BMJ Open

Adjuvant chemotherapy and survival outcomes in older women with HR+/HER2− breast cancer: a propensity score-matched retrospective cohort study using the SEER database

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To cite: Ma X, Wu S, Zhang X, *et al*. Adjuvant chemotherapy and survival outcomes in older women with HR+/HER2− breast cancer: a propensity score-matched retrospective cohort study using the SEER database. *BMJ Open* 2024;**14**:e078782. doi:10.1136/bmjopen-2023-078782

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2023-078782).

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Received 14 August 2023
Accepted 04 March 2024

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ABSTRACT

Objectives This study aimed to investigate the impact of adjuvant chemotherapy (ACT) on survival outcomes in older women with hormone receptor-positive and human epidermal growth factor receptor 2-negative (HR+/HER2−) breast cancer (BC).

Design A retrospective cohort study using data from the Surveillance, Epidemiology, and End Results database, which contains publicly available information from US cancer registries.

Setting and participants The study included 45 762 older patients with BC aged over 65 years diagnosed between 2010 and 2015.

Methods Patients were divided into two groups based on age: 65–79 years and ≥80 years. Propensity score matching (PSM) was employed to balance clinicopathological characteristics between patients who received ACT and those who did not. Data analysis used the χ^2 test and Kaplan-Meier method, with a subgroup analysis conducted to identify potential beneficiaries of ACT.

Outcome measures Overall survival (OS) and cancer-specific survival (CSS).

Results Due to clinicopathological characteristic imbalances between patients with BC aged 65–79 years and those aged ≥80 years, PSM was used to categorise the population into two groups for analysis: the 65–79 years age group (n=38 128) and the ≥80 years age group (n=7634). Among patients aged 65–79 years, Kaplan-Meier analysis post-PSM indicated that ACT was effective in improving OS (p<0.05, HR=0.80, 95% CI 0.73 to 0.88), particularly in those with advanced disease stages, but did not show a significant benefit in CSS (p=0.09, HR=1.13, 95% CI 0.98 to 1.31). Conversely, for patients aged ≥80 years, ACT did not demonstrate any improvement in OS (p=0.79, HR=1.04, 95% CI 0.79 to 1.36) or CSS (p=0.09, HR=1.46, 95% CI 0.69 to 2.26) after matching. Subgroup analysis also revealed no positive impact on OS and CSS.

Conclusions Patients with HR+/HER2− BC ≥80 years of age may be considered exempt from ACT because no benefits were found in terms of OS and CSS.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a systematic analysis that used a large sample from the Surveillance, Epidemiology, and End Results (SEER) database.
⇒ This study eliminated the effects of relevant factors in the group receiving ACT and the group not receiving ACT by use of propensity score matching.
⇒ The impact of comorbidities, endocrine therapy and ACT regimens on survival could not be assessed due to limitations of the SEER database.
⇒ The effect of selection bias could not be excluded entirely due to limitations of retrospective studies.

INTRODUCTION

Along with the increase in population ageing, the incidence of breast cancer (BC) in older women is also increasing worldwide annually.[1] There is currently no uniform definition of older patients with BC, female patients aged 65 years or older are generally considered older women. Approximately half of patients with BC are diagnosed at age 65 or older,[2 3] and patients aged ≥80 comprise a large percentage of this population. About one in four patients diagnosed with BC at over 65 years are 80 years of age or older, accounting for 10.6% of all patients with BC. Those diagnosed at ≥80 years have the highest mortality rate.[4 5] In addition, the proportion of new BC among women aged over 70 years is expected to increase from 24% in 2011 to 35% in 2030,[6] promoting the need to optimise cancer treatment recommendations for older adults.

Compared with younger patients, older patients are more likely to be hormone receptor-positive and human epidermal growth factor receptor 2-negative (HR+/HER2−), a subtype with a better prognosis.[7 8]

Some studies have demonstrated that BC in patients in older cohorts is less aggressive, with smaller tumour sizes and less or no lymph node involvement.[9–11] However, these patients carry a more significant burden of comorbidities and geriatric syndromes, such as cardiovascular and cerebrovascular diseases, functional cognitive impairment, malnutrition, polypharmacy and psychological distress.[12 13] The treatment of older patients with BC has always been controversial for several reasons. First, most clinical trials excluded elderly patients, and treatment strategies for elderly patients were often derived from an extended application of the evidence for treatment in the general age group. Second, the treatment strategy in older women is significantly inferior to that of younger patients due to older patients' higher rate of incompliance, toxic drug adverse effects and poorer health conditions.[14] Third, chronological age does not always coincide with biological age,[15] requiring clinical treatment decision-makers to assess patients more carefully and comprehensively.[16]

Patients with HR+/HER2− BC account for 70% of all BC cases.[17] Standard treatment varies depending on the risk of recurrence, and includes combinations of surgery, radiotherapy, adjuvant/neoadjuvant chemotherapy and endocrine therapy.[11 18] Previous studies have confirmed that endocrine therapy and surgery are associated with better overall survival in elderly patients with HR+ BC.[17 19–21] However, whether adjuvant chemotherapy (ACT) is beneficial in elderly patients, especially HR+/HER2− patients ≥80 years old, has rarely been studied. Recently updated American Society of Clinical Oncology (ASCO) practice guidelines recommend the use of multigene assays in HR+/HER2− early BC adjuvant decision-making, of which the 21-gene test (Oncotype DX) is the most widely used.[22] Although Oncotype DX is considered the genomic test of choice worldwide, the high cost and the remaining areas of uncertainty make the widespread use of this tool challenging.[23] This paper attempts to find a more straightforward way to measure the benefits of ACT in older patients with HR+/HER2− BC by determining whether this cohort should receive ACT by age alone.

In this study, we compared the clinical and pathological characteristics, treatments and long-term outcomes of patients with HR+/HER2− BC aged 65–79 years and those aged ≥80 years using the Surveillance, Epidemiology, and End Results (SEER) database, and investigated the impact of ACT on overall survival (OS) and cancer-specific survival (CSS) in both age cohorts of older women. This study aimed to evaluate the potential benefits of ACT to patients with BC aged ≥80 years.

METHODS

Data source

This retrospective study analysed the SEER 17 Registry maintained by the National Cancer Institute (NCI; 2000–2019; data set submitted in November 2021; www.seer.cancer.gov)[24].The SEER*Stat software (V.8.4.0) was used to extract clinicopathological and survival information from the database. The NCI (USA) provided permission to access the research data file in the SEER Registry (reference number 15031, November 2021).

Study cohort

Since the database only included HER2-related data after 2010 and to ensure a specific follow-up time, female patients diagnosed with HR+/HER2− primary invasive ductal BC (histological codes 8500, 8521, 8522 and 8523 of International Classification of Disease for Oncology third edition, ICD-O-3) between 2010 and 2015 were enrolled. All patients underwent surgery and received postoperative systemic therapy. Exclusion criteria included (1) male patients; (2) age <65 at diagnosis; (3) T0, Tx and Nx stage; (4) patients with distant metastases (M1 stage); and (5) missing data. According to age at diagnosis, patients were divided into two groups: 38 128 patients in the 65–79 years age group and 7634 patients in the older age group (≥80 years).

Exposures and covariates

The primary study endpoints were OS and CSS. Other covariates included race (white/black/others), tumour grade (I–II/III–IV), T stage (T1–T4), N stage (N0–N3), marital status (absence or presence of a marital partner at diagnosis of BC, indicated by 'No' or 'Yes', respectively), radiotherapy ('No/Unknown' or 'Yes'), chemotherapy ('No' or 'Yes') and surgery (breast-conserving surgery, mastectomy, modified radical mastectomy). Staging was classified according to the American Joint Committee on Cancer Tumor Node Metastasis (TNM) Sixth Edition.

Outcomes

OS was calculated from the date of diagnosis to the date of death from any cause. CSS was measured from the date of diagnosis to the date of direct or indirect death from BC. The SEER database shows the survival status as 'Vital Status'.

Statistical analysis

The baseline characteristics of elderly patients with BC aged 65–79 years and ≥80 years with HR+/HER2− were compared using χ^2 or Fisher's exact test. We then further studied the two cohorts separately. Each cohort was subdivided into two groups based on whether the patient received ACT, that is, the group receiving ACT and the group not receiving ACT. To reduce possible confounding factors, we used a 1:1 propensity score matching (PSM) to balance important clinicopathological characteristics between the group receiving and not receiving ACT, with a calliper value of 0.0001 for the 65–79 years age group and 0.001 for the ≥80 years age group. Variables in the PSM analysis included age, race, marital status, grade, T stage, N stage, radiotherapy and surgery. The Kaplan-Meier method was used to calculate the OS and CSS curves for patients who received ACT and those who did not receive ACT before and after PSM. The log-rank test

was performed to determine statistical significance. After PSM, the Cox proportional hazards regression model was used to explore subgroups that might benefit from ACT. Subgroups were analysed according to age, race, marital status, grade, T stage, N stage, radiotherapy and surgery. In cases where the HR and 95% CI were between 0 and 1, a smaller HR meant the patient benefited more from ACT. In cases where the HR and 95% CI were more significant than 1, a larger HR meant the patient did not benefit more from ACT. HR and 95% CI were calculated and a two-sided p value <0.05 was considered statistically significant. Statistical analyses were performed using R software (V.4.2.2).

Patient and public involvement

None.

RESULTS

Clinicopathological characteristics

The baseline clinical characteristics of older patients with HR+/HER2− BC who had undergone surgery are shown in table 1. There were 45 762 eligible patients in this study, including patients aged 65–79 years (n=38 128) and patients aged ≥80 years (n=7634). Compared with the 65–79 years age group, at initial diagnosis, the ≥80 years age group had higher tumour histological grade (III/IV: 17.1% vs 19.1%, p<0.05), later T stage (T3: 1.87% vs 2.92%; T4: 0.60% vs 2.16%, p<0.05) and N stage (N2: 3.23% vs 3.89%; N3: 1.44% vs 1.70%, p<0.05), a relatively low proportion with marital partners (54.1% vs 32.3%, p<0.05), and a lower ratio receiving radiotherapy (63.2% vs 40.3%, p<0.05) and chemotherapy (20.7% vs 3.76%, p<0.05). They all differed statistically, confirming significant differences in the clinicopathological characteristics of patients with HR+/HER2− BC aged 65–79 and ≥80 years.

Table 1 Comparison of the clinical characteristics of patients with HR+/HER2− breast cancer between the 65–79 years age group and the ≥80 years age group

Characteristics	65–79 years	≥80 years	P value
Patients, n	38 128	7634	
Race, n (%)			<0.001
White	32 285 (84.7)	6667 (87.3)	
Black	2696 (7.1)	487 (6.4)	
Other/unknown	3147 (8.3)	480 (6.3)	
Marital status, n (%)			<0.001
No	16 502 (43.3)	5044 (66.1)	
Yes	21 626 (56.7)	2590 (33.9)	
Grade, n (%)			<0.001
I/II	31 596 (82.9)	6175 (80.9)	
III/IV	6532 (17.1)	1459 (19.1)	
T stage, n (%)			<0.001
T1	28 806 (75.6)	4978 (65.2)	
T2	8380 (22.0)	2268 (29.7)	
T3	713 (1.9)	223 (2.9)	
T4	229 (0.6)	165 (2.2)	
N stage, n (%)			0.007
N0	29 525 (77.4)	5832 (76.4)	
N1	6820 (17.9)	1375 (18.0)	
N2	1233 (3.2)	297 (3.9)	
N3	550 (1.4)	130 (1.7)	
Radiotherapy, n (%)			<0.001
No/unknown	14 028 (36.8)	4561 (59.7)	
Yes	24 100 (63.2)	3073 (40.3)	
ACT, n (%)			<0.001
No	30 218 (79.3)	7347 (96.2)	
Yes	7910 (20.7)	287 (3.8)	
Surgery, n (%)			<0.001
BCS	26 355 (69.1)	5114 (67.0)	
MAST	7938 (20.8)	1571 (20.6)	
MRM	3835 (10.1)	949 (12.4)	

ACT, adjuvant chemotherapy; BCS, breast conservative surgery; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MAST, mastectomy; MRM, modified radical mastectomy; N stage, lymph node stage; T stage, tumour stage.

Survival outcomes before and after PSM

The variables before and after matching are shown in table 2 for patients with BC aged 65–79 years and in table 3 for patients with BC aged ≥80 years. There were 5543 patients with BC in the ACT and non-ACT groups in the matched cohort of patients aged 65–79 years and 232 patients with BC in the ACT and non-ACT groups in the matched cohort of patients aged ≥80 years. After PSM, the p values of the statistical tests for each variable in the groups receiving and not receiving ACT were close to '1', suggesting that PSM minimised the bias caused by other variables.

Interestingly, before matching, the results of the Kaplan-Meier survival curves showed that ACT did not improve OS and CSS in both groups and decreased patient survival time (figure 1A–D). After matching, ACT was effective in improving OS (p<0.001; figure 2A) but not CSS (p=0.092; figure 2B) in patients in the 65–79 years age group. For patients in the ≥80 years age group, ACT treatment had no noticeable effect on OS (p=0.79; figure 2C) and CSS (p=0.091; figure 2D).

In the subgroup survival analysis, ACT improved the OS in all age and histological grade subgroups in the 65–79 years age group. Also, for more advanced T stages (T2–T4) and N stages (N1–N3), ACT was effective in improving OS (online supplemental figure 1). Similarly, ACT improved CSS in T3, T4, N2 and N3 patients

Table 2 Clinicopathological features of patients aged 65–79 years with or without ACT before and after PSM

	Before PSM			After PSM		
	Without ACT	With ACT		Without ACT	With ACT	
Variables	n=30 218	n=7910	P value	n=5433	n=5433	P value
Age, n (%)			<0.001			1
65–69	12 417 (41.1)	4551 (57.5)		2853 (52.5)	2853 (52.5)	
70–79	17 801 (58.9)	3359 (42.5)		2580 (47.5)	2580 (47.5)	
Race, n (%)			<0.001			0.999
White	25 721 (85.1)	6564 (83.0)		4646 (85.5)	4646 (85.5)	
Black	1954 (6.5)	742 (9.4)		404 (7.4)	405 (7.5)	
Other/unknown	2543 (8.4)	604 (7.6)		383 (7.1)	382 (7.0)	
Marital status, n (%)			1			1
No	13 078 (43.3)	3424 (43.3)		2339 (43.1)	2338 (43.0)	
Yes	17 140 (56.7)	4486 (56.7)		3094 (56.9)	3095 (57.0)	
Grade, n (%)			<0.001			0.968
I/II	26 865 (88.9)	4731 (59.8)		3563 (65.6)	3566 (65.6)	
III/IV	3353 (11.1)	3179 (40.2)		1870 (34.4)	1867 (34.4)	
T stage, n (%)			<0.001			0.984
T1	24 913 (82.4)	3893 (49.2)		3134 (57.7)	3135 (57.7)	
T2	4915 (16.3)	3465 (43.8)		2121 (39.0)	2122 (39.1)	
T3	291 (1.0)	422 (5.3)		148 (2.7)	149 (2.7)	
T4	99 (0.3)	130 (1.6)		30 (0.6)	27 (0.5)	
N stage, n (%)			<0.001			0.969
N0	26 222 (86.8)	3303 (41.8)		3013 (55.5)	3013 (55.5)	
N1	3679 (12.2)	3141 (39.7)		2162 (39.8)	2162 (39.8)	
N2	231 (0.8)	1002 (12.7)		193 (3.6)	188 (3.5)	
N3	86 (0.3)	464 (5.9)		65 (1.2)	70 (1.3)	
Radiotherapy, n (%)			<0.001			1
No/unknown	10 745 (35.6)	3283 (41.5)		2256 (41.5)	2256 (41.5)	
Yes	19 473 (64.4)	4627 (58.5)		3177 (58.5)	3177 (58.5)	
Surgery, n (%)			<0.001			1
BCS	22 134 (73.2)	4221 (53.4)		3211 (59.1)	3210 (59.1)	
MAST	6057 (20.0)	1881 (23.8)		1400 (25.8)	1400 (25.8)	
MRM	2027 (6.7)	1808 (22.9)		822 (15.1)	823 (15.1)	

ACT, adjuvant chemotherapy; BCS, breast conservative surgery; MAST, mastectomy; MRM, modified radical mastectomy; PSM, propensity score matching; N stage, lymph node stage; T stage, tumour stage.

(online supplemental figure 2). However, the subgroup analysis for patients with BC aged ≥80 showed that ACT did not improve prognosis in terms of OS or CSS in each subgroup (online supplemental figures 3 and 4).

DISCUSSION

With population ageing, the number of Americans aged 65 and older is expected to reach 88.5 million by 2050. Many older women with HR+/HER2− BC are diagnosed with stage II–III disease.[25] There is no consensus definition for elderly patients; however, in the context of clinical trials, female patients older than 65 years old are usually considered older women.[26] This group is less likely to receive guideline-concordant treatment, including chemotherapy, partly due to their reduced tolerance to treatment.[27–30] Comorbidities and geriatric syndromes such as cardiovascular and cerebrovascular diseases, functional cognitive impairment, malnutrition polypharmacy, psychological distress and diabetes have been shown to lower the ability of patients to tolerate chemotherapy.[31–35] Older patients with BC have a higher risk of adverse events such as electrolyte imbalances, acute kidney injury, and cardiotoxicity and haematotoxicity than younger patients.[36] Also, BC treatment in older women often relies

Table 3 Clinicopathological features of patients aged ≥80 years with or without ACT before and after PSM

	Before PSM			After PSM		
	Without ACT	With ACT		Without ACT	With ACT	
	n=7347	n=287	P value	n=232	n=232	P value
Age, n (%)			<0.001			1
80–84	4719 (64.2)	237 (82.6)		189 (81.5)	189 (81.5)	
85+	2628 (35.8)	50 (17.4)		43 (18.5)	43 (18.5)	
Race, n (%)			0.002			1
White	6425 (87.5)	242 (84.3)		208 (89.7)	208 (89.7)	
Black	455 (6.2)	32 (11.1)		18 (7.8)	18 (7.8)	
Other/unknown	467 (6.4)	13 (4.5)		6 (2.6)	6 (2.6)	
Marital status, n (%)			0.007			1
No	4876 (66.4)	168 (58.5)		138 (59.5)	138 (59.5)	
Yes	2471 (33.6)	119 (41.5)		94 (40.5)	94 (40.5)	
Grade, n (%)			<0.001			1
I/II	6023 (82.0)	152 (53.0)		134 (57.8)	134 (57.8)	
III/IV	1324 (18.0)	135 (47.0)		98 (42.2)	98 (42.2)	
T stage, n (%)			<0.001			1
T1	4856 (66.1)	122 (42.5)		109 (47.0)	109 (47.0)	
T2	2145 (29.2)	123 (42.9)		100 (43.1)	100 (43.1)	
T3	199 (2.7)	24 (8.4)		14 (6.0)	14 (6.0)	
T4	147 (2.0)	18 (6.3)		9 (3.9)	9 (3.9)	
N stage, n (%)			<0.001			1
N0	5725 (77.9)	107 (37.3)		101 (43.5)	101 (43.5)	
N1	1274 (17.3)	101 (35.2)		84 (36.2)	84 (36.2)	
N2	240 (3.3)	57 (19.9)		39 (16.8)	39 (16.8)	
N3	108 (1.5)	22 (7.7)		8 (3.5)	8 (3.5)	
Radiotherapy, n (%)			<0.001			1
No/unknown	4421 (60.2)	140 (48.8)		113 (48.7)	113 (48.7)	
Yes	2926 (39.8)	147 (51.2)		119 (51.3)	119 (51.3)	
Surgery, n (%)			<0.001			1
BCS	4985 (67.9)	129 (44.9)		121 (52.2)	121 (52.2)	
MAST	1507 (20.5)	64 (22.3)		48 (20.7)	48 (20.7)	
MRM	855 (11.6)	94 (32.8)		63 (27.2)	63 (27.2)	

ACT, adjuvant chemotherapy; BCS, breast conservative surgery; MAST, mastectomy; MRM, modified radical mastectomy; PSM, propensity score matching; N stage, lymph node stage; T stage, tumour stage.

on extrapolated evidence from younger populations.[37] The above reasons lead to treatment of older patients with BC not being standardised and to few clinical trials being conducted specifically for this group, increasing their risk of recurrence. In addition, Oncotype DX is considered the genomic assay of choice worldwide and its primary purpose is to assess the risk of early HR+/ HER2– BC local and distant recurrence so that patients could be exempted from receiving ACT. However, it has the disadvantages of high price and uncertainty.[23] Using data from a large sample based on the SEER database, this study concluded that further age stratification was necessary for older women with HR+/HER2– BC over 65 years of age. According to our age classification, ACT improved the prognosis of patients aged 65–79. In contrast, ACT did not provide survival benefit and was even harmful to those aged ≥80 years.

In the entire patient population of older women, most of the elderly patients had lower tumour histological grade, earlier tumour stage and negative lymph node involvement. These findings are consistent with previous studies[10 38] and may explain why, of all age groups, the highest percentage of patients with BC who underwent breast-conserving surgery is in older patients.[39] We

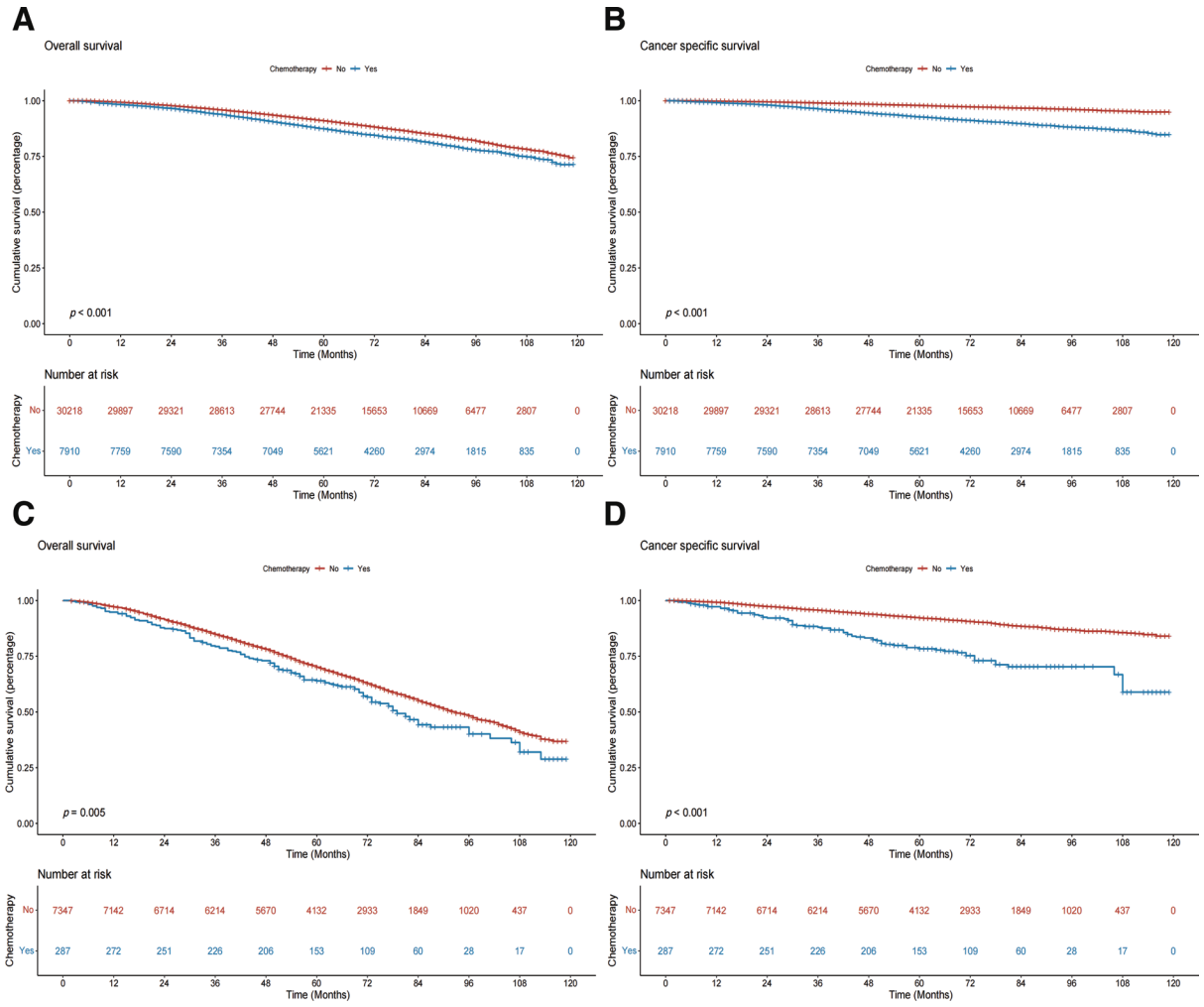

Figure 1 Overall survival (A) and cancer-specific survival (B) in the group of patients with breast cancer aged 65–79 years, and overall survival (C) and cancer-specific survival (D) in the group of patients with breast cancer aged ≥80 years, before matching.

demonstrated significant differences in clinical characteristics and treatment patterns between female patients aged 65–79 years and ≥80 years with primary invasive ductal BC. In the two subgroups, the ≥80 years age group manifested more aggressive and advanced tumour stage, with larger tumour size and more advanced lymph node staging, than the 65–79 years age group, which may explain the concept that mortality increases with age.[11]

A retrospective study from Japan including 12 727 older patients with BC aged >75 years found lower chemotherapy use in older women with stage II/III BC. Still, chemotherapy improved OS in luminal and HER2-positive patients.[40] It should be noted that the proportion of HR+/HER2− patients in their study was small, accounting for only 9.2%, and the sample size was much smaller than in our study, indicating that our findings are more reliable. A recently published retrospective study that included 1703 elderly patients with BC over 65 years of age found that ACT improved OS in older patients, particularly those with larger tumour diameters and positive lymph nodes.[41] The study included a higher percentage of HR+/HER2− patients, at 70%. However, its sample size was much smaller than our study. Our study also showed that ACT improved survival in patients aged 65–79 years and was more pronounced in patients with more advanced staging, consistent with their study. However, our analysis of patients aged ≥80 years did not find a survival advantage for ACT, which was complementary to their results because the sample size of their study's ≥80 years of age population was much smaller than ours.

In a study that included 592 patients with BC over 70 years with complications and lymph node-positive disease, those who received ACT had better survival rates than those who did not (HR=0.67, 95% CI 0.48 to 0.98).[42] Another multicentre prospective observational study of 3456 patients with BC aged ≥70 years showed that chemotherapy reduced the risk of metastasis but did not significantly improve OS and CSS. Chemotherapy improved OS and CSS only in patients with HR− BC.[43] In a study designed to assess the impact of chemotherapy on patients over 70 years of age, it was shown that older women with BC who are in good health may tolerate chemotherapy as well as younger patients. Still, the number of patients meeting the criteria was too small.[44] Overall, most of the studies on the choice of chemotherapy for older women with BC had small sample sizes. Most of these studies did

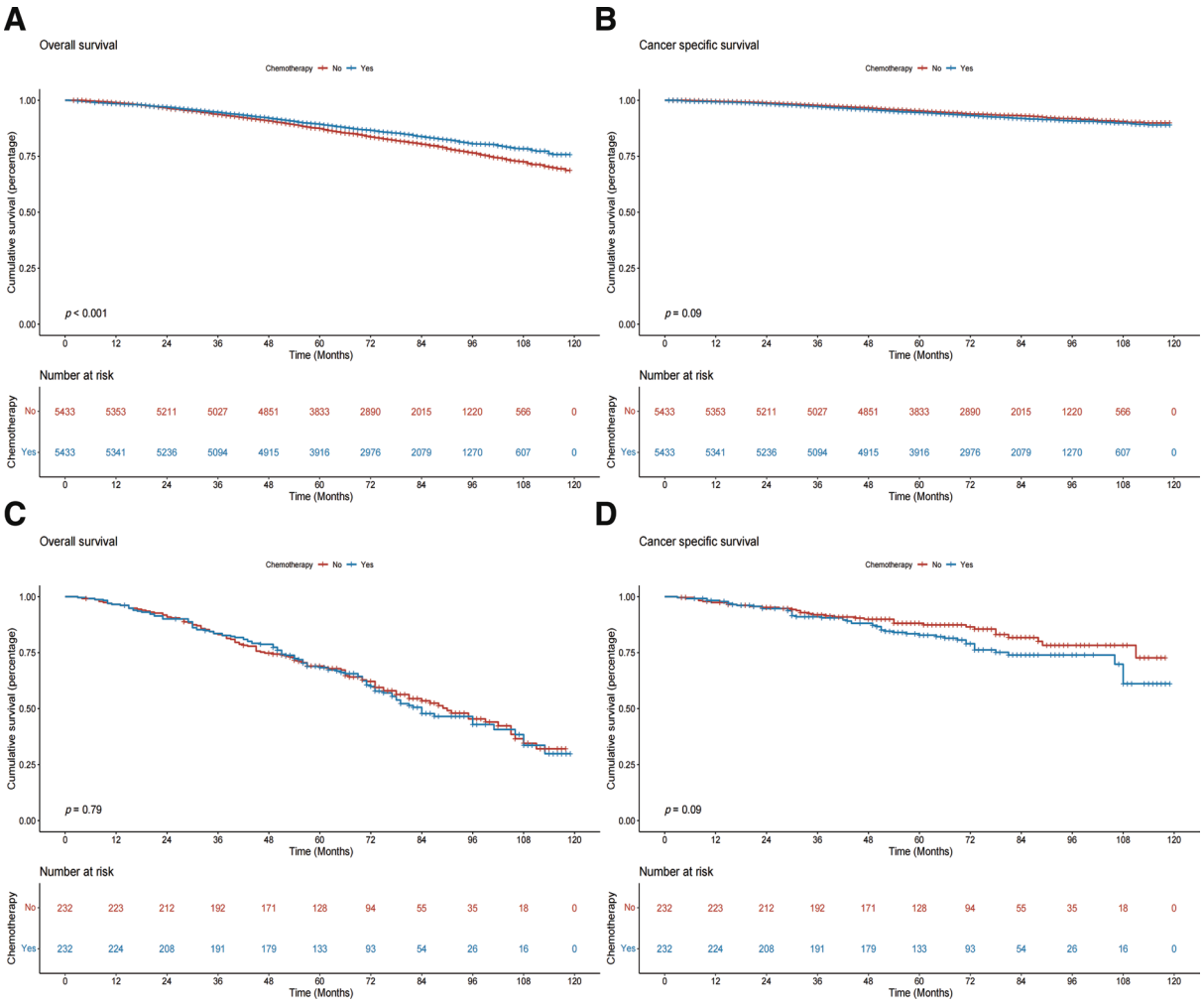

Figure 2 Overall survival (A) and cancer-specific survival (B) in the group of patients with breast cancer aged 65–79 years, and overall survival (C) and cancer-specific survival (D) in the group of patients with breast cancer aged ≥80 years, after matching.

not further stratify by age because older patients became less tolerant of chemotherapy with age. In contrast, our study took advantage of a large sample size and subdivided older women over 65 into two groups: the 65–79 years age group and the ≥80 years age group. In the 65–79 years age group, we reached conclusions consistent with most previous studies. However, in the ≥80 years age group, our study concluded that ACT did not improve long-term survival, including OS and CSS.

Based on our findings and on previous studies,[17 45] endocrine therapy could be an alternative treatment. Several classes of endocrine therapies have been developed, including selective oestrogen receptor modulators, selective oestrogen receptor downregulators, aromatase inhibitors, luteinising hormone-releasing hormone agonists, high-dose oestrogens and primarily targeted therapies.[46 47] Several clinical studies have shown that cyclin-dependent kinase 4/6 (CDK4/6) inhibitors or histone deacetylase (HDAC) inhibitors combined with conventional endocrine therapy had comparable efficacy to chemotherapy in patients with advanced BC, with low adverse drug reactions.[48–50] If patients with BC cannot tolerate chemotherapy, CDK4/6 or HDAC inhibitors combined with conventional endocrine therapy might be a good option. Of course, clinical safety and survival benefits require rigorous clinical trials.

Equally important, deciding on treatment strategies based solely on chronological age increases the risk of overtreatment or undertreatment in older patients.[51] Chronological age, based on date of birth, is the traditional criterion for assessing ageing, and the degree of ageing can vary widely between individuals,[52] making chronological age not the best indicator for assessing the degree of ageing in humans. Biological age is often used as an alternative to chronological age to assess ageing.[53] Based on tens of thousands of genetic samples from human tissues, Steve Horvath found the pattern of DNA methylation in the ageing process and developed a tool for measuring physiological age—epigenetic clock—with an accuracy of 98%.[54] The value of physiological age should be fully considered in practical treatment decisions.[15] Geriatric assessment (GA) helps estimate life expectancy better and contributes to therapeutic decision-making in geriatric oncology. GA usually includes several dimensions, such as physical performance, risk of falls, functional status, multiple comorbidities, polypharmacy status, depressive

symptoms, cognitive ability, psychosocial distress, nutritional status and socioeconomic support.[55] The European Society of Breast Cancer Specialists and the International Society of Geriatric Oncology recommend that GA be used in the management of all elderly patients with BC.[56] Our study further demonstrates the importance of performing GA for older patients with BC to make sound decisions when considering cancer treatment to maximise benefit and minimise harm to each patient.

We need to point out some limitations to this study. First, this was a regression study, and despite using statistical methods, such as PSM, selection bias and other problems could not be eliminated. Second, some patients were recorded as not receiving ACT in the SEER database; however, they may also have received chemotherapy during follow-up treatment which may not have been recorded. Also, data on endocrine therapy were not available in the database. Third, data on recurrence or metastasis during follow-up were also not available in the database. Fourth, the SEER database did not provide specific information on comorbidities other than cancer in older patients, the ACT regimen used, the dose received, the number of cycles given and the ACT complications. In this study, we defined receiving systemic therapy postoperatively and receiving ACT as chemotherapy. Future studies with large sample sizes and incorporating endocrine therapy conditions, comorbidities and adverse effects are needed to investigate the absolute clinical benefit of ACT in older women.

CONCLUSIONS

Our study suggests that older women with BC over 65 years of age should be further stratified according to age. Patients with HR+/HER2− BC aged ≥80 years may be considered exempt from receiving ACT, while ACT could be considered in patients with HR+/HER2− BC aged 65–79 years, especially in those with advanced tumour stage.

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Contributors Paper concept and design: YL, XM and SW. Review of the literature: YL, XM, SW, XZ, CheY and MC. Data analysis and interpretation: XM, NC, ChaY and KD. Manuscript editing and critical review: all authors. Approval of the final draft: all authors. YL approved the submission of the manuscript. YL has full responsibility for the overall content as the guarantor, had access to the data andcontrolled the decision to publish.

Funding This study was supported by Project '100 Foreign Experts Plan of Hebei Province', China (no: 2022001).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The SEER database was used as the data source for this study. The SEER database has been approved by the NIH Ethics Program (Office of Ethics, NIH and the ethics programmes of the institutes and centres).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository.

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