Prevalence of Breast Edema Following Conservative Breast Therapy in Israeli Patients

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ABSTRACT **Background:** Breast edema, characterized by fluid accumulation in breast tissue, is a common yet understudied complication following breast-conserving surgery (BCS) and radiotherapy for breast cancer. Its impact on physical and emotional well-being highlights the need for deeper exploration of its prevalence, risk factors, and clinical management.

Objectives: To evaluate the prevalence of breast edema following breast surgery, investigate its association with arm lymphedema, and explore links to surgical interventions.

Methods: We analyzed 105 breast cancer patients treated with BCS and axillary interventions, including sentinel lymph node biopsy (SLNB), lymph node sampling, or axillary lymph node dissection (ALND). Comprehensive evaluations included physical exams, arm circumference measurements, and a thorough review of patient demographics, medical history, and disease progression to assess the presence and severity of breast and arm lymphedema.

Results: Breast edema prevalence was 7.6%, with rates significantly influenced by surgical extent. None of the SLNB patients exhibited breast edema, compared to 23.5% of ALND patients. Significant predictors included arm lymphedema (OR 57.54, $P = 0.024$), body mass index (OR 0.65, $P = 0.016$), and tumor grade (OR 51.78, $P = 0.040$). Co-occurrence of breast and arm lymphedema was observed in 50% of cases.

Conclusions: Breast edema is a significant postoperative complication influenced by surgical extent and lymphatic disruption. Improved diagnostic methods, multidisciplinary care, and innovative surgical strategies are essential for mitigating this condition and enhancing patient outcomes.

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KEY WORDS: axillary lymph node dissection (ALND), breast cancer, breast edema, lymphedema, sentinel lymph node biopsy (SLNB)

Breast edema, characterized by the accumulation of fluid within breast tissue leading to swelling, is a significant clinical concern, particularly for breast cancer patients. Even after successful treatment, this condition can persist as a distressing reminder of the illness, contributing to physical discomfort and negatively impacting emotional well-being and overall quality of life [1].

Breast edema can result from various causes, with breast-conserving surgery (BCS) and radiotherapy being the most prevalent, primarily due to their propensity to disrupt the lymphatic system. This disruption leads to fluid accumulation and subsequent swelling [2]. Consequently, the compromised lymphatic system struggles to manage the fluid load, resulting in edema. Less common causes include inflammatory breast carcinoma, which induces lymphatic blockage through tumor activity; lymphatic obstruction from axillary, chest wall, or intrathoracic lesions; metastasis; mastitis; breast lymphoma; congestive heart failure; and trauma [3].

Clinically, breast edema manifests through symptoms such as skin changes, hardness, pain, and pitting edema [4-6] [Figure 1]. However, the absence of visible swelling in some cases complicates diagnosis [6]. The diagnostic challenge is further compounded by the lack of standardized objective measures. It is not clear how long after treatment edema is considered pathological, resulting in wide variability in reported incidences of breast edema following BCS, which range from 10% to 90.4% [1,2,7].

Breast edema is typically classified into two main types: parenchymal edema, which involves generalized swelling of the breast tissue itself, and cutaneous edema, marked by alterations in the epidermis and dermis [8]. It is also categorized into three stages based on changes in the breast's appearance, volume, and pain presence [6,9].

The objective of this study was to evaluate the prevalence of breast edema following breast surgery, investi-

gate its association with arm lymphedema, and explore links to surgical interventions. We aimed to fill gaps in existing literature by providing a detailed analysis of breast edema, an area often overshadowed by the broader focus on lymphedema, thereby contributing valuable insights to improve patient care. By improving our understanding of this condition, we emphasize the importance of early diagnosis, timely intervention, long-term monitoring, and meticulous surgical planning to minimize lymphatic system disruption.

Figure 1. A 42-year-old female patient diagnosed with right invasive ductal carcinoma

The patient underwent neoadjuvant chemotherapy, followed by a right lumpectomy with axillary lymph node dissection and oncoplastic breast reduction. Subsequently, she received radiotherapy and hormonal therapy. Over time, she developed significant breast edema, characterized by an increase in breast size of more than one cup, accompanied by hardness, swelling, and pain.

PATIENTS AND METHODS

The study cohort included 105 breast cancer patients who underwent BCS that included one of the following axillary interventions: sentinel lymph node biopsy (SLNB), lymph node sampling, or axillary lymph node dissection (ALND). These represent a spectrum of procedures with varying degrees of invasiveness. SLNB involves identifying and removing only the first few lymph nodes (sentinel nodes) to which cancer is likely to spread, minimizing complications and preserving lymphatic function. ALND is the most extensive procedure, involving the removal of multiple lymph nodes from the axilla to address advanced disease or confirm staging, but it carries a higher risk of complications such as lymphedema.

The axilla is bound by the axillary vein superiorly, the serratus medially, the latissimus laterally, the clavipectoral fascia anteriorly, and the subscapularis posteriorly. The inferior boundary of the axilla is less well-defined but should reach the axillary tail of the breast. The extent of ALND within these boundaries is defined as level I (lateral to the pectoralis minor), level I–II (extending posterior to the Pectoralis minor), or level I–III (extending to the apex of the axilla, Halsted's ligament) and should be based on tumor characteristics, patient anatomy, and intraoperative findings. Any procedure considered by the surgeons as more than an SLNB and less extensive than a proper ALND was classified as lymph node sampling.

The study was conducted between 2016 and 2020 at the Tel Aviv Sourasky Medical Center, a tertiary care oncology center. The study was approved by the ethics committee (reference 0935-20-TLV).

A thorough review of patient demographics, medical history, and disease progression was conducted for all participants. This workup included collecting information on age, co-morbid conditions such as diabetes and hypertension, tumor characteristics (including grade and subtype), and treatment details such as the type of surgical intervention and receipt of adjuvant therapies. This comprehensive data collection ensured a robust analysis of factors potentially influencing the development of breast edema and arm lymphedema. Each patient underwent a thorough physical examination by a blinded examiner to assess the presence and severity of both lymphedema and breast edema, which was consistent with the criteria described by Wratten [8] Delay [9] and colleagues.

Breast edema can be classified into three stages based on the severity and extent of symptoms. Stage 1 involves thickening of the skin without a change in breast volume, indicating early edema and minimal fluid accumulation. In stage 2, edema is visible with possible asymmetry between breasts, dilated skin pores, heaviness, pain, and pitting edema, reflecting moderate severity with noticeable swelling and discomfort. Stage 3 presents similar symptoms to stage 2 but involves more extensive pain and significant skin changes, indicating severe edema with pronounced fluid retention and skin alterations. The first stage correlates to what Wratten and co-authors [8] described as the cutaneous type, which can be clinically diagnosed by thickening of the skin and peau d'orange appearance. A positive diagnosis included visible edema, with either tenderness or heaviness, or dilated skin pores (peau d'orange). The severity of the edema was not rated.

Arm lymphedema was also evaluated through arm circumference measurements and volume calculations using the frustum-of-a-cone formula. Relative excess arm volume was determined using the formula: Absolute difference volumes between both arms / (V_1 swollen limb + V_2 unaffected limb)/2 × 100. Patients were diagnosed with lymphedema based on an absolute interlimb difference > 2 cm and a relative volume increase > 3%, with adjustments made for the non-dominant arm based on established correction factors [10]. There were no data in regard of arm measurements before surgery.

RESULTS

We analyzed data from 105 patients who underwent BCS. The patient cohort had a mean age of 56 years, with demographic details including a range spanning 35 to 75 years. Co-morbidities such as diabetes and hypertension were present in 20% of the patients. Of these patients, 30 underwent SLNB, 58 underwent lymph node sampling, and 17 underwent ALND. Most participants were treated for invasive ductal carcinoma with adjuvant radiation therapy [Table 1].

Lymphedema and breast edema prevalence varied by surgical procedure. Of the 30 SLNB patients, 4 (13.33%) developed lymphedema while none exhibited breast edema. Among the 58 lymph node sampling patients, 13 (22.4%) were diagnosed with lymphedema and 4 (6.89%) had breast edema. In the 17 ALND patients, 5 (29.4%) demonstrated lymphedema and 4 (23.5%) exhibited breast edema [Figure 2]. Fisher's exact test revealed a significant association between procedure type (in the axilla) and breast edema prevalence ($P < 0.05$). Subsequent pairwise comparisons using Bonferroni correction confirmed a significantly lower prevalence in SLNB compared to ALND ($P < 0.05$).

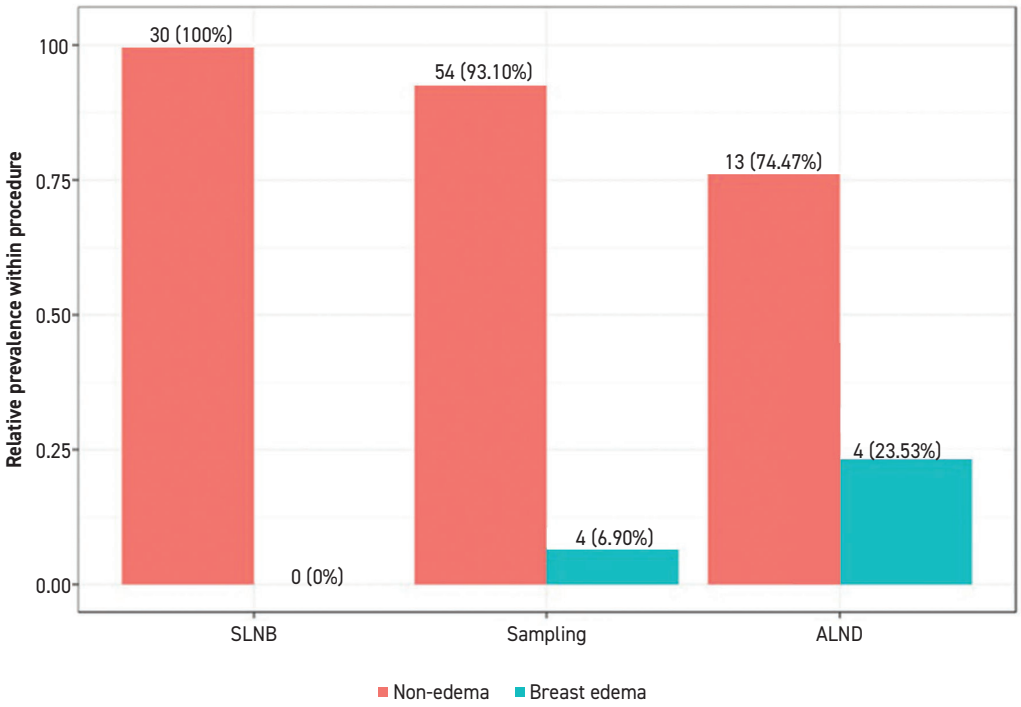
Table 1. Patient characteristics compared between the different axillary procedures

	SLNB (N=30)	LN sampling (N=58)	ALND (N=17)	Overall (N=105)	*P*-value
Body mass index					
Mean ± SD	26.8 ± 5.80	25.8 ± 4.83	28.4 ± 5.55	26.5 ± 5.28	0.216
Median [min–max]	25.0 [18.3–40.0]	24.2 [18.4–40.0]	29.0 [20.9–39.5]	24.8 [18.3–40.0]	
Missing	0	1 ± 1.7%	0	1 ± 1.0%	
Age at surgery, in years					
Mean ± SD	60.2 ± 12.3	55.3 ± 10.7	51.3 ± 11.3	56.0 ± 11.6	0.0464
Median [min–max]	63.5 [32.0–79.0]	58.0 [36.0–75.0]	48.0 [36.0–69.0]	59.0 [32.0–79.0]	
Type of cancer					
IDC	27 ± 90.0%	51 ± 87.9%	12 ± 70.6%	90 ± 85.7%	0.224
ILC	3 ± 10.0%	5 ± 8.6%	3 ± 17.6%	11 ± 10.5%	
Mucinous carcinoma	0 ± 0%	2 ± 3.4%	2 ± 11.8%	4 ± 3.8%	
BRCA 1\2 gene					
Negative	29 ± 96.7%	49 ± 84.5%	16 ± 94.1%	94 ± 89.5%	0.683
Positive	1 ± 3.3%	6 ± 10.3%	1 ± 5.9%	8 ± 7.6%	
Missing	0 ± 0%	3 ± 5.2%	0 ± 0%	3 ± 2.9%	
Neoaduvant therapy					
No	20 ± 66.7%	45 ± 77.6%	8 ± 47.1%	73 ± 69.5%	0.0557
Yes	10 ± 33.3%	13 ± 22.4%	9 ± 52.9%	32 ± 30.5%	
Adjuvant radiation therapy					
No	8 ± 26.7%	8 ± 13.8%	2 ± 11.8%	18 ± 17.1%	0.288
Yes	22 ± 73.3%	50 ± 86.2%	15 ± 88.2%	87 ± 82.9%	

IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, SD = standard deviation

Figure 2. Prevalence of breast edema across the different procedures

No patients presented with SLNB had breast edema. In lymph nodes sampling and ALND the prevalence was 6.9%(4) and 23.53% (4), respectively. ALND = axillary lymph node dissection, SLNB = sentinel lymph node biopsy



Eighteen patients did not receive adjuvant radiation therapy, and none of these patients developed breast edema. However, due to the small sample size, the results did not achieve statistical significance.

A logistic regression model was employed to identify risk factors for breast edema. Predictors included procedure type, adjuvant radiation therapy, and body mass index (BMI). Using stepwise model selection based on AIC values, significant predictors identified were arm lymphedema (OR 57.54, $P = 0.024$), BMI (OR 0.65, $P = 0.016$), and tumor grade (OR 51.78, $P = 0.040$). Other variables, such as BRCA status and age, were non-significant. The model had a Tjur's R^2 value of 0.560 and included data from 94 patients.

The relationship between breast and arm lymphedema was examined using Fisher's exact test, yielding a *P*-value of 0.058, indicating a trend toward significance.

DISCUSSION

Breast-conserving surgery combined with radiotherapy is a cornerstone of early-stage breast cancer treatment; however, it carries the risk of complications such as breast edema. With a minimal follow-up of 3 years, our study documented a prevalence of 7.6%, which, while lower than the wide range reported in previous studies (10–90.4%), highlights the importance of rigorous diagnostic criteria and extended follow-up. Surgical interventions significantly influenced breast edema development, with ALND patients showing a markedly higher prevalence compared to those undergoing SLNB.

Previous literature identifies key risk factors for breast and arm lymphedema, including the extent of surgical intervention, intensity of radiation treatment, initial presence of inflammatory breast carcinoma, postoperative infection, larger breast and tumor size, obesity, and diabetes [1-3]. In our study, the significant predictors of breast edema were the extent of axillary surgical intervention, arm lymphedema, and tumor grade. While our findings are consistent with the role of axillary intervention and tumor characteristics, we did not observe significant associations with inflammatory breast carcinoma or postoperative infection, likely due to a small sample size). In contrast to previous findings, we found that a high BMI was a protective factor; however, we did not have any data on the size of breasts or the extent of resection, which could have been a confounding factor. The co-occurrence of breast and arm lymph-

edema in 50% of cases underscores the shared lymphatic pathways of the breast and arm.

Incorporating advanced imaging modalities, such as indocyanine green (ICG) lymphography, could enhance early detection and differentiation of subclinical breast edema from other conditions [11,12]. In addition, our findings of lymphedema prevalence across the different procedures align with commonly reported trends in the literature, which reinforces the established association between more extensive surgical interventions, such as ALND, and higher rates of lymphedema [13,14].

Limitations of the study include the relatively small sample size and the lack of advanced imaging techniques, which could have provided additional diagnostic precision. Furthermore, the single-center study design may limit the generalizability of findings, and variability in physical examination methods could introduce measurement bias. The absence of detailed analysis of radiotherapy techniques and the psychosocial impact of breast edema also leaves room for further investigation. There were no data about the amount of breast resection (weight or percentage of the breast) nor whether the breast was reconstructed. Oncoplastic-associated procedures, such as tissue rearrangement or secondary flap as mobilization of breast tissues, can theoretically add internal scars to the breast tissue and may burden the lymphatic pathways. Future studies should integrate imaging methods to distinguish breast edema from similar conditions and identify early-stage changes. Thorough clinical evaluation remains essential for accurate diagnosis. Advanced imaging modalities, such as ICG lymphography, hold promise for improving diagnostic precision and early intervention.

CONCLUSIONS

Breast edema is a clinically significant complication following breast-conserving surgery and radiotherapy, with a prevalence of 7.6% observed in this study. Lymphatic disruption, particularly from ALND, plays a critical role in its development. Meticulous surgical planning, long-term patient monitoring, and a multidisciplinary approach are vital for minimizing complications and improving outcomes. Continued research is necessary to develop innovative strategies to preserve lymphatic function, reduce the burden of breast edema, and mitigate associated lymphedema.

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For many years, I thought a poem was a whisper overheard, not an aria heard.

Rita Dove (Born 1952), American poet and essayist