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Comparison of breast-conserving surgery and mastectomy in early breast cancer using observational data revisited: a propensity score-matched analysis

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Recent observational studies showed that breast-conserving surgery (BCS) resulted in superior survival compared to mastectomy in breast cancer patients. This study compared the clinical outcomes of BCS and mastectomy using propensity score (PS) matching analysis, which had advantages over conventional methods in reducing bias. Nonmetastatic breast cancer patients who underwent BCS and mastectomy were matched 1:1 based on their PS. We used the Kaplan-Meier method and Cox-regression model to estimate the treatment effects. A total of 2,866 patients with a median follow-up time of 67 months were included in the original study population. Although the mastectomy cohort (N=1,219) had more advanced disease compared to the BCS cohort (N=1,647), LRFS was similar between the two groups (93.8% vs. 92.4%, P>0.05). BCS (vs. mastectomy) was associated with improved DFS (73.8% vs. 58.7%, P<0.01) and CSS (91% vs. 78.2%, P<0.01) in the original population. In the PS-matched population (N=1,668), clinicopathological features were equally distributed between the two cohorts. BCS (vs. mastectomy) was not associated with improved DFS (70.7% vs. 66.9%, P>0.05) or CSS (87.5% vs. 84.9%, P>0.05). We found that PS methods reduce bias when estimating treatment effects using observational data. BCS and mastectomy show equivalent outcomes in nonmetastatic breast cancer patients.

breast-conserving surgery, mastectomy, breast cancer, propensity score, survival

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INTRODUCTION

From the Halstedian era until the end of the last century, mastectomy was considered the standard surgical treatment for breast cancer. However, the strategy for surgical treatment has since changed from a "maximum-tolerated approach" to a "minimum-effective approach". In 2002, long-term follow-up data from the NASBP B-06 (Fisher et al., 2002) and Milan (Veronesi et al., 2002) trials was published, demonstrating the oncological safety of BCS in early-stage breast cancer patients. This was further confirmed in other prospective randomized trials (Black et al., 2013; van Tien-

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hoven et al., 1999). Today, BCS is the preferred surgical therapy for early-stage breast cancer patients and recommended by the NCCN and ESMO clinical guidelines.

However, these previous prospective randomized trials were started in between 1970 and 1980, when the adjuvant systemic therapies following surgery were incomparable to those in use today. In addition, these randomized trials enrolled highly selected patients. Therefore, whether BCS is still oncologically safe in a real-world scenario remains unclear. In the past decade, several studies comparing the effectiveness of mastectomy versus BCS using large-scale data from the national cancer registry showed that BCS had superior survival compared to mastectomy, even after adjusting for known clinicopathological features. Since all of these retrospective studies used observational data, selection bias certainly existed. For example, patients with advanced disease were more likely to receive a mastectomy than BCS. Thus, the estimation of treatment effects could be compromised.

Propensity score (PS) matching analysis is widely used to reduce bias in the estimation of treatment effects in observational datasets. Based on the patients' clinicopathological features, the PS was developed to indicate the probability of a patient receiving the treatment of interest (e.g., BCS). For example, patients with less advanced disease and who were younger were more likely to receive BCS than mastectomy, thus these patients have a higher PS for BCS. In this scenario, the estimation of the treatment effects of BCS versus mastectomy in patients with a similar PS would be more appropriate and accurate. To our knowledge, recent studies that compared the survival of patients who underwent BCS versus mastectomy did not use PS matching to reduce the selection bias. In this study, we compared the clinical outcomes of breast cancer patients who underwent a mastectomy or BCS at our institution using PS matching analysis.

RESULTS

Baseline characteristics

A total of 2,866 patients were included in the original study population (Table 1). Of these, 1,647 (57.5%) and 1,219 (42.5%) patients received BCS and mastectomy, respectively. Compared to the BCS cohort, the mastectomy cohort was more likely to be older (P<0.001), to have a larger tumor (P<0.001), to have node-positive disease (P<0.001) and to have received more chemotherapy (P<0.001). The ER status, HER2 status and tumor grade were also significantly different between the two cohorts. The median follow-up time was 67 months, and the 5-year and 10-year cumulative LRFS, DFS and CSS are summarized in Table 2. The BCS and mastectomy cohorts had similar LRFS (Figure 1A), regardless of the lymph node status. The BCS cohort had significantly improved DFS (P<0.01, Figure 1B) and CSS (P<0.01, Figure 1C) compared to the mastectomy cohort according to univariate analysis (log-rank test, Table 2). The DFS and CSS advantage of BCS over mastectomy was more apparent in LN-positive patients, than in LN-negative patients (Figure 1B and C). When we controlled for confounding factors, BCS maintained improved DFS (HR=0.72, 95%CI 0.60–0.88) and CSS (HR=0.63, 95%CI 0.47–0.84) compared to mastectomy in the original study population (Table 3).

PS matching analysis

The logistic regression model was used to develop a propensity score (PS, 0–1) for each patient. The full PS model is shown in Table S1 in Supporting Information. The area under the curve (AUC) value of the PS model was 0.763. Patients with a higher PS were more likely to receive BCS than mastectomy. The distributions of the PS in patients receiving the two different surgeries are shown in Figure 2A. We matched a total of 1,668 patients who received BCS with those who received mastectomy based on their PS (Table 1). The 5-year and 10-year LRFS, DFS and CSS were similar between the original and PS-matched populations (Table 2, Figure S1 in Supporting Information). In the matched population, we noticed that the T-stage, N-stage, histology, ER status, PR status, HER2 status, tumor grade, patient age and chemotherapy characteristics were equally distributed between the BCS and mastectomy cohorts, suggesting that tumor burden and the propensity to receive BCS or mastectomy were similar between the two cohorts. Absolute standard differences were all less than 0.1 in the PS-matched population, suggesting that the clinicopathological features between the two cohorts were well-balanced (Figure 2B). In the PS-matched population, BCS was not associated with improved LRFS (Figure 1D), DFS (Figure 1E) or CSS (Figure 1F) compared to mastectomy (Table 2), regardless of the lymph node status. The differences of DFS and CSS between the BCS and mastectomy patients were significantly lower in the matched population, than in the original population (Figure S1 in Supporting Information).

DISCUSSION

Prospective, multicenter, randomized clinical trials that demonstrated the efficacy of BCS were initiated between 1970 and 1980 when systemic adjuvant therapies and local radiotherapy were incomparable to those in use today. More recently, observational real-world studies (Agarwal et al., 2014; Chen et al., 2015; Hartmann-Johnsen et al., 2015; Hwang et al., 2013; van Maaren et al., 2016) using data from

Table 1 Baseline characteristics of the study population[a)]

	Original population					PS-matched population				
	BCS		Mastectomy		*P*	BCS		Mastectomy		*P*
	n	%	*n*	%		*n*	%	*n*	%	
T-stage										
T1	937	56.89	468	38.39		384	46.0	392	47.0	
T2	386	23.44	432	35.44		282	33.8	268	32.1	
T3–4	17	1.03	91	7.47	<0.001	17	2.0	17	2.0	NS
Tis	139	8.44	90	7.38		77	9.2	74	8.9	
Tx	168	10.20	138	11.32		74	8.9	83	10.0	
N-stage										
N0	1,150	69.82	555	45.53		447	53.6	478	57.3	
N1	334	20.28	288	23.63		229	27.5	208	24.9	
N2	88	5.34	138	11.32	<0.001	83	10.0	82	9.8	NS
N3	36	2.19	130	10.66		36	4.3	30	3.6	
Nx	39	2.37	108	8.86		39	4.7	36	4.3	
Histology										
IDC	1,307	79.36	967	79.33		640	76.7	653	78.3	
DCIS	111	6.74	85	6.97	NS	65	7.8	62	7.4	NS
Others	229	13.90	167	13.70		129	15.5	119	14.3	
Estrogen receptor										
Negative	276	16.76	231	18.95		112	13.4	122	14.6	
Positive	1,312	79.66	896	73.50	<0.001	669	80.2	665	79.7	NS
Unknown	59	3.58	92	7.55		53	6.4	47	5.6	
Progesterone receptor										
Negative	276	16.76	74	6.07		48	5.8	67	8.0	
Positive	1,215	73.77	815	66.86	<0.001	644	77.2	621	74.5	NS
Unknown	156	9.47	330	27.07		142	17.0	146	17.5	
Her2										
Negative	1,138	69.10	741	60.79		526	63.1	540	64.7	
Positive	304	18.46	279	22.89	<0.001	177	21.2	177	21.2	NS
Unknown	205	12.45	199	16.32		131	15.7	117	14.0	
Tumor grade										
Before 2010	546	33.15	468	38.39		326	39.1	306	36.7	
After 2010, Grade I	96	5.83	26	2.13		16	1.9	26	3.1	
After 2010, Grade II	348	21.13	169	13.86	<0.001	123	14.7	140	16.8	NS
After 2010, Grade III	327	19.85	206	16.90		150	18.0	153	18.3	
After 2010, Unknown	330	20.04	350	28.71		219	26.3	209	25.1	
Age										
<50 years	1,015	61.63	635	52.09	<0.001	449	53.8	484	58.0	NS
≥50 years	632	38.37	584	47.91		385	46.2	350	42.0	
Chemotherapy										
No	208	12.63	108	8.86		86	10.3	89	10.7	
Adjuvant Chemotherapy	1,192	72.37	812	66.61	<0.001	574	68.8	585	70.1	NS
Neoadjuvant Chemotherapy	186	11.29	243	19.93		137	16.4	124	14.9	
Unknown	61	3.70	56	4.59		37	4.4	36	4.3	
Radiotherapy										
No	152	9.23	565	46.35		97	11.6	460	55.2	
Yes	1,297	78.75	584	47.91	<0.001	652	78.2	346	41.5	<0.001*
Unknown	198	12.02	70	5.74		85	10.2	28	3.4	

a) ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; IDC, invasive ductal carcinoma; DCIS, ductal carcinoma *in situ*; BCS, breast conserving surgery; NAC, neo-adjuvant chemotherapy; NS, non-significant; *, Radiotherapy was not included in the PSM model, because radiotherapy was not a determinant of the surgical choice. In contrast, the surgical choice is a major determinant of the use of radiotherapy.

Table 2 Summary of LRFS, DFS and CSS in the study population[a)]

		Overall population (%)		Stratified by surgery (%)			P^*
		5-year	10-year		5-year	10-year	
Original population	LRFS	95.8	93.3	BCS	96	93.8	NS
				Mastectomy	95.6	92.4	
	DFS	86.8	67.1	BCS	91	73.8	<0.01
				Mastectomy	81.2	58.7	
	CSS	92.1	85.4	BCS	95.7	91	<0.01
				Mastectomy	87.1	78.2	
PS-matched population	LRFS	95.6	93.0	BCS	95.4	92.9	NS
				Mastectomy	95.9	93.2	
	DFS	87.9	68.8	BCS	88.8	70.7	NS
				Mastectomy	87	66.9	
	CSS	92.8	86.2	BCS	93.7	87.5	NS
				Mastectomy	91.8	84.9	

a) *, Log-rank test. LRFS, local recurrence free survival; DFS, disease free survival; CSS, cancer-specific survival. NS, non-significant.

the national cancer registry showed that BCS was superior to mastectomy in terms of cancer-specific survival/overall survival. However, these retrospective studies were biased by "treatment by indications". For example, patients with more advanced disease were more likely to receive a mastectomy, which has been associated with inferior survival. Therefore, PS matching was proposed to reduce the "treatment by indications" bias (Haukoos and Lewis, 2015).

In our study, we noticed that patients with higher tumor burden, such as larger tumor size and hormone receptor negative diseases, tended to receive mastectomy. BCS was significantly associated with improved DFS and CSS in the original population compared to mastectomy, even after adjusting for confounding factors. Interestingly, in the PS-matched population where clinicopathological features were equally distributed between the BCS and mastectomy cohorts, BCS failed to show any advantage in DFS and CSS compared to mastectomy. We believe that estimation of the treatment effects in the PS-matched population is more reliable. The variables were well-balanced between the two treatment cohorts; therefore, PS matching is similar to performing a pseudo-randomization, in which patients are pseudorandomized to different treatment cohorts. Thus, comparing the treatment effects would be more reasonable in this situation. Recent studies (Abdulkarim et al., 2011; Agarwal et al., 2014; Hartmann-Johnsen et al., 2015; Hwang et al., 2013; Onitilo et al., 2014; van Maaren et al., 2016) that compared the survival of patients who underwent BCS and mastectomy using the national cancer registry data did not use the PS matching method, which might explain why these studies observed superior survival for BCS compared to mastectomy.

Although PS matching failed to demonstrate an advantage of BCS versus mastectomy with respect to DFS and CSS, caution should be exercised when interpreting these results, as the treatment effects estimated in the matched population may differ from the effects in the original population. Thus, additional statistical analyses are needed. In addition to PS matching analysis, there are other ways to use the PS in the original population without sacrificing the patients who cannot be matched into the PS-matched population. We used PS covariate adjustment, inverse probability weighting (IPW) with PS, and PS stratification analysis in the original population and obtained results similar to the original analysis without PS, namely, that BCS is associated with improved DFS and CSS compared to mastectomy (Supplementary File 1 and Figure S2 in Supporting Information). Thus, the appropriate application of PS matching remains unclear. Elze et al. (Elze et al., 2017) compared the four PS methods with a traditional regression model using four large-scale cardiovascular observational studies. Their study showed that the four PS methods were unlikely to produce significantly different results than those obtained by the traditional regression model. However, their study also revealed that the absolute standardized differences in the variables were lower using the PS-matching methods, suggesting a potential advantage of PS-matching analysis over others.

Whether less surgery is associated with improved clinical outcomes is an interesting question. Tata reported a randomized trial (Badwe et al., 2015) that compared locoregional versus no treatment of the primary tumor in metastatic breast cancer patients. The investigators observed that locoregional treatment significantly decreased the distant metastatic free survival. Thus, it is possible that, in some cases, less extensive surgery might lead to better clinical outcomes. Evidence from colon cancer research also supports this theory. For example, Lacy et al. (Lacy et al., 2002) reported a ran-

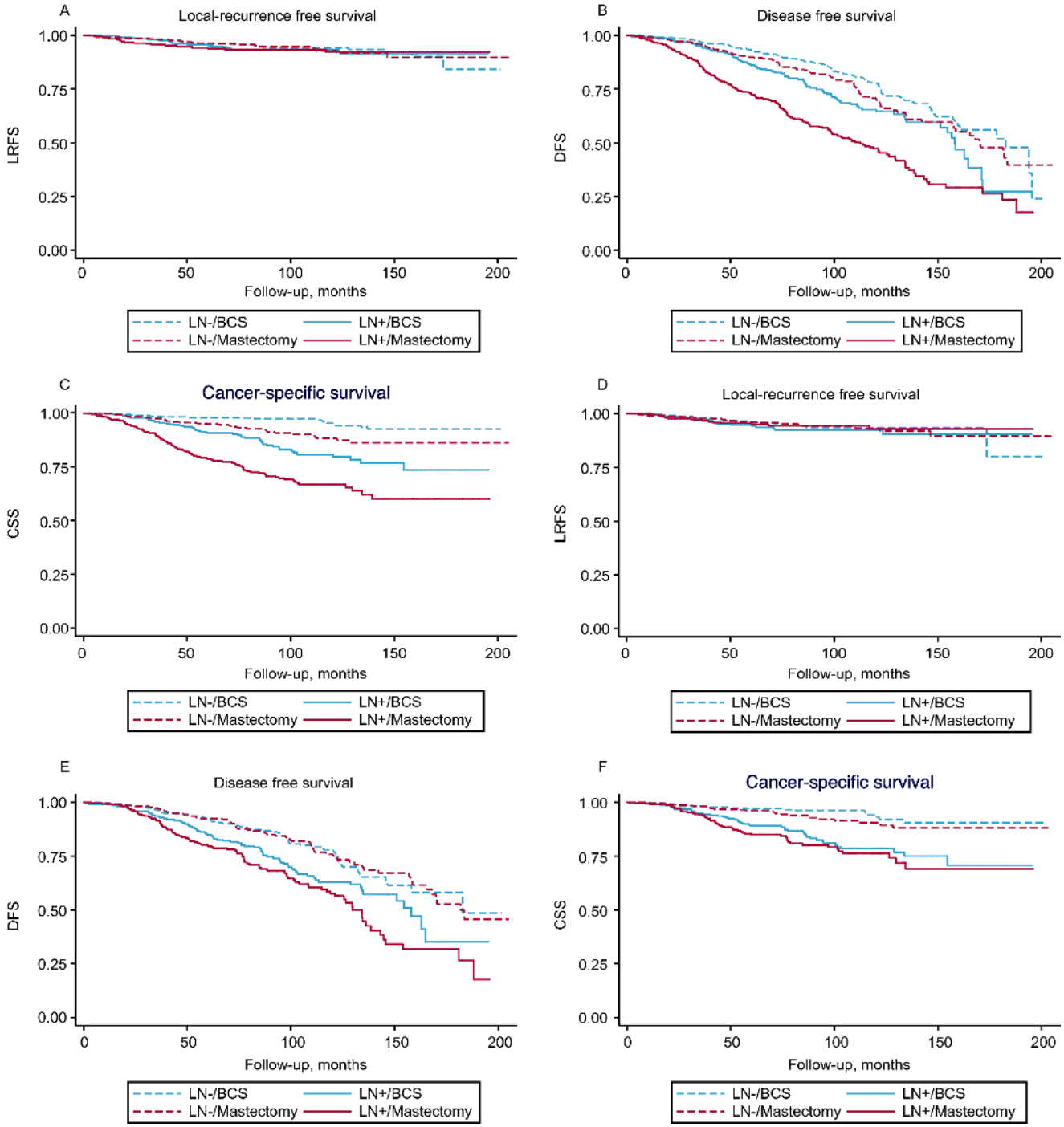

Figure 1 Comparison of the clinical outcomes of different surgical treatments stratified by lymph node status. A, Local-recurrence free survival in original population. B, Cancer-specific survival in original population. C, Disease-free survival in original population. D, Local-recurrence free survival in PS-matched population. E, Cancer-specific survival in PS-matched population. F, Disease-free survival in PS-matched population. PS, propensity score.

domized clinical trial involving colon cancer patients and showed that laparoscopy-assisted colectomy had superior cancer-specific survival compared to open colectomy. Possible biological explanations for this observation were described in a recent study by Krall et al. (Krall et al., 2018) in which a model system was used to show a link between surgery and the subsequent wound-healing response and outgrowth of tumor cells at distant anatomical sites. This study also showed that tumor cells can be restricted by a tumor-specific T cell response and that this T cell response can be disrupted by the inflammatory response after surgery. Hence, the investigators suggested that peri-operative anti-inflammatory treatment should be considered in breast cancer patients.

Table 3 Univariate and multivariate analysis of risk factors for DFS and CSS in the original population[a)]

Variables	DFS				CSS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*
T-stage								
T1	1		1		1		1	
T2	1.75(1.47–2.09)	<0.001	1.36(1.13–1.63)	0.001	2.22(1.69–2.92)	<0.001	1.55(1.17–2.05)	0.003
T3–4	2.53(1.82–3.51)	<0.001	1.26(0.89–1.79)	0.191	5.14(3.43–7.70)	<0.001	1.83(1.17–2.85)	0.008
Tis	0.97(0.67–1.40)	0.86	1.21(0.74–1.96)	0.449	0.52(0.24–1.12)	0.093	1.02(0.42–2.47)	0.974
Tx	1.83(1.43–2.33)	<0.001	1.24(0.95–1.63)	0.117	2.02(1.38–2.95)	<0.001	1.10(0.73-1.68)	0.643
N-stage								
N0	1		1		1		1	
N1	1.64(1.35–1.99)	<0.001	1.49(1.19–1.85)	<0.001	2.83(2.06–3.89)	<0.001	2.63(1.81–3.81)	<0.001
N2	2.29(1.78–2.93)	<0.001	1.86(1.40–2.47)	<0.001	4.64(3.20–6.71)	<0.001	3.57(2.28–5.58)	<0.001
N3	5.71(4.53–7.19)	<0.001	3.90(2.94–5.16)	<0.001	14.44(10.48–19.89)	<0.001	8.92(5.86–13.56)	<0.001
Nx	1.74(1.25–2.44)	0.001	1.33(0.91–1.92)	0.136	1.76(0.93–3.31)	0.081	1.16(0.59–2.30)	0.667
Grade								
After 2010/Grade I–II	1		1		1		1	
After 2010/Grade III	1.66(1.24–2.22)	<0.001	1.35(1.01–1.82)	0.045	2.26(1.39–3.66)	<0.001	1.60(0.98–2.63)	0.061
After 2010/Unknown	1.50(1.13–1.97)	0.004	1.30(0.96–1.75)	0.095	2.04(1.28–3.25)	0.003	1.61(0.98–2.64)	0.059
Before 2010	0.62(0.47–0.82)	<0.001	0.54(0.40–0.72)	<0.001	1.91(1.24–2.94)	0.003	1.40(0.90-2.19)	0.138
Histology								
IDC	1		1		1		1	
DCIS	0.65(0.43–0.97)	0.036	0.66(0.38–1.13)	0.131	0.10(0.03–0.42)	0.001	0.19(0.04–0.86)	0.031
Others	0.80(0.64–1.00)	0.046	0.82(0.64–1.05)	0.122	0.76(0.53–1.08)	0.123	0.85(0.57–1.25)	0.401
Estrogen Receptor								
Negative	1		1		1		1	
Positive	0.75(0.62–0.89)	0.001	0.73(0.60–0.87)	<0.001	0.56(0.43–0.72)	<0.001	0.56(0.43–0.74)	<0.001
Unknown	0.77(0.53–1.12)	0.175	0.64(0.44–0.95)	0.026	0.79(0.47–1.33)	0.368	0.67(0.37–1.22)	0.187
Progesterone Receptor								
Negative	1				1		Not included	
Positive	0.95(0.75–1.21)	0.682	Not included		0.83(0.58–1.19)	0.312		
Unknown	1.35(1.02–1.78)	0.036			1.54(1.03–2.31)	0.036		
HER2								
Negative	1				1		1	
Positive	1.18(0.97–1.43)	0.09	Not included		1.40(1.05–1.85)	0.02	1.02(0.76–1.37)	0.9
Unknown	1.00(0.80–1.25)	0.988			1.24(0.90–1.72)	0.191	1.00(0.70–1.45)	0.982
Age								
<50yrs	1		1		1		Not included	
>=50yrs	1.25(1.07–1.46)	0.005	1.21(1.03–1.42)	0.018	1.05(0.83–1.32)	0.708		
Chemotherapy								
No	1		1		1		1	
Adjuvant chemotherapy	1.22(0.88–1.68)	0.232	1.02(0.72–1.44)	0.897	3.13(1.47–6.67)	0.003	1.42(0.65–3.10)	0.379
Neoadjuvant chemotherapy	2.87(2.04–4.04)	<0.001	1.83(1.25–2.68)	0.002	11.00(5.12–23.63)	<0.001	3.29(1.47–7.40)	0.004
Unknown	2.26(1.32–3.86)	0.003	1.86(1.07–3.24)	0.028	3.26(1.10–9.72)	0.034	2.46(0.80–7.54)	0.115
Radiotherapy								
No	1		1		1		1	
Yes	1.27(1.05–1.52)	0.013	0.98(0.77–1.23)	0.845	1.65(1.21–2.24)	0.001	0.81(0.55–1.18)	0.267
Unknown	1.04(0.77–1.40)	0.802	1.31(0.95–1.81)	0.101	1.22(0.75–2.00)	0.42	1.82(1.06–3.12)	0.031
Surgery								
Mastectomy	1		1		1		1	
Breast-conserving surgery	0.55(0.48–0.65)	<0.001	0.72(0.60–0.88)	<0.001	0.35(0.27–0.45)	<0.001	0.63(0.47–0.84)	0.002

a) HR, hazard ratio; CI, confidence interval; IDC, infiltrating duct carcinoma; DCIS, ductal carcinoma *in situ*. DFS, disease-free survival; CSS, cancer-specific survival; HER2, human epidermal growth receptor 2.

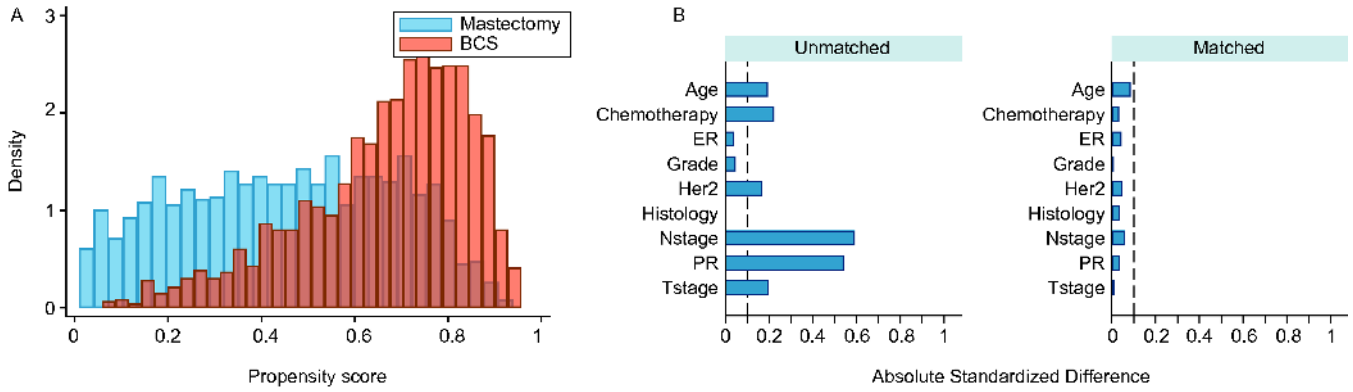

Figure 2 Propensity score matching analysis of patients with mastectomy and breast-conserving surgery. A, Distribution of the PS in patients who underwent breast-conserving surgery or mastectomy in the PS-matched population. B, Absolute standardized differences of variables in the original and PS-matched populations. PS, propensity score.

Pathological examination of lumpectomy margins is mandatory for BCS. 18%–40% of breast cancer patients have positive margins after BCS and require a second surgery (Morrow et al., 2012; Tang et al., 2017). In our institution, we assessed the cavity margin status but not the lumpectomy margin status. We used frozen section analysis intraoperatively and formalin-fixed, paraffin-embedded tissue postoperatively to assess cavity margins. Our previous studies (Chen et al., 2012; Yang et al., 2012) showed that this strategy leads to satisfactory local control and a very low second surgery rate (3.5%). These results were confirmed in our current study as patients who underwent BCS had similar LRFS compared to mastectomy patients. The joint analysis of two large-scale randomized trials, EORTC 10801 and DBCG-82TM (van Tienhoven et al., 1999), showed similar locoregional recurrence rates between BCS and mastectomy at 5 years (5%–7%) and 10 years (8%–9%) posttreatment. A more recent retrospective study with breast cancer patients diagnosed from 1999 to 2008 also confirmed that BCS and mastectomy had similar local control rates after a median follow-up time of 78.3 months. Thus, we suggest that BCS with intraoperative assessment of cavity margins is safe and effective.

Several limitations exist in our study. First, some information was lacking and limited our ability to control for confounding factors during the analysis. For example, Ki67, the response to chemotherapy, and the use of trastuzumab and endocrine therapy were not available in our study. In our institution, the current ratio of endocrine therapy for HR-positive breast cancer patients (diagnosed between 2017 and 2018) is 94.8%. However, the actual number of the patients with full adherence to their planned endocrine therapy (completion of 5 years of endocrine therapy) is not clear. Gao et al. (Gao et al., 2018) reported that the adherence (to endocrine therapy) rate was only 63.1% in Chinese population. Sociodemographic characteristics of patients, clinical- and medication-related characteristics and patients' attitudes were associated with the adherence to endocrine therapy. Second, the quality of the PS estimation was determined by the variables that were incorporated in the logistic regression model. Many factors that influence the choice of surgical treatment were not included in this study, such as the presence of extensive microcalcification or spiculate lesions in the mammogram, multifocal/multicenter disease, and patients' willing to pursue postmastectomy breast reconstruction. Therefore, we should be aware of these limitations. Additionally, the pre-operative patient consultation about the cost and side effects of adjuvant radiotherapy after BCS may also affect the surgical decision. However, we cannot include the radiotherapy in the PS model, otherwise, the proportion of patients who received radiotherapy between BCS and mastectomy in the matched population would be similar, which is not in accordance with the real-world scenario. In an ideal randomized clinical trial that compares the BCS vs. mastectomy, the rate of radiotherapy should be different between the two groups. Patients with node-negative diseases did and did not need radiotherapy after BCS and mastectomy, respectively. Thus, how the radiotherapy contributed to the clinical outcomes of the BCS group is still unclear, which is a limitation of our study. Third, there were 13.7% of the patients who were excluded due to the lack of follow-up information, which could potentially cause bias for the study.

In summary, we observed that BCS had equivalent local control compared to mastectomy. After adjusting for confounding factors, BCS was associated with improved DFS and CSS in the original study population compared to mastectomy. In the PS-matched population, BCS was not associated with improved DFS and CSS compared to mastectomy. Taken together, we suggest that BCS and mastectomy result in equivalent clinical outcomes. Using observational data to estimate treatment effects should be exercised with caution, and PS matching analysis is helpful to reduce potential bias.

METHODS

We identified 3,659 nonmetastatic breast cancer patients who received surgical treatment at Sun Yat-sen Memorial Hospital in Guangdong, China between 1 January 1998 and 31 December 2014, from the REDcap database system, maintained by Sun Yat-sen Memorial Hospital, Sun Yat-sen University. We excluded 338 patients with inflammatory breast cancer, bilateral breast cancer or phyllodes tumors of the breast. Furthermore, 13.7% (455/3,321) of the patients were excluded due to the lack of follow-up information. Patients were followed-up via telephone call and clinic interviews, which were performed by the Breast Disease Registry of Breast Tumor Center, Sun Yat-sen Memorial Hospital. The decision to perform BCS or mastectomy was determined based on patients' clinicopathological features and their personal preference. All specimens underwent pathological examination. In our institution, the hormonal status (estrogen receptor (ER) and progesterone receptor (PR)) was reported as negative, 1+, 2+ and 3+ before 2007. Since 2007, the detailed percentage of ER- or PR-positive tumor cells was reported. In this study, we defined patients with 1–3+ (before 2007) or >1% ER- or PR-positive tumor cells (after 2007) as hormonal positive patients. To determine the human epidermal growth factor receptor 2 (HER2) status, we used the HercepTest method. Samples were considered HER2-positive if the score was 3+ or 2+ with HER2 gene amplification as determined by fluorescence *in situ* hybridization (FISH). HercepTest scores of 1 or less, or scores of 2 without HER2 gene amplification were considered HER2-negative. This retrospective study consisted of de-identified data collected from a database. Ethical approval and patient consent were not needed based on our institutional policy. Since tumor grade was not available before 2010, we characterized tumor samples as belonging to one of five categories as follows: Before 2010; After 2010 & Grade I; After 2010 & Grade II; After 2010 & Grade III and After 2010 Grade unknown.

Our institution followed the NCCN guidelines for routine clinical practice in diagnosing and treating breast cancer. The following issues should be noted. (i) For BCS, we used frozen section analysis to evaluate the cavity margin status intraoperatively and formalin-fixed, paraffin-embedded tissue to confirm the margin status postoperatively, as previously reported (Chen et al., 2012). We did not routinely evaluate the lumpectomy margin status. We have previously shown that this strategy for marginal evaluation is oncologically safe (Chen et al., 2012; Yang et al., 2012). (ii) For clinically node-negative patients, SLNB was performed using radioisotope and blue dye techniques before 2012. After 2012, we used only the blue dye technique for SLNB. (iii) For patients with 1–3 positive axillary lymph nodes, a multidisciplinary team determined whether the patient received postmastectomy radiotherapy. (iv) Trastuzumab was not widely used in HER2-positive patients before 2009. (v) The 21 gene assay for hormone receptor positive, node-negative patients was not available during the study period.

We conducted descriptive analysis of the baseline clinicopathological features of the included patients. The chi-square test was used to compare the clinicopathological features of patients who underwent BCS versus mastectomy. We used Kaplan-Meier survival analysis to estimate the cumulative survival of the population and the log-rank test to compare survival between different treatment cohorts. The endpoints of the comparison included local recurrence-free survival (LRFS), disease-free survival (DFS) and cancer-specific survival (CSS). Local recurrence was defined as ipsilateral in-breast recurrence after BCS and chest-wall recurrence after mastectomy. The following events were included in DFS analysis: local and/or regional recurrence, distant metastasis, contralateral breast cancer, secondary malignancy, and death without evidence of cancer. The amount of time to reach these endpoints was calculated from the date of surgery. Univariate and multivariate Cox-regression analyses were used to characterize the risk factors associated with the endpoints.

The logistic regression model with variables (T-stage, N-stage, ER status, PR status, HER2 status, etc.) was used to estimate the PS for BCS versus mastectomy. Radiotherapy was not included in the PS model. After the PS had been calculated, patients that underwent BCS versus mastectomy were matched 1:1 based on a similar PS using the nearest neighbor method within a caliper of 0.05. In the PS-matched population, we used the chi-square test and absolute standardized differences to assess the balance of the variables between the two cohorts. Patients who were not matched were not included in the PS-matched population.

In this study, P values less than 0.05 were considered statistically significant. Data analyses were performed using Stata version 13.1 software (StataCorp, College Station, Texas, USA).

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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SUPPORTING INFORMATION

Figure S1 Comparison of the clinical outcomes of the matched and original population. a, Local-recurrence free survival. b, Cancer-specific survival. c, Disease-free survival. Comparison of the clinical outcomes of patients with breast-conserving surgery and mastectomy stratified by the matching status. d, Local-recurrence free survival. e, Cancer-specific survival. f, Disease-free survival.

Figure S2 Estimation of the treatment effects on (a) disease-free survival and (b) cancer-specific survival using different PS methods.

Table S1 Propensity score model

Supplementary File 1

The supporting information is available online at http://life.scichina.com and https://link.springer.com. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.