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Original article

Adjuvant chemotherapy could benefit early-stage ER/PR positive mucinous breast cancer: A SEER-based analysis

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ABSTRACT

Purpose: The aim of this study was to explore the value of adjuvant chemotherapy in patients with early-stage ER/PR-positive mucinous carcinoma.
Methods: We identified early-stage ER/PR-positive mucinous carcinoma patients in the Surveillance, Epidemiology, and End Results (SEER) database. We used propensity-score matching (PSM) analysis to eliminate selection bias and differences in baseline characteristics. Univariate and multivariate analyses were performed to identify significant prognostic factors. The primary outcomes were overall survival (OS) and breast cancer-specific survival (BCSS), which were evaluated with the Kaplan-Meier method.
Results: After propensity score matching, 805 pairs were selected. Patients with early-stage ER/PR-positive mucinous adenocarcinoma in the chemotherapy group had a better OS, but not BCSS, than those in the nonchemotherapy group after PSM (OS: $p < 0.001$; BCSS: $p = 0.285$). After stratifying by tumor size and lymph node status, adjuvant chemotherapy could significantly improve the OS of early-stage ER/PR-positive patients with tumors larger than 3 cm ($p = 0.004$) if they had negative lymph nodes (LNs). For patients positive LNs, the OS was significantly different between the chemotherapy group and the non-chemotherapy group when the tumors were larger than 1 cm (T = 1–2.9 cm, $p = 0.006$; T > 3 cm, $p = 0.049$, respectively).
Conclusion: Adjuvant chemotherapy maybe improves prognosis in patients with negative LNs and tumors larger than 3 cm, or patients with LNs metastasis and tumors larger than 1 cm. We suggest considering clinical characteristics meanwhile when deciding chemotherapy or not. Randomized controlled trials (RCT) are expected to confirm our results in the future.

Introduction

Mucinous carcinoma is a special histologic type of breast cancer, and its incidence ranges from 1% to 6% of all invasive breast carcinomas [1–3]. Previous studies have found that mucinous breast tumors have specific characteristics, such as higher estrogen receptor (ER) and progesterone receptor (PR) expression, lower expression of human epidermal growth factor receptor 2 (HER2), lower grade, and lower risk of nodal metastasis than other types of breast tumors [4–6]. It was reported that mucinous adenocarcinoma is associated with a good prognosis and has a better prognosis than invasive carcinoma [7,8]. Adjuvant chemotherapy always plays an important role in invasive breast cancer.

Didonato stated that the majority of mucinous breast cancer is mainly treated with surgery and adjuvant therapy, including anti-estrogen therapy [9]. The National Comprehensive Cancer Network (NCCN) guidelines recommend treating mucinous breast cancer according to hormone receptor status and lymph node status. These guidelines recommend that patients who are hormone receptor-positive receive endocrine therapy alone if they have negative lymph nodes, while those who have positive lymph nodes (one or more metastases > 2 mm) are recommended to consider adjuvant endocrine therapy plus adjuvant chemotherapy [10]. However, because of the rarity of ER/PR-positive mucinous

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List of abbreviations

estrogen receptor and progesterone receptor ER/PR
human epidermal growth factor receptor 2 HER2
The National Comprehensive Cancer Network NCCN
Surveillance, Epidemiology and End Results SEER
propensity-score matching PSM
Randomized controlled trials RCT
hazard ratio HR
confidence interval CI
overall survival OS
breast cancer-specific survival BCSS
lymph node LN

carcinoma, there is no clinical study has proved that adjuvant chemotherapy can be omitted. The value of adjuvant chemotherapy in the treatment of ER/PR positive mucinous breast cancer is still uncertain. Therefore, using the Surveillance, Epidemiology, and End Results (SEER) database, we aimed to investigate the role of adjuvant chemotherapy in patients with early-stage ER/PR-positive mucinous adenocarcinoma of the breast, and these findings may provide useful information for oncologists to make more precise clinical decisions.

Patients and methods

Database

The Surveillance, Epidemiology, and End Results (SEER)database, a National Cancer Institute-sponsored program, aims to collect information about cancer incidence and outcomes, including data on patient demographics, clinicopathologic features, and cancer-associated treatment of the US population [11]. We used the latest SEER*Stat software (version 8.3.6) to conduct this study.

Patients and variables

In this study, we screened 10918 female early-stage ER/PR positive breast cancer patients with histologically proven mucinous adenocarcinoma between 1998 and 2016 from the SEER database. The inclusion criteria for data extraction were as follows: (1) pathologically confirmed mucinous adenocarcinoma; (2) age $\geq$ 20 years and surgery at the primary tumor site; and (3) available follow-up data. The following patients were excluded: (1) male patients; (2) patients with multiple cancers or a prior diagnosis of other tumors; (3) patients with distant metastasis; (4) patients with an unknown lymph node status and no surgical information; (5) patients who died within 3 months after surgery; and (6) patients with ER-negative or PR-negative cancer or an unknown ER or PR status. The patient selection process is summarized in Fig. 1. The primary end-points of interest were overall survival (OS) and breast cancer-specific survival (BCSS). OS was defined as the time from diagnosis to death or last follow-up and BCSS was defined as the

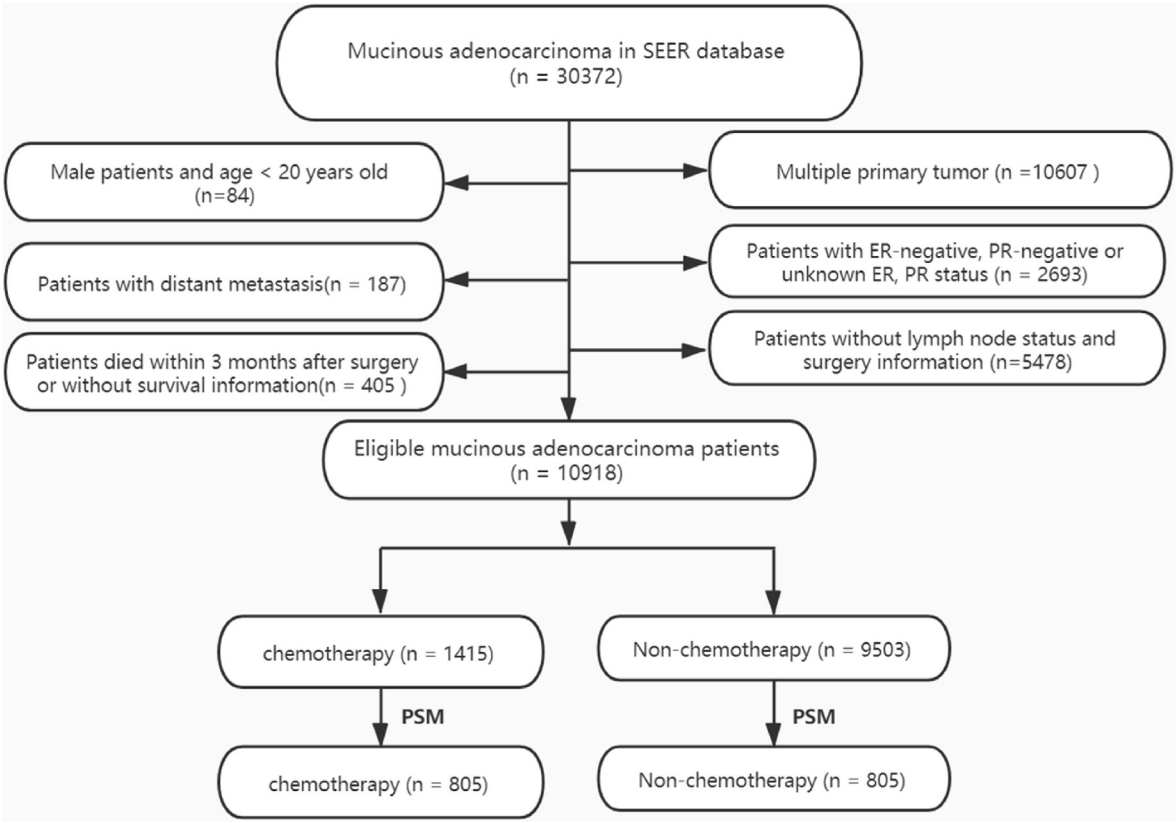

Fig. 1. Flow chart for screening patients; SEER, Surveillance Epidemiology, and End Results; PSM, propensity score matching.

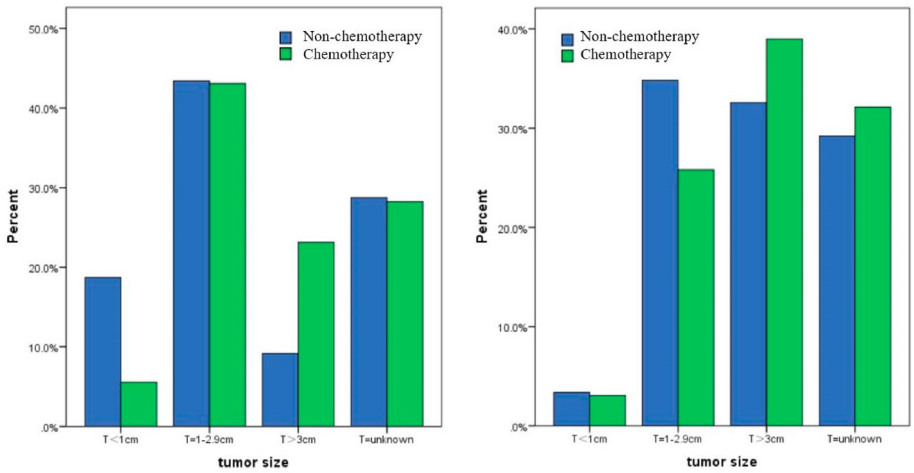

Fig. 2. The proportion of chemotherapy and non-chemotherapy stratified by tumor size and lymph node status. (A) lymph node-negativity; (B) lymph node metastasis.

survival time from the date of the diagnosis of breast cancer to the date of death caused by breast cancer [12]. Informed consent was not required from the patients in this study because the SEER patient information is deidentified.

Statistical analysis

The patients were divided into two groups according to whether they received chemotherapy. All statistical analyses were carried

Table 1
Patients' demographics and clinicopathological characteristics.

Variables	Data before PSM			Data after PSM		
	Chemotherapy (n = 1415)	Non-Chemotherapy (n = 9503)	P value	Chemotherapy (n = 805)	Non-Chemotherapy (n = 805)	P value
Age (year, %)			<0.001			0.521
<50	661 (46.7)	1083(11.4)		276(34.3)	276(34.3)	
≥50	754 (53.3)	8420(88.6)		529(65.7)	529(65.7)	
Marital status (%)			<0.001			0.642
Unmarried	582(41.1)	4597(48.4)		354(44.0)	350(43.5)	
Married	792(56.0)	4476(47.1)		439(54.5)	438(54.4)	
Unknown	41(2.9)	430(4.5)		12(1.5)	17(2.1)	
Race (%)			<0.001			0.349
White	975(68.9)	7570(79.7)		592(73.5)	600(74.5)	
Black	203(14.3)	875(9.2)		92(11.4)	75(9.3)	
Other	237(16.7)	1058(11.1)		121(15.0)	130(16.1)	
Grade (%)			<0.001			0.100
I/II	1109(78.4)	8021(84.4)		697(86.6)	702(87.2)	
III/IV	139(9.8)	230(2.4)		31(3.9)	17(2.1)	
Unknown	167(11.8)	1252(13.2)		77(9.6)	86(10.7)	
Laterality (%)			0.512			0.378
Left	713(50.4)	4901(51.6)		416(51.7)	396(49.2)	
Right	700(49.5)	4595(48.4)		389(48.3)	408(50.7)	
Unknown	2(0.1)	7(0.1)		0(0.0)	1(0.1)	
Stage			<0.001			0.155
I	432(30.5)	6723(70.7)		378(47.0)	382(47.5)	
II	730(51.6)	2585(27.2)		394(48.9)	383(47.6)	
III	252(17.8)	152(1.6)		33(4.1)	35(4.3)	
Unknown	1(0.1)	43(0.5)		0(0.0)	5(0.6)	
Tumor size (cm, %)			<0.001			0.766
T < 1	65(4.6)	1709(18.0)		45(5.6)	47(5.8)	
1≤T ≤ 2.9	514(36.3)	4087(43.0)		357(44.3)	340(42.2)	
T > 3	415(29.3)	975(10.3)		166(20.6)	163(20.2)	
Unknown	421(29.8)	2732(28.7)		237(29.4)	255(31.7)	
LN status (%)			<0.001			0.696
Negative	861(60.8)	9058(95.3)		659(81.9)	665(82.6)	
Positive	554(39.2)	445(4.7)		146(18.1)	140(17.4)	
HER status (%)			<0.001			0.123
Negative	404(28.6)	4030(42.4)		236(29.3)	238(29.6)	
Positive	106(7.5)	69(0.7)		40(5.0)	24(3.0)	
Unknown	905(64.0)	5404(56.9)		529(65.7)	543(67.5)	
Surgery			0.002			0.653
Done	1396(98.7)	9245(97.3)		796(98.9)	794(98.6)	
None	19(1.3)	258(2.7)		9(1.1)	11(1.4)	
Radiation			<0.001			0.960
Done	869(61.4)	4756(50.0)		460(57.1)	461(57.3)	
None	546(38.6)	4747(50.0)		345(42.9)	344(42.7)	

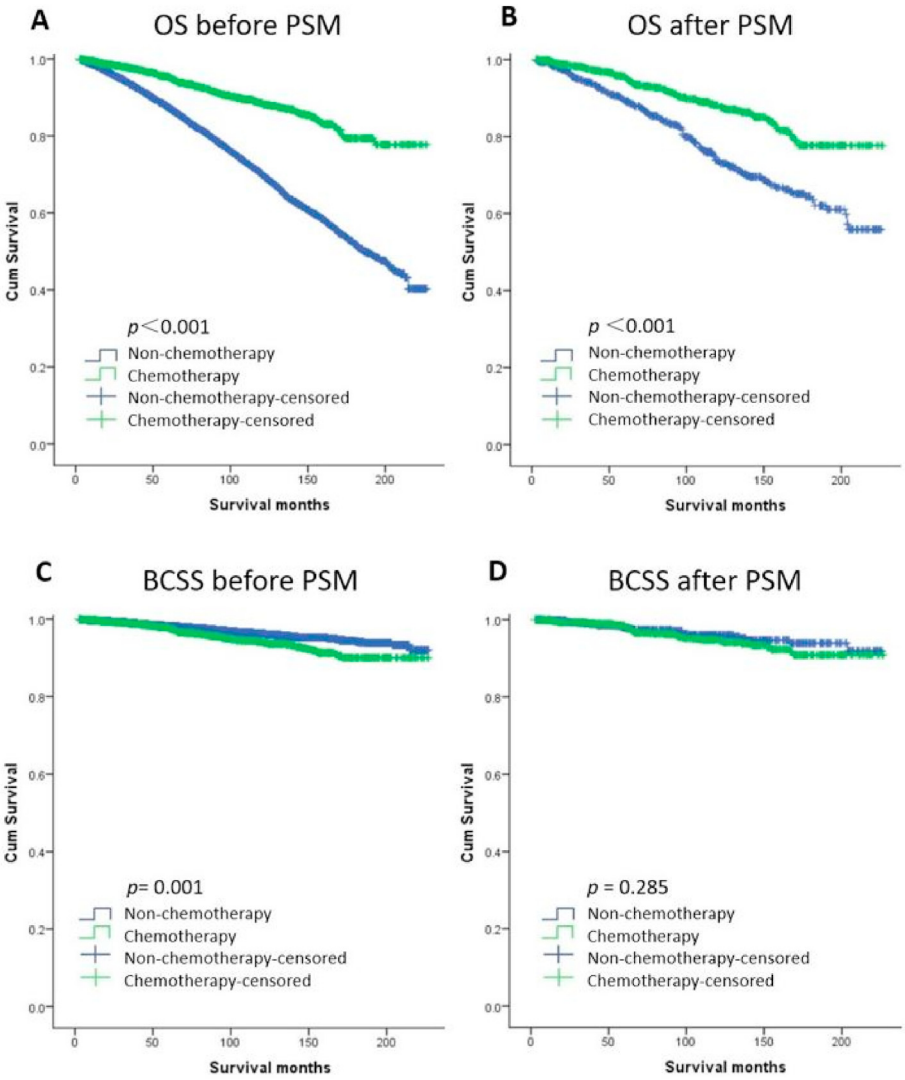

Fig. 3. Comparison of OS and BCSS between the chemotherapy and the non-chemotherapy groups. A, OS before PSM; B, OS after PSM. C, BCSS before PSM; D, BCSS after PSM. OS, overall survival; BCSS, breast cancer specific-survival; PSM, propensity score matching.

out using the IBM SPSS Statistics software package (version 25.0). The chi-square test and Fisher's test were used to analyze differences in clinical characteristics between the chemotherapy and nonchemotherapy groups, as appropriate. We carried out univariate and multivariate Cox proportional hazard regression analyses to identify the independent prognostic factors associated with improved OS and BCSS and reported the corresponding hazard ratios (HRs) and 95% confidence intervals (CIs). To eliminate the obvious differences in baseline covariates and inherent selection bias, we conducted a propensity score matching (PSM) analysis between the patients who underwent chemotherapy and those who did not (nonchemotherapy group). PSM is a tool for narrowing selection bias in nonrandomized studies and achieving balanced variables across treatment groups [13]. Using the chi-square test, twelve variables that may contribute to the survival of patients with mucinous adenocarcinoma were chosen for the propensity model to generate a matching ratio of 1:1, including age at diagnosis, marital status, race, tumor grade, stage, tumor size, lymph node status, ER status, PR status, HER2 status, surgery, and radiation. The standardized difference of <10% or a p-value>0.05 was reliably used to estimate the balance between variables before and after PSM [14]. The survival analysis between the chemotherapy and nonchemotherapy groups was performed by using the Kaplan-Meier method with the log-rank test. Two-sided p-values < 0.05 were considered to be statistically significant.

Results

Baseline patient characteristics

A total of 10918 patients with early-stage ER/PR positive mucinous adenocarcinoma were eligible from the SEER database, including 1415 patients who underwent chemotherapy and 9503 who did not receive chemotherapy. The median follow-up duration was 74 months (range: 3–227 months). The median age of the patients was 68 years, and the majority of (84.0%) patients were aged older than 50 years. Of all the patients, 9499 (83.0%) had grade I/II disease, and 1419 (13.0%) have grade III disease. Of all the patients, 999 (9.2%) had LN metastasis and 9919 (90.8%) did not. Furthermore, 861 (8.7%) of the patients with negative LNs had received chemotherapy, while 554 (55.5%) of the patients with positive LNs had received chemotherapy. Compared with the nonchemotherapy group, there were more patients with tumors larger than 3 cm in the chemotherapy group, regardless of lymph

Table 2
Univariate and multivariate Cox regression model analysis of OS between the Chemotherapy group and the Non-chemotherapy group.

Characteristics	Univariate analysis			Multivariate analysis		
	P value	Hazard ratio	95.0% CI for Exp(B)	P value	Hazard ratio	95.0% CI for Exp(B)
Age(year)						
<50years	Reference			Reference		
≥50years	**<0.001**	5.051	3.474–7.346	**<0.001**	4.311	2.935–6.332
Marital status						
Unmarried	Reference			Reference		
Married	**<0.001**	0.519	0.406–0.662	**0.001**	0.642	0.500–0.824
Unknown	0.457	0.713	0.292–1.739	0.247	0.577	0.228–1.462
Race						
White	Reference			Reference		
Black	0.436	1.164	0.794–1.706	0.434	1.168	0.792–1.722
Other	**0.007**	0.567	0.375–0.859	0.125	0.720	0.472–1.096
Grade						
I/II	Reference					
III/IV	0.279	1.397	0.763–2.561			
Unknown	0.658	1.079	0.769–1.515			
Laterality						
Left	Reference					
Right	0.622	0.942	0.741–1.197			
Unknown	0.102	5.155	0.720–36.910			
Stage						
I	Reference			Reference		
II	**<0.001**	2.154	1.653–2.808	0.066	1.355	0.980–1.874
III	**<0.001**	6.147	4.043–9.345	**<0.001**	2.691	1.542–4.698
Unknown	0.943	0	0–5.551E+90	0.933	0	0–3.918E+105
Tumor size(cm)						
T < 1	Reference			Reference		
1≤T ≤ 2.9	0.069	2.924	0.921–9.283	**0.041**	3.386	1.051–10.907
T > 3	**0.002**	6.507	2.042–20.739	**0.014**	4.482	1.346–14.920
Unknown	0.016	4.135	1.310–13.055	**0.023**	3.926	1.209–12.747
LN status						
Negative	Reference			Reference		
Positive	**<0.001**	2.241	1.730–2.904	0.863	1.029	0.742–1.428
HER status						
Negative	Reference			Reference		
Positive	0.326	0.488	0.117–2.041	0.871	0.887	0.208–3.776
Unknown	0.217	0.771	0.509–1.165	0.185	0.745	0.482–1.151
Surgery						
None	Reference			Reference		
Done	**<0.001**	0.200	0.099–0.406	**<0.001**	0.208	0.099–0.438
Chemotherapy						
None	Reference			Reference		
Done	**<0.001**	0.468	0.363–0.604	**<0.001**	0.427	0.331–0.552
Radiation						
None	Reference			Reference		
Done	**<0.001**	0.590	0.465–0.750	**<0.001**	0.646	0.505–0.826

node status. When the patients had negative LNs, the proportion of patients with tumors smaller than 1 cm or between 1 and 2.9 cm was lower in the chemotherapy group than in the non-chemotherapy group (5.6% vs 18.7%, 43.1% vs 43.4%, respectively, $p < 0.001$), and the proportion of patients with tumors larger than 3 cm (23.1%) were higher in the chemotherapy group than in the nonchemotherapy group (9.2%). Similarly, when the patients had LN metastasis, the proportion of patients with tumors smaller than 1 cm or between 1 and 2.9 cm was lower in the chemotherapy group than in the nonchemotherapy group (3.1% vs 3.4%, 25.8% vs 34.8%, respectively, $p = 0.016$), while patients with tumors larger than 3 cm accounted for 39.0% of the chemotherapy group and 32.6% of the nonchemotherapy group (Fig. 2). The detailed clinicopathologic characteristics of the patients with mucinous adenocarcinoma before or after PSM are shown in Table 1.

Survival analysis for OS and BCSS

Before PSM, among all patients, those who received adjuvant chemotherapy showed significantly better OS but worse BCSS (OS: $p < 0.001$, BCSS: $p = 0.001$, respectively) than the patients in the nonchemotherapy group (Fig. 3A and C).

After 1:1 matching, 805 patients in the chemotherapy group were matched and compared with 805 patients in the non-chemotherapy group. No demographic variables with significant differences were included ($p > 0.05$).

After eliminating the differences in covariates that might affect OS and BCSS by using PSM, we found that patients with ER/PR-positive mucinous adenocarcinoma in the chemotherapy group achieved a significantly better OS than those in the non-chemotherapy group ($p < 0.001$; Fig. 3B). However, chemotherapy was associated with only improved OS, not BCSS ($p = 0.285$; Fig. 3D). The 5-year OS and BCSS rates of the two cohorts are reported in Table 4. The 10-year OS and BCSS rates of the two cohorts are reported in Table 5. After stratifying patients by tumor size and lymph node status, for patients with negative LNs, we found that OS was significantly better in the chemotherapy group than in the nonchemotherapy group for patients with tumors larger than 3 cm ($p = 0.004$, Fig. 4C), while adjuvant chemotherapy showed no significant effects on OS in patients with tumors < 3 cm (T < 1 cm, $p = 0.625$, T = 1–2.9 cm, $p = 0.055$, respectively; Fig. 4A and B). For patients with positive LNs, the chemotherapy group had a longer OS than the nonchemotherapy group among patients with tumors ≥1 cm (T = 1–2.9 cm, $p = 0.006$, T > 3 cm, $p = 0.049$, respectively;

Table 3
Univariate and multivariate Cox regression model analysis of BCSS between the Chemotherapy group and the Non-chemotherapy group.

Characteristics	Univariate analysis			Multivariate analysis		
	P value	Hazard ratio	95.0% CI for Exp(B)	P value	Hazard ratio	95.0% CI for Exp(B)
Age(year)						
<50years	Reference			Reference		
≥50years	0.193	1.421	0.837–2.414	0.684	0.888	0.501–1.574
Marital status						
Unmarried	Reference					
Married	0.095	0.658	0.403–1.075			
Unknown	0.961	0	0–7.975E+190			
Race						
White	Reference			Reference		
Black	0.163	1.621	0.823–3.194	0.205	1.566	0.782–3.136
Other	**0.036**	0.288	0.090–0.922	**0.048**	0.305	0.094–0.991
Grade						
I/II	Reference			Reference		
III/IV	**0.040**	2.610	1.043–6.530	**0.038**	2.700	1.058–6.890
Unknown	0.379	0.684	0.293–1.594	0.569	0.775	0.322–1.864
Laterality						
Left	Reference					
Right	0.140	1.454	0.885–2.388			
Unknown	0.975	0	1.047E+212			
Stage						
I	Reference			Reference		
II	**0.002**	2.481	1.392–4.420	0.367	1.392	0.678–2.858
III	**<0.001**	10.875	5.070–23.328	**0.011**	4.123	1.379–12.332
Unknown	0.975	0	0–5.517E+212	0.972	0	0–4.568E+263
Tumor size(cm)						
T < 1	Reference			Reference		
1≤T ≤ 2.9	0.883	5739.705	0–7.712E+53	0.887	4953.918	0–4.609E+54
T > 3	0.865	21805.989	0–2.929E+54	0.876	11636.225	0–1.083E+55
Unknown	0.874	11257.050	0–1.512E+54	0.879	9129.244	0–8.493E+54
LN status						
Negative	Reference			Reference		
Positive	**<0.001**	3.186	1.927–5.268	0.182	1.592	0.805–3.150
HER status						
Negative	Reference			Reference		
Positive	0.967	0	0–2.795E+237	0.928	0	0–4.600E+82
Unknown	**0.013**	0.408	0.202–0.825	**0.009**	0.350	0.159–0.771
Surgery						
None	Reference			Reference		
Done	**<0.001**	0.124	0.039–0.399	**0.011**	0.202	0.059–0.691
Chemotherapy						
None	Reference			Reference		
Done	0.286	1.310	0.797–2.152	0.524	1.178	0.712–1.950
Radiation						
None	Reference			Reference		
Done	**0.008**	0.513	0.313–0.841	0.131	0.675	0.405–1.125

Fig. 4D and E). However, there was no difference in BCSS between the chemotherapy group and the nonchemotherapy group, regardless of tumor size or lymph node status (LNs-negative: T = 1–2.9 cm, $p = 0.347$; T > 3 cm, $p = 0.847$; LNs-positive: T = 1–2.9 cm, $p = 0.697$; T > 3 cm, $p = 0.815$, respectively; Fig. 5).

Prognostic factors for mucinous adenocarcinoma

We performed univariate and multivariate analyses to investigate the prognostic factors that could predict OS and BCSS in the matched-cohort. As shown in Table 2, univariate analyses revealed that age ($p < 0.001$), marital status ($p < 0.001$), race ($p = 0.007$), stage ($p < 0.001$), tumor size ($p = 0.002$), LN status ($p < 0.001$), surgery ($p < 0.001$), chemotherapy ($p < 0.001$), and radiation ($p < 0.001$) were important factors affecting OS. After we included the covariates that were clinically worth exploring or had $p < 0.05$ in the univariate analysis into the multivariate analysis, race ($p = 0.036$), grade ($p = 0.040$), stage ($p < 0.001$), tumor size ($p = 0.041$), surgery ($p < 0.001$), chemotherapy ($p < 0.001$) and radiation ($p < 0.001$) were independent prognostic factors of OS in patients with mucinous adenocarcinoma. As shown in Table 3, univariate analyses revealed that race ($p = 0.007$), grade

Table 4
5-year overall survival (OS) and breast cancer-specific survival (BCSS) of the two groups.

Group	5-year OS		5-year BCSS	
	Before matching	After matching	Before matching	After matching
Chemotherapy	95.4%	95.7%	97.8%	98.6%
Non-chemotherapy	87.4%	89.4%	98.2%	98.0%
P value	<0.001	<0.001	0.001	0.285
Total	88.5%	92.5%	98.1%	98.3%

Table 5
10-year overall survival (OS) and breast cancer-specific survival (BCSS) of the two groups.

Group	10-year OS		10-year BCSS	
	Before matching	After matching	Before matching	After matching
Chemotherapy	88.7%	88.2%	94.2%	94.8%
Non-chemotherapy	70.2%	73.8%	96.2%	96.0%
P value	<0.001	<0.001	0.001	0.285
Total	72.8%	80.9%	95.9%	95.4%

($p = 0.006$), stage ($p < 0.001$), LN status ($p < 0.001$), HER status ($p = 0.013$), surgery ($p < 0.001$) and radiation ($p = 0.008$) were important factors affecting BCSS. After we included the covariates that were clinically worth exploring or had $p < 0.05$ in the univariate analysis into the multivariate analysis, race ($p = 0.048$), grade ($p = 0.038$), stage ($p = 0.011$), HER status ($p = 0.009$) and surgery ($p = 0.011$) were independent prognostic factors of BCSS in patients with mucinous adenocarcinoma.

Discussion

In this SEER-based study, we observed an association between adjuvant chemotherapy and survival in patients with early-stage ER/PR-positive mucinous adenocarcinoma from 1998 to 2016. The median age of the enrolled patients was 68 years, which was older than the average age at diagnosis for invasive breast carcinoma [15]. Patients with mucinous adenocarcinoma were more likely to have a significantly better differentiated histologic grade, and lower risk of LN positivity, which is consistent with previous studies [1,3,6].

In our study, patients with early-stage ER/PR positive mucinous adenocarcinoma in the chemotherapy group had obviously better OS than those in the nonchemotherapy group, even after matching clinicopathological factors by PSM. However, our findings are not consistent with the conclusions from some other studies.

A previous study showed that node-negative, estrogen receptor-positive breast cancer patients did not equally benefit from adjuvant chemotherapy compared to patients with other types of breast cancer [16]. A clinical trial has reported that luminal A patients even in the high-risk premenopausal population derive no benefit from adjuvant chemotherapy [17]. Unfortunately, these studies were not specifically focused on mucinous carcinoma.

Hyung et al.'s retrospective analysis which included 3076

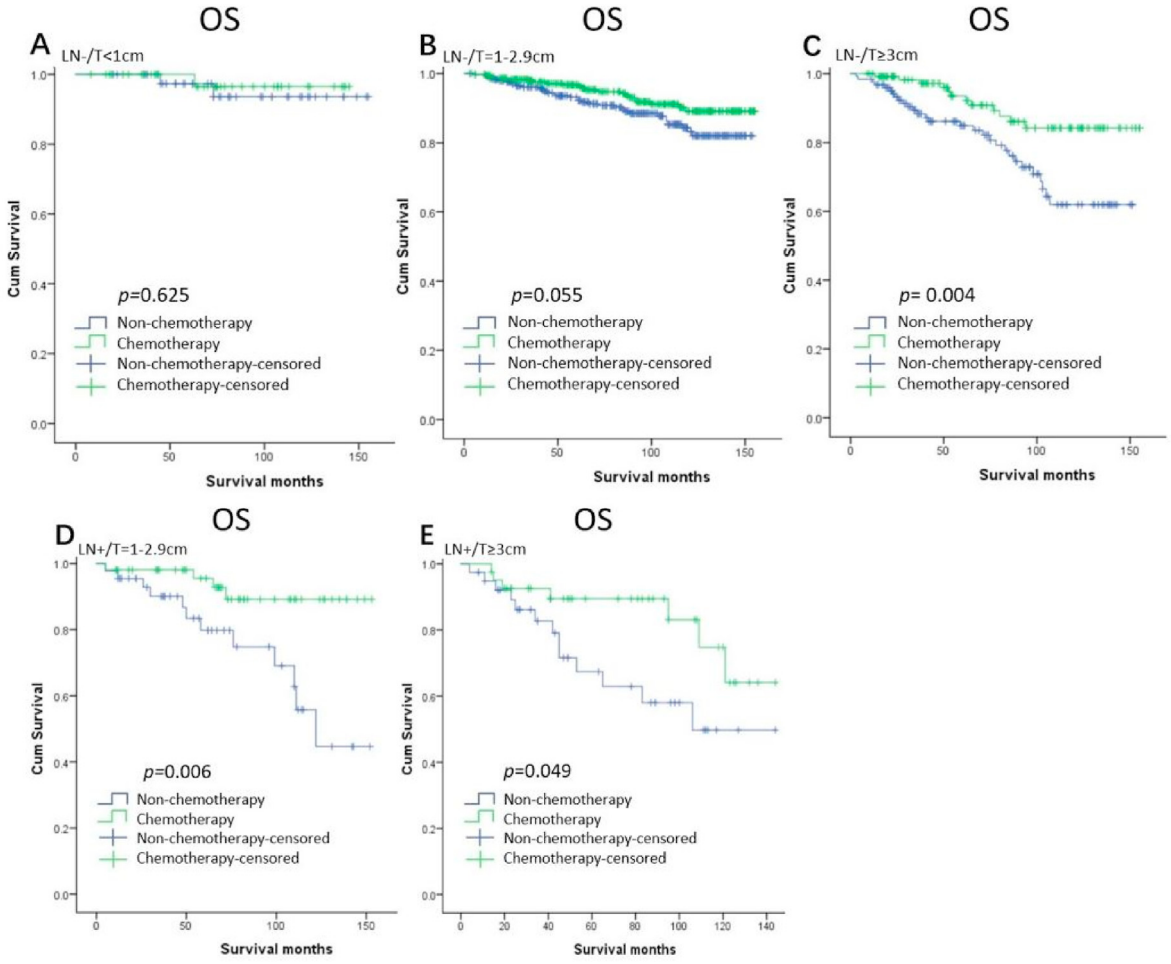

Fig. 4. Comparison of the OS of ER/PR positive patients between the chemotherapy and the non-chemotherapy groups stratified by tumor size and lymph node after matching. OS, overall survival; ER, estrogen receptor; PR, progesterone receptor; T, tumor size; LN, lymph node.

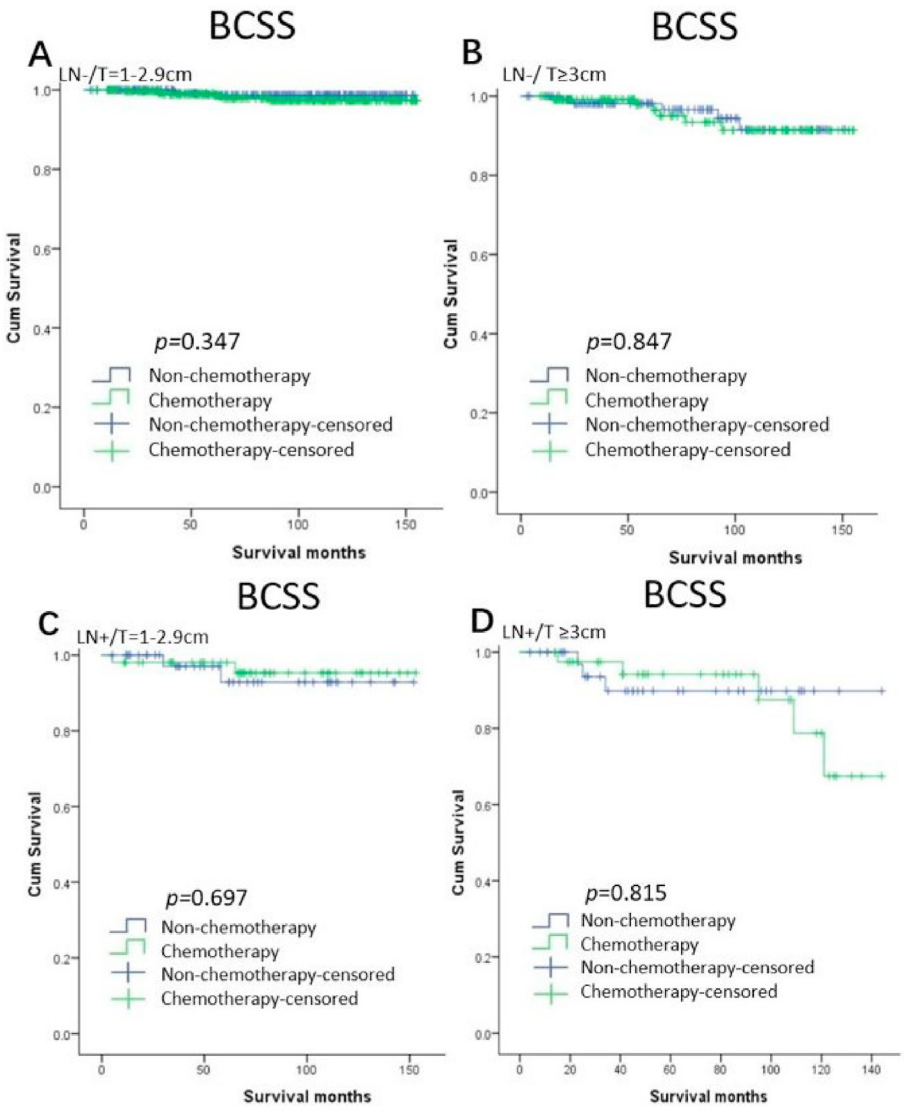

Fig. 5. Comparison of the BCSS of ER/PR positive patients between the chemotherapy and the non-chemotherapy groups stratified by tumor size and lymph node after matching. BCSS, breast cancer specific-survival; ER, estrogen receptor; PR, progesterone receptor; T, tumor size; LN, lymph node.

patients revealed that most ER-positive mucinous breast cancer patients did not benefit from adjuvant chemotherapy. They stated that chemotherapy can be omitted in the treatment of most ER-positive mucinous carcinomas [18].

The NCCN guidelines consider using hormone receptor status as the most important factor in making clinical decisions for the treatment of mucinous adenocarcinoma. ER-/PR-positive patients are recommended to consider adjuvant chemotherapy if they have LN metastasis, while adjuvant chemotherapy is not recommended for patients with negative LNs [10]. However, mucinous carcinoma is different from invasive breast cancer, and the uniqueness of mucinous carcinoma should be taken into consideration in clinical practice. Few clinical trials specifically focus on adjuvant chemotherapy to treat mucinous adenocarcinoma. Therefore, we tried to investigate the association between adjuvant chemotherapy and the survival of early-stage ER/PR-positive mucinous breast cancer patients. We found that the benefits obtained from adjuvant chemotherapy in ER/PR-positive mucinous adenocarcinoma depended on tumor size. In general, our study showed that early-stage ER/PR-positive patients in the chemotherapy group could have a better OS, but not BCSS, than those in the nonchemotherapy group. After stratifying by tumor size and lymph node status, our results are different from the NCCN guidelines.

When ER/PR-positive patients have negative LNs, the guidelines recommend adjuvant endocrine therapy alone regardless of tumor size. However, we found that patients could benefit from adjuvant chemotherapy if they had tumors larger than 3 cm because such patients had a better OS in the chemotherapy group than in the non-chemotherapy group.

When ER/PR-positive patients have LN metastasis, the guidelines recommend adjuvant endocrine therapy combined with or without adjuvant chemotherapy. However, the guidelines do not point out when these patients should and should not receive adjuvant chemotherapy. We found that those patients do not need adjuvant chemotherapy if they had tumors smaller than 1 cm. Patients with tumors larger than 1 cm had better OS in the chemotherapy group than in the nonchemotherapy group.

Therefore, patients with negative LNs should consider adjuvant chemotherapy if they have tumors larger than 3 cm and patients with LNs could consider omitting adjuvant chemotherapy if they

have tumors smaller than 1 cm.

Currently, genetic testing plays an important role in identifying the individual risk of recurrence for luminal patients to avoid the side effects of unnecessary adjuvant chemotherapy [19]. However, according to a previous study, genetic testing cannot be used to predict recurrence risk in mucinous breast cancer due to the abundant mucinous content [20]. To the best of our knowledge, this is the first SEER population-based study using PSM analysis to assess the value of adjuvant chemotherapy in treating mucinous breast cancer.

However, our study should be considered with several limitations. First, it is a retrospective study, which may inevitably result in selection bias even when using PSM. Second, chemotherapy regimens were not available, which may influence the effect of chemotherapy on OS and BCSS. Third, we did not assess the toxicity and side effects of the treatment for mucinous adenocarcinoma, which may affect the quality of life and compliance of patients.

Although our study provides evidence that ER/PR-positive patients with negative LNs and tumors larger than 3 cm and those with positive LNs and tumors larger than 1 cm could benefit from adjuvant chemotherapy, further clinical trials, and prospective studies should be conducted to validate our results and treatment guidelines for mucinous carcinoma.

Conclusion

Adjuvant chemotherapy may improve the prognosis of early-stage ER/PR-positive mucinous adenocarcinoma patients. Patients with negative LNs should consider adjuvant chemotherapy if they have tumors larger than 3 cm, while patients with positive LNs may consider adjuvant chemotherapy if they have tumors larger than 1 cm. We also suggest considering clinical characteristics meanwhile when deciding chemotherapy or not. These results could help oncologists to treat patients more precisely in the future. Randomized controlled trials (RCT) are expected to confirm our results in the future.

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Declaration of competing interest

All authors declare no conflicts of interest in this work.

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