

# Breast Conserving Surgery (BCS) is Superior to Mastectomy in Early Stage Triple Negative Breast Cancer (TNBC) a Comparative Study

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## Abstract

## Original Research Article

**Background:** Breast cancer is the most prevalent form of cancer in women worldwide and the second-leading cause of death from cancer in women. Because the estrogen receptor, progesterone receptor, and HER2 are not expressed, triple-negative breast cancer (TNBC) has an aggressive clinical history. The highest rates of recurrence and survival, higher average grades, and larger tumor sizes at diagnosis are all characteristics of TNBC. **Objective:** To compare between breast conserving surgery (BCS) and mastectomy patients with early stage Triple negative breast cancer (TNBC). **Materials and Methods:** We conducted a comparative retrospective monocentric study that evaluated TNBC patients treated with upfront surgery at CMH Dhaka, CMH Bogura and Kurmitola General Hospital, Dhaka. The observation period was from 1 January 2021 to 31 December 2022. All patients received biopsy to obtain the pathological tissue before treatment, and their immunohistochemical results met the diagnostic criteria for TNBC. Study patients divide into two group 40 surgeries with primary site were categorized as receiving BCS and other hand 40 surgeries with categorized as receiving mastectomy. BCSS and OS were the primary outcomes of our study. **Results:** Tumor grade II, tumor size >20.0 mm and lymph node 2 were significantly associated with breast cancer-specific survival. Tumor size >20.0 mm and lymph node 2 were significantly associated with TNBC survival. **Conclusion:** TNBC is a breast cancer type that is aggressive and has a bad prognosis. With regard to breast cancer-specific survival, advanced age, being single, left side of laterality, tumor grades II and III, large tumor size, and lymph node 2 were all substantially related. **Keywords:** Breast cancer-specific survival, overall survival, triple-negative breast cancer.

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## INTRODUCTION

Breast cancer is the most common cancer in females around the world and the second leading cause of female cancer death worldwide [1]. TNBC, defined by the absence of protein expression of the estrogen receptor (ER), progesterone receptor (PR), and HER2, is a subtype of breast cancer with a more invasive capability than the other subtypes, accounting for 15-20% of all breast cancers [2,3]. Triple-negative breast cancer (TNBC) is a kind of breast cancer that has an aggressive clinical history due to a lack of expression of the estrogen receptor, progesterone receptor, and HER2. TNBC has the highest recurrence and survival rates, is typically of higher grade, and has a greater tumor size at diagnosis. Triple-negative breast cancer (TNBC) tumors are particularly aggressive as they arise at a younger age, and have showcased much worse disease-free and overall

survival rate because they recur and metastasis earlier [4]. Because TNBC tumors do not express HER2 or the progesterone or estrogen receptors, neither hormone treatment nor HER2-blocking drugs are used to treat TNBC patients [5].

This begs the question of whether the poor prognosis of TNBC justifies a more aggressive surgical strategy, as well as if there is merit in expanding the use of radiation therapy among women with TNBC who undergo mastectomy. Breast-conserving surgery (BCS) and mastectomy are the two surgical choices for people with early stage (Stage I and Stage II) breast cancer [6,7].

Currently, modified radical mastectomy (MRM) is the standard procedure for operable breast cancer, although data indicates that breast-conserving surgery (BCS) is the recommended technique for early

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breast cancer [8]. There are still no general consensus on the best technique for treating early stage TNBC as some studies have shown that BCS is equivalent to mastectomy [9].

Through strong evidence, we intended to explore the effect of BCT versus mastectomy on overall survival (OS), as well as a hazard regression model through solid evidential data.

## MATERIALS AND METHODS

We conducted a comparative retrospective monocentric study that evaluated TNBC patients treated with upfront surgery at Combined Military Hospital, Dhaka, Combined Military Hospital, Bogura and Kurmitola General Hospital, Dhaka. The observation period was from 1 January 2021 to 31 December 2022. All patients received biopsy to obtain the pathological tissue before treatment, and their immunohistochemical results met the diagnostic criteria for TNBC. Study patients divide into two groups, 40 surgeries with primary site were categorized as receiving BCS and other hand 40 surgeries with categorized as receiving mastectomy. BCSS and OS were the primary outcomes of our study. BCSS was defined as the time from the date of diagnosis to death due to breast cancer or the final follow-up, whereas OS was defined as the date from diagnosis to death from all causes (including breast cancer) or the last follow-up. The following were the inclusion criteria: (1) patients aged 26 to 72; (2) patients not receiving any other treatments; (3) the patient was pathologically diagnosed with breast cancer; (4) clinical stage I or II breast cancer; and (5) a single breast tumor with a diameter less than 4 cm. 40 cases met the inclusion

criteria. The following were the exclusion criteria: (1) patients with poor compliance; (2) pregnant or lactating women; (3) patients who did not meet the TNBC diagnostic criteria; (4) patients with poor heart, liver, and kidney function who cannot tolerate chemotherapy; (5) patients who had serious adverse reactions and changed or refused chemotherapy; (6) patients who discovered distant metastases prior to treatment; and (7) patients with other malignant tumors. Continuous variables were characterized using mean standard deviation (SD) (median and interquartile range), and risk subclass comparisons were conducted using a Student's t-test. The chi-square test was used to analyze connections between categorical variables, which were described using absolute number and percentage. All statistical assessments were two-tailed and considered significant if the p-value was less than 0.05 ( $p < 0.05$ ). The SPSS ver. 26.0 program (Statistical Package for Social Science) was used for the statistical analysis.

## RESULTS

Table 1 shows that age, marital status, histopathological type, laterality, tumor grade, tumor size chemotherapy received were not statistically significant ( $p > 0.05$ ) between two groups. Table 2 shows that 43(87.5%) patients were overall survival in BCS group and 34(85.0%) in TNBC group. The difference was not statistically significant ( $p > 0.05$ ) between two groups. Tumor grade II, tumor size  $> 20.0$  mm and lymph node 2 were significantly associated with breast cancer-specific survival (Table-3). Tumor size  $> 20.0$  mm and lymph node 2 were significantly associated with TNBC survival (Table-4).

**Table 1: Baseline characteristics of the study populations (n=80)**

	BCS (n=40)		TNBC (n=40)		P value
	n	%	n	%	
Age (years)					
≤50	19	47.5	22	55.0	
>50	21	52.5	18	45.0	
Mean±SD	58.2	±10.8	56.4	±11.1	0.465
Marital status					
Married	39	97.5	38	95.0	0.556
Unmarried	1	2.5	2	5.0	
Histopathological type					
Ductal carcinoma	38	95.0	39	97.5	0.603
Lobular carcinoma	1	2.5	1	2.5	
Adenocarcinoma	1	2.5	0	0.0	
Laterality					
Left	22	55.0	24	60.0	0.651
Right	18	45.0	16	40.0	
Tumor grade					
Grade I	4	10.0	1	2.5	0.235
Grade II	12	30.0	9	22.5	
Grade III	24	60.0	30	75.0	
Tumor size					
≤5.0 mm	3	7.5	2	5.0	

	BCS (n=40)		TNBC (n=40)		P value
	n	%	n	%	
5.1-10.0 mm	4	10.0	2	5.0	0.551
10.1-20.0 mm	17	42.5	14	35.0	
>20.0 mm	16	40.0	22	55.0	
Lymph node involvement					0.207
N0	16	40.0	19	47.5	
N1	17	42.5	19	47.5	
N2	7	17.5	2	5.0	
Chemotherapy received					0.485
Yes	24	60.0	27	67.5	
No	16	40.0	13	32.5	

**Table 2: Overall survival of the study populations (n=80)**

Overall survival	BCS (n=40)		TNBC (n=40)		P value
	n	%	n	%	
Yes	35	87.5	34	85.0	0.745
No	5	12.5	6	15.0	

**Table 3: Overall survival in BCS of the study populations (n=80)**

	Total	Overall survival		P value
		Yes	No	
Age (years)				0.120
≤50	19	15	4	
>50	21	20	1	
Marital status				0.702
Married	39	34	5	
Unmarried	1	1	0	
Histopathological type				0.583
Ductal carcinoma	38	33	5	
Lobular carcinoma	1	1	0	
Adenocarcinoma	1	1	0	0.701
Laterality				0.810
Right	18	16	2	
Left	22	19	3	
Tumor grade				0.426
Grade I	4	4	0	
Grade II	12	12	0	
Grade III	24	19	5	0.117
Tumor size				0.049
≤5.0 mm	3	3	0	
5.1-10.0 mm	4	4	0	
10.1-20.0 mm	17	17	0	
>20.0 mm	16	11	5	0.903
Lymph node involvement				0.032
N0	16	16	0	
N1	17	16	1	
N2	7	3	4	
Chemotherapy received				1.000
No	16	14	2	
Yes	24	21	3	

**Table 4: Overall survival in TNBC of the study populations (n=80)**

	Total	Overall survival		P value
		Yes	No	
Age (years)				
≤50	22	17	5	0.130
>50	18	17	1	
Marital status				
Married	38	32	6	0.542
Unmarried	2	2	0	
Histopathological type				
Ductal carcinoma	39	33	6	0.670
Lobular carcinoma	1	1	0	
Laterality				
Right	16	14	2	0.718
Left	24	20	4	
Tumor grade				
Grade I	1	1	0	0.670
Grade II	9	8	1	0.710
Grade III	30	25	5	0.609
Tumor size				
≤5.0 mm	2	2	0	0.542
5.1-10.0 mm	2	2	0	0.542
10.1-20.0 mm	14	14	0	0.051
>20.0 mm	22	16	6	0.016
Lymph node involvement				
N0	19	18	1	0.100
N1	19	16	3	0.894
N2	2	0	2	0.001
Chemotherapy received				
No	13	11	2	0.962
Yes	27	23	4	

## DISCUSSION

In this study showed that age, marital status, histopathological type, laterality, tumor grade, tumor size chemotherapy received were not statistically significant ( $p > 0.05$ ) between two groups. Guo *et al.*, [10]. reported age at diagnosis, ethnicity, primary tumor site, grade, tumor size and lymph node status among the three groups ( $\chi^2$  values were 507.07, 59.70, 375.59, 11.78, 2086.50 and 2575.07, respectively, all  $P < 0.05$ ). Patients with older, black, located in the axillary tail, lower tumor grade, smaller tumor and less lymphatic metastasis were more likely to be treated with radiotherapy after breast-conserving surgery. Guo *et al.*, [10]. also reported according to age, tumor size and lymph node status, when the age was less than 55 years old, at T4, N2 or N3 category, there was no statistical significance between the BCS + RT group and the Mastectomy+RT group in OS or BCSS (all  $P > 0.05$ ). Young breast cancer patients were a unique group, usually with more aggressive tumors and a worse prognosis [11-13]. This study suggested that breast-conserving surgery with radiotherapy was still feasible for young TNBC patients, which was basically consistent with the conclusions of Vila *et al.*, [14]. However, Bhoo-Pathy *et al.*, [15]. carried out a large multi-center retrospective study of 775 Asian patients with T1-2, N0-

1, M0 TNBC, and found there was no significant difference in survival rates between patients who received only total mastectomy and those who received breast-conserving postoperative radiotherapy, which was slightly different from the results of Guo *et al.*, [10] study. In study of Afifi reported the age of the patients ranged between 41-65 years in the BCS group compared with 45-70 years with a mean age [16]. In BCS group 6 (60 %) of patients were married compared with 4 (40 %) in the MRM group of patients. In BCS group 6 (60 %) of patients were affected on the left side compared with 5 (50 %) in the MRM group of patients [16]. There was no statistically significant difference in this distribution. In BCS group tumor size was  $< 2$  cm in 6 (60%) of patients compared with 5 (50%) in MRM group of patients. In BCS group tumor grade II was in 3 (30%) of patients compared with 2 (20%) in the MRM group of patients. In BCS group N0 presented in 7 (70%) of patients compared with 8 (80 %) in the MRM group of patients. This was statistically significant difference. On the other hand, another study reported that TNBC tumors were associated with lower risk of axillary LN involvement, and reported the size of the tumor to be an unreliable factor in predicting the involvement of the lymph nodes [17].

In this study, it is showed that 43(87.5%) patients were overall survival in BCS group and 34(85.0%) in TNBC group. The difference was not statistically significant ( $p>0.05$ ) between two groups. Abdulkarim *et al.*, reported better locoregional control in the BCT group, but similar OS outcomes ( $n = 468$ ) [18]. Similarly, others [15,19]. reported comparable OS between the BCT and total mastectomy groups in early stage TNBC patients. In contrast, Kindts *et al.*, [20]. studied 439 non metastatic TNBC patients and reported better BCSS for those who underwent BCT as compared to mastectomy [20].

Tumor grade II, tumor size  $>20.0$  mm and lymph node 2 were significantly associated with breast cancer-specific survival. Tumor size  $>20.0$  mm and lymph node 2 were significantly associated with TNBC survival. Guo *et al.*, [10] reported that the 3-year OS and 3-year BCSS of all patients in this study were 86.8 and 88.2%, respectively. The 3-year OS of patients who received BCS + RT, Mastectomy alone and Mastectomy+RT were 92.9, 86.0 and 74.3%, respectively, and the 3-year BCSS of patients in the three groups were 93.6, 87.9 and 76.2%, respectively. The 5-year OS and 5-year BCSS of all patients in this study were 80.5 and 82.6%, respectively. The 5-year OS of patients who received BCS + RT, Mastectomy alone and Mastectomy+RT were 87.9, 79.6, and 65.5%, respectively, and the 5-year BCSS of patients in the three groups were 89.2, 82.3, and 68.3%, respectively. Survival analyses showed that patients with TNBC who received BCS + RT had better OS and BCSS (all log-rank  $P < 0.05$ ). From the KM survival curve, we could also observe that the OS curve and BCSS curve of patients in the three groups showed a separation trend. After adjusting age at diagnosis, ethnicity, marital status, laterality, primary tumor site, grade, tumor size and lymph node status, we constructed a multivariate Cox proportional risk regression model to explore the effect of local treatment methods on overall survival. The results of multivariate Cox proportional risk regression model showed that Mastectomy alone group (HR = 1.49; 95%CI: 1.31–1.70) and Mastectomy+RT group (HR = 1.24; 95%CI: 1.08–1.43) were worse in BCSS than in the BCSS+RT group, and Mastectomy+RT group (HR = 0.83; 95%CI: 0.74–0.94) was better in OS than Mastectomy alone group. Afifi study reported no significant difference between loco-regional treatments in grade I (HR, 0.529; 95% CI, 0.032 to 8.626;  $P = 0.655$ , for OS) and stage I (HR, 0.737; 95% CI, 0.497 to 1.095;  $P = 0.131$ , for OS). Many previous prospective and retrospective randomized controlled trials reported similar results where long-term survival of early-stage breast cancer patients managed with BCS was superior to patients managed with mastectomy [21]. Saifi reported [4] 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 [4].

## CONCLUSION

TNBC is an aggressive form of breast cancer with poor prognosis. Advance age, unmarried, left side of laterality, tumor grade II and III, large tumor size and lymph node 2 were significantly associated with breast cancer-specific survival. Proportional hazard regression model, tumor size  $>20.0$  mm and lymph node 2 were significantly associated with TNBC survival. There were no representative clinical trials that compared BCS to mastectomy in these patients. Our propensity-matched analysis study found that when combined with lumpectomy, RT is associated with improved OS and BCSS than mastectomy. More research should be done to optimize the therapy technique based on breast cancer biology.

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