



Is Breast-Conserving Therapy Appropriate for Male Breast Cancer Patients? A National Cancer Database Analysis

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ABSTRACT

Background. Current treatment guidelines for male breast cancer are predominantly guided by female-only clinical trials. With scarce research, it is unclear whether breast-conserving therapy (BCT) is equivalent to mastectomy in men. We sought to compare overall survival (OS) among male breast cancer patients who underwent BCT versus mastectomy.

Methods. We performed a retrospective analysis of 8445 stage I–II (T1–2 N0–1 M0) male breast cancer patients from the National Cancer Database (2004–2014). Patients were grouped according to surgical and radiation therapy (RT). BCT was defined as partial mastectomy followed by RT. Multivariable and inverse probability of treatment-weighted (IPTW) Cox proportional hazards models were used to compare OS between treatment groups, controlling for demographic and clinicopathologic characteristics.

Results. Most patients underwent total mastectomy (61.2%), whereas 18.2% underwent BCT, 12.4% underwent total mastectomy with RT, and 8.2% underwent

partial mastectomy alone. In multivariable and IPTW models, partial mastectomy alone, total mastectomy alone, and total mastectomy with RT were associated with worse OS compared with BCT ($p < 0.001$ all). Ten-year OS was 73.8% for BCT and 56.3, 58.0 and 56.3% for other treatment approaches. Older age, higher T/N stage, histological grade, and triple-negative receptor status were associated with poorer OS ($p < 0.05$). Subgroup analysis by stage demonstrated similar results.

Conclusions. In this national sample of male breast cancer patients, BCT was associated with greater survival. The underlying mechanisms of this association warrant further study, because more routine adoption of BCT in male breast cancer appears to translate into clinically meaningful improvements in survival.

With approximately 2400 estimated new cases in the United States in 2017, male breast cancer is a rare disease comprising less than 1% of all new breast cancer diagnoses.¹ As such, research investigating optimal local regional treatment for male breast cancer is sparse, and current treatment guidelines for men are predominantly based on clinical trials comprised of female participants.² For example, the landmark National Surgical Adjuvant Breast and Bowel Project (NSABP) B-06 study compared total mastectomy to breast-conserving therapy [BCT, i.e. partial mastectomy followed by radiation therapy (RT)] only in women. This study still strongly influences breast cancer treatment recommendations due to the finding of equivalent overall survival (OS) for BCT and mastectomy.³ Although this recommendation is applied to men, high-level evidence supporting this recommendation is lacking.

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Moreover, the few retrospective studies investigating male breast cancer have largely consisted of small cohorts and/or have been descriptive in nature.^{4–12} One exception, Cloyd et al. performed a retrospective analysis comparing partial to total mastectomy in male breast cancer patients using the Surveillance, Epidemiology and End Results (SEER) database; however, RT, an important factor for local recurrence and survival, was not used to categorize patients and was reported at low rates, potentially secondary to underreporting.^{13,14}

Such limitations in male breast cancer research are significant, because they impair treating clinicians' ability to provide evidence-based recommendations to male breast cancer patients. Although the National Comprehensive Cancer Network guidelines recommend that men be treated similar to postmenopausal women, a multidisciplinary expert panel has advised that male breast cancer is distinct from female breast cancer with significant biologic, clinicopathologic, and prognostic differences and should be treated accordingly.^{2,15–18} For example, a recent population-based study found significant differences in tumor gene expression in male breast cancer patients compared with female patients.¹⁸ This is problematic, because we are currently using female data to make assumptions about male patients. Thus, there is a need for greater research investigating the impact of different therapeutic modalities on outcomes in male breast cancer patients to optimize therapy and patient counseling. The purpose of this study was to compare OS among male breast cancer patients treated with BCT, partial mastectomy alone, and total mastectomy with and without RT using a large national database: the National Cancer Database (NCDB). We hypothesized that BCT will be equivalent to total mastectomy with and without RT, whereas partial mastectomy alone will be associated with worse OS.

METHODS

We performed a retrospective analysis of male breast cancer patients using the NCDB from 2004 to 2014. The NCDB is a joint American College of Surgeons and American Cancer Society project, in which patient-level data has been collected from all cancer patients seen at Commission on Cancer (COC) sites.^{19,20} Although approximately 30% of U.S. hospitals are COC sites, NCDB captures data from 70% of all newly diagnosed cancer patients in the United States.

We identified 18,984 male patients with invasive breast cancer, not including sarcomas and lymphomas. We excluded patients with stage III–IV/unknown, T3–T4, multicentric/diffuse, or Paget's disease to replicate the NSABP B-06 cohort clinicopathologic characteristics

(Supplement, Fig. S1). RT was defined as postoperative external beam RT to the breast and/or chest wall \pm axilla. Patients with unknown RT, including sequence/type/location, who underwent brachytherapy or preoperative RT were excluded. Patients were excluded if survival data were missing/unknown or if they did not undergo surgery with partial or total mastectomy. The final cohort consisted of 8445 patients, categorized into the following groups based on surgery and RT: 1539 BCT patients (partial mastectomy with RT), 695 partial mastectomy-alone patients, 5165 total mastectomy alone patients, and 1046 total mastectomy with RT patients. Because patient information was deidentified, the study protocol was exempt from the University of California, Davis Institutional Review Board approval.

We abstracted patient demographic, clinicopathologic characteristic, and treatment information from NCDB. The Charlson-Deyo comorbidity index (CDCI) measured patient medical comorbidities. Tumors were classified by histology based on international classification of disease oncology codes (ICD-O-3; Supplement). Staging was defined by AJCC TNM pathologic stage and only by clinical stage if pathologic staging data were missing ($n = 581$, 6.9%). Immunotherapy was categorized as "chemotherapy," because Trastuzumab was classified as chemotherapy until 2013. Because NCDB reports the number of lymph nodes examined and not the type of nodal surgery performed, we defined sentinel lymph node biopsy (SLNB) as examining 1–5 nodes and axillary lymph node dissection (ALND) as examining ≥ 6 nodes based on previously described methods and the limited clinical utility in obtaining 5 nodes in a SLNB.^{21–23} Patients' vital status and months from diagnosis to last contact and/or death were used to determine OS.

Statistical Analysis

Patient demographics, clinicopathologic characteristics, and additional therapies were compared between treatment groups using Chi Square, Kruskal–Wallis, and ANOVA for categorical, nonnormally distributed continuous, and normally distributed continuous variables respectively. We compared OS between groups using the Kaplan–Meier method, log-rank test, and Cox proportional hazards models. We performed both multivariable and inverse probability of treatment-weighted (IPTW; using propensity scores) Cox regression models to account for selection bias/confounding and determine clinical factors associated with OS.^{24,25} Propensity scores were created by estimating the probability of selection into the four treatment groups with a multinomial logistic regression model consisting of covariates associated with treatment group differences in univariate analyses ($p \leq 0.15$). The same covariates were

clinically relevant to OS and, therefore, also included in the multivariable Cox model. Model covariates included age, race, CDCI, income, insurance, facility, histology, grade, hormone receptor/HER-2 status, T/N/overall stage, axillary nodal surgery, surgical margins, chemotherapy, hormone therapy, and year of diagnosis. Evaluation of standardized differences determined appropriate balance of all covariates after IPTW. The proportional hazards assumption was not violated as assessed by Schoenfeld residuals. Missing data were incorporated into the model as “unknown” for each respective covariate.

HER-2 was not reported until 2010; therefore, 45.8% of patients had missing/unknown HER-2 status ($n = 3,871$). We performed sensitivity analyses comparing multivariable Cox models for OS of all patients and with HER-2 unknown patients excluded. Because there were no significant differences between models, we are presenting analyses including all patients.

Subgroup analyses by overall and T stage were performed using multivariable Cox proportional hazards regression models controlling for the same covariates as performed on the entire cohort. Statistical analysis was performed using SAS (version 9.4, SAS Institute, Cary, NC). All tests were two sided. p values < 0.05 were considered significant.

RESULTS

Of the 8445 males with invasive breast cancer, most underwent total mastectomy alone (61.2%, $n = 5165$), whereas 18.2% ($n = 1539$) underwent BCT, 12.4% ($n = 1046$) underwent total mastectomy with RT, and 8.2% ($n = 695$) underwent partial mastectomy alone. Table 1 describes key demographic and clinicopathologic characteristics by treatment approach. There were significant differences between treatment groups for age, race, CDCI, histology, tumor size, grade, T, N, and overall stage, hormone receptor/HER-2 status, surgical margins, nodal surgery, chemotherapy, and hormone therapy between treatment groups ($p < 0.05$). Hormone receptor-positive/HER-2-negative disease was more common among patients who underwent total mastectomy alone and with RT compared with BCT and partial mastectomy-alone patients (45.5% and 47.1% vs. 40.4% and 35.5%), whereas rates of triple-negative receptor status were greatest among BCT patients compared with patients who underwent partial mastectomy alone, total mastectomy alone, and total mastectomy with RT (4.9% vs. 3.0, 1.4 and 1.4%, $p < 0.0001$). Median follow-up for the entire cohort was 52 months [interquartile range (IQR) 30–79].

After controlling for demographic and clinicopathologic group differences, in both the multivariable (Table 2) and IPTW models, partial mastectomy alone (multivariable: aHR 1.73, 95% confidence interval [CI] 1.39–2.14, $p < 0.0001$; IPTW: HR 1.60, 95% CI 1.14–2.24, $p = 0.006$), total mastectomy alone (multivariable: aHR 1.54, 95% CI 1.29–1.83, $p < 0.0001$; IPTW: HR 1.62, 95% CI 1.27–2.07, $p < 0.0001$) and total mastectomy with RT (multivariable: aHR 1.44, 95% CI 1.16–1.79, $p = 0.001$; IPTW: HR 1.58, 95% CI 1.15–2.18, $p = 0.005$) were associated with poorer OS compared with BCT. Older age, higher CDCI scores, histological grade, T and N stage, and triple-negative receptor status were associated with worse OS, whereas SLNB, ALND, hormone therapy, and chemotherapy were associated with improved OS (Table 2). Figure 1a, b illustrate crude and IPTW Kaplan–Meier survival curves by treatment approach. At 5 and 10 years, OS rates (with IPTW adjustment) were 86.8% and 73.8% for BCT, 84.9% and 56.3% for partial mastectomy alone, 80.6% and 58.0% for total mastectomy alone, and 81.9% and 56.3% for total mastectomy with RT patients.

Subgroup analyses by overall and T stage are presented in Figs. 2a, b and 3a, b and Table S1 (Supplement). For stage I and T1 disease, there were no OS differences for BCT and total mastectomy with RT patients ($p > 0.05$; Table S1). Total and partial mastectomy alone were associated with worse OS compared with BCT ($p < 0.05$; Table S1). For stage II and T2 disease, total mastectomy alone and with RT and partial mastectomy alone were associated with worse OS compared with BCT ($p < 0.05$; Table S1).

DISCUSSION

In this NCDB analysis of male breast cancer patients, despite total mastectomy being performed more commonly, BCT was associated with greater survival compared with total mastectomy with and without RT and partial mastectomy alone. These findings were surprising, because current consensus guidelines based on randomized, clinical trials with female patients regard BCT and total mastectomy to be oncologically equivalent.^{2,3,26} Therefore, these findings are particularly important, because they underscore the need for greater consideration and adoption of BCT for male breast cancer patients.

This study strengthens the current limited body of research investigating oncologic outcomes among male breast cancer patients. In a retrospective SEER analysis, Cloyd et al.¹³ found equivalent disease-specific and OS among men with breast cancer who underwent partial mastectomy compared with those who underwent total

TABLE 1 Patient demographics and clinicopathologic characteristics by treatment approach

	Breast-conserving therapy <i>N</i> = 1539		Partial mastectomy alone <i>N</i> = 695		Total mastectomy alone <i>N</i> = 5165		Total mastectomy with radiation <i>N</i> = 1046		<i>p</i> value
	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	
Age (mean, SD, years)	61.4	12.0	66.7	14.7	66.3	12.6	63.4	12.5	< 0.001
Race									
Caucasian	1305	84.8%	586	84.3%	4495	87.0%	879	84.0%	0.0006
African American	179	11.6%	68	9.8%	501	9.7%	132	12.6%	
Asian/Pacific Islander	29	1.9%	15	2.2%	89	1.7%	17	1.6%	
Other/unknown	26	1.7%	26	3.7%	80	1.6%	18	1.7%	
Charlson–Deyo Comorbidity Index									
0	1326	86.2%	576	82.9%	3921	75.9%	846	80.9%	< 0.0001
1	174	11.3%	83	11.9%	939	18.2%	161	15.4%	
2	34	2.2%	25	3.6%	236	4.6%	30	2.9%	
≥ 3	5	0.3%	11	1.6%	69	1.3%	9	0.9%	
Income									0.15
< \$38,000	220	14.3%	102	14.7%	714	13.8%	167	16.0%	
\$38,000–47,999	339	22.0%	171	24.6%	1061	20.5%	212	20.3%	
\$48,000–62,999	413	26.8%	165	23.7%	1363	26.4%	279	26.7%	
≥ \$63,000	559	36.3%	248	35.7%	1984	38.4%	380	36.3%	
Unknown	8	0.5%	9	1.3%	43	0.8%	8	0.8%	
Insurance status									< 0.0001
Uninsured	22	1.4%	12	1.7%	82	1.6%	25	2.4%	
Private	833	54.1%	286	41.2%	2099	40.6%	486	46.4%	
Government	657	42.7%	386	55.5%	2918	56.5%	527	50.4%	
Unknown	27	1.8%	11	1.6%	66	1.3%	9	0.9%	
Facility type									0.0006
Comprehensive cancer	730	47.4%	318	45.8%	2373	45.9%	519	49.6%	
Community cancer	207	13.5%	102	14.7%	578	11.2%	122	11.7%	
Academic/research	385	25.0%	176	25.3%	1545	29.9%	278	26.7%	
Other	217	14.1%	99	14.2%	669	13.0%	127	12.1%	
Histology									
Invasive ductal (IDC)	1211	78.7%	555	79.9%	4387	84.9%	929	88.8%	< 0.0001
Invasive lobular (ILC)	163	10.6%	50	7.2%	205	4.0%	45	4.3%	
Mixed IDC/ILC	58	3.8%	21	3.0%	179	3.5%	33	3.2%	
Medullary	3	0.2%	2	0.3%	5	0.1%	2	0.2%	
Papillary	17	1.1%	21	3.0%	179	3.5%	8	0.8%	
Mucinous	33	2.1%	16	2.3%	62	1.2%	5	0.5%	
NOS	54	3.5%	30	4.3%	148	2.9%	24	2.3%	
Tumor size (median, IQR, cm)	1.4	0.9–2.0	1.5	1.0–2.2	1.8	1.3–2.5	2.3	1.7–3.0	< 0.0001
T stage									
T1	1197	77.8%	493	70.9%	3090	59.8%	443	42.4%	< 0.0001
T2	342	22.2%	202	29.1%	2075	40.2%	603	57.7%	
N stage									
N0	1251	81.3%	588	84.6%	3856	74.7%	343	32.8%	< 0.0001
N1	288	18.7%	107	15.4%	1309	25.3%	703	67.2%	
Stage									
1	1040	67.6%	439	63.2%	2545	49.3%	160	15.3%	< 0.0001
2	499	32.4%	256	36.8%	2620	50.7%	886	84.7%	

TABLE 1 continued

	Breast-conserving therapy <i>N</i> = 1539		Partial mastectomy alone <i>N</i> = 695		Total mastectomy alone <i>N</i> = 5165		Total mastectomy with radiation <i>N</i> = 1046		<i>p</i> value
	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	<i>N</i> /mean	%/SD	
Grade									
Well differentiated	398	25.9%	163	23.5%	773	15.0%	95	9.1%	< 0.0001
Moderately differentiated	656	42.6%	281	40.4%	2697	52.2%	507	48.5%	
Poorly differentiated/anaplastic	382	24.8%	196	27.8%	1460	28.3%	405	38.7%	
Unknown	103	6.7%	55	7.9%	235	4.6%	39	3.7%	
ER status									
Positive	1284	83.5%	567	81.6%	4789	92.7%	985	94.2%	< 0.0001
Negative	225	14.6%	83	11.9%	223	4.3%	42	4.0%	
Unknown	29	1.9%	45	6.5%	153	3.0%	19	1.8%	
PR status									
Positive	1162	75.5%	499	71.8%	4372	84.6%	892	85.3%	< 0.0001
Negative	344	22.4%	150	21.6%	624	12.1%	132	12.6%	
Unknown	33	2.1%	46	6.6%	169	3.3%	22	2.1%	
HER-2 status									
Positive	105	6.8%	46	6.6%	424	8.2%	95	9.1%	< 0.0001
Negative	698	45.4%	268	38.6%	2429	47.0%	509	48.7%	
Unknown	736	47.8%	381	54.8%	2312	44.8%	442	42.3%	
Negative surgical margins	1478	96.0%	626	90.1%	5040	97.6%	1004	96.0%	< 0.0001
Nodal surgery									
None	75	4.9%	174	25.0%	164	3.2%	21	2.0%	< 0.0001
Sentinel lymph node biopsy	1093	71.0%	361	51.9%	2500	48.4%	298	28.5%	
Axillary dissection	354	23.0%	145	20.9%	2472	47.9%	720	68.8%	
Unknown	17	1.1%	15	2.2%	29	0.6%	7	0.7%	
Chemotherapy ^a	572	37.2%	153	22.0%	1565	30.3%	685	65.5%	< 0.0001
Hormone therapy	1038	67.5%	220	31.7%	3074	59.5%	796	76.1%	< 0.0001

SD standard deviation, NOS not otherwise specified

^aChemotherapy includes immunotherapies (i.e., Trastuzumab)

mastectomy. Although Cloyd et al. included RT in the multivariable analysis, they did not stratify partial mastectomy patients by receipt of RT. As shown in our analysis, there were significant differences in age, comorbidities, surgical margins, and systemic therapy for BCT and partial mastectomy alone patients, suggesting that partial mastectomy patients who did and did not undergo RT are distinct patient cohorts. Additionally, after controlling for these group differences, we found that BCT was associated with greater survival compared with partial mastectomy alone. These findings highlight the importance of RT to improve oncologic outcomes in male breast cancer patients who undergo partial mastectomy.

Although the oncologic benefit of RT in breast cancer has been widely cited in female literature, RT in male breast cancer research is predominantly limited to retrospective single institution studies (many including patients

from the 1960s and 1970s).^{27–30} Although a number of these male-specific studies have shown an improvement in locoregional control with RT, few have observed a survival benefit.^{29,31,32} Therefore, the findings from the present study are noteworthy; they highlight a survival benefit associated with RT in male breast cancer. Additionally, the equivalent survival observed for stage I and T1 tumors treated with BCT or total mastectomy with RT suggests that RT may provide greater oncologic benefit than extensive surgical resection in small tumors. A recent study by Jatoi et al.³³ suggested an “abscopal effect” to explain such findings. The “abscopal effect” refers to the potential for RT to have both a localized and systemic antitumor effect from immunostimulation, leading to lower incidence of distant recurrence and greater survival. Despite such oncologic benefits, multiple studies have observed lower rates of RT compliance among male breast cancer patients

TABLE 2 Multivariable model for overall survival of male breast cancer patients (*N* = 8445)

	Hazard ratio	95% CI	<i>p</i> value
Surgery			
Breast-conserving therapy	Reference		
Partial mastectomy alone	1.73	1.39–2.14	< 0.0001
Total mastectomy alone	1.54	1.29–1.83	< 0.0001
Total mastectomy with radiation	1.44	1.16–1.79	0.001
Age	1.05	1.04–1.05	< 0.0001
Race			
Caucasian	Reference		
African American	1.17	1.00–1.38	0.06
Asian/Pacific Islander	0.82	0.52–1.31	0.41
Charlson–Deyo Comorbidity Index			
0	Reference		
1	1.69	1.51–1.89	< 0.0001
2	2.68	2.24–3.21	< 0.0001
≥ 3	3.53	2.67–4.68	< 0.0001
Income			
< \$38,000	Reference		
\$38,000–47,999	1.02	0.87–1.19	0.83
\$48,000–62,999	1.01	0.87–1.17	0.90
≥ \$63,000	0.83	0.72–0.96	0.02
Insurance status			
Uninsured	Reference		
Private	0.69	0.44–1.09	0.11
Government	0.92	0.59–1.45	0.73
Facility type			
Comprehensive cancer	Reference		
Community cancer	1.06	0.92–1.22	0.43
Academic/research	0.77	0.69–0.87	< 0.0001
Histology			
Invasive ductal (IDC)	Reference		
Invasive lobular (ILC)	0.86	0.68–1.08	0.18
Mixed IDC/ILC	1.05	0.79–1.39	0.73
Medullary	0.37	0.05–2.63	0.32
Papillary	1.04	0.76–1.43	0.81
Mucinous	0.78	0.48–1.27	0.32
Grade			
Well differentiated	Reference		
Moderately differentiated	1.32	1.14–1.54	0.0003
Poorly differentiated	1.66	1.41–1.96	< 0.0001
Hormone receptor/HER-2			
HR+/HER-2–	Reference		
HR+/HER-2+	1.20	0.94–1.53	0.15
HR–/HER-2+	1.68	0.79–3.58	0.19
HR–/HER-2–	1.87	1.26–2.77	0.002
Stage II	0.97	0.82–1.16	0.76
T2	1.58	1.36–1.83	< 0.0001
N1	1.53	1.34–1.74	< 0.0001

TABLE 2 continued

	Hazard ratio	95% CI	<i>p</i> value
Nodal surgery			
None	Reference		
Sentinel lymph node biopsy	0.47	0.40–0.57	< 0.0001
Axillary dissection	0.54	0.45–0.65	< 0.0001
Positive surgical margins	1.03	0.79–1.36	0.81
Hormone therapy	0.74	0.67–0.82	< 0.0001
Chemotherapy ^a	0.70	0.61–0.80	< 0.0001

CI confidence interval

^aChemotherapy includes immunotherapies (i.e., Trastuzumab)

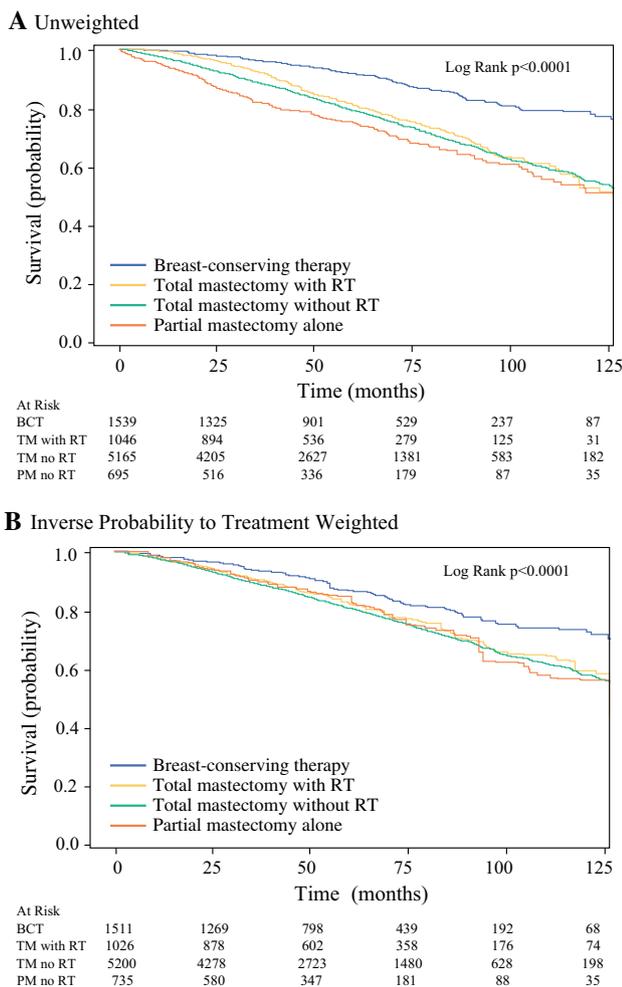


FIG. 1 Crude (a) and inverse probability of treatment weighted (b) overall survival for male breast cancer patients with breast-conserving therapy (BCT), total mastectomy with (TM with RT) and without radiation therapy (TM no RT), and partial mastectomy alone (PM no RT)

compared with female patients.^{11,12} Therefore, although our findings suggest BCT is appropriate therapy in men, BCT is only beneficial in those in which RT is feasible, because lumpectomy alone is not associated with the same survival benefit.

Although we acknowledge the potential influence of selection bias in this retrospective analysis, the similarities in tumor size, nodal disease, and surgical margins between patients who underwent BCT and mastectomy alone provides further confidence in the validity of our findings. Although the median tumor size was slightly larger for total mastectomy alone patients, the median tumor size for both groups was small (1.4–1.8 cm). Additionally, most patients in both cohorts were without nodal metastases (75–81%) and had high rates of negative surgical margins (96–98%). We acknowledge that the mastectomy with RT patients are a distinct group with larger tumors (median 2.3 cm) and high rates of nodal disease (67%) and, therefore, at greater risk of confounding. However, the clinical similarities between patients who underwent BCT and mastectomy alone (in addition to stratification by stage and robust multivariable and propensity score analyses) provides credence to our findings of a survival benefit associated with BCT compared with total mastectomy alone.

Additionally, recent retrospective, population-based studies comparing BCT to total mastectomy alone has observed similar results in female breast cancer patients, further validating our results.^{34–37} Agarwal et al.³⁵ performed a retrospective analysis comparing BCT to total mastectomy in female breast cancer patients with tumors ≤ 4 cm and ≤ 3 positive lymph nodes using the SEER database and found greater survival in BCT patients compared with women who underwent total mastectomy with and without RT. A separate SEER analysis of female patients by Bagaria et al.³⁴ found similar results, with worse disease-specific survival among women who

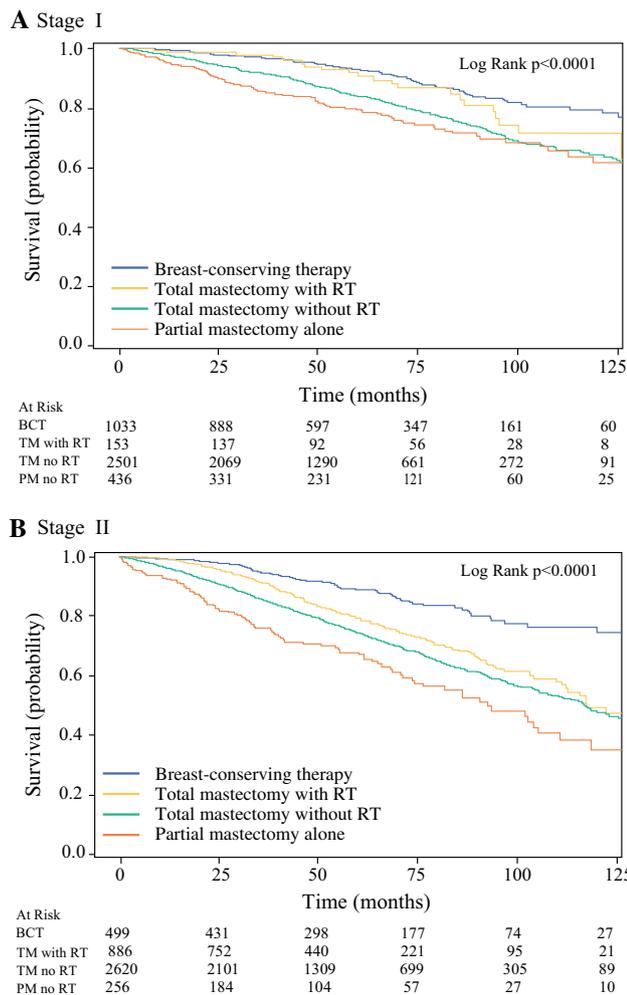


FIG. 2 Univariate overall survival for breast-conserving therapy (BCT) compared with partial mastectomy alone (PM no RT), total mastectomy alone (TM no RT), and total mastectomy with radiation therapy (TM with RT) by stage

underwent total mastectomy compared to BCT in low-, intermediate-, and high-risk tumors based on hormone status and grade. Furthermore, in a multicenter, prospective, cohort study of young women with breast cancer in the United Kingdom, although BCT was associated with earlier local recurrence, BCT was associated with improved distant disease-free interval and OS compared with total mastectomy.³⁷ Our findings complement this body of research by demonstrating similar findings in male patients, specifically that BCT is associated with improved survival compared with total mastectomy.

The present study has important implications for post-therapeutic surveillance in male breast cancer. Current guidelines for post-therapeutic surveillance in men are the same as those recommended for women, which include history and physical examination every 4–6 months for the first 5 years and annually afterwards.^{2,38} BCT patients also

should undergo annual mammography. Future research is needed to determine if this surveillance regimen is adequate in men, because these guidelines were created based on research with predominantly female patients.

Despite this study's strengths, it does have limitations inherent to administrative data. This study was retrospective, and patients were not randomized to treatment approaches. Despite extensive multivariable analyses and model adjustment with propensity scores, our results may still have been confounded by selection bias related to nuanced clinical, pathologic, or sociodemographic features that could affect choice of therapy, including patients' and physicians' preferences. For example, in addition to the higher rate of triple-negative receptor status among BCT patients compared with mastectomy alone patients (4.9% vs. 1.4%, which we controlled for in our IPTW and

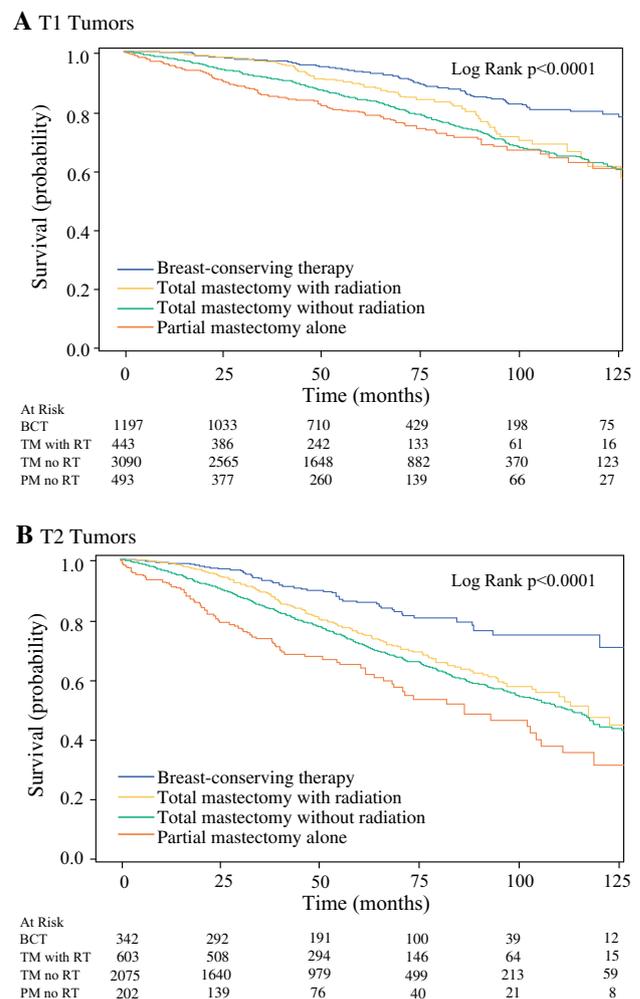


FIG. 3 Univariate overall survival for breast-conserving therapy (BCT) compared with partial mastectomy alone (PM no RT), total mastectomy alone (TM no RT) and total mastectomy with radiation therapy (TM with RT) by T stage

multivariable analyses), patient preferences may potentially explain why BCT patients were more commonly treated with adjuvant systemic therapies compared with mastectomy-alone patients. BCT patients may have been more amenable to additional therapies in general, including systemic therapy and RT, whereas mastectomy-alone patients may have preferred to avoid additional therapies, which is why they selected total mastectomy over BCT. We acknowledge that many patients had missing HER-2 status. However, this likely had negligible influence on our results. Most male breast cancer patients have been shown to be HER-2-negative, and our sensitivity analyses revealed no significant survival differences when excluding HER-2 unknown patients.¹² Because NCDB does not provide detailed information regarding systemic therapeutics, we were not able to control for specific adjuvant regimens or assess whether patients completed their entire course of adjuvant therapy. NCDB does not provide data on cause of death or recurrence, limiting our primary outcome to OS. Lastly, we lacked information regarding treatment complications and adverse side-effects, which have the potential to influence surgical and RT treatment decisions and patient quality of life.

CONCLUSIONS

In this analysis of a large, national cohort of male breast cancer patients, although total mastectomy was more commonly performed, BCT was associated with improved survival compared to total mastectomy. These findings suggest that BCT is a viable treatment approach for male breast cancer patients and should be given greater consideration by surgeons and oncologists. However, because RT compliance is an essential component in BCT, careful, personalized, shared decision-making between physicians and male breast cancer patients is necessary to ensure the selected treatment approach, whether BCT or mastectomy, is reasonable for the patient.

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