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DATABASE ANALYSIS

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Nomogram for Predicting Breast Cancer-Specific Mortality of Elderly Women with Breast Cancer

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Background: The objectives of this study were to evaluate the cumulative incidence of breast cancer-specific death (BCSD) and other cause-specific death in elderly patients with breast cancer (BC) and to develop an individualized nomogram for estimating BCSD.

Material/Methods: Data were retrieved from the Surveillance, Epidemiology, and End Results program. A total of 25 241 patients older than 65 years with stage I–III BC diagnosed between 2004 and 2008 was included in the study cohort. We used the cumulative incidence function (CIF) to describe the cause-specific mortality and Gray's test to compare the differences in CIF among the groups. Fine and Gray's proportional subdistribution hazard model was applied to validate the independent prognostic factors, upon which the competing-risks nomogram and web-based calculator was built. The performance of the nomogram was assessed with the C-indexes and calibration plot diagrams.

Results: After data screening, 25 241 cases were included for statistical analysis. In the training cohort, the 5-, 8-, and 10-year cumulative incidence of BCSD was 5.7, 8.1, and 9.1%, respectively. Ten independent prognostic factors associated with BCSD were identified. The C-index of the nomogram was 0.818 (0.804–0.831) in the training cohort and 0.808 (0.783–0.833) in the validation cohort. Calibration plot diagrams showed near-ideal consistency between the predicted probabilities and actual observations.

Conclusions: We built a reliable dynamic nomogram for predicting BCSD in elderly patients, and this individualized predictive tool is favorable for risk classification and complex personalized treatment decision making in clinical practice.

MeSH Keywords: Breast Neoplasms • Mortality • Nomograms • Prognosis • SEER Program

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Background

Breast cancer (BC) is the most common cancer and was the leading cause of cancer death in females worldwide in 2018, accounting for an estimated 24.2% of new cancer diagnoses and 15.0% of cancer deaths [1]. In the United States, there were 317 468 new cases in 2011–2015, of which approximately 43.2% were in women 65 years or older [2]. The probability of developing invasive BC among women ages >70 has increased to 1 in 15, compared with 1 in 52 among women ages <49 in 2018 [3]. With the world population aging [4], the elderly will continue to be a large component of BC patients.

BC in older women, compared with their younger counterparts, has distinctive biological and clinical characteristics. Syed et al. [5] reported that a high expression of estrogen receptor (ER), progesterone receptor (PR), BCL2, and MUC1, along with a low expression of human epidermal growth factor receptor-2 (HER-2), epidermal growth factor receptor, Ki-67, and p53, is more frequently observed in the tumor biology of the elderly. According to the San Antonio Breast Cancer Database and the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute, the proportion of ER-positive patients in the 65-year-old group is 4–8% more than those in the 55- to 64-year-old group [6], who are good candidates for endocrine therapy.

Increasing age, however, confers high risks for loss of function and numerous chronic health problems, such as ischemic heart disease, diabetes, hypertension, and arthritis [7]. Inevitably, physiological decline signifies a reduced tolerance to treatments. Additionally, corresponding to the lack of prospective studies for the elderly with BC [8–10], the evidence and guidelines for treatment in this population are insufficient. Given all these complexities, clinicians are challenged with proposing reasonable treatment strategies for this population.

Consequently, it is of great significance to develop a model for evaluating disease risk on a personalized level. Nomograms constructed on the basis of prognostic factors are increasingly becoming widely applied to quantify the likelihood of the specific events of interest [11–14]. Likewise, this kind of convenient and practical tool can be used to predict the mortality resulting from BC for elderly patients, potentially facilitating the screening of individuals in need of positive treatment strategies and intensive caring intervention. In this study, a nomogram was built by competing-risks analysis based on data from the SEER database, and after validation, the nomogram manifested an excellent predictive ability.

Material and and Methods

Study population

Data for this retrospective study were obtained from the SEER program, which consists of 18 population-based cancer registries, for the period 1973–2015 [15]. To ensure integrated data and adequate follow-up time, the clinicopathological information of patients diagnosed between 2004 and 2008 was collected from SEER*Stat Version 8.3.5 (*http://www.seer.cancer.gov/seerstat*). The inclusion criteria to identify eligible patients were as follows: 1) female; 2) age 65 years or older at diagnosis; 3) BC as the first and only primary malignancy; 4) diagnosis confirmed by positive histology other than by autopsy or death certificate only; 5) unilateral BC; 6) breast-adjusted American Joint Committee on Cancer (AJCC) 6th edition (1998+) stage I–III; 7) surgical treatment with either breast-conserving surgery (BCS) or mastectomy; and 8) active follow-up. Simultaneously, patients diagnosed with inflammatory BC or Paget's disease were excluded, as were those with missing information on marital status, race, histological grade, tumor (T) and nearby lymph node (N) stage, ER and PR status, and survival data. After a detailed screening, a total of 25 241 patients was eventually enrolled in our study. Data were analyzed according to the following clinicopathological characteristics: age (65–75 or 75+ years), marital status (unmarried or married), race (white, black, or others), histological type (invasive ductal carcinoma [IDC], invasive lobular carcinoma, or others), histological grade (I, II, or III/IV), laterality (left or right), ER and PR status (positive or negative), T stage (T1, T2, T3, or T4), N stage (N0, N1, N2, or N3), and surgery (BCS or mastectomy).

Statistical analysis

To establish and validate a competing-risks nomogram, the eligible patients were divided randomly into a training cohort (20 798) for building the model and a validation cohort (4443) for evaluating model performance. Breast cancer-specific death (BCSD) was measured as the time from the date of diagnosis to death attributed to BC, the date of the last follow-up or December 31, 2015 (if date of last contact was after 2015). Other cause-specific death (OCSD) was defined as competing outcomes. Cumulative incidence function (CIF) was applied to describe the probability of BCSD and OCSD grouped by age, marital status, race, histological type, histological grade, laterality, T and N stage, ER and PR status, and surgery; the differences of cause-specific deaths in CIF among the categorical groups were estimated with Gray's test [16].

Variables with $P<0.05$ in the univariate analysis were entered into a multivariate competing-risks survival analysis via the proportional subdistribution hazard model by Fine and Gary [17]. Subsequently, we constructed a competing-risks nomogram

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on the basis of the model we developed to predict the probability of mortality due to BC at 5, 8, and 10 years. To evaluate the model performance, the nomogram was subjected to validation both internally and externally with a 1000-resampling bootstrap method. The concordance index (C-index) value was used to quantify the discrimination performance [18], and calibration curves were plotted to visually assess the calibration, which compared the nomogram-predicted probabilities with the observed marginal cumulative incidence. The C-index ranges from 0.5 to 1.0, indicating random chance to a perfectly precise discrimination. For a well-calibrated model, the dots in the calibration curve should be located close to a 45° diagonal line. Finally, we used the "shiny" and "DNbuilder" packages to generate a web-based BCSD calculator, which can dynamically predict cancer-specific death rates (*https://www.shiny apps.io/*).

All statistical analyses were performed using SPSS software, version 23 (IBM Corporation, Armonk, NY, USA) and R version 3.5.2 software (Institute for Statistics and Mathematics, Vienna, Austria; *http://www.r-project.org/*), with the R packages cmprsk [19], rms [20], and mstate [21] for developing the model and nomogram and the package pec [22] for evaluating model performance. All *P*-values were two sided and $P<0.05$ was considered statistically significant.

Results

Patient's baseline characteristics

A total of 25 241 eligible patients (20 798 patients in the training cohort and 4443 patients in the validation cohort) with histologically confirmed invasive BC was included in this study. The demographic and baseline characteristics of these patients are shown in Table 1. In the entire population, the majority of patients were married (85.4%) and white (86.7%). Of all the histological types, most cases were of infiltrating ductal carcinoma (72.6%). Of the patients treated with surgery, 64.8% underwent BCS, whereas 35.2% received mastectomy.

Univariate and multivariate analysis

The median follow-up time was 98 (interquartile range 84–117) months. In total, 7480 patients (29.6%) died during the follow-up period, of whom 2271 patients (9.0%) died from BC and 5209 patients (20.6%) died from other causes. For the training cohort, the 5-, 8-, and 10-year cumulative incidences of BCSD stratified by clinicopathological parameters are shown in Table 2, and those of OCSD are displayed in Supplementary Table 1. The 5-, 8-, and 10-year estimates of the crude cumulative incidence of BCSD were 5.7, 8.1, and 9.1%, respectively, and that of OCSD were 9.1, 17.3, and 23.0%, respectively, which were almost twice as much as that of BCSD. The cumulative incidences of BCSD were strongly associated with all the variables ($P<0.001$), except laterality ($P=0.170$), and OCSD differed significantly between those with different ages ($P<0.001$), marital status ($P<0.001$), race ($P<0.001$), T stage ($P<0.001$), and surgery ($P<0.001$) in the univariate analysis. The differences of BCSD and OCSD discovered by Gray's test in all categorical variables were presented visually in Figure 1 and Supplementary Figure 1, respectively.

Multivariate analysis further validated the following variables used for building the BCSD model: age, marital status, race, histological type, histological grade, ER and PR status, T and N stage, and surgery. Coefficients and subdistribution hazard ratios ($_{sd}$HRs) from the multivariable analysis for building the model are presented in Table 3. Both age and marital status were significant independent predictors for BCSD, with a $_{sd}$HR of 1.43 (1.30–1.58) and 0.73 (0.65–0.82) for patients older than 75 years and who were married, respectively. Patients with grade III/IV or II were more likely to die of BC than those with grade I. Moreover, positive ER and PR predicted a lower incidence of BCSD, with $_{sd}$HR values of 0.33 (0.20–0.37) and 0.38 (0.35–0.42), respectively. Notably, advanced T and N stages led to a higher likelihood of BCSD. Compared with patients who underwent BCS, patients who underwent mastectomy had an increase in the probability of BCSD, with a $_{sd}$HR of 2.81 (2.56–3.10).

Construction and validation of the competing-risks nomogram

All of the validated factors were incorporated to develop the competing-risks nomogram for predicting the 5-, 8-, and 10-year probability of BCSD by calculating the sum of the point values corresponding to each patient's characteristics. Figure 2 shows that the N stage was the strongest contributor to BCSD, followed by the T stage and histological grade. The model showed a great discriminative ability in both the internal and external calibrations, with C-indexes of 0.818 (0.804–0.831) and 0.808 (0.783–0.833), respectively. The calibration plots in Figure 3 indicated that the nomogram was well calibrated because the predicted probability of mortality and the actual observations showed near-ideal consistency. According to these results, we built a web-based calculator (*https://bcsd.shinyapps.io/DynNomapp/*) to predict the BCSD of the elderly patients on the basis of the nomogram. As shown in Figure 4, the dynamic nomogram predicted the mortality of patients according to their clinical characteristics. For example, the 8-year BCSD was approximately 47.0% (95% confidence interval 39.0–58.0%) for patients ages 65–74 years, married, black race, IDC, grade II, with T3, N2 disease, ER negative, PR negative, with mastectomy.

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Table 1. Patients' demographics and baseline characteristics.

Characteristics	All patients N=25 241		Training cohort N=20 798		Validation cohort N=4443	
	n	%	n	%	n	%
Age						
65–74	16 183	64.1	13 348	64.2	2835	63.8
75+	9058	35.9	7450	35.8	1608	36.2
Marriage						
Unmarried	3680	14.6	3039	14.6	641	14.4
Married	21 561	85.4	17 759	85.4	3802	85.6
Race						
White	21 887	86.7	18 031	86.7	3856	86.8
Black	1591	6.3	1299	6.2	292	6.6
Other*	1763	7.0	1468	7.1	295	6.6
Histology						
IDC	18 320	72.6	15 140	72.8	3180	71.6
ILC	2085	8.3	1761	8.5	324	7.3
Other**	4836	19.2	3897	18.7	939	21.1
Grade						
I	6734	26.7	5535	26.6	1199	27.0
II	11 491	45.5	9487	45.6	2004	45.1
III/IV	7016	27.8	5776	27.8	1240	27.9
Laterality						
Left	12 842	50.9	10 607	51.0	2235	50.3
Right	12 399	49.1	10 191	49.0	2208	49.7
ER status						
Negative	4137	16.4	3381	16.3	756	17.0
Positive	21 104	83.6	17 417	83.7	3687	83.0
PR status						
Negative	7400	29.3	6011	28.9	1389	31.3
Positive	17 841	70.7	14 787	71.7	3054	68.7
T stage						
T1	17 419	69.0	14 386	69.2	3033	68.3
T2	6532	25.9	5341	25.7	1191	26.8
T3	785	3.1	664	3.2	121	2.7
T4	505	2.0	407	2.0	98	2.2
N stage						
N0	18 679	74.0	15 455	74.3	3224	72.6
N1	4683	18.6	3854	18.5	829	18.7

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Table 1 continued. Patients' demographics and baseline characteristics.

Characteristics	All patients N=25 241		Training cohort N=20 798		Validation cohort N=4443	
	n	%	n	%	n	%
N2	1192	4.7	933	4.5	259	5.8
N3	687	2.7	556	2.7	131	2.9
Surgery						
BCS	16345	64.8	13514	65.0	2831	63.7
Mastectomy	8896	35.2	7284	35.0	1612	36.3
Cause of death						
No events	17 761	70.4	15 084	72.5	2677	60.3
BCSD	2271	9.0	1748	8.4	523	11.8
OCSD	5209	20.6	3966	19.1	1243	28.0

IDC – infiltrating ductal carcinoma; ILC – infiltrating lobular carcinoma; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery; BCSD – breast cancer-specific death; OCSD – other cause-specific death; T – tumor stage; N – nearby lymph node stage. * Including American Indian/Alaskan native and Pacific Islander; ** including other histology of invasive breast cancer except IDC and ILC.

Table 2. 5-, 8-, 10-Year cumulative incidences of BCSD among patients with breast cancer in the training cohort.

Characteristics	BCSD				
	Events (%)	5-y (%)	8-y (%)	10-y (%)	*P*-value
Total	1748 (100.0)	5.7	8.1	9.2	
Age					<0.001
65–74	981 (56.1)	4.6	7.0	8.2	
75+	767 (43.9)	7.6	10.1	11.0	
Marriage					<0.001
Unmarried	325 (18.6)	7.5	10.6	11.6	
Married	1423 (81.4)	5.4	7.7	8.8	
Race					<0.001
White	1475 (84.4)	5.5	7.9	9.0	
Black	166 (9.5)	9.4	12.7	13.4	
Other*	107 (6.1)	5.0	7.2	8.1	
Histology					<0.001
IDC	1326 (75.9)	6.2	8.5	9.6	
ILC	172 (9.8)	5.0	9.2	11.3	
Other**	250 (14.3)	4.3	6.2	6.9	
Grade					<0.001
I	138 (7.9)	1.3	2.4	2.7	
II	648 (37.1)	4.0	6.4	7.8	
III/IV	962 (55.0)	12.8	16.4	17.7	

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Table 2 continued. 5-, 8-, 10-Year cumulative incidences of BCSD among patients with breast cancer in the training cohort.

Characteristics	BCSD				
	Events (%)		5-y (%)	8-y (%)	10-y (%)	*P*-value
Laterality						0.170
Left	919	(52.6)	5.8	8.3	9.6	
Right	829	(47.4)	5.6	7.9	8.8	
ER status						<0.001
Negative	611	(35.0)	15.0	18.0	18.8	
Positive	1137	(65.0)	3.9	6.2	7.4	
PR status						<0.001
Negative	877	(50.2)	11.5	14.4	15.4	
Positive	871	(49.8)	3.4	5.6	6.7	
T stage						<0.001
T1	587	(33.6)	2.5	3.9	4.6	
T2	811	(46.4)	10.6	14.9	16.5	
T3	193	(11.0)	20.6	28.0	31.4	
T4	157	(9.0)	30.3	38.5	39.7	
N stage						<0.001
N0	688	(39.4)	2.8	4.3	5.0	
N1	561	(32.1)	9.9	14.0	15.8	
N2	257	(14.7)	19.8	26.9	29.6	
N3	242	(13.8)	32.3	42.8	47.0	
Surgery						<0.001
BCS	719	(41.1)	3.5	5.0	6.0	
Mastectomy	1029	(58.9)	9.9	13.9	15.2	

IDC – infiltrating ductal carcinoma; ILC – infiltrating lobular carcinoma; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery; BCSD – breast cancer-specific death; OCSD – other cause-specific death; T – tumor stage; N – nearby lymph node stage. * Including American Indian/Alaskan native and Pacific Islander; ** including other histology of invasive breast cancer except IDC and ILC.

Discussion

With the rapid development of precision medicine, clinicians need to develop individualized treatment and follow-up strategies for patients, which requires more reliable and convenient assessment models. Nomograms integrate both clinical and demographic characteristics into a comprehensive model for predicting the long-term survival of patients. Furthermore, web-based calculators based on the nomogram improve the approachability of the predictive model. In this study, we identified 10 predictors for BCSD by means of a competing-risk analysis that included age, marital status, race, histological type, histological grade, ER and PR status, T and N stage, and surgery, and then established a novel dynamic nomogram. Therefore, clinicians could evaluate a patient's BCSD much more effectively and then create personalized treatment strategies and follow-up plans. To the best of our knowledge, this is the first nomogram constructed for predicting BCSD in elderly patients.

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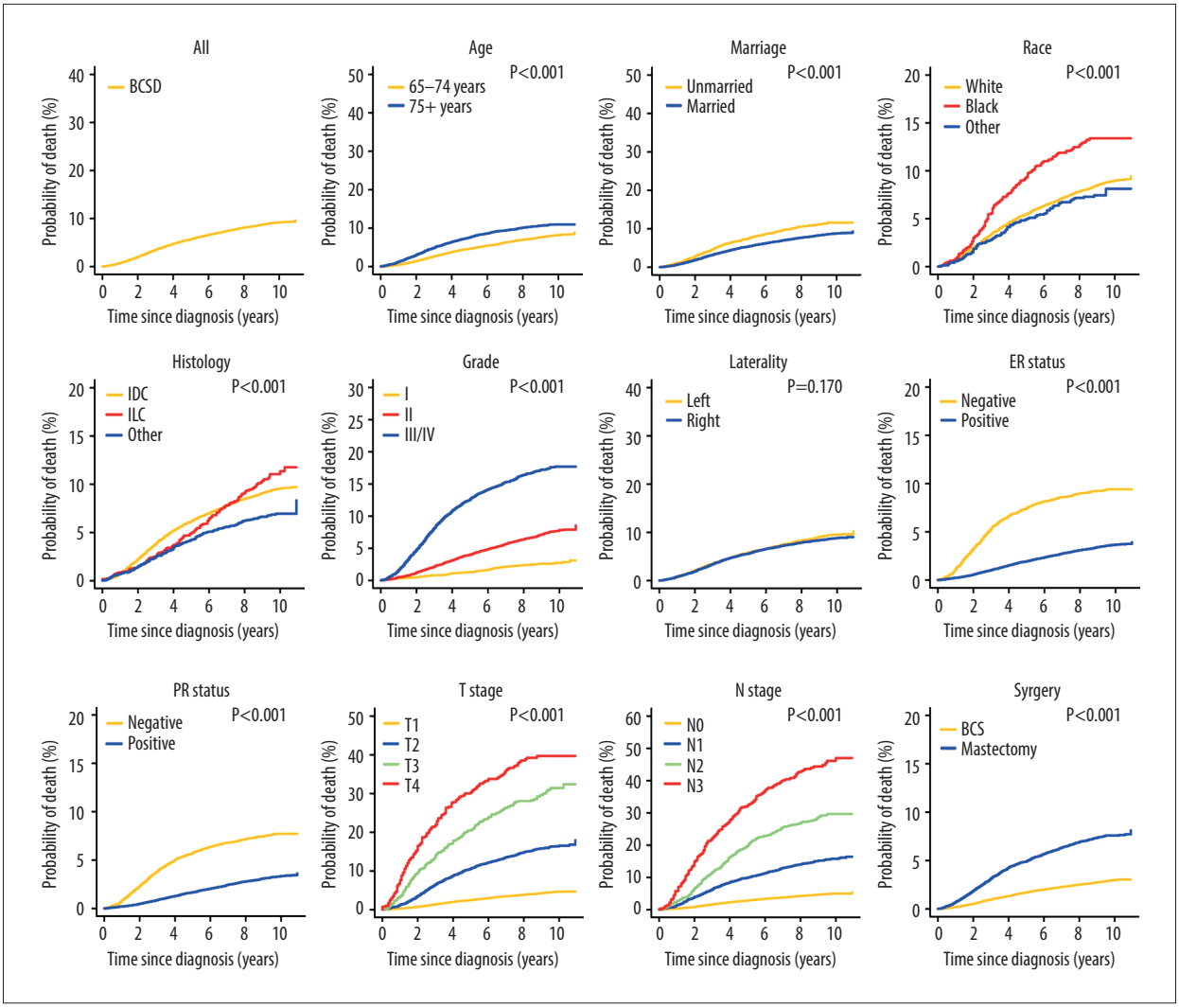

Figure 1. Cumulative incidence functions curves of breast cancer-specific death (BCSD) by patients' characteristic.

Competing-risks events pervasively exist in clinical studies for elderly patients, a frail population commonly accompanied by various chronic diseases, and the occurrence of death due to other causes may arise before and preclude that of the event of interest. Considering this, the Kaplan-Meier method and Cox proportional hazards regression model, which are usually used in survival analysis, were not appropriate for the competing-risks framework because the use of the Kaplan-Meier survival function leads to crude estimates of incidence biased upward, regardless of whether the competing events are independent of one another [23,24]. To address this problem, Gray's test and the proportional subdistribution hazard model are recommended for statistical analysis in the presence of competing risks.

Bastiaannet et al. [25] proved that the percentage of patients above age 75 who die from their BC is less than 50% and the percentage of deaths due to other causes increases with age. Similarly, our results showed that the incidence of OCSD is higher than that of BCSD at any time point for patients over 65 years in all categories, except for those with T3 and T4 stage and N2 and N3 stage. As Supplementary Table 1 showed, the factors associated with OCSD are age, marriage, race, T stage, and surgery. Of interest, there are six other factors including N stage that showed no statistical significance with OCSD in our research. OCSD is literally defined as the death caused by reasons other than breast cancer. It is certain that the clinicopathologic factors of breast cancer, such as N stage, have less influence on OCSD than BCSD. As the follow-up continued, the percentage gain of OCSD was much greater than that of BCSD. As previously mentioned, it is necessary to consider competing-risk events when evaluating a patient's disease-specific mortality.

In our study, we found that increasing age was a strongly independent predictive factor for an elevated probability of BCSD.

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Table 3. Proportional subdistribution hazard model of probabilities of BCSD for patients in the training cohort.

Characteristics	Coefficient	$_{sd}$HR (95% CI)	*P*-value
Age			
65–74	Reference		
75+	0.360	1.43 (1.30–1.58)	<0.001
Marriage			
Unmarried	Reference		
Married	–0.314	0.73 (0.65–0.82)	<0.001
Race			
White	Reference		
Black	0.482	1.62 (1.38–1.90)	<0.001
Other*	–0.108	0.90 (0.74–1.09)	0.280
Histology			
IDC	Reference		
ILC	0.100	1.11 (0.94–1.29)	0.210
Other**	–0.332	0.72 (0.63–0.82)	<0.001
Grade			
I	Reference		
II	1.030	2.80 (2.33–3.37)	<0.001
III/IV	1.980	7.25 (6.07–8.66)	<0.001
ER status			
Negative	Reference		
Positive	–1.107	0.33 (0.20–0.37)	<0.001
PR status			
Negative	Reference		
Positive	–0.969	0.38 (0.35–0.42)	<0.001
T stage			
T1	Reference		
T2	1.383	3.99 (3.59–4.43)	<0.001
T3	2.130	8.41 (7.14–9.91)	<0.001
T4	2.506	12.30 (10.20–14.70)	<0.001
N stage			
N0	Reference		
N1	1.245	3.47 (3.11–3.88)	<0.001
N2	1.472	4.36 (3.83–4.96)	<0.001
N3	1.589	4.90 (4.30–5.58)	<0.001
Surgery			
BCS	Reference		
Mastectomy	1.035	2.81 (2.56–3.1)	<0.001

IDC – infiltrating ductal carcinoma; ILC – infiltrating lobular carcinoma; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery; BCSD – breast cancer-specific death; OCSD – other cause-specific death; $_{sd}$HR – subdistribution hazard ratio; CI – confidence interval; T – tumor stage; N – nearby lymph node stage. * Including American Indian/Alaskan native and Pacific Islander; ** including other histology of invasive breast cancer except IDC and ILC.

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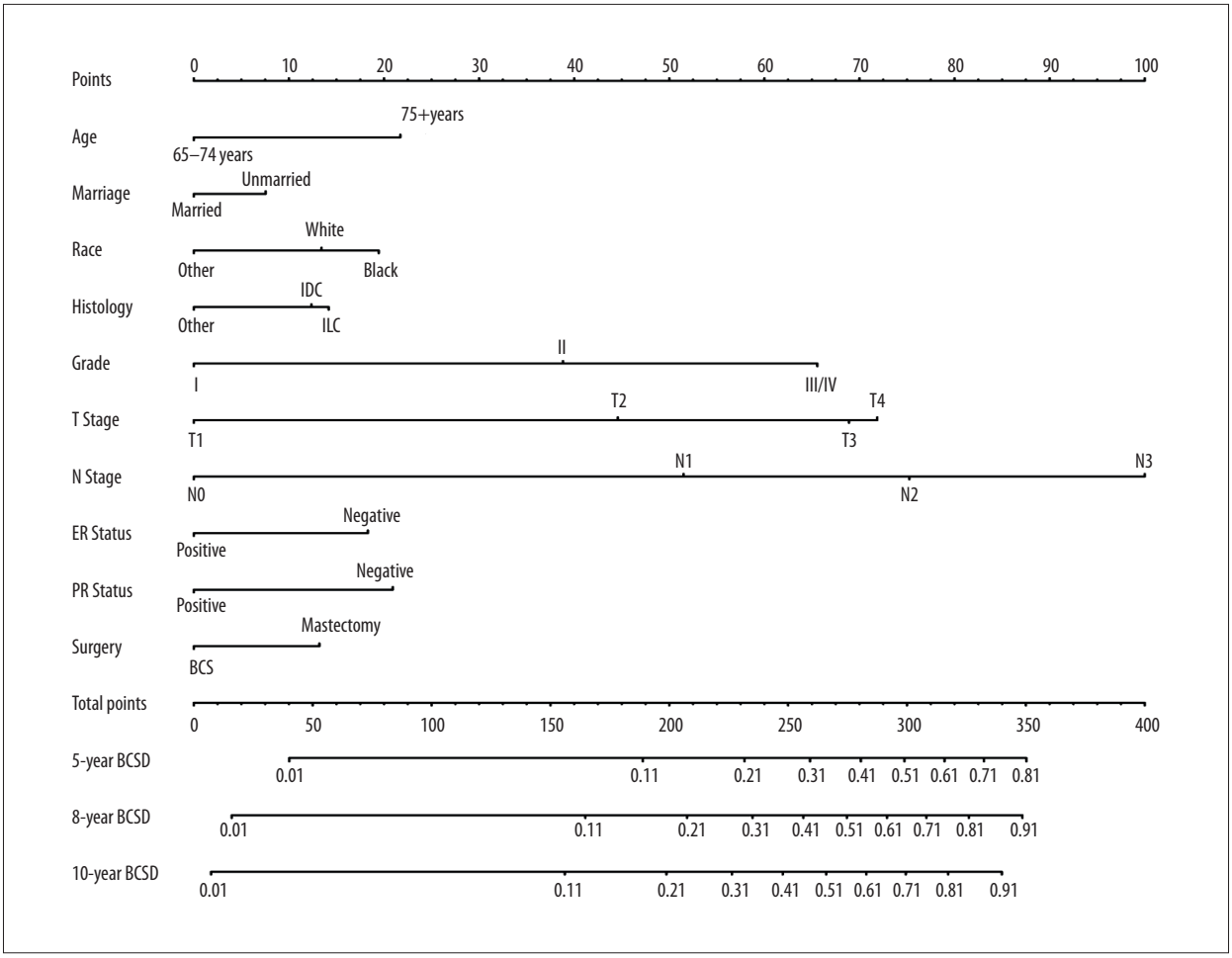

Figure 2. Competing-risks nomogram for predicting 5-, 8- and 10-year probabilities of breast cancer-specific death (BCSD) in elderly patients with breast cancer.

This finding was consistent with the findings from a prospective study of postmenopausal women [26], in which the HRs for patients ages 65–74 years and ≥75 years were 1.12 (95% CI, 0.94–1.34) and 1.66 (95% CI, 1.34–2.06), respectively, with patients ages <65 years as the reference. On one hand, age added a layer of biological complexity beyond BC molecular subtypes and classic pathological and clinical variables [27]. On the other hand, compared with their younger counterparts, older patients are prone to nonstandard treatment due to a lower tolerance to surgery, chemotherapy, and radiotherapy [28,29].

Multiple clinical trials have proved that BCS+radiotherapy (RT) has an equal or better effect than mastectomy [30–32]. However, in our study, we found that surgery is an independent prognostic factor, unlike previous studies. For this result, we think there are two reasons: One is that we didn't include RT data. We dropped the treatment data because of the lack of RT information. This may lead to bias of surgery result. The other is that the choice of treatment options are influenced by the patient's wishes and their physical condition, especially for elderly patients. For example, some early-stage patients with a poor physical condition may refuse RT considering its side effects. Surgery is an independent factor in our results, but it is influenced by certain factors in reality. Actually, among four main therapies including surgery, chemotherapy, endocrine therapy, and RT, endocrine therapy is offered for treatment strategies more frequently. ER and PR positivity is more common in elderly patients than in younger patients [6,33], indicating that the elderly are more likely to be sensitive to endocrine therapy. Additionally, endocrine therapy offers great benefit to elderly patients considering its equivalent efficacy to chemotherapy with a low risk of toxicities if appropriately used [34]. Although the conventional treatment for breast cancer is surgical resection, several prospective clinical trials have indicated much better outcomes for older patients with small, HR-positive tumors who receive tamoxifen alone than surgery [35]. The information above is consistent with our finding that ER and PR were protectors against BCSD. However, because of the limited access to the SEER database, information on endocrine treatment can't be acquired. This hinders us from further exploration.

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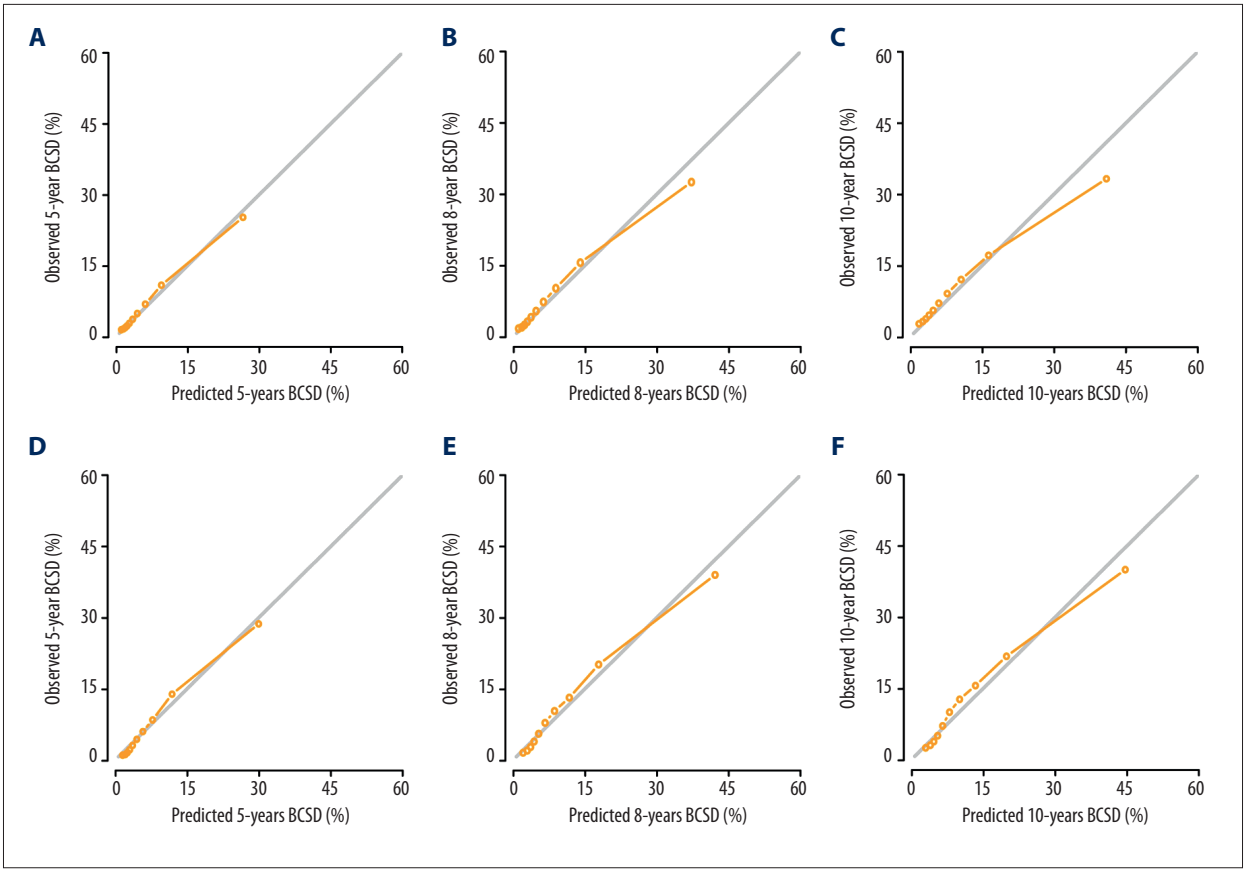

Figure 3. Internal calibration curves for (**A**) 5-, (**B**) 8-, and (**C**) 10-year breast cancer-specific death (BCSD) and external calibration curves for (**D**) 5-, (**E**) 8-, and (**F**) 10-year BCSD.

Figure 4. A patient age 65–74 years, married, black race, invasive ductal carcinoma (IDC, grade II, with tumor (T)3, nearby lymph node (N)2 disease, estrogen receptor (ER)-negative, progesterone (PR)-negative with mastectomy was evaluated using the web-based calculator.

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Before applying treatment to patients, it's necessary to build an effective and convenient tool to identify high-risk patients who need intensive treatment and clinical care. Though the TNM staging system for BC is an important prognostic predictor, the fact that certain significant prognostic factors such as age are not included cannot be ignored and may result in bias to some extent when evaluating a patient's survival. This nomogram incorporates not only parameters from the international AJCC but also some individual demographic and pathological characteristics and presents a prognostic numerical value. Thus, it provides enhanced comprehensiveness and convenience. Nevertheless, unavailable data on some characteristics regarding geriatric assessment is not included in the models, such as comorbidities, physical function status, mental health, and social support, which may make a difference in prognosis and clinical decision making [9,36]. This important part in optimal treatment tailoring must be considered when applying our nomogram.

There were certain limitations in our study that should be mentioned. First, adjuvant therapies such as chemotherapy and RT are not included in this study because of their incomplete and ambiguous data; for example, the categories "no treatment" and "unknown if patients received treatment" can't be distinguished for RT, and because of the large possibility of undertreatment in adjuvant therapies for elderly patients, bias may be involved in the statistical analysis if they were selected as candidate factors in the model, so we excluded this information even if it made a difference in prognosis. Unfortunately, several significant characteristics and follow-up information associated with prognosis were also not provided by the SEER database, including HER-2 status, Ki-67 positivity, tumor progression, and subsequent metastasis, which affects the effectiveness of our model certainly. Second, nearly half of the patients were excluded because of a lack of specific data. As a result, selection bias could affect our findings because of this underlying preference. Third, this was a single data-set study. To enhance the persuasiveness of the model, investigation from other centers or databases is needed for model validation. Finally, subject to retrospective methodology, the nomogram is supposed to be confirmed and supplemented via further prospective studies before clinical application.

Conclusions

In conclusion, we estimated the cumulative incidence of BCSD and OCSD in elderly patients diagnosed with BC on the basis of a large population-based cohort. A web-based dynamic nomogram predicting the 5-, 8-, and 10-year incidence of BCSD was built on the basis of 10 independent prognostic factors identified by a competing-risks analysis. The model performed excellently, and we hope that it can help clinicians evaluate patient risk of BCSD more effectively and propose individualized treatment strategies.

Acknowledgments

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Conflicts of interest

None.

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Supplementary Data

Supplementary Table 1. 5-, 8-, 10-Year cumulative incidences of OCSD among patients with breast cancer in the training cohort.

Characteristics	OCSD				
	Events (%)	5-y (%)	8-y (%)	10-y (%)	*P*-value
Total	3966 (100.0)	9.1	17.3	23.0	
Age					<0.001
65–74	1450 (36.6)	4.8	9.7	13.4	
75+	2516 (63.4)	17.0	30.8	39.9	
Marriage					<0.001
Unmarried	765 (19.3)	13.2	23.3	30.0	
Married	3201 (80.7)	8.4	16.2	21.8	
Race					<0.001
White	3483 (87.8)	9.2	17.5	23.2	
Black	286 (7.2)	11.5	20.4	26.2	
Other*	197 (5.0)	5.9	11.7	17.6	
Histology					0.621
IDC	2864 (72.2)	9.1	17.1	23.0	
ILC	327 (8.3)	9.5	17.4	21.8	
Other**	775 (19.5)	9.0	17.7	23.5	
Grade					0.537
I	1031 (26.0)	8.3	16.7	23.0	
II	1832 (46.2)	9.2	17.5	23.3	
III/IV	1103 (27.8)	9.8	17.3	22.3	
Laterality					0.086
Left	1969 (49.6)	9.2	16.9	22.2	
Right	1997 (50.4)	9.1	17.7	23.8	
ER status					0.987
Negative	643 (16.2)	10.2	17.3	22.4	
Positive	3323 (83.8)	8.9	17.3	23.1	
PR status					0.631
Negative	1158 (29.2)	10.0	17.6	22.4	
Positive	2808 (70.8)	8.8	17.1	23.2	
T stage					<0.001
T1	2524 (63.6)	7.7	15.6	21.7	
T2	1187 (30.0)	11.9	20.6	25.6	
T3	147 (3.7)	13.3	20.5	24.8	
T4	108 (2.7)	17.7	24.9	30.1	
N stage					0.222
N0	2986 (75.3)	9.0	17.4	23.6	
N1	707 (17.8)	9.1	16.5	21.5	
N2	183 (4.6)	11.2	18.4	21.8	
N3	90 (2.3)	9.9	16.0	17.4	

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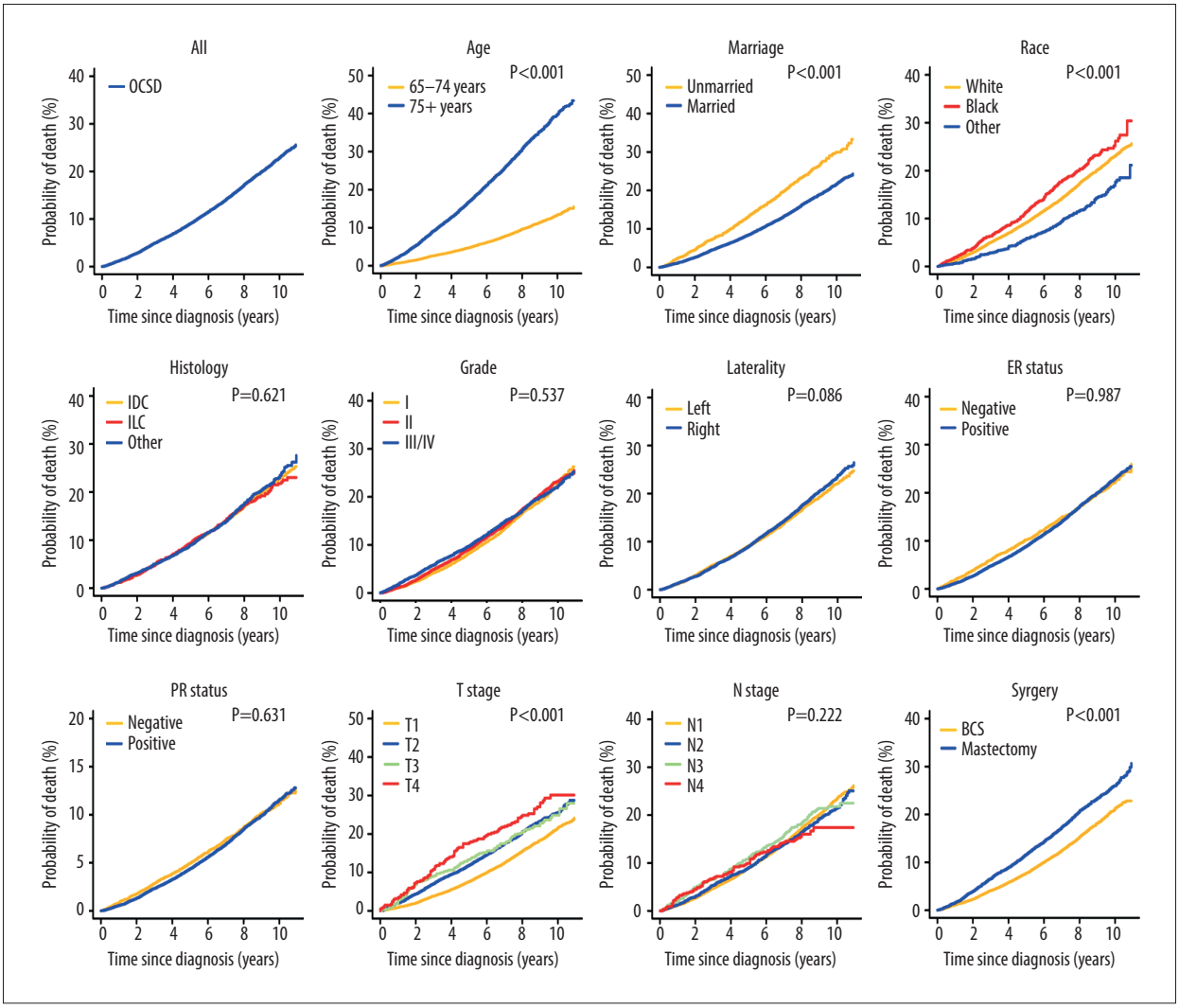
Supplementary Table 1 continued. 5-, 8-, 10-Year cumulative incidences of OCSD among patients with breast cancer in the training cohort.

Characteristics	OCSD					
	Events (%)		5-y (%)	8-y (%)	10-y (%)	*P*-value
Surgery						<0.001
BCS	2341	(59.0)	7.8	15.4	21.3	
Mastectomy	1625	(41.0)	11.7	20.8	26.0	

IDC – infiltrating ductal carcinoma; ILC – infiltrating lobular carcinoma; ER – estrogen receptor; PR – progesterone receptor; BCS – breast-conserving surgery; BCSD – breast cancer-specific death; OCSD – other cause-specific death; T – tumor stage; N – nearby lymph node stage. * Including American Indian/Alaskan native and Pacific Islander; ** including other histology of invasive breast cancer except IDC and ILC.



Supplementary Figure 1. Cumulative incidence function curves of OCSD by patients' characteristics.

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