Original Article

Clinical characterization and prognostic modeling of bladder cancer patients with a history of prior tumors: a SEER database analysis

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Background: Bladder cancer is one of the most prevalent malignancies within the urinary system, with incidence and mortality rates showing a global upward trend. This study aims to examine the clinical characteristics of bladder cancer patients with a history of prior malignancies and to develop a prognostic model using extensive data from the Surveillance, Epidemiology, and End Results (SEER) database to inform clinical treatment strategies.

Methods: Data from bladder cancer patients diagnosed between 2011 and 2015 were extracted using SEER*Stat software. Statistical analyses, including Kaplan-Meier survival curves, and Cox regression, were conducted using R software version 3.6.1 to develop a nomogram model. The predictive performance of the nomogram was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC) and the concordance index (C-index).

Results: A total of 12,260 bladder cancer patients were analyzed, including 8,959 individuals with no prior tumor history and 3,301 individuals with a history of previous tumors. The mean survival duration for patients with a prior tumor history was 56.04±39.96 months, significantly lower than the 70.28±39.36 months for patients without a prior tumor history (P<0.001). Significant differences were observed between the two groups across various clinical characteristics, such as age, race, gender, marital status, tumor location, tumor stage, and tumor grade. Multifactorial analysis identified age, race, gender, marital status, tumor grade, tumor stage, tumor histological type, surgical intervention, radiotherapy, chemotherapy, and prior tumor history as independent prognostic factors influencing survival. A nomogram was subsequently developed to predict overall mortality risk and 3- and 5-year survival rates, demonstrating robust predictive performance with a C-index and AUC exceeding 0.70.

Conclusions: Patients with a history of tumors exhibited lower survival rates and distinct clinical characteristics. The developed nomogram accurately predicts overall mortality and 3- and 5-year survival rates, offering potential for personalized prognostic assessments in clinical practice. Future research should validate the model's generalizability and include additional biological factors to enhance its predictive power.

Keywords: Bladder cancer; clinical features; nomogram; Surveillance, Epidemiology, and End Results database (SEER database); prognostic analysis

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Introduction

Bladder cancer is one of the most prevalent malignant neoplasms within the urinary system, with incidence and mortality rates showing a global upward trend (1). The disease encompasses various histological subtypes, including urothelial carcinoma (formerly transitional cell carcinoma), squamous cell carcinoma, adenocarcinoma, urachal carcinoma, mesenchymal tumors, mixed carcinoma, sarcomatoid carcinoma, and metastatic carcinoma (2). Urothelial carcinoma is the most common subtype, accounting for over 90% of bladder cancer cases (3). Current treatment strategies primarily involve surgical procedures, chemotherapy, radiotherapy, and other modalities (4). The etiology of bladder cancer is multifactorial, influenced by genetic and environmental factors such as gender, age, occupational exposure, smoking, genetic predispositions, dietary patterns, and exposure to environmental pollutants (5-8). Despite recent advances in diagnosis and treatment, the prognosis for bladder cancer remains poor. A history of prior tumors is a significant prognostic factor, as patients with previous malignancies often have worse outcomes (9). Research suggests that individuals with a history of prior tumors have an elevated risk of recurrence during subsequent survival (10). However, the impact on overall survival (OS) can vary depending on the tumor type and the specific population subgroup (11,12). Therefore, the clinical presentation and prognosis of bladder cancer patients with a history of prior tumors may be more complicated (13). The exclusion of these patients from many clinical trials has limited the understanding of their unique clinical characteristics and prognostic factors, potentially leading to less precise or limiting the individualized treatment and prognostic assessments for this group. There is a notable lack of research on the clinical characteristics and prognosis of bladder cancer patients with a history of prior tumors, especially in studies utilizing large-scale databases.

The Surveillance, Epidemiology, and End Results (SEER) database, maintained by the National Cancer Institute, is a widely used public resource in clinical practice, containing a vast collection of retrospective clinical data on oncology patients. It serves as an authoritative source for cancer incidence and survival statistics (14). By utilizing SEER data, researchers can conduct comprehensive analyses of the clinical characteristics and prognoses of cancer patients, providing a robust scientific foundation for clinical treatment strategies. This study aims to leverage the extensive dataset available in the SEER database to conduct a comprehensive analysis of the clinical characteristics of bladder cancer patients with a history of prior tumors and to develop a prognostic model. The research seeks to improve our understanding of the disease profile in this patient cohort, offer insights for clinical management, and serve as a reference for future studies. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1530/rc).

Highlight box

Key findings

- Constructed a nomogram model revealing shorter survival for bladder cancer patients with a history of prior cancer, identifying distinct clinical characteristics associated with prognosis.

What is known and what is new?

- Prior cancer history affects patient prognosis.
- Specific clinical differences and a predictive model for bladder cancer patients with prior cancer are identified.

What is the implication, and what should change now?

- The study implies the need for personalized treatment strategies for bladder cancer patients with prior cancer history. Clinical practice should consider incorporating predictive models into treatment planning.

Methods

Patient selection

Patients diagnosed with bladder cancer between 2011 and 2015 were identified using SEER*Stat software (version 8.3.9; https://seer.cancer.gov/data-software/documentation/seerstat/) from the SEER public database (https://seer.cancer.gov/). Data on patient demographics, clinical characteristics, and survival outcomes were collected, including age at diagnosis, gender, race, marital status, tumor grade, histologic type, tumor stage, primary tumor site, surgical intervention, radiation therapy, chemotherapy, prior oncologic history, and life status follow-up. The primary survival outcome was the time from diagnosis to death, with survival status confirmed through follow-up records in the SEER database. Inclusion criteria included confirmed pathological diagnosis, complete clinical information, and available survival follow-up data. Patients were excluded if they had missing data on race, tumor grade, tumor stage, survival time, marital status, surgical

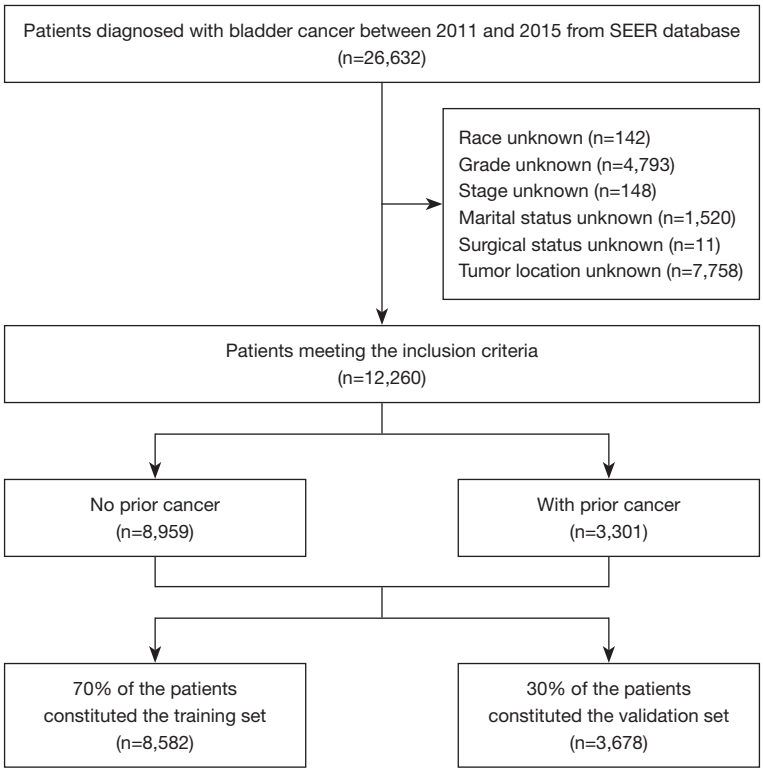

Figure 1 Data screening and analysis flowchart. SEER, Surveillance, Epidemiology and End Results database.

history, tumor site, or prior tumor history. A flowchart of the patient data screening process is provided in *Figure 1*. A total of 12,260 patients with bladder cancer were included in this study. All patient data were complete, with no missing data in the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Statistical analysis

Statistical analyses were performed using SPSS version 20.0 and GraphPad version 8.0 software. Patients were divided into two groups based on the presence or absence of a prior tumor history: the prior tumor history group and the no prior tumor history group. Categorical variables were presented as frequencies and percentages (n and %) and analyzed using the χ^2 test. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the *t*-test. Hazard ratios (HRs) for OS and cancer-specific survival (CSS) were estimated using multivariate Cox proportional hazards regression analysis. Kaplan-Meier survival curves were generated, and the log-rank test was used to compare survival distributions. Variables with P<0.1 in the univariate analysis were included in the multivariate regression analysis, followed by the application of a stepwise bidirectional regression method. Subsequently, a nomogram was constructed to predict the outcomes. Model validation was performed by randomly dividing the dataset into a training set and a validation set in a 7:3 ratio. The training set was used to develop the predictive model, while the validation set was used to assess the external performance of the model. There were no significant differences in clinical and pathological features between the two sets, as shown in Table S1. The predictive performance of the nomograms was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC) and the concordance index (C-index). Statistical significance was set at P<0.05.

Results

Clinical characterization of bladder cancer patients

A total of 12,260 bladder cancer patients were included in the study based on the established inclusion and

exclusion criteria. Of these, 8,959 patients (73%) had no prior history of tumors, while 3,301 patients (27%) had a documented history of tumors. The demographic and clinical characteristics of the patients are detailed in *Table 1*. Significant differences (P<0.05) were observed between the two groups across several key characteristics, including age, race, gender, marital status, tumor site, tumor stage, tumor grade, surgical intervention, radiotherapy and chemotherapy. The mean survival time was 70.28± 39.36 months for patients without a history of prior tumors, compared to 56.04±39.96 months for those with a prior tumor history. Most patients in both groups were over 60 years of age and predominantly Caucasian. Additionally, male gender and married status were more common in both cohorts. The bladder wall was the most frequent tumor site, with grade IV tumors and the histological type of urothelial carcinoma being the most prevalent. Most patients presented with localized tumors, and surgical intervention was the primary treatment modality. Notably, among patients without a prior tumor history, 18.33% were under 60 years old, and 23.65% were over 80 years old. In contrast, among patients with a prior tumor history, 6.33% were under 60 years old, and 40.96% were over 80 years old. Regarding tumor staging, the percentage of patients with localized and regional tumors was 87.69% versus 71.71% and 8.55% versus 24.33% in the no prior tumor history group and prior tumor history group, respectively. These findings suggest that bladder cancer patients with a prior tumor history exhibit distinct clinical characteristics compared to those without such a history.

HR analysis

We further analyzed the risk factors influencing OS and CSS in bladder cancer patients. *Figure 2A* illustrates the impact of various clinical and pathological factors on OS. Age was a significant risk factor, with HRs increasing progressively with age compared to patients younger than 60 years. Specifically, the HR was 1.57 [95% confidence interval (CI): 1.41–1.76, P<0.001] for patients aged 60–69 years, 2.63 (95% CI: 2.37–2.93, P<0.001) for those aged 70–79 years, and 5.36 (95% CI: 4.82–5.95, P<0.001) for patients aged 80 years and older. The risk was lower in Caucasians (HR =0.81, 95% CI: 0.71–0.91, P<0.001) and other races (HR =0.69, 95% CI: 0.59–0.81, P<0.001) compared to Blacks. Regarding gender, male patients (HR =1.18, 95% CI: 1.11–1.26, P<0.001) had a slightly higher risk of death than female patients. Marital status was also correlated with OS, with single patients (HR

Table 1 Clinical characteristics of bladder cancer patients with and without a history of prior cancer

Variables	Total (n=12,260)	Prior cancer		Statistic	P
		No (n=8,959, 73%)	Yes (n=3,301, 27%)		
Survival (months)	66.45±40.02	70.28±39.36	56.04±39.96	t=17.57	<0.001
Age				χ^2=557.34	<0.001
<60 years	1,851 (15.10)	1,642 (18.33)	209 (6.33)		
60–69 years	3,242 (26.44)	2,572 (28.71)	670 (20.30)		
70–79 years	3,696 (30.15)	2,626 (29.31)	1,070 (32.41)		
≥80 years	3,471 (28.31)	2,119 (23.65)	1,352 (40.96)		
Race				χ^2=12.75	0.002
Black	525 (4.28)	396 (4.42)	129 (3.91)		
White	10,950 (89.31)	7,950 (88.74)	3,000 (90.88)		
Others[†]	785 (6.40)	613 (6.84)	172 (5.21)		
Sex				χ^2=4.54	0.03
Female	2,819 (22.99)	2,104 (23.48)	715 (21.66)		
Male	9,441 (77.01)	6,855 (76.52)	2,586 (78.34)		

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Total (n=12,260)	Prior cancer		Statistic	P
		No (n=8,959, 73%)	Yes (n=3,301, 27%)		
Marital				χ^2=26.29	<0.001
Married	7,879 (64.27)	5,735 (64.01)	2,144 (64.95)		
Single	1,373 (11.20)	1,079 (12.04)	294 (8.91)		
Others‡	3,008 (24.54)	2,145 (23.94)	863 (26.14)		
Primary site				χ^2=27.54	<0.001
Bladder neck	664 (5.42)	428 (4.78)	236 (7.15)		
Overlapping lesion of bladder	2,074 (16.92)	1,543 (17.22)	531 (16.09)		
Ureteric orifice and Urachus	724 (5.91)	536 (5.98)	188 (5.70)		
Wall of bladder	8,798 (71.76)	6,452 (72.02)	2,346 (71.07)		
Grade				χ^2=56.35	<0.001
Grade I	1,510 (12.32)	1,195 (13.34)	315 (9.54)		
Grade II	3,281 (26.76)	2,439 (27.22)	842 (25.51)		
Grade III	1,667 (13.60)	1,247 (13.92)	420 (12.72)		
Grade IV	5,802 (47.32)	4,078 (45.52)	1,724 (52.23)		
Histologic				χ^2=5.11	0.16
Transitional cell carcinoma	11,820 (96.41)	8,643 (96.47)	3,177 (96.24)		
Adenocarcinoma	123 (1.00)	95 (1.06)	28 (0.85)		
Squamous cell carcinoma	158 (1.29)	116 (1.29)	42 (1.27)		
Others§	159 (1.30)	105 (1.17)	54 (1.64)		
Stage				χ^2=543.27	<0.001
Localized	10,223 (83.38)	7,856 (87.69)	2,367 (71.71)		
Regional	1,569 (12.80)	766 (8.55)	803 (24.33)		
Distant	468 (3.82)	337 (3.76)	131 (3.97)		
Surgery				χ^2=26.01	<0.001
No	242 (1.97)	142 (1.58)	100 (3.03)		
Yes	12,018 (98.03)	8,817 (98.42)	3,201 (96.97)		
Radiation				χ^2=3.16	0.08
No/unknown	11,552 (94.23)	8,462 (94.45)	3,090 (93.61)		
Yes	708 (5.77)	497 (5.55)	211 (6.39)		
Chemotherapy				χ^2=23.98	<0.001
No/unknown	7,884 (64.31)	5,646 (63.02)	2,238 (67.80)		
Yes	4,376 (35.69)	3,313 (36.98)	1,063 (32.20)		

Data are presented as mean ± standard deviation or n (%). *t*: *t*-test; χ^2: Chi-squared test. †, American Indian/AK Native, Asian/Pacific Islander; ‡, widowed/divorced/separated/unmarried or domestic partner; §, neuroendocrine carcinoma of other sites/other epithelial tumors of bladder/soft tissue sarcomas of other genitourinary.

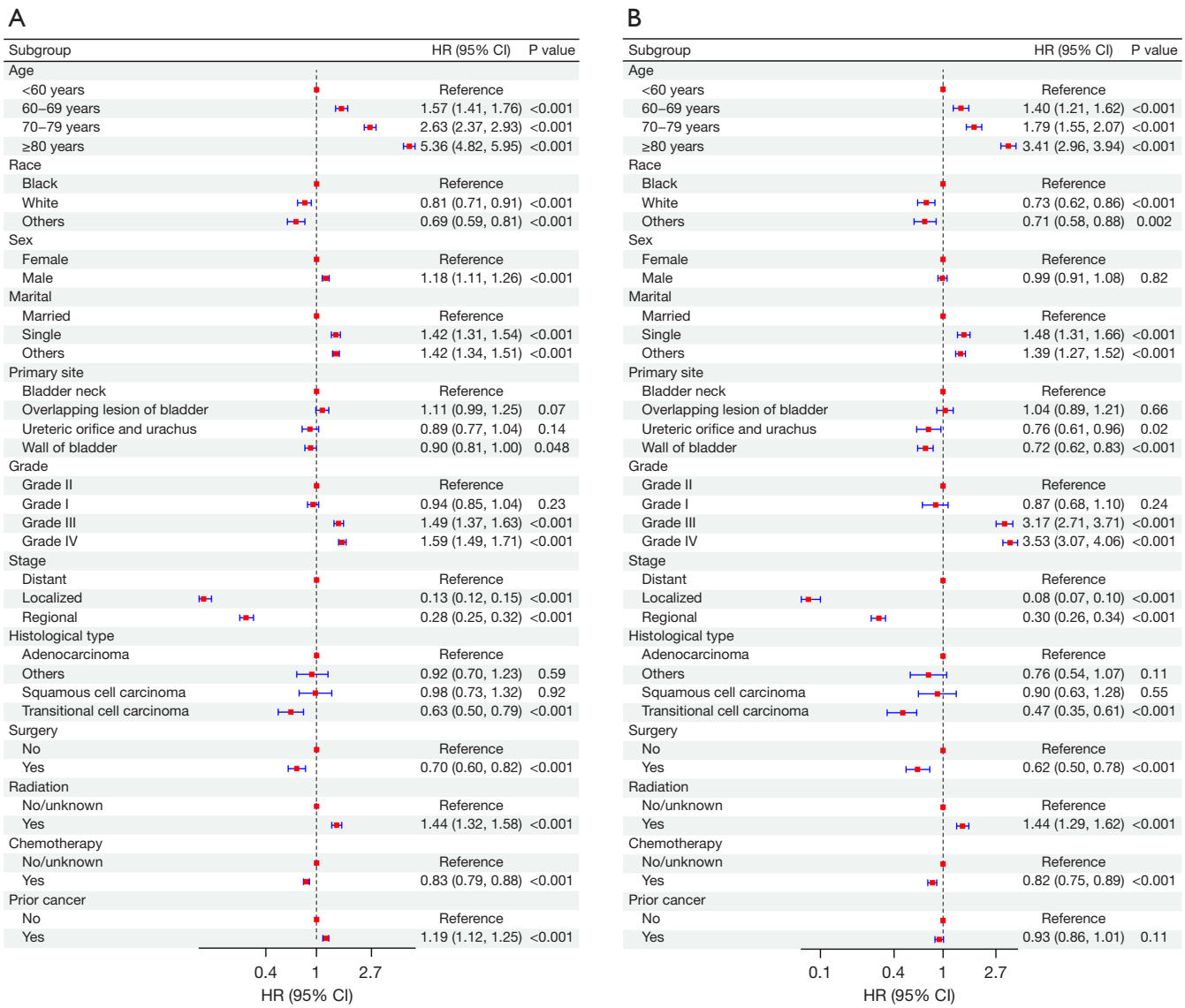

Figure 2 HR analysis. (A) Analysis of hazard ratios affecting OS in bladder cancer patients; (B) analysis of risk ratios affecting CSS in bladder cancer patients. CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; OS, overall survival.

=1.42, 95% CI: 1.31–1.54, P<0.001) and patients with other marital statuses (HR =1.42, 95% CI: 1.34–1.51, P<0.001) having a slightly higher risk of death than married patients. Patients with bladder wall tumors had a lower risk of death than those with bladder neck tumors (HR =0.90, 95% CI: 0.81–1.00, P=0.048). Tumor grade and stage significantly impacted OS, with an increased risk of death in patients with grade III (HR =1.49, 95% CI: 1.37–1.63, P<0.001) and grade IV (HR =1.59, 95% CI: 1.49–1.71, P<0.001) tumors. Patients with localized tumors (HR =0.13, 95% CI: 0.12–0.15, P<0.001) and regional tumors (HR =0.28, 95% CI: 0.25–0.32, P<0.001) had a significantly lower risk of death compared to those with distant metastases. Patients with urothelial carcinoma had a lower risk of death than those with adenocarcinoma (HR =0.63, 95% CI: 0.50–0.79, P<0.001). Surgical treatment (HR =0.70, 95% CI: 0.60–0.82, P<0.001) and chemotherapy (HR =0.83, 95% CI: 0.79–0.88, P<0.001) were associated with a reduced risk of death, while radiotherapy (HR =1.44, 95% CI: 1.32–1.58, P<0.001) was associated with an increased risk of death. Notably, having a prior tumor history (HR =1.19, 95% CI: 1.12–1.25, P<0.001) was associated with an increased risk of

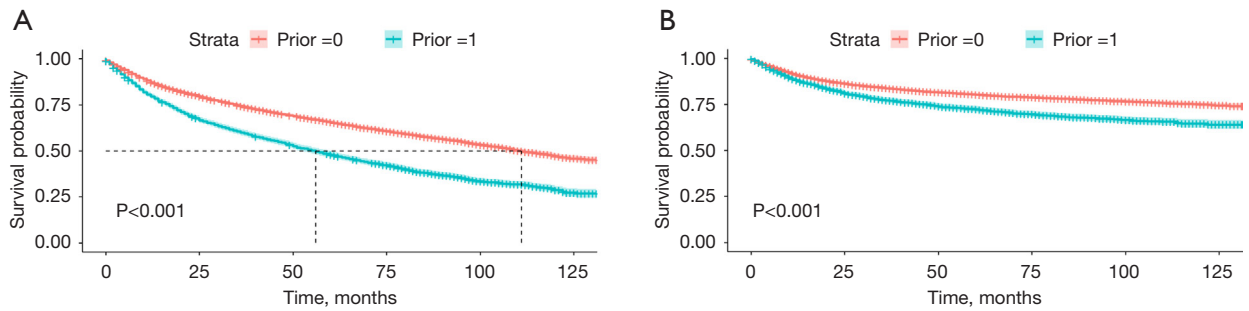

Figure 3 Kaplan-Meier curves evaluating the impact of prior tumor history on OS (A) and CSS (B) in bladder cancer patients. Prior =0: no prior cancer; prior =1: with prior cancer. CSS, cancer-specific survival; OS, overall survival.

death. *Figure 2B* provides an analysis of risk factors affecting CSS. Similar to the OS results, age, race, marital status, tumor site, tumor grade, tumor stage, tumor histological type, surgery, radiotherapy, and chemotherapy were independent predictors of CSS. Although a prior tumor history was associated with a reduced risk of CSS, the effect was not statistically significant (HR =0.93, 95% CI: 0.86–1.01, P=0.11).

Kaplan-Meier survival analysis

To further elucidate the impact of prior tumor history on OS and CSS in bladder cancer patients, Kaplan-Meier survival curves were generated for both endpoints. As depicted in *Figure 3*, the survival outcomes for bladder cancer patients with a history of prior tumors were significantly worse compared to those without such a history, as demonstrated by the log-rank test (P<0.001).

Multi-factor Cox proportional hazards modeling

Multifactorial Cox regression analysis

The survival data of bladder cancer patients were analyzed using a comprehensive multifactorial Cox proportional hazards model to identify independent prognostic factors influencing OS (*Table 2*). Age significantly impacted survival, with patients over 80 years exhibiting a markedly higher risk of death (HR =5.23, 95% CI: 4.62–5.93, P<0.001) compared to those under 60 years. Patients aged 60–69 years (HR =1.52, 95% CI: 1.33–1.73, P<0.001) and 70–79 years (HR =2.56, 95% CI: 2.25–2.90, P<0.001) also demonstrated an elevated risk of mortality. Compared to Black patients, those of other races (HR =0.73, 95% CI: 0.61–0.88, P<0.001) and White patients (HR =0.79, 95% CI: 0.68–0.91, P=0.001) exhibited a lower risk of death. Patients who were single (HR =1.34, 95% CI: 1.21–1.48, P<0.001) or of other marital statuses (HR =1.34, 95% CI: 1.25–1.43, P<0.001) exhibited an increased risk of death compared to married patients. Patients with overlapping bladder lesions exhibited a higher risk of death compared to those with bladder neck tumors (HR =1.16, 95% CI: 1.01–1.34, P=0.036). Patients with Grade III (HR =1.55, 95% CI: 1.36–1.76, P<0.001) and Grade IV (HR =1.63, 95% CI: 1.46–1.82, P<0.001) tumors had a significantly higher risk of death compared to those with grade I tumors. The risk of death was lower in patients with transitional cell carcinoma (HR =0.66, 95% CI: 0.50–0.86, P=0.002) compared to adenocarcinoma. Patients who received surgical treatment had a lower risk of death compared to those who did not (HR =0.71, 95% CI: 0.59–0.85, P<0.001). Patients who received radiotherapy had an increased risk of death compared to those who did not receive radiotherapy or whose treatment status was unknown (HR =1.41, 95% CI: 1.27–1.58, P<0.001). Patients with localized (HR =0.16, 95% CI: 0.14–0.18, P<0.001) and regional (HR =0.32, 95% CI: 0.28–0.37, P<0.001) tumors exhibited a significantly lower risk of death compared to those with distant metastases. Patients with a history of prior tumors had an increased risk of death compared to those without such a history (HR =1.19, 95% CI: 1.11–1.27, P<0.001).

Construction and validation of nomograms for Cox regression analysis

Based on the results of the Cox regression analysis, variables such as age of onset, race, marital status, tumor site, tumor grade, tumor histological type, surgery, radiotherapy, and the presence of prior tumor history were used as independent predictors to construct a nomogram. Each level of the predictors was assigned a corresponding score, and the total score for an individual patient was calculated

Table 2 Multifactor Cox regression analysis

Variables	β	SE	Z	P	HR (95% CI)
Age					
<60 years					1.00 (reference)
≥80 years	1.66	0.06	25.93	<0.001	5.23 (4.62–5.93)
60–69 years	0.42	0.07	6.09	<0.001	1.52 (1.33–1.73)
70–79 years	0.94	0.06	14.65	<0.001	2.56 (2.25–2.90)
Race					
Black					1.00 (reference)
Others	−0.32	0.09	−3.33	<0.001	0.73 (0.61–0.88)
White	−0.24	0.07	−3.25	0.001	0.79 (0.68–0.91)
Marital					
Married					1.00 (reference)
Others	0.29	0.03	8.44	<0.001	1.34 (1.25–1.43)
Single	0.29	0.05	5.70	<0.001	1.34 (1.21–1.48)
Primary site					
Bladder neck					1.00 (reference)
Overlapping lesion of bladder	0.15	0.07	2.10	0.04	1.16 (1.01–1.34)
Ureteric orifice and urachus	−0.08	0.10	−0.88	0.38	0.92 (0.76–1.11)
Wall of bladder	−0.06	0.07	−0.95	0.34	0.94 (0.82–1.07)
Grade					
Grade I					1.00 (reference)
Grade II	0.03	0.06	0.45	0.65	1.03 (0.91–1.16)
Grade III	0.44	0.07	6.67	<0.001	1.55 (1.36–1.76)
Grade IV	0.49	0.06	8.54	<0.001	1.63 (1.46–1.82)
Histology					
Adenocarcinoma					1.00 (reference)
Others	−0.03	0.17	−0.15	0.88	0.97 (0.69–1.37)
Squamous cell carcinoma	0.07	0.18	0.37	0.71	1.07 (0.76–1.51)
Transitional cell carcinoma	−0.42	0.14	−3.06	0.002	0.66 (0.50–0.86)
Surgery					
No					1.00 (reference)
Yes	−0.35	0.10	−3.62	<0.001	0.71 (0.59–0.85)
Radiation					
No/unknown					1.00 (reference)
Yes	0.35	0.05	6.33	<0.001	1.41 (1.27–1.58)

Table 2 (*continued*)

Table 2 (*continued*)

Variables	β	SE	Z	P	HR (95% CI)
Stage					
Distant					1.00 (reference)
Localized	−1.85	0.06	−28.69	<0.001	0.16 (0.14–0.18)
Regional	−1.13	0.07	−16.50	<0.001	0.32 (0.28–0.37)
Prior cancer					
No					1.00 (reference)
Yes	0.17	0.03	5.14	<0.001	1.19 (1.11–1.27)

CI, confidence interval; HR, hazards ratio; SE, standard error.

by summing these scores. A higher total score indicated a poorer prognosis. In the nomogram, a vertical line is drawn from the total score of each bladder cancer patient to predict their 3- and 5-year survival rates (*Figure 4A*). To assess the predictive efficacy of the nomogram, the AUC and C-index were calculated. The validation results showed that the C-index for the training and validation sets were 0.747 (95% CI: 0.714–0.780) and 0.752 (95% CI: 0.751–0.753), respectively. Additionally, the AUC for the training and validation sets were 0.800 (95% CI: 0.790–0.810) and 0.810 (95% CI: 0.790–0.820), indicating that the model has relatively accurate predictive ability (*Figure 4B*).

Discussion

Bladder cancer, more prevalent in men and increasing with age, ranks as the fourth most common cancer among men, constituting 6% of new cases and 4% of cancer-related deaths (8,15). Understanding the factors that influence bladder cancer prognosis and addressing the specific needs of different patient populations are crucial for developing personalized treatment strategies and improving patient management.

A history of prior tumors increases the risk of recurrent malignancy. Studies have shown that the impact of prior tumor history on a patient's prognosis depends on factors such as tumor type, stage, and the interval between diagnoses (16,17). However, whether a prior tumor history negatively affects survival remains controversial. Recent research by Yin *et al.* (18) has found that gastric cancer patients with a history of previous cancer do not have worse survival than those with primary gastric cancer, and in some cases, they even have improved CSS. Zhou *et al.* analyzed data from the SEER database for 20 types of cancer and found that patients with a history of uterine, breast, prostate, and bladder cancer had worse OS, while those with nasopharyngeal, esophageal, and hepatocellular carcinoma had similar OS to patients without a history of tumors (19). Additionally, prior tumor history was a significant risk factor for non-thymic malignancy-related death in patients who underwent resection of thymic epithelial tumors (20).

This study found that bladder cancer patients with prior tumors had shorter OS, likely due to shared risk factors such as smoking and occupational exposures, which can exacerbate tumor severity and progression (13,21). In addition, the treatment of the previous tumor may have affected the overall health status of the patients (22). It is speculated that these factors may have intensified the malignancy and progression speed of the tumor, thereby affecting the treatment response and prognosis of bladder cancer. Our multifactorial analysis showed that a history of prior tumors was associated with an increased risk of death (HR =1.19, 95% CI: 1.12–1.25). Kaplan-Meier curves for OS and CSS demonstrated that bladder cancer patients with a history of prior tumors had significantly lower survival than those without such a history. This finding was further confirmed by multifactorial logistic regression and Cox proportional hazards models, which identified prior tumor history as an independent risk factor for bladder cancer prognosis. Additionally, bladder cancer patients with a history of prior tumors exhibited significant differences in several key clinical characteristics compared to those without such a history, including age, sex, race, marital status, tumor site, tumor grade, tumor stage, surgical intervention, and chemotherapy. These disparities may be attributable to the biological behavior of the tumor, the

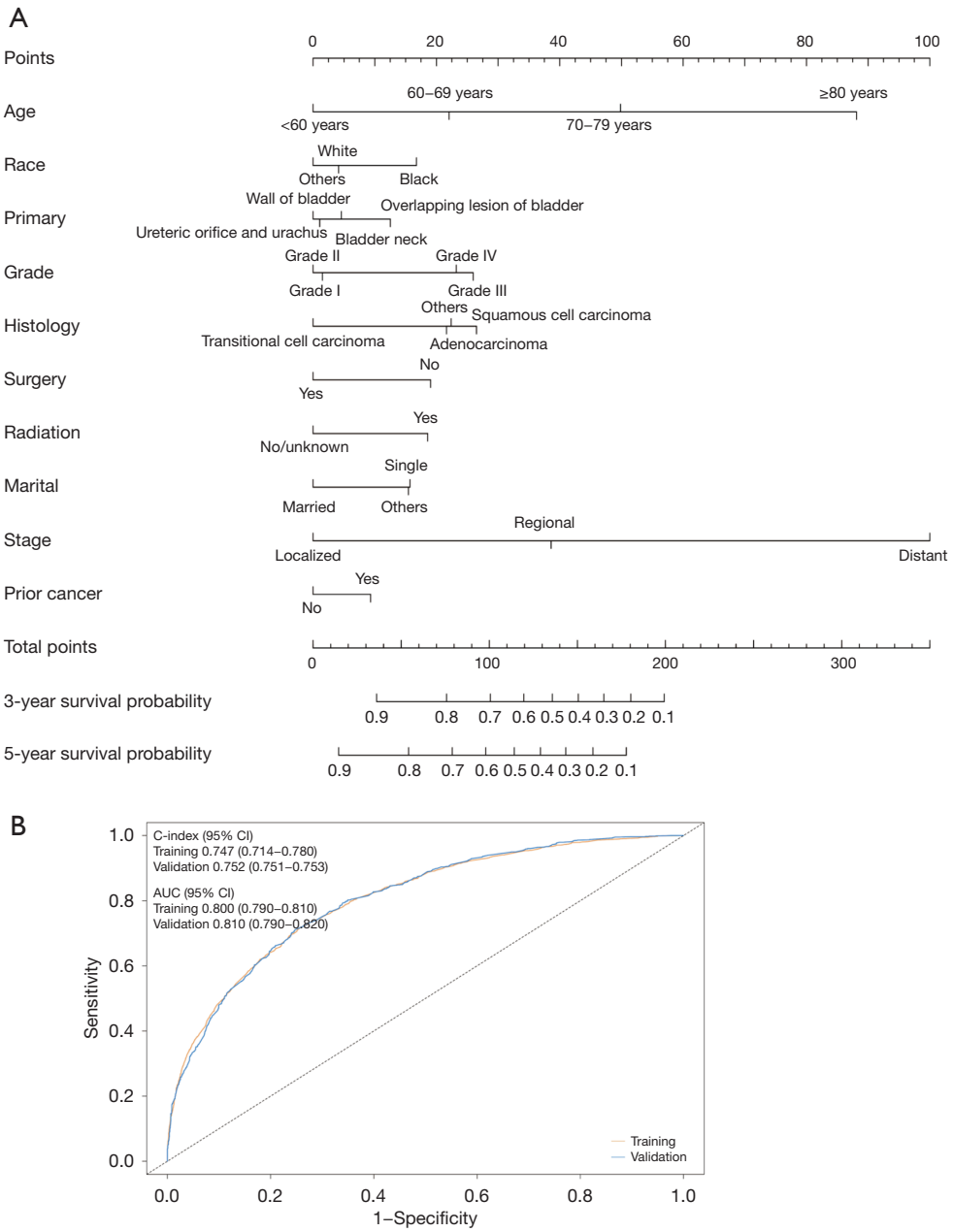

Figure 4 Cox regression analysis for bladder cancer patients. (A) Nomogram; (B) 36-month prognostic survival ROC curve. AUC, area under the curve; CI, confidence interval; C-index, concordance index; ROC, receiver operating characteristic curve.

patient's physiological condition, and their response to treatment. Our study's multifactorial analysis confirmed that age, race, gender, marital status, tumor grade, and stage significantly impact OS and CSS in bladder cancer patients, consistent with previous research and highlighting their prognostic importance (23). Studies indicate that older patients with advanced tumor grade and stage have shorter survival. Gender and marital status also influence treatment response and survival, with men showing higher incidence and mortality rates for bladder cancer, possibly due to hormone levels and smoking habits (24,25). Married patients have a lower mortality risk, potentially due to the stability of their social and emotional support networks, which may improve treatment adherence, mental health,

and resources for managing disease challenges (26).

Moreover, the study identified that White patients and those of other racial backgrounds had a lower mortality risk compared to Black patients. This racial disparity may be due to genetic susceptibility and differences in access to healthcare resources, both of which could indirectly influence patient prognosis (27). Radiotherapy, often used alongside other cancer treatments, can control tumor growth, reduce local recurrence rates, and improve survival. However, this study found that radiotherapy was associated with an increased risk of death from bladder cancer, possibly due to factors such as radiation dose, treatment accuracy, tumor biology, and patient variability. A study noted that while radiotherapy is a key treatment for muscle-invasive bladder cancer, its effectiveness can be limited by radiotherapy resistance due to the tumor's hypoxic and immunosuppressive microenvironments (28). Additionally, the SEER database may have limitations regarding radiotherapy information, as only 708 out of 12,260 bladder cancer patients received radiotherapy. This discrepancy could be due to underreporting or selection bias, limiting the evaluation of radiotherapy efficacy. The multifactorial analysis revealed a markedly elevated risk of mortality among older patients and those with advanced-stage tumors. Furthermore, approximately 10% of young cancer patients had a history of previous cancer, a figure that increased to about 25% in older patients. Notably, in the cohort of bladder cancer patients over 80 years old, 40.96% had a history of tumors compared to 23.65% of those without such a history. The percentage of locoregional cases was higher in the prior tumor group compared to the no prior tumor group (24.33% *vs.* 8.55%), while the percentage of localized cases was lower in the prior tumor group compared to the no prior tumor group (71.71% *vs.* 87.69%). These findings highlight the need for closer monitoring and more aggressive treatment strategies for high-risk patients in clinical practice.

Nomograms, which serve as models for probabilistic prediction of specific outcomes, facilitate the visualization of prognostic factors and allow for the convenient individualization of patient prognosis, informing clinical decision-making. These tools are now widely used across a broad spectrum of diseases (29,30). Independent prognostic factors for bladder cancer patients were identified using multifactorial logistic regression and Cox proportional hazards regression analyses. A nomogram was subsequently developed to predict overall mortality risk and 3- and 5-year survival rates, demonstrating robust predictive performance with both the C-index and AUC exceeding 0.70. This tool aids clinicians in assessing individualized patient prognosis and enhances patient understanding of their disease status and treatment expectations.

Despite offering valuable insights, our study has limitations. First, SEER data, mostly from the U.S., may not fully represent global patient populations. Second, SEER lacks details on treatment specifics (e.g., radiation, chemotherapy), genetic information, and lifestyle factors (e.g., smoking, occupational exposure), which are significant bladder cancer risk factors (6,7). The absence of this data may have hindered our ability to comprehensively understand the multifaceted risks associated with bladder cancer. For instance, the study by Kufukihara *et al.* (13) has highlighted the negative impact of a history of prior non-uroepithelial malignancies on clinical outcomes of non-muscle invasive bladder cancer patients in current smokers, revealing that smoking and prior tumor history may co-affect tumor recurrence and progression. This is something that our research has not fully explored. What's more, the nomogram survival model developed here was validated internally but lacks external validation, limiting its generalizability. Future studies will gather large clinical datasets to further validate the nomogram and explore more prognostic factors.

Conclusions

Analysis of the SEER database revealed that patients with a history of prior tumors exhibited lower average survival rates and distinct clinical characteristics, including differences in age, race, gender, marital status, and tumor grading and staging, when compared to those without a history of prior tumors. The prognostic model developed in this study integrates these clinical factors to improve the accuracy of survival predictions, thereby supporting more informed clinical treatment decisions.

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Footnote

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

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