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Geriatric Nutritional Risk Index as a prognostic marker for predicting survival outcomes in patients with UTUC after radical nephroureterectomy

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The purpose of this study was to determine the prognostic value of the Geriatric Nutritional Risk Index (GNRI) in patients with upper tract urothelial carcinoma (UTUC) after radical nephrectomy (RNU). A retrospective study of UTUC patients was conducted at West China Hospital between May 2016 and June 2019. The optimal cut-off point for GNRI was determined using the X-Tile procedure. Univariate and multivariate analyses were performed to identify predictors, and two- and four-year cancer-specific survival (CSS) prediction nomograms were created based on the results of the multivariate analyses. Furthermore, time-dependent ROC curve, calibration curve and decision curve analyses were conducted. A total of 219 patients with UTUC following RNU were identified and subsequently divided into three groups based on the critical values of GNRI (91.2, 98.8). GNRI was identified as a significant risk factor for CSS, with patients exhibiting higher GNRI demonstrating elevated CSS (hazard ratio = 0.58; 95% confidence interval, 0.32–0.92; P = 0.037). Furthermore, the GNRI-based nomogram demonstrated high predictive capacity for CSS, with areas under the curve of 0.810 and 0.842 for 2- and 4-year CSS, respectively. Preoperative GNRI is an independent predictor for CSS in UTUC patients who underwent RNU and should be considered as a promising personalized tool for clinical decision-making.

Keywords Geriatric nutritional risk index, Upper tract urothelial carcinoma, Prognosis, Nomogram

Abbreviations

UTUC	Upper tract urothelial carcinoma
RNU	Radical nephroureterectomy
CSS	Cancer-specific survival
CSM	Cancer-specific mortality
ROC	Receiver operating characteristic
DCA	Decision curve analyses
GNRI	Geriatric nutritional risk index
LVI	Lymphovascular invasion
EAU	European Association of Urology
CT	Computed tomography
IQRs	Interquartile ranges
HRs	Hazard ratios
CIs	Confidence intervals

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Upper tract urothelial carcinoma (UTUC), accounting for merely 5%-10% of urothelial carcinomas, originates from the renal pelvis and ureter, with an estimated incidence rate of approximately 2 per million annually[1]. Despite significant advancements in our understanding of UTUC risks, progression, and particularly the therapeutic modalities encompassing surgery, radiochemotherapy, and immunotherapy, UTUC remains a formidable neoplasm with unsatisfactory long-term prognoses[1–3]. Consequently, the identification of an accessible prognostic predictor with substantial accuracy for personalized and precise clinical treatment is both urgent and indispensable.

The current standard intervention for UTUC is radical nephroureterectomy (RNU)[1]. Post-RNU, multimodal treatment strategies, including optimal nutritional interventions, are pivotal for enhancing patient outcomes. Intriguingly, recent studies have indicated that nutrition and diet can influence the outcomes of cancer patients[4–6]. Therefore, recognizing patients at risk of malnutrition plays a critical role in the post-RNU management of UTUC patients. Malnutrition may stem directly from the primary tumor or as a side effect of treatments, particularly radiotherapy and chemotherapy[6,7]. These conditions can severely impact daily energy intake and are associated with increased mortality and morbidity. Given that a significant portion of UTUC patients require dietary supplementation and enteral feeding during treatment, managing their nutrition is an integral component of therapy. Beyond conventional clinicopathological variables, the newly emerged Geriatric Nutritional Risk Index (GNRI) has proven to be an effective and independent factor in cancer patients' tumor prognoses[8–10]. The GNRI, based on weight, height, and serum albumin levels, is readily assessable and implementable in routine clinical practice, recommended as a promising prognostic predictor for cancer patients. It has been widely used to assess the risk of malnutrition in hospitalized adults over 65 years of age or in those younger[8–10].

To our knowledge, the prognostic utility of GNRI in UTUC patients post-RNU has not been investigated with a nomogram centered around GNRI as the principal factor. Thus, this study aims to ascertain the prognostic value of GNRI in UTUC patients undergoing RNU and to establish a nomogram utilizing GNRI for survival prediction.

Methods and materials

Patients and data

The study was approved by the Ethics Committee of West China Hospital, Chengdu, China (2021–1209). Due to the retrospective design, anonymous data, and confidential information of included patients, the local institutional review board granted a waiver of informed consent for the study. All methods were performed in accordance with the relevant guidelines and regulations and all research participants have been performed in accordance with the Declaration of Helsinki. The initial cohort comprised 289 UTUC patients who had undergone RNU between May 2016 and June 2019. Patients with incomplete long-term prognostic information, patients without records of serum albumin or weight and height, patients who underwent neoadjuvant therapy, and patients with pathologically confirmed non-urothelial carcinoma were excluded from the present study. The final cohort consisted of 219 patients, who were included for further analysis.

The clinicopathological data were collected from the medical records, including the chronological age in the year of surgery, gender, weight and height, and albumin within two weeks before RNU. Additionally, the tumour characteristics were recorded, including tumour location, tumour stage, tumour grade, tumour size, tumor necrosis, lymph node metastasis, lymphovascular invasion (LVI), hydronephrosis, surgical margin, and smoking.

The specimens obtained by RNU were subjected to independent review by our professional genitourinary pathologists. Subsequently, the histopathological staging was conducted in accordance with the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system, while the histopathologic grading was performed in alignment with the WHO/ISUP recommendation grading system. The diagnosis of variant histology has been widely accepted by the urological pathological community and numerous experts. The diagnostic criteria are outlined in the WHO classification of tumors.

Follow-up and outcomes

The follow-up period commenced at two to three weeks post-RNU, coinciding with the delivery of the final pathology report. The initial follow-up was designed to examine the characteristics of the primary tumor and inform the development of subsequent therapeutic plans. In general, the follow-up protocol was in accordance with the guidelines set forth by the European Association of Urology (EAU)[1]. The follow-up interval was initially every three months for the first year, then every six months for the second year, and subsequently annually, provided that no signs of recurrence or unusual symptoms were observed. The routine content of the follow-up procedure included a physical examination, laboratory tests (including blood and urine analysis), a contrast-enhanced computed tomography (CT) scan of the chest and abdomen, and cystoscopy.

The endpoints of interest were CSS and the corresponding events, namely cancer-specific mortality (CSM). CSS was defined as the period between RNU and death from urothelial transitional cell carcinoma of the UTUC.

GNRI

The nutritional status was calculated according to the following formula: The GNRI is calculated using the following formula: GNRI = 1.489 × serum albumin level (g/L) + 41.7 × (actual body weight [kg]/ideal body weight [kg]). The ideal body weight was calculated as follows: [height (m)]^2 × 22 (kg/m^2). In instances where the subject's actual body weight exceeded their ideal body weight, the value of the actual body weight divided by the ideal body weight was set to 1.

The optimal cut point for the GNRI was identified using the X-Tile 3.6.1 software (Yale University)[11] based on the lowest P values and the maximum chi-square of log-rank tests.

Statistical analysis

The data were analysed using the statistical software R (available at http://www.r-projiect.org; version 4.1.3) and Empower (available at http://www.empowerstats.com, X&Y Solutions). Continuous variables were found to conform to a normal distribution, as described by the mean plus or minus the standard deviation. Categorical variables were described based on numbers and percentages. To ascertain significant differences in clinicopathological characteristics, Student's t-test or the Mann–Whitney U test was employed, as was the chi-square or Fisher's exact test.

The CSS was calculated using the Kaplan–Meier method and compared using the log-rank test. Cox proportional hazard regression models were employed to ascertain the prognostic value of GNRI on CSM in UTUC patients following RNU. Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to evaluate the risk of cancer-specific death. All variables with a P value of less than 0.1 in the univariate Cox regression were included in the multivariate Cox regression for further analysis. Moreover, predictors with P values less than 0.05 in multivariate analyses were employed to construct a nomogram for the prediction of cancer-specific survival at two-year and four-year intervals. The performance of the nomogram was evaluated using time-dependent ROC curves, calibration curves, and decision curve analysis (DCA). All results were deemed statistically significant with a two-sided P-value of less than 0.05.

Results

Baseline characteristic

A total of 219 UTUC participants who had undergone RNU were enrolled in this study, with a median age of 67.7 years and a male-to-female ratio of 115:104. Subsequently, the optimal cut-off value for GNRI was identified through the utilisation of the X-Tile 3.6.1 software, which employed the lowest P values and the maximum chi-square of log-rank tests as the determining factors. The resulting optimal cut-off values were established as 91.2 and 98.8 (Supplementary Fig. 1). Consequently, 32 patients (14.61%) were classified as belonging to the low-GNRI group, 50 patients (22.83%) were assigned to the medium-GNRI group, and the remaining 137 patients (62.56%) were categorised as high-GNRI. Significant differences were observed between the low-GNRI and high-GNRI groups in terms of albumin levels, age, weight, GNRI, and tumour characteristics (stage, grade, size, hydronephrosis). Further details are provided in Table 1.

Kaplan–Meier analysis and Cox analysis

Kaplan–Meier plots indicated that, in comparison to patients in the low-GNRI group, patients in the high-GNRI group exhibited a significantly poorer CSS (P = 0.024) (Fig. 1). Subsequently, univariable and multivariable analyses were conducted to ascertain predictors of CSS in UTUC patients following RNU. In order to include as many clinical indicators as possible, all variables with a P value of less than 0.100 in the univariate Cox regression were included in the multivariate Cox regression. The results demonstrated that GNRI (HR: 0.58, 95% CI 0.32–0.92, P = 0.037), tumour location (HR: 12.33, 95% CI 4.71–32.29, P < 0.001), tumour stage (HR: 2.57, 95% CI 1.48–4.46. These findings were statistically significant (P < 0.001), as were those pertaining to tumour grade (HR: 4.46, 95% CI 1.72–11.54, P = 0.002) and surgical margin status (HR: 2.13, 95% CI 1.01–4.48, P = 0.047). These factors were identified as independent predictors of CSS (Table 2).

Nomogram construction and validation

The results of the multivariate Cox analysis indicated that five variables should be included in the nomogram. The GNRI, tumour location, tumour grade, tumour stage and surgical margin were identified as predictors of the two-year and four-year CSS (Fig. 2). The calibration curves demonstrated a high degree of consistency between the predicted and observed survival probabilities, indicating reliable reproducibility (Fig. 3A). Furthermore, time-dependent ROC curves were employed to assess the predictive accuracy of the nomograms. The results demonstrated that the nomograms exhibited robust performance in predicting CSS, with AUCs of 0.810 (0.746–0.874) and 0.842 (0.766–0.918) for 2-year CSS and 4-year CSS, respectively (Fig. 3B). Furthermore, the decision curve analysis (DCA) curves demonstrated that the nomogram was more effective than the conventional models comprising tumour location, tumour grade, and tumour stage in predicting 2-year and 4-year cancer-specific survival (CSS) (Fig. 4a and b).

Discussion

In this study, we conducted a retrospective analysis of 219 upper tract urothelial carcinoma (UTUC) patients who underwent radical nephroureterectomy (RNU) in Southwest China. Our findings demonstrate the significant prognostic utility of the Geriatric Nutritional Risk Index (GNRI) in predicting cancer-specific survival (CSS) among UTUC patients. Multivariate analysis identified the GNRI as an independent prognostic determinant for CSS, with lower preoperative GNRI values being significantly associated with poorer outcomes. Additionally, we developed and validated a nomogram that integrates the GNRI with four other clinicopathological variables to predict 2-year and 4-year CSS.

In an effort to improve the prognosis of UTUC patients, numerous studies over the past decade have sought to identify reliable predictors that stratify patients by risk, thereby facilitating personalized treatment approaches[12,13]. The GNRI, which combines preoperative height, weight, and serum albumin levels, offers a comprehensive reflection of an individual's nutritional status. Low serum albumin, a surrogate marker for sarcopenia, has been consistently linked to adverse oncologic outcomes. For instance, a systematic review by Gupta et al. in 2010 underscored the prognostic value of pretreatment serum albumin levels in various malignancies, including gastrointestinal, lung, and bladder cancers[14]. The association between hypoalbuminemia and poorer cancer outcomes may be attributed to its role as an indicator of a systemic inflammatory response

Variables	Total patients (n = 219)	GNRI categorical			P value
		≤ 91.2 (n = 32)	> 91.2, ≤ 98.8 (n = 50)	> 98.8 (n = 137)	
Age (year)	67.70 ± 10.17	70.22 ± 8.70	69.96 ± 9.21	66.29 ± 10.62	0.029
Albumin	39.58 ± 5.85	30.50 ± 6.64	37.27 ± 3.42	42.54 ± 3.23	< 0.001
Height (cm)	160.82 ± 7.09	158.66 ± 7.61	160.66 ± 7.94	161.39 ± 6.57	0.143
Weight (kg)	59.72 ± 9.89	50.74 ± 6.70	55.17 ± 9.23	63.48 ± 8.65	< 0.001
GNRI	102.10 ± 11.44	83.14 ± 8.92	95.36 ± 2.41	108.99 ± 6.37	< 0.001
Age categorical, n (%)					0.081
< 65	74 (33.79%)	6 (18.75%)	15 (30.00%)	53 (38.69%)	
≥ 65	145 (66.21%)	26 (81.25%)	35 (70.00%)	84 (61.31%)	
Gender, n (%)					0.942
Male	115 (52.51%)	16 (50.00%)	26 (52.00%)	73 (53.28%)	
Female	104 (47.49%)	16 (50.00%)	24 (48.00%)	64 (46.72%)	
Tumor location, n (%)					0.100
Ureter	168 (76.71%)	21 (65.62%)	45 (90.00%)	102 (74.45%)	
Renal pelvis	45 (20.55%)	10 (31.25%)	4 (8.00%)	31 (22.63%)	
Both	6 (2.74%)	1 (3.12%)	1 (2.00%)	4 (2.92%)	
Tumor stage, n (%)					0.008
pT1	80 (36.87%)	4 (12.50%)	21 (42.86%)	55 (40.44%)	
pT2	38 (17.51%)	7 (21.88%)	5 (10.20%)	26 (19.12%)	
pT3	74 (34.10%)	17 (53.12%)	13 (26.53%)	44 (32.35%)	
pT4	25 (11.52%)	4 (12.50%)	10 (20.41%)	11 (8.09%)	
Tumor grade, n (%)					0.047
Low	57 (26.39%)	3 (9.38%)	16 (33.33%)	38 (27.94%)	
High	159 (73.61%)	29 (90.62%)	32 (66.67%)	98 (72.06%)	
Tumor size(cm), n (%)					0.041
< 3	71 (32.72%)	12 (37.50%)	9 (18.00%)	50 (37.04%)	
≥ 3	146 (67.28%)	20 (62.50%)	41 (82.00%)	85 (62.96%)	
Tumor necrosis, n (%)					0.456
No	208 (94.98%)	30 (93.75%)	46 (92.00%)	132 (96.35%)	
Yes	11 (5.02%)	2 (6.25%)	4 (8.00%)	5 (3.65%)	
Lymph node metastasis, n (%)					0.600
No	16 (7.37%)	4 (12.50%)	2 (4.00%)	10 (7.41%)	
Yes	15 (6.91%)	1 (3.12%)	4 (8.00%)	10 (7.41%)	
Unidentified	186 (85.71%)	27 (84.38%)	44 (88.00%)	115 (85.19%)	
Lymphovascular invasion, n (%)					0.948
No	194 (89.40%)	29 (90.62%)	45 (90.00%)	120 (88.89%)	
Yes	23 (10.60%)	3 (9.38%)	5 (10.00%)	15 (11.11%)	
Hydronephrosis, n (%)					0.001
No	83 (38.25%)	3 (9.38%)	20 (40.82%)	60 (44.12%)	
Yes	134 (61.75%)	29 (90.62%)	29 (59.18%)	76 (55.88%)	
Surgery margin, n (%)					0.407
Negative	201 (93.06%)	28 (87.50%)	46 (93.88%)	127 (94.07%)	
Positive	15 (6.94%)	4 (12.50%)	3 (6.12%)	8 (5.93%)	
Smoking, n (%)					0.346
No	156 (71.89%)	22 (68.75%)	40 (80.00%)	94 (69.63%)	
Yes	61 (28.11%)	10 (31.25%)	10 (20.00%)	41 (30.37%)	

Table 1. The clinical and pathological characteristics of patients. GNRI: geriatric nutritional risk index.

leading to protein catabolism[15,16]. However, fluctuations in serum albumin due to hydration status and its relatively long half-life limit its effectiveness as a standalone predictor[17]. Consequently, composite indices that integrate albumin with other parameters, such as complete blood count metrics (hemoglobin, lymphocytes, and platelets)[18], fibrinogen[19], and inflammatory markers (CRP and neutrophils)[20], have garnered increased attention for their enhanced prognostic value in clinical practice.

Our study further reinforces the promise of the GNRI as a robust marker for nutritional assessment and prognostic prediction. We demonstrated a significant association between preoperative GNRI values and patient outcomes, underscoring its reliability as a prognostic biomarker in UTUC patients post-RNU. These findings

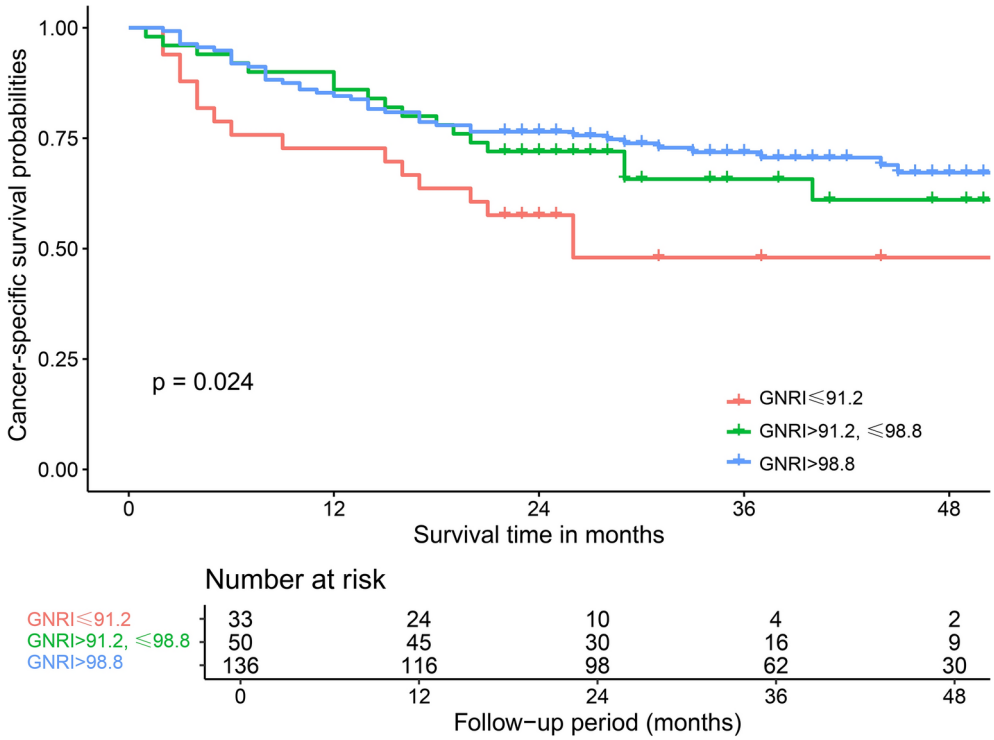

Fig. 1. Kaplan–Meier curves for cancer-specific survival stratified by GNRI.

align with previous research that has highlighted the prognostic significance of the GNRI across diverse clinical settings, including localized cancer[21], metastatic disease[22], and in the context of chemoradiotherapy[23]. For example, Hayama et al. retrospectively evaluated 259 patients with stage I–III colorectal cancer who underwent curative resection and reported that lower preoperative GNRI values were significantly associated with reduced overall and recurrence-free survival[21]. Similarly, Zeynep et al. demonstrated in a cohort of 185 patients with metastatic colorectal cancer that the GNRI not only correlated with CT-diagnosed sarcopenia but also served as a practical predictor of oncologic outcomes[22]. Moreover, Hass et al. found that among 162 patients with recurrent or metastatic head and neck cancer receiving immune checkpoint inhibitors, a lower GNRI (≤ 98) was significantly linked to poorer disease control[24]. Beyond oncology, the GNRI has been applied in prognostic evaluations for conditions such as heart failure[25], uremia[26], and stroke-associated pneumonia[27]. Nonetheless, as the current evidence is predominantly based on retrospective studies, well-designed prospective trials are needed to further validate the prognostic relevance of the GNRI. An important question for clinicians is whether targeted nutritional interventions, such as preoperative albumin supplementation in hypoproteinemic patients, can improve outcomes, a topic that merits additional investigation.

We also constructed a nomogram incorporating the GNRI alongside four other clinicopathological factors that reached statistical significance ($P < 0.05$) in the multivariate Cox regression for 2-year and 4-year CSS prediction. Calibration curves and time-dependent receiver operating characteristic (ROC) analyses confirmed the promising performance of this model. In contrast to previously established nomograms for UTUC, which have primarily relied on demographic and pathological features without considering nutritional status[28–30], the inclusion of the GNRI may enhance predictive accuracy. For example, a systematic review by Pallauf et al. highlighted nomograms based on pathological tumor stage, age, and lymphovascular invasion (LVI) that demonstrated excellent discriminative ability for CSS prediction[31]. However, as personalized treatment strategies evolve, these parameters alone may not suffice for accurate individual prognostication. Thus, our nomogram, which integrates a measure of nutritional status, could offer superior clinical utility. Nonetheless, the absence of external validation limits the generalizability of our findings, and further studies are required to confirm its applicability in diverse clinical settings. Importantly, our analysis reaffirms the prognostic significance of the GNRI and lays the groundwork for future predictive modeling in UTUC.

The results of our study should be interpreted in the context of several limitations. First, the retrospective, single-center design may introduce inherent biases, including data homogeneity, a limited sample size, and the lack of detailed information on patient comorbidities. Second, the cutoff values for the GNRI (91.2 and 98), determined using X-Tile 3.6.1 software (Yale University), might not be directly transferable to other populations given the variability observed across studies with different tumor types and geographic regions. Third, the lack of external validation constrains the clinical applicability of our nomogram, and the tangible benefits of employing such models in patient management remain to be elucidated. Finally, our analysis focused solely on the prognostic value of the GNRI without incorporating other established biomarkers, such as the systemic

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value
Age (year)				
< 65	Reference		Not included	
≥ 65	1.00 (0.98, 1.03)	0.667		
Gender				
Male	Reference		Not included	
Female	1.40 (0.88, 2.20)	0.154		
GNRI				
≤ 91.2	Reference		Reference	
> 91.2, ≤ 98.8	0.54 (0.27, 1.08)	0.082	0.66 (0.31, 1.38)	0.266
> 98.8	0.45 (0.25, 0.81)	0.008	0.58 (0.32, 0.92)	0.037
Tumor location				
Ureter	Reference		Reference	
Renal pelvis	2.06 (1.24, 3.41)	0.005	1.73 (1.00, 2.98)	0.048
Both	5.41 (2.30, 12.72)	< 0.001	12.33 (4.71, 32.29)	< 0.001
Tumor stage				
≤ pT2	Reference		Reference	
> pT2	4.26 (2.56, 7.10)	< 0.001	2.57 (1.48, 4.46)	< 0.001
Tumor grade				
Low	Reference		Reference	
High	5.18 (2.24, 11.95)	< 0.001	4.46 (1.72, 11.54)	0.002
Tumor size (cm)				
< 3	Reference		Reference	
≥ 3	1.82 (1.06, 3.13)	0.030	1.58 (0.90, 2.79)	0.112
Tumor necrosis				
No	Reference		Not included	
Yes	0.47 (0.11, 1.90)	0.286		
Lymph node metastasis				
No	Reference		Reference	
Yes	2.94 (1.08, 7.97)	0.034	2.23 (0.79, 6.25)	0.128
Unidentified	0.78 (0.33, 1.80)	0.556	1.36 (0.56, 3.31)	0.498
Lymphovascular invasion				
No	Reference		Reference	
Yes	2.32 (1.27, 4.24)	0.006	1.43 (0.77, 2.65)	0.260
Hydronephrosis				
No	Reference		Not included	
Yes	0.99 (0.62, 1.58)	0.966		
Surgery margin				
Negative	Reference		Reference	
Positive	2.86 (1.42, 5.79)	0.003	2.13 (1.01, 4.48)	0.047
Smoking				
No	Reference		Not included	
Yes	0.86 (0.51, 1.45)	0.577		

Table 2. Univariate and multivariate Cox proportional hazards regression analyses of variables associated with cancer-specific survival. [a]The results of univariate and multivariate analysis. Variables included in the multivariate analysis were extracted from variables with P value of less than 0.1 in univariate analysis. [b]HR: hazard ratio, CI: confidence interval, GNRI: geriatric nutritional risk index, UTUC: upper tract urothelial carcinoma.

immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), lymphocyte–monocyte ratio (LMR), and prognostic nutritional index (PNI). We are currently undertaking further studies to address these limitations.

Conclusion

Preoperative GNRI, composed of preoperative height weight, and albumin level, is an independent predictor for CSS in UTUC patients who underwent RNU. In addition, the nomogram based on the GNRI is a promising

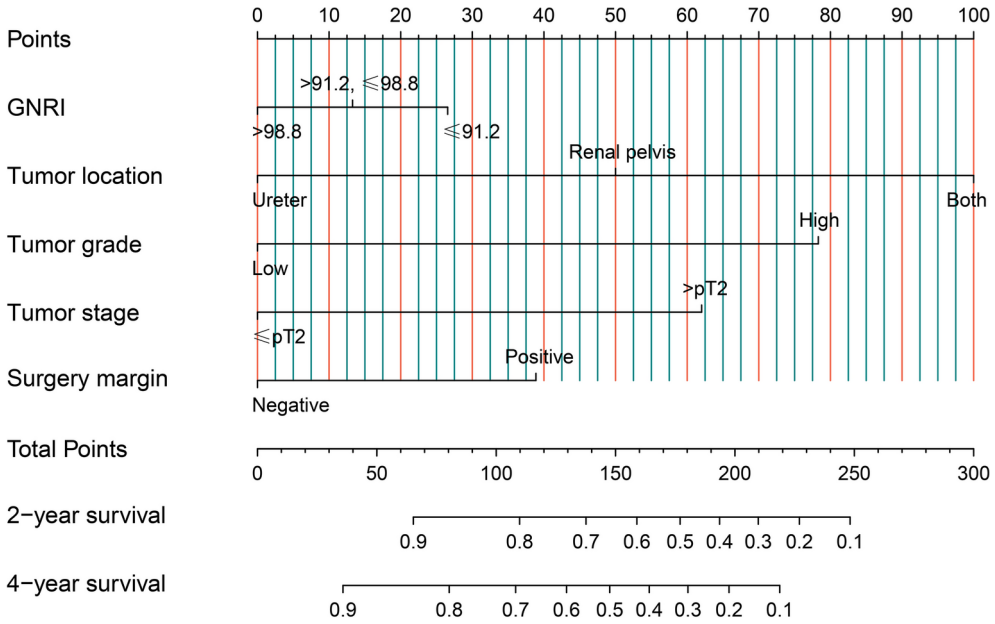

Fig. 2. A nomogram for predicting 2-year or 4-year cancer-specific survival.

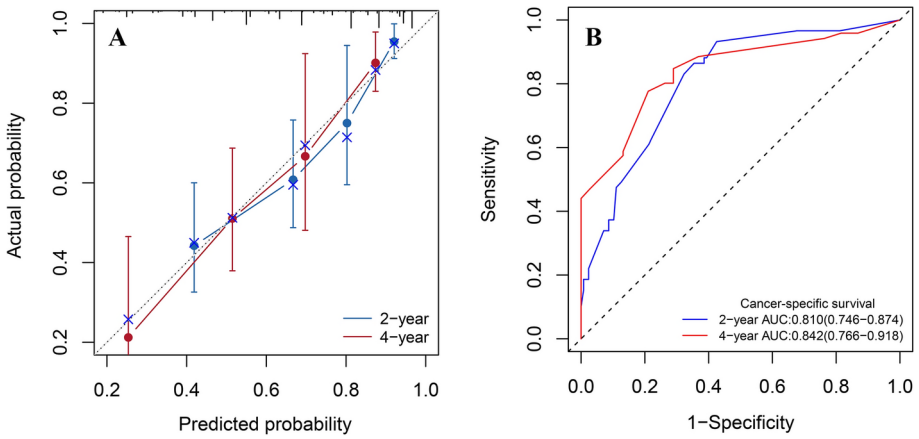

Fig. 3. Calibration curves of 2-year and 4-year cancer-specific survival (**A**) and ROC curve for assessing the calibration and discrimination of the nomogram in predicting 3-year or 5-year cancer-specific survival (**B**).

personalization tool to provide reliable prognostic information for achieving the greatest survival benefits in UTUC patients, but further external validation is needed.

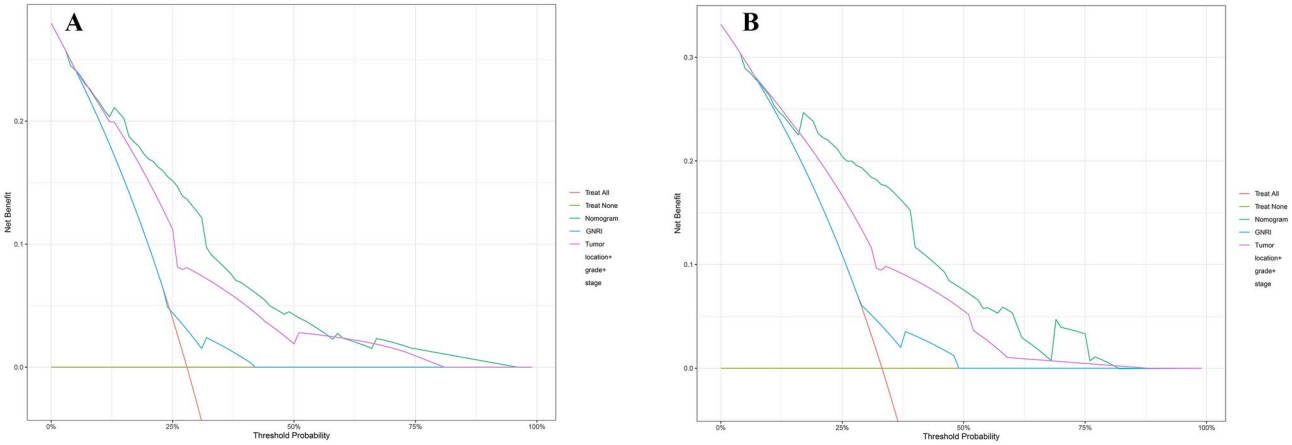

Fig. 4. Decision curve analysis of the nomogram about 2-year cancer-specific survival benefit (**a**) and 4-year cancer-specific survival benefit (**b**).

Data availability

The data that support the findings of this study are available upon request from the corresponding author, upon reasonable request.

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Declarations

Ethical statement

All methods were performed in accordance with the relevant guidelines and regulations and all research participants have been performed in accordance with the Declaration of Helsinki.

Consent for publication

All authors have approved the manuscript and agree with the submission to your journal.

Competing interests

The authors declare no competing interests.

Additional information

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