Original Article

Prognostic role of radiotherapy in low-risk elderly breast cancer patients after breast-conserving surgery: a cohort study

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Background: Previous research suggested that radiotherapy (RT) had a small absolute benefit in patients with low-risk breast cancer over the age of 65. To reduce the patient's treatment burden and cost, as well as the damage to normal tissue, this study sought to explore the prognostic role of RT after breast-conserving surgery (BCS) in elderly patients.

Methods: Patients who were aged ≥65 years, stage T1N0M0, and estrogen receptor/progesterone receptor positive (ER^+/PR^+) were included in this study. Age, marital status, histology, race, grade, human epidermal growth factor receptor 2 (HER2), subtype, treatment method, and survival were also collected from the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2015. We compared overall survival (OS) and breast cancer-specific survival (BCSS) before and after propensity score matching (PSM) in the patients who underwent BCS with or without RT. Kaplan-Meier method and Cox proportional hazards regression analyses were used in our study.

Results: The data of 3,623 patients were analyzed in this study. Among them, 2,851 (78.69%) patients had received RT. The multivariate analyses before PSM showed that RT resulted in better OS [hazard ratio (HR) 0.51, 95% confidence interval (CI): 0.42–0.62, P<0.001], and BCSS (HR 0.40, 95% CI: 0.27–0.58, P<0.001). The multivariate analyses after PSM (n=1,538) confirmed that patients who received RT (n=769) had a longer survival time than those who did not (n=769) (OS: HR 0.73, 95% CI: 0.57–0.95, P=0.018; and BCSS: HR 0.57, 95% CI: 0.35–0.93, P=0.025). The survival analysis showed that patients receiving RT had a better OS (P=0.028) and BCSS (P=0.016) than those who did not receive RT. However, there were no significant differences in patients' OS and BCSS with or without RT across the different age subgroups (P>0.05).

Conclusions: In our study, patients who received RT had a longer survival time. However, the age subgroup analysis showed that RT did not have any survival benefit in elderly patients with T1N0M0 and ER^+/PR^+ breast cancer. Furthermore, at the age of 65–69 years, the P value for OS approached 0.05, which suggests that the decision to administer RT in this patient group should be made based on each patient's condition.

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Introduction

Breast cancer is a common malignant tumor in women. With approximately 280,000 new cases of breast cancer and about 40,000 new deaths reported in 2021, it ranks first in terms of incidence and second in terms of mortality among female malignant tumors (1). Breast cancers are divided into the following 3 groups (2): (I) breast cancers expressing hormone receptors [estrogen receptor (ER)$^+$ or progesterone receptor (PR)$^+$]; (II) breast cancers expressing human epidermal growth factor receptor 2 (HER2)$^+$; and (III) triple-negative breast cancers (TNBC), ER$^-$, PR$^-$, HER2$^-$.

The comprehensive treatment of breast cancer includes surgery, endocrine therapy, chemotherapy, radiotherapy (RT), and targeted therapy (3). For early breast cancer, breast-conserving therapy (BCT) is a safe treatment modality. BCT is the embodiment of a multidisciplinary complex treatment mode, including adjuvant RT and chemotherapy after breast-conserving surgery (BCS) (4). In the inchoate stage of BCS for breast cancer, RT can decrease local recurrence (LR); however, due to insufficient follow-up periods, the overall survival (OS) benefit of RT is not yet known (5).

Many researchers have begun to examine the status and significance of RT after BCS for early breast cancer patients. Studies have found (6-8) that in the vast majority of patients with early breast cancer, RT is an effective and safe treatment after local surgery that ameliorates the success rate of BCS. The treatment mode of breast cancer is well established, but the treatment compliance of elderly patients is poor, as most elderly breast cancer patients have systemic diseases. Currently, no consensus has been reached as to the beneficial effects of RT after BCS in elderly patients. The CALGB-9493 study found (9) that the benefit of RT is limited in clinical stage T1N0M0, ER$^+$ patients, aged >70 years, and as a result, this treatment was subsequently omitted from the National Comprehensive Cancer Network (NCCN) guidelines.

Currently, the World Health Organization (10) defines breast cancer patients aged >65 years as "elderly" in clinical practice. Older age is one of the biggest risk factors for new breast cancer, with >40% of breast cancer patients being aged ≥65 years (11,12). As older patients have been underrepresented in clinical studies, there is limited evidence-based data on the best treatment for such patients. If the age at which RT was omitted was lowered to 65 years, the adverse and economic pressure placed on elderly breast cancer patients undergoing breast-conserving postoperative RT would be reduced; however, doing so, would give rise to other issues. The PRIMEII (13) study showed that the recurrence of 5-year ipsilateral breast tumors was statistically significant in both experimental and control groups of patients who were aged ≥65 years, negative margins after BCS, Primary tumor <3cm and ER$^+$/PR$^+$ (4.1% and 1.3%, respectively). However, the clinical significance of this difference is questionable, and the clinical benefit of RT after BCS for patients is unknown. Without a doubt, RT remains the gold standard of treatment for the majority of breast-conserving patients, but when selecting patients for RT, it is critical to ensure that they have a net benefit. According to the current study findings (9), patients over the age of 70, in stage T1, and with ER$^+$ can avoid RT. According to the findings of the PRIMEII study (13), the age of omitted RT may be reduced in the future to 65 years. Thus, more studies need to be conducted to verify and support these findings.

In this study, data were extracted from the Surveillance, Epidemiology, and End Results (SEER) database for patients who had received a pathological diagnosis of breast cancer from 2004 to 2015, were aged ≥65 years, had a primary tumor <3 cm, and had ER$^+$/PR$^+$ status after BCS. The effects of RT and other clinical factors on the prognosis of patients after BCS were evaluated using the traditional method and the propensity score matching (PSM) method. We present the following article in accordance with the STROBE reporting checklist (available at https://gs.amegroups.com/article/

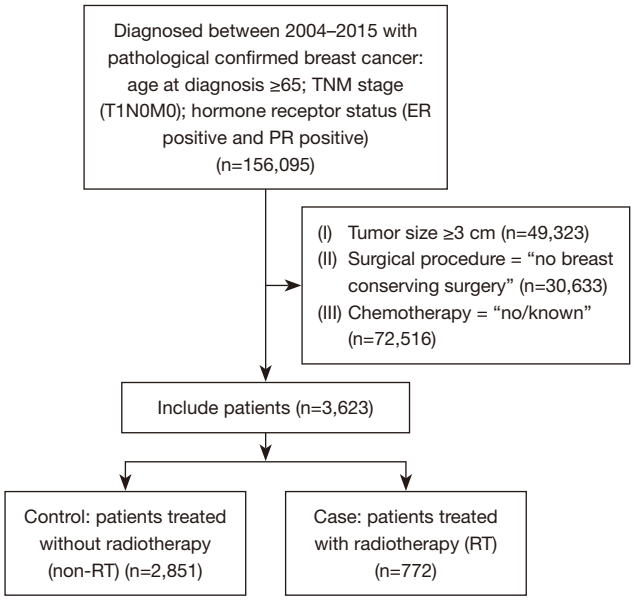

Figure 1 Flow diagram of study cohort selection. ER, estrogen receptor; PR, progesterone receptor.

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Methods

Study population and data sources

The case list option for survival in the SEER*Stat software program was used to retrieve the patient list from the SEER 18 database. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). To be eligible for inclusion in the cohort study, patients had to meet the following inclusion criteria: (I) be male or female; (II) be aged ≥65 years; (III) have been site coded (breast) and pathologically diagnosed as having a malignant tumor; (IV) be stage T1N0M0; (V) have been diagnosed between 2004 and 2015; (VI) be ER^+/PR^+; and (VII) have undergone adjuvant chemotherapy after BCS. The follow-up cut-off was 31 December 2016. The following clinical factors were analyzed: age, marital status, histology, race, grade, HER2, subtype, the way of treatment.

In our study, the primary endpoints were OS and breast cancer-specific survival (BCSS). OS was defined as the time from the date of diagnosis to the date of death from all causes or the last follow-up. BCSS was defined as the time from the date of diagnosis to the date of death from breast cancer or the last follow-up.

PSM

PSM is an instrument used to reduce selection bias in non-randomized studies and to achieve balanced covariates between treatment groups (14). The ratio of RT group to non-RT group was 4:1, in order to reduce selection bias, our study used PSM to create a matched data set in which the covariables were age, marital status, race, histology, tumor grade, HER2 status, subtype, and treatment choice (i.e., RT or no RT). PSM was then performed using nearest neighbor matching (at a 1:1 ratio) to create matching pairs between the RT and non-RT groups.

Statistical analysis

Stata13 software was used for the statistical analysis, and the chi-square test was both used to examine differences in the demographic characteristics and tumor characteristics between the RT and non-RT groups before and after PSM. The Kaplan-Meier method was also both used to evaluate OS and BCSS, and the log-rank test was used to evaluate survival differences before and after PSM. The Cox proportional risk regression model was both used to conduct the univariate and multivariate analyses of OS and BCSS in patients aged ≥65 years who were treated with RT after BCS before and after PSM. The multivariable Cox regression analysis adjusting for other prognostic factors including age, marital status, histology, race, grade, HER2, subtype and chemotherapy were performed to evaluate the effect of treatment type on OS and BCSS. The effects of treatment style on OS and BCSS were evaluated using hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical significance was defined as a two-sided P value <0.05.

Results

Patient demographic and clinical characteristics

We identified 3,623 patients with T1N0M0 stage, who were aged ≥65 years, had a primary mass <3 cm, had ER^+/PR^+ status, and who received adjuvant chemotherapy after BCS from 2004 to 2015 in the SEER database. The patients were divided into the following 2 groups: (I) the RT group (n=2,851); and (II) the non-RT group (n=772) (see *Figure 1*). *Table 1* sets out the demographic, oncological, and therapeutic characteristics of the patients. Due to the significant differences between the 2 groups, PSM was used to balance the distribution of the demographic and clinical features. Before PSM, the age group, marital

Table 1 Demographics and tumor characteristics in the SEER database study population for study groups before and after PSM

Variables	Before PSM (n=3,623), n (%)			After PSM (n=1,538), n (%)		
	Yes	No	P value	Yes	No	P value
Age group			<0.001			0.317
65–69 years	1,662 (58.30)	379 (49.09)		402 (52.28)	379 (49.28)	
70–74 years	782 (27.43)	246 (31.87)		219 (28.48)	246 (31.99)	
≥75 years	407 (14.28)	147 (19.04)		148 (19.25)	144 (18.73)	
Race			0.739			0.967
White	2,426 (85.09)	665 (86.14)		660 (85.83)	663 (86.22)	
Black	250 (8.77)	58 (7.51)		62 (8.06)	57 (7.41)	
Other	171 (6.00)	48 (6.22)		46 (5.98)	48 (6.24)	
Unknown	4 (0.14)	1 (0.13)		1 (0.13)	1 (0.13)	
Marital status			0.004			0.362
Unmarried	1,061 (37.22)	333 (43.13)		311 (40.44)	331 (43.04)	
Married	1,689 (59.24)	406 (52.59)		431 (56.05)	405 (52.67)	
Unknown	101 (3.54)	33 (4.27)		27 (3.51)	33 (4.29)	
Histology			0.551			0.659
IDC	2,299 (80.64)	605 (78.37)		598 (77.76)	604 (78.54)	
ILC	180 (6.31)	52 (6.74)		56 (7.28)	52 (6.76)	
IDC + ILC	169 (5.93)	52 (6.74)		44 (5.72)	52 (6.76)	
Other	203 (7.12)	63 (8.16)		71 (7.93)	61 (7.93)	
Grade			0.766			0.962
1	443 (15.54)	123 (15.93)		116 (15.08)	122 (15.86)	
2	1,347 (47.25)	361 (46.76)		369 (47.98)	360 (46.81)	
3 or 4	991 (34.76)	264 (34.20)		261 (33.94)	263 (34.20)	
Unknown	70 (2.46)	24 (3.11)		23 (2.99)	24 (3.12)	
HER2 status			0.021			0.188
Negative	1,002 (35.15)	272 (35.23)		265 (34.46)	272 (35.37)	
Positive	709 (24.87)	226 (29.27)		201 (26.14)	226 (29.39)	
Unknown	1,140 (39.99)	274 (35.49)		303 (39.40)	271 (35.24)	
Subtype			0.021			0.188
Luminal A	1,002 (35.15)	272 (35.23)		265 (34.46)	272 (35.37)	
Luminal B	709 (24.87)	226 (29.27)		201 (26.14)	226 (29.39)	
Unknown	1,140 (39.99)	274 (35.49)		303 (39.40)	271 (35.24)	

PSM, propensity score matching; SEER, Surveillance, Epidemiology, and End Results; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2.

status, HER2 status, and tumor subtype in patients differed significantly between the 2 groups, but the other clinical and pathological indicators did not differ significantly between the 2 groups. There were no significant differences in the clinical and pathological indicators between the 2 groups after PSM. A large proportion of the patients (78.69%) received RT after BCS. Most of the patients had invasive ductal carcinoma (IDC) (80.15%), and middle- and high-grade breast cancer (G2: 47.14%, G3/G4: 34.64%). A relatively high proportion of patients had the luminal A subtype (35.16% *vs.* 25.18%) (see *Table 1*).

Survival analyses in the whole SEER cohort

We investigated the prognostic factors for OS and BCSS in patients with breast cancer aged ≥65 years after BCS. The univariate Cox regression analysis revealed that other than histology, the rest of the variables were significantly associated with OS, but only age, marital status, grade, and RT were significantly associated with BCSS (see *Table 2*). The results showed that patients treated with RT had superior OS and BCSS than those who did not receive adjuvant RT (OS: HR 0.48, 95% CI: 0.39–0.59, P<0.001; and BCSS: HR 0.39, 95% CI: 0.27–0.57, P<0.001).

The results of the multivariate Cox regression analysis were consistent with those of the univariate analysis. In the multivariate analysis, the patients treated with RT also had a longer survival time than those who did not receive adjuvant RT (OS: HR 0.51, 95% CI: 0.42–0.62, P<0.001, and BCSS: HR 0.40, 95% CI: 0.27–0.58, P<0.001; see *Table 2*). The Kaplan-Meier analysis showed that patients aged ≥65 years who received RT after BCS had a longer survival time than those who did not (see *Figure 2A*,*2B*).

Survival analysis in the PSM cohort

The univariate analysis showed that the prognostic factors for OS were age, marital status, grade, and RT, but only age, grade and RT were significantly associated with BCSS (see *Table 3*). The multivariate analysis showed that the prognostic factors for OS, including age, marital status, HER2 status, tumor subtype, RT, while age, grade, HER2 status, tumor subtype, RT were significantly associated with BCSS. Additionally, the univariate and multivariate analyses showed that patients who received RT survived significantly longer than those who did not (OS: HR 0.73, 95% CI: 0.56–0.94, P=0.017; HR 0.73, 95% CI: 0.57–0.95, P=0.018; and BCSS: HR 0.58, 95% CI: 0.36–0.95, P=0.030; HR 0.57, 95% CI: 0.35–0.93, P=0.025; see *Table 3*). The survival curves also showed that patients who received RT after BCS had a longer survival time than those who did not receive RT after BCS (see *Figure 3A*,*3B*).

Subgroup analysis

To identify the specific subgroups that could benefit from RT, we further stratified the PSM-matched patients by age, histology, HER2 status, and tumor subtype. In the three age subgroups, there were no significant differences between the RT and non-RT groups (see *Figure 4*). However, RT provided a significant survival advantage in the invasive lobular carcinoma (ILC) and tumor grade 2 subgroups (see *Figure 5A*,*5B*). In the subgroup of HER2 status and subtype, the survival rate of patients who received RT was higher than those who did not receive RT in the luminal A type and HER2 negative subgroup (see *Figure 5C*,*5D*).

Discussion

Breast cancer, lung cancer, and colorectal cancer, are the three most common cancers in women worldwide (1). The global incidence of breast cancer ranges from 27 per 100,000 in Africa and East Asia to 97 per 100,000 in North America, which suggests that its incidence is correlated to economic development and social and lifestyle factors (15). In recent years, the mortality rate of breast cancer patients has decreased in some regions and countries, which may be attributed to early prevention, diagnosis, and treatment (16,17). Currently, there is no clear definition of early breast cancer. Most scholars believe that tumors in early breast cancer should be <2 cm, the metastatic axillary lymph node should not be involved, and there should be no distant metastasis (18). Elderly patients often have relatively more favorable biological characteristics than younger patients; however, due to their hormone receptor status, tumor grade, and proliferation rate at the time of diagnosis, most elderly breast cancer patients are in the advanced stage (19).

Local treatment methods for early breast cancer include BCS, mastectomy, and postoperative RT, and systemic treatments include endocrine therapy and postoperative chemotherapy (18,20). RT after BCS is the standard of treatment, and has a survival rate comparable to that of mastectomy for early breast cancer (21). Due to improvements in modern imaging technology, the dose of RT can be controlled with increasing accuracy, but the adjacent organs and tissues are irradiated and damaged to

Table 2 Univariate and multivariate analyses of OS and BCSS in the BCS patients before PSM

Variables	Univariate analysis				Multivariate analysis			
	BCSS		OS		BCSS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age group								
65–69 years	Reference	–	Reference	–	Reference	–	Reference	–
70–74 years	1.32 (0.85–2.03)	0.211	1.92 (1.53–2.40)	<0.001	1.26 (0.82–1.95)	0.294	1.87 (1.49–2.34)	<0.001
≥75 years	1.47 (1.17–1.84)	0.001	1.78 (1.58–1.99)	<0.001	1.45 (1.16–1.83)	0.001	1.71 (1.52–1.93)	<0.001
Race								
White	Reference	–	Reference	–	Reference	–	Reference	–
Black	0.98 (0.50–1.94)	0.960	1.71 (1.28–2.28)	<0.001	0.88 (0.44–1.76)	0.722	1.56 (1.16–2.09)	0.003
Other	0.98 (0.67–1.44)	0.912	0.94 (0.76–1.16)	0.579	0.97 (0.66–1.42)	0.858	0.93 (0.75–1.15)	0.490
Unknown	–	–	–	–	–	–	–	–
Marital status								
Unmarried	Reference	–	Reference	–	Reference	–	Reference	–
Married	0.65 (0.45–0.94)	0.021	0.63 (0.52–0.76)	<0.001	0.70 (0.48–1.02)	0.064	0.72 (0.59–0.87)	<0.001
Unknown	0.83 (0.50–1.38)	0.479	0.86 (0.66–1.11)	0.235	0.83 (0.50–1.37)	0.462	0.85 (0.66–1.09)	0.200
Histology								
IDC	Reference	–	Reference	–	Reference	–	Reference	–
ILC	0.58 (0.58–2.26)	0.703	1.09 (0.76–1.58)	0.635	1.00 (0.50–1.99)	0.972	1.07 (0.74–1.55)	0.717
IDC + ILC	0.83 (0.55–1.26)	0.391	0.94 (0.78–1.14)	0.534	0.81 (0.54–1.23)	0.322	0.91 (0.75–1.10)	0.308
Other	0.90 (0.70–1.17)	0.432	1.01 (0.90–1.13)	0.850	0.90 (0.69–1.16)	0.405	0.98 (0.88–1.10)	0.741
Grade								
1	Reference	–	Reference	–	Reference	–	Reference	–
2	1.79 (0.91–3.53)	0.093	0.81 (0.63–1.03)	0.089	2.06 (1.03–4.13)	0.041	0.91 (0.70–1.17)	0.459
3 or 4	1.63 (1.16–2.29)	0.005	0.84 (0.73–0.96)	0.013	1.65 (1.16–2.34)	0.005	0.88 (0.76–1.02)	0.091
Unknown	1.43 (1.00–2.04)	0.050	1.13 (0.96–1.32)	0.138	1.56 (1.07–2.26)	0.021	1.19 (1.00–1.39)	0.039
HER2 status								
Negative	Reference	–	Reference	–	Reference	–	Reference	–
Positive	0.60 (0.29–1.26)	0.177	0.70 (0.47–1.04)	0.080	0.50 (0.24–1.05)	0.070	0.62 (0.41–0.92)	0.019
Unknown	1.12 (0.88–1.42)	0.355	1.56 (1.08–2.25)	0.018	1.11 (0.88–1.41)	0.378	1.01 (0.88–1.16)	0.840
Subtype								
Luminal A	Reference	–	Reference	–	Reference	–	Reference	–
Luminal B	0.60 (0.29–1.26)	0.177	0.70 (0.47–1.04)	0.080	0.50 (0.24–1.05)	0.070	0.62 (0.41–0.92)	0.019
Unknown	1.06 (0.94–1.19)	0.355	1.16 (1.03–1.31)	0.018	1.11 (0.88–1.41)	0.378	1.01 (0.88–1.16)	0.840
Radiation								
No	Reference	–	Reference	–	Reference	–	Reference	–
Yes	0.39 (0.27–0.57)	<0.001	0.48 (0.39–0.59)	<0.001	0.40 (0.27–0.58)	<0.001	0.51 (0.42–0.62)	<0.001

BCS, breast-conserving surgery; BCSS, breast cancer-specific survival; CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; OS, overall survival; PSM, propensity score matching.

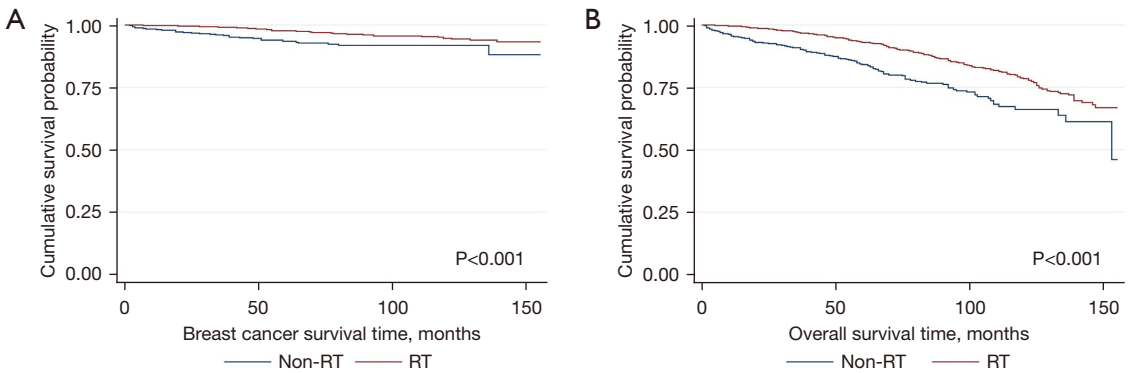

Figure 2 The Kaplan-Meier analysis showed that the RT cohort had a longer survival time than the non-RT cohort before PSM. BCSS (A) and OS (B) curves of the RT cohort *vs.* the non-RT cohort before PSM. BCSS, breast cancer-specific survival; OS, overall survival; PSM, propensity score matching; RT, radiotherapy.

a certain extent. For most patients, the benefits of RT far exceed the risks; however, RT for low-risk breast cancer patients following BCS may pose an unreasonable risk of side effects in elderly patients with a brief life expectancy. Additionally, given the economic costs of RT and the presence of comorbidities in most elderly patients, adjuvant RT after BCS should not be administered when its absolute benefit to patients is very small.

In this study, we screened 3,623 patients aged ≥65 years diagnosed with T1N0M0 from 2004 to 2015 identified in the SEER database and matched by PSM. The patients were divided into RT and non-RT groups. Stata software was used for the data analysis. The univariate and multivariate analyses showed that there were significant differences in OS and BCSS between the RT and non-RT groups. The survival curve analysis suggested that the elderly breast cancer patients in the RT group had better OS and BCSS than those in the non-RT group. However, among the patients aged ≥65 years, there was no significant difference in the survival time between the RT and non-RT groups in the age subgroup analysis.

The survival curve analysis showed that RT failed to improve the OS and BCSS (BCSS: P=0.108, OS: P=0.050) of patients in the 65–69-year-old subgroup. Our research results support those of previous studies (12,22-24). For example, Clement *et al.* found that women aged >65 years had a similar incidence of LR in RT and non-RT groups (5.8% *vs.* 5%, P=0.838) (22). Similarly, Wu *et al.* (23) found that postoperative RT did not improve BCSS rates compared to no RT (P=0.134). Additionally, a study published in the *European Journal of Surgical Oncology* indicated that BCS and endocrine therapy without RT appeared to be safe treatment options for women aged ≥65 years with early breast cancer and favorable histopathology (24). However, our results showed that the P value of OS between the 2 groups approached 0.05, which is a critical state that indicates a significant difference. Thus, careful consideration should be given as to whether to administer breast-conserving postoperative RT based on the individual condition of each patient.

The survival curves in the subgroups of patients aged 70–74 years and those aged ≥75 years revealed no significant difference between the RT and non-RT groups in terms of OS and BCSS (BCSS: P=0.144, P=0.514; OS: P=0.438, P=0.259). These research results were consistent with the study of CALGB-9493 (9), which suggested that RT be omitted in patients aged >70 years, an approach that has been adopted by the NCCN guidelines. Stueber *et al.* analyzed patients aged ≥70 years suffering from low-risk early breast cancer treated with guideline adherent (GA)-BCS and suggested that they could avoid breast irradiation with a <3% chance of relapse (25).

In summary, our research results are consistent with the recommendations set out in the NCCN guidelines; that is, we found that RT can be omitted in patients with low-risk breast cancer aged ≥70 years. Our study demonstrated that ILC was a significant factor determining the OS benefits derived from RT. ILC depends on hormonal status, is more common in older aged patients, and tends to be multicentric, ER^+/PR^+, and HER2-negative. The results in patients with luminal A and HER2 negative were analogous. A previous study showed that patients with ILC had better disease-specific survival and disease-free survival rates than those with IDC (26).

Table 3 Univariate and multivariate analyses of OS and BCSS in the BCS patients after PSM

Variable	Univariate analysis				Multivariate analysis			
	BCSS		OS		BCSS		OS	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age group								
65–69 years	Reference	–	Reference	–	Reference	–	Reference	–
70–74 years	1.27 (0.71–2.27)	0.428	1.94 (1.42–2.65)	<0.001	1.24 (0.69–2.23)	0.473	1.90 (1.39–2.61)	<0.001
≥75 years	1.50 (1.12–2.00)	0.006	1.78 (1.52–2.09)	<0.001	1.49 (1.12–2.00)	0.007	1.73 (1.47–2.03)	<0.001
Race								
White	Reference	–	Reference	–	Reference	–	Reference	–
Black	0.54 (0.17–1.73)	0.302	1.49 (1.00–2.23)	0.052	0.46 (0.14–1.47)	0.189	1.27 (0.84–1.92)	0.260
Other	1.08 (0.68–1.71)	0.738	0.91 (0.68–1.22)	0.523	1.07 (0.68–1.70)	0.761	0.89 (0.66–1.19)	0.434
Unknown	–	–	–	–	–	–	–	–
Marital status								
Unmarried	Reference	–	Reference	–	Reference	–	Reference	–
Married	0.68 (0.42–1.10)	0.116	0.66 (0.51–0.85)	0.002	0.73 (0.45–1.20)	0.217	0.73 (0.56–0.95)	0.019
Unknown	0.74 (0.36–1.50)	0.399	0.76 (0.53–1.09)	0.138	0.74 (0.36–1.51)	0.412	0.79 (0.55–1.13)	0.194
Histology								
IDC	Reference	–	Reference	–	Reference	–	Reference	–
ILC	1.12 (0.48–2.61)	0.791	1.22 (0.78–1.90)	0.379	1.03 (0.44–2.40)	0.948	1.24 (0.79–1.93)	0.346
IDC + ILC	0.75 (0.42–1.34)	0.334	0.91 (0.70–1.18)	0.478	0.72 (0.40–1.30)	0.275	0.88 (0.67–1.16)	0.365
Other	0.86 (0.61–1.21)	0.380	1.00 (0.86–1.16)	0.949	0.87 (0.62–1.22)	0.407	0.94 (0.81–1.10)	0.451
Grade								
1	Reference	–	Reference	–	Reference	–	Reference	–
2	2.04 (0.79–5.28)	0.140	0.76 (0.55–1.05)	0.095	2.41 (0.90–6.41)	0.079	0.83 (0.59–1.17)	0.287
3 or 4	1.88 (1.17–3.01)	0.009	0.81 (0.68–0.98)	0.028	1.91 (1.17–3.13)	0.010	0.83 (0.68–1.01)	0.070
Unknown	0.98 (0.48–2.00)	0.952	0.86 (0.61–1.21)	0.427	1.06 (0.49–2.31)	0.874	0.94 (0.73–1.21)	0.657
HER2 status								
Negative	Reference	–	Reference	–	Reference	–	Reference	–
Positive	0.90 (0.37–2.19)	0.810	0.69 (0.42–1.14)	0.147	0.76 (0.31–1.90)	0.557	0.68 (0.41–1.13)	0.019
Unknown	1.38 (0.99–1.91)	0.057	1.09 (0.92–1.31)	0.322	1.40 (1.00–1.94)	0.047	1.08 (0.90–1.29)	0.388
Subtype								
Luminal A	Reference	–	Reference	–	Reference	–	Reference	–
Luminal B	0.90 (0.37–2.19)	0.810	0.69 (0.42–1.14)	0.147	0.76 (0.31–1.90)	0.557	0.68 (0.41–1.13)	0.019
Unknown	1.38 (0.99–1.91)	0.057	1.09 (0.92–1.31)	0.322	1.40 (1.00–1.94)	0.047	1.08 (0.90–1.29)	0.388
Radiation								
No	Reference	–	Reference	–	Reference	–	Reference	–
Yes	0.58 (0.36–0.95)	0.030	0.73 (0.56–0.94)	0.017	0.57 (0.35–0.93)	0.025	0.73 (0.57–0.95)	0.018

BCS, breast-conserving surgery; BCSS, breast cancer-specific survival; CI, confidence interval; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; OS, overall survival; PSM, propensity score matching.

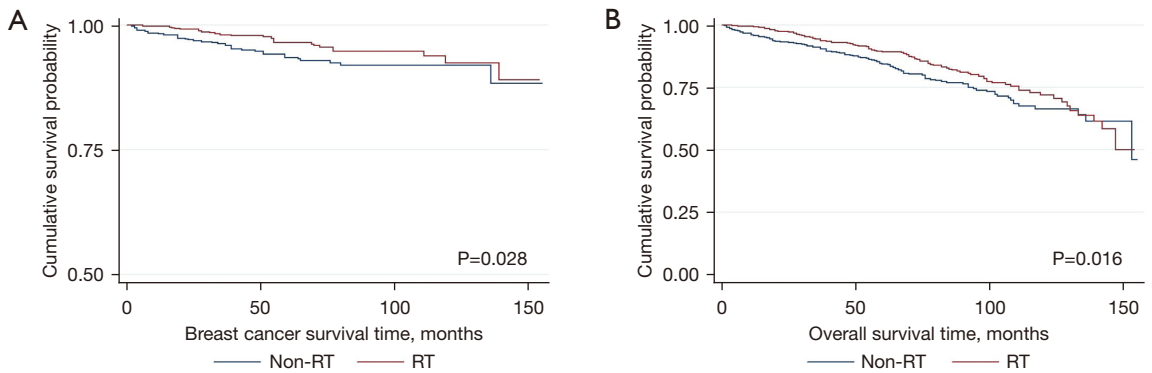

Figure 3 The Kaplan-Meier analysis showed that the RT cohort had a longer survival time than the non-RT cohort after PSM. BCSS (A) and OS (B) curves of the RT cohort *vs.* the non-RT cohort after PSM. BCSS, breast cancer-specific survival; OS, overall survival; PSM, propensity score matching; RT, radiotherapy.

In studies of elderly patients with breast cancer, different thresholds have been used to define old age, including >50 years (27), 55 years (28), 65 years (12), or 70 years (29). One study (30) showed that breast cancer patients aged ≥80 years received less treatment than younger patients, but had a higher cancer-specific mortality rate. The NCCN recommends selective RT for women aged ≥70 years with stage I breast cancer (31). The International Society of Geriatric Oncology, the European Association of Breast Cancer Specialists, and the 14th St. Gallen International Breast Cancer Conference all suggest that RT shouldn't be omitted based solely on age (29,32). Thus, unless the patient has a short life expectancy or comorbidities, the omission of RT in elderly and low-risk patients should only be considered if the absolute benefit of postoperative RT is minimal and consideration should also be given to each patient's hormonal status, tumor size, and tumor grade. There is a general need to decrease treatment for aged patients in clinical practice (28,33). However, low-risk elderly breast cancer should not be under-treated to address issues of over-treatment, and patients who receive RT should be carefully selected.

Our study had a number of limitations, as the data collected from the registry lacked comprehensive clinical information. First, as no information was provided in the SEER 18 database on hormone therapy, it was not possible to evaluate its effects. However, as hormone therapy is the standard treatment for patients with HR^+ breast cancer, it is likely that the majority of these patients received hormone therapy. Second, there was no information regarding LR or distant metastasis in the database. Additionally, while the chemotherapy data of patients could be screened out from the database, information on patients' exact chemotherapy regimens could not be obtained. Finally, there is currently no information in the database on comorbidities, lymphatic vascular invasion, surgical margin status, HER2 status, and radiation dose. Additionally, PSM has some limitations. First, PSM cannot solve the endogenous problems caused by selection bias or omitted variables. Second, PSM cannot be called a quasi-experiment, nor can it simulate experimental conditions. Finally, PSM systematically excludes samples lacking control groups, which worsened the sample representativeness and affected the external validity of the research results.

Conclusions

In conclusion, in elderly patients aged ≥65 years with ER^+/PR^+ early-stage breast cancer (T1N0M0), receiving RT did not improve the BCSS and OS of patients in different age groups; thus, omitting RT is a possible treatment option for such patients. However, in patients with a histology of ILC, tumor grade 2, luminal A type, and $HER2^-$, RT significantly increased the patients' BCSS and OS. Additionally, in the age subgroup of 65–69 years, due to its particularity, omitting RT should only be considered with caution.

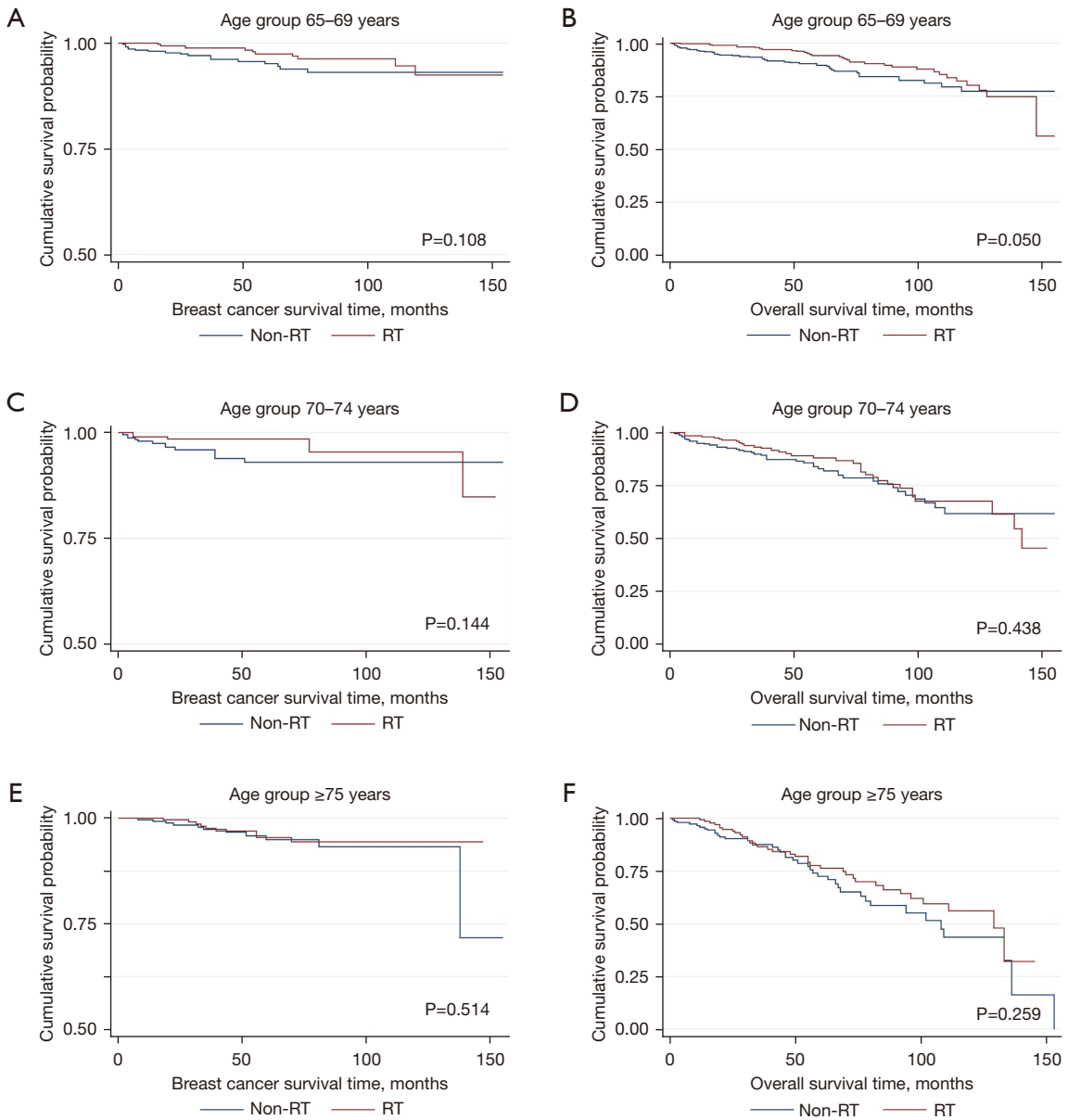

Figure 4 No significant differences were found between the RT and non-RT groups. BCSS (A) and OS (B) curves of the 65–69-year-old subgroup with or without RT after PSM. BCSS (C) and OS (D) curves of the 70–74-year-old subgroup with or without RT after PSM. BCSS (E) and OS (F) curves of ≥75-year-old subgroup with or without RT after PSM. BCSS, breast cancer-specific survival; OS, overall survival; PSM, propensity score matching; RT, radiotherapy.

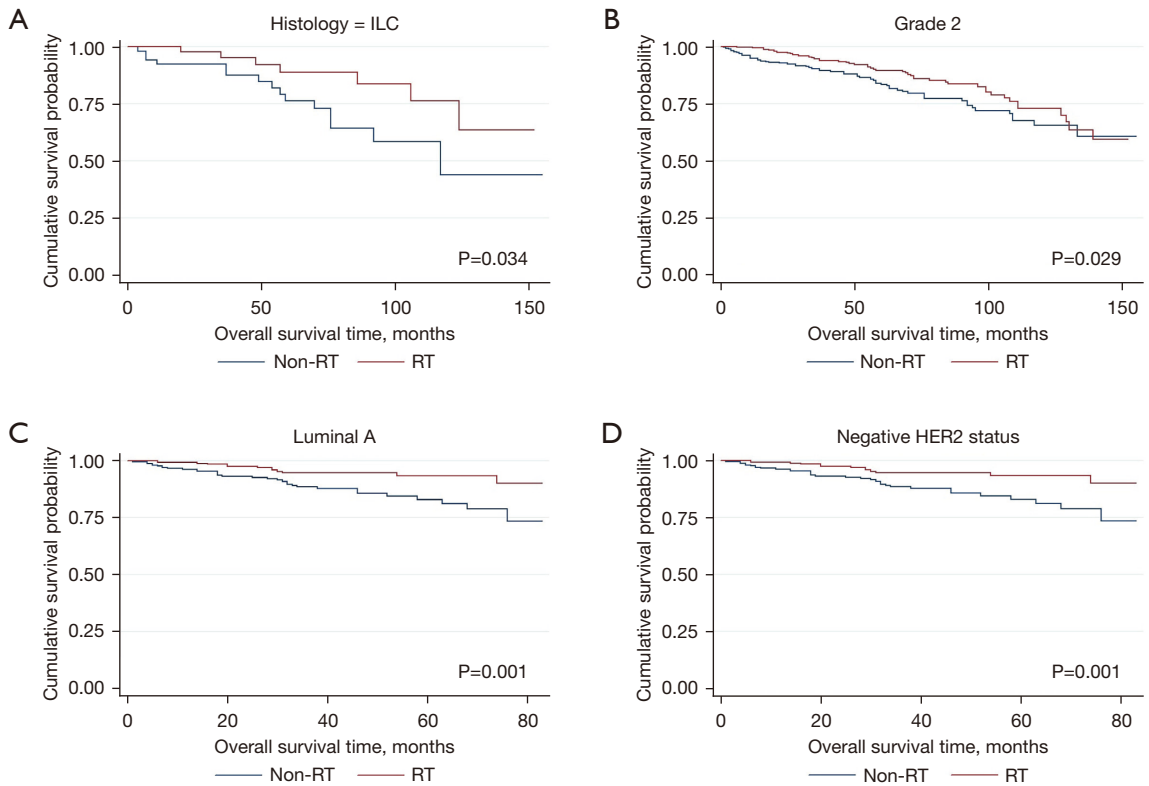

Figure 5 RT maintained a significant survival advantage in the ILC, grade 2, luminal A and HER2 negative subgroups. (A) OS curves of ILC subgroup with or without RT after PSM. (B) OS curves of tumor grade 2 subgroup with or without RT after PSM. (C) OS curves of luminal A subgroup with or without RT after PSM. (D) OS curves of HER2 negative status subgroup with or without RT after PSM. HER2, human epidermal growth factor receptor 2; ILC, invasive lobular carcinoma; OS, overall survival; PSM, propensity score matching; RT, radiotherapy.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-22-235/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-235/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. As no experiments with human participants or animals were conducted in this study, ethical approval was not required. Informed consent was not obtained, as the data were obtained from the Surveillance Epidemiology and End Results registry. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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