Incidence, prognostic factors and survival in bladder cancer patients: a population-based study

Shun-De Wang[1,2]^, Cheng-Guo Ge[2]^, Jun-Yong Zhang[2]^

[1]Department of Urology, The ChenJiaqiao Hospital of ShaPingba District of Chongqing City, Chongqing, China; [2]Department of Urology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing, China

Contributions: (I) Conception and design: All authors; (II) Administrative support: JY Zhang, CG Ge; (III) Provision of study materials or patients: SD Wang, JY Zhang; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Cheng-Guo Ge. Department of Urology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China. Email: kinghongyi@163.com; Jun-Yong Zhang. Department of Urology, The Second Affiliated Hospital of Chongqing Medical University, Chongqing 400010, China. Email: zhangmachine@cqmu.edu.cn.

Background: The aim of this study was to investigate the incidence, epidemiologic characteristics, prognostic factors and survival of patients with bladder cancer.

Methods: Bladder cancer patients diagnosed between 2010 and 2015 were identified from the Surveillance, Epidemiology, and End Results (SEER) database. Univariate and multivariate Cox proportional hazards regression analyses were used to identify the independent prognostic factors for overall survival. Kaplan-Meier survival analysis and nomogram analysis were constructed based on the identified independent prognostic factors.

Results: A total of 95,329 eligible bladder cancer patients were included in this study. Eight independent risk factors, including age, histologic type, race, tumor, node and metastasis (TNM) stage, American Joint Committee on Cancer (AJCC) stage, surgery, tumor metastasis and summary stage, were recognized by using multivariate logistic regression models. By comprising these factors, a predictive nomogram was constructed to predict the 1-, 3-, and 5-year overall survival possibilities. The concordance index and calibration curve showed that the nomogram had robust and accurate performance.

Conclusions: Bladder cancer is the most common cancer of the urinary system, but the overall incidence has been decreasing yearly since 1992. Our results demonstrate eight factors significantly associated with overall survival in bladder cancer patients. Based on these factors, we established and validated a nomogram, which has the potential to provide an individualized prediction of overall survival in patients with bladder cancer.

Keywords: Bladder cancer (BC); multivariate; overall survival (OS); Surveillance, Epidemiology, and End Results (SEER)

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^ ORCID: Shun-De Wang, 0000-0001-5973-8390; Cheng-Guo Ge, 0000-0003-4347-5463; Jun-Yong Zhang, 0000-0001-7753-9520.

Introduction

Bladder cancer (BC) is the 10th most common cancer in the world and the 13th leading cause of cancer-related death (1), with nearly 549,000 new cases and 200,000 deaths each year (2).

Previous studies have shown that multiple factors, such as sex, age, smoking, and race, can affect the survival probability of BC (3-5). Study shows that the incidence of BC is three to four times higher in men than in women (6). The incidence of BC increases with age: more than 90% of patients are over 55 years old, with an average age of approximately 73 years (1). Whites are more likely to develop BC than people of other races (7). Survival probability is a prediction of the likelihood that a patient will continue to survive (8-10). Because each survival probability is a prediction based on finite conditions, the survival probability can only be used as a reference, and the survival probability cannot provide a definite answer.

The purpose of this study was to understand the incidence, prognostic factors, and survival trends in BC patients. This study was based on a larger population derived from the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute. We also characterized independent prognostic factors associated with BC and sought to build prognostic nomograms that could assist clinicians in evaluating prognosis. We present the following article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-46/rc).

Methods

Data source

The data for this study were obtained retrospectively from the SEER database. To extract data, select cases, and define variables, SEER*Stat (version 8.3.9.2) was used. The case listing was created using the incidence-SEER 18 Registers Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (1975-2016 varying). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Patient identification

Patients diagnosed with malignant BC by histology between 2010 and 2015 were included in this study. *Table 1* shows the inclusion and exclusion criteria for this study.

Variables from the selected cohort included sex, race, age at diagnosis, histologic type, TNM-T, TNM-N, TNM-M, AJCC stage, surgery of primary site, bone metastasis, brain metastasis, liver metastasis, lung metastasis, summary stage, survival months, and vital status. The main endpoint was overall survival (OS).

The age at diagnosis was divided into five subgroups: <50, 51–60, 61–70, 71–80, and >80 years. We classified the histological type into transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, neuroendocrine carcinoma and other epithelial tumors of the bladder using the ICD-0-3 morphological code.

Statistical analysis

The incidence rates of BC were calculated per 100,000 person-years and age-adjusted to the 2,000 US Standard Population [19 age groups, United States Bureau of the Census, Current Population Reports, Publication 25-1130 (Census P25-1130)] using SEER*Stat (version 8.3.9.2). Annual percentage changes (APCs) were calculated using the weighted least squares method.

Estimated OS was calculated with the Kaplan-Meier method and compared by the log-rank test. Univariate and multivariate Cox regression analyses were performed to identify independent prognostic factors associated with OS in BC patients.

All statistical analyses were performed in R (Version 4.1.1, R Foundation; R packages: rms, survival, survminer, ggplot2). Statistical significance was set at a two-sided P value <0.05.

Nomogram construction

R 4.1.1 was used to construct a nomogram based on the results of multivariate analysis of the Cox proportional hazards model. The maximum score for each variable was set to 100. We also built calibration curves to identify whether the predicted and actual survival were in agreement.

Results

Baseline characteristics

A total of 95,329 eligible BC patients from 2010 to 2015 were included in this study. *Table 2* shows the comparison of baseline characteristics and chi-square test results for patients with BC clustered by age. Of all patients, 4,139

Table 1 Inclusion and exclusion criteria of population selection and classification

Inclusion criteria
Patients diagnosed with malignant bladder cancer
The histologic type of patients should be available
The survival time and vital status should be available
Clinicopathological information for the age at diagnosis, race, surgery, tumor stage and other baseline information should be available
Exclusion criteria
Patients with bladder cancer found during an autopsy or on a death certificate
Unknown ethnicity
Unknown survival time
Unknown AJCC-stage
Unknown summary stage
Unknown surgical status
Unknown TNM-T/N/M stage
Unknown age
Unknown vital status

AJCC, American Joint Committee on Cancer; TNM, tumor, node, metastasis.

(4.30%) patients were aged less than 51 years, 12,536 (13.20%) patients were aged 51–60 years, 25,979 (27.30%) patients were aged 61–70 years, 28,868 (30.20%) patients were aged 71–80 years and 23,807 (25.00%) patients were aged over 80 years. According to the chi-square test, sex (P<0.001), race (P<0.001), diagnosis year (P<0.001), histologic type (P<0.001), TNM-T (P<0.001), TNM-N (P<0.001), TNM-M (P<0.001), AJCC stage (P<0.001), surgery (P<0.001), bone metastasis (P<0.001), brain metastasis (P=0.045), and summary stage (P<0.001) were all factors that were significantly different among age groups, except for liver metastasis (P=0.851) and lung metastasis (P=0.101).

Males accounted for approximately 70% of the patients in each group. Patients over 61 years old accounted for approximately 80% of the sample in each group. Based on TNM stage, summary stage and AJCC-stage system, most patients were in the early stage of cancer (in situ, localized, AJCC-stage 0a, AJCC-stage 0is, AJCC-stage I, AJCC-stage II, TaN0M0 and T1N0M0); therefore, more than 80% of patients underwent transurethral resection of bladder tumor (TURBT). According to histological type, transitional cell carcinoma accounted for more than 90% of patients in each group. The incidence of brain metastases was the lowest compared to other distant organ metastases.

Cox proportional hazards model

Univariate and multivariate risk analyses of OS are shown in *Table 3*. Univariate risk analyses revealed that sex, age, histologic type, race, TNM stage, AJCC stage, surgery, tumor metastasis and summary stage were significant prognostic factors of OS. Variables in univariate risk analyses with a P value of less than 0.01 were included in multivariate risk analyses. The results indicated that age, histologic type, race, TNM stage, AJCC stage, surgery, tumor metastasis and summary stage were independent prognostic factors for OS.

Incidence of BC

The trend in the incidence of BC has decreased since 1992, with an APC of –0.59 (95% CI: –0.79 to –0.39, P<0.05) (*Figure 1A*). This trend was more remarkable among male patients (*Figure 1B*), white patients (*Figure 1C*), patients aged less than 70 years (*Figure 1D*) and patients with *in situ* and localized tumor stage (*Figure 1E*). The overall annual age-adjusted incidences of BC from 1992 to 2018 were 20.7, 20.2, 20.1, 20.2, 20.5, 20.6, 20.7, 20.7, 0.8, 20.3, 20.9, 21, 20.9, 20.4, 20.9, 20.3, 19.9, 20.4, 19.4, 19.6, 19, 19, 18.7, 18.5, 17.8, and 16.8/100,000 persons, respectively.

Table 2 Baseline characteristics

Factors	ALL, n (%)	Age group, n (%)					P value
		<51 years	51–60 years	61–70 years	71–80 years	>80 years	
Total	95,329 (100.00)	4,139 (4.30)	12,536 (13.20)	25,979 (27.30)	28,868 (30.20)	23,807 (25.00)	
Gender							<0.001
Male	73,059 (76.64)	3,072 (4.20)	96,006 (13.10)	20,236 (27.80)	22,515 (30.80)	17,630 (24.10)	
Female	22,270 (23.36)	1,067 (4.80)	2,930 (13.20)	5,743 (25.80)	6,353 (28.50)	6,177 (27.70)	
Race							<0.001
White	85,577 (89.77)	3,593 (4.20)	10,951 (12.70)	23,260 (27.20)	26,071 (30.50)	21,702 (25.40)	
Black	5,443 (5.71)	342 (6.30)	987 (18.10)	1,615 (29.70)	1,497 (27.50)	1,002 (18.40)	
API	3,997 (4.19)	178 (4.50)	534 (13.40)	1,014 (25.40)	1,222 (30.50)	1,049 (26.20)	
AIAN	312 (0.33)	26 (8.30)	64 (20.50)	90 (28.80)	78 (25.00)	54 (17.30)	
Diagnosis year							<0.001
2010	15,561 (16.32)	740 (4.80)	2,113 (13.50)	4,174 (26.80)	4,667 (30.00)	3,867 (24.90)	
2011	15,543 (16.30)	731 (4.70)	2,034 (13.10)	4,214 (27.10)	4,636 (29.80)	3,928 (25.30)	
2012	15,994 (16.78)	720 (4.50)	2,068 (12.90)	4,336 (27.10)	4,828 (30.20)	4,042 (25.30)	
2013	15,822 (16.60)	674 (4.30)	2,027 (12.80)	4,418 (27.90)	4,724 (29.90)	3,979 (25.10)	
2014	16,174 (16.97)	631 (3.90)	2,195 (13.60)	4,395 (27.20)	4,916 (30.30)	4,037 (25.00)	
2015	16,235 (17.03)	643 (4.00)	2,099 (12.90)	4,442 (27.30)	5,097 (31.40)	3,954 (24.40)	
Histologic type							<0.001
Tcc	91,963 (96.47)	3,900 (4.20)	12,049 (13.10)	25,147 (27.30)	27,915 (30.40)	22,952 (25.00)	
Scc	1,265 (1.33)	82 (6.50)	182 (14.40)	279 (22.10)	360 (28.50)	362 (28.50)	
Ac	845 (0.89)	121 (14.30)	174 (20.60)	223 (26.40)	185 (21.90)	142 (16.80)	
Nec	788 (0.83)	20 (2.50)	86 (10.90)	209 (26.60)	247 (31.30)	226 (28.70)	
Oet	468 (0.49)	16 (3.40)	45 (9.60)	121 (25.90)	161 (34.40)	125 (26.70)	
TNM-T							<0.001
Ta	46,421 (48.70)	2,444 (5.30)	6,579 (14.10)	13,257 (28.60)	13,991 (30.10)	10,150 (21.90)	
Tis	4,052 (4.25)	131 (3.20)	468 (11.50)	1,103 (27.20)	1,350 (33.40)	100 (24.70)	
T0	1 (0.00)	0 (0.00)	0 (0.00)	1 (0.00)	0 (0.00)	0 (0.00)	
T1	23,616 (24.77)	776 (3.30)	2,774 (11.70)	6,161 (26.10)	7,248 (30.70)	6,657 (28.20)	
T2	14,382 (15.09)	427 (3.00)	1,664 (11.50)	3,478 (24.20)	4,154 (28.90)	4,659 (32.40)	
T3	3,977 (4.17)	219 (5.50)	607 (15.30)	1,192 (30.00)	1,252 (31.40)	707 (17.80)	
T4	2,880 (3.02)	142 (4.90)	444 (15.40)	787 (27.30)	873 (30.30)	634 (22.00)	
TNM-N							<0.001
N0	91,377 (95.85)	3,875 (4.20)	11,751 (12.90)	24,772 (27.10)	27,756 (30.40)	23,223 (25.40)	
N1	1,544 (1.62)	105 (6.80)	295 (19.10)	487 (31.50)	426 (27.60)	231 (15.00)	
N2	1,938 (2.03)	129 (6.70)	400 (20.60)	569 (29.30)	544 (28.10)	296 (15.30)	
N3	470 (0.49)	60 (6.40)	90 (19.10)	151 (32.10)	142 (30.20)	57 (12.10)	

Table 2 (*continued*)

Table 2 (*continued*)

Factors	ALL, n (%)	Age group, n (%)					P value
		<51 years	51–60 years	61–70 years	71–80 years	>80 years	
TNM-M							<0.001
M0	92,977 (97.53)	4,016 (4.30)	12,170 (13.10)	25,376 (27.30)	28,161 (30.30)	23,254 (25.00)	
M1	2,352 (2.47)	123 (5.20)	366 (15.60)	603 (25.60)	707 (30.10)	553 (23.50)	
AJCC stage							<0.001
Stage 0a	46,421 (48.70)	2,444 (5.30)	6,579 (14.10)	13,257 (28.60)	13,991 (30.10)	10,150 (21.90)	
Stage 0is	4,052 (4.25)	131 (3.20)	468 (11.60)	1,103 (27.20)	1,350 (33.30)	1,000 (24.70)	
Stage I	23,054 (24.18)	737 (3.20)	2,675 (11.60)	6,025 (26.10)	7,093 (30.80)	6,524 (28.30)	
Stage II	12,275 (12.88)	335 (2.70)	1,309 (10.70)	2,886 (23.60)	3,541 (28.80)	4,204 (34.20)	
Stage III	3,896 (4.09)	164 (4.20)	501 (12.90)	1,080 (27.70)	1,253 (32.20)	898 (23.00)	
Stage IV	5,631 (5.91)	328 (5.80)	1,007 (17.80)	1,628 (28.90)	1,640 (29.20)	1,031 (18.30)	
Surgery							<0.001
TURBT	84,713 (88.86)	3,523 (4.20)	10,656 (12.60)	22,477 (26.50)	25,568 (30.20)	22,489 (26.50)	
PC	1,265 (1.33)	95 (7.50)	202 (16.00)	327 (25.80)	359 (28.40)	282 (22.30)	
RC	9,351 (9.81)	521 (5.60)	1,678 (17.80)	3,175 (34.00)	2,941 (31.50)	1,036 (11.10)	
Metastasis							
Bone	94,491 (99.12)	4096 (4.30)	12,378 (13.10)	25,760 (27.30)	28,625 (30.30)	23,632 (25.00)	<0.001
Brain	95,266 (99.93)	4135 (4.30)	12,525 (13.10)	25,954 (27.30)	28,853 (30.30)	23,799 (25.00)	0.045
Liver	94,852 (99.50)	4115 (4.30)	12,468 (13.10)	25,856 (27.30)	28,752 (30.30)	23,688 (25.00)	0.851
Lung	94,552 (99.18)	4,100 (4.30)	12,419 (13.10)	25,798 (27.30)	28,627 (30.30)	13,608 (25.00)	0.101
Summary stage							<0.001
In situ	49,517 (51.94)	2,535 (5.10)	6,932 (14.00)	14,111 (28.50)	15,056 (30.40)	10,883 (22.00)	
Localized	35,803 (37.56)	1,094 (3.10)	4,047 (11.30)	9,065 (25.30)	10,767 (30.10)	10,830 (30.20)	
Regional	6,967 (7.31)	343 (4.90)	1,064 (15.30)	1,992 (28.60)	2,140 (30.70)	1,428 (20.50)	
Distant	3,042 (3.19)	167 (5.50)	493 (16.20)	811 (26.60)	905 (29.80)	666 (21.90)	

AIAN, American Indian/Alaska Native; API, Asian or Pacific Islander; TURBT, transurethral resection of bladder tumor; PC, partial cystectomy; RC, radical cystectomy; Tcc, transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors.

Kaplan-Meier survival analysis

To evaluate the impact of different factors on the OS of BC patients, Kaplan-Meier survival analysis was performed in all patients. As shown in *Figure 2A*, the overall survival decreases significantly as the age of diagnosis increases. *Figure 2B* shows the survival probability of patients of four races except for black patients was > 50% at 80 months. Asian or Pacific Islander patients had the highest survival probability, followed by white and American Indian/

Alaska Native patients. *Figure 2C* shows that once the summary stage starts to progress, the overall survival decreases significantly. AJCC stage IV had the worst survival probability, and the survival probability for AJCC stage 0a-I patients was >50% at 80 months (*Figure 2D*). Neuroendocrine carcinoma of the bladder has the worst survival probability, while transitional cell carcinoma of the bladder has the best survival probability (*Figure 2E*). *Figure 2F* shows that patients who underwent radical cystectomy had the worst survival probability, which was

Table 3 Cox proportional-danger model analysis of bladder cancer patients

Factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender		<0.001		
Male	Reference		Reference	
Female	1.070 (1.043–1.098)	<0.001	0.981 (0.956–1.007)	0.154
Age		<0.001		
0–50 years	Reference		Reference	
51–60 years	1.391 (1.268–1.527)	<0.001	1.330 (1.212–1.460)	<0.001
61–70 years	1.738 (1.593–1.897)	<0.001	1.734 (1.589–1.892)	<0.001
71–80 years	2.830 (2.597–3.083)	<0.001	2.748 (2.612–3.102)	<0.001
>81 years	5.814 (5.340–6.330)	<0.001	5.693 (5.226–6.202)	<0.001
Histologic type		<0.001		
Tcc	Reference		Reference	
Scc	3.056 (2.849–3.278)	<0.001	1.821 (1.696–1.956)	<0.001
Ac	1.804 (1.638–1.987)	<0.001	1.097 (0.994–1.211)	0.067
Nec	3.718 (3.420–4.043)	<0.001	1.244 (1.142–1.356)	<0.001
Oet	1.548 (1.352–1.773)	<0.001	1.201 (1.046–1.379)	0.009
Race		<0.001		
White	Reference		Reference	
Black	1.327 (1.270–1.386)	<0.001	1.270 (1.215–1.328)	<0.001
API	0.900 (0.849–0.955)	<0.001	0.844 (0.796–0.896)	<0.001
AIAN	1.170 (0.970–1.413)	0.101	1.117 (0.926–1.349)	0.248
TNM-T		<0.001		
Ta	Reference		Reference	
Tis	1.405 (1.319–1.497)	<0.001	1.255 (1.166–1.351)	<0.001
T0*	–	–	–	–
T1	1.965 (1.907–2.025)	<0.001	5.729 (4.571–7.181)	<0.001
T2	4.949 (4.805–5.098)	<0.001	6.156 (4.988–7.599)	<0.001
T3	4.784 (4.574–5.004)	<0.001	8.059 (6.520–9.962)	<0.001
T4	8.483 (8.098–8.888)	<0.001	9.524 (7.703–11.774)	<0.001
TNM-N		<0.001		
N0	Reference		Reference	
N1	3.400 (3.197–3.615)	<0.001	0.953 (0.849–1.030)	0.172
N2	4.876 (4.632–5.134)	<0.001	1.269 (1.163–1.384)	<0.001
N3	5.368 (4.850–5.941)	<0.001	1.063 (0.939–1.204)	0.332

Table 3 (*continued*)

Table 3 (*continued*)

Factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
TNM-M		<0.001		
M0	Reference		Reference	
M1	8.824 (8.438–9.228)	<0.001	0.996 (0.884–1.123)	0.951
AJCC stage		<0.001		
Stage 0a	Reference		Reference	
Stage 0is	1.405 (1.319–1.497)	<0.001	–	–
Stage I	1.872 (1.815–1.930)	<0.001	0.257 (0.214–0.307)	<0.001
Stage II	4.434 (4.297–4.575)	<0.001	0.640 (0.546–0.750)	<0.001
Stage III	4.569 (4.364–4.783)	<0.001	0.564 (0.509–0.625)	<0.001
Stage IV	9.549 (9.209–9.902)	<0.001	–	–
Surgery		<0.001		
TURBT	Reference		Reference	
PC	1.201 (1.097–1.315)	<0.001	0.519 (0.472–0.571)	<0.001
RC	1.595 (1.544–1.648)	<0.001	0.528 (0.507–0.551)	<0.001
Tumor metastasis				
Bone		<0.001		
No	Reference		Reference	
Yes	9.716 (9.047–10.435)	<0.001	1.448 (1.324–1.584)	<0.001
Brain		<0.001		
No	Reference		Reference	
Yes	12.727 (9.936–16.301)	<0.001	1.930 (1.501–2.482)	<0.001
Liver		<0.001		
No	Reference		Reference	
Yes	12.104 (11.298–13.619)	<0.001	1.638 (1.473–1.821)	<0.001
Lung		<0.001		
No	Reference		Reference	
Yes	9.466 (8.788–10.196)	<0.001	1.193 (1.088–1.307)	<0.001
Summary stage		<0.001		
In situ	Reference		Reference	
Localized	2.492 (2.429–2.557)	<0.001	1.212 (1.059–1.387)	0.005
Regional	4.972 (4.797–5.153)	<0.001	1.412 (1.175–1.697)	<0.001
Distant	14.457 (13.843–15.098)	<0.001	2.057 (1.653–2.558)	<0.001

*, there was only one T0 stage patient, the result is not informative. AIAN, American Indian/Alaska Native; API, Asian or Pacific Islander; Tcc, transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors; TURBT, transurethral resection of bladder tumor; PC, partial cystectomy; RC, radical cystectomy.
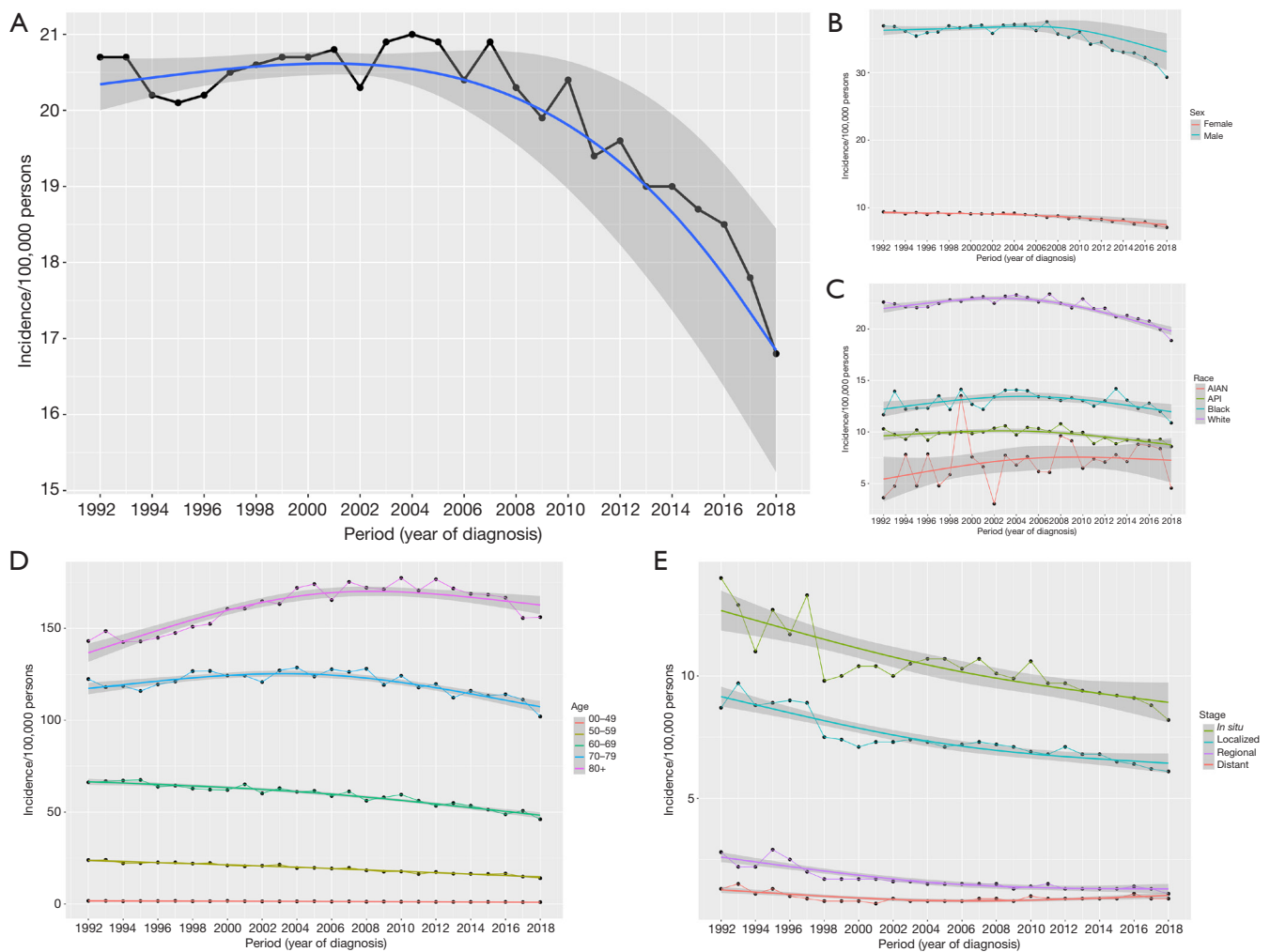
Figure 1 Annual age-adjusted incidence of bladder cancer decreased from 1992 to 2018 (A), and stratified by sex (B), race (C), age (D), and tumor stage (E).

associated with the fact that most of the patients in this group were in an advanced stage of cancer.

Figure 3 shows the survival probability for patients with five histologic types of BC (transitional cell carcinoma, squamous cell carcinoma, adenocarcinoma, neuroendocrine carcinoma and other epithelial tumors of the bladder) after undergoing different surgical approaches. Patients with transitional cell carcinoma have the highest survival probability after TURBT, in contrast to BC patients with the other four histologic types. Patients with squamous cell carcinoma have the highest survival probability after partial cystectomy, which is similar to adenocarcinoma.

Figure 4A shows that neuroendocrine carcinoma of the bladder had the worst survival probability among male patients, but among female patients, both neuroendocrine

carcinoma of the bladder and squamous cell carcinoma of the bladder had a lower survival probability. *Figure 4B* shows significant differences in survival probability among the four ethnic groups of BC patients, and this was more remarkable in female patients.

Prognostic nomogram

A nomogram was constructed based on the Cox proportional hazard model to predict the 1-, 3-, and 5-year OS in BC patients (*Figure 5*). Each subgroup variable was assigned a corresponding score to construct this nomogram. A scoring system was used to assign a score from 0 to 100 to each subgroup variable based on its contribution. These scores are added to the registered variables to generate a

2750

Wang et al. Incidence, prognosis and survival in bladder cancer patients
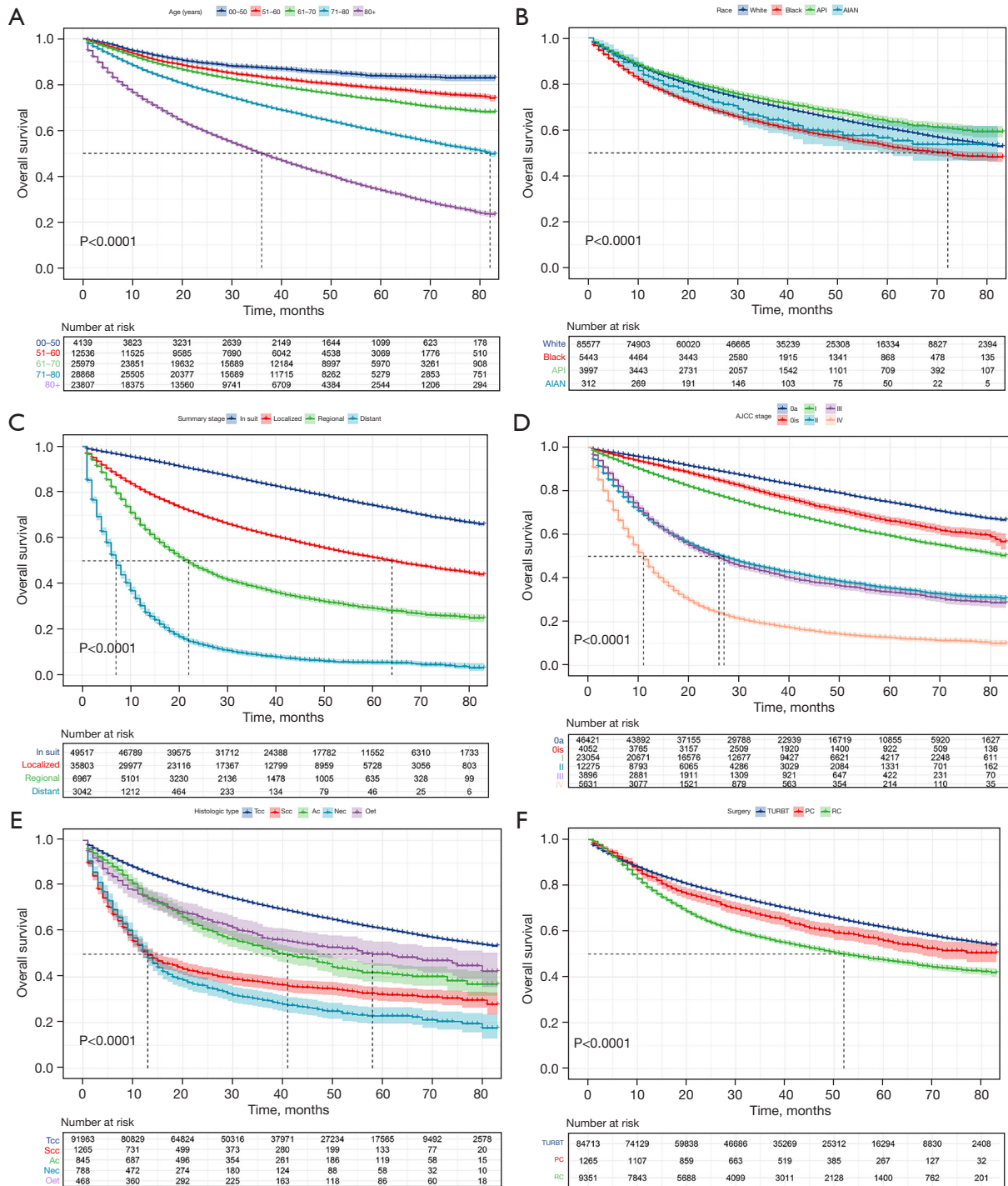
Figure 2 Kaplan-Meier survival curves for overall patients with bladder cancer in different conditions: age (A), race (B), summary stage (C), AJCC stage (D), histologic type (E), surgery (F). API, Asian or Pacific Islander; AIAN, American Indian/Alaska Native; Tcc, transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors; TURBT, transurethral resection of bladder tumor; PC, partial cystectomy; RC, radical cystectomy.
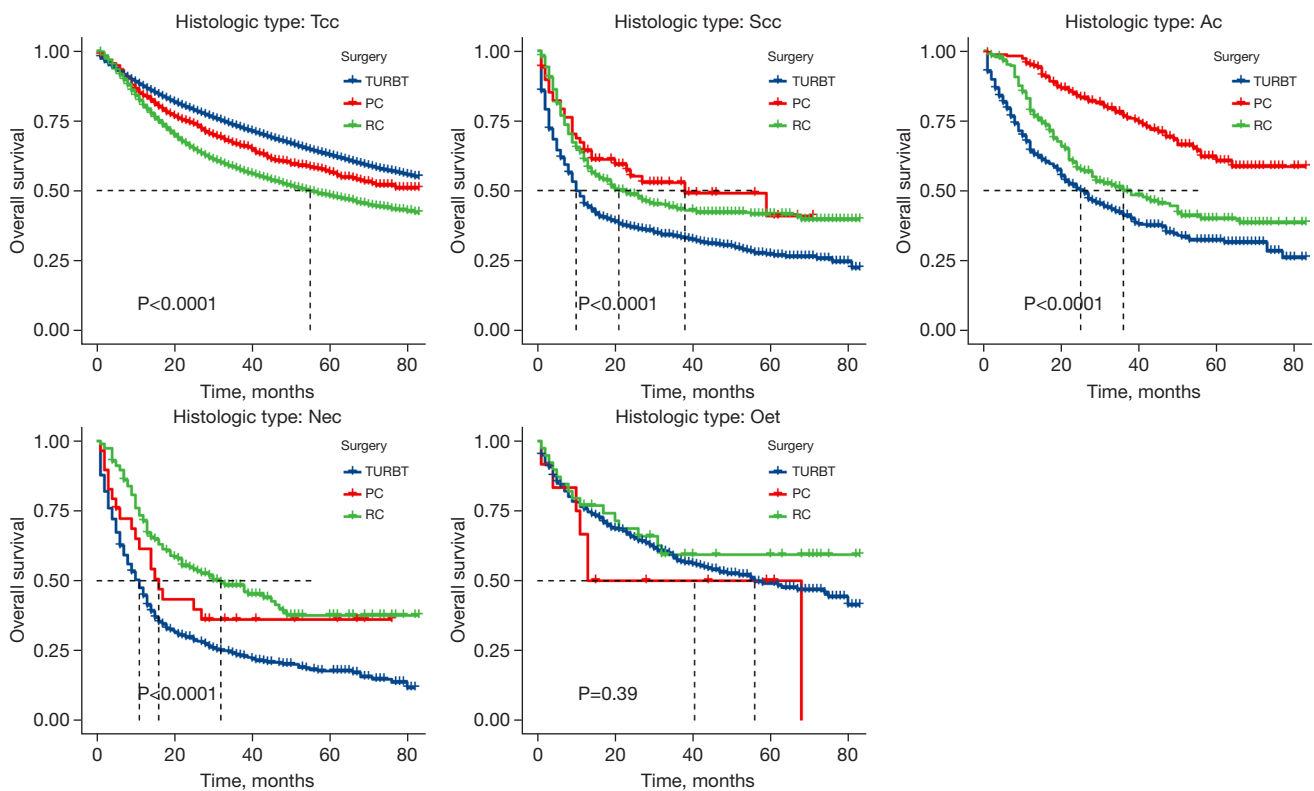
Figure 3 Kaplan-Meier survival curves for different histologic types in different surgeries of bladder cancer patients. Tcc, transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors; TURBT, transurethral resection of bladder tumor; PC, partial cystectomy; RC, radical cystectomy.

total score for the bottom scale, which was then converted to predict the corresponding OS.

Validation of the nomogram

The calibration curve was used to validate the model's ability to predict 1-, 3-, and 5-year OS in BC patients. As shown in *Figure 6*, a perfect correlation between nomogram prediction and observed outcomes demonstrated the great reliability of our nomogram. The C-index is 0.768, which is greater than 0.7. These results suggested that the newly established nomogram was considerably accurate.

Discussion

BC is the ninth most common cancer in the world and one of the most common cancers of the urinary system (2,11). Although our results showed that the overall incidence of BC showed a downward trend, there was still an increasing trend in patients aged >80 years. Despite the fact that

we now have more treatment options available for BC patients, including molecular targeted drugs, neoadjuvant chemotherapy, and immunotherapy, older patients do not seem to benefit from these promising therapies.

In this study, we obtained data from 95,329 BC patients, and by the Kaplan-Meier method, we found that the OS of BC patients not only had racial differences but was also related to TNM stage, histological type, and surgery. Meanwhile, a subgroup analysis was performed and showed that OS differed by histological type in patients of different sexes or after different surgical procedures and that OS also differed between female patients of different races.

We found that the number of men with BC was much higher than the number of women, and most patients were aged over 50 years. Most BCs were transitional cell carcinoma. Several studies have previously been performed to illustrate why BC is more likely to occur in men (2,12-15): one reason is the interaction of estrogen, androgens and the liver, and another reason is related to smoking, which increases the risk of BC because more men smoke than
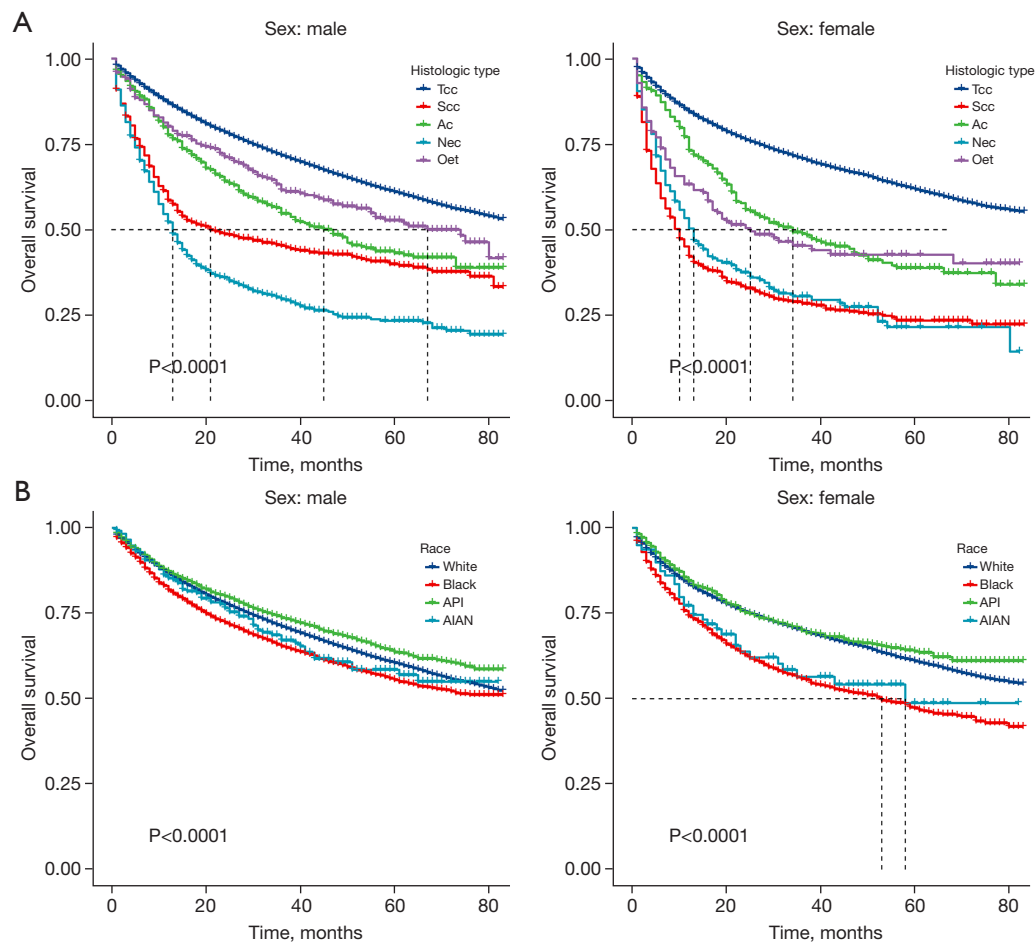
Figure 4 Kaplan–Meier survival for different histologic types (A) and races (B) in bladder cancer patients by sex. API, Asian or Pacific Islander; AIAN, American Indian/Alaska Native; Tcc, transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors.

women (13,16). In addition, older patients are susceptible to BC due to degeneration of the body's immune system, leading to an increase in cancer incidence year by year (17-19). Additionally, the decline in bladder function and the development of benign prostatic hyperplasia in male patients as they aged leads to chronic urinary retention (20), which increases exposure to carcinogens and increases the risk of developing BC.

We used univariate and multivariate risk analyses to evaluate various risk factors that have a significant impact on OS in patients with BC. Multivariate analyses showed that all factors, except sex and TNM-M stage, had a significant effect on overall survival in bladder cancer, which is consistent with published studies (6,13,21).

OS was lowest for patients who underwent radical cystectomy due to the higher tumor stage (T2–4), with

or without lymph nodes or distant metastases, with approximately 76% of patients being older than 60 years. In contrast, patients who underwent TURBT had the best OS; although more than 80% of this group of patients were older than 60 years, these patients tended to have an earlier tumor stage. Our findings showed that the risk of death increased with age and tumor stage (TNM stage, AJCC stage). A review of the literature shows that as patients age, immunity and physical function decline, which exacerbates the impact of the disease on patients to some extent (22-24). In addition, as patients age, exposure to carcinogens may increase (24), which may affect patient OS. As tumor grading increases, the chances of tumor cell spreading and metastasis increase, which makes treatment more difficult.

The nomogram is widely used to predict OS in oncology patients (25-28). It has been proven that multivariate
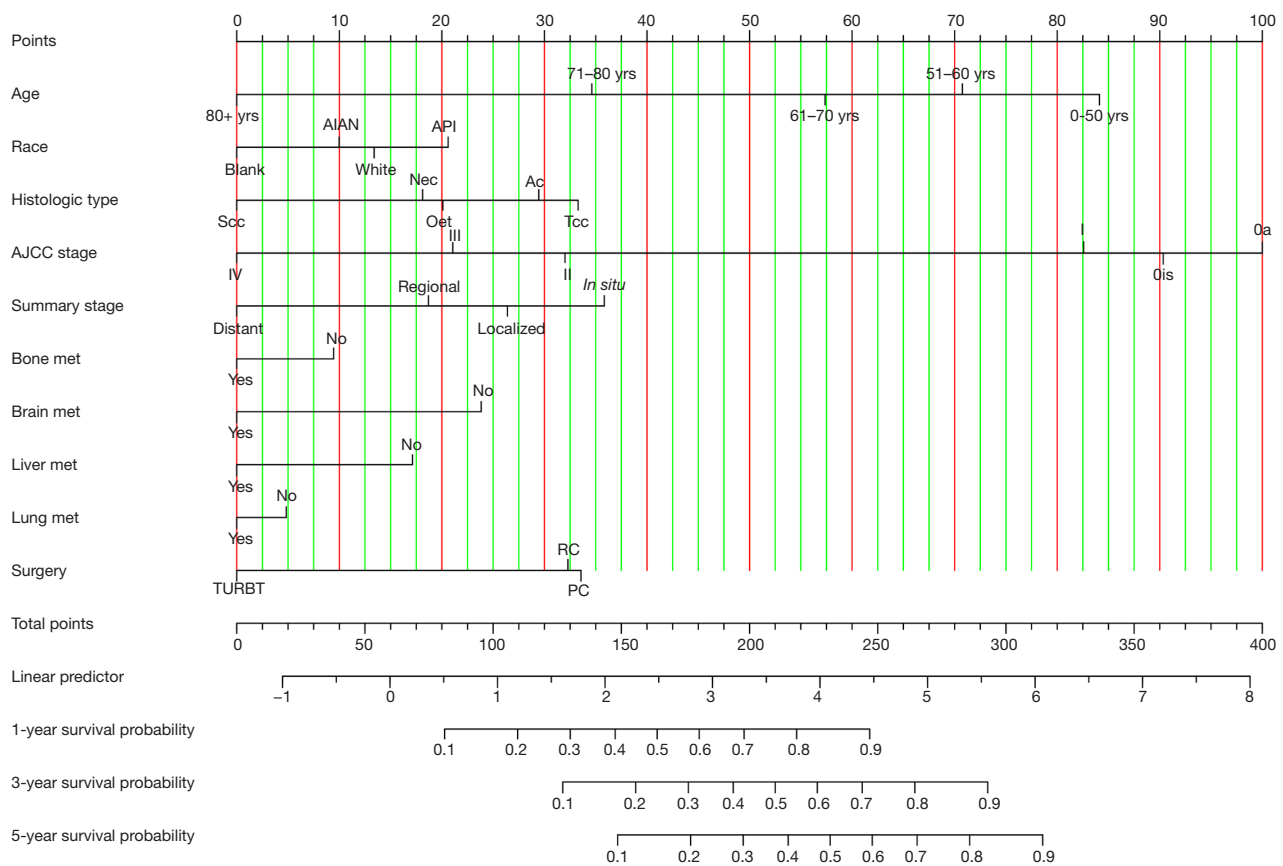
Figure 5 Nomogram of prediction for 1-, 3- and 5-year overall survival of bladder cancer. API, Asian or Pacific Islander; AIAN, American Indian/Alaska Native; Tcc, Transitional cell carcinoma; Scc, squamous cell carcinoma; Ac, adenocarcinoma; Nec, neuroendocrine carcinoma; Oet, other epithelial tumors; TURBT, transurethral resection of bladder tumor; PC, partial cystectomy; RC, radical cystectomy.

prediction models predict cancer outcomes more accurately than the cancer stage system (29,30). Our nomogram incorporates more risk factors, which to some extent increases its personalized prediction, and decisions about follow-up and surveillance of cancer patients are made based on risk. Patients predicted to be at higher risk need to receive more intensive follow-up and more accurate treatments, and the inclusion of more risk factors allows us to make more reliable predictions. The C-index of the nomogram was 0.768, indicating that the nomogram is an accurate model for predicting OS.

There are certain shortcomings in this study. First, the SEER database includes less than 30% of the U.S. population, indicating that the scope of the database is not large enough. For example, due to the limited number of patients with TNM-T0 stage, we lacked additional data to analyses the survival differences in patients with T0 stage. Therefore, our survival analyze for this period did not

provide additional results. Second, we did not include other factors that may affect OS, such as economic conditions (31), marital status (32), genetic factors (33-35), posttreatment care status (36,37), and patient physical status. The inclusion of these factors would further make the nomogram more accurate. Finally, chemotherapy, radiotherapy and other novel therapy strategies may affect the OS of BC patients. However, some of the SEER data do not provide this important information. Therefore, more studies are needed to identify risk factors that affect OS in BC patients.

Conclusions

Our study showed that the overall incidence of BC has been decreasing year by year since 1992. Meanwhile, we found that age, race, histologic type, tumor stage, and organ metastasis were independent predictors of OS in BC patients. To better predict the 1-, 3-, and 5-year OS in
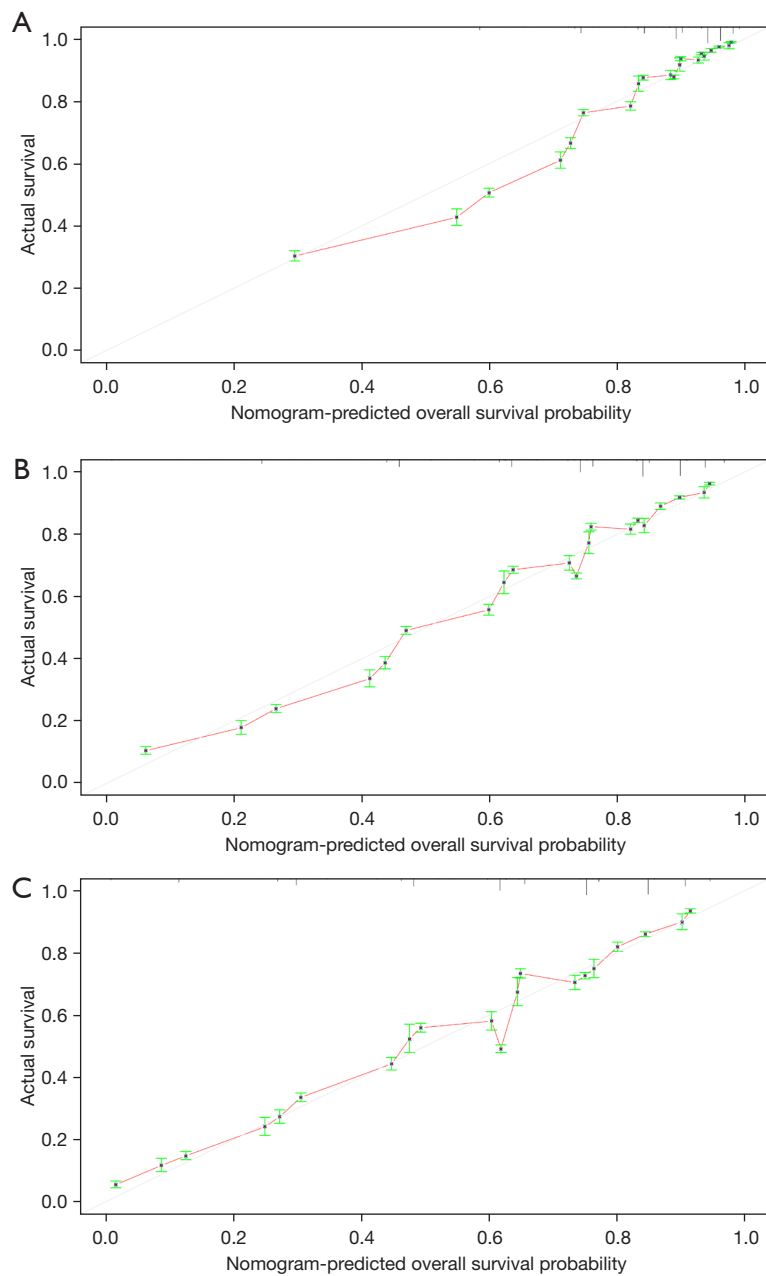
Figure 6 Calibration curves of the nomogram-predicted 1- (A), 3- (B) and 5-year (C) overall survival.

BC patients, we constructed a nomogram based on specific characteristics. The C-index was satisfactory in internal validation. This prediction tool will help physicians assess individualized survival predictions and could provide better surveillance strategies for BC patients.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-46/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-46/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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