

Predictors of Surgery Types after Neoadjuvant Therapy for Advanced Stage Breast Cancer: Analysis from Florida Population-Based Cancer Registry (1996–2009)

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ABSTRACT

PURPOSE: Despite the established guidelines for breast cancer treatment, there is still variability in surgical treatment after neoadjuvant therapy (NT) for women with large breast tumors. Our objective was to identify predictors of the type of surgical treatment: mastectomy versus breast-conserving surgery (BCS) in women with T3/T4 breast cancer who received NT.

METHODS: Population-based Florida Cancer Data System Registry, Florida's Agency for Health Care Administration, and US census from 1996 to 2009 were linked for women diagnosed with T3/T4 breast cancer and received NT followed by either BCS or mastectomy. Analysis of multiple variables, such as sociodemographic characteristics (race, ethnicity, socioeconomic status, age, marital status, and urban/rural residency), tumor's characteristics (estrogen/progesterone receptor status, histology, grade, SEER stage, and regional nodes positivity), treatment facilities (hospital volume and teaching status), patients' comorbidities, and type of NT, was performed.

RESULTS: Of 1,056 patients treated with NT for T3/T4 breast cancer, 107 (10%) had BCS and 949 (90%) had mastectomy. After adjusting with extensive covariables, Hispanic patients (adjusted odds ratio (aOR) = [3.50], 95% confidence interval (CI): 1.38–8.84, $P = 0.008$) were more likely to have mastectomy than BCS. Compared to localized SEER stage, regional stage with direct extension (aOR = [3.24], 95% CI: 1.60–6.54, $P = 0.001$), regional stage with direct extension and nodes (aOR = [4.35], 95% CI: 1.72–11.03, $P = 0.002$), and distant stage (aOR = [4.44], 95% CI: 1.81–10.88, $P = 0.001$) were significantly more likely to have mastectomy than BCS. Compared to patients who received both chemotherapy and hormonal therapy, patients who received hormonal NT only (aOR = [0.29], 95% CI: 0.12–0.68, $P = 0.004$) were less likely to receive mastectomy.

CONCLUSION: Our study suggests that Hispanic ethnicity, advanced SEER stage, and type of NT are significant predictors of receiving mastectomy after NT.

KEYWORDS: neoadjuvant, breast cancer, mastectomy, lumpectomy, predictors, SEER

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Introduction

Neoadjuvant therapy (NT) is often the first-line treatment for locally advanced breast cancer (LABC), providing systemic therapy early on and increasing the possibility of breast conservation. However, after NT, the decision regarding the surgical approach is not always clear. The choice of mastectomy versus breast-conserving surgery (BCS) is often influenced by multiple medical and social considerations. It is well recognized that race, ethnicity, and socioeconomic status (SES) correlate with survival rates and treatment approach for women with breast cancer. African-American women are more likely to present with more advanced stages compared to White women.^{1,2} White women are shown to have higher survival rates compared to other racial groups.^{2,3} Furthermore, SES has been

shown to correlate more favorably with presentation stage, treatment provided, and five-year survival.^{4–6} As the treatment of breast cancer is ever changing and improving, it is important to identify how social and clinical variables correlate with the use of developing treatment approaches. Although originally controversial, the use of BCS post NT in LABC has been shown in multiple studies to be oncologically safe.⁷ The rates of ipsilateral recurrence and locoregional recurrence were comparable in patients undergoing mastectomy versus BCS post neoadjuvant chemotherapy (NCT) for LABC.^{7–9} In spite of the recent increase in the use of BCS post NT for LABC, there remains variability in the choice of surgery type. This article aims to identify factors that correlate with the choice of surgery type in the treatment of LABC following NT.



Materials and Methods

Study population. Population-based Florida Cancer Data System (FCDS) Registry from 1996 to 2009 was screened for women diagnosed with T3/T4 breast cancer and received NT followed by either BCS or mastectomy. Florida’s Agency for Health Care Administration (AHCA) database provided procedure and diagnoses information from all inpatient and outpatient facilities, and data from the US census provided a proxy for individual SES. Female patients of 18 years or older were included if they resided in Florida during the study period. Patients with carcinoma in situ or with missing data on age, race, ethnicity, or SES were excluded from the study, resulting in a total sample size of 1,056 patients.

Variables. The dichotomous primary outcome variable was whether the patient had mastectomy versus BCS. Patients’ sociodemographic variables were age at diagnosis (years), race (White, Black, and others), ethnicity (Hispanic and non-Hispanic), neighborhood SES based on the percentage of individuals living below the federal poverty line from US census tract-level information (lowest: ≥20%; middle-low: ≥10% and <20%; middle-high: ≥5% and <10%; highest: <5%), and primary payer at diagnosis (private insurance, Medicare, Medicaid, defense/military, Indian Health Service, other insurance, or uninsured). Histological characteristics included SEER stage, regional nodes status, estrogen receptor (ER), progesterone receptor (PR), histological type, and histological differentiation grade. Clinical variables included

aggregated comorbidity based on 31-item Elixhauser Index (none, 1–2, 3–4, and >4) and type of NT received (hormonal therapy, chemotherapy, or both).

Statistical analysis. Demographic and clinical characteristics of patients were calculated as frequencies and percentages for categorical variables and means and standard deviations for continuous variables for all the patients in this study and then for patients with BCS or mastectomy. A multivariable logistic regression model (mastectomy versus BCS), by taking into account treating facilities as clustering, was used to identify significant predictors of the type of surgery, such as sociodemographic characteristics (race, ethnicity, SES, age, marital status, and urban/rural residency), tumor’s characteristics (ER/PR status, histology, grade, SEER stage, and regional nodes positivity), treatment facilities (hospital volume and teaching/nonteaching), type of NT, and patients’ comorbidity index. Adjusted odds ratios (aORs) and 95% confidence intervals (CI) were calculated. Type I error rate is set to 5%. All statistical analyses were performed using the SAS software version 9.3 for Windows (SAS Institute Inc.). This study was approved by the institutional review boards of both the University of Miami and Florida Department of Health.

Results

We were able to analyze 1,056 female patients treated with NT for T3/T4 breast cancer. The sociodemographic characteristics of the patients are presented in Table 1. Of 1,056 patients,

Table 1. Demographic characteristics of patients by surgery type after neoadjuvant therapy.

| | ALL PATIENTS N (%) | | SURGERY | | | |
|--------------------------|--------------------|-------|------------------|-------|-------------|-------|
| | N | COL % | BCS ^a | | MASTECTOMY | |
| | N | COL % | N | COL % | N | COL % |
| All | 1,056 | 100.0 | 107 | 10.0 | 949 | 90.0 |
| Status | | | | | | |
| Dead | 260 | 24.6 | 20 | 18.7 | 240 | 25.3 |
| Alive | 796 | 75.4 | 87 | 81.3 | 709 | 74.7 |
| Age at diagnosis | | | | | | |
| 17< to 54 | 532 | 50.4 | 57 | 53.3 | 475 | 50.1 |
| 54< to high | 524 | 49.6 | 50 | 46.7 | 474 | 49.9 |
| Age at diagnosis (years) | | | | | | |
| Mean (STD) | 55.5 (13.5) | | 56.1 (14.5) | | 55.4 (13.4) | |
| Median (Q1; Q3) | 54 (46; 64) | | 54 (46; 65) | | 54 (46; 64) | |
| Min; max | 22; 95 | | 29; 91 | | 22; 95 | |
| Race | | | | | | |
| White | 811 | 76.8 | 75 | 70.1 | 736 | 77.6 |
| Black | 226 | 21.4 | 29 | 27.1 | 197 | 20.8 |
| Other | 19 | 1.8 | 3 | 2.8 | 16 | 1.7 |
| Hispanic origin | | | | | | |
| No | 919 | 87.0 | 99 | 92.5 | 820 | 86.4 |
| Yes | 137 | 13.0 | 8 | 7.5 | 129 | 13.6 |

(Continued)



Table 1. (Continued)

| | ALL PATIENTS N (%) | | SURGERY | | | |
|--|--------------------|-------|------------------|-------|------------|-------|
| | N | COL % | BCS ^a | | MASTECTOMY | |
| | | | N | COL % | N | COL % |
| Neighborhood poverty status ^b | | | | | | |
| Lowest | 181 | 17.1 | 16 | 15.0 | 165 | 17.4 |
| Middle-low | 341 | 32.3 | 40 | 37.4 | 301 | 31.7 |
| Middle-high | 344 | 32.6 | 35 | 32.7 | 309 | 32.6 |
| Highest | 190 | 18.0 | 16 | 15.0 | 174 | 18.3 |
| Marital status | | | | | | |
| Unknown | 19 | 1.8 | 2 | 1.9 | 17 | 1.8 |
| Never married | 224 | 21.2 | 27 | 25.2 | 197 | 20.8 |
| Married | 520 | 49.2 | 51 | 47.7 | 469 | 49.4 |
| Divorced/separated/widowed | 293 | 27.7 | 27 | 25.2 | 266 | 28.0 |
| Insurance status | | | | | | |
| Unknown | 14 | 1.3 | 1 | 0.9 | 13 | 1.4 |
| Uninsured | 117 | 11.1 | 14 | 13.1 | 103 | 10.9 |
| Private insurance | 449 | 42.5 | 43 | 40.2 | 406 | 42.8 |
| Medicaid | 110 | 10.4 | 6 | 5.6 | 104 | 11.0 |
| Medicare | 263 | 24.9 | 27 | 25.2 | 236 | 24.9 |
| Defense/military/veteran | 18 | 1.7 | 1 | 0.9 | 17 | 1.8 |
| Indian/public | 4 | 0.4 | | | 4 | 0.4 |
| Insurance, NOS | 81 | 7.7 | 15 | 14.0 | 66 | 7.0 |
| Tobacco use | | | | | | |
| Never | 574 | 54.4 | 63 | 58.9 | 511 | 53.8 |
| History | 193 | 18.3 | 23 | 21.5 | 170 | 17.9 |
| Current | 155 | 14.7 | 12 | 11.2 | 143 | 15.1 |
| Unknown | 134 | 12.7 | 9 | 8.4 | 125 | 13.2 |
| Hospital volume | | | | | | |
| Low | 583 | 55.2 | 60 | 56.1 | 523 | 55.1 |
| High | 473 | 44.8 | 47 | 43.9 | 426 | 44.9 |
| Teaching hospital ^c | | | | | | |
| No | 864 | 81.8 | 89 | 83.2 | 775 | 81.7 |
| Yes | 192 | 18.2 | 18 | 16.8 | 174 | 18.3 |
| Residency | | | | | | |
| Rural | 40 | 3.8 | 1 | 0.9 | 39 | 4.1 |
| Urban | 1,016 | 96.2 | 106 | 99.1 | 910 | 95.9 |

Notes: ^aBCS: Breast conserving surgery. ^bEquivalent to Socioeconomic status: percent of households at the tract level living below the federal poverty line, lowest ($\geq 20\%$), middle-low ($\geq 10\%$ and $< 20\%$), middle-high ($\geq 5\%$ and $< 10\%$), and highest ($< 5\%$). ^cTeaching Hospital: Teaching hospitals listed in AAMC (Association of American Medical Colleges) 2005.

107 (10%) patients had BCS and 949 (90%) had mastectomy. In the last follow-up, it is noted that 81.3% of the patients who received BCS and 74.7% of the patients who received mastectomy were alive. The mean age in the BCS group was 56.1 years and ranged between 29 and 91 years, and in the mastectomy group, it was 55.4 years and ranged between 22 and 95 years. Most of our samples were White females: ~70% of the BCS patients and 77.6% of mastectomy patients. Similarly, patients of non-Hispanic origin dominated the sample: 92.5% of the BCS group and 86.4% of the mastectomy group. The percentage

distribution of the neighborhood poverty (equivalent to SES) in the BCS and mastectomy groups was 15% versus 17.4% for lowest, 37.4% versus 31.7% for middle-low, 32.7% versus 32.6% for middle-high, and 15% versus 18.3% for the highest SES status, respectively. A total of 47.7% and 49.4% of the BCS and mastectomy patients were married, 25.2% and 20.8% were never married, and 25.2% and 28% were divorced/separated or widowed, respectively. Most of the patients in BCS (40.2%) and mastectomy (42.8%) groups had private insurance, 25.2% and 24.9% had Medicare, 5.6% and 11% had Medicaid, and



13.1% and 10.9% were uninsured, respectively. Few patients in each group had defense/military/veteran insurance, and the rest had either unspecified or unknown insurance. More than half (58.9%) of the patients with BCS have never smoked, 21.5% had past history of smoking, and 11.2% were current smokers compared to 53.8%, 17.9%, and 15.1% of the women with mastectomy, respectively. Hospital volume was equally distributed between the two categories. A total of 56.1% of BCS and 55.1% of mastectomy patients were treated in low volume, and the majority of the hospitals in each group (83.2% in BCS and

81.7% in mastectomy) were nonteaching hospitals. Almost all the patients in our sample (1,016; 96.2%) were from urban areas.

The clinical and histopathological characteristics of the patients are presented in Table 2. More than half of the patients in BCS group (62.6%) and mastectomy group (64.1%) had more than four comorbidities, and the number of comorbidities was comparable between the two populations. The tumors were positive for ER in 56.1% and for PR in 42.1% of the BCS patients compared to 49% and 37.1%, respectively, in the mastectomy patients. Receptor status was unknown in 14.9% of the

Table 2. Clinical characteristics of patients by surgery type after neoadjuvant therapy.

| | ALL PATIENTS N (%) | | SURGERY | | | |
|----------------------------------|--------------------|-------|------------------|-------|------------|-------|
| | N | COL % | BCS ^a | | MASTECTOMY | |
| | N | COL % | N | COL % | N | COL % |
| All | 1,056 | 100.0 | 107 | 10.0 | 949 | 90.0 |
| Estrogen receptor (ER) assay | | | | | | |
| Unknown | 157 | 14.9 | 10 | 9.3 | 147 | 15.5 |
| Positive | 525 | 49.7 | 60 | 56.1 | 465 | 49.0 |
| Negative | 374 | 35.4 | 37 | 34.6 | 337 | 35.5 |
| Progesterone receptor (PR) assay | | | | | | |
| Unknown | 167 | 15.8 | 12 | 11.2 | 155 | 16.3 |
| Positive | 397 | 37.6 | 45 | 42.1 | 352 | 37.1 |
| Negative | 492 | 46.6 | 50 | 46.7 | 442 | 46.6 |
| Co-morbidity ^b | | | | | | |
| None | 61 | 5.8 | 7 | 6.5 | 54 | 5.7 |
| 1-2 | 112 | 10.6 | 13 | 12.1 | 99 | 10.4 |
| 3-4 | 208 | 19.7 | 20 | 18.7 | 188 | 19.8 |
| >4 | 675 | 63.9 | 67 | 62.6 | 608 | 64.1 |
| Histology | | | | | | |
| Ductal carcinoma | 843 | 79.8 | 89 | 83.2 | 754 | 79.5 |
| Lobular carcinoma | 139 | 13.2 | 10 | 9.3 | 129 | 13.6 |
| Other | 74 | 7.0 | 8 | 7.5 | 66 | 7.0 |
| Stage T | | | | | | |
| III | 461 | 43.7 | 72 | 67.3 | 389 | 41.0 |
| IV | 595 | 56.3 | 35 | 32.7 | 560 | 59.0 |
| SEER stage | | | | | | |
| Localized | 97 | 9.2 | 25 | 23.4 | 72 | 7.6 |
| Regional, direct extension | 138 | 13.1 | 16 | 15.0 | 122 | 12.9 |
| Regional, lymph nodes only | 249 | 23.6 | 28 | 26.2 | 221 | 23.3 |
| Regional, extension and nodes | 422 | 40.0 | 25 | 23.4 | 397 | 41.8 |
| Distant | 150 | 14.2 | 13 | 12.1 | 137 | 14.4 |
| Grade | | | | | | |
| Unknown/not stated | 142 | 13.4 | 13 | 12.1 | 129 | 13.6 |
| Well-differentiated | 44 | 4.2 | 2 | 1.9 | 42 | 4.4 |
| Moderately-differentiated | 270 | 25.6 | 30 | 28.0 | 240 | 25.3 |
| Poorly-differentiated | 584 | 55.3 | 61 | 57.0 | 523 | 55.1 |
| Undifferentiated | 16 | 1.5 | 1 | 0.9 | 15 | 1.6 |

(Continued)



Table 2. (Continued)

| | ALL PATIENTS N (%) | | SURGERY | | | |
|-------------------------|--------------------|-------|------------------|-------|------------|-------|
| | N | COL % | BCS ^a | | MASTECTOMY | |
| | | | N | COL % | N | COL % |
| Regional nodes positive | | | | | | |
| Unknown | 131 | 12.4 | 23 | 21.5 | 108 | 11.4 |
| No | 251 | 23.8 | 36 | 33.6 | 215 | 22.7 |
| Yes | 674 | 63.8 | 48 | 44.9 | 626 | 66.0 |
| Chemotherapy | | | | | | |
| Unknown | 7 | 0.7 | | | 7 | 0.7 |
| No | 59 | 5.6 | 14 | 13.1 | 45 | 4.7 |
| Yes | 990 | 93.8 | 93 | 86.9 | 897 | 94.5 |
| Hormone therapy | | | | | | |
| Unknown | 63 | 6.0 | 7 | 6.5 | 56 | 5.9 |
| No | 753 | 71.3 | 71 | 66.4 | 682 | 71.9 |
| Yes | 240 | 22.7 | 29 | 27.1 | 211 | 22.2 |
| Radiation therapy | | | | | | |
| Unknown | 48 | 4.5 | 3 | 2.8 | 45 | 4.7 |
| No | 623 | 59.0 | 61 | 57.0 | 562 | 59.2 |
| Yes | 385 | 36.5 | 43 | 40.2 | 342 | 36.0 |

Notes: ^aBCS: Breast conserving surgery. ^bCo-morbidities: Aggregated variable by summing all 31 Elixhauser Comorbidity Index.

sample for ER and in 15.8% for PR. Invasive ductal carcinoma (IDC) dominated the histological type in 83.2% of the BCS patients and 79.5% of the mastectomy patients, which is followed by invasive lobular carcinoma (ILC) in 9.3% and 13.6%, respectively. The nuclear grade was comparable between the two groups, and more than half were poorly differentiated. Data for the status of the lymph node involvement were missing in 32.9% of patients. For the patients with a known lymph node status, 44.9% had metastasis to lymph nodes in BCS group compared to 66% in mastectomy group, and 33.6% had no lymph node involvement in the BCS group compared to 22.7% in mastectomy group. Our sample composed of only stage T3 and T4 breast cancers. About two-thirds (67.3%) of patients with BCS had T3 tumors compared to 41% in mastectomy patients. Comparing BCS versus mastectomy using the SEER stage at diagnosis, disease was localized in 23.4% versus 7.6%, regional with direct extension in 15% versus 12.9%, regional with lymph nodes only in 26.2% versus 23.3%, regional with direct extension to surrounding structures and with lymph node involvement in 23.4% versus 41.8%, and distant metastatic disease was present in 12.1% versus 14.4%, respectively. The type of systemic NT provided had similar pattern between the two groups. NCT was provided to 86.9% of the BCS patients and 94.5% of the mastectomy patients. However, only 27.1% of the BCS patients and 22.2% of the mastectomy patients received hormonal therapy. Adjuvant radiation therapy was provided to 40.2% of the BCS patients and 36% of the mastectomy patients. Examples of the percentage distribution of some socioeconomic and clinical variables are illustrated in Figure 1.

After adjusting for the abovementioned characteristics, a multivariate logistic regression model was used to identify significant predictors of the extent of surgery performed after NT for T3/T4 breast cancers (Table 3). Among the sociodemographic variables, the patients of Hispanic origin were 3.5 times more likely to receive mastectomy compared to the patients of non-Hispanic origin (aOR = [3.5], 95% CI: 1.38–8.84, $P = 0.008$). There was no statistically significant difference in the type of surgery, considering race, SES, age at diagnosis, marital status, residential area, hospital volume, or teaching versus nonteaching hospital (all P -values > 0.05).

For clinical and pathological data, compared to patients who received both chemotherapy and hormonal therapy, patients who received systemic hormonal therapy alone (71%) were less likely to undergo mastectomy than to BCS (aOR = [0.29], 95% CI: 0.12–0.68, $P = 0.004$). Also compared to localized disease SEER stage, regional disease with direct extension (aOR = [3.24], 95% CI: 1.6–6.54, $P = 0.001$), regional disease with direct extension and lymph node involvement (aOR = [4.35], 95% CI: 1.72–11.03, $P = 0.002$), and distant metastatic disease (aOR = [4.44], 95% CI: 1.81–10.88, $P = 0.001$) were all associated with higher odds of receiving mastectomy. There was a trend toward more mastectomy for ILC compared to IDC (aOR = [1.86], 95% CI: 0.99–3.51, $P = 0.055$). However, it did not reach statistical significance. Other variables such as ER/PR status, nuclear grade, regional lymph node status, and number of comorbidities did not show statistically significant associations.

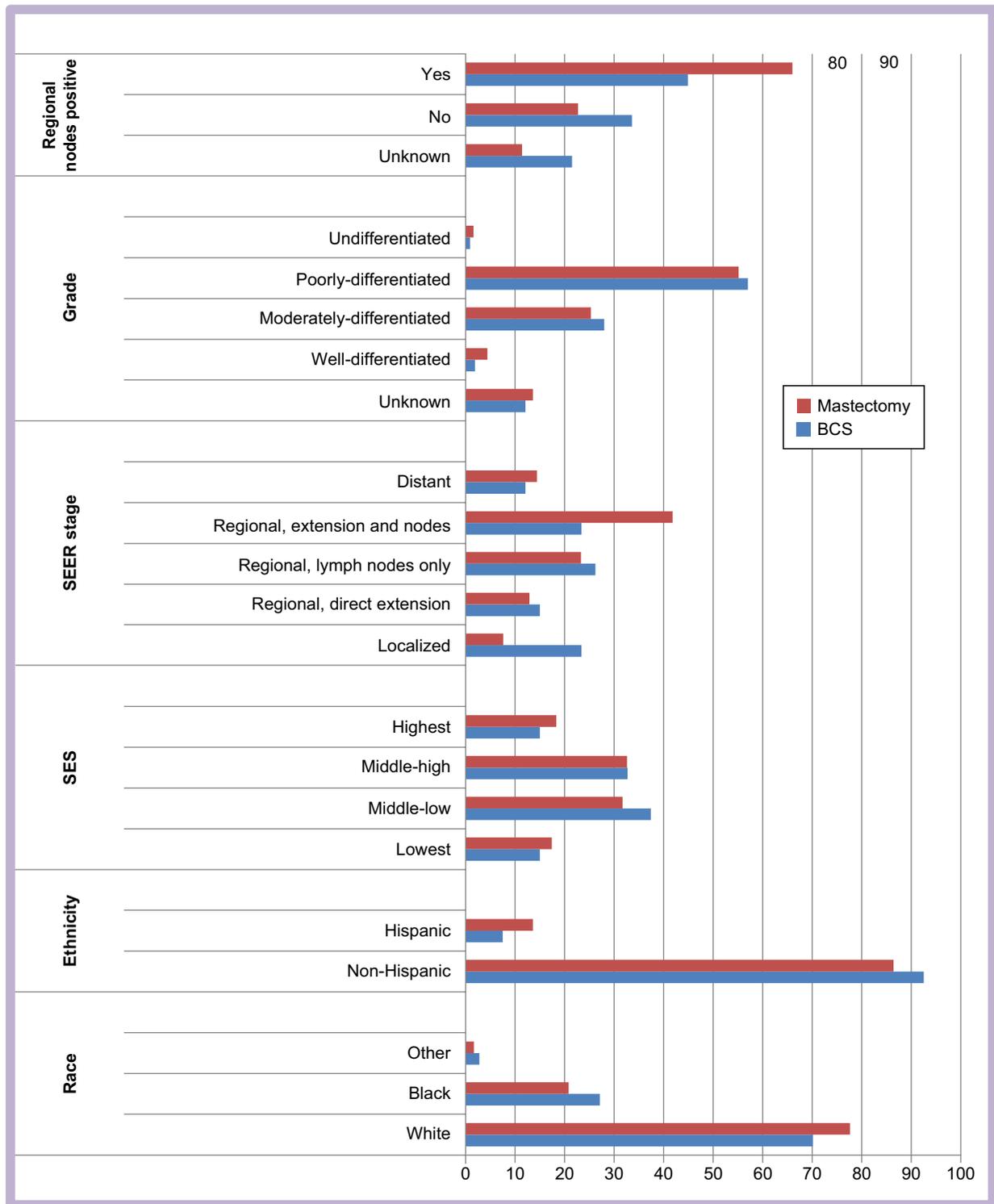


Figure 1. Socio-demographic and clinical characteristics (% by surgery type).
Abbreviations: BCS, Breast conserving surgery; SES, Socio-economic status.

Discussion

The working hypothesis at the outset of this study was that significant differences would be identified in the rate of breast conservation after NT between certain socioeconomic groups, as well as between academic- and community-based institutions and between urban and rural areas. Contrary to

our hypothesis, we have not been able to identify significant disparities in the use of BCT after NT for LABC.

Despite these negative findings, we identified significant ethnicity-related, stage-related, and treatment-related differences. Hispanic ethnicity, advanced SEER stage, and type of NT were significant predictors of mastectomy after NT.

**Table 3.** A multivariable logistic regression model for type of surgery (mastectomy versus BCS^b).

| VARIABLE | CATEGORY | OR ^a (95% CI) | P-VALUE |
|---------------------------|-------------------------------|--------------------------|---------|
| Treatment | Chemo/hormonal therapy | 1.00 (ref) | |
| | Chemotherapy | 0.92 (0.49, 1.73) | 0.807 |
| | Hormonal therapy | 0.29 (0.12, 0.68) | 0.004 |
| Race | White | 1.00 (ref) | |
| | Black | 0.83 (0.45, 1.52) | 0.539 |
| | Other | 1.16 (0.29, 4.63) | 0.839 |
| Hispanic | No | 1.00 (ref) | |
| | Yes | 3.5 (1.38, 8.84) | 0.008 |
| SES | Lowest | 1.00 (ref) | |
| | Middle-low | 0.76 (0.35, 1.66) | 0.496 |
| | Middle-high | 0.87 (0.4, 1.88) | 0.725 |
| | Highest | 0.95 (0.33, 2.72) | 0.930 |
| Marital status | Never married | 1.00 (ref) | |
| | Married | 1.1 (0.65, 1.86) | 0.730 |
| | Divorced/separated/widowed | 1.28 (0.63, 2.57) | 0.494 |
| | Unknown | 0.99 (0.31, 3.15) | 0.983 |
| Residency | Urban | 1.00 (ref) | |
| | Rural | 5.35 (0.85, 33.58) | 0.074 |
| Teaching hospital | Yes | 1.00 (ref) | |
| | No | 0.93 (0.46, 1.88) | 0.848 |
| Hospital volume | High | 1.00 (ref) | |
| | Low | 0.89 (0.57, 1.41) | 0.631 |
| ER | Negative | 1.00 (ref) | |
| | Unknown | 4.9 (1.13, 21.24) | 0.034 |
| | Positive | 0.66 (0.32, 1.38) | 0.269 |
| PR | Negative | 1.00 (ref) | |
| | Unknown | 0.36 (0.08, 1.71) | 0.200 |
| | Positive | 1.14 (0.59, 2.21) | 0.688 |
| Histology | Ductal carcinoma | 1.00 (ref) | |
| | Lobular carcinoma | 1.86 (0.99, 3.51) | 0.055 |
| | Other | 1.03 (0.44, 2.38) | 0.948 |
| SEER stage | Localized | 1.00 (ref) | |
| | Regional, direct extension | 3.24 (1.6, 6.54) | 0.001 |
| | Regional, lymph nodes only | 2.09 (0.91, 4.79) | 0.082 |
| | Regional, extension and nodes | 4.35 (1.72, 11.03) | 0.002 |
| | Distant | 4.44 (1.81, 10.88) | 0.001 |
| Grade | Well-differentiated | 1.00 (ref) | |
| | Moderately-differentiated | 0.36 (0.08, 1.76) | 0.208 |
| | Poorly-differentiated | 0.38 (0.08, 1.75) | 0.212 |
| | Undifferentiated | 0.71 (0.08, 6.51) | 0.759 |
| | Unknown/not stated | 0.33 (0.06, 1.67) | 0.179 |
| Regional nodes positive | None | 1.00 (ref) | |
| | Yes | 1.61 (0.71, 3.66) | 0.255 |
| | Unknown | 0.47 (0.23, 0.97) | 0.040 |
| Co-morbidity ^c | None | 1.00 (ref) | |
| | 1–2 | 1.46 (0.54, 3.97) | 0.455 |
| | 3–4 | 1.41 (0.56, 3.58) | 0.465 |
| | >4 | 1.31 (0.57, 3.02) | 0.531 |

Notes: ^aOR: Odds ratio; 95% CI: 95% confidence interval. ^bBCS: Breast conserving surgery. ^cCo-morbidities: Aggregated variable by summing all 31 Elixhauser Comorbidity Index.



Our results demonstrate that Hispanic women are 3.5 times more likely to undergo mastectomy versus BCS for LABC post NT than non-Hispanic women. This difference in treatment, however, seems to be ethnic and cultural and was not related to SES, hospital type, or domicile location. This is an interesting finding because many previous studies have not identified ethnic-only predictors of the type of breast surgery. A previous study, however, identified significant differences between patients' surgical choices related to whether the decision was left to the patient alone, dictated by the surgeon, or reached by patient and surgeon jointly. In that same study, Hispanic patients were least likely to change their choices because of surgeon's recommendations.¹⁰ Considering BCS post NT for LABC has only recently become more popular; resistance to it despite its proven oncologic safety may be explained by a general disinclination to receive the latest advances in medical and surgical therapy. In this regard, trends in receiving BCS post NT may be compared to trends in enrollment in breast cancer clinical trials. It has been shown that minority women, specifically Black women, are more reluctant to participate in clinical trials.¹¹ Reluctance of Black women to participate in cutting edge technology, such as BCS post NT for LABC, may transcend to all minority women, including Hispanic women. It has also been shown that trial enrollment is decreased in women of lower SES.¹² It has been speculated that certain racial and socioeconomic group are more likely to be denied access to clinical trials and therefore may not be offered the latest advances in surgical therapy.¹³ Our data did not show SES to be a significant factor in the choice of surgery after NT.

Decreased access to adjuvant radiotherapy may explain why 57% of the 107 patients who received BCS did not receive adjuvant radiotherapy in our study. It may also explain why most women in our study were more likely to receive mastectomy versus BCS post NT for LABC. For example, it has been demonstrated that women cared for at smaller hospitals are less likely to receive indicated radiation therapy post lumpectomy.¹⁴ This finding has been shown to correlate with race. Black women are more likely than White women to have cancer surgery at institutions with lower rates of radiation use following lumpectomy for LABC.¹⁵ This same trend encompasses women of all minority groups. For example, Freedman et al demonstrated that Hispanic women have the lowest rates of definitive primary surgical treatment for LABC of any racial group, and Asian women have the highest rates than White women.¹⁶ Similar disparities in the choice of surgery type for treatment of LABC have been shown to correlate with age. Women who are younger than 60 years or older than 70 years are less likely to receive definitive primary therapy, ie, BCS without radiation when indicated, compared to women aged 61–70 years.¹⁶ Furthermore, the presence of distant metastatic disease in 12% of the BCS group might also explain why those patients did not complete their locoregional therapy with radiation. It is speculated that there are multiple reasons for which women may choose to forego radiation therapy post

BCS. This may be an issue of physicians providing insufficient patient education, failing to specifically communicate the importance of radiation therapy after BCS, and social or financial issues limiting compliance with multiple treatment sessions of radiation therapy. Further studies are needed to determine whether the approach of physician to discuss about radiotherapy varies with race or ethnicity of the patient.

Another reason that may explain why mastectomy was more prevalent than BCS post NT is that BCS is generally underutilized across race. A study in New York City demonstrated the aforementioned disparity in the utilization of BCS among minority women; one in three Black women and one in four Hispanic women underused adjuvant therapies. However, the same study demonstrated that one in six White women did not utilize the available adjuvant therapies.¹⁷

The data in this study did not support existing literature that thoroughly demonstrates the presence of racial disparities in breast cancer treatment. Black women are less likely to receive hormonal therapy,¹⁸ less likely to receive sentinel lymph node biopsy,¹⁹ less likely to receive necessary adjuvant chemotherapy and radiotherapy for early stage breast cancer,¹⁷ and less likely to receive testing for biomarkers in the treatment of breast cancer.²⁰ Black women are more likely to experience treatment delays,¹⁸ more likely to receive fragmented care,²¹ and more likely to undergo early discontinuation of therapy.²² In our study, however, there was no statistically significant difference in surgical approach between Black and White women. This could be because most of our samples (76.8%) comprised White women.

Although the breast cancer histological type was not a significant predictor of surgery type in our study, there was a trend for mastectomy in patients with ILC. This could probably show significance with larger sample size because only 13.2% of our population had ILC. The trend, however, is concordant with the literature supporting total mastectomy for ILC as a safer option to control local disease.²³ On the contrary, other studies showed that ILC can be safely treated with BCS with no difference in local recurrence or survival.^{24,25} One reason why ILC is more likely to be treated with mastectomy is that ILC is associated with diffusely infiltrative growth pattern and the absence of surrounding desmoplastic reaction, resulting in difficulty obtaining negative margins after BCS.^{26–28} Moreover, ILC is less likely to respond significantly to NT; the clinical and pathological responses are lower in ILC compared to IDC,²⁹ which occludes the feasibility of BCS due to inadequate downsizing of the tumor mass. With this knowledge, surgeons should be careful in their approach for treating ILC and should tailor the treatment considering other prognostic factors in each case. Nevertheless, adequate patient counseling regarding positive margins is essential if planning BCS for ILC.

Our data lack the information on the Her2–Neu receptor status. However, the ER and PR receptor status did not seem to affect the choice of surgical approach in our



population. A study of 519 women with breast cancer, of which 90 were with triple-negative breast cancer (TNBC), showed that after BCS with radiation, women with TNBC had a higher rate of locoregional recurrence compared to after mastectomy with radiation. However, following multivariate analysis, this difference was not statistically significant.³⁰ The assumption that more aggressive treatment is better for more aggressive disease, like receptor negative cancer, has changed after multiple studies showing controversy in the survival outcome measures. For example, in a study of 117 TNBC patients who received BCS, there was no evidence that these patients are at higher risk for local relapse after conservative surgery and radiation.³¹ On the other hand, a study comparing the outcome for 688 breast cancer patients after BCS showed that a significant difference was observed for survival between subtypes for locoregional recurrence ($P = 0.012$), distant disease free survival ($P = 0.0035$), and breast cancer-specific death ($P = 0.0482$) in the favor of luminal A subtype.³²

Advanced SEER stage was a significant predictor of mastectomy in our study. Moreover, there was a linear relationship between SEER stage and odds for mastectomy; the higher the SEER stage, the higher the odds ratio for mastectomy was 3.24, 4.35, and 4.44 for direct extension, extension with lymph nodes, and distant disease, respectively. This is concordant with the current literature, considering direct extension as a contraindication to BCS.³³ Our study lacks the data on the purpose of mastectomy in patients with distant metastasis at diagnosis. However, we anticipate that it was for palliation. In such patients, BCS is not an option.

Although the percentage of patients with positive lymph nodes was more in the mastectomy group (66% versus 44.9%), on the multivariate analysis, the regional SEER stage with lymph node involvement only did not seem to impact the surgical procedure type ($P = 0.082$). The positive axilla, compared to negative, did not show statistically significant odds for mastectomy ($P = 0.25$). These findings are concordant with the evidence in literature that the presence of axillary lymph node metastasis is not a contraindication to BCS.³⁴

The type of NT was a significant predictor of extent of surgery in our study. Patients who received neoadjuvant hormonal therapy alone (71%) were less likely to undergo mastectomy compared to patients who received both chemo and hormonal therapy (aOR = [0.29], 95% CI: 0.12–0.68, $P = 0.004$). This could be explained by the less aggressive clinical behavior of ER positive (luminal A) breast cancer due to their low expression of proliferative genes compared to the basal-like (ER negative and triple negative) breast cancer,³⁵ making BCS a reasonable choice for these patients.

There are a few limitations to this study that are based on a statewide cancer database. The FCDS and AHCA databases do not contain detailed information on post-NT tumor response, nor does it include information on multifocality and multicentricity or on additional risk factors, such as genetic

and familial predisposition. Nonetheless, this study is based on a large statewide cancer registry database and allows us to examine a wide variety of associations of ethnicity, SES, statewide geographic differences, hospital type, and demographic, clinical, and comorbid characteristics, with choice surgery type after NT. Thus, it paves the way for subsequent studies that will look more in depth into factors predicting the type of surgical intervention after NT and in general.

Conclusion

For locally advanced T3/T4 breast cancer, the decision regarding the extent of surgery (BCS versus mastectomy) after NT is very important, as it could result in a significant impact on the treatment approach and treatment-related morbidity. In the absence of clear guidelines, additional tools are required to guide the decision-making. Our study suggests that Hispanic ethnicity and advanced SEER stage are significant predictors for mastectomy, while neoadjuvant hormonal therapy is a significant predictor for BCS after NT. More prospective studies are needed to further explore additional factors that can predict the choice of surgery after NT and facilitate patient counseling.

Author Contributions

Conceived and designed the experiments: EA, TK. Analyzed the data: FM, TK. Wrote the first draft of the manuscript: JA, TK. Contributed to the writing of the manuscript: CS. Agree with manuscript results and conclusions: EA, JA, TK, MB. Jointly developed the structure and arguments for the paper: JA, CS. Made critical revisions and approved final version: EA, TK. All authors reviewed and approved of the final manuscript.

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