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Impact of Neoadjuvant Chemotherapy on Breast Reconstruction

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Abstract

BACKGROUND—With advances in oncologic treatment, cosmesis after mastectomy has assumed a pivotal role in patient and provider decision making. Multiple studies have confirmed the safety of both chemotherapy before breast surgery and immediate reconstruction. Little has been written about the effect of neoadjuvant chemotherapy on decisions about reconstruction.

METHODS—The authors identified 665 patients with stage I through III breast cancer who received chemotherapy and underwent mastectomy at Dana-Farber/Brigham & Women's Cancer Center from 1997 to 2007. By using multivariate logistic regression, reconstruction rates were compared between patients who received neoadjuvant chemotherapy (n = 180) and patients who underwent mastectomy before chemotherapy (n = 485). The rate of postoperative complications after mastectomy was determined for patients who received neoadjuvant chemotherapy compared with those who did not.

RESULTS—Reconstruction was performed immediately in 44% of patients who did not receive neoadjuvant chemotherapy but in only 23% of those who did. Twenty-one percent of neoadjuvant chemotherapy recipients and 14% of adjuvant-only chemotherapy recipients underwent delayed reconstruction. After controlling for age, receipt of radiotherapy, and disease stage, neoadjuvant recipients were less likely to undergo immediate reconstruction (odds ratio [OR], 0.57; 95% confidence interval [CI], 0.37, 0.87) but were no more likely to undergo delayed reconstruction (OR, 1.29; 95% CI, 0.75, 2.20). Surgical complications occurred in 30% of neoadjuvant chemotherapy recipients and in 31% of adjuvant chemotherapy recipients.

CONCLUSIONS—The current results suggest that patients who receive neoadjuvant chemotherapy are less likely to undergo immediate reconstruction and are no more likely to

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undergo delayed reconstruction than patients who undergo surgery before they receive chemotherapy.

Keywords

neoadjuvant chemotherapy; breast reconstruction; breast cancer; mastectomy; postoperative complications

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With advances in oncologic treatment, cosmesis after breast surgery has assumed a pivotal role in patient and provider decision making. Reconstruction, once was delayed for months after surgery, has proven oncologically sound and presents little additional risk of morbidity —whether autologous or prosthetic—when undertaken simultaneously with primary breast surgery.[1–3] By avoiding an additional procedure and achieving an immediate improvement in cosmetic result, the advantages for patients, both psychological and financial, have made immediate reconstruction a desired option for many.[4–6]

Neoadjuvant chemotherapy also has become a critical component of modern breast cancer care. By reducing tumor burden in both the breast and the axilla, women may achieve complete resections with less extensive operations.[7,8] To date, randomized controlled trials have reported equivalent recurrence rates, disease-free survival rates, and overall survival rates for neoadjuvant chemotherapy and adjuvant chemotherapy.[7,9] In addition, neoadjuvant therapy has both prognostic and prescriptive value. Treatment response is predictive of long-term survival, whereas nonresponse may inform future chemotherapy choices.[8,10]

However, despite their independent advantages, little is known about how decisions for neoadjuvant chemotherapy and immediate reconstruction influence each other when used concurrently.[11] Although it has been demonstrated that apprehensions about delays in adjuvant treatment after neoadjuvant chemotherapy and immediate reconstruction are largely unwarranted,[12] the interaction between neoadjuvant chemotherapy and the receipt of reconstruction is not well-described. The use of neoadjuvant chemotherapy is 1 of several clinical scenarios in which individual surgeon preference may have an impact on the timing of reconstruction. In the current study, we sought to characterize how neoadjuvant chemotherapy influenced the use of immediate breast reconstruction in a cohort of patients from a large tertiary cancer center with a multiprovider, multipractice, multisite plastics and reconstructive referral network. We hypothesized that patients who received neoadjuvant chemotherapy would be less likely to undergo immediate reconstruction after controlling for other clinical characteristics, possibly because of complications during chemotherapy or treatment fatigue.

MATERIALS AND METHODS

Identification of Cohort and Data Abstraction

The Breast Oncology Center at Dana-Farber/Brigham & Women’s Cancer Center includes surgical oncologists, medical oncologists, radiation oncologists, radiologists, pathologists, and plastic surgeons, among others, in a large, multidisciplinary care team. Patients are referred to 1 of 12 plastic surgeons at the discretion of the breast surgical oncologist after initial consultation. The decision for referral is individually based; patients with advanced breast cancer may be candidates for breast reconstruction. These plastic surgeons represent 3 different practices at 2 different hospitals; therefore, the approach to reconstruction is heterogeneous at our institution.

We identified 791 patients with stage I through III breast cancer who received chemotherapy and underwent mastectomy at Dana-Farber/Brigham & Women’s Cancer Center between

1997 and 2007. Eighty-one patients were excluded secondary to unclear details regarding either the timing of their chemotherapy, the timing of their surgery, and/or the laterality of their disease. We identified variables concerning demographics (age, race, marital status), overall health (body mass index [BMI], smoking status, number of comorbidities, presence of diabetes, premastectomy clinical status), disease status (stage, tumor size, presence of lymph node metastases, estrogen receptor [ER]/progesterone receptor [PR]/human epidermal growth factor receptor 2 [Her-2] status), and treatment (start and end dates for chemotherapy regimen, use of radiation therapy, use of hormone therapy, surgical procedures, and procedure dates) from our internally maintained, prospectively collected database.

Recipients of neoadjuvant therapy underwent an additional chart review to obtain detailed information on the development of complications during neoadjuvant therapy (inpatient admission, neutropenic fever, infectious complications, other severe side effects), the operation (mastectomy type, timing of reconstruction), and the development of surgical complications (seroma requiring drainage, hematoma, surgical site infection, dehiscence/open wound, skin necrosis, flap failure/loss, thromboembolism) within 60 days of mastectomy. A similar chart review was performed for the adjuvant-only group to confirm the operative history (presence/absence and timing of reconstruction) and the development of any 60-day postmastectomy surgical complications.

Patients with simultaneous bilateral cancer (n = 23), who had not undergone mastectomy with the intention of curing a primary cancer (n = 14), who were men (n = 3), and who had received atypical chemotherapy regimens (eg, bone marrow transplantation; n = 5) were excluded, leaving a final sample of 485 recipients of adjuvant therapy only and 180 recipients of neoadjuvant therapy (N = 665).

Data Analysis

Variables—Several variables were dichotomized based on a priori judgment and/or to increase power: These included marital status (single/divorced/widowed vs married), smoking status (never/past smoker vs current smoker), number of comorbidities (0–1 vs ≥ 2), lymph node (N) metastasis (N0 vs ≥ N1), tumor (T) classification (tumor in situ [Tis]-T2 vs ≥ T3), neoadjuvant complications (none vs any), mastectomy type (skin sparing vs simple/modified radical), reconstruction type (autologous flap vs implant/tissue expander), and surgical complications (none vs any). Race was dichotomized (white vs nonwhite) for the multivariate analyses only; all race/ethnicity groups are included in the tables, reflecting univariate analyses. Age (< 50 years, 50–70 years, ≥ 70 years) and BMI (underweight [< 18.5 kg/m^2], normal [18.5–25 kg/m^2], overweight [25–30 kg/m^2], or obese [≥ 30 kg/m^2]) were categorized in univariate analyses for ease of display and were retained as continuous variables for multivariate analyses. Length of neoadjuvant therapy was calculated in days and was retained as a continuous variable for all analyses.

There were 2 primary outcomes: receipt of immediate reconstruction (vs delayed/no reconstruction) and, among patients who did not undergo immediate reconstruction, delayed reconstruction (vs no reconstruction). The primary predictor of interest was treatment with neoadjuvant chemotherapy. We controlled for other covariates of clinical significance, as described above.

Univariate analyses—Recipients of neoadjuvant and adjuvant-only chemotherapy were compared first by using the Fisher exact and, where appropriate (age group, weight, preprocedure clinical status, stage), the Mantel-Haenszel chi-square test for trend. Recipients of immediate reconstruction (n = 256) were compared with recipients of nonimmediate (delayed or no) reconstruction (n = 409) using the Fisher exact test and the Mantel-Haenszel

chi-square test. The same analyses were repeated for the subgroup that did not undergo immediate reconstruction to identify univariate predictors of undergoing delayed reconstruction (n = 106) versus no reconstruction (n = 303). Additional variables (the development of neoadjuvant complications, length of neoadjuvant therapy) were evaluated for their impact on the receipt of immediate reconstruction in the neoadjuvant population alone. Finally, patients who developed surgical complications were compared with those who did not using the Fisher exact test and the Mantel-Haenszel chi-square test.

Multivariate analyses—Multivariate logistic regressions for both outcome comparisons (immediate vs delayed/no reconstruction, delayed vs no reconstruction) and the development of surgical complications were performed next using covariates that were of a priori interest and that had been significant in univariate analyses. Remaining covariates of interest were forced back into the model to check for confounding, which was defined as a change > 20% in the odds ratio (OR) for any other covariate. By using the ASSESS statement in SAS Proc Genmod (SAS Institute Inc., Cary, NC), a goodness-of-fit test statistic based on the sum of the residuals was checked for both logistic regression models.[13] All analyses were performed using SAS version 9.1. Significance was set at a 2-sided *P* value of .05.

RESULTS

The majority of patients in our population were aged < 50 years, white, married, not overweight, nonsmokers, and had few comorbidities. Table 1 lists the characteristics of our study population according to our main predictor of interest: receipt of neoadjuvant chemotherapy. Neoadjuvant chemotherapy was administered as follows: doxorubicin/cyclophosphamide (17.8%), doxorubicin/cyclophosphamide/paclitaxel (32.8%), paclitaxel (9.4%), and other (40%). Adjuvant chemotherapy regimens for both the neoadjuvant chemotherapy group and the adjuvant chemotherapy group are provided in Table 1. Transverse rectus abdominus myocutaneous (TRAM) flaps were the most commonly performed type of reconstruction (44.8%) followed by tissue expanders (30.4%), latissimus dorsi flaps with implants (10.2%), latissimus dorsi flaps alone (5.3%), immediate implants (5.0%), deep inferior epigastric perforator flaps (3.9%), and free flaps (0.6%). Alloderm was used in 72.7% of the tissue expanders, in 50% of the immediate implants, and in 6.8% of the TRAM flaps.

Results of the univariate analysis predicting immediate reconstruction are provided in Table 2. Recipients of neoadjuvant therapy were less likely to undergo immediate reconstruction (16.4% vs 33.7%; $P < .01$). Immediate reconstruction was associated with younger patients (aged < 50 years: 65.6% vs 51.3%; $P < .01$), higher preprocedural functional status (full activity: 81.6% vs 72.4%; $P = .01$), less aggressive disease (stage I: 25.8% vs 12.2%; $P < .01$; ≥ T3: 12.6% vs 28.6%; $P < .01$; ≥ N1: 57.4% vs 72.6%; $P < .01$), low or normal weight (BMI < 25 kg/m^2: 59.2% vs 50.7%; $P = .03$), nonreceipt of radiotherapy (55.7% vs 30.1%; $P < .01$), and adjuvant chemotherapy type (doxorubicin/cyclophosphamide: 42.6% vs 30.8%; other: 19.5% vs 23.5%; $P = .01$). Among neoadjuvant chemotherapy recipients, length of neoadjuvant therapy (82.8 days vs 86.7 days; $P = .41$) and the rate of complications during neoadjuvant therapy (38.1% vs 39.9%; $P = .86$) were similar for those who did and did not undergo immediate reconstruction.

In the remaining patients (those who did not undergo immediate reconstruction), delayed reconstruction was predicted only by younger age (< 50 years: 74.5% vs 43.2%; $P < .01$), lower BMI (< 25 kg/m^2: 67.4% vs 45.3%; $P < .01$), and the lack of diabetes (99.1% vs 93.4%; $P = .02$). All other covariates were nonsignificant on univariate analysis.

Patients who developed surgical complications tended to be older (aged ≥ 50 years: 53.6% vs 38.4%; $P < .01$) and overweight/obese (BMI ≥ 25: 56.9% vs 41.2%; $P < .01$). Patients who underwent more extensive surgery (reconstruction at the time of mastectomy) tended to experience complications more frequently, as expected: 37.1% of patients who underwent immediate reconstruction developed postmastectomy complications compared with only 24.5% of patients who underwent delayed reconstruction and 27.7% of patients who did not undergo reconstruction ($P = .02$). Of those who underwent reconstruction, the complication rate was higher among those who received autogenous tissue flaps than those who received expanders or implants (39.7% vs 21.9%; $P < .01$). The receipt of neoadjuvant chemotherapy was not associated with the development of postmastectomy complications, as indicated in Table 3. This result did not change when the analysis was stratified by timing of reconstruction. After undergoing mastectomy alone, 28.3% of patients who received neoadjuvant chemotherapy developed a complication compared with 26.2% of patients who received adjuvant chemotherapy only ($P = .72$). With the addition of immediate reconstruction, these rates increased to 35.7% and 37.4%, respectively, but remained statistically similar across groups ($P = 1.00$).

After controlling for age, disease stage, and the receipt of radiotherapy, the receipt of neoadjuvant therapy reduced the odds of undergoing immediate reconstruction by more than half (adjusted OR, 0.57; 95% confidence interval [CI], 0.37–0.87; $P < .01$). The adjusted predicted probability of undergoing immediate reconstruction in recipients of neoadjuvant therapy was 0.28 (95% CI, 0.21–0.36), compared with 0.40 (95% CI, 0.36–0.45) in patients receiving only adjuvant therapy.

Among the remaining patients who did not undergo immediate reconstruction, multivariate regression produced only 2 significant predictors of the receipt of delayed reconstruction: younger age (adjusted OR, 0.93/year; 95% CI, 0.90–0.96; $P < .01$) and lower BMI (0.90/point; 95% CI, 0.85–0.95; $P < .01$). After controlling for those covariates, receipt of neoadjuvant therapy was no longer a significant predictor of undergoing delayed reconstruction (adjusted OR, 1.29; 95% CI, 0.75–2.20; $P = .36$). The goodness-of-fit test produced P values of .724 (for the immediate vs delayed/no reconstruction) and .506 (for delayed vs no reconstruction), suggesting that these logistic regression models are appropriate.

The multivariate model predicting surgical complications contained 4 significant covariates. Each year of age increased the adjusted odds of developing a complication by 1.03 (95% CI, 1.01–1.05; $P < .01$). Similarly, with each point increase in BMI, the adjusted odds increased by 1.06 (95% CI, 1.02–1.09; $P < .01$). Compared with patients who had smaller tumors, patients who had ≥ T3 tumors had an adjusted OR of 1.06 (95% CI, 1.03–2.51; $P = .03$). Immediate reconstruction, as expected, had the largest impact, with an adjusted OR of 2.08 (95% CI, 1.4–3.05; $P < .01$). Receipt of neoadjuvant chemotherapy was nonsignificant (OR, 0.99; 95% CI, 0.65–1.52; $P = .96$).

DISCUSSION

Research has confirmed the safety and efficacy of both neoadjuvant chemotherapy alone[7–10] and immediate reconstruction alone[1–3,12,14–18], but data addressing both concurrently are limited. In 1 study of 22 patients with locally advanced (stage IIB or III) cancer who received neoadjuvant chemotherapy and underwent immediate reconstruction, there was no delay in adjuvant treatment, but the perioperative morbidity rate was 14%.[19] Another series of 31 patients after neoadjuvant chemotherapy and immediate TRAM flap reconstruction demonstrated an adjuvant treatment delay of 6% and a postoperative complication rate of 55%.[20] In 48 other patients who received neoadjuvant chemotherapy and underwent

immediate reconstruction, the mean time between surgery and adjuvant chemotherapy was 26 days.[16] Azzawi et al did not observe any differences in the time to adjuvant therapy or in failure, reoperation, or minor complication rates between recipients and nonrecipients of neoadjuvant chemotherapy in a single surgeon's immediate breast reconstruction population.[21] Similarly, in the study by Warren Peled et al, a cohort of 57 neoadjuvant and 41 adjuvant-only chemotherapy recipients demonstrated no differences in reoperation, skin necrosis, implant/expander/flap loss, seroma, or ventral hernia rates after immediate reconstruction.[11] All of those studies had small sample sizes, few included a comparison with delayed or no reconstruction[16] or adjuvant-only chemotherapy,[11,21] and none adequately addressed both the timing of reconstruction and the timing of chemotherapy simultaneously.

Current practices in the timing of reconstruction seem to vary according to disease stage and provider/institutional philosophies about the risks associated with the administration of neoadjuvant chemotherapy, adjuvant chemotherapy, and/or radiation therapy. Some centers favor postponing all reconstructions if postmastectomy radiation therapy is likely,[22] such that patients who eventually do not require radiation are forced to endure a delay and to forgo a skin-sparing mastectomy.[23] Others routinely perform immediate reconstruction despite the need for radiation,[21,24] which may have an impact on both the quality of radiation delivery and the esthetic outcome.[25,26] At The University of Texas M. D. Anderson Cancer Center, Kronowitz and colleagues have pioneered the delayed-immediate approach, in which patients with stage II (and select patients with stage I) disease who desire reconstruction undergo immediate tissue expander placement followed either by reconstruction within 2 weeks if radiation is not required or by deflation (immediately before delivery), reinflation (2 weeks after delivery), and delayed reconstruction (within 3 months of delivery) if radiation is required. Receipt of neoadjuvant chemotherapy is yet another consideration within this algorithm; for patients who receive neoadjuvant chemotherapy, the expander is left inflated for the 4-week to 6-week period between mastectomy and radiation.[23,27] Although these reports all contribute to our understanding about the appropriate times at which reconstruction should be offered to breast cancer patients, none characterize the frequency of actual receipt.

Our study revealed that recipients of neoadjuvant therapy are less likely to undergo immediate reconstruction, even after controlling for age, disease stage, and receipt of radiotherapy. Accounting for these variables, the average neoadjuvant chemotherapy recipient has a 28% chance of undergoing immediate reconstruction compared with 40% for the average patient who receives only adjuvant chemotherapy. These neoadjuvant recipients, however, are not more likely to progress to delayed reconstruction. Only younger age and lower BMI seem to predict delayed reconstruction among patients who do not undergo immediate reconstruction. Because Alderman et al observed an increased likelihood of delay in the receipt of adjuvant chemotherapy in patients with higher BMI who underwent immediate reconstruction,[14] delayed reconstruction appears to be a prudent choice in this population. However, our results demonstrate a diminishing likelihood of undergoing delayed reconstruction with increasing BMI. Patient or surgeon preference may contribute to these findings. Another explanation may be treatment fatigue; neoadjuvant chemotherapy recipients already have submitted themselves to additional weeks of an exhausting therapy before mastectomy and, thus, may be less willing to schedule an additional elective operation. Future research should address this issue.

The failure to demonstrate a statistically significant increase in delayed reconstruction procedures among neoadjuvant chemotherapy recipients also may be an issue of power. We would have needed 916 neoadjuvant recipients and 2618 adjuvant recipients to detect our

observed OR of 1.29 with 80% power (and $\alpha = .05$), assuming a similar study and a similar ratio of neoadjuvant-to-adjuvant chemotherapy recipients.

Contrary to our hypothesis, immediate reconstruction is not predicted by the length of neoadjuvant therapy (as a measure of delay) or by complications during neoadjuvant therapy. However, our chart reviewers noted qualitatively that many patients who received neoadjuvant chemotherapy either planned to undergo or demonstrated an interest in undergoing delayed reconstruction at presentation, but they experienced a range of social and/or medical complications (eg, divorce, death of a loved one, loss of family income, development of a second primary cancer, chemotherapy-induced cardiomyopathy) that seemingly precluded eventual reconstruction. Again, treatment fatigue may be an important issue to investigate. Because >95% of our patients received adjuvant chemotherapy, we cannot address the potential role played by adjuvant chemotherapy (compared with no adjuvant chemotherapy) in this cohort.

In our study, the rate of complications in patients who underwent reconstruction after receiving neoadjuvant chemotherapy was 37.1%, which was higher than the 26.9% rate among patients who underwent mastectomy alone. This trend is consistent with prior work[17,28] and is not surprising, as the addition of a reconstruction necessarily makes any procedure more extensive. Our rates compare favorably with those reported elsewhere. Fifty-five percent of the 31 patients reported by Deutsch et al developed a complication after receiving neoadjuvant chemotherapy and undergoing immediate TRAM reconstruction.[20] The Michigan Breast Reconstruction Outcome Study, which includes 23 plastic surgeons at 12 centers, reported a complication rate of 45.4%.[28] Thirty-one percent of the 163 patients reported by Warren Peled et al who underwent immediate reconstruction developed a complication that required a return to the operating room.[11] In a cohort of 62 patients who underwent immediate reconstruction, Mortensen et al reported that 22.3% experienced complications.[17] Similarly, Furey et al documented a complication rate of 27.8% in 36 patients who underwent immediate reconstruction and received adjuvant chemotherapy.[29]

Factors that predispose patients to the development of postoperative complications are important to investigate, as low-risk patients may be targeted for immediate, rather than delayed, reconstruction. The only factors that we identified as predictive of surgical complications in our neoadjuvant population were age, tumor size, and BMI. Weight has been correlated previously with postoperative complications. Alderman et al calculated an 8% increase in risk with each additional point in BMI.[28] Chang et al estimated that a BMI ≥ 25 kg/m^2 doubled the incidence of both flap and donor site complications in free TRAM reconstructions, even after controlling for the receipt of preoperative radiotherapy and neoadjuvant chemotherapy.[30] We did not observe that smoking was related significantly to the development of complications; however, the number of smokers was limited to 16 within our neoadjuvant cohort. The existing data on the effect of smoking is conflicting. Both Alderman et al[28] and Deutsch et al[20] failed to observe any significant differences in complication rates between smokers and nonsmokers; however, Chang et al[31] demonstrated an increase in mastectomy skin flap necrosis, abdominal flap necrosis, and hernia among free TRAM flap recipients. The occurrence of mastectomy skin flap necrosis was accentuated when the reconstruction was timed to coincide with the mastectomy; hence, the group at The University of Texas M. D. Anderson Cancer Center advocates delaying these reconstructions in active smokers.[31]

This work represents a single-institution experience; therefore, generalizability is a concern. Because the Dana-Farber Cancer Institute is a large, comprehensive cancer center associated with a tertiary care institution, the availability and use of certain services (eg, plastic/reconstructive surgery) may differ from that of the general community. The most predictive

factor of undergoing reconstruction is documentation of a patient-provider discussion regarding reconstruction,[32] and surgeons who have high clinical breast surgery volumes and who work in cancer centers are known to have higher referral rates to plastic surgery for breast reconstruction.[33] Our work may be subject to reviewer subjectivity, a problem inherent to chart review, although we believe we minimized this problem by standardizing variable definitions (eg, infectious complication during neoadjuvant chemotherapy required antibiotic administration) using physicians with clinical surgical experience as reviewers and adjudicating disputes with a breast surgical oncologist.

We were unable to capture any events that were not documented in the electronic medical records. If, for example, a patient was seen for a chemotherapy-related or postoperative complication at another hospital, then we would not have been able to identify it unless it was mentioned explicitly by a Dana-Farber provider in a note filed within the defined neoadjuvant chemotherapy or 60-day postmastectomy periods. Therefore, our estimates of complication and reconstruction rates are potentially biased in a conservative direction. However, because our reviewers indicated that these notes were exceptionally thorough, with detailed weekly assessments that frequently incorporated medical and social events external to the system, we believe the effect of said bias is likely minimal.

We have demonstrated that women who receive neoadjuvant chemotherapy are significantly less likely to undergo immediate reconstruction and are no more likely to undergo delayed reconstruction than patients who undergo mastectomy before they receive chemotherapy. This phenomenon does not appear to be the result of neoadjuvant-related complications. It will be important to investigate other measures of treatment fatigue for both adjuvant and neoadjuvant chemotherapy recipients. Considering the recent expansion of the neoadjuvant population (as criteria for neoadjuvant treatment are broadened) and the importance of cosmesis in quality of life, patients and providers alike are in need of this type of evidence regarding the interaction between medical, surgical, and radiation therapies in the treatment of breast cancer. Further research is needed to corroborate and build upon our findings.

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Table 1

Characteristics of Recipients of Adjuvant-Only and Neoadjuvant Chemotherapy

Variable	No. of Patients (%)		
	Adjuvant Only, n = 485	Neoadjuvant, n = 180	*P*
Age, y			.08[a,b]
<50	287 (59.2)	91 (50.6)	
From ≥50 to <70	188 (38.8)	86 (47.8)	
≥70	10 (2.1)	3 (1.7)	
Race			.38
White	438 (90.3)	166 (92.2)	
Asian	7 (1.4)	3 (1.7)	
Black/AA	13 (2.7)	5 (2.8)	
Hispanic/Latino	16 (3.3)	1 (0.6)	
Other	11 (2.3)	3 (1.7)	
Marital status			.03[a]
Single/divorced/widowed	108 (22.6)	55 (31.3)	
Married	369 (77.4)	121 (68.8)	
Weight: BMI, kg/m^2			.02[a,b]
Underweight: <18.5	16 (3.5)	1 (0.6)	
Normal: ≥18.5 to <25	241 (52.9)	77 (47)	
Overweight: ≥25 to <30	119 (26.1)	48 (29.3)	
Obese: ≥30	80 (17.5)	38 (23.2)	
Risk factors			
Current smoker	39 (8.3)	16 (9.1)	.75
≥2 Comorbidities	68 (14.2)	23 (12.9)	.80
Diabetes mellitus	16 (3.3)	11 (6.1)	.12
Functional status before procedure			<.01[a,b]
Fully functional	275 (82.3)	112 (63.3)	
Restricted	48 (14.4)	52 (29.4)	
Can walk and take care of self	5 (1.5)	7 (4)	
Needs some help	4 (1.2)	6 (3.4)	
Cannot take care of self	2 (0.6)	0 (0)	
Stage			<.01[a,b]
I	111 (22.9)	5 (2.8)	
II	281 (57.9)	91 (50.6)	
III	93 (19.2)	84 (46.7)	
Lymph node status ≥N1	318 (65.6)	125 (69.8)	.31
Tumor classification ≥T3	66 (13.6)	82 (46.6)	<.01[a]
Hormone receptor status			
ER+	385 (79.4)	122 (67.8)	<.01[a]

Variable	No. of Patients (%) Adjuvant Only, n = 485	Neoadjuvant, n = 180	*P*
PR+	365 (75.7)	114 (63.3)	<.01[a]
HER2+	104 (22.6)	63 (35.6)	<.01[a]
Treatments			
Radiotherapy	248 (51.2)	151 (83.9)	<.01[a]
Bevacizumab	14 (2.9)	14 (7.8)	<.01[a]
Adjuvant chemotherapy[c]			
AC	193 (39.8)	42 (23.3)	<.01[a]
AC+paclitaxel	203 (41.9)	23 (12.8)	
Paclitaxel	9 (1.9)	20 (11.1)	
Other	80 (16.5)	66 (36.7)	
None[d]	0 (0)	29 (16.1)	
Autologous flap reconstructions	183 (64.9)	51 (63.8)	.89
Reconstruction timing			<.01[a]
Immediate	214 (44.1)	42 (23.3)	
Delayed	68 (14)	38 (21.1)	
None	203 (41.9)	100 (55.6)	

AA indicates African American; BMI, body mass index; ER+, estrogen receptor-positive; PR+, progesterone receptor-positive; HER2+, human epidermal growth factor receptor 2-positive; AC, doxorubicin/cyclophosphamide.

[a] Significant at $P < .05$

[b] Mantel-Haenzel chi-square trend tests were used.

[c] Represents the adjuvant chemotherapy regimen only. The neoadjuvant chemotherapy regimen is described in the text.

[d] Patients who did not receive adjuvant chemotherapy did receive neoadjuvant chemotherapy.

Table 2

Univariate Predictors of Immediate Reconstruction

Variable	No. of Patients (%)		*P*
	Delayed/No Reconstruction, n = 409	Immediate Reconstruction, n = 256	
Neoadjuvant chemotherapy	138 (33.7)	42 (16.4)	<.01[a]
Age, y			<.01[a,b]
<50	210 (51.3)	168 (65.6)	
From ≥50 to <70	187 (45.7)	87 (34)	
≥70	12 (2.9)	1 (0.4)	
Race			.25
White	371 (90.9)	233 (91.4)	
Asian	8 (2)	2 (0.8)	
Black/AA	10 (2.5)	8 (3.1)	
Hispanic/Latino	13 (3.2)	4 (1.6)	
Other	6 (1.5)	8 (3.1)	
Marital status			.93
Single/divorced/widowed	102 (25.2)	61 (24.6)	
Married	303 (74.8)	187 (75.4)	
Weight: BMI, kg/m^2			.03[a,b]
Underweight: <18.5	9 (2.4)	8 (3.3)	
Normal: ≥18.5 to <25	181 (48.3)	137 (55.9)	
Overweight: ≥25 to <30	106 (28.3)	61 (24.9)	
Obese: ≥30	79 (21.1)	39 (15.9)	
Risk factors			
Current smoker	35 (8.8)	20 (8)	.77
≥2 Comorbidities	56 (13.8)	35 (13.8)	1.00
Diabetes mellitus	21 (5.1)	6 (2.3)	.10
Clinical status before procedure			.01[a,b]
Fully functional	236 (72.4)	151 (81.6)	
Restricted	71 (21.8)	29 (15.7)	
Can walk and take care of self	9 (2.8)	3 (1.6)	
Needs some help	8 (2.5)	2 (1.1)	
Cannot take care of self	2 (0.6)	0 (0)	
Stage			<.01[a,b]
I	50 (12.2)	66 (25.8)	
II	221 (54)	151 (59)	
III	138 (33.7)	39 (15.2)	
Lymph node status ≥N1	296 (72.6)	147 (57.4)	<.01[a]
Tumor classification ≥T3	116 (28.6)	32 (12.6)	<.01[a]
Hormone receptor status			

Variable	No. of Patients (%)		*P*
	Delayed/No Reconstruction, n = 409	Immediate Reconstruction, n = 256	
ER+	306 (74.8)	201 (78.5)	.30
PR+	286 (70.3)	193 (75.7)	.15
HER2+	104 (26)	63 (26.6)	.93
Treatments			
Radiotherapy	286 (69.9)	113 (44.3)	<.01[a]
Bevacizumab	19 (4.7)	9 (3.5)	.56
Neoadjuvant chemotherapy[c]			.01[a]
AC	24 (17.4)	8 (19.1)	
AC+paclitaxel	45 (32.6)	14 (33.3)	
Paclitaxel	12 (8.7)	5 (11.9)	
Other	57 (41.3)	15 (35.7)	
Adjuvant chemotherapy[c]			.01[a]
AC	126 (30.8)	109 (42.6)	
AC+paclitaxel	143 (35)	83 (32.4)	
Paclitaxel	21 (5.1)	8 (3.1)	
Other	96 (23.5)	50 (19.5)	
None[d]	23 (5.6)	6 (2.3)	

AA indicates African American; BMI, body mass index; ER+, estrogen receptor-positive; PR+, progesterone receptor-positive; HER2+, human epidermal growth factor receptor 2-positive; AC, doxorubicin/cyclophosphamide.

[a] Significant at $P < .05$

[b] Mantel-Haenzel chi-square trend tests were used.

[c] Represents the adjuvant chemotherapy regimen only. The neoadjuvant chemotherapy regimen is described in the text.

[d] Patients who did not receive adjuvant chemotherapy did receive neoadjuvant chemotherapy.

Table 3

Distribution of Surgical Complications in Recipients of Neoadjuvant Therapy[a]

Surgical Complication	No. of Patients (%)		
	No Neoadjuvant, n=485	Neoadjuvant, n=180	*P*
Any[b]	151 (31.1)	54 (30)	.85
Seroma	59 (12.2)	27 (15)	.36
Hematoma	26 (5.4)	5 (2.8)	.21
Surgical site infection	52 (10.7)	18 (10)	.89
Dehiscence/open wound	25 (5.2)	6 (3.3)	.41
Skin necrosis	45 (9.3)	13 (7.2)	.44
Flap failure/loss	1 (0.2)	2 (1.1)	.18
Thromboembolism	3 (0.6)	2 (1.1)	.62
Tissue expander/implant removal	3 (0.6)	0 (0)	.39

[a] In the 60 days after mastectomy.

[b] "Any" is not the sum of all complications; some patients developed more than 1 complication.