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Is breast conservation superior to mastectomy in early stage triple negative breast cancer?

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Is breast conservation superior to mastectomy in early stage triple negative breast cancer?

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ABSTRACT

Purpose: Compare overall survival (OS) and breast cancer-specific survival (BCSS) outcomes of breast conservative therapy (BCT) and mastectomy in a large cohort of patients with early-stage triple negative breast cancer (TNBC), using a propensity score-based matching approach.
Methods: Surveillance, Epidemiology, and End Results (SEER) database was used to study the role of RT in early stage TNBC. Primary end points were OS and BCSS. Cox proportional hazard regression models and Kaplan-Meier plots were used to generate the desired outcomes. Propensity score matching was done to minimize bias.
Results: 12,761 patients with T1-2N0M0 TNBC as their first malignancy were retrieved. Of these 7237 had lumpectomy with RT, and 5524 had mastectomy only. Age, race, marital status, tumor laterality, grade and stage, and receipt of chemotherapy were prognostic variables for OS and BCSS. Among 4848 matched subjects, the 5-year OS was significantly higher in patients with lumpectomy and RT (89%) compared to mastectomy alone (84.5%) (p-value <0.001). Similarly, BCSS was significantly higher in patients with lumpectomy and RT (93%) compared to mastectomy alone (91%) (p-value <0.001). On subgroup analysis, patients who are younger than 40 had similar survival outcomes after either mastectomy alone or lumpectomy with RT. However, those who are older than 60, have any grade or T stage had better survival outcomes with lumpectomy and RT.
Conclusions: Overall, lumpectomy followed by RT is associated with better OS and BCSS compared to mastectomy in T1-2N0M0 TNBC patients. Further research is needed to determine the optimal treatment strategy for specific patient subgroups.

1. Introduction

Breast cancer is the most common malignant tumor in women worldwide, with around 2 million novel cases annually [1]. While high-income countries have seen a decline in mortality rates through changes in both clinical presentation and management [2], improvements can still be made to ensure better outcomes for patients. Triple-negative breast cancer (TNBC) tumors are particularly aggressive, occur at a younger age and have worse disease-free and overall survival as they tend to recur and metastasize earlier [3].

Historically, clinical trials [4–7] have demonstrated the equivalence of lumpectomy with radiotherapy, also known as breast conservative therapy (BCT), to mastectomy in early stage breast cancer. These trials did not account for specific breast cancer subtypes such as triple negative. To date, there is no consensus on the optimal approach for treatment of early stage TNBC. Some studies have showcased the equivalence of BCT to mastectomy [8], while others showed superiority of BCT in early-stage TNBC [9]. Such studies are limited and lack certain treatment related variables such as type and sequence of chemotherapy.

The current study utilizes a recent cohort from the SEER database on TNBC. Using a propensity-matched analysis., we evaluate survival (BCSS and OS) of early stage TNBC based on treatment modality.

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2. Methods

2.1. Patient population

SEER*Stat statistical software version 8.3.61 was used to conduct a case-listing session. Starting in 2010, SEER database began to include data on HER-2 receptor status. Accordingly, all cases of early stage TN breast cancer diagnosed between 2010 and 2015 were retrieved from the SEER research database. All selected patients were (clinical or pathologic) T1-2N0M0 based on the 7th edition of the American Joint Committee on Cancer. Among the selected cases, those with unknown stage, unknown laterality, no or unknown type of surgery, unknown tumor grade, unknown race, unknown insurance status, unknown marital status, radiation other than adjuvant, mastectomy followed by radiotherapy, lumpectomy without radiotherapy, duplicates, and previous malignancies were excluded. No IRB approval was required as this study did not involve patient interaction, informed consents, or patient identification.

For each case, information on age at diagnosis, race, insurance status, marital status, tumor laterality, tumor size, tumor grade, tumor histology, TNM stage, type of surgery, use of radiotherapy, use of chemotherapy, and cause of death were collected. Primary end points were overall survival (OS) and breast cancer specific survival (BCSS). OS was measured from the date of diagnosis to the date of death from any cause or last follow-up. BCSS was measured from the date of diagnosis to the date of death due to breast cancer or last follow-up.

Cases were categorized into 2 groups: lumpectomy with RT, and mastectomy alone. The groups were compared for a range of demographic, pathologic, and treatment variables.

2.2. Matching

Lumpectomy with RT patients were matched to the mastectomy alone patients on the propensity for having lumpectomy + RT. The calipers used were ±0.25*std of logit propensity scores. For each case, a control subject was randomly selected from the potential pool of controls defined by the calipers. The propensity for lumpectomy with RT was estimated using a logistic regression model with the response variable being lumpectomy with RT (Y/N), and the independent variables being age, marital status, insurance, race, T stage, laterality, grade, histology and receipt of chemotherapy. Patients who were missing at least one of these variables were excluded from the matching process. Standardized mean difference (SMD) was calculated to reflect the size of the difference between the two groups in each variable. SMD<0.1 was considered a small difference.

2.3. Statistical analysis

Statistical analysis was performed using SPSS 25.0 software. Continuous data were reported as means and standard deviations or medians and ranges while categorical data were reported as counts and percentages. Comparisons between different demographic and tumor characteristics between the 2 groups were done using the chi-square test, independent *t*-test, and nonparametric independent samples median test, as appropriate. OS and BCSS for the matched cohort were estimated by Kaplan-Meier survival curves, and survival differences were assessed by the log-rank test. The Cox proportional hazards regression model was conducted on univariable and multivariable analyses of OS and BCSS in the whole cohort.

Univariate Cox regression analysis was performed for each prognostic variable. Multivariate Cox regression analysis (stepwise backward likelihood ratio) adjusting for other prognostic factors including age, race, marital status, laterality, tumor grade, tumor size (T-stage), and chemotherapy was performed to evaluate the effect of variables and treatment on OS and BCSS. Hazard ratio (HR) with 95% confidence interval (CI) for each variable and treatment group was calculated. All reported P values were 2 sided, and differences were considered statistically significant at $P < 0.05$.

3. Results

3.1. Study population

We retrieved 12,761 T1-2N0M0 TNBC patients diagnosed between 2010 and 2015 who met our inclusion criteria. Of those, 7237 (57%) had lumpectomy followed by RT, and 5524 (43%) had mastectomy alone. Table 1 demonstrates the patients' demographics and tumor characteristics. Except for marital status, laterality and tumor grade, all variables were significantly different between the 2 treatment groups. Lumpectomy with RT patients were older (mean age 60) compared to mastectomy patients (mean age 57). On the other hand, the mastectomy group had a higher proportion of tumor size >2 cm (49%) compared to the lumpectomy with RT (34%) group. Among the 2 groups, most patients were white (74%), insured (99%), married (60%), received chemotherapy (71%), and had ductal (90%) and poorly differentiated grade 3 (78%) carcinoma.

Using propensity score matching, 4848 pairs of patients in the lumpectomy with RT and mastectomy groups were matched on age, marital status, insurance, race, T stage, laterality, tumor grade, histology and receipt of chemotherapy using an SMD<0.1 as illustrated in Supplements 1 and Table 2.

3.2. Outcomes

On univariate cox proportional hazard regression, several variables proved to have a significant prognostic effect on the OS and BCSS in the whole cohort of TNBC patients. Asian or Pacific Islander race, being married, right-sided tumor, lower grade disease, and receipt of chemotherapy were significantly associated with better OS and BCSS. Younger age and smaller tumor size had a significant protective effect in terms of OS only. Using a multivariate cox proportional hazard regression model, Asian or Pacific Islander race, being married, right sided tumor, lower grade disease, and the receipt of chemotherapy retained significance as prognostic variables associated with better BCSS. These variables in addition to younger age and smaller tumor size also retained significance as prognostic variables associated with better OS (Table 3).

Among the propensity-matched cohort, the hazards ratio (HR) for death associated with mastectomy alone vs. lumpectomy with RT was 1.5 (95% CI: 1.33–1.73; P value < 0.001) for OS and 1.4 (95% CI: 1.18–1.66; P value < 0.001) for BCSS (Table 4). Furthermore, lumpectomy with RT group had better OS and BCSS as illustrated in the Kaplan-Meier plots in Figs. 1 and 2 respectively. The 5-year OS was significantly higher in patients with lumpectomy and RT (89%) compared to mastectomy alone (84.5%) (p-value <0.001). Similarly, BCSS was significantly higher in patients with lumpectomy and RT (93%) compared to mastectomy alone (91%) (p-value <0.001). To eliminate the uncertainty of the receipt of chemotherapy (patients with no/unknown status), survival analysis was repeated only on patients who received chemotherapy (lumpectomy + RT n = 3327; mastectomy n = 3415). Despite the receipt of chemotherapy, lumpectomy with RT had significantly higher 5-year OS (91.2% vs 89%, p = 0.007) and BCSS (93.3% vs 91.5%, p = 0.021) compared to mastectomy as illustrated in the Kaplan-Meier plots in Figs. 3 and 4, and the hazards ratios in Table 4.

Subgroup analysis was done for multiple variables (Table 5). BCSS and OS were similar in the 2 groups for patients less than 40 years old or aged 40–60 years. However, lumpectomy with RT had better survival outcomes in those aged >60. Lumpectomy with RT had better BCSS compared to mastectomy in grade 1, 2 and 3 disease in terms of OS and in grades 3 in terms of BCSS. Regardless of race, tumor size and the recipient of chemotherapy, lumpectomy with RT was associated with better outcomes.

Table 1
Baseline characteristics of all patients with triple negative T1-2N0M0, according to treatment group.

Variable		Number (%)			*p* value	SMD[a]
		Total	Lumpectomy + RT	Mastectomy Alone		
Patients		12,761	7237	5524		
Age at Diagnosis (years)	Mean (SD)	58.74 (13.18)	60.02 (12.10)	57.06 (14.51)	**<0.001**	0.221
	Median (Range)	59 (22–99)	60 (22–99)	56 (22–98)	**<0.001**	
	<40	959 (7.5)	326 (4.5)	633 (11.5)	**<0.001**	
	40–60	6059 (47.5)	3377 (46.7)	2682 (48.6)		
	>60	5743 (45.0)	3534 (4.8)	2209 (40.0)		
Race	White	9481 (74.3)	5312 (73.4)	4169 (75.5)	**<0.001**	0.168
	Black	2283 (17.9)	1457 (20.1)	826 (15.0)		
	Asian or Pacific Islander	931 (7.3)	434 (6.0)	497 (9.0)		
	American Indian/Alaska Native	66 (0.5)	34 (0.5)	32 (0.6)		
Marital Status	Married	7657 (60.0)	4343 (60.0)	3314 (60.0)	0.98	<0.001
	Unmarried	5104 (40.0)	2894 (40.0)	2210 (40.0)		
Insurance Status	Insured	1257 (98.6)	7130 (98.5)	5446 (98.6)	0.76	0.057
	Uninsured	185 (1.4)	107 (1.5)	78 (1.4)		
Laterality	Right	6226 (48.8)	3505 (48.4)	2721 (49.3)	0.36	0.017
	Left	6535 (51.2)	3732 (51.6)	2803 (50.7)		
Histology	Ductal Carcinoma	11,446 (89.7)	6545 (90.4)	4901 (88.7)	**0.005**	0.064
	Lobular Carcinoma	119 (0.9)	58 (0.8)	61 (1.1)		
	Adenocarcinoma	234 (1.8)	134 (1.9)	100 (1.8)		
	Other	962 (7.5)	500 (6.9)	462 (8.4)		
Tumor Grade	I - Well Differentiated	372 (2.9)	235 (3.2)	137 (2.5)	**0.02**	0.054
	II - Moderately Differentiated	2502 (19.6)	1436 (19.8)	1066 (19.3)		
	III - Poorly Differentiated	9887 (77.5)	5566 (76.9)	4321 (78.2)		
T Stage/Tumor size (mm)	T1mic (microscopic foci)	142 (1.1)	76 (1.1)	66 (1.2)	**<0.001**	0.322
	T1a (≤5 mm)	804 (6.3)	486 (6.7)	318 (5.8)		
	T1b (>5 mm–10 mm)	1933 (15.1)	1319 (18.2)	614 (11.1)		
	T1c (>10 mm–20 mm)	4730 (37.1)	2896 (40.0)	1834 (33.2)		
	T2 (>20 mm–50 mm)	5152 (40.4)	2460 (34.0)	2692 (48.7)		
Chemotherapy Received	Yes	9060 (71.0)	5324 (73.6)	3736 (67.6)	**<0.001**	0.131
	No/Unknown	3701 (29.0)	1913 (36.4)	1788 (32.4)		

[a] Standardized Mean Difference.

Table 2
Baseline characteristics of propensity matched patients with triple negative T1-2N0M0, according to treatment group.

Value		Number (%)			SMD[a]
		Total	Lumpectomy + RT	Mastectomy Alone	
Patients		9696 (100)	4848 (50)	4848 (50)	
Age at Diagnosis (years)	Mean (SD)	58 (14)	58 (13)	58 (14)	0.011
	Median (Range)	58 (22–99)	58 (22–99)	58 (22–98)	
	<40	762 (7.9)	320 (6.6)	442 (9.1)	
	40–60	4806 (49.6)	2481 (51.2)	2325 (48.0)	
	>60	4128 (42.6)	2047 (42.2)	2081 (42.9)	
Race	White	7253 (74.8)	3608 (74.4)	3645 (75.2)	0.022
	Black	1636 (16.9)	830 (17.1)	806 (16.6)	
	Asian or Pacific Islander	753 (7.8)	385 (7.9)	368 (7.6)	
	American Indian/Alaska Native	54 (0.6)	25 (0.5)	29 (0.6)	
Marital Status	Married	5855 (60.4)	2957 (61.0)	2898 (59.8)	0.025
	Unmarried	3841 (39.6)	1891 (39.0)	1950 (40.2)	
Insurance Status	Insured	9551 (98.5)	4771 (98.4)	4780 (98.6)	0.043
	Uninsured	145 (1.5)	77 (1.6)	68 (1.4)	
Laterality	Right	4947 (51.0)	2354 (48.6)	2395 (49.4)	0.017
	Left	4749 (49.0)	2494 (51.4)	2453 (50.6)	
Histology	Ductal Carcinoma	8632 (89.0)	4290 (88.5)	4342 (89.6)	0.034
	Lobular Carcinoma	96 (1.0)	50 (1.0)	46 (0.9)	
	Adenocarcinoma	180 (1.9)	94 (1.9)	86 (1.8)	
	Other	788 (8.1)	414 (8.5)	374 (7.7)	
Tumor Grade	I - Well Differentiated	288 (3.0)	159 (3.3)	129 (2.7)	0.038
	II - Moderately Differentiated	1918 (19.8)	958 (19.8)	960 (19.8)	
	III - Poorly Differentiated	7490 (77.2)	3731 (77.0)	3759 (77.5)	
T Stage/Tumor size (mm)	T1mic (microscopic foci)	125 (1.3)	65 (1.3)	60 (1.2)	0.097
	T1a (≤5 mm)	637 (6.6)	333 (6.9)	304 (6.3)	
	T1b (>5 mm–10 mm)	1362 (14.0)	756 (15.6)	606 (12.5)	
	T1c (>10 mm–20 mm)	3456 (35.6)	1692 (34.9)	1764 (36.4)	
	T2 (>20 mm–50 mm)	4116 (42.5)	2002 (41.3)	2114 (43.6)	
Chemotherapy Received	Yes	6742 (69.5)	3327 (68.6)	3415 (70.4)	0.039
	No/Unknown	2954 (30.5)	1524 (31.4)	1433 (29.6)	

[a] Standardized Mean Difference.

Table 3
Univariable and multivariable cox proportional hazard regression model of OS and BCSS in the whole cohort.

Univariable Cox Proportional Hazard Regression Model of OS and BCSS					
Variable		OS		BCSS	
		HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age	<40	Reference		Reference	
	40–60	1.0 (0.73–1.30)	0.86	0.87 (0.64–1.19)	0.39
	>60	2.3 (1.77–3.08)	**<0.001**	1.3 (0.92–1.70)	0.15
Race	White	Reference		Reference	
	Black	1.0 (0.87–1.18)	0.84	1.1 (0.89–1.32)	0.41
	Asian or Pacific Islander	0.61 (0.46–0.81)	**0.001**	0.6 (0.41–0.86)	**0.006**
	American Indian/Alaska Native	1.1 (0.48–2.39)	0.87	0.92 (0.30–2.86)	0.89
Marital Status	Married	Reference		Reference	
	Unmarried	1.65 (1.45–1.85)	**<0.001**	1.408 (1.236–1.603)	**<0.001**
Insurance Status	Insured	Reference		Reference	
	Uninsured	1.1 (0.69–1.75)	0.69	1.4 (0.79–2.38)	0.26
Laterality	Right	Reference		Reference	
	Left	1.14 (1.02–1.28)	**0.027**	1.2 (1.01–1.37)	**0.036**
Histology	Ductal Carcinoma	Reference		Reference	
	Lobular Carcinoma	1.1 (0.64–1.92)	0.7	0.72 (0.30–1.74)	0.47
	Adenocarcinoma	1.0 (0.66–1.56)	0.95	0.3 (0.12–0.88)	**0.026**
	Other	1.2 (0.96–1.44)	0.13	1.1 (0.85–1.45)	0.45
Tumor Grade	I - Well Differentiated	Reference		Reference	
	II - Moderately Differentiated	1.4 (0.87–2.24)	0.17	1.8 (0.83–3.92)	0.13
	III - Poorly Differentiated	1.8 (1.06–2.64)	**0.027**	2.7 (1.28–5.71)	**0.009**
T Stage/Tumor size (mm)	Tmic (microscopic foci)	Reference		Reference	
	T1a (≤5 mm)	2.0 (0.62–6.61)	0.24	793.9 (0.0–2.1E+20)	0.74
	T1b (>5 mm–10 mm)	2.4 (0.76–7.56)	0.14	1393.2 (0.0–3.7E+20)	0.72
	T1c (>10 mm–20 mm)	4.1 (1.33–12.85)	**0.01**	2799.7 (0.0–7.3E+20)	0.7
	T2 (>20 mm–50 mm)	6.5 (2.010–20.26)	**0.001**	5233.4 (0.0–1.4E+21)	0.68
Chemotherapy Received	No	Reference		Reference	
	Yes	0.4 (0.38–0.48)	**<0.001**	0.8 (0.68–0.94)	**0.006**
Multivariate Cox Proportional Hazard Regression Model of OS and BCSS					
Variable		**OS**		**BCSS**	
		HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age	<40	Reference			
	40–60	1.1 (0.79–1.41)	0.71		
	>60	2.1 (1.61–2.83)	**<0.001**		
Race	White	Reference		Reference	
	Black	1.0 (0.89–1.21)	0.64	1.0 (0.84–1.25)	0.8
	Asian or Pacific Islander	0.64 (0.48–0.84)	**0.002**	0.6 (0.42–0.89)	**0.01**
	American Indian/Alaska Native	0.86 (0.48–2.40)	0.86	0.9 (0.30–2.87)	0.89
Marital Status	Married	Reference		Reference	
	Unmarried	1.3 (1.15–1.46)	**<0.001**	1.3 (1.07–1.46)	**0.005**
Laterality	Right	Reference		Reference	
	Left	1.1 (1.01–1.28)	**0.03**	1.2 (1.02–1.38)	**0.029**
Tumor Grade	I - Well Differentiated	Reference		Reference	
	II - Moderately Differentiated	1.6 (1.005–2.60)	**0.048**	1.9 (0.87–4.10)	0.11
	III - Poorly Differentiated	2.5 (1.57–3.93)	**0.002**	3.0 (1.44–6.47)	**0.004**
T Stage/Tumor size (mm)	Tmic (microscopic foci)	Reference			
	T1a (≤5 mm)	2.2 (0.67–7.14)	0.2		
	T1b (>5 mm–10 mm)	3.1 (0.99–9.87)	0.052		
	T1c (>10 mm–20 mm)	6.7 (2.15–20.93)	**0.001**		
	T2 (>20 mm–50 mm)	11.9 (3.82–37.17)	**<0.001**		
Chemotherapy Received	No/Unknown	Reference		Reference	
	Yes	0.4 (0.35–0.45)	**<0.001**	0.7 (0.62–0.86)	**<0.001**

4. Discussion

Previous historical landmark studies and clinical trials showed that radiation added to lumpectomy is equivalent to mastectomy in early stage breast cancer patients [4–7]. Similarly, the largest observational study to date recently revealed the comparable efficacy of BCT to mastectomy [10]. However, recent observational studies suggested that BCT is superior to mastectomy in early stage breast cancer [11–15]. Therefore, it is essential to reconsider the comparison between BCT and mastectomy in the modern era.

Few studies reported mixed results when comparing BCT to mastectomy in early stage TNBC. Abdulkarim et al. reported better locoregional control in the BCT group, but similar OS outcomes (n = 468) [16]. Similarly, others [17,18] reported comparable OS between the BCT and total mastectomy groups in early stage TNBC patients. In contrast, Kindts et al. studied 439 non metastatic TNBC patients and reported better BCSS for those who underwent BCT as compared to mastectomy [19]. More recently a large, non-propensity matched SEER analysis on early stage TNBC showed BCT to be associated with better OS and BCSS compared to mastectomy [20]. Such discrepancies can be attributed to differences in the study populations, the limited power of the statistical comparisons, the effect of confounders and selection bias.

To better address the above question, we used the SEER database and performed propensity score matching in order to minimize selection bias. As shown in Figs. 1 and 2, BCT was superior to mastectomy alone in terms of OS (log rank $p < 0.001$) and BCSS (log rank $p < 0.001$). This concurs with the above mentioned non-propensity matched SEER analysis study [20] and with a recent report whereby patients with T1N0 disease treated with BCT had better 10-year OS and distant metastasis-free survival compared to those who had mastectomy [21].

Table 4
OS and BCSS hazard ratios associated with radiation and extent of surgery in the matched cohort.

Comparison	OS for all patients		OS for patients who received chemotherapy	
	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
Lumpectomy + RT	1 [Reference]	<0.001	1 [Reference]	0.007
Mastectomy	1.5 (1.33–1.73)		1.3 (1.07–1.55)	
Comparison	**BCSS for all patients**		**BCSS for patients who received chemotherapy**	
	Hazard Ratio (95% CI)	**P Value**	**Hazard Ratio (95% CI)**	**P Value**
Lumpectomy + RT	1 [Reference]	<0.001	1 [Reference]	0.022
Mastectomy	1.4 (1.18–1.66)		1.3 (1.04–1.58)	

Similarly, others showed superiority of BCT for early stage breast cancer regardless of subtype [11–15].

We stratified the matched cohort based on select clinical variables to account for possible cofounding effects. For patients younger than 40 years old or aged 40–60 years, the treatment modality did not affect the cancer specific and overall survival. This is supported by the results of some observational studies that showed no significant difference between BCT and mastectomy in early stage breast cancer patients aged less than 40 years [22,23]. In terms of BCSS and tumor grade, lumpectomy with RT had protective effect for grade 3 disease only. This might indicate that treatment modality does not make a difference for low grade tumors (1–2). As shown in Table 5, other subcategories, demonstrated better survival outcome with BCT vs. mastectomy.

There are multiple potential explanations for the additional benefit RT adds to lumpectomy when compared to mastectomy. RT might help eliminate microscopic disease and possible microscopic LN involvement that are not targeted by mastectomy alone reducing locoregional

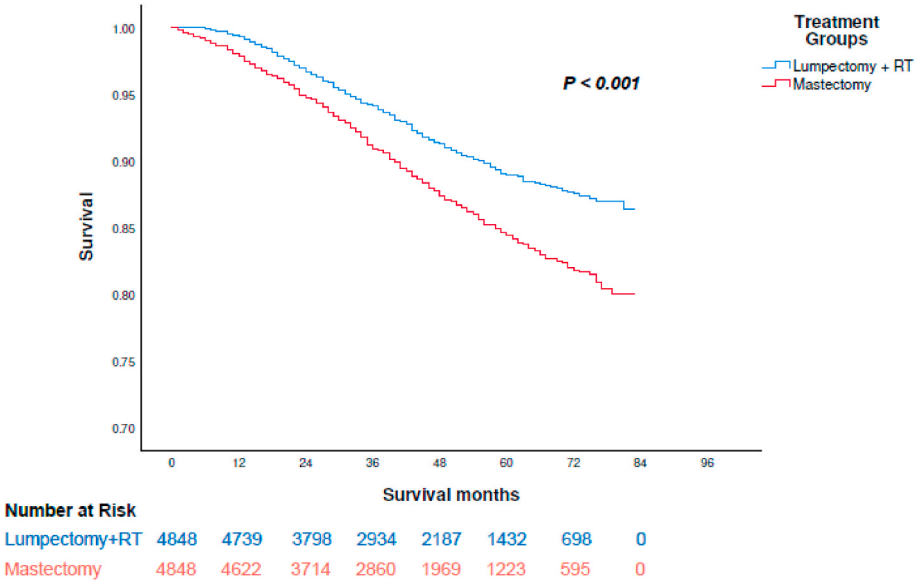

Fig. 1. Kaplan-Meier plot of overall survival (OS) by treatment group in the matched cohort.

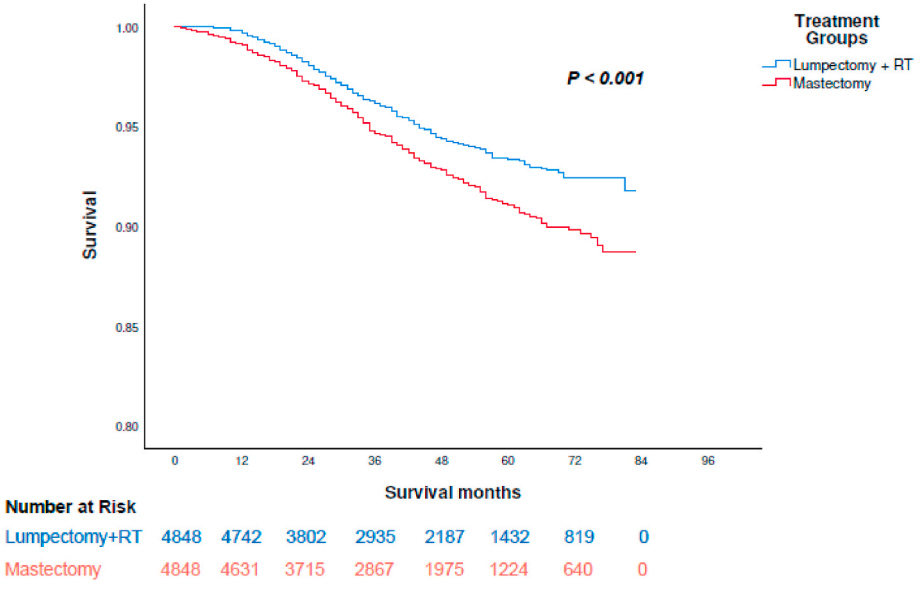

Fig. 2. Kaplan-Meier plot of breast cancer specific survival (BCSS) by treatment group in the matched cohort.

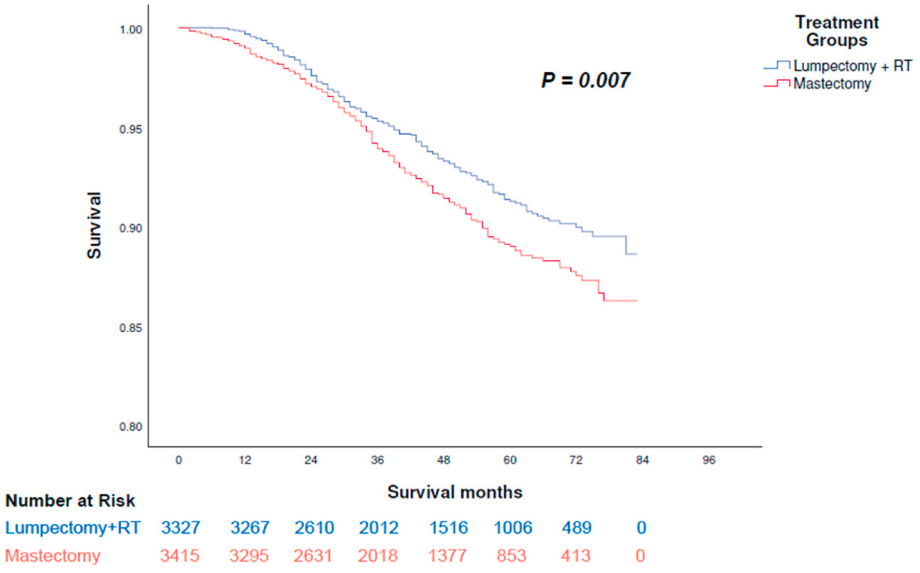

Fig. 3. Kaplan-Meier Plot of Overall Survival (OS) by Treatment Group in the Matched Cohort for Patients who Received Chemotherapy.

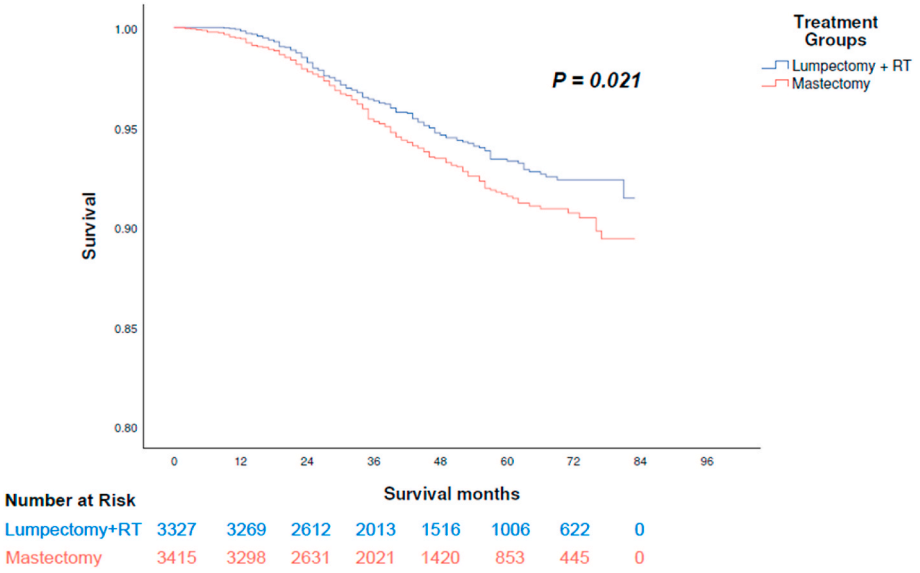

Fig. 4. Kaplan-Meier Plot of Breast Cancer Specific Survival (BCSS) by Treatment Group in the Matched Cohort for Patients who Received Chemotherapy.

recurrence (LRR). Onitilo et al. reported better LRR and OS for patients receiving lumpectomy followed by RT compared to mastectomy [24]. Furthermore, TNBC patients are more likely to have BRCA mutations [25], rendering the tumor unable to repair the DNA damage. This can lead to increased radio-sensitivity [26] which might explain the better outcomes associated with RT in our study. Unfortunately, we were unable to obtain data on BRCA status through SEER, which limits our ability to confirm this hypothesis. Finally, mastectomy is known to be more morbid than BCT, although efforts have been spent to decrease its morbidity by changing the surgery technique [27]. However, one should note that despite minimizing the effect of confounding with propensity score matching, some confounders are not available and cannot be easily adjusted for. For example, SEER does not record mode of presentation (screening or symptomatic) as screen-detected disease have a better prognosis than its symptomatic counterpart. Screen-detected patients are more likely to be treated by BCT and thus have improved survival outcomes. The observation that the apparent improvements in survival after BCT in our study were evident in older patients but not in younger patients (who are less likely to be detected through screening) is in keeping with this possibility.

As for the prognostic factors, Asian and non-pacific race had better survival. This concurs with previously reported results that showed lower breast cancer actuarial risk of death among Asian women [28]. Being married conferred a survival effect as well. This can be attributed to the parity, breastfeeding and social support effect which is proven to decrease the risk of breast cancer [29] even in TNBC [30]. Lower grade disease and smaller tumor size also provided survival benefit in these patients. Furthermore, the receipt of chemotherapy contributed to better survival in these patients. Chemotherapy currently serves as the backbone of systemic therapy in TNBC as such tumors lack sensitivity to ER and HER-2 blockade targeting agents [31]. It is worth mentioning that BCT was also associated with better OS and BCSS compared to mastectomy in patients who received chemotherapy indicating the added benefit radiation can provide despite the receipt of systemic therapies.

Although it stands as one of the largest studies on the topic, the current analysis has several limitations that are worth discussing. First,

Table 5
Hazard Ratios for BCSS and OS Associated with Lumpectomy and Radiotherapy vs Mastectomy Alone for Various Propensity-Matched Patient Subgroups.

Subgroup		Comparison	HR for BCSS (CI 95%)	*p* value	HR for OS (CI 95%)	*p* value
Age at Diagnosis (years)	<40	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.5 (0.77–2.77)	0.25	1.7 (0.89–3.12)	0.11
	40–60	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.2 (0.95–1.63)	0.11	1.1 (0.87–1.40)	0.42
	>60	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.5 (1.18–1.91)	**0.001**	1.7 (1.48–2.05)	**<0.001**
Race	White	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.4 (1.14–1.68)	**0.001**	1.5 (1.29–1.73)	**<0.001**
	Black	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.4 (0.93–2.01)	0.11	1.5 (1.12–2.06)	**0.007**
Tumor Grade	I - Well Differentiated	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	7.4 (0.90–61.57)	0.06	3.5 (1.27–9.80)	**0.016**
	II - Moderately Differentiated	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.2 (0.76–1.86)	0.44	1.6 (1.19–2.22)	**0.003**
	III - Poorly Differentiated	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.4 (1.16–1.69)	**<0.001**	1.5 (1.26–1.69)	**<0.001**
T Stage/Tumor Size	T1mic + T1a (≤5 mm)	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.3 (1.06–1.65)	**0.012**	1.6 (1.32–1.88)	**<0.001**
	T1b (>5 mm–10 mm)	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	2.3 (1.13–4.66)	**0.022**	1.6 (1.03–2.61)	**0.037**
	T1c (>10 mm–20 mm)	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.3 (0.92–1.71)	0.15	1.3 (1.03–1.61)	**0.03**
	T2 (>20 mm–50 mm)	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.3 (1.06–1.65)	**0.012**	1.6 (1.32–1.88)	**<0.001**
Chemotherapy Received	Yes	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.3 (1.04–1.58)	**0.022**	1.3 (1.07–1.55)	**0.007**
	No/Unknown	Lumpectomy Plus Radiotherapy	Reference		Reference	
		Mastectomy	1.7 (1.25–2.25)	**0.01**	1.8 (1.53–2.22)	**<0.001**

this is a retrospective non-randomized study, where treatment might have been given according to physician preferences and some specific factors that are not captured by the dataset. Second, SEER database does not have data on locoregional recurrence, which is an important endpoint for radiotherapy. Furthermore, SEER has data on HER-2 receptor status as of 2010, limiting the study cohort to 5 years only (2010–2015). Moreover, important variables such as BRCA mutation or the sequence of chemotherapy could not be retrieved. Other major limitations include the inability to capture the sequence of chemotherapy (neoadjuvant vs adjuvant) and its definite absence in the treatment paradigm. Moreover, we did not provide further analysis on ethnicity, rather we limited it to race only.

5. Conclusion

TNBC is an aggressive form of breast cancer with poor prognosis. No representative clinical trials assessed the difference between BCT and mastectomy in these patients. Our propensity-matched analysis study revealed that RT when added to lumpectomy is associated with better OS and BCSS compared to mastectomy. Further studies should be conducted to optimize the treatment modality according breast cancer biology.

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Ethical approval

The project did not require Institutional Review Boards (IRB) approval as it did not involve human subjects and was merely based on online databases.

Authors contributions

Conception and design: OS, MC, JH, LAV, YHZ, Provision of study materials or patients: OS, MC, JH, ZL, JP, LAV, YHZ, Collection and assembly of data: OS, MC, JH, Data analysis and interpretation: OS, MC, JH, ZL, JP, LAV, YHZ, Manuscript writing: All authors, Final approval of manuscript: All author, Accountable for all aspects of the work: All authors.

Declaration of competing interest

The authors declare to conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2022.02.006.

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