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ORIGINAL ARTICLE
Reconstructive

Immediate Lymphatic Reconstruction May Decrease the Incidence of Lymphedema in Patients Undergoing Axillary Lymph Node Dissection

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Background: Approximately one-third of patients undergoing axillary lymph node dissection (ALND) for breast cancer will develop breast cancer–related lymphedema (BCRL). To prevent BCRL, immediate lymphatic reconstruction (ILR) has been proposed, whereby lymphatics cut during the ALND are anastomosed to adjacent veins to restore lymphatic drainage. As evidence for ILR grows, the aim of this study was to investigate its efficacy at our institution.

Methods: This prospective single-center study included 17 women undergoing ALND with ILR. Our primary outcome was the incidence of BCRL, diagnosed using a greater than 10% relative difference in arm volume. Use of compression therapy was also followed. Our secondary outcome was patient-reported outcome measures, determined by the validated Lymphedema Quality of Life (LYMQOL-Arm) survey. Postoperatively, patients were followed up at regular intervals for a minimum of 18 months.

Results: The median age of included patients was 49 (interquartile range [IQR] 46–58). The average follow-up time was 34.4 months (range 18–42 mo). Two patients met the criteria for BCRL. Patients with BCRL had a significantly higher median arm volume difference of 27.5% (IQR 21.8%–33.2%) versus 4.2% (IQR 1.6%–7%; $P = 0.02$). Three patients used compression to control symptoms. Patients without lymphedema scored better in several domains of the LYMQOL-Arm survey, including function, appearance, and overall quality of life; however, these results did not meet statistical significance.

Conclusions: ILR in patients undergoing ALND is associated with a low incidence of BCRL. Our study is one of the first to use patient-reported outcome measures to study ILR. *(Plast Reconstr Surg Glob Open 2025; 13:e6543; doi: 10.1097/GOX.0000000000006543; Published online 12 February 2025.)*

INTRODUCTION

Breast cancer–related lymphedema (BCRL) is a challenging yet common complication that can develop following axillary lymph node dissection (ALND).[1] A recent systematic review from our institution found the incidence of BCRL to be as high as 34% in patients undergoing ALND, whereas some individual studies have found rates up to 60%.[2,3] Typically presenting as heavy arm swelling, BCRL can have a very negative impact on patients, resulting in pain, joint stiffness, and cellulitis, ultimately impacting functional status and reducing overall quality of life.[3–8]

Given the negative impacts of BCRL, coupled with an increased focus on quality of life due to the steadily rising rates of survival following breast cancer treatment, there is interest in both the treatment and prevention of BCRL. Prophylactic techniques such as immediate lymphatic reconstruction (ILR) using lymphovenous anastomosis (LVA) completed at the time of ALND is one such technique that has been developed to prevent BCRL.[2,9] This procedure involves the identification and preservation of lymphatic vessels during the ALND and subsequent anastomosis of these vessels into a branch of a regional vein, allowing for ongoing lymphatic drainage through existing lymphatic channels that would have otherwise been no longer functional.[10] Although the initial use of LVA

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focused on treating existing lymphedema, ILR was first described by Boccardo et al[10] as far back as 2009. Since then, interest in the procedure has grown, with recent studies finding a reduction in the rate of BCRL by as much as 67%, while also finding it to be cost-effective.[2,9–15] These initial studies have sparked ongoing interest in the procedure and the need for further research into its efficacy.

Our primary aim of this study was to investigate the efficacy of ILR in preventing BCRL at a single tertiary care center. An additional aim was to investigate differences in patient-reported outcome measures (PROMs) using the Lymphedema Quality of Life (LYMQOL-Arm) survey, as PROMs have been rarely studied in ILR literature thus far.[12,16]

Takeaways

Question: Does immediate lymphatic reconstruction (ILR) following axillary lymph node dissection (ALND) prevent or reduce breast cancer–related lymphedema?

Findings: Our prospective cohort study of 17 breast cancer patients undergoing ILR following ALND demonstrated an 11% lymphedema rate.

Meaning: ILR following ALND may reduce the incidence of breast cancer–related lymphedema.

METHODS

Study Design and Patient Selection

The protocol for this single-center prospective cohort study was approved by our institutional review board under the ethics ID HREBA.CC-22-0176. Our study population included adult women with lymph node–positive breast cancer who were undergoing a planned completion ALND at our center in Calgary, Alberta, Canada, from October 2020 to March 2022. No patients were excluded if they agreed to undergo ILR. Patients were approached by their surgical oncologist about the procedure and referred to a plastic surgeon (C.T.O.) for further information and consent. Demographic information, cancer diagnosis, operative details, limb measurements, compression use, and patient-reported outcomes were collected for all patients included in the study.

ILR Procedure

All ALNDs were carried out by a surgical oncologist. The plastic surgeon was present throughout the oncological portion of the procedure to first identify and then preserve lymphatics before completing the LVA. Identification of prospective lymphatic channels for the LVA was carried out using dual lymphatic mapping before the ALND with both indocyanine green (ICG) injected into the ipsilateral first dorsal web space and Patent Blue dye injected into the ipsilateral inner upper arm. The standard procedure for ICG was to inject 1 mL and use a gentle milking technique to move the dye up the arm. Approximately 15 minutes later, the SPY Portable Handheld Imager (Stryker, MI) device was used to visualize lymphatic channels through the skin as they entered the axillary basin.

The surgical oncologist then performed the ALND, during which any lymphatic channels identified by either the SPY Portable Handheld Imager or direct visualization of Patent Blue dye were cut and tagged using a hemoclip and a 5-mm piece of 3-0 Vicryl by the plastic surgeon. Microclamps were not used for this purpose due to the frequency of them becoming dislodged and leading to an incorrect surgical count.

Following the completion of the ALND, a branch of either the axillary vein or the thoracodorsal vein, if no suitable smaller vein was available, was identified for the LVA. From there, the LVA was completed under an operative microscope using either an end-to-end or end-to-side intussusception technique with as many lymphatic channels of adequate length as were available into the same vein branch using either a 9-0 or 10-0 nylon suture. Patency was confirmed by Patent Blue Dye and ICG flow across the anastomosis.[17]

Follow-up and Measurements

All patients were seen by both their surgical oncologist and their plastic surgeon at a routine 2- to 4-week initial follow-up visit. From there, any complications were followed up as required through additional visits. For patients receiving adjuvant chemotherapy and/or radiation, this was started 2 to 4 weeks postoperatively, or once their incisions were well healed, and sequenced with chemotherapy before radiation. Bilateral arm measurements were collected at the time of their visits with their plastic surgeon at 4 cm intervals up each arm, from the wrist crease to the shoulder, using a flexible measuring tape (Fig. 1). Either 10 or 11 measurements were collected depending on the length of patients' arms. A truncated cone formula was then used to calculate bilateral limb volumes, and the difference in volume was converted to a percentage.[18] All patients were brought back for additional measurements at approximately 6-month intervals from their initial surgery. Patients were also asked to fill out the LYMQOL-Arm survey at each follow-up visit.[16] If the patient was referred to the lymphedema clinic by any practitioner, limb volumes were also collected from that source. Patients were followed up for a minimum of 18 months.

Diagnosis of BCRL

For our study, a greater than 10% relative limb volume difference between the operative and nonoperative limb was used to diagnose BCRL.[19] We have found that this is a practical and reproducible diagnostic method that is reasonably efficient and does not add additional cost to patient care. Along with these patients, any patients who went on to develop a subjective unilateral arm swelling or discomfort or clinically noticeable arm swelling that did not meet diagnostic cutoffs were referred to our local lymphedema clinic for further evaluation and treatment, which typically involves targeted physiotherapy and prolonged use of custom-fitted compression garments.

Outcomes

Our primary outcome was the incidence of BCRL in our ILR population, as determined by the number of patients who developed lymphedema based on the above

Fig. 1. An example of the setup for arm measurement collection. With the patient in a seated position, flexible measuring tapes were placed along both arms and held in place with tape. A second flexible measuring tape was then used to collect circumferential measurements at 4 cm intervals beginning at the wrist creases.

diagnostic criteria. The number of patients who went on to be referred to a lymphedema clinic for compression despite not meeting the greater than 10% difference in limb volume was also recorded. Our secondary outcome was differences in PROMs as determined by LYMQOL-Arm survey results between patients who developed lymphedema and those who did not.

Statistical Analysis

The Mann-Whitney U test and the Fisher exact test were used to compare demographic data. The Mann-Whitney *U* test was used to determine whether there were significant differences between lymphedema and nonlymphedema groups in terms of quality-of-life outcome measures. Survival plots were constructed using Kaplan–Meier survival analysis, with 95% confidence intervals. The survival curve was calculated as the time from surgery to the diagnosis of lymphedema. All statistical analyses were performed using Lifelines and SciPy libraries in Python (version 3.7.9).

RESULTS

Our study ultimately included 17 patients for whom demographic information is shown in Table 1. The median age of patients included in the study was 49.0 years of age (interquartile range [IQR] 46–58), with the most common diagnosis being unilateral invasive ductal carcinoma (71%). Fifteen patients received adjuvant radiation as part of their treatment. The median follow-up time was 34.4 months (IQR 32–37). The median number of LVAs per patient was 2.0 (IQR 2–3).

Two patients met limb volume diagnostic criteria for BCRL, with 16% and 39% volume increases compared with their contralateral arms. Their BCRL diagnoses were made at 5 and 21 months postoperatively, as shown in Figure 2. Kaplan–Meier survival analysis demonstrated that that the chance of lymphedema-free survival was 88% at 42 months (95% confidence interval: 0.61–0.97; Fig. 3). Both BCRL patients, along with 1 additional patient with subjective but not measurement-proven arm swelling, were referred to our local lymphedema clinic and underwent compression therapy.

Patients without lymphedema had a significantly lower difference in limb volume between their operative and nonoperative arms, with a median volume difference of 4.2% (IQR 1.6%–7%) compared with 27.50% (IQR 21.8%–33.2%; $P = 0.15$) for our patients with BCRL (Fig. 4).

All 17 participants completed the LYMQOL-Arm survey. Patients without BCRL scored slightly better than those with BCRL in 2 domains, including function (1.2 of 4 versus 1.6 of 4; $P = 0.17$) and appearance (1.2 of 4 versus 1.3 of 4; $P = 0.65$), as well as rated their overall quality of life higher (8 of 10 versus 7 of 10; $P = 0.42$). Both groups scored the same in the symptoms domain (1.6 of 4 versus 1.6 of 4; $P = 0.57$), whereas patients without BCRL scored slightly worse in the mood domain (1.6 of 4 versus 1.0 of 4; $P = 0.09$) (Figs. 5, 6).

DISCUSSION

Our prospective cohort study found the incidence of BCRL was 11% in patients who underwent ILR at the time of ALND. Median limb volume differences were significantly higher in patients with BCRL versus those without. Overall quality of life, function, and appearance were rated as better in patients without lymphedema. These findings are consistent with those published in recent literature and seem to be an overall reduction in the rate of BCRL compared with historical controls. Preliminary results of a randomized clinical trial at Memorial Sloan Kettering Cancer Center found a 9.7% lymphedema rate in patients who underwent ILR at the time of ALND compared with a rate of 32% in the control group.[12] A recent 4-year retrospective review of 90 patients who underwent ILR similarly demonstrated a 9% rate of BCRL.[14] Before these 2 publications, a systematic review and meta-analysis out of our own institution found a 6.7% rate of lymphedema in patients who underwent ILR in comparison to a rate of 34% in the control group who underwent ALND without ILR.[2]

The addition of radiation seems to significantly increase the rate of BCRL in patients undergoing ALND when compared with ALND alone, as demonstrated by a review by Johnson et al,[20] which found a BCRL rate of 33.4% in patients who underwent ALND and radiation compared with a rate of 14.1% in those who underwent ALND alone. As the majority of our patients also received

Table 1. Demographic Data

		Overall	No Lymphedema	Lymphedema	*P*
n		17	15	2	
Age, y, median [Q1, Q3]		49.0 [46.0, 58.0]	48.0 [45.5, 50.5]	61.5 [59.8, 63.2]	0.06
Diagnosis, n (%)	Metastatic adenocarcinoma of the axilla, presumed breast origin	2 (11.8)	2 (13.3)		1
	Unilateral ductal carcinoma in situ	1 (5.9)	1 (6.7)		
	Unilateral invasive ductal carcinoma	12 (70.6)	10 (66.7)	2 (100.0)	
	Unilateral invasive lobular carcinoma	1 (5.9)	1 (6.7)		
	Unilateral locally advanced inflammatory breast cancer	1 (5.9)	1 (6.7)		
Length of follow-up, median [Q1, Q3]		34.0 [32.0, 37.0]	36.0 [32.0, 38.5]	34.0 [34.0, 34.0]	0.7
Radiation, n (%)	Adjuvant	15 (88.2)	13 (86.7)	2 (100.0)	1
	Declined	2 (11.8)	2 (13.3)		
Chemotherapy, n (%)	Adjuvant	3 (17.6)	3 (20.0)		1
	Declined	3 (17.6)	3 (20.0)		
	Neoadjuvant	5 (29.4)	4 (26.7)	1 (50.0)	
	Neoadjuvant and adjuvant	6 (35.3)	5 (33.3)	1 (50.0)	
Endocrine therapy, n (%)	Adjuvant	9 (52.9)	7 (46.7)	2 (100.0)	0.603
	Declined	1 (5.9)	1 (6.7)		
	Neoadjuvant and adjuvant	1 (5.9)	1 (6.7)		
	No	6 (35.3)	6 (40.0)		
No. LVA anastomoses, median [Q1, Q3]		2.0 [2.0, 3.0]	2.0 [2.0, 3.0]	3.5 [3.2, 3.8]	0.7
BMI, n (%)	Nonobese (BMI < 30 kg/m^2)	11 (64.7)	9 (60.0)	2 (100.0)	0.515
	Obese (BMI > 30 kg/m^2)	6 (35.3)	6 (40.0)		
Clinical stage, n (%)	IIA	2 (11.8)	2 (13.3)		0.7
	IIB	4 (23.5)	4 (26.7)		
	IIIA	7 (41.2)	5 (33.3)	2 (100.0)	
	IIIC	1 (5.9)	1 (6.7)		
	Unstageable	3 (17.6)	3 (20.0)		
Complications, n (%)	Cellulitis	2 (11.8)	2 (13.3)		1
	None	15 (88.2)	13 (86.7)	2 (100.0)	

BMI, body mass index.

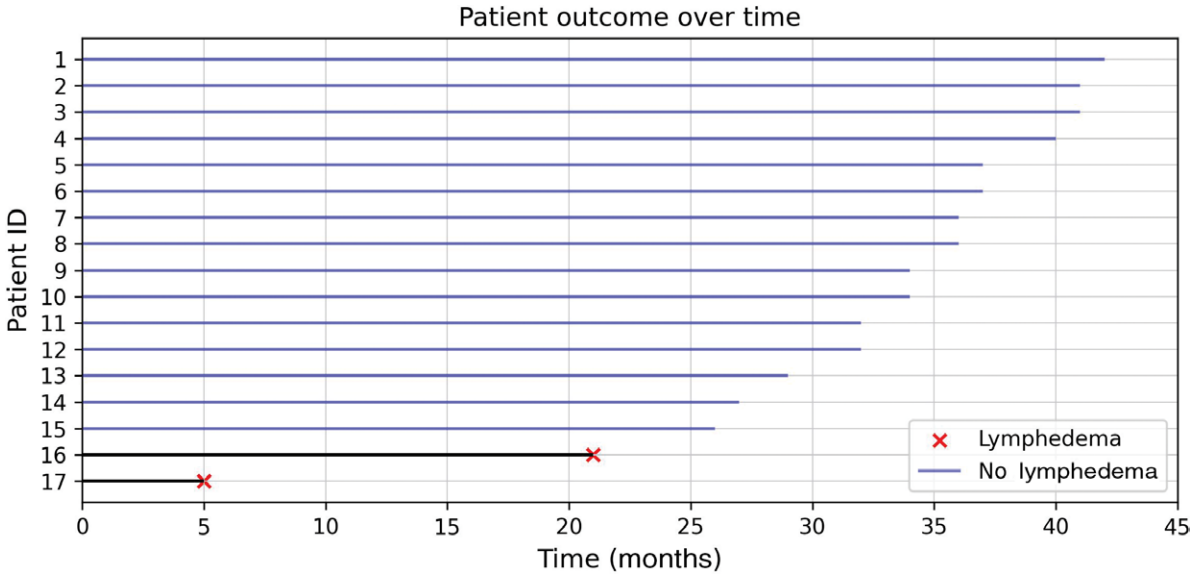

Fig. 2. Life history of lymphedema in patients receiving ILR. Two of 17 total patients developed lymphedema, at 5 and 21 months postoperatively.

radiation following ALND, they would fall into this higher risk group, further illustrating the efficacy of ILR in reducing rates of BCRL.

It is worth noting that although many recent publications have shown promise for ILR, a 2022 4-year retrospective review by Levy et al[21] did not find any difference in

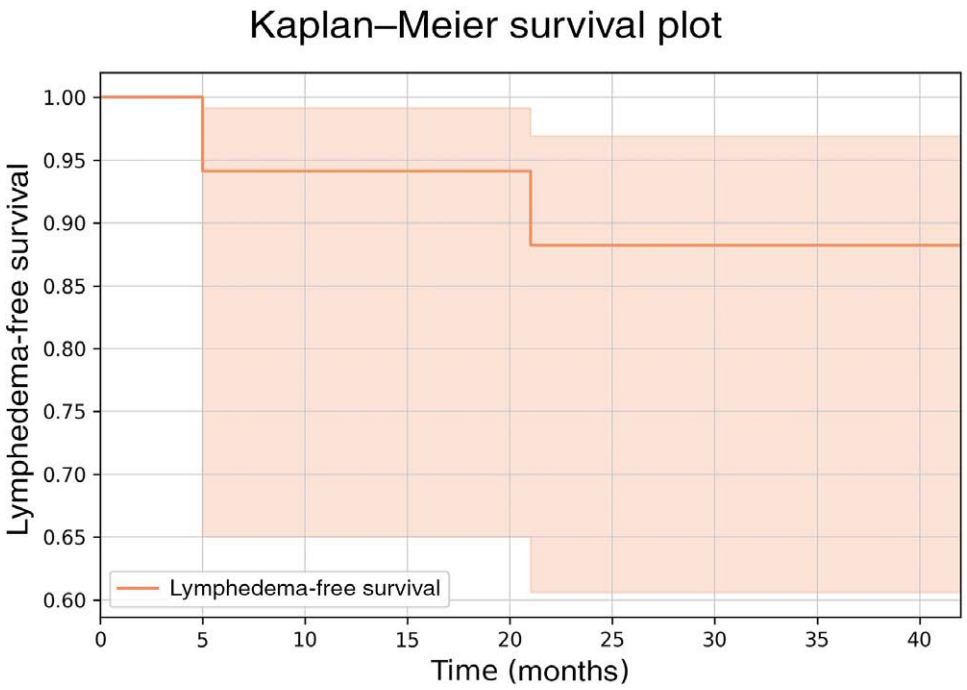

Fig. 3. Kaplan–Meier survival analysis demonstrated that patients undergoing ILR had an 88% chance of lymphedema-free survival at 42 months postoperatively (95% confidence interval: 0.61–0.97).

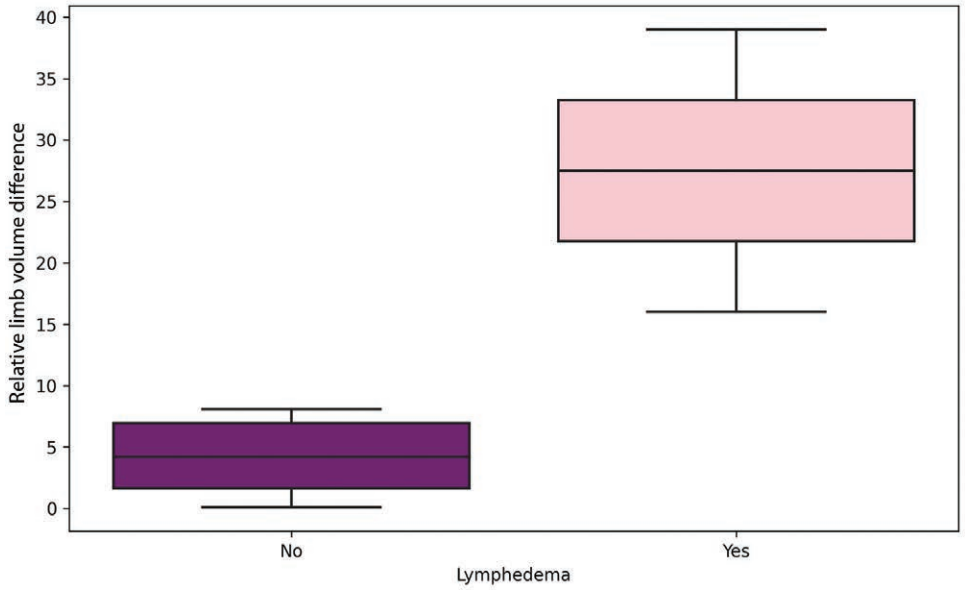

Fig. 4. Median differences in limb volume measurements.

lymphedema rates between patients undergoing ILR following ALND and those who did not. Although the follow-up time in this article was adequately long, the authors note that lymphedema was diagnosed clinically rather than based on objective measurements, which may have increased their diagnosis rate compared with other studies. As evidence mounts for IRL, it is critical to continue to publish all clinical results to better understand the efficacy of the procedure, and we commend the authors for publishing a negative study.

Despite a large volume of research surrounding BCRL, its diagnosis, particularly in the context of ILR, remains inconsistent. Our method of using a greater than 10% relative volume difference between sides postoperatively has been commonly used in the BCRL literature but may have been more accurate using a greater than 10% relative volume change from pre- and postoperative measurements.[19,22,23] A recent publication by Le et al[15] on the efficacy of ILR utilized a greater than 5% relative volume change to diagnose lymphedema

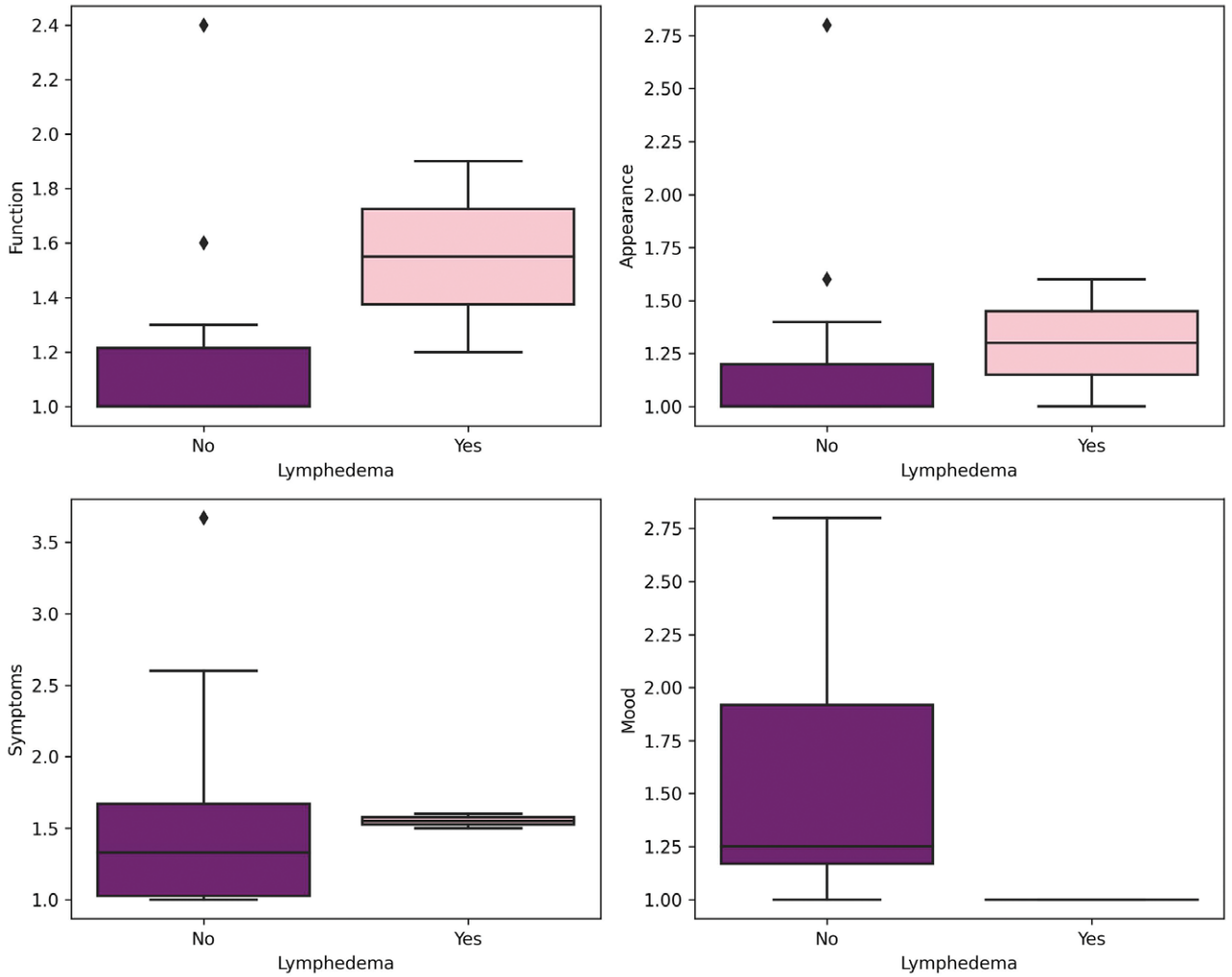

Fig. 5. Box plot illustration of the distribution of patient-reported outcomes from the LYMQOL-Arm survey showing results for function, appearance, symptoms, and mood in patients without ("no") and with ("yes") BCRL. Average scores for each group are shown. LYMQOL-Arm domains were scored using the following: 1, not at all; 2, a little; 3, quite a bit; 4, a lot.

in their study, finding an overall lymphedema rate of 4.8% out of 252 patients undergoing ILR, which is a departure from the typical 10% diagnostic cutoff. There is currently little data on how much swelling, in terms of increased limb volume, is expected in patients with BCRL specifically following ALND in the absence of treatment or prevention. One available study found that patients undergoing ALND are at a significantly higher risk of developing a greater than 10% limb volume increase in their operative arm.[23] In these very high-risk patients, perhaps we are preventing more severe swelling using ILR, making the procedure successful despite an eventual clinical diagnosis of lymphedema based on our current definitions. Differences in diagnostic criteria, therefore, have the potential to greatly influence results and echo the need for a universal definition used in all ILR studies to better determine the efficacy of the procedure.

The use of compression garments is a mainstay in the treatment of lymphedema.[24] Its preventative use, however, has yet to be fully studied, especially in the context of ILR, which, as we have argued in a prior publication, may interfere with our current ILR studies.[25] As there is research to suggest that the use of early physiotherapy can prevent patients with limb volume changes in the 5%–10% range from progressing to worsening lymphedema, ILR studies may, therefore, be underdiagnosing lymphedema in patients who undergo early compression, as the addition of compression may prevent patients from reaching diagnostic thresholds rather than the ILR alone.[23,24,26,27] In addition, there are currently no standardized referral criteria or protocols for compression use, making it difficult to study compression use in ILR studies. In our study, 1 additional patient beyond our 2 BCRL patients was referred to the lymphedema clinic due to subjective arm swelling and pain despite no objective measurements confirming BCRL and subsequently underwent a period of compression therapy. On the other hand, Campisi et al[28] suggested that early compression use after an LVA is essential to stimulate and maintain the anastomosis and

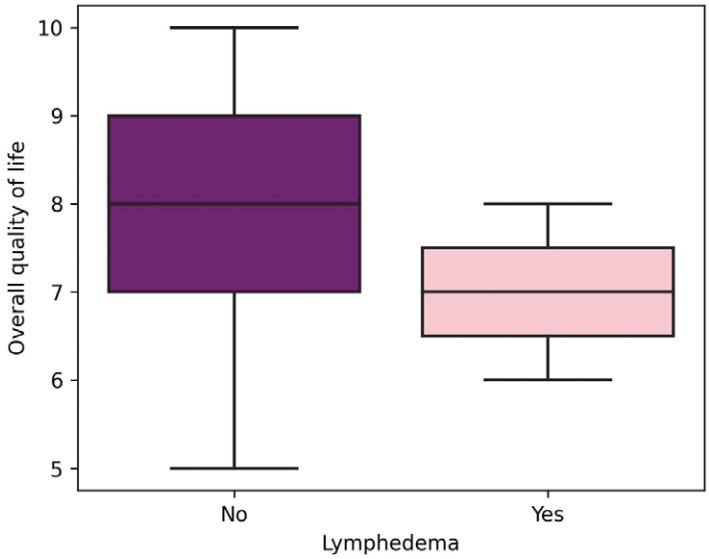

Fig. 6. Box plot illustration of the distribution of patient-reported outcomes from the LYMQOL-Arm survey showing results for overall quality of life in patients without ("no") and with ("yes") BCRL. The overall quality of life was ranked out of 10.

may, therefore, be a necessary component of postoperative care; however, it is unclear if this is solely in the context of LVAs for established lymphedema treatment or is also essential in ILR. In their early RCT results, Coriddi et al[12] noted compression use in both ILR and control groups, but found a decrease in the reliance on compression in patients who underwent ILR compared with their control group, potentially defining another modality to determine the success of ILR without compression use being a confounding variable.

When we compare our 2 patients who developed BCRL to the 15 who did not, no clear differences in risk factors could be identified, other than that both patients had an elevated body mass index and were slightly older than the nonlymphedema group (Table 1). As noted above, risk factors for developing BCRL include radiation therapy, as well as obesity, and the number of lymph nodes removed.[29,30] Despite our patients having minimal differences in these characteristics, this comparison is limited by the low sample size in our study. It is also equally possible that either the LVAs failed in these patients, or the amount of lymphatic flow reestablished by the LVAs was insufficient to prevent arm swelling in their specific cases. Additionally, although patency is tested at the completion of the procedure, we do not routinely image patients postoperatively to confirm ongoing flow.

Patients in our study reported overall good LYMQOL-Arm scores, with slightly better scores noted in non-BCRL patients. Differences in scores among groups were not found to be statistically significant, likely due to limitations in analysis with our small sample size. Similar results were found by Coriddi et al[12] who also utilized the LYMQOL-Arm survey. The evaluation of lymphedema using both PROMs and limb measurements has been suggested by Armer et al[3,31] as a surveillance tool for patients undergoing ALND to expedite treatment referrals and prevent the worsening of the condition. As noted above, diagnosis of lymphedema using limb measurements alone is inconsistent. Studies have shown that patients may more accurately detect changes in limb volumes through symptom reporting, even before volume-based diagnostic criteria are met or at volume changes lower than current diagnostic thresholds. In a 2009 article by Cormier et al,[32] the authors found that limb volume changes of 5% occur in up to 61.3% of breast cancer survivors and are associated with an increase in symptoms and a decrease in patient-reported quality of life. Although not specifically validated in patients who underwent ALND, given this significant change in PROMs despite small changes in limb volume, perhaps PROMs may actually be a better diagnostic and assessment tool for BCRL and even the success of ILR, rather than the clinical evaluation of lymphedema alone. This is reflected in one of our patients who, despite developing a moderate difference in limb volume of 8%, scored the lowest of all patients on the LYMQOL-Arm survey and required compression therapy for symptomatic relief. More research is certainly needed in this area, especially for patients undergoing ILR.

Our study benefited from a long follow-up time and the use of both quantitative limb measurements and qualitative PROMs to track outcomes. Along with the Coriddi et al article, this is one of the first ILR studies to use both objective measurement and PROM data. One major limitation of this study is the lack of a control group that would have allowed for a direct comparison of outcomes between reconstructed and nonreconstructed patients. Additionally, our small sample size may have restricted the statistical significance of our results. As we did not collect preoperative limb

measurements, we also could not determine how much limb volumes changed in individual patients pre- and postoperatively. As noted above, the greater than 10% difference in limb volume to diagnose lymphedema has been utilized in prior studies; however, there continues to be a lack of a clear definition of lymphedema across studies. Given this lack of clear diagnostic criteria, additional methods to diagnose lymphedema including bioimpedance spectroscopy and lymphoscintigraphy may have strengthened our results; however, in a resource-constrained medical system, they would have added additional costs to patient care.

CONCLUSIONS

This study demonstrates that ILR is associated with a low incidence of BCRL in a high-risk group of breast cancer patients. Our findings are in keeping with other recently published studies on ILR and are strengthened by their prospective nature, long follow-up time, and use of PROMs. Going forward, PROMs seem to be an essential component in the evaluation of lymphedema as the current clinical diagnostic criteria remain very unclear. As the field of lymphatic surgery progresses, ongoing research is still needed to further evaluate the efficacy of ILR.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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