The Different Outcomes Between Breast-Conserving Surgery Plus Radiotherapy and Mastectomy in Breast Ductal Carcinoma In Situ with Microinvasion

Lin-Yu Xia (lylc1023@163.com)
The First Affiliated Hospital of Chengdu Medical College https://orcid.org/0000-0003-4802-2359
Wei-Yun Xu
Mianyang Central Hospital
Qing-Lin Hu
The First Affiliated Hospital of Chengdu Medical College

Research

Keywords: breast cancer, intraductal, microinvasion, breast-conserving surgery, mastectomy,survival outcomes

Posted Date: May 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-525726/v1

Abstract

Background: Ductal carcinoma in situ with microinvasion (DCIS-MI) is a subtype of breast cancer with good prognosis, for which both breast conserving surgery plus radiotherapy (BCS+RT) and mastectomy are feasible surgical methods, but their effects on the prognosis of patients are still unclear.

Methods: We used the Surveillance, Epidemiology and End Results (SEER) database to extracted DCIS-MI patients who underwent BCS+RT or mastectomy between 2000 and 2014. Participants were divided into BCS+RT group and mastectomy group. We compared the breast cancer-specific survival (BCSS) and overall survival (OS) of the two groups using Kaplan -Meier method and Cox proportional hazard regressions before and after propensity score matching (PSM) with the landmark. Results: We selected 5432 patients, among which 2834 patients (52.17%) were in the BCS+RT group and 2598 patients (47.83%) were in the mastectomy group. With a 101 months median follow-up time in the overall cohort, both univariate and multivariate analysis showed that BCS + RT group showed significantly higher OS and BCSS compared with patients in the mastectomy group (P<0.001). After PSM, the BCS+RT and mastectomy groups consisted of 1902 patients, respectively. multivariate analysis also showed that compared with mastectomy, the BCS+RT showed significantly higher OS and BCSS (HR = 0.676, 95% CI = 0.540-0.847, P<0.001; HR = 0.565,95% CI = 0.354-0.903, P= 0.017). In addition, the subgroup analysis showed that BCS + RT is at least equivalent to mastectomy with respect to OS and BCSS in any subgroup.

Conclusion: For patients with DCIS-MI, the prognosis of BCS+RT was superior to mastectomy.

Introduction

Ductal carcinoma in situ with microinvasion (DCIS-MI) is a special type of breast cancer, accounting for 0.6–3.4% of breast cancer [1, 2]. It refers to cancer cells breaking through the basement membrane to infiltrate adjacent tissues, but the maximum lesion scope is less than 1mm[3, 4]. According to the American Joint Committee on Cancer (AJCC), lesions that meet this definition are regarded as a subtype of stage T1 breast cancer and classified as T1mic stage [5]. Most scholars believe that DCIS-MI is the intermediate stage of DCIS and invasive ductal carcinoma (IDC), with a prognosis between the two [6–9]. However, some scholars believe that DCIS-MI has the same prognosis as DCIS [10, 11]. The early-stage proposed by DCIS-MI lacks a unified diagnostic standard, the disease is relatively rare, and the study sample size is small. Therefore, there are many controversies in the treatment.

Currently, many studies have demonstrated that for early breast cancer, patients receiving BCS + RT have the same prognosis as patients receiving mastectomy [12–14]. Mamtani et al. compared the prognosis of BCS + RT and mastectomy in patients with DCIS and found that BCS + RT was superior to mastectomy in OS or DFS of DCIS [15]. Both BCS + RT and mastectomy are currently available surgical methods for DCIS-MI. However, considering the good prognosis of DCIS-MI and patients' postoperative life quality, it is worth exploring whether BCS + RT is the best choice for DCIS-MI. At present, there are few studies on the surgical methods of DCIS-MI [16–18].The prognosis of BCS + RT or mastectomy for patients with DCIS-MI is still unclear.We conducted this study to determine which surgical procedure is better for patients with DCIS-MI. This study compared the long-term outcomes of patients with DCIS-MI receiving BCS + RT and mastectomy using the SEER database.

Methods

Patients

This study was conducted using the SEER database published in November 2018. Patients who were diagnosed with DCIS-MI from 2000 to 2014 were eligible for recruitment. The inclusion criteria included: (1) 20–79 years old; (2) A mastectomy or breast-conserving surgery was performed. Exclusion criteria included :(1) Patients with tumor metastasis; (2) patients combined with other malignant tumors; (3) Patients who did not receive radiotherapy after breast-conserving surgery.

Data collection and outcome measures

We collected the following factors: year of diagnosis, age, race, marital status, histological grade, lymph node status, estrogen receptor (ER), progesterone receptor (PR), surgical method, chemotherapy and radiotherapy. Our study's main outcomes were OS and BCSS, OS was defined as the time from the date of diagnosis to the date of death, and BCSS was measured from the date of diagnosis to the date of death due to breast cancer.

Statistical analysis

Propensity score matching(PSM) was applied to create a matched pair between the two groups to eliminate the selection bias of this study population[19]. We performed PSM for all the variables included in the study. Landmark analysis was used to eliminate a lead time bias among the propensity-matched cohort[20]. With the landmark, analysis was restricted to patients who survived to 6 months without death .X^2 test was used to compare the distribution of the clinical and pathological features between the two groups before and after PSM. The OS and BCSS survival curves were plotted through the Kaplan-Meier method and compared by the log-rank test. The cox regression model was used for the univariate and multivariate analyses of the BCSS and OS. All *P* values were two-sided, and $P < 0.05$ was considered significant. The SPSS 20.0 (IBM SPSS Statistics, Chicago, IL, US)was used for these analyses.

Ethics statement

The informed consent is not required for that the study obtained data from the SEER database.

Results

Baseline characteristics

In total, 5432 patients with DCIS-MI from 2000 to 2014 were included in the study through the SEER database. We divided the patients into two groups :BCS + RT group (2834,52.17%) and mastectomy group (2598,47.83%). Table 1 summarizes the patient clinical characteristics of the two groups. Compared with mastectomy group, the patients in the BCS group were older (78.9% VS. 64.2%; $P < 0.001$)and had lower histological grade (grade I + II,65.6% VS. 56.4%; $P < 0.001$), less lymph node metastasis(N0, 96.7% VS. 87.5%; $P < 0.001$). Further, the BCS group had a higher ER(76.7% VS. 67.4%; $P < 0.001$) and PR (62.9% VS. 55.4%; $P < 0.001$) positive rates and were less likely to receive chemotherapy (6.2% VS. 14.8%; $P < 0.001$). After PSM, the two groups consisted of 1902 pairs. There was no significant difference in clinicopathological characteristics between the two groups.

Table 1
Baseline characteristics of the study population and tumor

Characteristics		before PSM			after PSM		
		BCS + RT (n,%)	Mastectomy (n,%)	*P*	BCS + RT (n,%)	Mastectomy (n,%)	*P*
No. of patients		2834	2598(47.83%)		1902	1902	
Year of diagnosis	2004–2009	1304(46%)	1181(45.5%)	0.682	851(44.7%)	849(44.6%)	0.948
	2010–2014	1530(54%)	1417(54.5%)		1051(55.3%)	1053(55.4%)	
Age (years)	20–49	597(21.1%)	931(35.8%)	**< 0.001**	488(25.7%)	489(25.7%)	0.970
	50–80	2237(78.9%)	1667(64.2%)		1414(74.3%)	1413(74.3%)	
Race	White	2179(76.9%)	1944(74.8%)	0.205	1476(77.6%)	1481(77.9%)	0.888
	Black	333(11.8%)	335(12.9%)		210(11.0%)	214(11.2%)	
	Other	322(11.4%)	319(12.3%)		216(11.4%)	207(10.9%	
Marital status	Married	963(34%)	840(32.3%)	0.198	628(33.0%)	622(32.7%)	0.836
	Not married	1871(66%)	1758(67.7%)		1274(67.0%)	1280(67.3%)	
Grade	I	748(26.4%)	473(18.2%)	**< 0.001**	408(21.5%)	408(21.5%)	1
	II	1112(39.2%)	993(38.2%)		761(40.0%)	761(40.0%)	
	III	848(29.9%)	995(38.3%)		652(34.3%)	652(34.3%)	
	IV	126(4.4%)	137(5.3%)		81(4.3%)	81(4.3%)	
Nodal status	N0	2741(96.7%)	2274(87.5%)	**< 0.001**	1840(96.7%)	1841(96.8%)	1
	N1	78(2.8%)	273(10.5%)		55(2.9%)	54(2.8%)	
	N2	11(0.4%)	35(1.3%)		6(0.3%)	6(0.3%)	
	N3	4(0.1%)	16(0.6%)		1(0.1%)	1(0.1%)	
ER	Negative	660(23.3%)	846(32.6%)	**< 0.001**	523(27.5%)	523(27.5%)	1
	Positive	2174(76.7%)	1752(67.4%)		1379(72.5%)	1379(72.5%)	
PR	Negative	1050(37.1%)	1159(44.6%)	**< 0.001**	752(39.5%)	756(39.7%0	0.895
	Positive	1784(62.9%)	1439(55.4%)		1150(60.5%)	1146(60.3%)	

PSM = propensity score matching; BCS + RT = Breast conserving surgery plus radiotherapy

Characteristics		before PSM			after PSM		
		BCS + RT (n,%)	Mastectomy (n,%)	*P*	BCS + RT (n,%)	Mastectomy (n,%)	*P*
Chemotherapy	yes	177(6.2%)	384(14.8%)	< 0.001	102(5.4%)	103(5.4%)	0.943
	no	2657(93.8%)	2214(85.2%)		1800(94.6%)	1799(94.6%)	
Radiotherapy	yes	2834(100%)	184(7.1%)		1902(100%)	85(4.5%)	
	no	0(0%)	2414(92.9%)		0(0%)	1817(95.5%)	
PSM = propensity score matching; BCS + RT = Breast conserving surgery plus radiotherapy							

Prognostic factors associated with OS and BCSS

Before PSM, The median follow-up time for these patients was 101 months. The 5-year and 10-year OS for patients in BCS + RT and mastectomy groups were 97.3% vs. 95.4% and 91.2% vs. 88.5% respectively (log-rank $P = 0.001$, Fig. 1A). The 5-year and 10-year BCSS for patients in BCS + RT and mastectomy groups were 99.1% vs. 97.8% and 98.0% vs. 95.9% (log-rank $P < 0.001$, Fig. 1B). After adjusting for the prognostic variables in the univariate analysis (Supplementary Table 1), the multivariate analysis indicated that black and more lymph node metastases are associated with poor OS and BCSS (all $P < 0.05$). BCS + RT group showed significantly higher OS and BCSS compared with patients in the mastectomy group (HR = 0.686, 95% CI = 0.571–0.825, $P < 0.001$; HR = 0.596,95% CI = 0.411–0.865, $P = 0.007$). Besides, patients at a younger age and not married had better OS relatively while patients without chemotherapy had lower BCSS (all $p < 0.05$) (Table 2).

Table 2
Prognostic factors for OS and BCSS in multivariate analysis

Characteristics		OS		BCSS	
		HR(95%CI)	*P*	HR(95%CI)	*P*
Year of diagnosis	2000–2007	Ref.	Ref.	Ref.	Ref.
	2008–2014	0.795(0.625–1.011)	0.061	0.902(0.603–1.349)	0.614
Age (years)	20–49	Ref.	Ref.	Ref.	Ref.
	50–80	2.806(2.158–3.648)	**< 0.001**	0.875(0.611–1.253)	0.465
Race	White	Ref.	Ref.	Ref.	Ref.
	Black	1.522(1.199–1.933)	**< 0.001**	1.900(1.261–2.863)	**0.002**
	Other	0.696(0.479–1.012)	0.058	0.782(0.393–1.555)	0.483
Marital status	Married	Ref.	Ref.	Ref.	Ref.
	Not married	0.615(0.513–0.738)	**< 0.001**	0.730(0.514–1.037)	0.079
Grade	I	Ref.	Ref.	Ref.	Ref.
	II	0.859(0.677–1.090)	0.212	0.904(0.543–1.504)	0.697
	III	0.808(0.623–1.048)	0.108	1.191(0.716–1.980)	0.500
	IV	0.735(0.479–1.128)	0.159	0.987(0.446–2.187)	0.975
Nodal status	N0	Ref.	Ref.	Ref.	Ref.
	N1	1.204(0.829–1.747)	0.330	1.941(1.113–3.384)	**0.019**
	N2	2.248(1.079–4.684)	**0.031**	2.961(1.163–7.540)	**0.023**
	N3	5.600(2.687–11.672)	**< 0.001**	10.648(4.298–26.381)	**< 0.001**
ER	Positive	Ref.	Ref.	Ref.	Ref.
	Negative	0.998(0.760–1.312)	0.990	1.354(0.838–2.189)	0.216
PR	Positive	Ref.	Ref.	Ref.	Ref.
	Negative	0.868(0.675–1.115)	0.268	0.692(0.444–1.078)	0.103
Chemotherapy	yes	Ref.	Ref.	Ref.	Ref.
	no	0.980(0.690–1.393)	0.910	1.747(1.042–2.930)	**0.034**
Surgical method	BCS + RT	0.686(0.571–0.825)	**< 0.001**	0.596(0.411–0.865)	**0.007**

OS = overall survival; BCSS = breast cancer-specific survival

Characteristics	OS		BCSS	
	HR(95%CI)	*P*	HR(95%CI)	*P*
Mastectomy	Ref.	Ref.	Ref.	Ref.
OS = overall survival; BCSS = breast cancer-specific survival				

After PSM with a 6-month landmark, the 5-year and 10-year OS for patients in BCS + RT and mastectomy groups were 97.4% vs. 95.9% and 92.1% vs. 89.1% respectively (log-rank $P = 0.001$, Fig. 2A). The 5-year and 10-year BCSS for patients in BCS + RT and mastectomy groups were 99.1% vs. 98.7% and 98.2% vs. 97.4% (log-rank $P = 0.016$, Fig. 2B). The multivariate cox regression analysis showed that OS's prognostic factors were the same as before PSM while the prognostic factors of BCSS had a little difference. Patients at grade III and patients without chemotherapy were associated with poor BCSS. Compared with mastectomy, the BCS + RT also showed significantly higher OS and BCSS (HR = 0.676, 95% CI = 0.540–0.847, $P < 0.001$; HR = 0.565,95% CI = 0.354–0.903, $P = 0.017$)(Table 3).

Table 3
Prognostic factors for OS and BCSS in multivariate analysis after PSM

Characteristics		OS		BCSS	
		HR(95%CI)	*P*	HR(95%CI)	*P*
Year of diagnosis	2000–2007	Ref.	Ref.	Ref.	Ref.
	2008–2014	0.751(0.544–1.018)	0.065	0.902(0.517–1.573)	0.717
Age (years)	20–49	Ref.	Ref.	Ref.	Ref.
	50–80	3.763(2.539–5.578)	**< 0.001**	1.007(0.592–1.711)	0.980
Race	White	Ref.	Ref.	Ref.	Ref.
	Black	1.634(1.200-2.226)	**0.002**	2.203(1.240–3.915)	**0.007**
	Other	0.534(0.311–0.916)	0.053	0.540(0.168–1.737)	0.301
Marital status	Married	Ref.	Ref.	Ref.	Ref.
	Not married	0.601(0.478–0.755)	**< 0.001**	0.703(0.432–1.146)	0.158
Grade	I	Ref.	Ref.	Ref.	Ref.
	II	0.900(0.666–1.215)	0.490	1.630(0.759–3.502)	0.210
	III	0.868(0.626–1.202)	0.394	2.210(1.022–4.778)	**0.044**
	IV	0.738(0.413–1.318)	0.304	1.383(0.372–5.142)	0.629
Nodal status	N0	Ref.	Ref.	Ref.	Ref.
	N1	1(0.509–1.964)	1	4.001(1.607–9.961)	**0.003**
	N2	7.004(1.931–25.403)	**0.003**	12.960(2.953–56.873)	**0.001**
	N3	36.754(4.349-310.608)	**0.001**	53.355(4.923–578.230)	**0.001**
ER	Positive	Ref.	Ref.	Ref.	Ref.
	Negative	0.897(0.622–1.292)	0.558	1.418(0.709–2.835)	0.323
PR	Positive	Ref.	Ref.	Ref.	Ref.
	Negative	0.993(0.706–1.396)	0.966	0.710(0.375–1.342)	0.292
Chemotherapy	yes	Ref.	Ref.	Ref.	Ref.
	no	0.916(0.505–1.661)	0.773	1.241(0.503–3.065)	0.639
Surgical method	BCS + RT	0.676(0.540–0.847)	**0.001**	0.565(0.354–0.903)	**0.017**
	Mastectomy	Ref.	Ref.	Ref.	Ref.

OS = overall survival; BCSS = breast cancer-specific survival;PSM = propensity score matching

Subgroup analysis of OS and BCSS

To further explore possible factors affecting the overall survival time for patients who had undergone two types of surgery, we performed a subgroup analysis of all patients after PSM. BCS + RT group showed significantly higher OS than mastectomy group for patients aged between 50–79 years, patients who married or not married, the white race group, patients with grade III + IV, patients with lymph nodal negative, patients with ER positive, patients with PR positive or negative and those who did not receive chemotherapy(all $P < 0.05$)(Fig. 3).Further, the BCT + RT group also showed BCSS benefit in patients who not married, patients with lymph nodal negative, patients with ER negative, and those who did not receive chemotherapy (Fig. 4). The OS and BCSS outcomes of mastectomy were not better than those of BCS + RT in any subgroup.

Discussion

DCIS-MI is a special type of breast cancer, and there is little evidence on the prognosis of patients with DCIS-MI undergoing BCS + RT and mastectomy. We found that the prognosis of patients with DCIS-MI after mastectomy is not better than those of BCS + RT in any subgroup by using the SEER database.

In the NCCN guidelines, DCIS-MI is classified as early-stage invasive breast cancer. All surgical options for early-stage invasive breast cancer are unified. There is no special explanation for the surgical options for DCIS-MI. In our study, 71.9% of patients with DCIS-MI were older than 50 years. Besides, patients with DCIS-MI had few lymph node metastases (92.3% without lymph nodal metastases), low histological grade (61.3% in GI + II), and high positive rates of ER and PR (72.3% and 59.3%), which was consistent with other studies [21, 22]. These results indicate that DCIS-MI has a good prognosis.

Although the clinicopathological features of DCIS-MI all indicate a good prognosis, at present, there are still a large number of DCIS-MI patients undergoing mastectomy. In our study, 47.83% of the patients received mastectomy. In Eastern countries, the proportion of patients with DCIS-MI undergoing mastectomy is higher, even as high as 80% [23, 24]. At present, the safety of mastectomy for DCIS-MI has been verified. Mamtani et al.studied the locoregional and distant recurrence after mastectomy for DCIS with or without microinvasion. It proved that locoregional recurrence after mastectomy for DCIS ± microinvasion is uncommon. Even in the age group with the highest recurrence rate, 10-year locoregional recurrence remains low at 4.2%[25]. DCIS-MI often has multiple minimally invasive foci, associated with a higher risk of ipsilateral recurrence [26, 27]. The study of Si et al. showed that 35.1% of DCIS-MI Patients have multiple foci, which had a worse disease-free survival rate compared with one-focus patients (98.29 vs. 93.01%, P = 0.032)[24]. The safety of BCS for DCIS-MI is worth exploring. Rakovitch compared the local recurrence rate after breast-conserving in patients with DCIS and DCIS-MI [17]. The results showed that multiple foci of MI are associated with an increased risk of invasive local recurrence in women with DCIS treated with BCS, but treatment with the whole breast and boost RT can mitigate this risk. The Yale School of Medicine retrospective clinical study of BCS included 72 patients with DCIS-MI and 321 patients with DCIS, all of whom received local radiotherapy. There was no difference in regional recurrence rates after 10 years between the DCIS-MI group and the DCIS group (8.3% vs. 6.8%) [18]. These studies proved that BCS + RT is safe for DCIS-MI.

Studies have confirmed the safety of BCS + RT in DCIS patients. Park et al. conducted a study on 3648 patients with DCIS younger than 40 years old, and the results showed that mastectomy does not offer survival benefits over BCS + RT [28]. Mamtani et al. also confirmed this [15]. To our knowledge, only Bartova et al. compare the prognostic difference between BCS and mastectomy in DCIS-MI. They followed up 41 patients with DCIS or DCIS-MI after BCS and mastectomy, and finally, only 27 patients completed the follow-up. There is no local recurrence occurred [16]. However, the sample size of this study was small, and no survival rate was reported. Our study

showed that the BCS + RT group showed significantly higher OS and BCSS than patients in the mastectomy group. In order to find out which subgroups of people can benefit from BCS + RT, we also conducted a subgroup analysis and found that the OS and BCSS outcomes of mastectomy were not better than those of BCS + RT in any subgroup. Furthermore, we observed that 95.5% of patients received mastectomy without RT in our study. Thus we think that BCS + RT showed a better prognosis than mastectomy may due to RT. Studies have confirmed that RT can reduce the local recurrence of breast cancer. Rakovitch et al. proved that postoperative radiotherapy could reduce the local recurrence rate in patients with DCIS-MI [17]. The EORTC study also demonstrated that adjuvant radiotherapy after BCS could reduce the risk of ipsilateral invasive recurrence by approximately 50% during 10 years of follow-up [29].

Similar to the result of aother study, chemotherapy cannot improve the survival of DCIS-MI. Pu et al. proved that postoperative chemotherapy did not improve DFS in patients with DCIS-MI after mastectomy (HR = 1.50, 95%CI 0.29–7.87, *P* = 0.63)[30]. Chen et al. analyzed 3198 DCIS-MI patients and concluded that chemotherapy was an independent factor for worse BCSS (P = 0.008) and there was no statistical significance for OS (P = 0.248) in patients with DCIS-MI [31].In our study's overall cohort, 6.2% and 14.8% of patients in the BCS + RT group and the mastectomy group received chemotherapy, respectively. There was no significant difference in OS and BCSS between those who did not receive chemotherapy and those who received chemotherapy (all $P > 0.05$) after PSM. However, further studies are needed to verify whether chemotherapy is beneficial to patients with DCIS-MI.

Our study had several limitations. Firstly, there may be residual confounders even though the propensity-matched landmark analysis was used. Secondly, the SEER database did not provide detailed information on breast multiple lesions and lacks data on postoperative breast reconstruction and postoperative local recurrence. Finally, there is no information on endocrine therapy and targeted therapy in the SEER database.

Conclusion

This population-based study based on SEER database revealed that the prognosis of patients who were diagnosed with DCIS-MI receiving mastectomy was not better than those receiving BCS + RT. We think that BCS + RT is more suitable for the DCIS-MI patients.

Abbreviations

DCIS-MI = ductal carcinoma in situ with microinvasion

BCS+ RT= breast conserving surgery plus radiotherapy

OS= overall survival

BCSS = breast cancer-specific survival

PSM = propensity score matching

ER = estrogen receptor

PR = progesterone receptor

Declarations

- Ethics approval and consent to participate

Not applicable.

- Consent to publish

Not applicable.

- Availability of data and materials

Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov)

SEER*Stat Database: Incidence - SEER 18 Regs Custom Data (with additional treatment fields), Available at: https://seer. cancer.gov/data/, Accessed June 23, 2020.

- Conflict of Interest

The author(s) declare that they have no competing interests.The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- Funding

Not applicable.

- Authors' Contributions

Protocol/project development: L.-Y.X and Q.-L.H. Data acquisition and interpretation of data:L.-Y.X. Statistics analysis of data: L.-Y.X and W.-Y.X Manuscript drafting: L.-Y.X and W.-Y.X . Manuscript Revision and accountable for all aspects of the study:L.-Y.X and Q.-L.H. All authors read and approved the final manuscript.

- Acknowledgments

Not applicable.

References

1. Singletary SE. Allred C, Ashley P. Bassett LW, Berry D. Bland KI, *et al.* Revision of the American joint committee on cancer staging system for breast cancer. J Clin Oncol. 2002;20:3628–36.
2. Pimiento JM. Lee MC, Esposito NN. Kiluk JV, Khakpour N. Carter WB, *et al.* Role of axillary staging in women diagnosed with ductal carcinoma in situ with microinvasion. J Oncol Pract. 2011;7(5):309–13. *doi*: 10.1200/JOP.2010.000096.
3. Bianchi S. Vezzosi V. Microinvasive carcinoma of the breast. Pathol Oncol Res. 2008;14:105–11. *doi*: 10.1007/s12253-008-9054-8.
4. Shatat L. Gloyeske N, Madan R. O'Neil M, Tawfifik O. Fan F. Microinvasive breast carcinoma carries an excellent prognosis regardless of the tumor characteristics. Hum Pathol. 2013;44: 2684–9. *doi*: 10.1016/j.humpath.2013.07.010.
5. Amin MB. Edge SB, Greene FL, et al AJCC Cancer Staging Manual.*8th ed. New York*:*Springer*,2016.

6. Mori M. Tsugawa K, Yamauchi H,Yagata H, Suzuki K. Ohde S, *et al.* Pathological assessment of microinvasive carcinoma of the breastBreast Cancer. 2013;20(4):331–5.*doi*: 10.1007/s12282-012-0339-0.
7. Wong JH. Kopald KH, Morton DL. The impact of microinvasion on axillary node metastases and survival in patients with intraductal breast cancer. Arch Surg. 1990;125:1298–301. *doi*: 10.1001/archsurg.1990.01410220082011.
8. Vieira CC. Mercado CL, Cangiarella JF. Moy L, Toth HK. Guth AA. Microinvasive ductal carcinoma in situ: clinical presentation, imaging features, pathologic fifindings, and outcome. Eur J Radiol. 2010;73:102–7. *doi*: 10.1016/j.ejrad.2008.09.037.
9. Thomas A. Weigel RJ, Lynch CF. Spanheimer PM, Breitbach EK. Schroeder MC.Incidence,characteristics,and management of recently diagnosed,microscopically invasive breast cancer by receptor status: Iowa SEER 2000 to 2013.Am J Surg.2017;214(2):323–8.*doi*:10.1016/j.amjsurg.2016.08.008.
10. Wang L. Zhang W, Lyu S. Liu X, Zhang T. Liu S, *et al.* Clinicopathologic characteristics and molecular subtypes of microinvasive carcinoma of the breast. Tumour Biol. 2015; 36: 2241–8. *doi*: 10.1007/s13277-014-2652-z.
11. Worni M. Akushevich I, Greenup R. Sarma D, Ryser MD. Myers ER, *et al.* Trends in Treatment Patterns and Outcomes for Ductal Carcinoma In Situ. J Natl Cancer Inst. 2015; 107: djv263.doi: 10.1093/jnci/djv263.
12. Fisher B. Anderson S, Bryant J. Margolese RG, Deutsch M. Fisher ER, *et al.* Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347:1233–41. *doi*: 10.1056/NEJMoa022152.
13. Blichert-Toft M. Nielsen M, During M. Moller S, Rank F. Overgaard M, *et al.* Long-term results of breast conserving surgery vs. mastectomy for early stage invasive breast cancer: 20-year follow-up of the Danish randomized DBCG-82TM protocol. Acta Oncol. 2008;47:672–81.*doi*: 10.1080/02841860801971439.
14. *van* Maaren MC, *de* Munck L, *de* Bock GH, Jobsen JJ. *van* Dalen T, Linn SC, *et al.* 10 year survival after breast-conserving surgery plus radiotherapy compared with mastectomy in early breast cancer in the Netherlands: a population-based study. The Lancet Oncology. 2016;17:1158–70. *doi*: 10.1016/s1470-2045(16)30067-5.
15. Mamtani A. Patil S, Stempel MM. Morrow M. Are there patients with T1 to T2, lymph node-negative breast cancer who are “high-risk” for locoregional disease recurrence? Cancer. 2017; 123: 2626–33.*doi*: 10.1002/cncr.30658.
16. Bartova M. Suska P, Pohlodek K. Local recurrence rate in patients with DCIS. Bratisl Lek Listy. 2012;113(1):30–4. *doi*: 10.4149/bll_2012_007.
17. Rakovitch E. Sutradhar R, Lalani N. Nofech Mozes S,Gu S. Goldberg M,*et al.* Multiple foci of microinvasion is associated with an increased risk of invasive local recurrence in women with ductal carcinoma in situ treated with breast-conserving surgery.Breast Cancer Res Treat.2019;178(1):169–76. *doi*: 10.1007/s10549-019-05364-z.
18. Parikh RR. Haffty BG, Lannin D. Moran MS. Ductal carcinoma in situ with microinvasion: prognostic implications, long-term outcomes, and role of axillary evaluation. Int J Radiat Oncol Biol Phys. 2012; 82: 7–13. *doi*: 10.1016/j.ijrobp.2010.08.027.
19. Austin PC. The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. Stat Med. 2014;33(7):1242–58. 10.1002/sim.5984. *doi.*
20. Giobbie-Hurder A. Gelber RD, Regan MM. Challenges of guarantee-time bias. J Clin Oncol. 2013;31(23):2963–9.*doi*:10.1200/JCO.2013.49.5283.

21. Hanna MG. Jaffer S, Bleiweiss IJ. Nayak A.Re-evaluating the role of sentinel lymph node biopsy in microinvasive breast carcinoma. Mod Pathol.2014;27(11): 1489–98.*doi*: 10.1038/modpathol.2014.54.
22. Francis AM. Haugen CE, Grimes LM. Crow JR, Yi M. Mittendorf EA, *et al.* Is sentinel lymph node dissection warranted for patients with a diagnosis of ductal carcinoma In situ? Ann Surg Oncol, 2015;22(13): 4270–9.*doi*: 10.1245/s10434-015-4547-7.
23. Li Y. Zhang S, Wei X. Zhang J. The clinical features and management of women with ductal carcinoma in situ with microinvasion: A retrospective Cohort study. Int J Surg (2015*)* 19:91–4. 10.1016/j.ijsu.2015.05.013.
24. Si J. Guo R, Pan H. Lu X, Guo Z. Han C, *et al. Multiple Microinvasion Foci in Ductal Carcinoma In Situ Is Associated With an Increased Risk of Recurrence and Worse Survival Outcome. Front Oncol*. 2020;*10*:*607502. doi*: 10.3389/fonc.2020.607502.
25. Mamtani A. Nakhlis F, Downs-Canner S. Zabor EC, Morrow M. King TA, *Van* Zee KJ. *Impact of Age on Locoregional and Distant Recurrence After Mastectomy for Ductal Carcinoma In Situ With or Without Microinvasion. Ann Surg Oncol*. 2019 *Dec;26*(*13*):*4264–4271. doi*: 10.1245/s10434-019-07693-1.
26. Shamliyan T. Wang SY, Virnig BA. Tuttle TM, Kane RL.Association between patient and tumor characteristics with clinical outcomes in women with ductal carcinoma in situ.J Natl Cancer Inst Monogr.2010;2010(41):121-9. *doi*: 10.1093/jncimonographs/lgq034.
27. He X. Ye F, Li M. Yu P, Xiao X. Tang H, *et al.*Application of a novel prognostic invasive lesion index in ductal carcinoma in situ with minimal invasion of the breast.Cancer Med.2017;6(11):2489-96. *doi*: 10.1002/cam4.1175.
28. Park HL. Chang J, Lal G. Lal K, Ziogas A. Anton-Culver H.Trends in Treatment Patterns and Clinical Outcomes in Young Women Diagnosed With Ductal Carcinoma In Situ. Clin Breast Cancer. 2018; 18: e179–85. *doi*: 10.1016/j.clbc.2017.08.001.
29. Wapnir IL. Dignam JJ, Fisher B. Mamounas EP, Anderson SJ. Julian TB, *et al.*Long-term outcomes of invasive ipsilateral breast tumor recurrences after lumpectomy in NSABP B-17 and B-24 randomized clinical trials for DCIS.J Natl Cancer Inst.2011;103(6):478 – 88. *doi*: 10.1093/jnci/djr027.
30. Pu T. Zhong X, Deng L. Li S, Qiu Y. Liu Y,*et al.* Long term prognosis of ductal carcinoma in situ with microinvasion: a retrospective cohort study.Int J Clin Exp Pathol. 2018;11(5):2665–74.
31. Chen C. Huang S, Huang A. Jia Y, Wang J. Zhang Z, *et al.* Risk factors for lymph node metastasis and the impact of adjuvant chemotherapy on ductal carcinoma in situ with microinvasion: a population-based study. Onco Targets Ther. 2018;11:9071–80. *doi*: 10.2147/OTT.S186228.

Figures

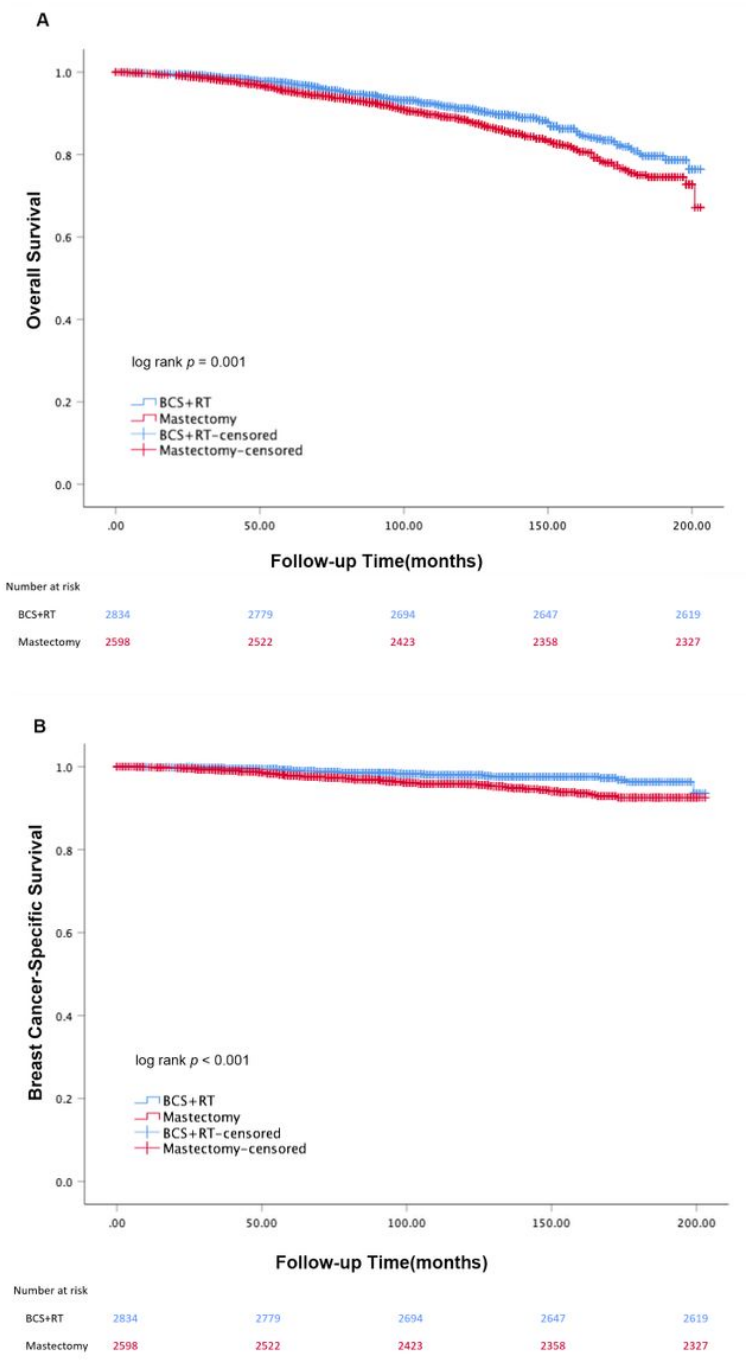

Figure 1

Kaplan-Meier curves of OS (A) and BCSS (B) for unmatched cohorts

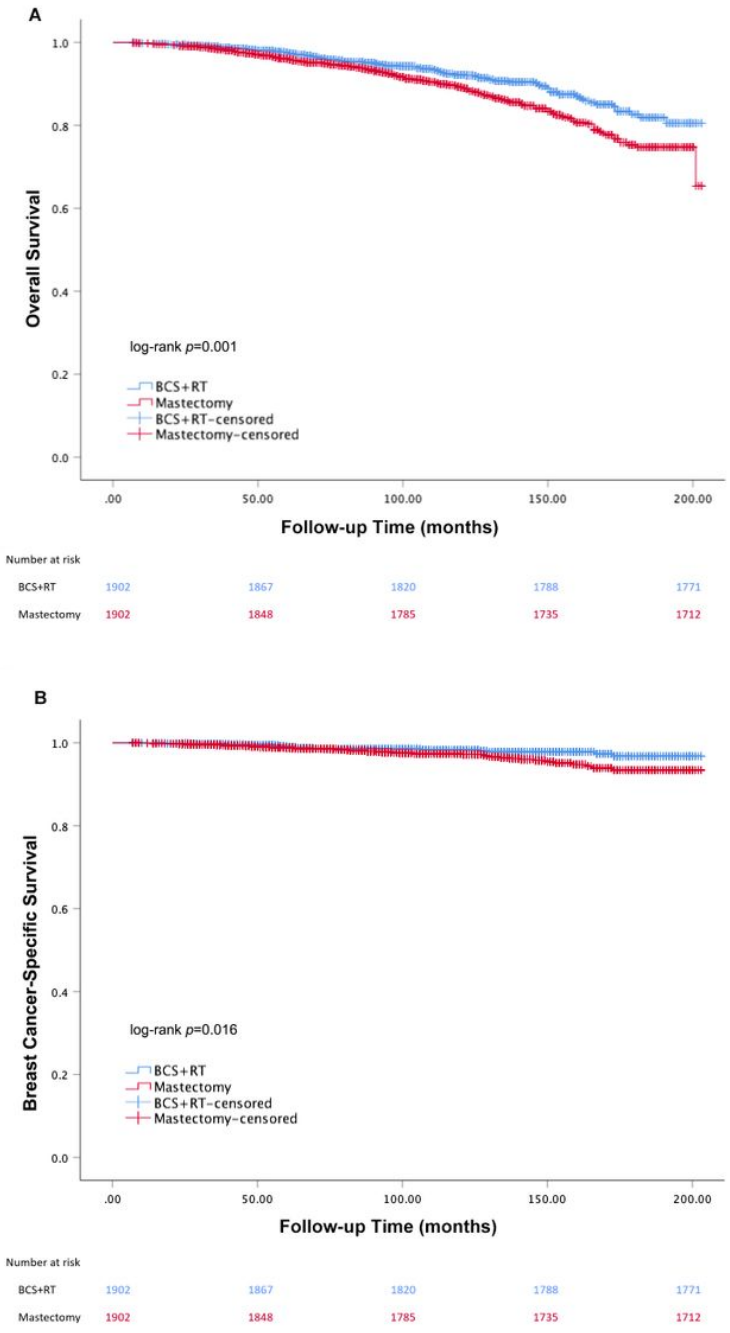

Figure 2

Kaplan-Meier curves of OS (A) and BCSS (B) : propensity matched landmark analysis

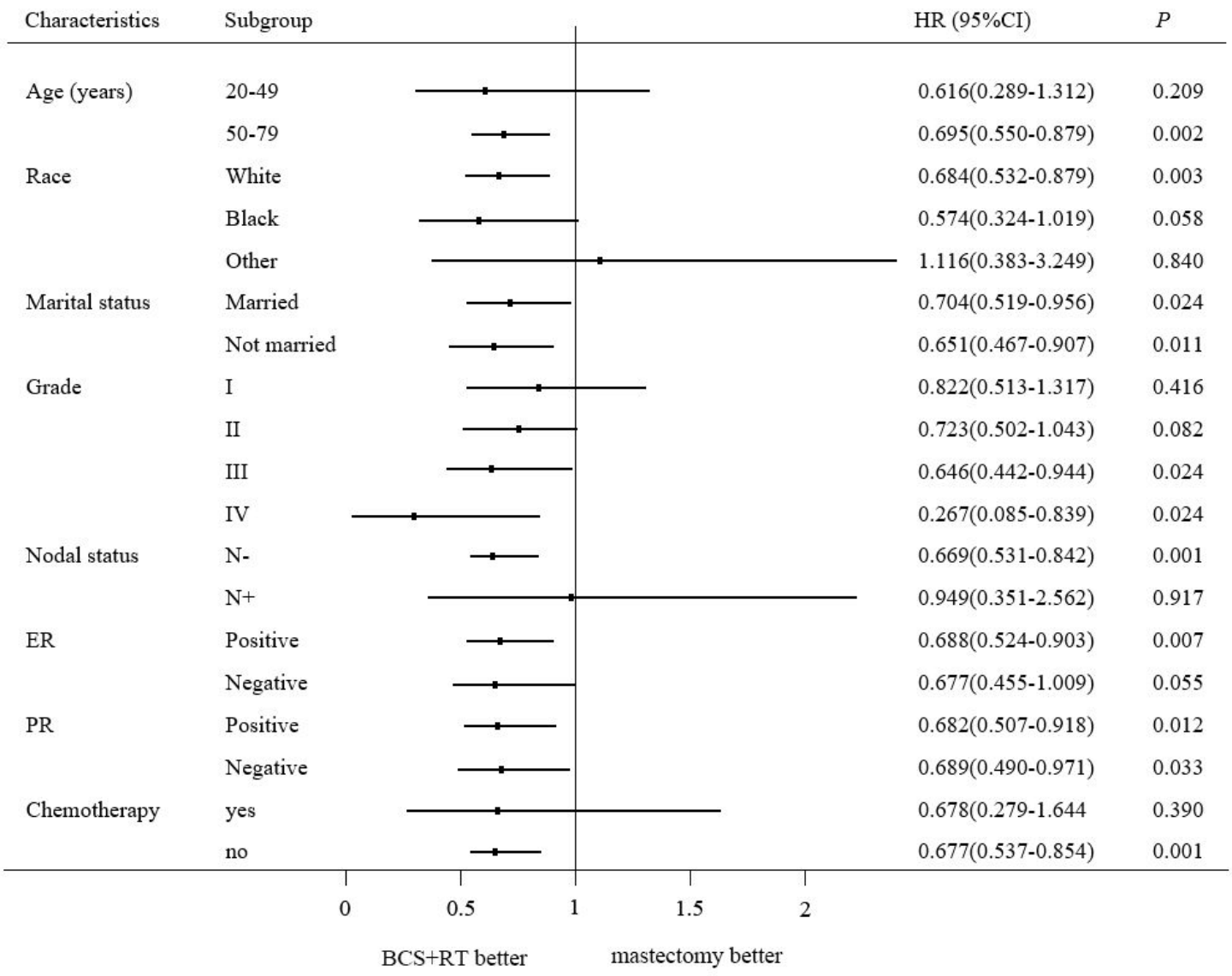

Figure 3

The forest plot of HR for OS between the BCS+RT group and mastectomy group according to different characteristics

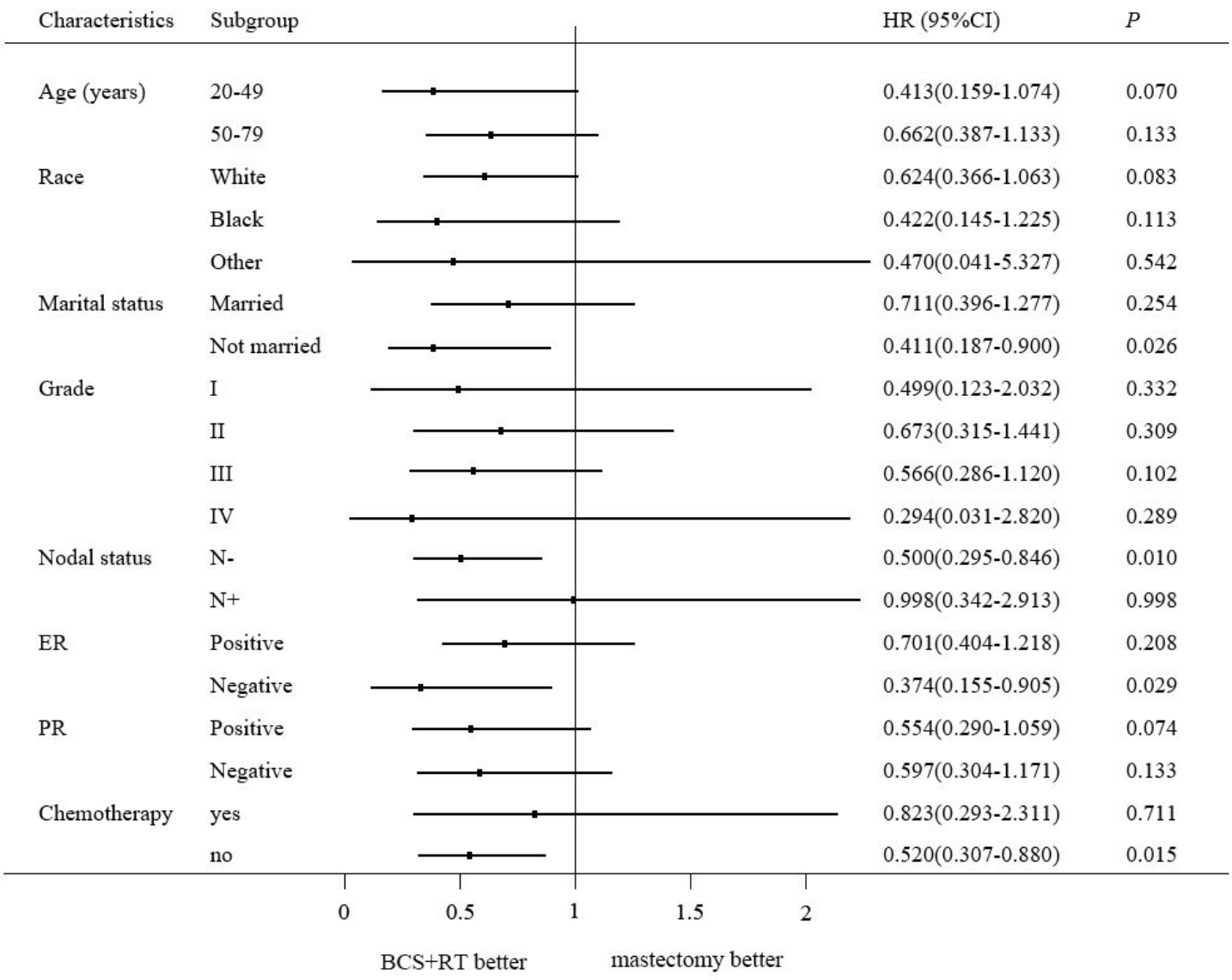

Figure 4

The forest plot of HR for BCSS between the BCS+RT group and mastectomy group according to different characteristics