**Efficacy of Immediate Lymphatic Reconstruction in Prevention of Breast Cancer–Related Lymphedema**

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**Introduction:** Breast cancer–related lymphedema (BCRL) is a chronic condition that can negatively affect the quality of life of breast cancer survivors. Immediate lymphatic reconstruction (ILR) at the time of axillary lymph node dissection is emerging as a technique for the prevention of BCRL. This study compared the incidence of BCRL in patients who received ILR and those who were not amenable to ILR.

**Methods:** Patients were identified through a prospectively maintained database between 2016 and 2021. Some patients were deemed nonamenable to ILR due to a lack of visualized lymphatics or anatomic variability (eg, spatial relationships or size discrepancies). Descriptive statistics, independent t test, and Pearson χ² test were used. Multivariable logistic regression models were created to assess the association between lymphedema and ILR. A loose age-matched subsample was created for subanalysis.

**Results:** Two hundred eighty-one patients were included in this study (252 patients who underwent ILR and 29 patients who did not). The patients had a mean age of 53 ± 12 years and body mass index of 28.6 ± 6.8 kg/m². The incidence of developing lymphedema in patients with ILR was 4.8% compared with 24.1% in patients who underwent attempted ILR without lymphatic reconstruction (P < 0.001). Patients who did not undergo ILR had significantly higher odds of developing lymphedema compared with those who had ILR (odds ratio, 10.7 [3.2–36.3], P < 0.001; matched OR, 14.2 [2.6–77.9], P < 0.001).

**Conclusions:** Our study showed that ILR was associated with lower rates of BCRL. Further studies are needed to determine which factors place patients at highest risk of developing BCRL.

**Key Words:** immediate lymphatic reconstruction, breast cancer–related lymphedema, axillary lymph node dissection

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Breast cancer–related lymphedema (BCRL) is caused by the chronic accumulation of interstitial protein-rich fluid due to the disruption of lymphatic flow either from the breast cancer disease itself or from its treatment.¹ This condition affects up to 45% of breast cancer survivors after surgery, and risk factors include invasive cancer, axillary lymph node dissection (ALND), postmastectomy radiation therapy, age older than 65 years, and body mass index (BMI) greater than 35 kg/m².²–³ The current standard of care is symptom management and palliative therapy, which typically entail lifelong interventions that can be beneficial but not curative.⁴ These include decongestive therapies, such as compression bandaging, pneumatic pumps, and physical therapy, which are time consuming, pose substantial difficulties with patient compliance, and are problematic for postsurgical quality of life.⁵

As such, BCRL can prolong a patient’s journey with breast cancer and contribute additional costs to our healthcare systems.⁶,⁷ Therefore, recent techniques have arisen to help mitigate the incidence of BCRL, substituting prevention where curative strategies have previously fallen short.⁵ Immediate lymphatic reconstruction (ILR) establishes an alternative pathway for lymphatic fluid to flow by connecting lymph vessels to venules at the time of ALND and tumor extirpation.⁸–¹¹ Immediate lymphatic reconstruction is gradually becoming accepted as the standard of care in the surgical community, as a growing body of literature has observed its association with lower rates of BCRL.¹² These includes studies by our group, which previously have demonstrated a reduced incidence of BCRL with ILR.¹³

Unfortunately, there are a subset of patients who have anatomic variations that make them unsuitable for ILR at the time of ALND. Therefore, this study aimed to compare the incidence of lymphedema in patients who received ILR and those who were not amenable at the time of ALND.

**METHODS**

A prospectively maintained database of patients referred to our multidisciplinary lymphedema clinic for ILR at the time of ALND between 2016 and 2021. The ALNDs were done in conjunction with the breast surgeon in efforts to preserve and restore as many functional lymphatics as possible. Patients were considered nonamenable for ILR if they lacked visualized lymphatics or had anatomic variations between identified lymphatics and preserved venules (eg, spatial relationships or size discrepancies). The techniques used for ILR have been described in a prior publication from the authors’ institution.¹⁴ Patients were excluded if they had preoperative ipsilateral lymphedema. Preoperative lymphedema was determined based on patient reported symptoms and elevated circumferential limb measurement compared with the opposite arm (>5% difference). The development of BCRL was assessed through patient reported symptoms, circumferential limb measurements performed by certified lymphedema therapists (>5% difference between affected and unaffected extremity), and bioimpedance spectroscopy (L-Dex score change of ±10 units).¹³

**Statistical Analysis**

Descriptive statistics for sociodemographic and clinical risk factors and complications of surgery were conducted, with significance determined by independent t test and Pearson χ² test. The sociodemographic and clinical risk factors include age, BMI, race, tobacco use, neoadjuvant/adjuvant radiation and chemotherapy, laterality of immediate lymphatic reconstruction, and type of mastectomy. The complications that were explored include seromas, hematomas, infection, nodal and locoregional recurrence, distant metastasis, mortality, development of lymphedema, and return to the operating room within the first 30 days. Bivariate and multivariable logistic regression models were created to assess the association between lymphedema and ILR. Crude and adjusted odds ratio (OR) and 95% confidence interval were calculated, and the fit of the final multivariable model was determined by Hosmer and Lemeshow goodness-of-fit test. To account for the high

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mismatch in the number of patients having undergone ILR and those who had not, a loose age-matched subsample was created for subanalysis. Significance was defined as a $P$ value $\leq 0.05$. The data were analyzed using SAS 9.4, accessed from the University of South Florida.

**RESULTS**

Our study included a total of 281 patients, with 252 patients who underwent ILR and 29 patients who did not. The matched subanalysis included 122 patients in the ILR group and 29 patients in the group undergoing attempted ILR without lymphatic reconstruction. The average age of the study population was 53 ± 12 years and average BMI was 28.6 ± 6.8 kg/m². Most patients were White (77% in the ILR group and 75.9% in the no ILR group; Table 1). In the ILR group, most patients received adjuvant radiation therapy (81.8%) and neoadjuvant chemotherapy (91.7%). The no ILR group also had a majority of the patients receiving adjuvant radiation (82.8%) and neoadjuvant chemotherapy (82.8%). For both the study population and subanalysis, there were no statistically significant differences in the sociodemographic and clinical risk factors of receiving ILR compared with not (Table 1).

There were no significant differences observed regarding surgical and oncologic complications between the 2 groups aside for infections treated with oral antibiotics (0.4% vs 10.3%, $P<0.01$, for ILR and no ILR groups, respectively; Table 2). The incidence of developing lymphedema was significantly higher in the group that did not undergo ILR (12.4% vs 0.0%, $P<0.001$, for ILR and no ILR groups, respectively; Table 3).

### Table 1. Sociodemographic and Clinical Risk Factors of Receiving ILR and Undergoing Attempted ILR Without Lymphatic Reconstruction

| Variable                        | ILR     | No ILR   | $P$      | Subanalysis $P$ |
|---------------------------------|---------|----------|----------|-----------------|
| Age (years)                     | 52.5 ± 12.3 | 54.4 ± 11.2 | 0.426     | 0.803           |
| BMI                             | 28.5 ± 6.8  | 28.9 ± 6.6  | 0.778     | 0.680           |
| Race                            |          |          |          |                 |
| White                           | 194 (77.0) | 22 (75.9)  |          |                 |
| Black                           | 25 (9.9)   | 5 (17.2)   |          |                 |
| Asian                           | 9 (3.6)    | 0 (0.0)    |          |                 |
| Hispanic                        | 13 (5.2)   | 0 (0.0)    |          |                 |
| Other                           | 11 (4.4)   | 2 (6.9)    |          |                 |
| Tobacco use                     |          |          | 0.082    | 0.113           |
| Nonsmoker                       | 161 (63.9) | 24 (82.8)  |          |                 |
| Former smoker                   | 68 (27.0)  | 5 (17.2)   |          |                 |
| Current smoker                  | 23 (9.1)   | 0 (0.0)    |          |                 |
| Neoadjuvant XRT                 | 11 (4.4)   | 2 (6.9)    | 0.632    | 0.620           |
| Adjuvant XRT                    | 206 (81.8) | 24 (82.8)  | 0.893    | 1.000           |
| Neoadjuvant chemotherapy        | 231 (91.7) | 24 (82.8)  | 0.165    | 0.146           |
| Adjuvant chemotherapy           | 64 (25.4)  | 9 (31.0)   | 0.512    | 0.312           |
| Laterality of ILR               |          |          | 0.544    | 0.617           |
| Right                           | 127 (50.4) | 12 (41.4)  |          |                 |
| Left                            | 123 (48.8) | 17 (58.6)  |          |                 |
| Bilateral                       | 2 (0.8)    | 0 (0.0)    |          |                 |
| Type of mastectomy              |          |          | 0.425    | 0.573           |
| Unilateral                      | 105 (41.8) | 9 (31.0)   |          |                 |
| Bilateral                       | 98 (39.0)  | 15 (51.7)  |          |                 |
| Lumpectomy                      | 16 (6.4)   | 3 (10.3)   |          |                 |
| ALND only                       | 31 (12.4)  | 2 (6.9)    |          |                 |
| Scar/skin resection only        | 1 (0.4)    | 0 (0.0)    |          |                 |

The bolded values indicate statistical significance.

IV, intravenous.

### Table 2. Complications of Undergoing and Not Undergoing ILR

| Variable                         | ILR     | No ILR   | $P$  | Subanalysis $P$ |
|----------------------------------|---------|----------|------|-----------------|
| Return to operating room         | 4 (1.6) | 1 (3.5)  | 0.422| 0.578           |
| Seroma                           | 9 (3.6) | 1 (3.5)  | 1.000| 1.000           |
| Hematoma                         | 2 (0.8) | 0 (0.0)  | 1.000| 1.000           |
| Infection—oral antibiotics       | 1 (0.4) | 3 (10.3) | 0.004| 0.007           |
| Infection—IV antibiotics         | 0 (0.0) | 1 (3.5)  | 0.103| 0.192           |
| Nodal recurrence                 | 3 (1.2) | 2 (6.9)  | 0.085| 0.167           |
| Locoregional recurrence          | 5 (2.0) | 1 (3.5)  | 0.483| 0.578           |
| Distant metastasis               | 18 (7.1)| 3 (10.3) | 0.464| 0.701           |
| Mortality                        | 8 (3.2) | 0 (0.0)  | 1.000| 1.000           |
| Lymphedema                       | 12 (4.8)| 7 (24.1) | 0.001| 0.006           |

The bolded values indicate statistical significance.

### Table 3. Bivariate and Multivariable Logistic Regression for Development of Lymphedema in Patients Who Did and Did Not Undergo ILR

| Variable                   | Unadjusted OR | $P$  | Adjusted OR | $P$  |
|----------------------------|---------------|------|-------------|------|
| Lymphedema                 | 6.4 (2.3–17.8)| <0.001| 10.7 (3.2–36.3)| <0.001|
| Age-matchehted lymphedema  | 5.9 (1.8–19.2)| 0.003| 14.2 (2.6–77.9)| 0.002|

The bolded values indicate statistical significance.
lymphedema was 4.8% for patients receiving ILR and 24.1% for patients without ILR ($P < 0.01$; Table 2).

When controlling for covariates, patients who did not undergo immediate lymphatic reconstruction had an OR of 10.7 (3.2–36.3, $P < 0.001$) for developing lymphedema. When the patients were matched by age, the patients without immediate lymphatic reconstruction had an OR of 14.2 (2.6–77.9, $P = 0.002$; Table 3).

**DISCUSSION**

Breast cancer related lymphedema is a debilitating disease that can have a substantial negative impact on quality of life for breast cancer survivors. Our study demonstrated that ILR was associated with a lower rate of BCRL (4.8% compared with 24.1% in patients without ILR). Patients who did not undergo immediate lymphatic reconstruction had significantly higher odds of developing lymphedema compared with those who had ILR (OR, 10.7). When the patients were matched by age, the patients without immediate lymphatic reconstruction still had higher odds of developing lymphedema (OR, 14.2).

The 24.1% incidence of BCRL in patients undergoing ALND with intraoperatively identified axillary lymphatic and venous anatomy preventing ILR is still much improved relative to a previously reported incidence of 44% from a retrospective control study from our institution. Here, we hypothesize this improvement demonstrates the potential value of having the plastic surgeon work in a collaborative fashion with the oncologic team during ALND. It has been observed that when present, functional lymphatic anatomy in close proximity to, but uninvolved with, axillary nodal contents can be reliably identified and preserved through reverse lymphatic mapping of the affected extremity. The increased focus on lymphatic anatomy that arises from a combined team surgical approach to the axilla results in a less traumatic extirpation of nodal tissue and can often translate to a greater preservation of arm draining lymphatic channels.

Immediate lymphatic reconstruction seems to be a safe procedure as the complications rates remained similar between the ILR and no ILR groups. The only significantly different complication were infections treated by oral antibiotics. We hypothesize that this may be related to the fact that BCRL has been associated with increased infection risk given the no ILR group had a significantly higher incidence of BCRL.

Some limitations of this study include a small sample size and a large mismatch of patients within each study group. We did attempt to minimize this with our matched subgroup analysis. Considerations for matching were made based on additional variables including chemotherapy and radiation exposure, but this resulted in too few control patients, which would have led to an meaningless subanalysis. Furthermore, there were no significant differences between radiation and chemotherapy in either the study population or subanalysis group, so we do not feel that this matching would have been necessary to create a representative control. Further studies are needed to determine which factors place patients at highest risk of developing BCRL. In the meantime, these patients will need close postoperative monitoring to help risk stratify this cohort of patients. Finally, randomized controlled trials are needed to fully elucidate the incremental benefit of ILR for breast cancer survivors, and we look forward to engaging with these ongoing studies.

In conclusion, our study demonstrated that immediate lymphatic reconstruction is associated with lower rates of BCRL. Breast cancer–related lymphedema is a devastating disease, and any effort toward prevention should be attempted. Immediate lymphatic reconstruction is a safe and effective procedure that can help improve many patients’ quality of life.

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