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Shen A, Qiang W, Zhang L, et al. Risk Factors for Breast Cancer-Related Lymphedema: An Umbrella Review. *Ann Surg Oncol* 2024;31:284-302.
2. McNeely ML, Courneya KS, Al Onazi MM, et al. Upper Limb Morbidity in Newly Diagnosed Individuals After Unilateral Surgery for Breast Cancer: Baseline Results from the AMBER Cohort Study. *Ann Surg Oncol* 2023;30:8389-97.
3. Boccardo F, Casabona F, De Cian F, et al. Lymphedema microsurgical preventive healing approach: a new technique for primary prevention of arm lymphedema after mastectomy. *Ann Surg Oncol* 2009;16:703-8.
4. Weinstein B, Le NK, Robertson E, et al. Reverse

- Lymphatic Mapping and Immediate Microsurgical Lymphatic Reconstruction Reduces Early Risk of Breast Cancer-Related Lymphedema. *Plast Reconstr Surg* 2022;149:1061-9.
5. Johnson AR, Fleishman A, Granoff MD, et al. Evaluating the Impact of Immediate Lymphatic Reconstruction for the Surgical Prevention of Lymphedema. *Plast Reconstr Surg* 2021;147:373e-81e.
 6. Le NK, Liu L, Jesus Cruz R, et al. Efficacy of Immediate Lymphatic Reconstruction in Prevention of Breast Cancer-Related Lymphedema. *Ann Plast Surg* 2023;90:S363-5.
 7. Hill WKF, Deban M, Platt A, et al. Immediate Lymphatic Reconstruction during Axillary Node Dissection for Breast Cancer: A Systematic Review and Meta-analysis. *Plast Reconstr Surg Glob Open* 2022;10:e4291.
 8. Levy AS, Murphy AI, Ishtihar S, et al. Lymphatic Microsurgical Preventive Healing Approach for the Primary Prevention of Lymphedema: A 4-Year Follow-Up. *Plast Reconstr Surg* 2023;151:413-20.
 9. La-Anyane O, Alba BE, Harmon KA, et al. United States insurance coverage of immediate lymphatic reconstruction. *J Surg Oncol* 2024;129:584-91.
 10. Rochlin DH, Coriddi MR, Nelson JA, et al. Immediate Lymphatic Reconstruction and the Current Value Problem. *Ann Surg* 2023;277:e1197-9.
 11. Coriddi M, Dayan J, Bloomfield E, et al. Efficacy of Immediate Lymphatic Reconstruction to Decrease Incidence of Breast Cancer-related Lymphedema: Preliminary Results of Randomized Controlled Trial. *Ann Surg* 2023;278:630-7.
 12. Guzzo HM, Valente SA, Schwarz GS, et al. Oncologic safety of axillary lymph node dissection with immediate lymphatic reconstruction. *Breast Cancer Res Treat* 2022;196:657-64.
 13. Lin YS, Kuan CH, Lo C, et al. Is Immediate Lymphatic Reconstruction on Breast Cancer Patients Oncologically Safe? A Preliminary Study. *Plast Reconstr Surg Glob Open* 2023;11:e5385.

Cite this article as: Otsuki Y, Nuri T, Ueda K. Immediate lymphatic reconstruction for breast cancer-related lymphedema: current status and challenges. *Gland Surg* 2024;13(3):455-457. doi: 10.21037/gs-23-527