The Efficacy of Axillary Reverse Mapping for the Prevention of Lymphedema

Amanda E. Ruffino[1†‡], Joshua D. Madera[1†‡], Makayla M. Dearborn[1†‡], and Jacqueline C. Oxenberg[2]
[1]Geisinger Commonwealth School of Medicine, Scranton, PA 18509
[2]Department of General Surgery, Geisinger Wyoming Valley Medical Center, Wilkes-Barre, PA 18711
[†]Doctor of Medicine Program
[‡]Authors contributed equally
Correspondence: amandaruffino@gmail.com

Abstract

Background: Lymphedema (LE) is the most notable complication of axillary surgery. The axillary reverse mapping (ARM) technique was created to decrease LE. This study aims to evaluate a single surgeon's experience with ARM in patients undergoing sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) for breast cancer.

Methods: We retrospectively analyzed 139 patients who underwent SLNB or ALND. Tumor characteristics and treatments received were evaluated. Surgical intervention and the use of ARM were compared to assess LE rates. A subgroup analysis was also performed of patients who underwent neoadjuvant chemotherapy (NAC).

Results: LE was initially reported in 7.1% (n=10) of patients; 3.3% (n=4) with SLNB and 35% (n=6) with ALND. At initial follow-up, LE was reported 16.4% more often in patients who underwent ALND with no ARM, and 38.8% more often in patients who underwent ALND plus ARM. An increased risk of LE was found in patients treated with ALND (OR = 16.0, $p < 0.001$). All patients who underwent ARM were 12.75% more likely to develop LE if they received NAC ($p < 0.05$). Patients in the ALND group who also received NAC were more likely to undergo ARM as compared with patients in the SLNB group ($p < 0.01$).

Conclusion: Our study found that ARM failed to decrease the incidence of LE. Until better surgical outcomes are shown for the prevention of LE using ARM, other approaches should be utilized. Future iterations might include larger prospective studies to better evaluate ARM.

Introduction

Lymphedema (LE) continues to be an unfortunate comorbidity following axillary surgery for breast cancer and can significantly affect patients' quality of life. While decades of research have endorsed deescalating the extent of axillary surgery, axillary sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) remain the standards of care for breast cancer (1–3). However, both procedures share a common notable complication of LE.

The prevalence of LE ranges from 16.5–24.6% following ALND, and 3.7–7.5% following SLNB (4). Striving to reduce morbidity and improve patient outcomes, axillary reverse mapping (ARM) was introduced in 2007 as a promising technique to better discern arm lymphatics from the breast (5). Once the arm nodes were visualized and identified, preserving them helped prevent most LE (5–6). A systematic review by Ahmed et al. reported LE rates ranging from 0–6% during ARM-assisted SLNB and 5.9–24% during ARM-assisted ALND (7). Realizing its benefit, this technique has been employed by many surgeons' treating breast cancer, as well as scrutinized further. While several studies have already assessed the efficacy, oncologic safety, and LE outcomes regarding ARM (4, 7–11), it has been less studied in patients with locally advanced breast cancer who underwent neoadjuvant chemotherapy (NAC) (12–13). Its role in preventing LE has also not been well investigated. This is an important outcome to highlight as it will elucidate patients who are more likely to benefit from ARM.

Therefore, this study aims to evaluate a single surgeon's experience with ARM in patients undergoing either SLNB or ALND for breast cancer. We hypothesized that using ARM would decrease the rate of LE by allowing preservation or identification for the repair of lymphatics, even in the setting of NAC. However, our study findings showed that LE rates did not improve with the use of ARM.

Methods

Appropriate IRB approval was obtained from the Geisinger Institutional Review Board and the study was determined to be exempt. A retrospective chart review was conducted for a single institution and a single surgeon for patients with non-metastatic breast cancer undergoing either SLNB or ALND from December 2018 to October 2021. Patients were included if they had stages 0–3 breast cancer and were excluded if they underwent surgery for non-breast cancers, had distant metastatic disease or did not undergo axillary surgery.

Patient and tumor characteristics obtained included age at diagnosis, tumor type, tumor grade, clinical stage, pathologic stage, and hormone receptor status. Treatment characteristics evaluated included chemotherapy, radiation, type of breast surgery (mastectomy vs. breast conservation), type of axillary surgery (SLNB vs ALND), number of nodes removed, and number of nodes found with metastatic disease. Final definitive surgical procedure was utilized if multiple surgeries were performed. Sentinel node biopsy was defined by complete excision of nodes identified by periareolar injection of intraoperative lymphatic mapping via the use of technetium-labeled sulfur colloid or lymphazurin blue. Axillary lymph node dissection was defined as dissection of axillary levels 1 and 2 lymph node basins with level 3 taken if clinically suspicious. Patients undergoing bilateral procedures were included and each side was analyzed separately given each axilla had its own individual risk.

Intraoperative factors that were evaluated include the use of ARM, if ARM lymphatics were seen, if ARM lymphatics had crossover with either the sentinel node or axillary dissection nodes and if repair of the arm lymphatics was performed. ARM was performed via injection of 4–5 mL lymphazurin blue subcutaneously in the upper inner arm medial intramuscular groove for localization of the lymphatics draining the arm (14). ARM was only utilized if adequate uptake was found with the utilization of technetium-labeled sulfur colloid if SLNB was being performed. When ARM was utilized, blue nodes were still removed if they were mapped to be the sentinel nodes or in the area of axillary dissection and were labeled as crossover nodes. In the case of ALND after NAC, lymphazurin blue was not injected for ARM until adequate axillary sampling (at least the clipped node and/or 3 nodes sampled) were able to be performed. Repair of lymphatics was performed by reapproximation with interrupted 4-0 vicryl if possible (5–6).

LE was measured during the first postoperative visit (defined as LE initially reported) and at the last follow-up visit (defined as patients' last recorded office visit in their chart). While bioimpedance spectroscopy and arm circumference measurements were attempted for all patients as screening modalities for lymphedema, these were unable to be utilized uniformly for lymphedema screening, given the time period during COVID-19. Therefore, any lymphedema diagnosis was recorded (subclinical and clinical) but lymphedema at the time of the last follow-up included only patients with clinically significant (Stage 2 per ISL criteria) LE requiring interventions (compression sleeves, physical therapy, etc.) (15). Patients referred to physical therapy early were also recorded as some did undergo early interventions with compression sleeves. The date of the last follow-up and disease status were also recorded. A subset analysis was performed for patients who underwent ARM and those who underwent NAC.

Descriptive statistics relating to patient, tumor, treatment, and surgery characteristics were calculated and presented. A combination of Wilcoxon rank sum tests, Fisher's exact tests, and Pearson's Chi-squared tests were used to test for associations between variables. Logistic regression models were created for the binary outcomes of lymphedema at initial follow-up and lymphedema at most recent follow-up using a variety of predictor variables. The backward selection procedure using Bayesian information criterion (BIC) was applied to identify simpler models from the full models. Results from these models were presented as odds ratios (ORs) and 95% confidence intervals (95% Cis). All p-values were two-tailed, and $p < 0.05$ was considered statistically significant. Analyses were performed using R Version 4.0.5.

Characteristics	Overall (n=140)	ARM Used: No (n=60)	ARM Used: Yes (n=80)	p-value
Age at Diagnosis, years, median (IQR)	62.8 (52.0, 72.6)	64.6 (52.0, 71.7)	62.3 (52.0, 72.7)	0.8721
(# missing)	1	0	1	
Histology, n (%)				0.549
Tubular adenocarcinoma	3 (2.1%)	0 (0%)	3 (3.8%)	
Mucinous adenocarcinoma	1 (0.7%)	0 (0%)	1 (1.2%)	
Intraductal adenocarcinoma, non-infiltrating	9 (6.4%)	2 (3.3%)	7 (8.8%)	
Ductal adenocarcinoma	7 (5.0%)	4 (6.7%)	3 (3.8%)	
Invasive carcinoma of no special type	87 (62%)	39 (65%)	48 (60%)	
Non-infiltrating intracystic carcinoma	2 (1.4%)	1 (1.7%)	1 (1.2%)	
Invasive micropapillary carcinoma	1 (0.7%)	0 (0%)	1 (1.2%)	
Pleomorphic lobular carcinoma in situ	1 (0.7%)	0 (0%)	1 (1.2%)	
Lobular carcinoma	16 (11%)	8 (13%)	8 (10%)	
Intraductal carcinoma and lobular carcinoma in situ	1 (0.7%)	0 (0%)	1 (1.2%)	
Infiltrating ductal and lobular carcinoma	10 (7.1%)	4 (6.7%)	6 (7.5%)	
Metaplastic carcinoma	2 (1.4%)	2 (3.3%)	0 (0%)	
Clinical N Stage, n (%)				0.478
0	121 (87%)	50 (83%)	71 (90%)	
1	13 (9.4%)	6 (10%)	7 (8.9%)	
2	1 (0.7%)	1 (1.7%)	0 (0%)	
2a	3 (2.2%)	2 (3.3%)	1 (1.3%)	
oi	1 (0.7%)	1 (1.7%)	0 (0%)	
(# missing)	1	0	1	
Pathologic N Stage, n (%)				**0.037**
0	99 (71%)	37 (62%)	62 (78%)	
0i	3 (2.1%)	1 (1.7%)	2 (2.5%)	
1	1 (0.7%)	0 (0%)	1 (1.2%)	
1a	9 (6.4%)	6 (10%)	3 (3.8%)	
1c	1 (0.7%)	0 (0%)	1 (1.2%)	
1mi	4 (2.9%)	2 (3.3%)	2 (2.5%)	
2	1 (0.7%)	0 (0%)	1 (1.2%)	
2a	2 (1.4%)	1 (1.7%)	1 (1.2%)	
3	1 (0.7%)	1 (1.7%)	0 (0%)	
oi	1 (0.7%)	1 (1.7%)	0 (0%)	
yo0	1 (0.7%)	1 (1.7%)	0 (0%)	
yp0	11 (7.9%)	9 (15%)	2 (2.5%)	
yp1	2 (1.4%)	1 (1.7%)	1 (1.2%)	
yp2a	3 (2.1%)	0 (0%)	3 (3.8%)	
ypn1mi	1 (0.7%)	0 (0%)	1 (1.2%)	
Grade, n (%)				0.222
G1: Low combined histologic grade (favorable), SBR score of 3-5 points	33 (24%)	11 (18%)	22 (28%)	
G2: Intermediate combined histologic grade (moderately favorable), SBR score of 6-7 points	54 (39%)	27 (45%)	27 (34%)	

ARM= Axillary Reverse Mapping
IQR= Interquartile Range
SBR= Scarff-Bloom-Richardson

Table 1. Patient and tumor characteristics of the study sample by use of ARM.

Results

A total of 140 breast/axillary surgeries were included in 139 patients (one had bilateral breast cancer). The median age of diagnosis for patients was 62.8 years old (IQR: 52-73 years old). The most common breast tumor type was invasive carcinoma of no special type (n=87) with 62.1%. Tumor characteristics including grade, clinical stage, and pathologic stage can be seen in Table 1. Sixteen patients (11.4%) had estrogen receptor negative (ER negative)/human epidermal growth factor receptor 2 (HER2) negative disease, 6 (4.3%) had ER negative/HER2 positive disease, 98 (70.0%) had ER positive/HER2 positive disease and 9 (6.4%) had ER positive/HER2 positive disease. Eleven patients had ductal carcinoma in situ (DCIS) with 9 ER+ and 2 ER-.

NAC was the treatment for 15.7% of patients (n=22) and 12.1% (n=17) received adjuvant chemotherapy. Most (77.1%) patients received radiation therapy (n=108), while 22.9% of patients were not treated with radiation (n=32). 62.1% of patients

Characteristics	Overall (n=140)	ARM Used No (n=60)	ARM Used Yes (n=80)	p-value
Age at Diagnosis, years, median (IQR)	62.8 (52.0, 72.6)	64.6 (52.0, 71.7)	62.3 (52.0, 72.7)	0.872[1]
(# missing)	1	0	1	
Neoadjuvant Chemotherapy, n (%)				0.240[2]
No	117 (84%)	48 (80%)	69 (87%)	
Yes	22 (16%)	12 (20%)	10 (13%)	
Radiation Received, n (%)				0.771[2]
No	32 (23%)	13 (22%)	19 (24%)	
Yes	108 (77%)	47 (78%)	61 (76%)	
Type of Surgery, n (%)				0.232[1]
Sentinel LN biopsy	123 (88%)	55 (92%)	68 (85%)	
Axillary dissection	17 (12%)	5 (8.3%)	12 (15%)	
Type of Breast Surgery, n (%)				0.801[1]
Breast Conservation	87 (62%)	38 (63%)	49 (61%)	
Mastectomy	53 (38%)	22 (37%)	31 (39%)	
Nodes Examined, median (range)	2.0 (1.0, 28.0)	2.0 (1.0, 20.0)	2.0 (1.0, 28.0)	0.899[2]
Nodes Positive, median (range)	0.0 (0.0, 28.0)	0.0 (0.0, 28.0)	0.0 (0.0, 7.0)	0.738[2]

[1]Pearson's Chi-squared test; [2]Wilcoxon rank sum test
ARM= Axillary Reverse Mapping
IQR= Interquartile Range
LN= Lymph Node

Table 2. Patient and surgery characteristics of the study population by use of ARM

	SLNB (n= 123)	ALND (n= 17)	Total (n= 140)
ARM Performed, n (%)	68 (55%)	12 (71%)	80 (57%)
Overall Lymphedema Rate, n (%)	4 (3.3%)	6 (35.3%)	10 (7.1%)
Blue Lymphatics Seen, n (%)	24 (19.5%)	8 (47.1%)	32 (22.9%)
Crossover Nodes, n (%)	12 (9.8%)	7 (41.2%)	19 (13.6%)
Blue Lymphatics Repaired, n (%)	10 (8.1%)	6 (35.3%)	16 (11.4%)
Lymphedema with ARM, n (%)	2 (2.9%)	5 (29.4%)	7 (5%)

ARM= Axillary Reverse Mapping
SLNB= Sentinel Lymph Node Biopsy
ALND= Axillary Lymph Node Dissection

Table 3. Intraoperative lymphatic findings with ARM for SLNB and ALND

Characteristic	Overall	ARM Used No	ARM Used Yes	p-value
LE Originally Reported, n (%)				0.516
No	130 (92.9%)	57 (95%)	73 (91.2%)	
Yes	10 (7.1%)	3 (5%)	7 (8.8%)	
LE at Last Follow-Up, n (%)				0.238
No	134 (95.7%)	59 (98.3%)	75 (93.8%)	
Yes	6 (4.3%)	1 (1.7%)	5 (6.2%)	

LE= Lymphedema
ARM= Axillary Reverse Mapping

Table 4. LE rates in ARM versus no ARM at initial and last follow-up

received breast conservation therapy (n=87) while 37.9% of patients received mastectomy alone (n=53). Most (87.9%, n=123) patients underwent SLNB, while 12.1% (n=17) patients underwent ALND. A median of 2 nodes were examined (range 1–28) with a median of 0 nodes positive (range 0–11).

Patients were stratified based on the use of ARM (n = 80, 57.1%) vs. no ARM (n=60, 42.9%). Results of surgery characteristics and treatment differences can be seen in Table 2. No significant differences between the ARM and no ARM group were seen for surgery characteristics or types of treatment. Intraoperative lymphatic findings with ARM can be seen in Table 3. Of the 80 patients who received ARM, arm lymphatics were identified in 40.0% of patients (n=32). Overlap between arm lymphatics and sentinel or axillary dissection nodes was observed in 23.8% of the 80 patients (n=19).

LE was initially reported in 7.1% (n=10) of all patients; 3.3% (n=4) with SLNB and 35.3% (n=6) with ALND. However, at a median follow-up of 15.7 months (range 8-20.3 months), only 4.3% (n=6) of all patients, 1.6% (n=2) with SLNB and 23.5% (n=4) with ALND, still had clinical signs of lymphedema or were still being treated (utilizing compression sleeves or seeing physical therapy). Median follow-up time was longer for the patients who did not undergo ARM (median 19.7 months (IQR 11.8-28.1) vs. 16.5 months (IQR 12.1-22.9), $p = 0.041$). No significant difference in lymphedema in the ARM vs. no ARM group was found (Table 4).

Stratification by type of surgery revealed that patients who underwent ALND had a higher risk of experiencing LE as compared with SLNB at both initial and final follow-up visits. At the initial follow-up visit, LE was reported 16.4% more often in patients who underwent ALND with no ARM, and 38.8% more often in patients who underwent ALND plus ARM as compared to SLNB. Similarly, at the final follow-up visit, patients who underwent ALND plus ARM experienced LE 31.9% more often. In contrast, LE was reported 1.6% less often at the final follow-up visit in patients who underwent ALND with no ARM compared to the SLNB group.

The logistic regression model for LE at initial follow-up with the eight predictors such as age at diagnosis, use of NAC, use of radiation, type of surgery, type of breast surgery, ARM used, number of regional lymph nodes examined, and number of regional lymph nodes positive did not reveal any significant explanatory variables associated with the development of LE (Figure 1, top). However, in a simpler model selected using backward selection with BIC, type of surgery (SLNB vs. ALND) was identified as a significant predictor with ALND patients having 15.95 times the odds (95% CI: 3.99-71.17) of presenting with lymphedema at initial follow-up than SLNB patients (Figure 1, bottom). In the logistic regression model for LE at most recent follow-up with the eight aforementioned predictors and LE reported at initial follow-up, only LE reported at initial follow-up was significantly associated with the outcome (Figure 2, top). Using the same backward selection procedure, LE reported at initial follow-up remained as the only significant covariate, with patients originally presenting with LE having 127 times the odds (95% CI: 16.74-2697.68) of presenting with LE at most recent follow-up than patients not originally presenting with lymphedema (Figure 2, bottom).

Examination of additional factors in all patients who underwent ARM revealed a 12.75% increase in the likelihood of LE development in those who received NAC as compared with those who did not ($p < 0.05$). Similarly, the presence of positive nodes in patients who underwent ARM led to the development of LE 30.2% more often than in patients with negative nodes ($p < 0.05$). However, no significant differences in LE rates were identified based on the use of radiation therapy or surgery type (mastectomy vs. breast conservation) patients received ($p > 0.05$). However, of those with LE who underwent ARM, 71.4% (n=5) had crossover nodes resected. Of patients with LE at last follow-up, 100% (n=5) had ARM lymphatics seen and had crossover nodes resected.

Subgroup analysis of patients undergoing NAC can be seen in Table 5. The number of nodes removed ranged from 1 to 28 nodes (median of 5 nodes) with a median of 0 nodes positive (range 0–6). Rates of LE were similar between all patients who received NAC, regardless of the use of ARM or type of mastectomy ($p > 0.05$). However, patients in the ALND group who also received NAC were more likely to undergo ARM as compared with patients in the SLNB group ($p < 0.01$). This same trend was observed for the number of nodes examined and the number of positive nodes, such that patients who received NAC had increased ARM usage ($p < 0.01$).

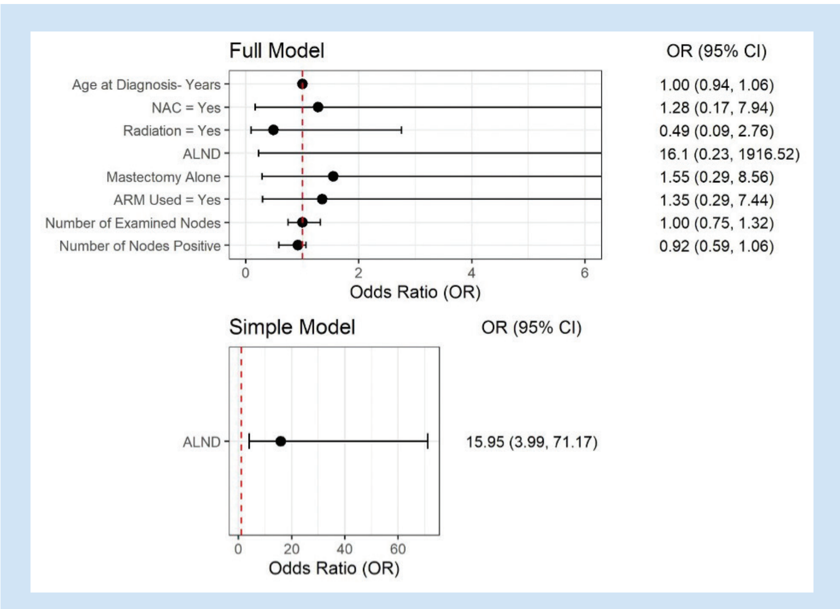

Figure 1. Effects of demographics, clinical, and surgery characteristics on lymphedema at initial follow-up. Full model results (top) and simple model results (bottom) are shown as odds ratios and 95% confidence intervals (CIs).

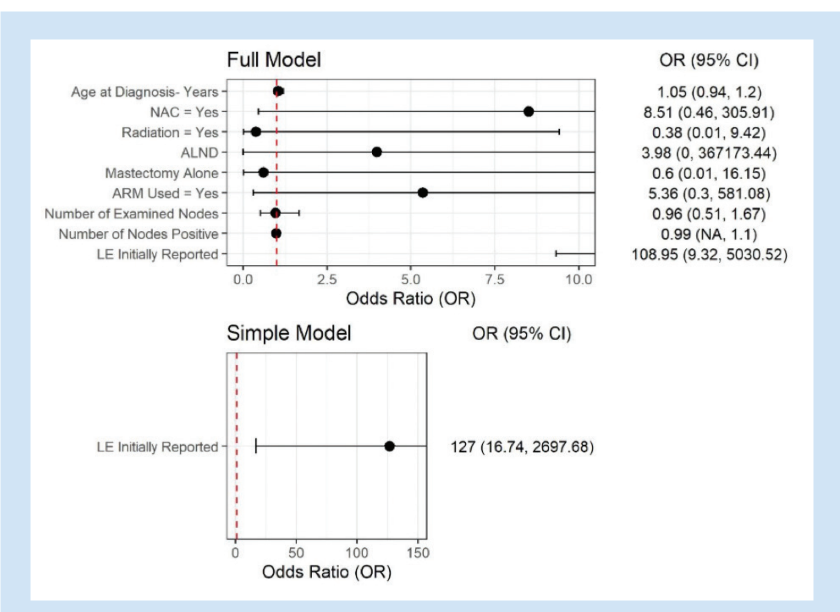

Figure 2. Effects of demographics, clinical, and surgery characteristics on lymphedema at most recent follow-up. Full model results (top) and simple model results (bottom) are shown as odds ratios and 95% confidence intervals (CIs).

Discussion

Our study showed that using ARM failed to decrease LE rates. While our findings are consistent with a systematic review published by Bakri et al., other studies have contradicted this (4, 7–8, 10). The muddled evidence has created a need for more conclusive studies, especially in the setting of advanced breast cancer. A study by Tummel et al. found objective lymphedema rates to be 6.9% in ALND and 1.2% in SLNB in patients whose arm nodes were successfully identified and preserved.10 Our overall LE rate with ARM was 7.1%, with 3.3% after SLNB and 35% after ALND. Moreover, evaluating the rate of LE following ARM in the setting of NAC or locally advanced breast cancer needed to be further assessed as varying evidence currently exists or has not been explored in this context (11, 16).

Our subgroup analysis of all patients who received NAC revealed that patients who underwent ALND had increased rates of ARM usage. However, we found no significant differences in LE rates at follow-up visits when assessing all patients who received NAC. This suggests that

Characteristic	Overall (n=22)	ARM Used		p-value
		No (n=12)	Yes (n=10)	
Age at diagnosis, median (IQR)	53.5 (47.8, 67.0)	52.0 (46.5, 71.9)	53.5 (49.3, 58.2)	1
Radiation, n (%)				1
Yes	17 (77%)	9 (75%)	8 (80%)	
No	5 (23%)	3 (25%)	2 (20%)	
Type of Surgery, n (%)				**0.002**
SLNB	13 (59%)	11 (92%)	2 (20%)	
ALND	9 (41%)	1 (8.3%)	8 (80%)	
Type of Breast Surgery, n (%)				1
Breast Conservation	9 (41%)	5 (42%)	4 (40%)	
Mastectomy	13 (59%)	7 (58%)	6 (60%)	
Nodes examined, median (range)	5 (1.0, 28)	3.5 (2.0, 20)	16.5 (1.0, 28)	**0.034**
Nodes positive, median (range)	0.0 (0.0, 95)	0.0 (0.0, 95)	2.0 (0.0, 6.0)	**0.024**
LE originally reported, n (%)				1
Yes	4 (18%)	2 (17%)	2 (20%)	
No	18 (82%)	10 (83%)	8 (80%)	
LE reported at most recent f/u, n (%)				0.571
Yes	3 (14%)	1 (8.3%)	2 (20%)	
No	19 (86%)	11 (92%)	8 (80%)	
F/u time in months, median (IQR?)	15.7 (8.0, 20.3)	15.1 (7.3, 19.7)	15.7 (8.6, 22.9)	0.497

NAC= Neoadjuvant Chemotherapy
ARM= Axillary Reverse Mapping
IQR= Interquartile Range
SLNB= Sentinel Lymph Node Biopsy
ALND= Axillary Lymph Node Dissection
LE= Lymphedema
F/u= Follow-Up

Table 5. NAC subset analysis of patient and surgery characteristics, intraoperative lymphatic findings, and lymphedema rates stratified by the use of ARM

patients with locally advanced breast cancer, requiring NAC or more extensive axillary dissections, may not have benefited from ARM. Since a large percentage of patients with LE were found to have crossover nodes, this may support that ARM may predict who is at risk for LE, but also questions the efficacy of lymphatic repair. Prior studies have demonstrated that immediate lymphatic repair, known as lymphatic microsurgical preventive healing approach (LYMPHA), during axillary surgery is a promising and safe approach for preventing LE in a high-risk patient population (17–18). However, a more novel surgical technique has been created, known as Simplified-LYMPHA (S-LYMPHA), which repairs lymphatics without utilizing a microscope (19). Utilizing these surgical techniques in the immediate and/or delayed setting can be better explored to reduce the clinical significance and morbidity of LE.

Limitations of this study include its small retrospective nature. Additionally, other factors such as body mass index (BMI) that can increase the risk for lymphedema were not included. Further, S-LYMPHA was not an adopted surgical approach to repair lymphatics and primary lymphatic repair was performed with simple reapproximation with a 4-0 vicryl.

Conclusion

Until we can show better surgical outcomes for the prevention of LE using ARM, other approaches including radiation therapy as well as utilizing NAC to downstage locally advanced axillary disease should be utilized. However, larger prospective studies are needed to evaluate ARM as well as standardization and more widespread training for formal lymphatic repairs before the preservation of arm nodes can consistently reduce the incidence of LE in patients.

Disclosures

The study authors reported no conflicts of interest.

References

1. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Ashikaga T, Weaver DL, Miller BJ, Jalovec LM, Frazier TG, Noyes RD. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: Results from the NSABP B-32 randomised phase III trial. *Lancet Oncol*. 2007 Oct 1;8(10):881-8.
2. Lucci A, McCall LM, Beitsch PD, Whitworth PW, Reintgen DS, Blumencranz BW, Leitch AM, Saha S, Hunt KK, Giuliano AE. Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol*. 2007 Aug 20;25(24):3657-63.
3. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, Cataliotti L, Westenberg AH, Klinkenbijl JH, Orzalesi L, Bouma WH. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): A randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol*. 2014 Nov 1;15(12):1303-10.
4. Bakri NA, Kwasnicki RM, Khan N, Ghandour O, Lee A, Grant Y, Dawidziuk A, Darzi A, Ashrafian H, Leff DR. Impact of axillary lymph node dissection and sentinel lymph node biopsy on upper limb morbidity in breast cancer patients: A systematic review and meta-analysis. *Ann Surg*. 2023 Apr 1;277(4):572-80.
5. Thompson M, Korourian S, Henry-Tillman R, Adkins L, Mumford S, Westbrook KC, Klimberg VS. Axillary reverse mapping (ARM): A new concept to identify and enhance lymphatic preservation. *Ann Surg Oncol*. 2007 Jun;14(6):1890-95.
6. Boneti C, Korourian S, Bland K, Cox K, Adkins LL, Henry-Tillman RS, Klimberg VS. Axillary reverse mapping: mapping and preserving arm lymphatics may be important in preventing lymphedema during sentinel lymph node biopsy. *J Am Coll Surg*. 2008 May 1;206(5):1038-42.
7. Ahmed M, Rubio IT, Kovacs T, Klimberg VS, Douek M. Systematic review of axillary reverse mapping in breast cancer. Br J Surg. 2016 Feb;103(3):170-8.

8. Han C, Yang B, Zuo WS, Zheng G, Yang L, Zheng MZ. The feasibility and oncological safety of axillary reverse mapping in patients with breast cancer: A systematic review and meta-analysis of prospective studies. *PLoS One*. 2016 Feb 26;11(2):e0150285.

9. Bedrosian I, Babiera GV, Mittendorf EA, Kuerer HM, Pantoja L, Hunt KK, Krishnamurthy S, Meric-Bernstam F. A phase I study to assess the feasibility and oncologic safety of axillary reverse mapping in breast cancer patients. *CA Cancer J Clin*. 2010 Jun 1;116(11):2543-8.

10. Tummel E, Ochoa D, Korourian S, Betzold R, Adkins L, McCarthy M, Hung S, Kalkwarf K, Gallagher K, Lee JY, Klimberg VS. Does axillary reverse mapping prevent lymphedema after lymphadenectomy? *Ann Surg*. 2017 May 1;265(5):987-92.

11. Khandelwal R, Poovamma CU, Shilpy C, Prema M, Anthony P. Axillary reverse mapping: Is it feasible in locally advanced breast cancer patients?. *Breast Dis*. 2014 Jan 1;34(4):151-5.

12. Yoon KH, Lim SM, Koo B, Kim JY, Park HS, Park S, Kim SI, Park BW, Cho YU. Conserving the lymphatics from the arm using fluorescence imaging in patients with breast cancer at high risk of postoperative lymphedema: A pilot study. *Gland Surg*. 2020 Jun;9(3):629.

13. Liu S, Wang N, Gao P, Liu P, Yang H, Xie F, Wang S, Liu M, Wang S. Using the axillary reverse mapping technique to screen breast cancer patients with a high risk of lymphedema. *World J Surg Oncol*. 2020 Dec;18(1):1-8.

14. Boneti C, Korourian S, Diaz Z, Santiago C, Mumford S, Adkins L, Klimberg VS. Scientific impact award: Axillary reverse mapping (ARM) to identify and protect lymphatics draining the arm during axillary lymphadenectomy. *Am J Surg*. 2009 Oct 1;198(4):482-7.

15. Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus document of the international society of lymphology. *Lymphology*. 2020;53(1):3-19. PMID: 32521126.

16. Gobardhan PD, Wijsman JH, van Dalen T, Klompenhouwer EG, van der Schelling GP, Los J, Voogd AC, Luiten EJ. ARM: Axillary reverse mapping–the need for selection of patients. *Eur J Surg Oncol*. 2012 Aug 1;38(8):657-61.

17. Johnson AR, Fleishman A, Granoff MD, Shillue K, Houlihan MJ, Sharma R, Kansal KJ, Teller P, James TA, Lee BT, Singhal D. Evaluating the impact of immediate lymphatic reconstruction for the surgical prevention of lymphedema. *Plast Recon Surg*. 2021 Mar 1;147(3): 373e-81e.

18. Lipman K, Luan A, Stone K, Wapnir I, Karin M, Nguyen D. Lymphatic microsurgical preventive healing approach (LYMPHA) for lymphedema prevention after axillary lymph node dissection—A single institution experience and feasibility of technique. *J Clin Med*. 2022 Jan;11(1):92.

19. Ozmen T, Lazaro M, Zhou Y, Vinyard A, Avisar E. Evaluation of simplified lymphatic microsurgical preventing healing approach (S-Lympha) for the prevention of breast cancer–related clinical lymphedema after axillary lymph node dissection. *Ann Surg*. 2019 Dec 1;270(6):1156-60.