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Immediate implant reconstruction is associated with a reduced risk of lymphedema compared to mastectomy alone: a prospective cohort study

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STRUCTURED ABSTRACT

Objective—We sought to determine the risk of lymphedema associated with immediate breast reconstruction compared to mastectomy alone.

Background—Immediate breast reconstruction is increasingly performed at the time of mastectomy. Few studies have examined whether breast reconstruction impacts development of lymphedema.

Methods—616 breast cancer patients who underwent 891 mastectomies between 2005–2013 were prospectively screened for lymphedema at our institution, with 22.2 months median follow-up. Mastectomies were categorized as immediate implant, immediate autologous, or no reconstruction. Arm measurements were performed pre-operatively and during post-operative follow-up using a Perometer. Lymphedema was defined as 10% arm volume increase compared to pre-operative. Kaplan-Meier and Cox regression analyses were performed to determine lymphedema rates and risk factors.

Results—Of 891 mastectomies, 65% (580/891) had immediate implant, 11% (101/891) immediate autologous, and 24% (210/891) no reconstruction. The two-year cumulative incidence of lymphedema was: 4.08% (95% CI: 2.59–6.41%) implant, 9.89% (95% CI: 4.98–19.1%) autologous, and 26.7% (95% CI: 20.4–34.4%) no reconstruction. By multivariate analysis, immediate implant (HR: 0.352, $p < 0.0001$) but not autologous (HR: 0.706, $p = 0.2151$)

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DISCLOSURES

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reconstruction was associated with a significantly reduced risk of lymphedema compared to no reconstruction. Axillary lymph node dissection ($p<0.0001$), higher Body Mass Index ($p<0.0001$), and greater number of nodes dissected ($p=0.0324$) were associated with increased lymphedema risk.

Conclusion—This prospective study suggests that in patients for whom implant-based reconstruction is available, immediate implant reconstruction does not increase the risk of lymphedema compared to mastectomy alone.

INTRODUCTION

Improvements in breast cancer treatment have led to increasing survival rates and enhanced cosmetic outcomes. Despite this, significant side effects of treatment still remain.

Lymphedema is a chronic condition characterized by swelling of the arm, hand, breast, or trunk which can result from breast cancer treatment due to the accumulation of lymphatic fluid in the interstitial tissues. The condition is known to significantly compromise quality of life due to body image changes, alterations in arm function, increased complications including infection and cellulitis, and significantly higher medical costs.^{1–5} The reported incidence of lymphedema is >20% following axillary lymph node dissection (ALND) and 3.5–11% after sentinel lymph node biopsy (SLNB).^{6–11}

Recent trends have demonstrated an increase in the number of patients who opt for immediate breast reconstruction following mastectomy.^{12,13} Immediate breast reconstruction has been shown to improve body image, psychological well-being, and overall quality of life in breast cancer patients.^{14–18} Numerous studies have demonstrated the oncologic safety of immediate breast reconstruction for patients with invasive breast cancer,^{19–21} and some argue that immediate compared with delayed breast reconstruction offers superior aesthetic and psychosocial benefits.^{22–24}

Commonly cited risk factors for lymphedema include ALND and higher Body Mass Index (BMI) or obesity, with mastectomy occasionally cited as a risk factor.^{1,6,8–10,25–37} In addition, several studies have shown that delayed autologous breast reconstruction may reduce the severity of existing post-mastectomy lymphedema resulting from a prior modified radical mastectomy. Until recently, there has been little data on the association of immediate breast reconstruction with development of lymphedema after mastectomy. Findings from recent studies suggest that immediate breast reconstruction may be associated with a reduced risk of post-mastectomy lymphedema.^{38–40} However, most studies were conducted retrospectively and utilized non-standardized methods of measuring and defining lymphedema.

In this study, we sought to determine the risk of lymphedema associated with immediate breast reconstruction compared to mastectomy alone. We evaluated rates of lymphedema in patients prospectively screened for the condition at our institution who underwent mastectomy with immediate implant, immediate autologous, or no reconstruction. Multivariate regression was utilized to identify independent risk factors for lymphedema.

MATERIAL AND METHODS

Study Design

Beginning in 2005, with Institutional Review Board approval, we prospectively obtained bilateral arm volume measurements on women diagnosed with breast cancer using a Perometer. The Perometer is an optoelectronic system that utilizes infrared light beams to measure circumference at regular intervals along the limb and calculates volume based on these measurements. Arm volume measurements were obtained pre- and post-operatively, during chemotherapy and/or radiation therapy, and at follow-up oncology visits after completion of breast cancer treatment. The protocol for lymphedema screening has previously been published.⁴¹

For this study, we utilized a weight-adjusted volume change equation which calculates change in arm volume compared to a pre-operative measurement and accounts for temporal changes in patient weight, which may cause arm size changes unrelated to lymphedema.⁴² Weight-adjusted arm volume change (WAC) was calculated for the left and right arm independently at each post-operative assessment according to the formula, $WAC = (A2*W1)/(W2*A1) - 1$, where A1 is pre-operative arm volume, A2 is arm volume at a post-operative assessment, and W1 and W2 are the patient's weights at these time points. Use of the WAC equation allowed for inclusion of patients who underwent bilateral mastectomy, since arm volume change can be assessed in each arm individually and does not rely on comparison of size between arms. All patients included in this analysis had a pre-operative measurement and at least one follow-up measurement occurring >3 months after surgery.

Lymphedema was defined as a measurement with ≥10% WAC, based on consensus in the literature.^{6,29,43} Measurements recorded within the first 3 months after surgery were not utilized for lymphedema assessment, because patients may experience transient increases in measured arm volume during this period related to post-surgical changes.⁴⁴ Measurements obtained after a patient was diagnosed with distant metastases or local recurrence were excluded to avoid potential confounding factors.

Patient Population

616 patients with a diagnosis of primary breast cancer who underwent 891 mastectomies at our institution between 9/2005–2/2013 were included in this analysis, with a median post-operative follow-up of 22.2 months (range 3.0–86.9). Each breast was considered individually, and mastectomies were categorized according to type of immediate breast reconstruction: implant (immediate tissue expander or immediate direct-to-implant, designated together as immediate implant), autologous, or no reconstruction. Mastectomies with delayed breast reconstruction were excluded from this analysis. Regional lymph node radiation included supraclavicular and/or axillary radiation. Patient demographics, surgical, radiation and medical oncology treatments were collected via medical record review to analyze as risk factors.

Breast Reconstruction

Implant reconstruction included immediate tissue expander placement with subsequent implant exchange and immediate direct-to-implant (single stage) placement. Tissue expanders were placed with total or partial muscle coverage, with or without acellular dermal matrix or vicryl mesh. Expanders were exchanged to implants in a second surgery. If the skin envelope was sufficient at the time of mastectomy, an implant was placed with partial muscle coverage and acellular dermal matrix or mesh in one stage.⁴⁵ Immediate autologous reconstruction included Transverse Rectus Abdominis Myocutaneous (TRAM) and Deep Inferior Epigastric Artery Perforator (DIEP) flaps. One patient underwent autologous reconstruction with a Superficial Inferior Epigastric Artery (SIEA) flap. Operations were performed at a single institution by 4 breast only surgeons and 5 dedicated reconstructive plastic surgeons. The decision regarding whether to perform reconstruction and which type of reconstruction to perform was made by a multidisciplinary team based on patient anatomy and comorbidities, concomitant therapy, and patient preference.

Statistical Analysis

Univariate and multivariate Cox proportional hazard models were used to evaluate risk factors for lymphedema. Time-dependent covariates were included for use of systemic therapies and radiation fields such that cases were included in the unexposed group prior to initiation of a given treatment and then were included in the exposed group after treatment. Regression parameters in the Cox models were estimated using a robust sandwich covariance matrix estimate to account for the correlation induced by including data from both sides for patients who had bilateral mastectomies.⁴⁶ Multivariate models were derived using backwards selection, starting with a model that included all variables that were significant ($p < 0.1$) in the univariate analysis, and removing non-significant variables one at a time until only significant variables ($p < 0.05$) remained. Two-way interactions were evaluated for all covariates included in the resulting model. The Kaplan-Meier method was used to estimate and plot cumulative incidence of lymphedema by type of reconstruction.

RESULTS

Patient Population

We included 616 patients who underwent 891 mastectomies, of which 73% (654/891) were for treatment of breast cancer and 27% (237/891) prophylactic. 282 of the 616 (46%) patients underwent bilateral mastectomies, 38 for a diagnosis of bilateral breast cancer and 244 for unilateral breast cancer with contralateral prophylactic mastectomy. Patients who underwent bilateral prophylactic mastectomies were excluded. Seven patients with unilateral mastectomy later underwent contralateral mastectomy with bilateral reconstruction (delayed on one side and immediate on the other), and therefore had one breast excluded from this analysis due to delayed reconstruction. The remaining 334 of 616 (54%) patients underwent unilateral mastectomy for a diagnosis of unilateral breast cancer.

Of the 891 mastectomies, 76% (681/891) were classified as immediate breast reconstruction and 24% (210/891) as no reconstruction. Among the immediate breast reconstructions, 85% (580/681) were immediate implant (309 immediate tissue expander and 271 direct-to-

implant) and 15% (101/681) autologous. Seventy-six of 101 (75%) autologous breast reconstructions utilized a TRAM flap, 24 (24%) utilized a DIEP flap, and 1 (1%) SIEA flap. Clinicopathologic factors of patients with and without reconstruction are listed in Table 1.

Excluding mastectomies performed prophylactically (n=243) and/or following neoadjuvant chemotherapy (n=128), 13% (74/551) were for AJCC stage 0, 41% (22/551) for stage I, 31% (169/551) for stage II, and 15% (86/551) for stage III breast cancer (Table 2). Eleven mastectomies were performed for stage T4d (inflammatory) breast cancer, all in the no reconstruction group and following neoadjuvant chemotherapy. 5 mastectomies were performed for cN2 breast cancer, 4 in the no reconstruction group and 1 in the immediate reconstruction group.

Cumulative Incidence of Lymphedema

The two-year cumulative incidence of lymphedema was 10.58% (95% CI: 8.41–13.27%), 5.13% (95% CI: 3.50–7.49%) for immediate breast reconstruction compared with 26.66% (95% CI: 20.38–34.43%) for no reconstruction. The incidence for implant reconstruction was 4.08% (95% CI: 2.59–6.41%), compared with 9.89% (95% CI: 4.98–19.13%) for autologous reconstruction (Fig. 1, Table 3). Among implant reconstructions, lymphedema incidence was similar for tissue expander (3.91%, 95% CI: 2.09–7.23%) and direct-to-implant (4.31%, 95% CI: 2.21–8.29%).

The two-year cumulative incidence of lymphedema was similar when prophylactic mastectomies were excluded, 5.46% (95% CI: 3.38–8.75%) for implant, 11.15% (95% CI: 5.40–22.28%) for autologous, and 30.35% (95% CI: 23.27–38.97%) for no reconstruction.

Univariate Analysis

By univariate analysis, immediate implant (HR: 0.172, $p<0.0001$) or autologous (HR: 0.467, $p=0.0077$) reconstruction was associated with a significantly reduced risk of lymphedema compared to no reconstruction. Univariate results for additional clinicopathologic risk factors are listed in Table 4.

Multivariate Analysis

Immediate breast reconstruction was associated with a significantly reduced risk of lymphedema compared to no reconstruction (HR: 0.432, $p<0.0001$) by multivariate analysis. According to type of reconstruction, implant (HR: 0.352, $p<0.0001$) but not autologous (HR: 0.706, $p=0.215$) reconstruction significantly reduced the risk of lymphedema compared to no reconstruction. The reduction in lymphedema risk was similar for implant reconstruction with direct-to-implant (HR: 0.433, $p=0.009$) or tissue expander (HR: 0.300, $p=0.0002$). There was a greater reduction in lymphedema risk for implant compared with autologous reconstruction by multivariate analysis (HR: 0.500, $p=0.0334$). Factors associated with a significantly increased risk of lymphedema by multivariate analysis included BMI ≥ 30 ($p<0.0001$), ALND ($p<0.0001$), and number of lymph nodes dissected ($p=0.0322$). Other significant univariate factors did not remain significant by multivariate analysis. [Table 4]

A multivariate model excluding prophylactic mastectomies similarly demonstrated a reduced risk of lymphedema associated with implant reconstruction (HR: 0.350, $p<0.0001$), as did a model excluding mastectomies performed for stage T4d and cN2 disease (HR: 0.378, $p=0.0002$).

DISCUSSION

In this series of 891 mastectomies from 616 patients prospectively screened for lymphedema using a Perometer, immediate breast reconstruction was associated with a significantly reduced risk of lymphedema compared to no reconstruction by multivariate analysis. According to type of reconstruction, immediate implant but not immediate autologous reconstruction was associated with reduced lymphedema risk. Other independent risk factors included ALND, greater number of lymph nodes dissected, and higher BMI at surgery.

Recent trends have demonstrated a rise in the rate of mastectomies performed, including among patients diagnosed with early-stage breast cancer.^{47–49} A corresponding increase in the number of patients undergoing immediate breast reconstruction at the time of mastectomy has also been observed.^{12,13} Immediate breast reconstruction has been demonstrated to improve body image, psychological well-being, and quality of life. Importantly, studies have confirmed the oncologic safety of immediate breast reconstruction for patients with invasive breast cancer.^{19–21}

Several studies evaluating the impact of delayed reconstruction on post-mastectomy lymphedema have shown that delayed autologous reconstruction reduces the severity of existing lymphedema.^{50–53} Chang et al retrospectively evaluated 444 delayed breast reconstructions, and found that some patients with existing lymphedema experienced reduced severity of lymphedema symptoms following delayed autologous reconstruction.⁵⁰ Based on prior studies demonstrating reestablishment of lymphatic pathways after microvascular free-tissue transfer,^{54,55} it was hypothesized that use of a healthy, well-vascularized tissue flap in autologous breast reconstruction may promote lymphatic vessel in-growth and thereby improve lymphedema symptoms.^{50,52}

Findings from recent studies suggest that immediate breast reconstruction may also be associated with a reduced risk of lymphedema.^{38–40} A 2010 study by Avraham et al prospectively evaluated the incidence of lymphedema after skin-sparing mastectomy with immediate tissue expander reconstruction compared with no reconstruction.³⁹ In this series of 316 patients, lymphedema was objectively defined as an increase in arm circumference of $>2\text{cm}$ or $>5\text{cm}$ compared to a pre-operative measurement, and was also subjectively evaluated utilizing a lymphedema symptoms questionnaire. The authors found that after adjusting for age, BMI, and post-operative weight gain, patients who underwent tissue expander reconstruction had a significant reduction in risk of lymphedema.

A 2012 study by Card et al retrospectively evaluated 574 matched patients who underwent mastectomy alone or with reconstruction using tissue expanders, latissimus dorsi flap with implants, or autologous tissue transfer.³⁸ The authors found that patients without reconstruction were significantly more likely to develop lymphedema by multivariate

analysis (HR= 0.37, $p<0.0001$) after matching patients on age, axillary radiation, and type of axillary surgery. Patients did not undergo a pre-operative arm measurement, and were evaluated for lymphedema in a non-standardized manner based on clinical assessment and confirmation with measurements not clearly defined in the manuscript. A letter to the editor responding to this manuscript suggested the potential for under-diagnosis of lymphedema due to subjective evaluation at irregular intervals, and cited the need for objective measurement data from centers with consecutive lymphedema information.⁵⁶

Most recently, Lee et al retrospectively evaluated the impact of immediate autologous reconstruction on lymphedema risk in 712 patients who underwent modified radical mastectomy.⁴⁰ Multivariate analysis demonstrated a significantly lower incidence of lymphedema in patients who underwent immediate autologous reconstruction compared to mastectomy alone (OR=0.461, $p=0.023$). However, as with the study by Card et al, patients in this series did not undergo a pre-operative measurement, and were evaluated for lymphedema in a non-standardized manner based on clinician assessment and confirmation with the Perometer.

In our series, immediate implant but not autologous reconstruction was associated with a significantly reduced risk of lymphedema compared to mastectomy alone by multivariate analysis. Importantly, our multivariate analysis adjusted for known lymphedema risk factors including ALND, BMI, number of lymph nodes dissected, and radiation therapy, which were not evenly distributed amongst the reconstruction and no reconstruction groups.^{1,6,8–10,25–37,57–63} Indeed, ALND, higher BMI at surgery, and greater number of lymph nodes dissected were significantly associated with increased risk of developing lymphedema by multivariate analysis. These factors have all been shown to increase lymphedema risk in previous studies.^{6,29}

There exist a number of possible explanations for our finding that immediate implant reconstruction is associated with reduced lymphedema risk. Patients undergoing immediate reconstruction typically have skin-sparing mastectomies, which preserves more of the skin envelope and therefore lymphatic channels under the skin, whereas patients without reconstruction undergo more resection of breast and axillary skin for optimal healing and cosmesis. Perhaps more importantly, patients who undergo mastectomy without reconstruction may experience tissue adhesion, fibrosis, and contracture of the breast skin, chest wall, and axilla, resulting in obstructed lymphatic flow and possibly lymphedema development.⁴⁰ Yet another theory suggests a role for tissue ischemia in lymphedema prevention. Tissue expansion and capsular contracture from implant reconstruction may induce tissue ischemia and lead to increased expression of vascular endothelial growth factor, resulting in tissue angiogenesis and possibly lymphangiogenesis.⁶⁴ Card et al propose that continued ischemia and capsular contracture from implant reconstruction may help prevent lymphedema development.³⁸

Despite findings from studies demonstrating that delayed autologous breast reconstruction may improve existing lymphedema, we did not find immediate autologous breast reconstruction to reduce risk of lymphedema in our series. This is in contrast with findings from Lee et al, who hypothesized that transferred skin flaps could reduce post-operative

fibrosis, contracture, and adhesion in the chest wall and axilla, and could contribute to reduced lymphatic obstruction.⁴⁰ The relatively small number of patients in our series with immediate autologous breast reconstruction (n=101) may account for our findings, as demonstrated by the large confidence interval for cumulative lymphedema incidence.

Additional explanations for the association of reduced lymphedema risk with immediate breast reconstruction include the positive impacts of reconstruction, and uncontrolled-for confounding. A recent study by McCarthy et al demonstrated that women who underwent immediate autologous or implant reconstruction following mastectomy experienced less chronic physical morbidity compared with those who underwent mastectomy alone, which could contribute to reduced long-term risk of lymphedema resulting from increased upper extremity use with breast reconstruction.⁶⁵ Another possibility is confounding caused by factors not accounted for in the multivariate model, resulting in a lower risk of lymphedema in patients who underwent reconstruction despite adjustment for known risk factors. In our series, patients in the no reconstruction group were more likely to undergo ALND, radiation therapy, have BMI ≥ 30 , and have more lymph nodes dissected, all of which are known risk factors but were adjusted for in the multivariate model.

Our study has a number of limitations, including the non-randomized selection of patients for immediate reconstruction versus mastectomy alone. There were significant differences in the distribution of risk factors for lymphedema among patients in the reconstruction and no reconstruction groups, which could at least partially account for our findings despite adjustment in the multivariate model. A greater proportion of patients in the no reconstruction group had stage IIb or stage III breast cancer compared with the immediate reconstruction groups; thus it is possible that the combination of extent of surgical procedure, radiation therapy, and receipt of neoadjuvant chemotherapy could have enhanced the risk of lymphedema in the no reconstruction group. However, we did adjust for post-mastectomy radiation and receipt of chemotherapy, which were not significant on multivariate analysis. Of note, exclusion of mastectomies for inflammatory (T4d) breast cancer and with matted axillary lymph nodes (cN2), which may be at higher risk for lymphedema due to more aggressive surgery and are not usually accompanied by reconstruction, did not affect our findings. Owing to these limitations, further research is warranted regarding the association of lymphedema with breast reconstruction and a possible mechanism by which immediate breast reconstruction may reduce the risk of lymphedema.

Strengths of this study include use of a large cohort of patients prospectively screened for lymphedema with objective arm volume measurements occurring pre-operatively and at regular intervals throughout breast cancer treatment and follow-up. Arm volumes were measured using the Perometer, a device with demonstrated validity for lymphedema assessment.^{66,67} To our knowledge, this cohort of 891 mastectomies (from 616 patients) represents one of the largest series in the literature on lymphedema, and certainly the largest in which risk of lymphedema was prospectively evaluated for association with immediate breast reconstruction. Patients included in our study underwent pre-operative and regular post-operative measurements, with a median follow-up of almost two years. We objectively quantified lymphedema using the validated WAC equation, which incorporates fluctuations

in patient weight to account for arm size changes unrelated to lymphedema.⁴² The importance of obtaining pre-operative assessments to account for asymmetry between arms and adjustment for factors unrelated to lymphedema has been previously demonstrated.^{41,68,69}

In conclusion, multivariate analysis of 891 mastectomies from patients prospectively screened for lymphedema demonstrated a reduced risk of lymphedema with immediate implant reconstruction compared to mastectomy alone, in patients for whom implant-based reconstruction was available. The mechanism by which immediate implant reconstruction may reduce lymphedema risk is not known, however, further research may offer novel treatment strategies for mastectomy patients. Furthermore, these findings can be utilized for patient counseling regarding reconstructive options following mastectomy.

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	No. at risk					
No reconstruction:	119	106	68	38	20	9
Autologous:	78	73	47	38	20	11
Implant:	316	303	182	112	59	28

Figure 1.
 Cumulative incidence of lymphedema (≥ 10% WAC) according to immediate breast reconstruction

Table 1

Clinical and pathologic characteristics of mastectomy cohort, as median (range) or n (%)

	Entire Cohort N= 891	Immediate Reconstruction N= 681	No Reconstruction N= 210	P value *
Patient Characteristics				
Age at surgery, years	50 (23–86)	48 (23–81)	58 (28–86)	<0.0001
Follow-up, months	22.2 (3.0–86.9)	21.6 (3.0–83.6)	24.5 (4.6–86.9)	0.0525
BMI at surgery[†]				<0.0001
<30 kg/m ²	691 (79%)	550 (82%)	141 (69%)	
≥30 kg/m ²	181 (21%)	117 (18%)	64 (31%)	
Axillary Surgery				<0.0001
None	102 (12%)	83 (12%)	19 (9%)	
SLNB	519 (58%)	433 (64%)	86 (41%)	
ALND	270 (30%)	165 (24%)	105 (50%)	
Tumor Type				<0.0001
None (Prophylactic)	243 (27%)	210 (31%)	33 (16%)	
Invasive Carcinoma	574 (64%)	412 (61%)	162 (77%)	
Ductal Carcinoma in Situ (DCIS)	74 (8%)	59 (9%)	15 (7%)	
Pathologic Characteristics				
Invasive tumor size, cm [‡]	1.8 (0.01–12.5)	1.7 (0.01–10.5)	2.3 (0.10–12.5)	0.0004
Number lymph nodes dissected	2 (0–43)	2 (0–43)	6.5 (0–41)	<0.0001
Number positive lymph nodes	0 (0–39)	0 (0–23)	0 (0–39)	<0.0001
Radiation Therapy				<0.0001
None	640 (72%)	522 (77%)	118 (56%)	
Chest Wall only	32 (4%)	27 (4%)	5 (2%)	
Chest Wall + RNLR	219 (25%)	132 (19%)	87 (41%)	
Neoadjuvant Chemotherapy				<0.0001
Yes	128 (14%)	78 (12%)	50 (24%)	
No	763 (86%)	603 (89%)	160 (76%)	
Adjuvant Chemotherapy				0.2253
Yes	478 (54%)	373 (55%)	105 (50%)	
No	413 (46%)	308 (45%)	105 (50%)	
Hormonal Therapy				0.5456

	Entire Cohort N= 891	Immediate Reconstruction N= 681	No Reconstruction N= 210	P value*
Yes	630 (71%)	485 (71%)	145 (69%)	
No	261 (29%)	196 (29%)	65 (31%)	

* P value for immediate reconstruction vs. no reconstruction

† 19 values missing for BMI

‡ Excludes mastectomies performed after neoadjuvant chemotherapy

Abbreviations: BMI = Body Mass Index, SLNB = Sentinel Lymph Node Biopsy, ALND = Axillary Lymph Node Dissection, RLNR = Regional Lymph Node Radiation

Table 2

AJCC staging for the cohort according to type of reconstruction, excluding mastectomies performed prophylactically and/or following neoadjuvant chemotherapy

AJCC Stage	Entire cohort N= 551 (100%)	Immediate Implant N= 350 (100%)	Immediate Autologous N= 66 (100%)	No Reconstruction N= 135 (100%)
0	74 (13%)	50 (14%)	9 (14%)	15 (11%)
I				
Ia	196 (36%)	127 (36%)	31 (47%)	38 (28%)
Ib	26 (5%)	20 (6%)	3 (5%)	3 (2%)
II				
IIa	105 (19%)	73 (21%)	13 (20%)	19 (14%)
IIb	64 (12%)	39 (11%)	4 (6%)	21 (16%)
III				
IIIa	67 (12%)	35 (10%)	4 (6%)	28 (21%)
IIIb	0 (0%)	0 (0%)	0 (0%)	0 (0%)
IIIc	19 (3%)	6 (2%)	2 (3%)	11 (8%)

Table 3

2-year cumulative incidence of lymphedema (10% WAC) overall and by type of immediate breast reconstruction

	N	2-year cumulative incidence	95% Confidence Interval	
Entire cohort	891	10.58%	8.41%	13.27%
Immediate Reconstruction	681	5.13%	3.50%	7.49%
Implant	580	4.08%	2.59%	6.41%
Autologous	101	9.89%	4.98%	19.13%
No reconstruction	210	26.66%	20.38%	34.43%

Table 4

Univariate and multivariate analysis of risk factors for lymphedema (10% WAC)

	Univariate Results		Multivariate Results	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Patient Characteristics				
Age at surgery, years *	1.04 (1.02, 1.06)	0.0003	NS [†]	NS
BMI at surgery, kg/m ² 30 vs. <30	4.13 (2.72, 6.26)	<0.0001	3.42 (2.23, 5.24)	<0.0001
Surgical Characteristics				
Axillary Surgery				
SLNB vs. no axillary surgery	2.37 (0.31, 18.17)	0.4065	[‡]	-
ALND vs. SLNB	13.11 (7.29, 23.57)	<0.0001	-	-
ALND vs. SLNB/no axillary surgery	-	-	7.53 (3.47, 16.35)	<0.0001
Number lymph nodes dissected *	1.11 (1.09, 1.12)	<0.0001	1.03 (1.00, 1.05)	0.0324
Immediate Reconstruction				
Implant vs. no reconstruction	0.17 (0.11, 0.28)	<0.0001	0.35 (0.21, 0.58)	<0.0001
Autologous vs. no reconstruction	0.47 (0.27, 0.82)	0.0077	0.71 (0.41, 1.23)	0.2151
Pathologic Characteristics				
Invasive tumor size, cm *	1.24 (1.12, 1.36)	<0.0001	NS	NS
Number positive lymph nodes *	1.11 (1.08, 1.14)	<0.0001	NS	NS
Systemic Therapy				
Neoadjuvant chemotherapy				
Yes vs. no	2.56 (1.61, 4.07)	<0.0001	NS	NS
Adjuvant chemotherapy				
Yes vs. no	1.82 (1.17, 2.83)	0.0081	NS	NS
Hormonal therapy				
Yes vs. no	1.24 (0.78, 1.98)	0.3649	-	-
Radiation Therapy				
Chest wall only vs. no radiation	3.96 (1.67, 9.39)	0.0018	NS	NS
Chest wall + RLNR vs. no radiation	6.57 (4.39, 9.84)	<0.0001	NS	NS

* Age at surgery, invasive tumor size, number of lymph nodes dissected and number of positive lymph nodes were analyzed as continuous variables such that the hazard ratios reflect the change in lymphedema risk associated with a 1-unit increase in the variable

[†]“NS” indicates the variable was not significant in multivariate analysis

[‡]“-” indicates the specified variable/comparison was not analyzed

Abbreviations: CI = confidence interval, BMI = body mass index, SLNB = sentinel lymph node biopsy, ALND = axillary lymph node dissection, RLNR = regional lymph node radiation

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