Original Article

Survival benefit of adjuvant chemotherapy in elderly patients with stage I triple-negative breast cancer: a cohort study based on the SEER database

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Background: This study analyzed the trend and prognostic role of postoperative adjuvant chemotherapy (POCT) in patients with stage I triple-negative breast cancer (TNBC) aged more than 65 years. In addition, the relationship between POCT and survival rate was also determined.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was collected to determine 3,307 TNBC elderly women aged ≥65 years between 2010 and 2016, and they were divided into POCT and non-POCT groups. Propensity score matching (PSM) method was used to offset the differences in baseline characteristics between the groups. Kaplan-Meier plots were tested to contrast overall survival (OS) and breast cancer-specific survival (BCSS) between the two groups. The Cox proportional hazard model was constructed to assess the prognostic factors affecting OS and BCSS.

Results: Younger age, higher histological grade, married, postoperative radiotherapy, lumpectomy, larger tumor, and closer year of diagnosis were related to an enhanced likelihood of adjuvant chemotherapy. After PSM, POCT was related to increased 5-year OS [hazard ratio (HR): 0.571, 95% confidence interval (CI): 0.432–0.753, respectively], without significant difference in BCSS improvement. Exploratory subgroup analysis demonstrated that POCT contributed to OS improvement in both IA and IB patients, but did not improve BCSS in IA and IB patients.

Conclusions: In elderly patients ≥65 years, POCT improved 5-year OS in stage I TNBC patients, while further exploration with larger prospective trials are needed.

Keywords: Triple-negative breast cancer (TNBC); adjuvant chemotherapy; elderly women; survival

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Introduction

Triple-negative breast cancer (TNBC), lacking estrogen receptor (ER) and progesterone receptor (PR) expression and human epidermal growth factor receptor 2 (HER2) gene amplification, accounting for 15–20% of all breast cancers, is the most destructive breast cancer with poor prognosis (1-3). TNBC cannot take advantage of targeted therapy and endocrine therapy without valuable therapeutic targets, and postoperative adjuvant chemotherapy (POCT) remains a helpful treatment for TNBC (4). According to current recommendations, most early TNBC patients should receive adjuvant chemotherapy (5). The National Comprehensive Cancer Network (NCCN) adopts adjuvant chemotherapy

as standard treatment for all lymph node positive and node-negative TNBC patients with a primary tumor above 1 cm. For TNBC patients with a diameter of less than 1 cm without lymph node metastasis, NCCN guidelines usually do not recommend adjuvant chemotherapy for T1a-TNBC, and for T1b-TNBC, the chemotherapy recommendation is not clear, suggesting that 'consider' adjuvant chemotherapy (4,6,7). The Chinese Society of Clinical Oncology (CSCO) guidelines suggest that all TNBC patients should receive POCT without any specific recommendations (6,8).

Around 40% of breast cancers are found in people over 65 years old, which has been an upward trend recently (9). Due to factors such as short life expectancy and many complications, clinical trials are generally excluded from the elderly population. Adjuvant chemotherapy is not widely studied in elderly women with breast cancer, and insufficient data are collected to support definitive chemotherapy recommendations. The effect of POCT in elderly patients with stage I TNBC has become a clinical issue. We explored the correlation between POCT and survival outcomes in stage I TNBC patients ≥65 years old based on large-scale Surveillance, Epidemiology, and End Results (SEER) database, providing a theoretical basis for clinical practice. We present this article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-123/rc).

Highlight box

Key findings

- In elderly patients ≥65 years, postoperative adjuvant chemotherapy (POCT) improved overall survival (OS) in stage I triple-negative breast cancer (TNBC) patients.

What is known and what is new?

- The National Comprehensive Cancer Network (NCCN) adopts adjuvant chemotherapy as standard treatment for all lymph node positive and node-negative TNBC patients with a primary tumor above 1 cm.
- There is no prospective or retrospective study to evaluate the survival outcomes of POCT for stage I TNBC older patients. Therefore, this study collected the patients of seer database above 65 years with stage I TNBC to analyze the correlation between their receipt of POCT and survival outcomes.

What is the implication, and what should change now?

- In our study, elderly female patients appeared to benefit from POCT. POCT may be a promising tool for elderly female patients with stage I TNBC in the future.

Methods

Data sources

The data are derived from the SEER database, a publicly available resource for cancer research in the USA. The SEER database gathers cancer cases data since 1973, including 18 cancer registration centers, covering about 28% of the population in the USA. We recruited the SEER*Stat software 8.3.6 to obtain the variables.

Study population

We retrospectively reviewed all information on patients with primary breast cancer from the SEER database between 2010 and 2017, and gathered pertinent pathology, population, and survival data. The inclusion criteria were as follows: (I) female patients aged ≥65 years; (II) TNBC subtype (negative expression of ER, PR, and HER2); (III) diagnosis of tumor stage I based on the 7th edition of the American Joint Committee on Cancer (AJCC) stage (converting 2016–2017 UICC stage to 7th edition AJCC stage); (IV) previous lumpectomy or mastectomy; (V) infiltrating carcinoma as the histology type (International Classification of Disease, 3rd edition, ICD-O-3 code 8500/3, 8522/3 and 8523/3). For better analysis, all quantitative data were converted to categorical variables using the X-tile software.

Statistical analysis

The study population was divided into POCT and non-POCT groups. Our outcomes included overall survival (OS) and breast cancer-specific survival (BCSS). OS was described as the interval from diagnosis to death, and BCSS as the period from diagnosis to the date of death from breast cancer. Univariate analysis was employed to assess risk factors related to chemotherapy ($P<0.05$), and multivariate stepwise logistic regression models were constructed based on univariate analyses ($P<0.05$). We carried out propensity score matching (PSM) to eliminate heterogeneity between the two groups. POCT groups and non-POCT groups were matched by nearest neighbor with caliper value of 0.01 in a 1:1 ratio. Kaplan-Meier plots were tested to compare OS and BCSS between POCT and non-POCT groups to determine survival differences, and log-rank tests were used to compare survival distributions. Subgroup analysis of the effects of OS and BCSS on the two groups

at different stages was carried out. Z test was performed to compare survival 5-year OS and BCSS rates between stage IA and stage IB tumors. Univariate and multivariate Cox proportional risk regression models were constructed to assess prognostic factors related to survival. All analyses were carried out with R 4.1.2 software, and P values <0.05 was regarded as statistically significant differences. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Results

Patient baseline characteristics

A total of 3,307 female TNBC patients aged ≥65 years were enrolled in this study, of whom 1,653 (50.0%) received chemotherapy and 1,985 (60.0%) received radiotherapy. The median survival time was 48 (range, 0–107) months. There were 1,281 (38.7%) patients aged 65–69 years, 948 (28.7%) patients aged 70–74 years, 614 (18.6%) patients aged 75–79 years, and 464 (14.0%) patients aged ≥80 years. In terms of the clinical stage of breast cancer, 3,216 (97.2%) patients had stage IA, 91 (2.8%) patients had stage IB. In addition, 1,748 (52.9%) of the patients were married. Their demographic and clinicopathologic characteristics are described in *Table 1*.

Predictors of POCT

The use of chemotherapy decreased with age in older patients. 68.2% of those aged 65–69, 54.2% of those aged 70–74, 34.0% of those aged 75–79, and 12.1% of those older than 80 received POCT. In multivariate analysis, younger age (P<0.001), higher tumor grade (P<0.001), married (P<0.001), postoperative radiotherapy (P<0.001), lumpectomy (P=0.014), larger tumor size (P<0.001), and recent year of diagnosis (P=0.030) were related to an added likelihood of receiving POCT. Univariate and multivariate logistic regressions of POCT outcomes, demographics and clinical characteristics of the study population are demonstrated in *Table 1*.

Survival outcomes

Obvious differences were shown between the POCT group and the non-POCT group at baseline for the original data in terms of age (P<0.001), marital status (P<0.001), year of diagnosis (P=0.003), grade (P<0.001), tumor size (P<0.001), type of surgery (P<0.001), and radiotherapy (P<0.001). We used PSM to eliminate the interference and balanced the heterogeneity. After PSM, the baseline data were essentially the same in the two groups (P>0.05), demonstrating that the variables were offsetting. Ultimately, 1,842 patients were enrolled, half of whom received chemotherapy. Their demographic and clinical characteristics before and after PSM treatment are demonstrated in *Table 2*.

The median follow-up time was 51 (range, 2–107) months and 51 (range, 0–107) months for the POCT and non-POCT groups, respectively. We evaluated OS and BCSS before and after PSM for TNBC patients at stage I using the Kaplan-Meier method. Overall, POCT notably improved OS (before PSM: P<0.0001, after PSM: P<0.0001) (*Figure 1*) rather than BCSS (before PSM: P=0.42, after PSM: P=0.26) (*Figure 1*). Before PSM, 5-year OS of the POCT group and the non-POCT group were 90.9% and 82.6%, respectively (P<0.001), while 5-year BCSS was similar, 94.2% and 93.4%, respectively (P=0.42); after PSM, the 5-year OS was 90.0% and 83.0% in the POCT and non-POCT groups, respectively (P<0.001), while the 5-year BCSS was similar in the POCT and non-POCT groups, 94.4% and 92.5%, respectively (P=0.26) (*Table 3*).

Subgroup analysis

We conducted a subgroup analysis to determine the impact of prognostic causes. Before PSM, POCT could improve OS (P<0.0001) but not BCSS (P=0.64) in patients with stage IA TNBC (*Figure 2A*,*2B*). After PSM, for TNBC patients in stage IA, POCT could improve OS in stage IA (P=0.00035) and could not improve BCSS (P=0.47) (*Figure 2C*,*2D*). Before PSM, for TNBC patients in stage IB, POCT could improve OS (P=0.0046) and BCSS (P=0.048) (*Figure 3A*,*3B*). After PSM, POCT could improve OS (P=0.0058), the improvement of BCSS was not statistically significant (P=0.053) (*Figure 3C*,*3D*).

Cox proportional hazards models for OS and BCSS

The correlation between clinical characteristics and OS, BCSS was shown using univariate and multifactorial Cox proportional risk regression models (*Table 4*). After PSM matching, univariate Cox regression showed that age (P<0.001), chemotherapy (P<0.001), marital status (P<0.001), race (P=0.005), radiotherapy (P=0.006), tumor stage (P<0.001), and tumor size (P<0.001) were significant factors affecting TNBC patients' predictors of OS. Age

Table 1 Univariate and multivariate logistic regressions of POCT outcomes, demographics and clinicopathologic characteristics of the study population

Variables	Case (%)	POCT		Univariable analysis			Multivariable analysis		
		No, n (%)	Yes, n (%)	OR	95% CI	P	OR	95% CI	P
Age (years)									
65–69	1,281 (38.7)	407 (31.8)	874 (68.2)		1 (reference)			1 (reference)	
70–74	948 (28.7)	434 (45.8)	514 (54.2)	0.552	0.464–0.656	<0.001	0.535	0.445–0.643	<0.001
75–79	614 (18.6)	405 (66.0)	209 (34.0)	0.240	0.196–0.295	<0.001	0.228	0.184–0.284	<0.001
80+	464 (14.0)	408 (87.9)	56 (12.1)	0.064	0.047–0.087	<0.001	0.056	0.041–0.077	<0.001
Grade									
I/II	1,063 (32.1)	642 (60.4)	421 (39.6)		1 (reference)			1 (reference)	
III/IV	2,244 (67.9)	1,012 (45.1)	1,232 (54.9)	1.856	1.600–2.153	<0.001	1.648	1.391–1.952	<0.001
Laterality									
Left	1,667 (50.4)	822 (49.3)	845 (50.7)		1 (reference)				
Right	1,640 (49.6)	832 (50.7)	808 (49.3)	0.945	0.824–1.083	0.414			
Marital status									
Married	1,748 (52.9)	767 (43.9)	981 (56.1)		1 (reference)			1 (reference)	
Unmarried	1,559 (47.1)	887 (56.9)	672 (43.1)	0.592	0.516–0.680	<0.001	0.731	0.624–0.857	<0.001
Race recode									
Black	548 (16.6)	255 (46.5)	293 (53.5)		1 (reference)				
White	2,539 (76.8)	1,284 (50.6)	1,255 (49.4)	0.851	0.707–1.024	0.087			
Other	220 (6.7)	115 (52.3)	105 (47.7)	0.795	0.581–1.087	0.150			
Radiation after surgery									
No	1,322 (40.0)	758 (57.3)	564 (42.7)		1 (reference)			1 (reference)	
Yes	1,985 (60.0)	896 (45.1)	1,089 (54.9)	1.633	1.420–1.880	<0.001	1.561	1.309–1.862	<0.001
Regional nodes examined									
>2	1,477 (44.7)	720 (48.7)	757 (51.3)		1 (reference)			1 (reference)	
1	976 (29.5)	517 (53.0)	459 (47.0)	0.844	0.718–0.993	0.041	0.831	0.690–1.001	0.051
2	854 (25.8)	417 (48.8)	437 (51.2)	0.997	0.842–1.180	0.97	0.977	0.805–1.186	0.815
Stage									
IA	3,216 (97.2)	1,617 (50.3)	1,599 (49.7)		1 (reference)				
IB	91 (2.8)	37 (40.7)	54 (59.3)	1.476	0.966–2.255	0.072			
Surgery									
Lumpectomy	1,745 (52.8)	798 (45.7)	947 (54.3)		1 (reference)			1 (reference)	
Mastectomy	1,562 (47.2)	856 (54.8)	706 (45.2)	0.695	0.606–0.797	<0.001	0.806	0.679–0.957	0.014
Tumor size (cm)									
1< T ≤2	2,017 (61.0)	828 (41.1)	1,189 (58.9)		1 (reference)			1 (reference)	
T ≤1	1,290 (39.0)	826 (64.0)	464 (36.0)	0.391	0.339–0.452	<0.001	0.307	0.260–0.362	<0.001

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Case (%)	POCT		Univariable analysis			Multivariable analysis		
		No, n (%)	Yes, n (%)	OR	95% CI	P	OR	95% CI	P
Year of diagnosis									
2010–2013	1,599 (48.4)	843 (52.7)	756 (47.3)	1 (reference)			1 (reference)		
2014–2017	1,708 (51.6)	811 (47.5)	897 (52.5)	1.233	1.076–1.414	<0.001	1.191	1.017–1.394	0.030

POCT, postoperative adjuvant chemotherapy; OR, odds ratio; CI, confidence interval.

Table 2 Patients' demographic and clinicopathologic characteristics before and after PSM

Variables	Before PSM			After PSM		
	Non-POCT (n=1,654), n (%)	POCT (n=1,653), n (%)	P	Non-POCT (n=921), n (%)	POCT (n=921), n (%)	P
Age (years)			<0.001			0.786
65–69	407 (24.6)	874 (52.9)		357 (38.8)	368 (40.0)	
70–74	434 (26.2)	514 (31.1)		304 (33.0)	310 (33.7)	
75–79	405 (24.5)	209 (12.6)		195 (21.2)	187 (20.3)	
80+	408 (24.7)	56 (3.4)		65 (7.1)	56 (6.1)	
Marital status			<0.001			0.709
Married	767 (46.4)	981 (59.3)		484 (52.6)	493 (53.5)	
Unmarried	887 (53.6)	672 (40.7)		437 (47.4)	428 (46.5)	
Race recode			0.181			0.372
Black	255 (15.4)	293 (17.7)		152 (16.5)	170 (18.5)	
Other	115 (7.0)	105 (6.4)		62 (6.7)	70 (7.6)	
White	1,284 (77.6)	1,255 (75.9)		707 (76.8)	681 (73.9)	
Year of diagnosis			0.003			0.243
2010–2013	843 (51.0)	756 (45.7)		451 (49.0)	425 (46.1)	
2014–2017	811 (49.0)	897 (54.3)		470 (51.0)	496 (53.9)	
Grade			<0.001			0.136
I/II	642 (38.8)	421 (25.5)		285 (30.9)	316 (34.3)	
III/IV	1,012 (61.2)	1,232 (74.5)		636 (69.1)	605 (65.7)	
Tumor size (cm)			<0.001			0.671
1< T ≤2	828 (50.1)	1,189 (71.9)		540 (58.6)	530 (57.5)	
T ≤1	826 (49.9)	464 (28.1)		381 (41.4)	391 (42.5)	
Stage			0.088			0.247
IA	1,617 (97.8)	1,599 (96.7)		901 (97.8)	892 (96.9)	
IB	37 (2.2)	54 (3.3)		20 (2.2)	29 (3.1)	

Table 2 *(continued)*

Table 2 *(continued)*

Variables	Before PSM			After PSM		
	Non-POCT (n=1,654), n (%)	POCT (n=1,653), n (%)	P	Non-POCT (n=921), n (%)	POCT (n=921), n (%)	P
Surgery			<0.001			0.816
Lumpectomy	798 (48.2)	947 (57.3)		476 (51.7)	470 (51.0)	
Mastectomy	856 (51.8)	706 (42.7)		445 (48.3)	451 (49.0)	
Radiation after surgery			<0.001			0.509
No	758 (45.8)	564 (34.1)		384 (41.7)	399 (43.3)	
Yes	896 (54.2)	1,089 (65.9)		537 (58.3)	522 (56.7)	
Regional nodes examined			0.089			0.347
>2	720 (43.5)	757 (45.8)		414 (45.0)	391 (42.5)	
1	517 (31.3)	459 (27.8)		265 (28.8)	293 (31.8)	
2	417 (25.2)	437 (26.4)		242 (26.3)	237 (25.7)	
Laterality			0.434			0.401
Left	822 (49.7)	845 (51.1)		458 (49.7)	439 (47.7)	
Right	832 (50.3)	808 (48.9)		463 (50.3)	482 (52.3)	

PSM, propensity score matching; POCT, postoperative adjuvant chemotherapy.

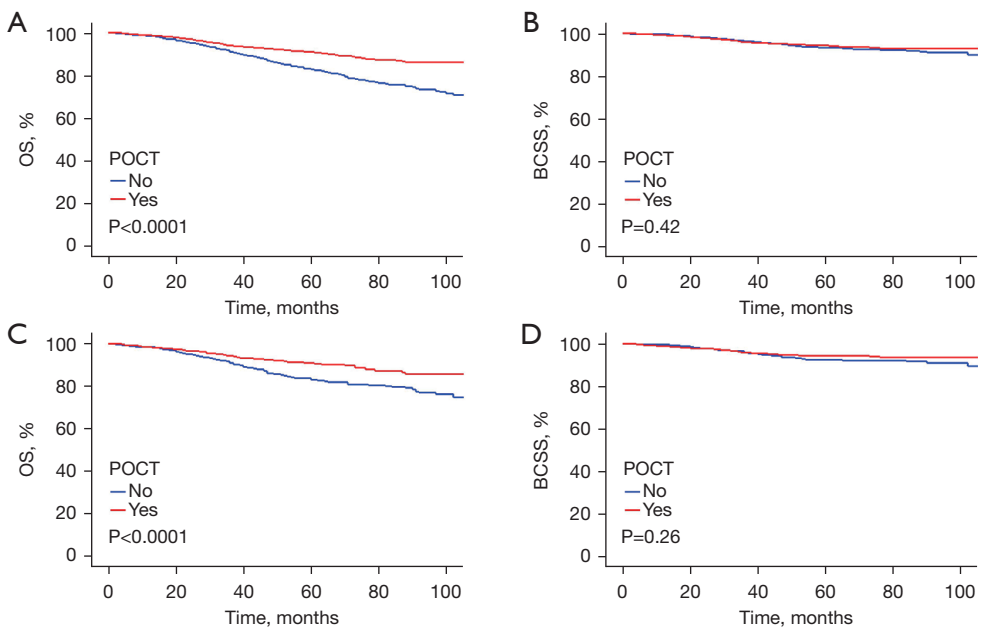

Figure 1 Kaplan-Meier curves comparing OS and BCSS for the POCT versus non-POCT groups in whole cohort. (A) OS before PSM. (B) BCSS before PSM. (C) OS after PSM. (D) BCSS after PSM. POCT, postoperative adjuvant chemotherapy; OS, overall survival; BCSS, breast cancer-specific survival; PSM, propensity score matching.

Table 3 Stage I tumor survival outcomes of patients following POCT

Outcomes	Non-POCT			POCT			P
	5-year estimate (%)	95% CI (%)	Total no. of events	5-year estimate (%)	95% CI (%)	Total no. of events	
Before PSM							
OS	82.6	80.5–84.8	4	90.9	89.2–92.5	2	<0.001
BCSS	93.4	91.9–94.8	1	94.2	92.9–95.6	1	0.42
After PSM							
OS	83.0	80.2–86.0	3	90.0	88.7–93.1	1	<0.001
BCSS	92.5	90.4–94.6	2	94.4	92.7–96.1	1	0.26

POCT, postoperative adjuvant chemotherapy; CI, confidence interval; PSM, propensity score matching; OS, overall survival; BCSS, breast cancer-specific survival.

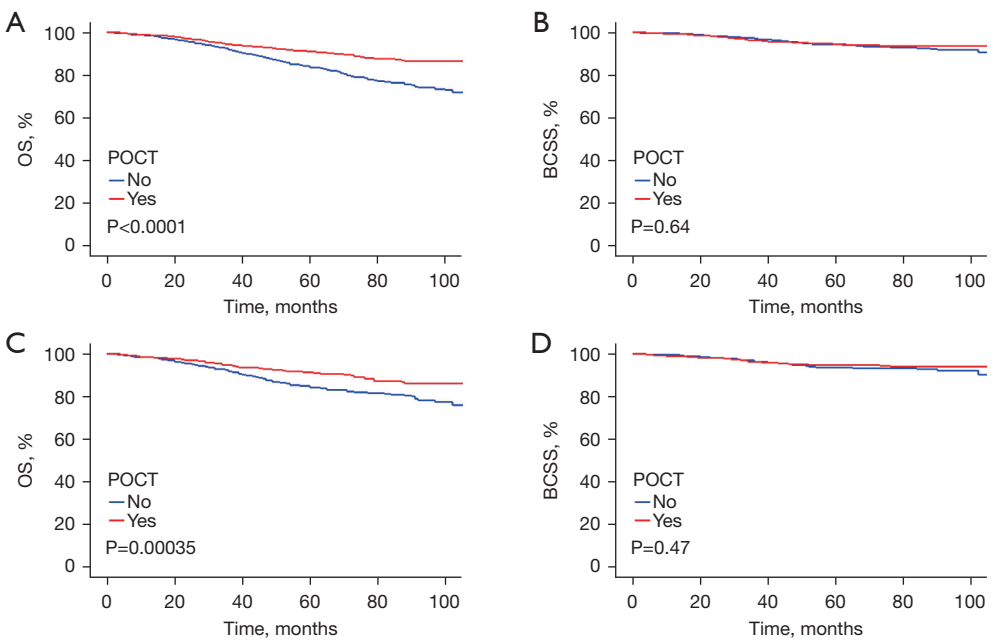

Figure 2 Kaplan-Meier curves comparing OS and BCSS for the POCT versus non-POCT groups in IA subgroup. (A) OS before PSM. (B) BCSS before PSM. (C) OS after PSM. (D) BCSS after PSM. POCT, postoperative adjuvant chemotherapy; OS, overall survival; BCSS, breast cancer-specific survival; PSM, propensity score matching.

(P=0.001), race (P<0.001), stage (P<0.001), and tumor size (P<0.001) were notable forecasters of BCSS. Statistically significant variables in the univariate were involved in multifactorial regression model, and multifactorial Cox regression analysis demonstrated that age (P=0.003), chemotherapy (P<0.001), race (P=0.011), radiotherapy (P=0.023), tumor stage (P<0.001), and tumor size (P=0.010) were independent prognostic factors for OS. Age (P=0.019), race (P<0.001), tumor stage (P<0.001), and tumor size (P<0.001) were independent prognostic factors for BCSS.

Discussion

Adjuvant chemotherapy can increase the prognosis of early TNBC patients and prolong their survival time (10-12). SEER database also demonstrates the important role of adjuvant chemotherapy in early stage TNBC (6,13). Meanwhile, the NCCN guidelines state that adjuvant

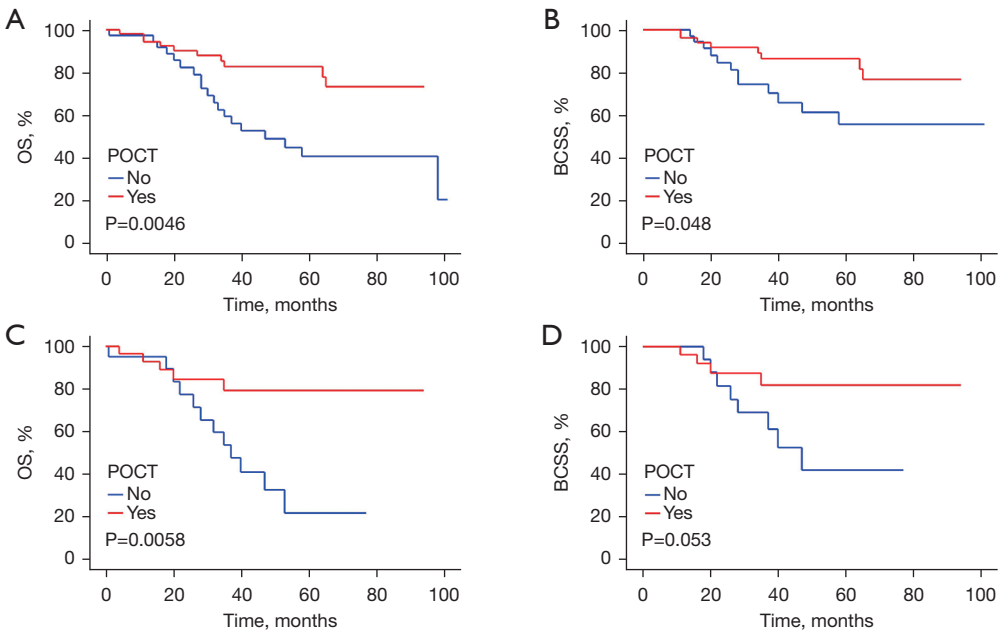

Figure 3 Kaplan-Meier curves comparing OS and BCSS for the POCT versus non-POCT groups in IB subgroup. (A) OS before PSM. (B) BCSS before PSM. (C) OS after PSM. (D) BCSS after PSM. POCT, postoperative adjuvant chemotherapy; OS, overall survival; BCSS, breast cancer-specific survival; PSM, propensity score matching.

chemotherapy is recommended to be "considered" for stage I (pT1bN0M0) TNBC patients (5). However, only a few elderly patients were enrolled in the above retrospective study. To our knowledge, there is no prospective or retrospective study to evaluate the survival outcomes of POCT for these specific older TNBC patients. Therefore, this study collected the patients of SEER database above 65 years with stage I TNBC from 2010 to 2016 to analyze the correlation between their receipt of POCT and survival outcomes.

The employment of adjuvant chemotherapy is limited in elderly patients. Studies have indicated that the likelihood of older patients with TNBC receiving chemotherapy is minimal, with the main factor being concerns about tolerability in people with reduced functional reserve (14-18). In our study, we observed that the ratio of elderly patients receiving POCT reduced with increasing age (68.2%, 54.2%, 34.0%, and 12.1% for 65–69, 70–74, 75–79, and ≥80 age subgroups, respectively), which is similar to that reported previous studies (16,19,20). Furthermore, our results also indicate that age is an independent predicator affecting survival, which is consistent with previous reports (15). However, some researches indicate that elderly patients with TNBC may own more sound outcomes than younger patients. Providing adjuvant chemotherapy based on age alone may have a negative impact on the prognosis of such patients (21-23). It may be because age-related alterations in TNBC and general breast cancer need to be viewed in the context of the underlying genomic phenotype. Patient age is interrelated with changes in Ki-67 expression, *PIK3CA* mutations, and luminal androgen receptor subtypes. Therefore, in addition to the age at diagnosis, more consideration should be given to the impact of tumor biology in making treatment decisions (17).

A retrospective study of 177 elderly patients with stage I–III TNBC in Peking Union Medical College Hospital showed that those receiving chemotherapy were younger with more advanced disease. Chemotherapy with more sound BCSS and OS, and the recurrence-free survival (RFS) rate receiving chemotherapy was improved (22). However, the impact of adjuvant chemotherapy on the survival outcome of stage I patients was not specifically assessed here. In this study, it was observed the 5-year OS of the POCT group was pronouncedly improved compared to that of the non-POCT group, both before and after matching. Difference of 5-year BCSS between POCT and non-POCT was not statistical. However, there are studies that are inconsistent with our results. It has been reported that adjuvant

Table 4 Univariable and multivariable Cox regression analyses for predictive factors of OS and BCSS after PSM

Variables	After PSM OS				After PSM BCSS			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age (years)								
65–69	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
70–74	1.188 (0.837–1.687)	0.335	1.140 (0.801–1.622)	0.467	1.380 (0.824–2.311)	0.221	1.281 (0.763–2.152)	0.349
75–79	2.027 (1.427–2.879)	<0.001	1.726 (1.202–2.477)	0.003	2.411 (1.445–4.025)	0.001	1.864 (1.107–3.140)	0.019
80+	2.943 (1.885–4.594)	<0.001	2.471 (1.565–3.900)	<0.001	1.693 (0.737–3.889)	0.215	1.524 (0.658–3.530)	0.326
Chemotherapy after surgery								
No	1 (reference)		1 (reference)		1 (reference)			
Yes	0.571 (0.432–0.753)	<0.001	0.569 (0.430–0.752)	<0.001	0.793 (0.531–1.184)	0.257		
Grade								
I/II	1 (reference)				1 (reference)			
III/IV	1.299 (0.963–1.753)	0.087			1.580 (0.989–2.522)	0.055		
Laterality								
Left	1 (reference)				1 (reference)			
Right	0.963 (0.737–1.258)	0.781			0.866 (0.581–1.290)	0.479		
Marital status								
Married	1 (reference)		1 (reference)		1 (reference)			
Unmarried	1.622 (1.238–2.126)	<0.001	1.273 (0.960–1.686)	0.093	1.371 (0.920–2.044)	0.121		
Race recode								
Black	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
White	0.638 (0.466–0.875)	0.005	0.658 (0.477–0.908)	0.011	0.392 (0.258–0.598)	<0.001	0.400 (0.262–0.611)	<0.001
Other	0.549 (0.287–1.053)	0.071	0.590 (0.307–1.136)	0.114	0.231 (0.071–0.753)	0.015	0.250 (0.076–0.816)	0.022
Radiation after surgery								
No	1 (reference)		1 (reference)		1 (reference)			
Yes	0.686 (0.525–0.897)	0.006	0.727 (0.552–0.956)	0.023	0.770 (0.517–1.146)	0.198		
Regional nodes examined								
>2	1 (reference)				1 (reference)			
1	1.315 (0.964–1.792)	0.084			1.535 (0.961–2.453)	0.073		
2	1.084 (0.768–1.514)	0.663			1.352 (0.818–2.233)	0.239		
Stage								
IA	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
IB	4.247 (2.585–6.975)	<0.001	3.963 (2.397–6.552)	<0.001	6.728 (3.672–12.328)	<0.001	5.359 (2.899–9.904)	<0.001
Surgery								
Lumpectomy	1 (reference)				1 (reference)			
Mastectomy	0.866 (0.662–1.132)	0.293			0.822 (0.551–1.227)	0.338		

Table 4 *(continued)*

Table 4 *(continued)*

Variables	After PSM OS				After PSM BCSS			
	Univariable analysis		Multivariable analysis		Univariable analysis		Multivariable analysis	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Tumor size (cm)								
1< T ≤2	1 (reference)		1 (reference)		1 (reference)		1 (reference)	
T ≤1	0.510 (0.379–0.687)	<0.001	0.662 (0.484–0.905)	0.010	0.343 (0.210–0.561)	<0.001	0.412 (0.249–0.681)	<0.001
Year of diagnosis								
2010–2013	1 (reference)				1 (reference)			
2014–2017	0.957 (0.700–1.307)	0.781			1.052 (0.685–1.616)	0.817		

OS, overall survival; BCSS, breast cancer-specific survival; PSM, propensity score matching; HR, hazard ratio; CI, confidence interval.

chemotherapy does not enhance the prognosis of elderly TNBC (24). Huang *et al.* suggested that chemotherapy did not improve the survival rate of elderly patients with stage I TNBC, while the situation for patients with stage II and III is the opposite (25).

In addition, we conducted exploratory subgroup analysis to determine the influence of prognostic factors. We divided stage I TNBC into stage IA and stage IB to compare the survival rate between POCT group and non-POCT group. There was an obvious difference between stage IA and stage IB in the benefit of POCT for TNBC patients in OS, but the benefits for BCSS were only significant in stage IB, and the difference in BCSS between the two groups in stage IA was not pronounced, indicating that POCT can decrease the risk of death from all causes or from breast cancer in stage IB, but not in stage IA death from breast cancer.

Limitations also exist here. First, the inherent selection bias is unavoidable in this retrospective analysis. Second, patients in the non-POCT group may be healthier than those in the POCT group. Third, the data for elderly patients were unevenly distributed, with few elderly patients in T1a or T1b tumors, so a more detailed subgroup analysis by stage was not possible. Fourth, some biological characteristics such as Ki-67, *BRCA1* and *BRCA2* mutations were not registered in the SEER database. Fifth, SEER did not record the whole-body specific treatment information such as adjuvant chemotherapy regimen, dose and number of adjuvant chemotherapy cycles, which may affect the impact of chemotherapy on OS and BCSS. Sixth, a notable shortcoming is that chemotherapy records in the SEER database are categorized as "no/unknown" and "yes". Data for 921 patients with definite chemotherapy were recorded, but it is not sure that whether the patients recorded as "no/unknown" had in fact not received chemotherapy. This study also has certain advantages. First, as the first study using PSM in elderly patients with stage I TNBC, the results are more dependable than those without PSM. This is the first retrospective study to analyze the effect of POCT on elderly patients with stage I TNBC using a public database. Secondly, the advantage of our research is to focus on the newest obtainable data in the SEER database and strictly exclude lost data to ensure the reliability of our research.

Although our study provides evidence that older women over 65 with stage I TNBC can benefit from POCT, more comprehensive genetic stratification with advanced molecular biology techniques is needed and should be performed in order to identify the appropriate chemotherapy population and decide on adjuvant chemotherapy regimens.

Conclusions

In our study, the use of POCT decreased with age in elderly female patients over 65 years with stage I TNBC, and elderly female patients appeared to benefit from POCT. POCT may be a promising tool for elderly female patients with stage I TNBC in the future.

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Footnote

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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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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