

# Impact of Surgery on Survival in Breast Cancer with Bone Metastases: a SEER database retrospective analysis

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## Research article

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# Abstract

**Purpose** It was controversial to operate on the primary site of breast cancer with simple bone metastasis<sup>1</sup> we found that the surgery could improve survival in patients with breast cancer with bone metastases via a SEER database retrospective analysis.

**Method** Totolly 2917 cases of breast cancer with bone metastasis, first diagnosed between 2010 and 2015 in the National Cancer Institute surveillance, Epidemiology, and Results Database (SEER).We assessed the effect of different surgical procedures on survival and prognosis by the correlation statistics.

**Results** Compared with the non-surgical group , the prognosis of patients on the primary tumor surgical group shows the statistical significance ( $c_2 = 146.023, P < 0.001$ ), the survival benefit of the breast-conserving group was the highest for 70 months( $c_2=157.117, P<0.001$ ). Compared with the non-surgery group, the median OS of primary surgery group was: HR=0.525, 95%CI=0.467-0.590, $P<0.001$ . In the breast-conserving group, the median operative OS: HR=0.394, 95%CI=0.325-0.478, $P<0.001$ .

**Conclusion:** This study showed that primary surgery could improve the prognosis and overall survival of women with advanced breast cancer with bone metastasis alone. Under the condition of low tumor burden, breast conserving surgery was a better choice.

## 1. Introduction

Breast cancer is the most common malignant tumor threatening women's health,there are over 270,000 new cases diagnosid yearly and approximately 42,000 raled deaths, ranking first in morbidity and second in mortality in the world <sup>1</sup>. Although with the improvement of people's health awareness and the development of medical technology, the screening and treatment of early breast cancer have been significantly improved, about 5% of patients still appear distant bone metastasis at the first diagnosis, and the incidence of bone metastasis is as high as 70% in advanced metastatic breast cancer <sup>2,3</sup>. Currently, for breast cancer with bone metastasis, the treatment principle is to relieve pain, restore function and improve the quality of life,increase the survival time,mainly comprehensive therapy including in Radiation and chemotherapy<sup>4-6</sup>.

There is growing evidence indicating that the active primary site surgery is associated with survival benefits in many retrospective studies<sup>7-15</sup><sup>1</sup>although prospective studies produced a small number of positive results<sup>16-18</sup>. the selective bias current guidelines do not recommend routine screening of bone metastases in patients with localized breast cancer only if directed by signs or symptoms.There is no definite result whether the operation on the primary site of breast cancer with bone metastasis benefits or not until now.

As for this, we used the Surveillance, Epidemiology, and End Results (SEER) database to investigate the effect of surgical operation on the prognosis of the patients with breast cancer with bone metastases

from 2010 to 2015.

## 2. Materials And Methods

### 2.1 Data

We obtained data from the Surveillance, Epidemiology, and End Results (SEER)–Medicare database , which consists of 18 population-based cancer registries. The SEER program of the National Cancer Institute collects and publishes cancer incidence and survival data encompassing approximately 28% of the United States population. In this study,we used SEER\*Stat Version 8.3.6 (<http://www.seer.cancer.gov/seerstat>) from the National Cancer Institute to survey eligible patients.

### 2.2 Patients

We collected breast cancer patients with bone metastases between 2010 and 2015 based on the 7th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual<sup>19</sup>. We further screened the patients through inclusion criteria and exclusion criteria, inclusion criteria: (1)Pathological diagnosis of breast cancer; (2)Age >18 years old female; (3) Simple distant bone metastases occurred clearly at the first diagnosis; (4)Complete clinicopathological information such as tumor pathological type and histological grade; (5)Complete treatment information; (6) Prognostic information is complete. Exclusion criteria: (1)Multiple primary carcinomas; (2)Bilateral breast cancer; (3)Patients with unknown T and N stages, such as T0,TX and NX, were excluded. After relevant screening, we finally leaved 2917 patients eligible for survival analyses and related reseach.

### 2.3 Clinicopathological parameters and control variables

Patients were divided into primary Surgery group and non-surgery group according to whether primary Surgery was performed. The Surgery group was divided into Breast Conservion Surgery (BCS) group, subcutaneous or simple Mastectomy group\&Mastectomy\&, modified Radical Mastectomy group and Radical Mastectomy group\&Radical mastectomy\&. Clinical pathology staging is based on AJCC 7th edition. The following clinicopathological characteristics were used as study factors: age, race, ethnic origin, marital status, T stage, N stage, laterality, behavior, ER, PR, HER2, tumor subtype and histological grade, radiotherapy, and chemotherapy.

### 2.4 Statistical analysis

Patient and tumor characteristics were summarized using descriptive statistics and compared using a two-sided  $\chi^2$  test for categorical variables and Student's t test for continuous variables. In the survival analysis, kaplan-Meier method was used to calculate the median survival time, and log-rank test was used for univariate analysis. Statistically significant factors in univariate analysis results were incorporated into COX proportional hazard regression model for multivariate analysis. All the above

statistical analyses were calculated by SPSS 22.0 statistical software. Two sided P values < 0.05 were considered statistically significant.

## 3. Results

### 3.1 Patient characteristics

A total of 2917 patients with breast cancer with simple bone metastasis were included in this study according to the inclusion criteria and exclusion criteria. Patient and tumor characteristics are listed in **table 1**. Among them, there were 1245 cases (42.7%, 1235/2917) in the primary surgery group and 1672 cases (57.3%, 1672/2917) in the non-surgery group. The clinicopathological parameters in surgical group with statistical significance were: marital status, age, histological grade, T stage, N stage, ER, molecular subtype, radiotherapy and chemotherapy compared with the non-surgical group. Compared with the non-operative patients, the proportion of young patients undergoing surgery was higher ( $c^2 = 21.613$ ,  $P < 0.001$ ). Compared with unmarried patients, married patients had a higher surgical rate (46.8% vs 38.8%). With the higher of tissue grade, the higher of T stage and N stage of tumor, the more proportion of the operation rate ( $P < 0.001$ ), and the more ratio of radiotherapy and chemotherapy of surgical patients significantly ( $P < 0.001$ ). Compared with ER positive, ER+/HER2- and ER+/HER2+ patients, ER negative, TNBC, and HER2-enriched breast cancer patients had higher surgical rates ( $P < 0.001$  and  $P = 0.009$ ). There were no significant differences in race, Ethnic origin, behavior, laterality, HER2 and PR expression between surgical patients and non-surgical patients.

### 3.2 Univariate analysis and multivariate analysis on the prognosis of breast cancer with bone metastasis

2917 cases of clinical pathology and prognosis of breast cancer with bone metastases of single factor analysis in the result analysis (**table 2**), the clinicopathological parameters influencing the prognosis of patients were race, histologic grade, marital status, age, histology, T stage, tumor radiotherapy and chemotherapy, ER, PR, and HER2, subtypes, primary tumors surgery and surgical procedure ( $P < 0.05$ ), and had no relevant to ethnic origin, laterality, and N staging ( $P > 0.05$ ). According to the results of single factor analysis, primary site surgical group significantly affected the prognosis of patients (**Figure 1**) compared to the non-surgical group ( $c^2 = 146.023$ ,  $P < 0.001$ ); In the surgery group, the survival time of the breast-conserving group (**Figure 2**) benefitted most for 70 month ( $c^2 = 157.117$ ,  $P < 0.001$ ). With the higher histological grading, higher T stage, the more the median survival time decreased ( $P < 0.001$ ). Compared with the black, the white and others got a longer survival time ( $c^2 = 35.071$ ,  $P < 0.001$ ); The expression of ER, PR, and HER2, histology of invasive ductal carcinoma, married patients, younger age, radiotherapy, and chemotherapy were all protective factors for breast cancer with bone metastasis ( $P < 0.001$ ). Single factor analysis results showed in the molecular subtype analysis, her2-positive breast cancer had the best prognosis, with the median survival time up to 73 months, while three-negative breast cancer had the worst prognosis, with the median survival time of 13 months, the difference was statistically significant ( $c^2 = 242.199$ ,  $P < 0.001$ ). COX multivariate regression analysis was performed on the pathological parameters significant by univariate analysis (**table 3**). The results showed that the

clinicopathological parameters with statistical significance were race, age, marital status, histological grade, histology, chemotherapy, ER, PR, HER2, molecular subtype, T stage, primary surgery and surgical mode. The results of univariate analysis were consistent with the above factors except the slight change of radiotherapy factors.

### 3.3 Comparison of baseline data among 1245 patients with different surgical modes

To further analyze the difference in survival analysis between different surgical methods, we used chi-square test to further analyze the baseline data of 1245 patients with different surgical methods.

According to the analysis of **table 4** results, there were statistically significant differences in T staging, N staging, radiotherapy and chemotherapy ( $P<0.05$ ) in baseline data of 1245 patients, with no significant differences in other variables. In the breast-conserving group, the proportion of T and N stages, radiotherapy and chemotherapy was higher: the clinical stages of breast-conserving patients were lower, the tumor burden was lower, and the treatment was more active.

## 4. Discussion

As is known to all, advanced breast cancer refers to a tumor that has metastasized to other organs of the body. Generally, it cannot be cured and has a poor prognosis. Therefore, it is the therapeutic goal to improve the overall survival and the quality of life of patients, and systemic treatment is the first choice. The intervention guideline of local surgery for breast cancer is to relieve symptoms, remove tumor rupture, bleeding, fungal infection and cancer pain without affecting the life of the patient<sup>6</sup>.

In our study, the pathology of breast cancer patients with bone metastasis was mostly LuminalA type (ER+/HER2-) (72.5%), which had good prognosis for the reason of the stable endocrine therapy and low proliferative index. According to the results of single factor analysis, primary site surgical group significantly affected the prognosis of patients (**Figure 1**) compared to the non-surgical group ( $c_2 = 146.023, P < 0.001$ ), benefitting most for 70 month (**Figure 2**) ( $c_2 = 157.117, P < 0.001$ ). For another, the expression of ER, PR, and HER2, histology of invasive ductal carcinoma, married patients, younger age, radiotherapy, and chemotherapy were all protective factors for breast cancer with bone metastasis ( $P<0.001$ ). Although the treatment of breast cancer is surgery-based comprehensive treatment, the survival benefit from primary surgery may be related to the following conditions: 1. Surgery can remove the primary tumor site, get rid of the primary tumor cell and tumor stem cells, and reduce the possibility of peripheral release and spread of circulating tumor cells<sup>24-26</sup>; 2. Primary surgery can play an important role at local control of on patients: Tumor ulcer, infection and other aspects, which improving patients' physical and psychological quality of life; 3. Primary surgery can reduce the burden of tumor and improve the curative effect of tumor chemotherapy<sup>22,27</sup>; 4. Resection of the primary tumor can reduce the immune suppression of the tumor on the body, activate CD4 and CD8 T lymphocytes, and stimulate the immune response of the body to tumor cells<sup>12,28,29</sup>

In the past related studies about advanced invasive carcinoma<sup>20-22</sup>, a phenomenon had been observed in gastric cancer, ovarian cancer, colon cancer that the reduction in tumor burden and an increase in overall survival were associated, but it was controversial that surgery did not take a survival benefit in advanced breast cancer<sup>5,16-18</sup>. However, in recent years, many retrospective studies<sup>7-15</sup> had shown that resection of the primary site of advanced breast cancer could bring survival benefits, which were most obvious in young patients with positive estrogen receptor, low tumor burden, negative human epidermal growth factor receptor, and simple bone metastasis.

Why were the conclusions of retrospective studies inconsistent with those of prospective studies? We analyzed the three prospective clinical studies. Firstly, the Translational Breast Cancer Research Consortium 013 (TBCRC-013 study) was a prospective multi-institutional registry trial which aimed to evaluate the role of surgery in stage IV breast cancer. Patients diagnosed with stage IV breast cancer at presentation (group A, n=112) or stage IV within 3 months of diagnosis (group B, n=16) were enrolled. Early results<sup>23</sup> from this study showed that surgery was associated with improved survival on multivariate analysis (HR 0.28, 95% CI 0.10–0.74, P = 0.01); In addition, 3-year overall survival results were demonstrated no difference in survival by the use of surgery among patients who responded to first-line therapy, the reason was that the patients treated with surgery were more likely to have larger tumors, the higher tumor burden<sup>16</sup>. Secondly, the prospective clinical trial was initiated at Tata Memorial Centre in India enrolling 350 patients to receive locoregional treatment (n=173) or no locoregional treatment (n=177). The result indicated the surgery could not take survival benefit because of unreasonable systemic therapy that they did not uniformly include taxanes, and most patients (92%) with HER2-positive breast cancer did not receive trastuzumab therapy; In addition, in the baseline data of the operation group, it had more of metastases number (75% vs 25%), the less of the bone metastases (29%)<sup>17</sup>. At last, the MF07-01 trial conducted by the Turkish Federation seemed to produce positive result. Although there was no difference in survival at 36 months, overall survival was improved for the surgery group at 41.6% as compared to 24.4% in the no surgery group at 5 years. (46 versus 37 months, P = 0.005). Subgroup analysis showed that the survival benefit was associated with ER positive and HER2/neu-negative disease, age under 55, and bone metastases only<sup>18</sup>.

Different primary tumor surgery methods took different survival benefit, which might be associated with baseline of patients undergoing surgery. For further analysis, we found that there was statistical significance on the baseline of the BCS group, Mastectomy group and Radicial Mastectomy group (**Table 4**) in terms of T stage, N stage, chemotherapy, radiation therapy; There were lower tumor load, T stage, N stage levels and higher proportion of chemotherapy, radiation therapy in the BCS group, which further confirmed the fact that the prognosis was better in patients with simple bone metastasis from breast cancer with a lower tumor burden. Studies<sup>7,30,31</sup> showed that there was no significant survival benefit in further expanding the scope of surgery and lymph node dissection. Axillary lymph node status was not correlated with prognosis and was not an independent factor affecting prognosis, which was consistent with the results of multi-factor analysis in our study, but surgical margin status was correlated with patient prognosis<sup>7</sup>. In addition, in the data analysis of breast cancer with bone metastasis, Her-2

overexpression was statistically significant in univariate and multivariate analyses ( $P<0.05$ ), and Her2 overexpression is a protective factor affecting breast cancer bone metastasis, which might be related to anti-Her-2 targeted therapy<sup>32,33</sup>.

Although positive results are obtained obviously, limitations of the study should be acknowledged. Firstly, we are lack of the whole information about systemic treatment, such as endocrine therapy, HER2-targeted therapy, or chemotherapy, which may lead to some bias in the survival analysis. Also, the short of data in the SEER database on events associated with bone metastasis as well as related systematic treatment<sup>34-36</sup>, has implications for the conclusions. Another potential issue is the possibility of incomplete or inaccurate claim entry as well as variability in coding practices among physicians. It is important to note that the tumor burden of patients selected for surgery is relatively low, which is also part of the surgical bias and has a certain impact on the results<sup>37</sup>.

To sum up, this study shows that primary surgery can improve the prognosis and overall survival of women with advanced breast cancer with simple bone metastasis. Under the premise of low tumor burden and comprehensive treatment, breast conserving surgery is a better choice. Although the application of primary surgery in advanced patients is controversial, the comprehensive treatment, systemic evaluation, and surgical timing, surgical mode selection of breast cancer for patients with simple bone metastasis from breast cancer need to be supported by prospective research data.

## Declarations

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### Availability of data and material

The datasets generated and analyzed in the study are available from Surveillance, Epidemiology, and End Results (SEER) Program ([www.seer.cancer.gov](http://www.seer.cancer.gov)) SEER\*Stat Database: Incidence - SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975-2016 varying) - Linked To County Attributes - Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2019, based on the November 2018 submission.

### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** For this type of study formal consent is not required.

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## Tables

**Table1** The baseline level of 2917 patients in the surgery group and the non-surgery group

variables	number	surgery (%)	non-surgery (%)	c2	P-value
Race					
white	2255	968(42.9%)	1287(57.1%)	0.567	0.753
black	462	190(41.1%)	272(58.9%)		
other	200	87(43.5%)	113(56.5%)		
Ethnic origin					
Spanish-Hispanic-Latino	289	136(47.1%)	153(52.9%)	2.513	0.113
Non-Spanish-Hispanic-Latino	2628	1109(42.2%)	1519(57.3%)		
Age					
≤35	134	67(50%)	67(50%)	21.613	<0.001
35<Age<60	1345	631(46%)	714(54%)		
≥60	1438	547(38%)	891(62%)		
Marital status					
married	1416	662(46.8%)	754(53.2%)	18.638	<0.001
unmarried	1501	583(38.8%)	918(61.2%)		
Grade					
1	287	99(34.5%)	188(65.5%)	37.276	<0.001
2	1440	560(38.9%)	880(68.1%)		
3-4	1190	586(49.2%)	604(50.8%)		
Laterality					
left	1525	656(43%)	869(57%)	0.147	0.701
right	1392	589(42.3%)	803(57.7%)		
Histology					
IDC	2351	1023(43.5%)	1328(56.5%)	3.433	0.064
non-IDC	566	222(39.2%)	344(60.8%)		
T stage					
T1	383	153(39.9%)	230(60.1%)	45.68	<0.001
T2	1158	569(49.1%)	589(50.9%)		
T3	553	242(43.8%)	311(56.2%)		

T4	823	281(34.1%)	542(65.9%)		
N stage					
N0	704	208(29.5%)	496(70.5%)	258.366	<0.001
N1	1326	463(34.9%)	863(65.1%)		
N2	406	261(64.3%)	145(35.7%)		
N3	481	313(65.1%)	168(34.9%)		
Radiation					
yes	1302	704(54.1%)	598(45.9%)	124.703	<0.001
no	1615	541(33.5%)	1074(66.5%)		
Chemotherapy					
yes	1564	803(51.3%)	761(48.7%)	103.411	<0.001
no	1353	442(32.7%)	911(67.3%)		
Subtype					
ER+/HER2-	2114	869(41.1%)	1245(58.9%)	11.671	0.009
ER+/HER2+	433	189(43.6%)	244(56.4%)		
HER2+	122	61(50%)	61(50%)		
TNBC	248	126(50.8%)	122(49.2%)		
ER					
positive	2532	1050(41.5%)	1482(58.5%)	11.512	0.001
negative	385	195(50.6%)	190(49.4%)		
PR					
positive	2121	886(41.8%)	1235(58.2%)	2.62	0.106
negative	796	359(45.1%)	437(54.9%)		
HER2					
positive	555	250(45%)	305(55%)	1.566	0.211
negative	2362	995(42.1%)	1367(57.9%)		

-ER, Estrogen receptor; Progesterone receptor;Her-2, Human epidermal growth factor receptor 2;IDC,infiltrating ductal carcinoma;TNBC, Triple-Negative Breast Cancer

**Table2 Single factor analysis of clinical pathology and prognosis of 2917 breast cancer patients with bone metastasis**

variables	number	median survival time (month)	95% confidence interval (CI)	c2	P-value
race					
white	2255	44	41.617-46.383	35.071	<0.001
black	462	31	27.607-34.393		
other	200	43	31.973-54.027		
grade					
1	287	46	37.721-54.279		
2	1440	46	42.998-49.002	45.128	<0.001
3-4	1190	34	31.198-37.002		
Marital					
married	1416	48	44.517-51.483	45.771	<0.001
unmarried	1501	36	33.209-38.791		
Age					
≤35	134	56	38.548-73.452		
35<Age<60	1345	46	42.387-49.613	70.468	<0.001
≥60	1438	36	33.066-38.934		
Ethnic origin					
Spanish-Hispanic-Latino	289	47	41.597-52.403	2.103	0.147
Non-Spanish-Hispanic-Latino	2628	41	38.983-43.017		
Laterality					
left	1525	42	39.446-44.554	0.017	0.896
right	1392	42	39.085-44.915		
Histology					
IDC	2351	44	41.537-46.463	25.295	<0.001
non-IDC	566	36	32.245-39.755		
T stage					
T1	383	47	38.824-55.176		
T2	1158	47	42.855-51.145	53.468	<0.001

T3	553	40	35.692-44.308		
T4	823	34	30.984-37.016		
N stage					
N0	704	39	34.668-43.332		
N1	1326	43	39.941-46.059	5.582	0.134
N2	406	43	37.639-48.361		
N3	481	42	38.004-45.996		
Radiation					
yes	1302	46	42.593-49.407	14.906	<0.001
no	1615	39	36.512-41.488		
Chemotherapy					
yes	1564	48	44.242-51.758	64.579	<0.001
no	1353	36	33.254-38.746		
subtype					
ER+/HER2-	2114	43	41.030-44.970		
ER+/HER2+	433	57	48.725-65.275	242.199	<0.001
HER2+	122	73	0		
TNBC	248	13	11.349-14.651		
ER					
positive	2532	44	42.077-45.923	91.338	<0.001
negative	385	18	14.319-21.681		
PR					
positive	2121	46	43.765-48.235	97.923	<0.001
negative	796	27	23.973-30.027		
HER2					
positive	555	58	46.618-69.382	30.843	<0.001
negative	2362	40	37.931-42.069		

Primary surgery						
operation	1245	56	51.508-60.492	146.023	<0.001	
non-operation	1672	33	30.830-35.170			
surgical mode						
non-operation	1672	33	30.830-35.170			
BCS	381	70	0	157.117	<0.001	
Mastectomy	255	59	45.751-72.249			
Radical mastectomy	609	48	43.369-52.631			

-ER, Estrogen receptor; Progesterone receptor;Her-2, Human epidermal growth factor receptor 2;IDC,infiltrating ductal carcinoma;BCS, Breast Conservion Surgery; TNBC,Triple-Negative Breast Cancer

**TABLE3 Clinical pathology and prognosis of 2917 cases of breast cancer with bone metastases by multivariate analysis**

variables	Regression coefficient	Standard error	P-value	HR	95%CI
Marital					
married	reference				
unmarried	0.193	0.056	0.001	1.213	1.087-1.354
Age					
≤35	reference				
35<Age<60	-0.07	0.147	0.635	0.933	0.700-1.243
≥60	0.258	0.147	0.08	1.294	0.970-1.727
race					
white	reference				
black	0.267	0.071	<0.001	1.306	1.135-1.502
other	0.001	0.113	0.995	1.001	0.802-1.248
Histology					
IDC	reference				
non-IDC	0.331	0.065	<0.001	1.392	1.225-1.583
Primary surgery					
non-operation	reference				
operation	-0.644	0.059	<0.001	0.525	0.467-0.590
Chemotherapy					
yes	reference				
no	0.383	0.061	<0.001	1.467	1.302-1.653
T stage					
T1	reference				
T2	0.116	0.091	0.2	1.123	0.940-1.341
T3	0.247	0.099	0.013	1.28	1.054-1.555
T4	0.321	0.093	0.001	1.379	1.149-1.654
Radiation					
yes	reference				
no	-0.011	0.055	0.849	0.99	0.888-1.103

grade						
1	reference					
2	0.234	0.1	0.02	1.263	1.038-1.538	
3-4	0.583	0.105	<0.001	1.791	1.459-2.199	
HER2						
positive	reference					
negetive	0.571	0.082	<0.001	1.771	1.508-2.079	
ER						
positive	reference					
negetive	0.589	0.095	<0.001	1.802	1.496-2.170	
PR						
positive	reference					
negetive	0.442	0.073	<0.001	1.556	1.348-1.797	
subtype						
ER+/HER2-	reference					
ER+/HER2+	-0.243	0.091	0.007	0.785	0.657-0.937	
HER2+	-2.024	0.353	<0.001	0.132	0.066-0.264	
TNBC	-0.547	0.322	0.089	0.579	0.308-1.088	
surgical mode						
non-operation	reference					
BCS	-0.93	0.099	<0.001	0.394	0.325-0.478	
Mastectomy	-0.702	0.108	<0.001	0.496	0.401-0.613	
Radical mastectomy	-0.488	0.071	<0.001	0.614	0.534-0.706	

-ER, Estrogen receptor; Progesterone receptor;Her-2, Human epidermal growth factor receptor  
2;IDC,infiltrating ductal carcinoma;BCS, Breast Conservion Surgery; TNBC,Triple-Negative Breast Cancer

**Table4 Baseline data analysis of 1245 patients with different surgical mode**

variables	BCS (%)	Mastectomy (%)	Radical Mastectomy (%)	c2	P-value
race					
white	297(78.0%)	204(80.0%)	467(76.7%)		
black	57(15.0%)	38(14.9%)	95(15.6%)	2.12	0.714
other	27(7.0%)	13(5.1%)	47(7.7%)		
Age					
≤35	13(3.4%)	16(6.3%)	38(6.2%)		
35<Age<60	181 47.5%	132(51.8%)	318(52.2%)	8.373	0.079
≥60	187 49.1%	107(42.0%)	253(41.5%)		
grade					
1	34(8.9%)	20(7.8%)	45(7.4%)	6.528	0.163
2	173 45.4%	129(50.6%)	258(42.4%)		
3-4	174 45.7%	106(41.6%)	306(50.2%)		
Laterality					
left	209(54.9%)	130(51.0%)	317(52.1%)	1.115	0.573
right	172(45.1%)	125(49.0%)	292(48.0%)		
Marital					
married	206(54.1%)	138(54.1%)	318(52.2%)		
unmarried	175(45.9%)	117(45.9%)	291(47.8%)	0.438	0.803
Ethnic origin					
Spanish-Hispanic-Latino	43(11.3%)	23(9.0%)	70(11.5%)	1.205	0.547
Non-Spanish-Hispanic-Latino	338(88.7%)	232(91.0%)	539(88.5%)		
Histology					
IDC	326(85.6%)	201(80.0%)	49(77.0%)	5.163	0.076
non-IDC	55(14.4%)	54(20.0%)	113(33.0%)		
T stage					

T1	91(23.9%)	21(8.2%)	41(6.7%)	158,845	<0.001
T2	22(58.3%)	109(42.7%)	238(39.10%)		
T3	37(9.7%)	59(23.1%)	146(24%)		
T4	31(8.1%)	66(25.9%)	184(30.20%)		
N stage					
N0	126(33.1%)	52(20.4%)	30(4.9%)		
N1	133(34.9%)	124(48.6%)	206(33.80%)	192.317	<0.001
N2	67(17.6%)	41(16.10%)	153(25.10%)		
N3	55(14.4%)	38(14.90%)	220(36.10%)		
Radiation					
yes	22(60.1%)	124(48.6%)	351(57.60%)		
no	15(39.9%)	131(51.40%)	258(42.40%)	8.765	0.012
Chemotherapy					
yes	20(54.9%)	171(69.50%)	423(67.10%)		
no	17(45.1%)	84(30.50%)	186(32.90%)	22.744	<0.001
subtype					
ER+/HER2-	276(72.4%)	177(69.4%)	416(68.3%)		
ER+/HER2+	54(14.2%)	34(13.3%)	101(16.6%)	6.514	0.368
HER2+	15(3.9%)	11(4.3%)	35(5.7%)		
TNBC	36(9.4%)	33(12.9%)	57(9.4%)		
ER					
positive	329(86.4%)	207(81.2%)	514(84.4%)	3.101	0.212
negative	52(13.6%)	48(18.8%)	95(15.6%)		
PR					
positive	281(73.8%)	176(69.0%)	429(70.4%)	1.97	0.373
negative	100(26.2%)	79(31.0%)	180(29.6%)		
HER2					
positive	69(18.1%)	45(17.6%)	136(22.3%)	3.786	0.151

negetive

312(81.9%)

210(82.4%)

473(77.7%)

-ER, Estrogen receptor; Progesterone receptor; Her-2, Human epidermal growth factor receptor 2; IDC, infiltrating ductal carcinoma; BCS, Breast Conservion Surgery; TNBC, Triple-Negative Breast Cancer

## Figures

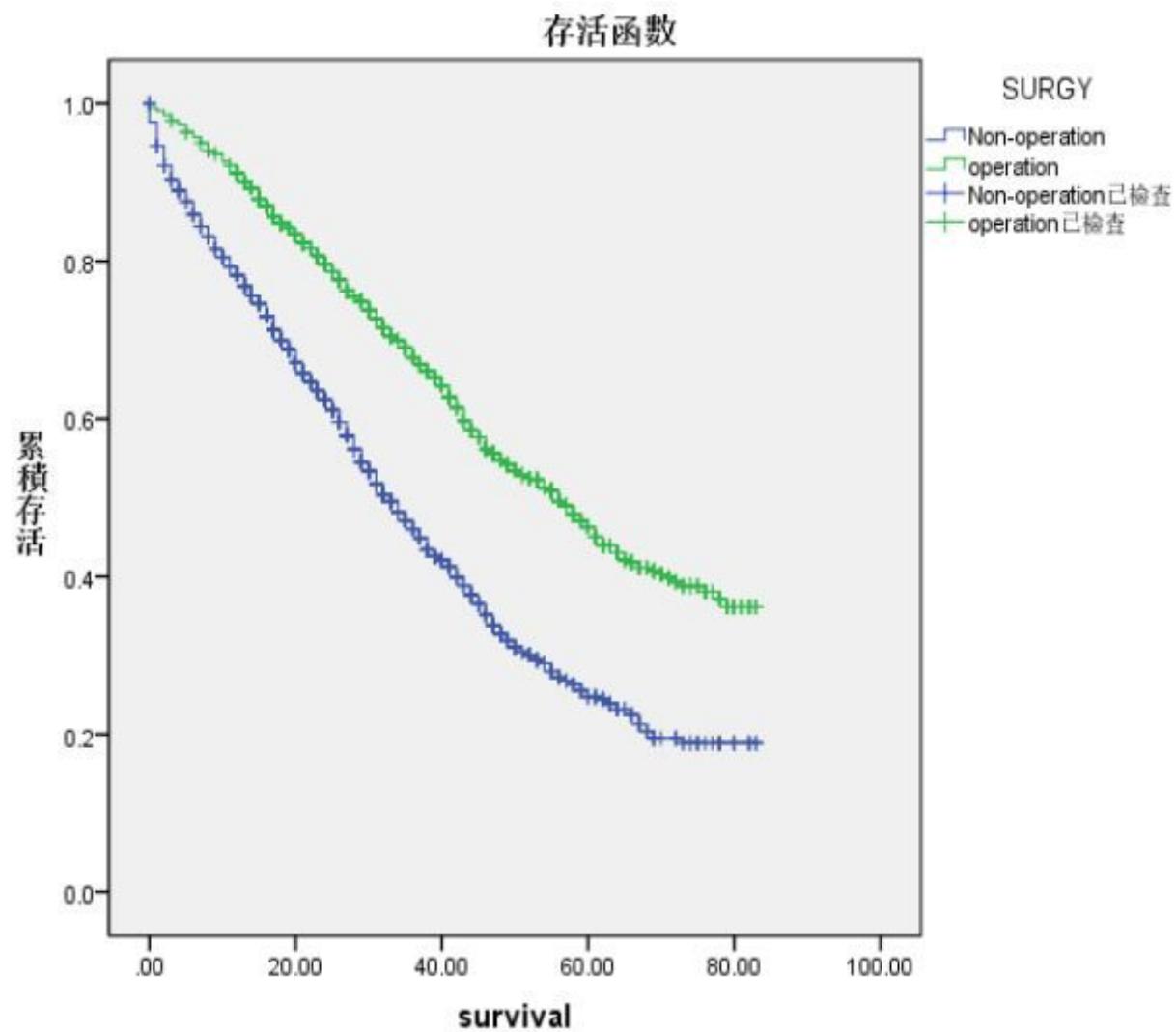


Figure 1

Surgical and nonsurgical effects on survival

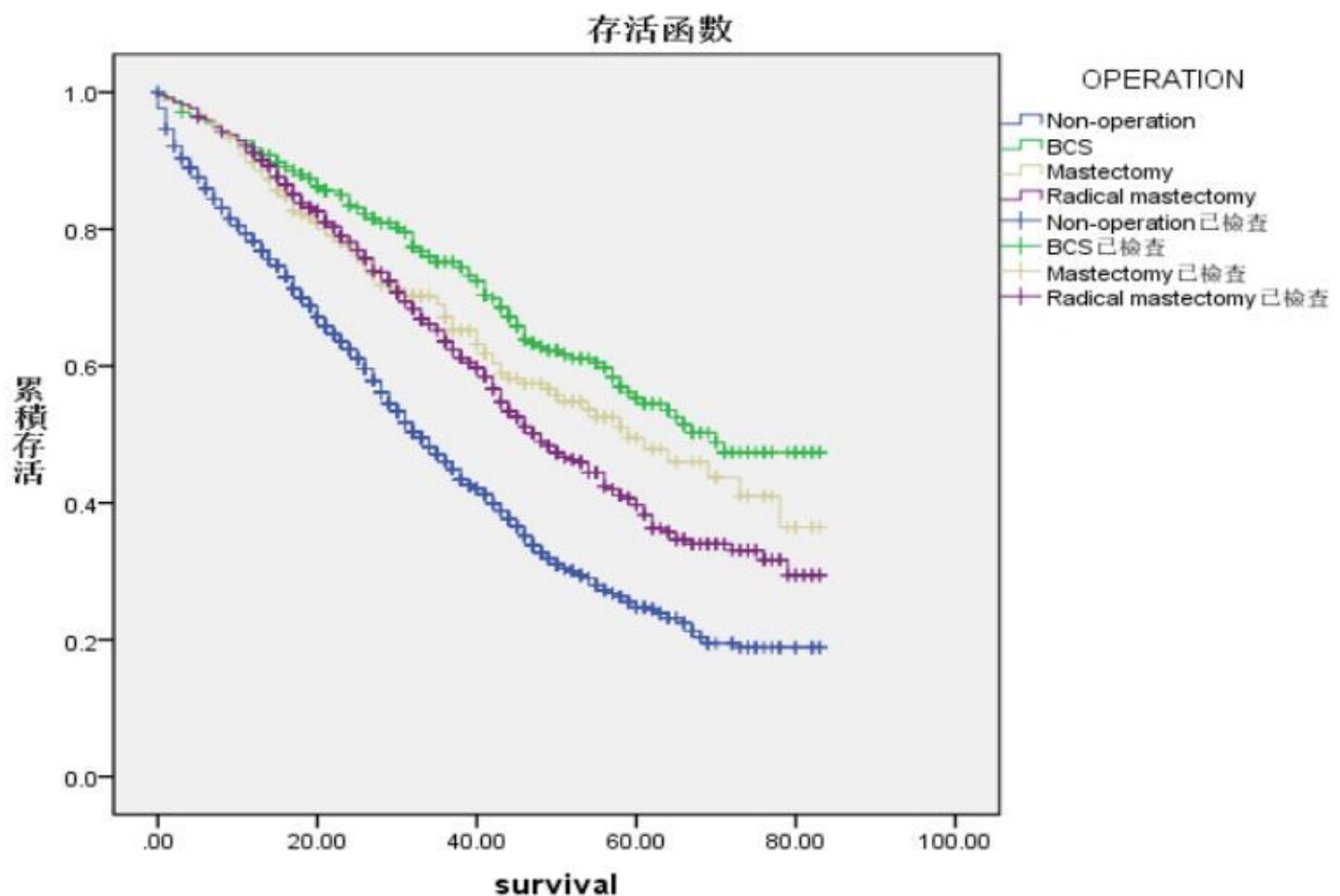


Figure 2

Effect of different surgical modes on survival