Trends of Incidence and Prognosis of Upper Tract Urothelial Carcinoma

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Research

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Abstract

Backgrud The purpose of this study was to investigate trends of incidence of upper tract urothelial carcinoma (UTUC) patients and establish reliable and practical nomogram based on significant clinical factors to predict the overall survival (OS) and cancer-specific survival (CSS) of UTUC patients.

Methods The Surveillance, Epidemiology, and End Results (SEER) database extracts UTUC patients between 1988 and 2015. Incidence was calculated using joinpoint regression software, and trends were quantified by annual percentage change (APC). A nomogram was constructed using R software to predict the OS and CSS probabilities of a single patient.

Results From 1988 to 2015, the incidence of UTUC showed a downward trend (1988: 1.57/100,000 to 2015: 1.51/100,000; APC=-0.1). After stratification according to sex, age and primary site, we found that the incidence of UTUC patients in male, 70+ years and renal pelvis were higher than those of female, <60 years,60-69 years and ureter UTUC patients. The nomogram based on age, sex, marital status, race, origin, primary site, histological type, grade, SEER stage, surgery, radiotherapy and chemotherapy variables showed good OS and CSS accuracy (OS: C-index=0.701, AUC=0.738; CSS: C-index=0.729, AUC=0.689). In addition, the calibration curves showed a good consistency between the predicted and actual 3-, 5- and 10-year OS and CSS rates of the nomogram.

Conclusion In the past 30 years, the incidence of UTUC showed a general downward trend, and the prognostic nomogram we established can provide a personalized risk assessment for the survival of UTUC patients.

Backgroud

Upper tract urothelial carcinoma (UTUC) is a relatively rare tumor, including carcinoma of the renal pelvis and carcinoma of the ureter, which accounting for about 5–10% of urothelial carcinoma (UC).[1, 2] In the United States, there were approximately 15,000 newly diagnosed cases of UTUC in 2014.[3] UTUC has the characteristics of multicentric tumor growth and urinary dissemination tendency, and has a higher grade and stage at the time of diagnosis.[4] The 5-year cancer-specific survival rate of UTUC patients is 50–80%.[5]

The incidence of UTUC is high in Taiwan, especially on the southwest coast of the island, which accounts for 20–25% of UC in the region.[6, 7] Some epidemiological studies have shown that the annual incidence rate in western countries is about 2 cases per 100,000 residents.[8] The majority of UTUC in European and the United States are male, with a male to female ratio of about 2: 1, which is more common in individuals aged 70–90 years, and the incidence of renal pelvic cancer is about twice that of ureter cancer.[9] However, to the best of our knowledge, it is unclear what the trends in UTUC have changed over the past three decades, and whether any changes have been driven by factors such as age, sex and primary site.

The American Joint Committee on Cancer (AJCC) tumor node metastasis (TNM) staging system is widely used to evaluate the prognosis of patients with UTUC.[10] However, other factors such as age, sex, race, marital status, SEER stage, grade and treatment pattern can also affect the outcome of UTUC patients. Therefore, it was necessary to establish a comprehensive prognostic assessment system including clinicopathological and demographic variables in clinical practice. The nomogram based on the equations derived from the regression coefficients of each variable integrates many prognostic factors, which can more accurately predict the individual survival of patients with UTUC.[11]

The purpose of the current study is to estimate the incidence of UTUC based on sex, age and primary site, and establish reliable and practical nomogram based on significant clinical factors to predict the overall survival (OS) and cancer-specific survival (CSS) of UTUC patients. Therefore, this study used the Surveillance, Epidemiology, and End Results (SEER) database to study the trend of incidence and establish prognostic nomogram in UTUC patients from 1988 to 2015. We hope that the results of this study can improve the OS and CSS rate of patients with UTUC.

Patients And Methods

Patients selection

The data used in our study was retrieved from the National Cancer Institute-funded Surveillance Epidemiology and End Results (SEER) database. The SEER database covers approximately 28% of the US population and includes demographic information and cancer characteristics, such as year of diagnosis, diagnosis age, sex, race, marital status, primary tumor site, tumor grade and stage, histological type, Tumor-Node-Metastasis (TNM) stage, treatment modality and survival time.[12]

Estimate trends of incidence of UTUC patients

We used SEER*Stat software version 8.3.6 (https://seer.cancer.gov/seerstat/) to collect incidence information (Incidence - SEER 9 Regs Research Data, Nov 2018 Sub (1975–2016) < Katrina/Rita Population Adjustment). The *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) site codes C65.9-Renal pelvis and C66.9-Ureter were used to identify patients diagnosed with UTUC between 1988 and 2015. We divide all patients into male and female based on gender. According to the age at diagnosis, the population was divided into three groups: <60 years group, 60–69 years group and 70 + years group. On the basis of the primary site, the patients were divided into renal pelvis cancer and ureter cancer.

Analyze the survival trends of UTUC patients

The National Cancer Institute's SEER*Stat software version 8.3.6 (https://seer.cancer.gov/seerstat/) (SEER 18 Regs Custom Data (with additional treatment fields), Nov 2018 Sub (1975–2016 varying)

database) was used to analyze the survival trends of UTUC patients. The exclusion criteria were as follows:(a) unknown marital status or domestic partner (n = 990); (b) age < 18 years (n = 7); (c) unknown survival time (n = 72); (d) with two or more primary tumor (n = 12,710) and (e) surgery unknown (n = 32). Finally, we left 10,852 eligible patients diagnosed with UTUC.

Variable definition information about age at diagnosis, sex, marital status, race, origin, primary site, histological type, grade, SEER stage, surgery, radiotherapy, chemotherapy, cause of death and survival time can be found in the SEER database. The starting point of the follow-up was the date of diagnosis of UTUC, and the end point was cancer-specific death or the last follow-up in December 2016. The overall survival (OS) time corresponded to the length of time from the date of diagnosis to the death from any cause or the date on which data were censored. When analyzing cancer-specific survival (CSS), mortality cases associated with other causes were excluded.

Statistical analysis

The incidence calculations are performed per 100,000 people and adjusted for the age of the 2000 standard United States population. In order to compare the incidence trends of UTUC from 1988 to 2015 in stages, we performed joinpoint regression analysis. Joinpoint regression software is a program of the National Cancer Institute's SEER program that detect trends in incidence, and can determine the starting and ending years in which incidence increases and/or decreases. the regression model is used to estimates the rates between the two joinpoint years, the annual percentage change (APC) of the rates and the 95% confidence interval (CI).

Univariate and multivariate Cox regression models were performed to estimate the hazard ratios (HR) and 95% CI to analyze independent prognostic factors of UTUC OS and CSS. Using R software, we constructed nomogram based on age at diagnosis, sex, marital status, race, origin, primary site, histological type, grade, SEER stage, surgery, radiotherapy and chemotherapy to predict the OS and CSS probabilities of individual patients. We use the MedCalc software (version 15.2.0) to generate the receiver operating characteristic (ROC) curve for the nomogram, and determined the area under the curve (AUC). In addition, by comparing the predicted survival time with the observed survival time, the predictive performance of the nomogram was evaluated using the consistency index (C-index) and calibration curve, and the nomogram was calibrated for 3-, 5- and 10-years OS and CSS. The C index was similar to the AUC, but seems to be more suitable for censored data. The value of the C-index statistic was between 0.5 (non-discrimination) and 1 (perfect discrimination), and a higher C-index value indicates a better prognostic model. These evaluations were performed using a bootstrap with 1000 resamples. Because there was no direct clinical interpretation for C-index. Therefore, we also analyzed the decision curve analysis (DCA), which is a novel method to evaluate the predictive model for evaluating net benefits from the perspective of clinical outcome.

SEER*Stat software version 8.3.6 (National Cancer Institute), Joinpoint regression program version 4.5.0.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National

Cancer Institute) and statistical software package R version 3.5.3 (http://www.r-project.org/) were used to calculate age-adjusted incidence. P-value ≤ 0.05 (two-sided) was considered statistically significant.

Results

Incidence trends of UTUC patients

From 1988 to 2015, the average age at onset of UTUC increased from 70.01 years in 1988 to 73.20 years in 2015, and mean age of onset of UTUC in female and ureter was higher than that in male and renal pelvis (Fig. 1).

The incidence of UTUC showed a downward trend (1988: 1.57/100,000 persons to 2015: 1.51/100,000 persons) between 1988 and 2015 (Fig. 2A). The average APC of age-adjusted incidence among all UTUC patients was − 0.1 (95% CI: -0.2 to 0.0). In the same period, the incidence of patients aged 70 + was significantly higher than that of patients < 60 years and 60–69 years (Fig. 2B). The incidence of UTUC patients aged < 60 years (APC=-2.1, 95% CI: -2.3 to -1.9) and 60–69 years (APC=-1.4, 95% CI: -1.5 to -1.2) was decreasing, while the incidence of 70 + years patients was increasing (APC = 0.7, 95% CI: 0.6 to 0.8) (Table 1). After stratification according to sex and primary site, we found that the incidence of UTUC patients in male and renal pelvis were higher than those of female and ureter UTUC patients (Fig. 2C, D).

Table 1
Changes in the incidence of upper tract urothelial carcinoma (UTUC) from 1988 to 2015.

Characteristic	Year	Annual Percent Change	95% CI
Total patients	1988–2015	-0.1	-0.2 to 0.0
Age			
< 60	1988–2015	-2.1	-2.3 to -1.9
60–69	1988–2015	-1.4	-1.5 to -1.2
70+	1988–2015	0.7	0.6 to 0.8
Sex			
Male	1988–1993	-3.6	-4.8 to -2.5
	1993–2015	0.0	-0.1 to 0.1
Female	1988–2015	0.2	0.0 to 0.3
Primary site			
Renal pelvis	1988–2015	-0.1	-0.2 to -0.1
Ureter	1988–2015	-0.1	-0.3 to 0.0

Subsequently, we stratified sex and primary site to detect the effect of age on incidence (**Supplemental Table 1**). Among the four groups of 70 + years, only the male 70 + years group experienced a decrease in incidence from 1988 to 1993 (**Fig. S1A**), while the remaining three groups of 70 + years showed an increasing trend. Both male and female, renal pelvis and ureter, the incidence of UTUC < 60 years and 60–69 years showed a decreasing trend (**Fig. S1B-D**).

Identification of prognostic factors of OS and CSS in GCTC patients

Univariate and multivariate Cox regression were used to analyze the related factors of OS and CSS in patients with GCTC (Table 2 **and** Table 3). Univariate Cox regression analysis showed that sex, age at diagnosis, marital status, histological type, SEER stage, grade, surgery, radiotherapy and chemotherapy were related factors of OS and CSS of UTUC patients. After incorporating factors related to univariate Cox regression into multiple Cox regression analysis, we found that age at diagnosis, marital status, histological type, SEER stage, grade, surgery, radiotherapy and chemotherapy were independent risk factors for OS and CSS in patients with UTUC.

Table 2
Univariate and multivariate analysis of overall survival (OS) rates.

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Sex				
Male	Reference		Reference	
Female	1.07 (1.02–1.12)	.003	0.89 (0.85–0.94)	< .001
Age at diagnosis				
< 60	Reference		Reference	
60–69	1.59 (1.46–1.73)	< .001	1.63 (1.50–1.78)	< .001
70+	2.63 (2.44–2.83)	< .001	2.60 (2.41–2.81)	< .001
Race				
White	Reference			
Black	1.07 (0.97–1.19)	.183		
Other	0.93 (0.85-1.00)	.058		
Origin				
Spanish-Hispanic-Latino	Reference			
Non-Spanish-Hispanic-Latino	1.05 (0.97–1.15)	.235		
Primary site				
Renal pelvis	Reference			
Ureter	1.01 (0.96–1.05)	.825		
Marital status				

Abbreviations:

OS, Overall survival; SEER, Surveillance, Epidemiology, and End Results.

Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.

[a]Model was adjusted by sex, age, marital status, histological type, grade, SEER stage and treatment pattern.

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
Married	Reference		Reference	
Divorced/separated	1.10 (1.01–1.19)	.027	1.16 (1.07–1.26)	< .001
Windowed	1.59 (1.51–1.67)	< .001	1.29 (1.21–1.36)	< .001
Single	1.09 (1.00-1.18)	.042	1.21 (1.12–1.32)	< .001
Histological Type				
Transitional cell carcinoma	Reference		Reference	
Others	1.53 (1.42–1.66)	< .001	1.16 (1.07–1.26)	< .001
SEER stage				
Localized	Reference		Reference	
Regional	1.75 (1.65–1.86)	< .001	1.73 (1.63–1.85)	< .001
Distant	6.33 (5.89–6.79)	< .001	5.08 (4.69–5.51)	< .001
Unstaged	2.11 (1.91–2.33)	< .001	1.30 (1.17–1.45)	< .001
Grade				
Grade I	Reference		Reference	
Grade II	1.20 (1.04–1.38)	.014	1.09 (0.95–1.26)	.235
Grade III	2.26 (1.98–2.58)	< .001	1.57 (1.37–1.80)	< .001
Grade IV	1.95 (1.70–2.23)	< .001	1.49 (1.30–1.71)	< .001
Unknown	2.98 (2.60–3.42)	< .001	1.46 (1.27–1.69)	< .001
Surgery				
No	Reference		Reference	
Yes	0.38 (0.36–0.40)	< .001	0.50 (0.47–0.54)	< .001

Abbreviations:

OS, Overall survival; SEER, Surveillance, Epidemiology, and End Results.

Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.

[a]Model was adjusted by sex, age, marital status, histological type, grade, SEER stage and treatment pattern.

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
Radiotherapy				
No	Reference		Reference	
Yes	2.06 (1.92–2.21)	< .001	1.35 (1.25–1.45)	< .001
Chemotherapy				
No	Reference		Reference	
Yes	1.31 (1.24–1.38)	< .001	0.81 (0.76–0.86)	< .001

Abbreviations:

OS, Overall survival; SEER, Surveillance, Epidemiology, and End Results.

Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.

[a]Model was adjusted by sex, age, marital status, histological type, grade, SEER stage and treatment pattern.

Table 3
Univariate and multivariate analysis of cancer-specific survival (CSS) rates.

Characteristic	CSS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Sex				
Male	Reference		Reference	
Female	1.14 (1.06–1.22)	< .001	-	.640
Age at diagnosis				
< 60	Reference		Reference	
60–69	1.30 (1.15–1.46)	< .001	1.31 (1.16–1.47)	< .001
70+	1.81 (1.63–2.01)	< .001	1.76 (1.57–1.96)	< .001
Race				
White	Reference			
Black	1.10 (0.95–1.28)	.218		
Other	0.99 (0.88–1.12)	.903		
Origin				
Spanish-Hispanic-Latino	Reference			
Non-Spanish-Hispanic-Latino	1.03 (0.91–1.17)	.645		
Primary site				
Renal pelvis	Reference		Reference	
Ureter	0.72 (0.67–0.77)	< .001	0.72 (0.67–0.78)	< .001
Marital status				

Abbreviations:

CSS, Cancer-specific survival; SEER, Surveillance, Epidemiology, and End Results.

Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.

[a]Model was adjusted by sex, age, primary site, marital status, histological type, grade, SEER stage and treatment pattern.

Characteristic	CSS			
	Univariate analysis		Multivariate analysis[a]	
Married	Reference		Reference	
Divorced/separated	1.05 (0.93–1.18)	.479	1.05 (0.93–1.19)	0.422
Windowed	1.47 (1.36–1.59)	< .001	1.24 (1.14–1.34)	< .001
Single	1.00 (0.88–1.13)	.947	1.05 (0.93–1.19)	0.426
Histological Type				
Transitional cell carcinoma	Reference		Reference	
Others	2.03 (1.83–2.26)	< .001	1.41 (1.27–1.59)	< .001
SEER stage				
Localized	Reference		Reference	
Regional	2.99 (2.66–3.36)	< .001	2.83 (2.51–3.19)	< .001
Distant	12.43 (10.98–14.07)	< .001	8.90 (7.77–10.20)	< .001
Unstaged	3.62 (3.05–4.29)	< .001	2.13 (1.78–2.55)	< .001
Grade				
Grade I	Reference		Reference	
Grade II	1.94 (1.40–2.68)	< .001	1.69 (1.22–2.34)	.001
Grade III	5.46 (4.02–7.43)	< .001	3.20 (2.34–4.36)	< .001
Grade IV	4.07 (2.99–5.54)	< .001	2.69 (1.97–3.68)	< .001
Unknown	6.75 (4.95–9.21)	< .001	2.58 (1.88–3.54)	< .001
Surgery				
No	Reference		Reference	
Yes	0.34 (0.32–0.37)	< .001	0.50 (0.45–0.55)	< .001

Abbreviations:

CSS, Cancer-specific survival; SEER, Surveillance, Epidemiology, and End Results.

Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.

[a]Model was adjusted by sex, age, primary site, marital status, histological type, grade, SEER stage and treatment pattern.

Characteristic	CSS			
	Univariate analysis		Multivariate analysis[a]	
Radiotherapy				
No	Reference		Reference	
Yes	2.37 (2.15–2.62)	< .001	1.44 (1.29–1.59)	< .001
Chemotherapy				
No	Reference		Reference	
Yes	1.50 (1.40–1.62)	< .001	0.77 (0.70–0.83)	< .001
Abbreviations:				
CSS, Cancer-specific survival; SEER, Surveillance, Epidemiology, and End Results.				
Grade I, Well differentiated; Grade II, Moderately differentiated; Grade III, Poorly differentiated; Grade IV, Undifferentiated.				
[a]Model was adjusted by sex, age, primary site, marital status, histological type, grade, SEER stage and treatment pattern.				

Prognostic nomograms for OS and CSS

Based on age at diagnosis, sex, marital status, race, origin, primary site, histological type, grade, SEER stage, surgery, radiotherapy and chemotherapy, we constructed 3-, 5- and 10-year OS and CSS prognostic nomogram for UTUC patients (Fig. 3). Each subtype of the variables on the nomogram corresponds to a point on the "Point" scale. By adding the scores associated with each variable and projecting the "Total point" to the lowest number, the probabilities of OS and CSS for 3-, 5-, and 10- years can be estimated.

The length of the line corresponding to each variable in the nomogram represents the influence of the predictive variable on the survival outcome. We found that, for the nomogram generated by all variables, age contributed the most to survival outcome in the OS nomogram, while SEER stage has the greatest contribution to the survival outcome in the nomogram of CSS.

Nomograms validation and calibration

Analysis of the time-dependent ROC curves across the entire cohort showed that the AUC of the nomogram used to predict OS and CSS based on all variables were 0.738 (95% CI = 0.729–0.746) and 0.689 (95% CI = 0.680–0.697), the C-index of the nomogram were 0.701 (95% CI = 0.695–0.707) and 0.729 (95% CI = 0.721–0.737), respectively (Fig. 4A, B). The result indicates that the model established by

the nomogram was quite accurate. In addition, DCA curves also shows better clinical utility of the nomogram (Fig. 4C, D). Moreover, we calibrated the 3-, 5- and 10-year OS and CSS nomogram of the entire cohort. The results show a good consistency between the prediction of the nomogram and the actual observation (Fig. 5).

Discussion

Although UTUC is a relatively rare solid tumor, accounting for 5–7% of all kidney tumors and 5–10% of all urothelial tumors.[13] However, 60% of UTUC were invasive at the time of diagnosis, 15–25% were associated with bladder tumor, 7% had metastasis, and the 5-year CSS rate was about 50–80%.[13, 14] Therefore, it is still very important to grasp the incidence trend of UTUC and build a model that can accurately predict the prognosis of UTUC patients.

In this about 30 years retrospective study, we first examined the incidence trend of UTUC. The results showed that the average age at onset of UTUC increased from 70.01 years in 1988 to 73.20 years in 2015. The mean age of onset of UTUC in female and ureter was higher than that in male and renal pelvis. Regarding the incidence of UTUC, we found that the incidence of UTUC decreased from 1.55/100,000 persons in 1988 to 1.52/100,000 persons (APC=-0.1). In the same period, the incidence of UTUC patients in male, 70 + years and renal pelvis were higher than those of female, < 60 years,60–69 years and ureter UTUC patients. Then, we constructed a reliable and accurate nomogram based on important clinical factors to predict OS and CSS in patients with UTUC.

Previous studies have also studied changes in the incidence of UTUC. Munoz et al.[15] assessed the changes in the incidence of UTUC from 1973 to 1996 with reference to the standardized to the 1980 United States census, and concluded that the incidence of ureteral tumors seemed to have increased slightly (0.69 to 0.73/100,000 person-years). Through the study of UTUC patients from 1973 to 2005, Raman et al.[16] found that the overall incidence of UTUC increased slowly (from 1.88 to 2.06 per 100,000 persons).

Our study found that the overall incidence of UTUC decreased slightly between 1988 and 2015, which may be due to in the article by Munoz et al used 1980 US standard population (21,526,796) as a standardized, while we used the 2000 US standard population (26,787,544) as a standardized, resulting in a lower overall incidence than Munoz et al. We speculate that the difference between our results and Raman et al due to the impact of different databases used.

Some studies have pointed out that the male-to-female ratio of UTUC is about 2:1, and the position of the renal pelvis is twice as common as that of the ureter.[17, 18] Our results are consistent with previous studies. In addition, we also found that in the same period, the incidence of patients over 70 years old was significantly higher than that of patients < 60 years and 60–69 years. The incidence of UTUC patients aged < 60 years (APC=-2.1, 95% CI: -2.3 to -1.9) and 60–69 years (APC=-1.4, 95% CI: -1.5 to -1.2) was decreasing, while the incidence of 70 + years patients was increasing (APC = 0.7, 95% CI: 0.6 to 0.8).

TNM staging and classification system is the basis of prognosis of patients with UTUC.[19] In this classification system, clinicians can determine the TNM stage according to the depth of tumor invasion (T), lymph node metastasis number (N) and distant metastasis (M), so that clinicians can make personalized treatment plans for patients and evaluate the prognosis of patients. How to better combine the tumor characteristics of patients with their own clinical factors, tailor-made patient risk assessment method has always been a challenge for clinicians.[20]

The nomogram is a visual tool for predicting prognosis based on multiple variables.[21] The model integrates a variety of prognostic factors and can make more preparations for evaluating the survival possibility of individual patients.[22] At present, many cancer nomograms have been developed and show a more accurate prediction of cancer prognosis than traditional TNM systems.[23] In addition, the line chart enables clinicians to include more prognostic factors in patients, assess patients' physical condition more intuitively, and specify personalized treatment plans. Therefore, the establishment of an effective and reliable map is of great significance to the prognosis of patients with UTUC and to provide them with personalized treatment.

The nomogram has been widely used in various malignant tumors of the urinary system.[24–26] Kattan et al. [27] constructed a nomogram that included pre-treatment serum prostate-specific antigen levels, biopsy Gleason scores and clinical stages, and found that it could predict the 5-year treatment failure probability with clinically localized prostate cancer who underwent radical prostatectomy. Similarly, Karakiewicz et al.[28] performed preoperative prediction of 726 patients treated with radical cystectomy and bilateral pelvic lymphadenectomy, and found that the multivariate nomogram was more accurate than the TUR T stage alone prediction.

At present, some studies have constructed the nomograms of UTUC prognosis.[29–31] Through the study of 227 patients underwent radical nephroureterectomy, Zeng et al.[30] found that the nomogram based on grade, stage, age, lymph node, bladder cancer concurrent, primary site, histological type and lymphovascular invasion can accurately predict the CSS of UTUC. Krabbe et al.[31] developed a prognostic nomogram composed of four variables: pT stage, pN stage, age and architecture, to predicted the relapse-free survival of patients with high grade UTUC after extirpative surgery. Zhang et al.[29] constructed a nomogram with stronger predictive power than the TNM staging system and SEER stage through 4,990 patients treated with surgery in the SEER database. The subjects of the above studies were UTUC patients who underwent surgery, and the researchers included fewer other prognostic variables. In our study, we developed a nomogram based on thirteen variables of age at diagnosis, sex, marital status, race, origin, primary site, histological type, grade, SEER stage, surgery, radiotherapy and chemotherapy, and showed better ability to predict the prognosis than the TNM stage nomogram. Using this nomogram, urologists can evaluate the prognostic survival of patients with UTUC, enabling personalized treatment and monitoring possible.

Our research still has some limitations. First, our study is a retrospective study with inevitable selection bias. Second, we cannot obtain detailed specific information about radiotherapy, chemotherapy and

information about the patient's physical condition and complications. Moreover, since 15–25% of UTUC patients were associated with bladder cancer, the data of this study did not consider simultaneous or heterochronous bladder cancer.

Conclusions

The incidence of UTUC has generally declined in the past 30 years, but it has increased in patients aged 70 + years. Moreover, the prognostic nomogram we established can provide a personalized risk assessment for the survival of UTUC patients.

Declarations

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Authors' contributions

WM, BX and MC studied the concept and design. WM, ZX and JL collected the data. WM, WC, QK and JW analyzed and interpreted the data. WM and ZX drafted the manuscript. BX and MC critically revised the manuscript for important intellectual content. WM and JL performed the statistical analysis.

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

We declare that there are no conflicts of interest between authors.

Consent for publication

This manuscript is approved by all authors for publication.

Research involving Human Participants and/or Animals

This article does not contain any studies with human participants or animals performed by any of the authors.

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Figures

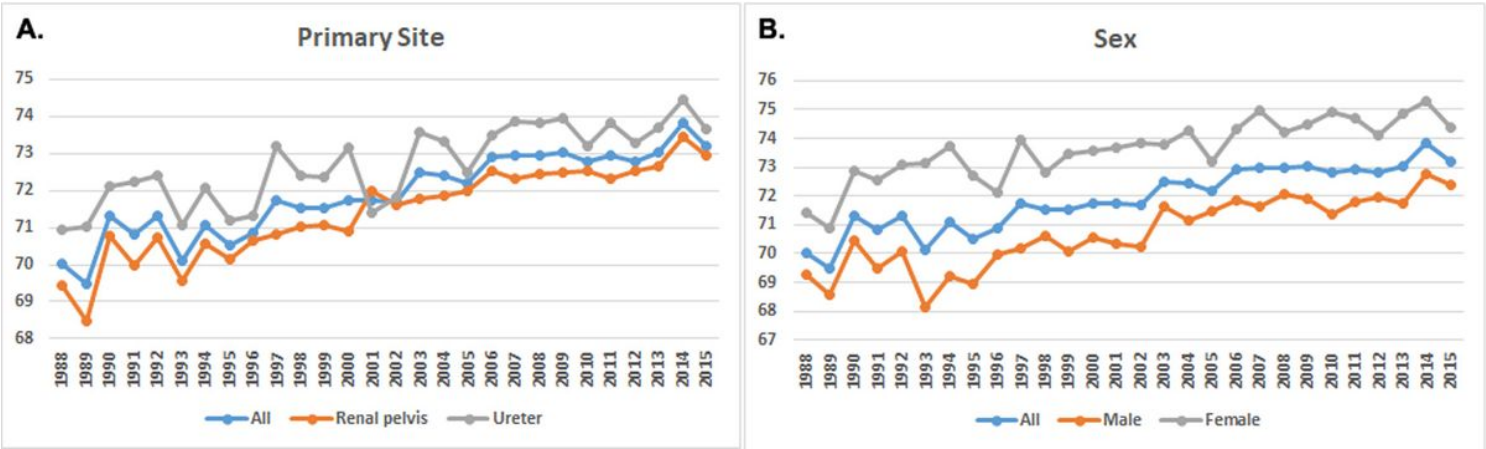

Figure 1

Change in average age at onset of UTUC patients from 1988 to 2015. A. Primary site; B. Sex.

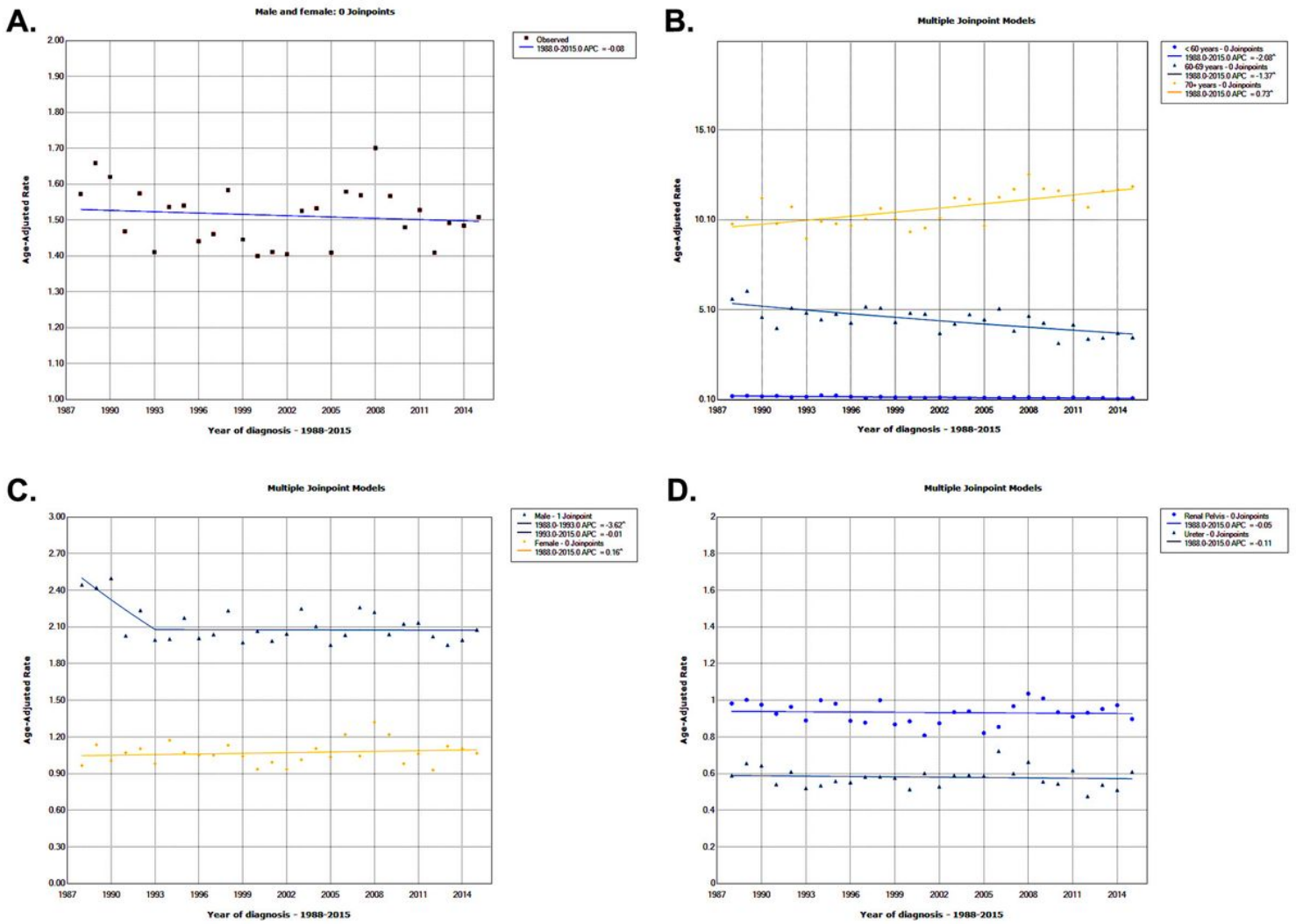

Figure 2

Change in the incidence of UTUC patients from 1988 to 2015. A. All patients; B. Grouped by age; C. Grouped by sex; D. Grouped by primary site.

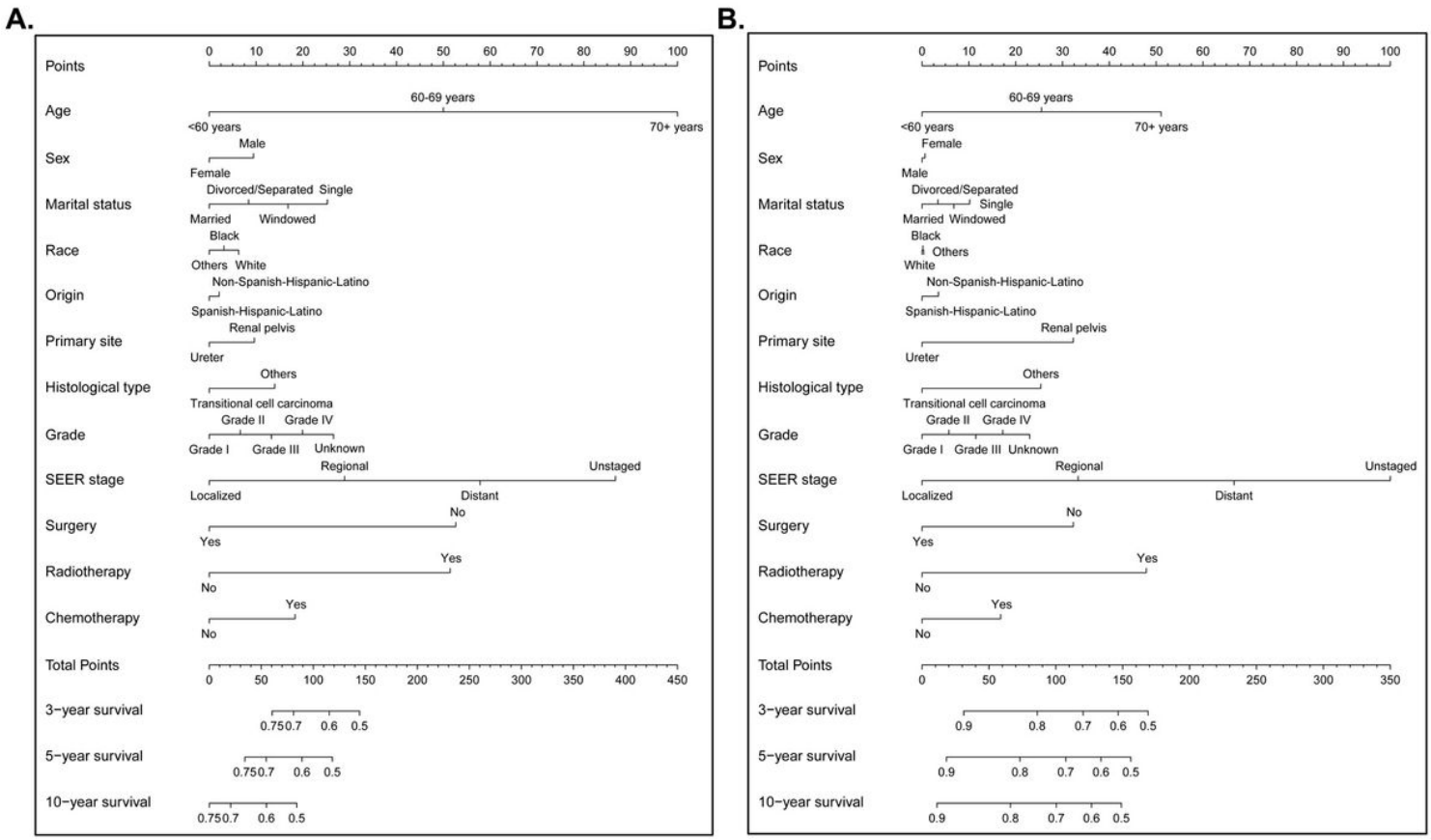

Figure 3

Nomogram predicting 3-, 5-, and 10-year overall survival (OS) and cancer-specific survival (CSS) rate of UTUC patients. A. OS rate; B. CSS rate.

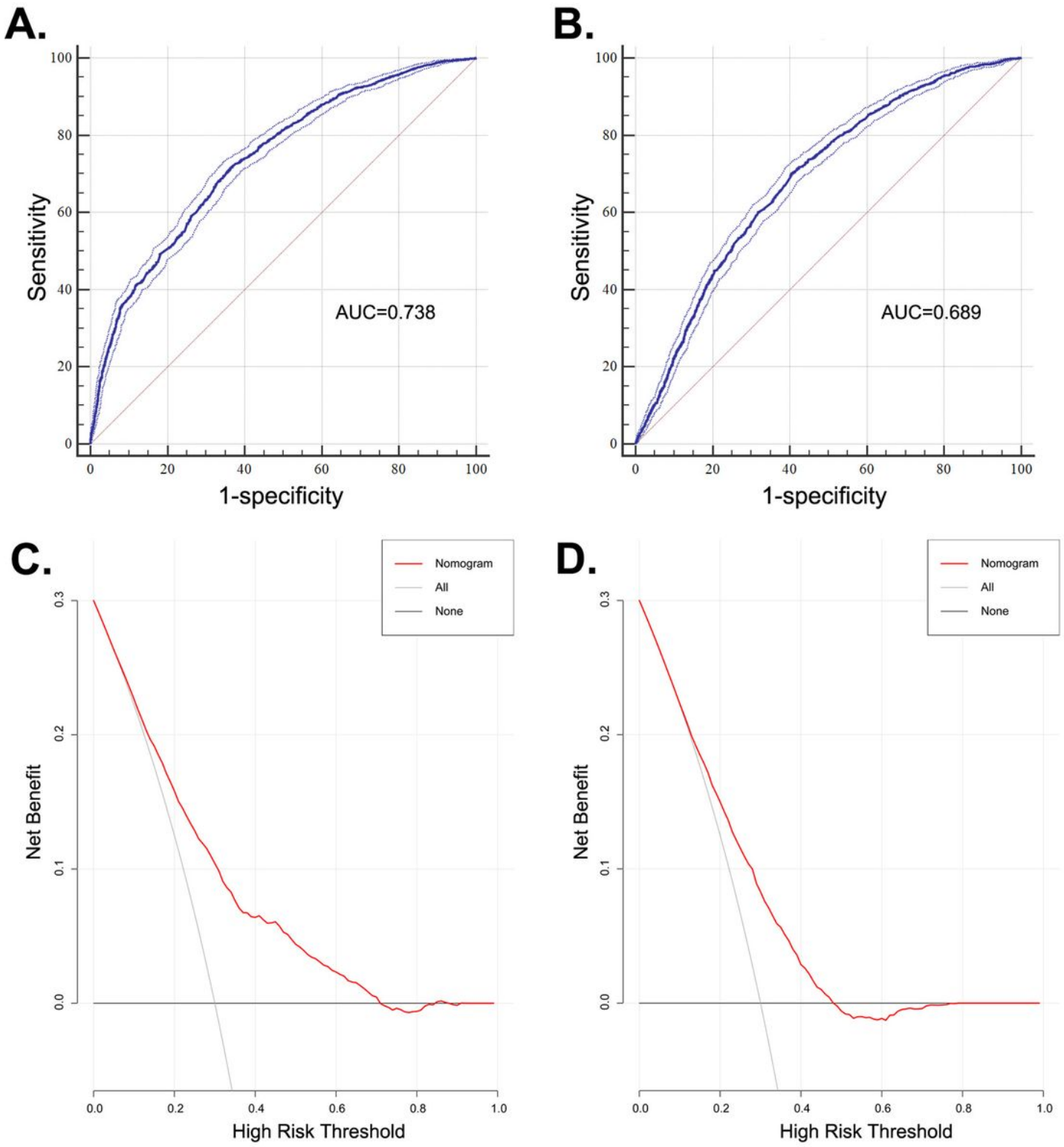

Figure 4

Receiver operating characteristic (ROC) curves and decision curve analysis (DCA) curves detects the predictive value of the nomograms in UTUC prognosis. A. ROC curve for Overall survival (OS). B. ROC curve for Cancer-specific survival (CSS); C. DCA curve for Overall survival (OS). D. DCA curve for Cancer-specific survival (CSS)

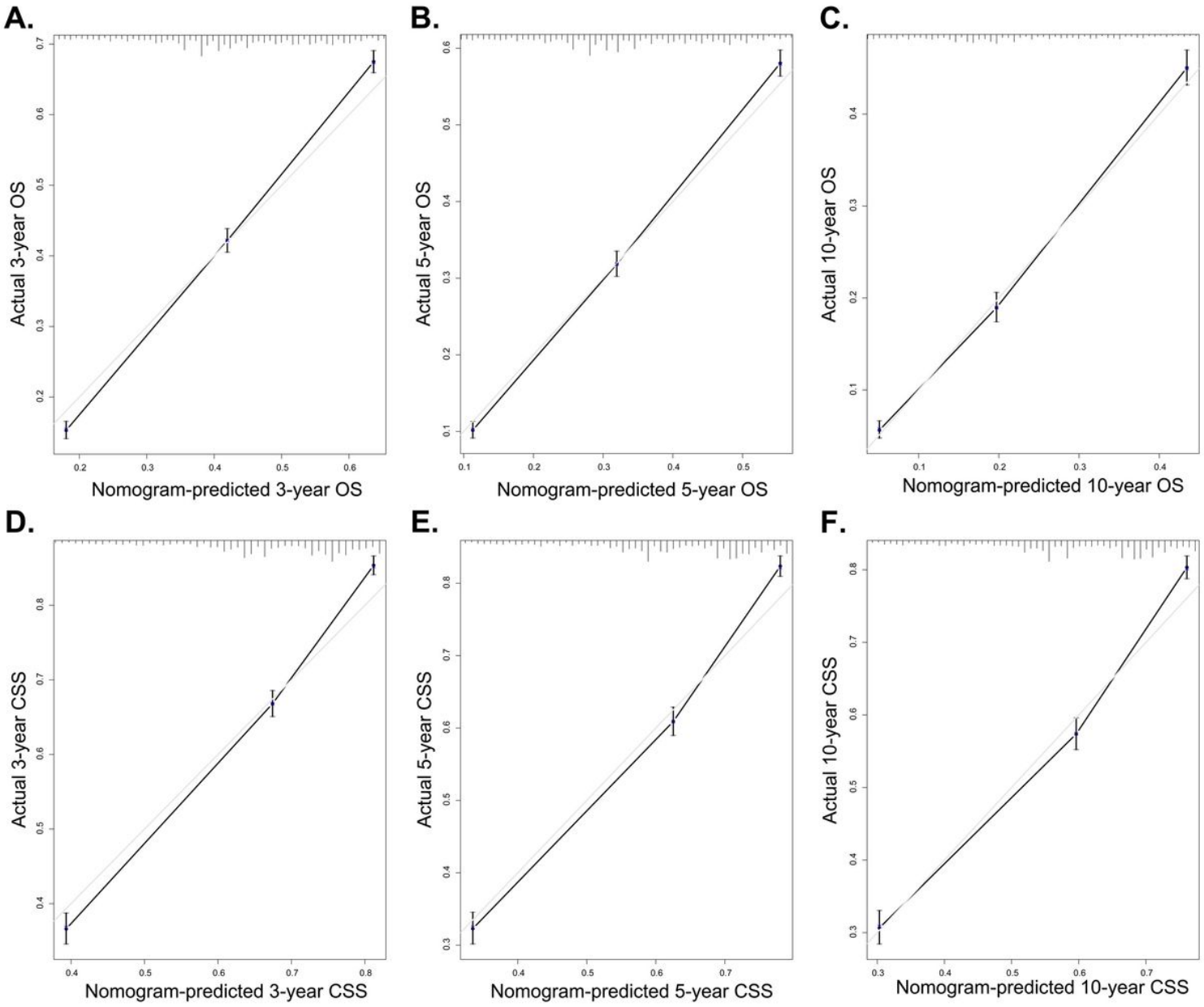

Figure 5

Calibration plot of the nomogram for predicting 3-, 5-, and 10-year overall survival (OS) and cancer-specific survival (CSS). A. 3-year OS; B. 5-year OS; C. 10-year OS; D. 3-year CSS; E. 5-year CSS; F. 10-year CSS.

Supplementary Files

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