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A nomogram for predicting cancer-specific survival in patients with non-metastatic primary renal cell carcinoma

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Abstract

Objectives: Renal cell carcinoma (RCC) is a common malignancy and has been on the rise in recent years. This study aimed to develop a nomogram prognostic model of cancer-specific survival (CSS) in patients with non-metastatic primary renal cell carcinoma (nmRCC). Patients and Methods: Patients diagnosed with Renal carcinoma (RC) from 2010 to 2015 were downloaded from the Surveillance, Epidemiology, and End Results (SEER) database. Patients were identified according to the inclusion and exclusion criteria and then randomly assigned to the training group (70%) and the validation group (30%). Univariate and multifactorial Cox regression analyses were used to identify significant independent prognostic factors in the training cohort of patients. Based on these independent factors, a nomogram was then constructed to predict 1-, 3-, and 5-year CSS in nmRCC primary patients. Nomogram was analyzed performance by concordance index (C-index), calibration curve, receiver operating characteristic curves (ROC), net reclassification improvement (NRI), integrated discriminant improvement (IDI), and decision curve analysis (DCA) was used to validate the clinical application value of the model. We compared the nomogram with the AJCC staging system. A risk stratification system was constructed and then validated by Kaplan-Meier survival analysis. Results: A total of 26372 patients participated in this study. These patients were randomly divided into a training set (N=18460) and a validation set (N=7912). Univariate and multivariate Cox regression analyses in the training set showed that age, marriage, tumor histology, AJCC, tumor size, tumor histological grade, surgical approach, radiotherapy, and chemotherapy were independent predictor factors. The C-index was 0.833 and 0.836 for the training set and validation set, respectively. In the training set, the AUC of the nomogram at 1-, 3-, and 5 years were 0.858, 0.872, 0.855, and the AUC of the AJCC staging system at 1-, 3-, and 5 years were 0.758, 0.770, 0.750, respectively. In the validation set, the AUC of the nomogram at 1-, 3-, and 5 years were 0.860, 0.861, 0.832, and the AUC of the AJCC staging system at 1-, 3-, and 5 years were 0.778, 0.768, 0.758, respectively. The calibration curves of the training and validation sets indicated that the model had good accuracy. The NRI and IDI results showed that the nomogram prediction ability is greatly improved compared with the traditional AJCC model. And the DCA also suggests that the model has potential clinical application. The risk stratification system can clearly distinguish patients with different survival risks. Conclusion: We developed the nomogram prediction model to predict CSS of nmRCC patients at 1-, 3-, and 5 years. The model has good accuracy and discriminatory ability, which can help physicians and patients in clinical decision-making and active monitoring of risk factors.

Keywords

Nomogram, nonmetastatic renal cell carcinoma, cancer-specific survival, SEER.

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1. Introduction

Renal cell carcinoma (RCC) is the most common type of renal malignancy in adults, accounting for 2-3% of adult malignancies[1]. The major cell subtypes of RCC are clear renal cell carcinoma (CCRCC), chromophobe renal cell carcinoma (CHRCC), and papillary renal cell carcinoma (PRCC)[2].

The incidence of RCC is increasing, and according to the American Cancer Society (ACS) 2023 cancer statistics, there will be 1,958,310 new cancer cases and 609,820 cancer deaths in the United States in that year [3]. The incidence of kidney cancer is increasing at a rate of approximately 1% per year. The incidence of kidney cancer is on a continuously increasing trend in many countries worldwide[4]. Studies have found a positive correlation between kidney cancer mortality and the economic level of national development[5]. Renal cell carcinoma is classified into metastatic renal cell carcinoma (mRCC) or non-metastatic renal cell carcinoma (nmRCC) according to whether the tumor is metastatic or not. NmRCC has a good prognosis, and a comprehensive treatment approach based on surgery is advocated for localized RCC [6]. NmRCC is considered to have the possibility of a complete cure[7]. 20-30% of patients with limited RCC will still recur after surgery[8].

The prognosis of patients with malignancy at this stage is mostly based on the American Joint Committee on Cancer (AJCC) established by the TNM staging system. The TNM staging system of AJCC is also the most commonly used prognostic assessment system for RCC[9]. However, considering that RCC is a highly heterogeneous disease, factors such as age[10], race[11], smoking[12], marriage[13], laterality[14] are risky prognostic factors. Several studies reported the prognostic impact of non-clinical multifactorial analysis on survival of nmRCC cases based on the SEER database. Tang et al. studied the global profile of cancer incidence, mortality and corresponding trends in people aged 15 to 39 years during 2010-2018. Cheng et al. studied nmRCC patients bas on the SEER database from 2010 to 2015[15-17]. However, these study samples only evaluated middle-aged and older patients and did not include specific surgical option factors and did not explore the prognosis of adjuvant therapy on patients, which are important influencing factors in other studies. Therefore, accurate predictive models are important for clinical decision-making, building patient confidence, and improving medical treatment decisions.

2. Patients and methods

2.1. Data Source and Data Extraction

This study obtained patients diagnosed with RCC in the United States from 2010 to 2015 from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (https://seer.cancer.gov/). The SEER database is a public database, the data are publicly available, and ethical approval and informed consent were not required for our study.

The data were obtained from the SEER 17 Regs Custom Data (with additional treatment fields), Nov 2021 Sub (2000-2019 variation) by using the SEER*Stat 8.4.0.1 software.

Patient demographic information and clinicopathological data included age, gender, race, marriage, tumor laterality, tumor histologic type, tumor size, histologic grade, TNM/AJCC staging system, surgery, radiotherapy, and chemotherapy. Inclusion criteria: (1) patients diagnosed with site code C64.9-Kidney; (2) Patients were diagnosed between 2010 and 2015. Exclusion criteria: (1) Patients were diagnosed with distant metastasis (M1); (2) Non-primary cell renal cell carcinoma; (3) unknown American Joint Committee (AJCC) on Cancer 7th TNM stage; (4) unknown race, unknown marital status; (5) pathological diagnosis of SEER database ICD-O-3 codes wasn't 8260, 8310, 8312, 8317; (6)unknown laterality or bilateral tumor; (7)

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unknown tumor size, unknown tumor grade; (8) surgical codes 00,20-27,30,50; (9) unknown survival time, unknown cause of death. The patient selection flow chart is shown in Figure 1.

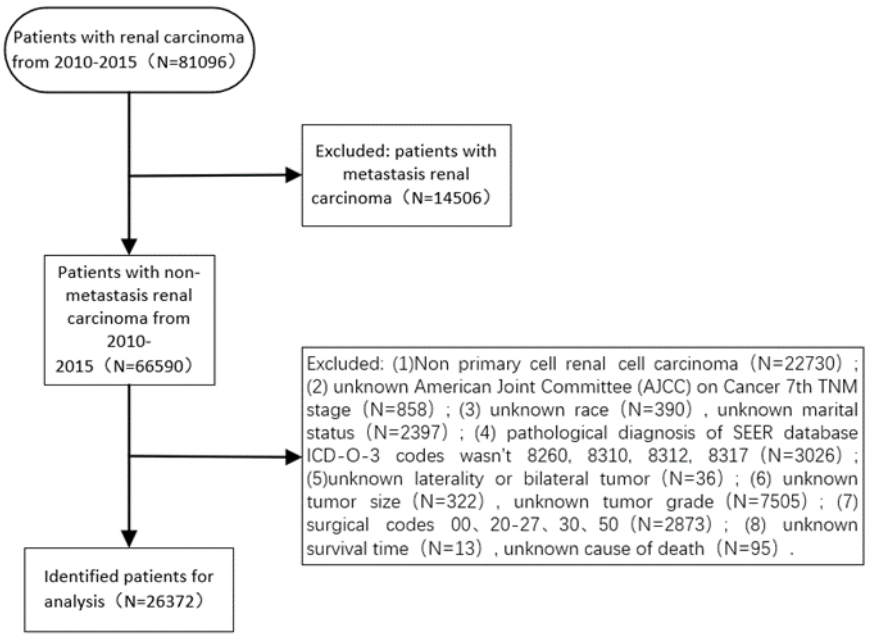

Figure 1. Flowchart for selecting patients

2.2. Statistical method

Included patients were randomly divided into a training set (N=18460) and a validation set (N=7912) in the ratio of 7:3. A chi-square test was performed on categorical variables to explore the baseline characteristics of patients in both sets. Categorical variables were reported as frequencies and proportions. The best cut-off value for age and tumor size was assessed using X-tile software. According to the surgical method, patients were divided into non-surgery(No), local tumor resection(LN), partial nephrectomy (PN), and radical total nephrectomy(RN) groups. Cox regression models were used to analyze the prognostic factors for patient survival. All analyses were performed using the statistical package R 4.1.2 (http://www.R-project.org). Bilateral p values < 0.05 were considered statistically significant.

2.3. Nomogram Construction for 1-, 3-, and 5-Year CSS

In the training set, one-way Cox regression analysis was performed to identify significant prognostic factors. They were included in multivariate Cox proportional risk regression models to further determine the association of each variable at p-values < 0.05 with survival outcomes in patients with nmRCC. All results were expressed as hazard ratios (HR) and 95% confidence intervals (95% CI). Nomogram plots were constructed using identified independent risk factors to predict CSS at 1, 3, and 5 years in patients with nmRCC.

2.4. Nomogram Validation and Clinical Utility

We use the consistency index (C-index), the area under the receiver operating curve (AUC) at 1, 3, and 5 years of the training and validation sets to test the discriminative power of the prediction model. The accuracy of the nomogram in predicting CSS at 1, 3, and 5 years was assessed by calibration charts. In addition, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were used to evaluate whether the nomogram was more accurate than the AJCC TNM staging system.

Decision curve analysis (DCA) was used to evaluate the clinical application value of the nomogram. In addition, we calculated the total score for each patient based on the nomogram.

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Based on the total score, we constructed a risk stratification model to divide all patients into two different risk groups (low-risk group and high-risk group). The optimal critical values were analyzed using X-tile software. We used log-rank test and Kaplan-Meier curve to compare the survival differences of patients in different groups. The patients were classified into two subgroups including low-risk, and high-risk groups. Kaplan-Meier curves and log-rank tests were used to compare the differences in risk model survival between groups.

3. Results

3.1. Clinical Characteristics

A total of 26372 patients were included in the study. They were randomly divided into a training set (N= 18460) and a validation set (N= 7912) according to a 7:3 ratio. Table 1 shows the clinical characteristics of all patients.

Table 1. Basic clinical characteristics of the training and test sets of patients with nmRCC

	All （N= 26372）	Training set （N= 18460）	Validation set (N= 7912)	p
Age n(%)				
<65	16980 (64.4)	11841 (64.1)	5139 (65.0)	0.214
≥65	9392 (35.6)	6619 (35.9)	2773 (35.0)	
Sex n(%)				
Female	10013 (38.0)	7041 (38.1)	2972(37.6)	0.382
Male	16359 (62.0)	11419 (61.9)	4940 (62.4)	
Race n(%)				
Black	2639 (10.0)	1875 (10.2)	7315 (92.5)	0.319
Other	1927 (7.3)	1330 (7.2)	597 (7.5)	
White	21806 (82.7)	15255 (82.6)	6551 (82.8)	
Marriage n(%)				
Married	18827 (71.4)	13144 (71.2)	5683 (71.8)	0.31
No	7545 (28.6)	5316 (28.8)	2229 (28.2)	
Histologic type n(%)				
CHRCC	1369 (5.2)	969 (5.2)	400 (5.0)	0.919
CCRCC	18710 (70.9)	13080 (70.9)	5630 (71.2)	
Unclassified	3169 (12.0)	2222 (12.0)	947 (12.0)	
PRCC	3124 (11.8)	2189 (11.9)	935 (11.8)	
AJCC n(%)				
I	18760 (71.1)	13097 (70.9)	1412 (17.8)	0.718
II	2662 (10.1)	1869 (10.1)	793 (10.0)	
III	4808 (18.2)	3396 (18.4)	44 (0.6)	
IV	142 (0.5)	98 (0.5)	5663 (71.6)	
Tumor size n(%)				
＜65mm	19723 (74.8)	13791 (74.7)	5932 (75.0)	0.658
≥65mm	6649 (25.2)	4669 (25.3)	1980 (25.0)	
Grade n(%)				
Well-differentiated	3038 (11.5)	2089 (11.3)	3631 (12.0)	0.401
Moderately differentiated	14417 (54.7)	10136 (54.9)	4281 (54.1)	
Poorly differentiated	7536 (28.6)	5273 (28.6)	2263 (28.6)	
Undifferentiated	1381 (5.2)	962 (5.2)	419 (5.3)	
Laterality n(%)				
Left	12866 (48.8)	9075 (49.2)	3791(47.9)	0.066
Right	13506 (51.2)	9385 (50.8)	4121 (52.1)	

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Surgery n(%)				
No	402 (1.5)	274 (1.5)	116 (1.5)	0.62
LN	358 (1.4)	242 (1.3)	128 (1.6)	
PN	11331 (43.0)	7927 (42.9)	3404 (43.0)	
RN	14281 (54.2)	10017 (54.3)	4264 (53.9)	
Radiation n(%)				
No/unknown	26286 (99.7)	18406 (99.7)	7880 (99.6)	0.179
Yes	86 (0.3)	54 (0.3)	32 (0.4)	
Chemotherapy n(%)				
No/unknown	25933 (98.3)	18154 (98.3)	7779 (98.3)	0.934
Yes	439 (1.7)	306 (1.7)	133 (1.7)	

3.2. Univariate and Multivariate Cox Regression Analysis and Nomogram construction

The results of Cox regression analysis as shown in Table 2 showed that age, marital status, pathological type, AJCC stage, tumor size, histological grade, surgical approach, radiotherapy, and chemotherapy variables were statistically significant($p < 0.05$). The variables of gender, race, and tumor laterality were not statistically significant ($p > 0.05$).

Table 2. Univariate and multivariate COX regression analyses in patients with primary nmRCC in the training set

	Univariate analysis			Multivariate analysis		
	HR	95%CI	P	HR	95%CI	P
Age						
＜65	Reference			Reference		
≥65	1.825	1.652-2.015	<0.001	1.815	1.644-2.004	<0.001
Sex						
Male	Reference					
Female	0.957	0.863-1.062	0.411			
Race						
White	Reference					
Black	1.069	0.899-1.272	0.448			
Other	1.038	0.863-1.248	0.693			
Marriage						
Married	Reference			Reference		
No	1.150	1.031-1.284	0.013	1.154	1.035-1.286	0.010
Histologic type						
CCRCC	Reference			Reference		
PRCC	1.363	1.162-1.599	<0.001	1.383	1.184-1.616	<0.001
CHRCC	0.424	0.305-0.589	<0.001	0.423	0.305-0.587	<0.001
Unclassified	1.150	1.001-1.322	0.049	1.153	1.003-1.324	0.045
AJCC						
I	Reference			Reference		
II	1.263	1.039-1.534	0.019	1.262	1.039-1.533	0.019
III	2.593	2.237-3.007	<0.001	2.592	2.236-3.004	<0.001
IV	6.333	4.712-8.513	<0.001	6.359	4.732-8.546	<0.001
Tumor size						
＜65mm	Reference			Reference		
≥65mm	1.911	1.661-2.199	<0.001	1.915	1.664-2.203	<0.001
Laterality						
Left	Reference					
Right	0.959	0.870-1.057	0.400			
Grade						
Well-differentiated	Reference			Reference		
Moderately differentiated	1.065	0.839-1.351	0.607	1.067	0.840-1.353	0.596

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Poorly differentiated	2.239	1.765-2.839	<0.001	2.258	1.781-2.863	<0.001
Undifferentiated	4.088	3.165-5.281	<0.001	4.105	3.178-5.303	<0.001
Surgery						
No	Reference			Reference		
LN	0.444	0.266-0.743	0.002	0.442	0.264-0.739	0.002
PN	0.119	0.088-0.161	<0.001	0.119	0.087-0.161	<0.001
RN	0.270	0.204-0.357	<0.001	0.269	0.203-0.356	<0.001
Radiation						
Yes	Reference			Reference		
No/unknown	0.316	0.227-0.441	<0.001	0.316	0.226-0.440	<0.001
Chemotherapy						
Yes	Reference			Reference		
No/unknown	0.484	0.406-0.577	<0.001	0.490	0.411-0.583	<0.001

According to the Nomogram model constructed, the total score of the patient could be relatively intuitively derived by summing all the variable scores. For example, a 65-year-old married patient was diagnosed with RCC with a tumor size of about 6 cm, underwent RN, and the postoperative pathology showed a T3N0M0 moderately differentiated grade PRCC, and no postoperative radiotherapy or chemotherapy was administered. Then the total score of this patient was 177.5 (age with a grade of 27.5, marriage with a grade of 0, PRCC with a grade of 55, tumor size with a grade of 0, AJCC stage with a grade of 55, tissue grading with a grade of 2.5, surgery with a grade of 37.5, radiotherapy with a grade of 0, chemotherapy with a grade of 0. The 5-year survival rate of this patient was approximately 87%.

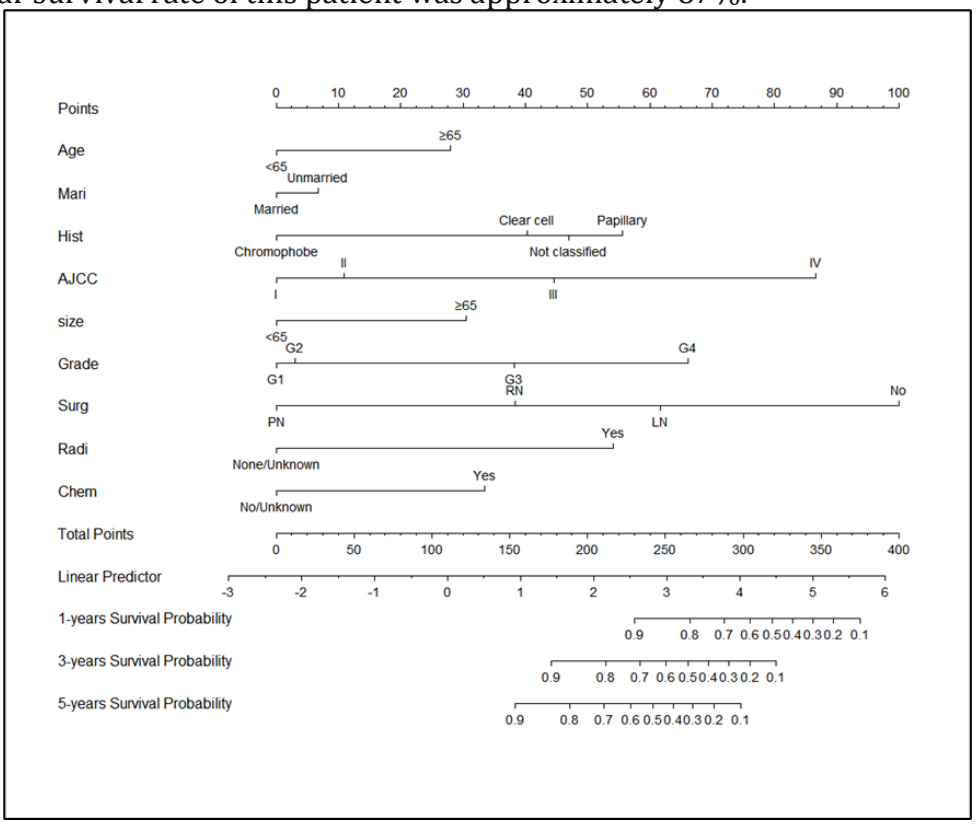

Figure 2. Nomogram model of predicted survival rates for 1-year, 3-year, and 5-year survival rates for patients with nmRCC

3.3. Validation of the nomogram

The C-index is 0.833 for the training set and 0.836 for the test set. In the AJCC staging system, the C-index is 0.738 for the training set and 0.742 for the test set. The ROC curves are shown in Figure 3, in the training set, the AUC of the new model is 0.858 for 1-year survival, 0.872 for 3-year survival, and 0.855 for 5-year survival; the AUC of the AJCC TNM staging system is In the test set, the AUC of the predicted model was 0.860 for 1-year survival, 0.861 for 3-year survival,

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and 0.832 for 5-year survival; the AUC of the AJCC staging model was 0.758 for 1-year survival, 0.770 for 3-year survival, and 0.750 for 5-year survival. The AUC for 1-year survival was 0.778, the AUC for 3-year survival was 0.768, and the AUC for 5-year survival was 0.758. The C-index, AUC values assess the performance of the model. It indicats that our model performed well in predicting performance.

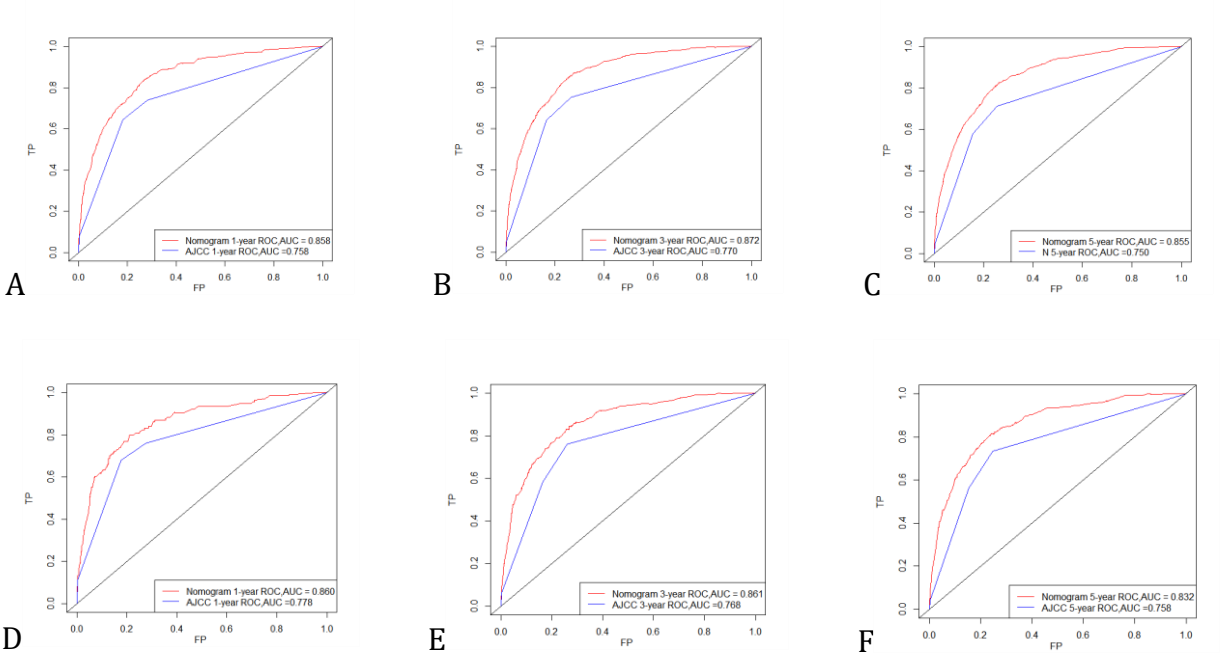

Figure 3. Comparison of the ROC curves of the nomogram model and the AJCC model of nmRCC patient. (A), (B) and (C) represent the ROC curves for 1, 3, and 5 years for the training set, respectively. (D), (E), (F) represent the 1, 3, and 5-year ROC curves for the test set, respectively.

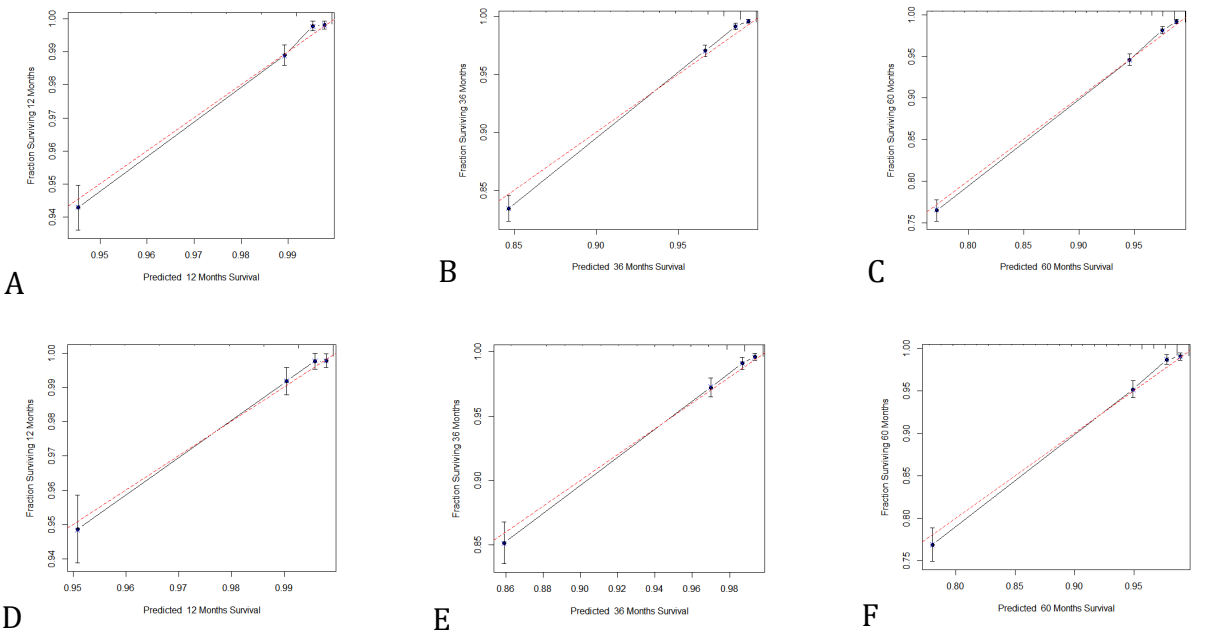

Figure 4. Calibration curves for the training and test sets. (A), (B), and (C) are curves of 1, 3, and 5 years for the training set, respectively; (D), (E), and (F) are curves of 1, 3, and 5 years for the test set, respectively.

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As shown in Figure 4, our new model calibration curves show that the predicted probabilities of 1-year survival, 3-year survival, and 5-year survival for the training and test sets are very close to the predicted probabilities of the actual situation.

The results are detailed in Tables 4 and 5. NRI and IDI of the nomogram model were compared with the AJCC staging model. In the NRI training set, the predictive ability of 1-year, 3-year, and 5-year survival was improved by 22.26%, 37.51%, and 37.74%, respectively. In the NRI test set, the prediction ability of the 1-year survival rate improved by 20.17%, the prediction ability of the 3-year survival rate improved by 40.09%, and the prediction ability of the 5-year survival rate improved by 40.23% compared with that of the AJCC staging model. In the IDI training set, the prediction ability of 1-year, 3-year, and 5-year survival was improved by 2.48%, 5.98%, and 8.06%. In the IDI test set, the predictive ability of 1-year survival improved by 2.35%, 3-year survival by 6.19%, and 5-year survival by 8.46% compared with the AJCC staging model.

Table 4. NRI of nomogram model compared with AJCC staging system

NRI	Training set	95%CI	Test set	95%CI
1-year CSS (%)	22.26	17.66~30.36	20.17	11.23~30.00
3-year CSS (%)	37.51	32.41~42.21	40.09	32.95~46.08
5-year CSS (%)	37.74	32.75~42.04	40.23	34.85~46.78

Table 5. IDI of nomogram model compared with AJCC staging system

IDI	Training set	P	Test set	P
1-year CSS (%)	2.48	<0.001	2.35	<0.001
3-year CSS (%)	5.98	<0.001	6.19	<0.001
5-year CSS (%)	8.06	<0.001	8.46	<0.001

As shown in Figure 5, the green line means that the gain is 0. Both the cyan and red lines lie above the orange and green lines, indicating that the clinical benefit can be obtained using either the nomogram model or the AJCC staging model, and the nomogram model yields a higher clinical benefit.

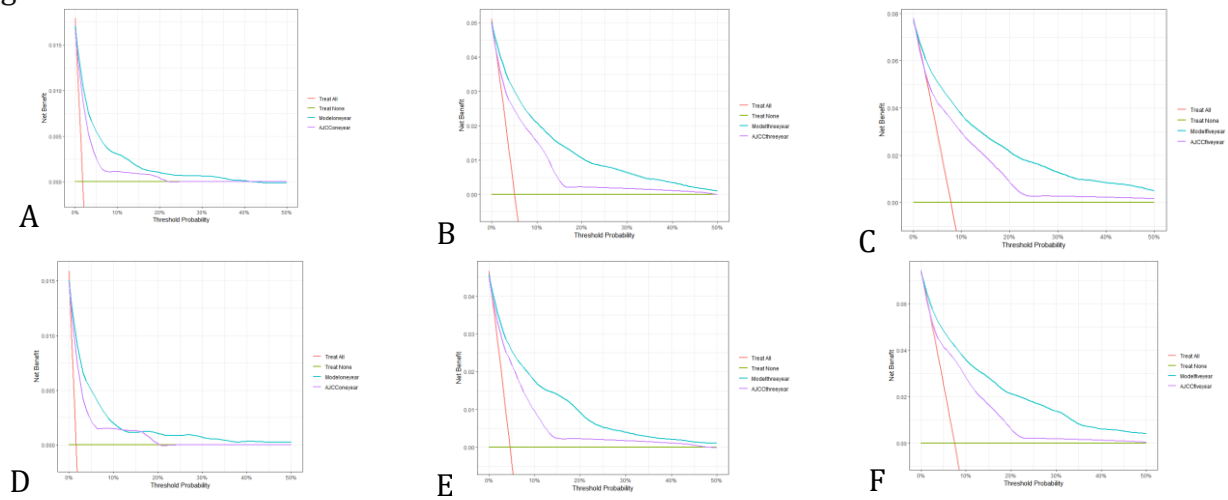

Figure 5. DCA curves of the nomogram model and AJCC staging model. (A), (B), and (C) are the DCA curves of the training set for 1-, 3-, and 5-year survival rates, respectively; (D), (E), and (F) are the DCA curves of the test set for 1-, 3-, and 5-year survival rates, respectively.

We calculated the total scores for all patients according to the nomogram model and then used the X-tile software to calculate the optimal cut-off values of the total score. Patients were divided into high-risk(≥190) and low-risk groups(＜190). There was a statistically significant difference between the two groups by Kaplan-Meier analysis (p< 0.0001) (Figure 6).

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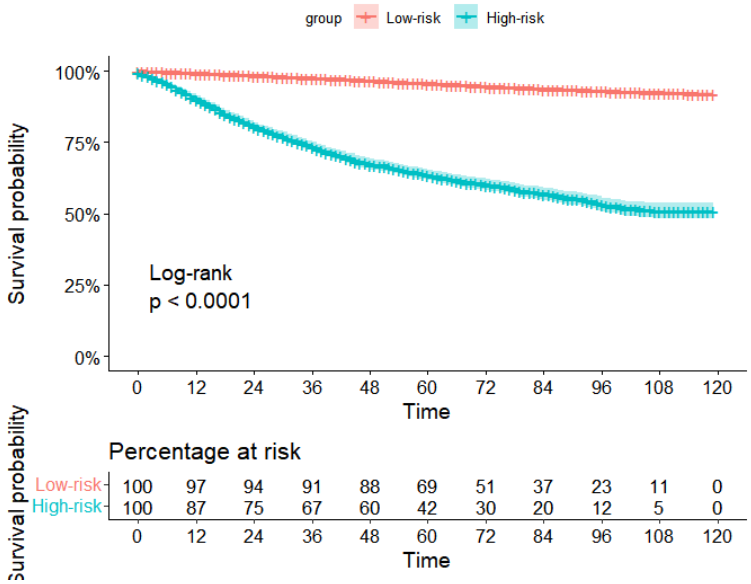

Figure 6. Kaplan-Meier curves of patients for CSS in the low-risk and high-risk groups of all patients.

4. Discussion

Renal cell carcinoma is a heterogeneous group of cancers derived from renal tubular epithelial cells, which includes a variety of histological and molecular subtypes. Of all pathological types, clear cell renal carcinoma is the most common type, and other pathological types including PRCC, CCHRCC or unclassified RCC[2, 18, 19]. With the development of imaging and health concepts, the incidence of early-stage renal cell carcinoma has gradually increased[20]. Patient diagnosis, prognosis and clinical decision-making are currently based on histological information (i.e. Fuhrman grading or MSKCC score and AJCC staging system[21, 22]. Tumor progression is a multistep process that is influenced by a variety of social, family, and other factors. A better understanding of the role of variables influencing tumor progression can help include the diagnosis, prevention, and treatment of kidney cancer. In this study, we constructed a more detailed predictive model of nmRCC than traditional AJCC staging system by collecting multiple variables such as age, gender, race, marriage, tumor size, pathological type, AJCC, tumor laterality, tumor histological grade, surgical approach, radiotherapy, and chemotherapy. We performed a more detailed analysis including demographic, tumor, and clinical information for predictive modeling to generate a series of meaningful results to better understand the factors affecting the prognosis of patients with renal cell carcinoma and to make more accurate clinical decisions.

AJCC staging system is the most important conventional prognostic factor for renal cell carcinoma. Data suggest that prognosis prediction based on it has reached its limits[23]. Significant progress has been made in analyzing diseases and establishing clinical prognosis models using various public databases such as the SEER database, MIMIC database, and Nhanes database. SEER database is an authoritative cancer statistical database established in the U.S. and includes various tumor types such as lung cancer, breast cancer, gastric cancer, colorectal cancer, prostate cancer, etc[24-26]. Huang et al. constructed a prognostic nomogram model for patients with single or multiple metastases of CCRCC[27]. Zhang et al. and Tang's team analyzed risk factors and plotted CSS and overall survival time (OS) using univariate and multivariate Cox regressions in elderly (age) and middle-aged nmRCC patients, respectively. No study has yet constructed a survival prognostic model analysis of patients with all-age nmRCC based on multiple factors such as demographics and clinical characteristics in the SEER database. To our knowledge, this study is the first to construct a survival prognostic prediction model based on

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Cox proportional risk regression. This model is suitable for use in patients of all ages with nmRCC, and the study aids clinicians and patients in clinical decision-making and active monitoring.

Our clinical experience is similar to the results of previous studies in that patient prognosis is closely related to age. Çakıcı,MÇ et al. retrospectively analyzed the effect of two borderline age groups on RCC survival, and despite similar pathology in both groups, the prognosis and survival were more favorable in younger[28]. Liao et al. retrospectively analyzed seven different age groups of kidney cancer patients and showed that age was negatively associated with survival in RCC patients[10].

Among the four pathological types in this study, the prognosis in order from good to poor was CHRCC, CCRCC, unclassified RCC, PRCC. Studies have shown that PRCC has a worse prognosis than patients with CCRCC [8, 29, 30]. Other studies showed CHRCC has a better prognosis than CCRCC[31]. It is known that the poorer the degree of tumor differentiation, the more malignant the tumor is and the worse the prognosis of the patients.

Li et al. showed that the probability of invasive tumors increased with tumor size[32]. A study retrospectively evaluated 286 patients with nmRCC undergoing RN and showed that the risk of postoperative recurrence and prognosis of patients were closely related to tumor size[33]. Similar to the previous studies, our findings suggest that patients with nmRCC ≥ 65 mm have a poorer prognosis. In the AJCC TNM staging group, stage I to IV prognosis becomes progressively worse.

Surgical excision and ensuring negative surgical margins remain effective treatment options. Compared with RN, PN provides better renal unit protection and decreased risk of serious postoperative complications while ensuring similar recurrence-free survival[34-37]. As the incidence of early-stage kidney cancer increases, more patients are treated with nonsurgical and nephron-sparing strategies[38]. Similar to previous studies, this study suggests that patients with PN have the best prognosis over RN. Patients who did not undergo surgery had the worst prognosis, and those who underwent tumor resection had a worse prognosis than those who underwent PN and RN. This may be because simple tumor resection has the potential to recur the tumor, although this is rare. In addition, when the tumor is small or in the early stage, clinicians choose PN treatment, and large size of the tumor also means that the tumor has a deeper degree of invasion, a wide range of invasion, and a late-clinical stage.

It is important to note that due to the limitations of the SEER database, we cannot know the specific information on radiotherapy and chemotherapy in patients, only "yes" and "no/unknown" results. It is generally believed that RC has low sensitivity to radiotherapy and chemotherapy. So radiotherapy and chemotherapy are not recommended as conventional means for postoperative treatment of tumor bed areas. There are still llittle data suggesting that adjuvant therapy can benefit the survival of patients with renal cancer[17, 39]. Grant, SR, et al. suggest that patients with T1N0M0 early-stage kidney cancer who receive high-dose radiation therapy have a longer survival[40]. Florent et al. evaluated a group of 4,350 patients who received chemoradiotherapy for childhood cancer, with radiation doses less than 1 Gy not receiving radiotherapy or renal absorption, with a 5.7-fold higher incidence of kidney cancer (95% CI: 1.4-14.7) and a 66.3-fold higher radiation dose of 10-19 Gy (95% CI: 23.8-142.5) and a 14.5-fold higher risk of kidney cancer (95% CI: 0.8-63.9) for larger radiation doses. Chemotherapy also increases the risk of kidney cancer. This incidence increases further as childhood cancer survivors move into old age[41]. Our model results suggest that chemoradiotherapy is a prognostic factor for kidney cancer, but the prognosis for patients receiving radiotherapy or chemotherapy is relatively poor compared with patients who do not receive chemoradiotherapy. This may be related to the side effects of chemoradiotherapy, or because radiotherapy is mostly used for locally advanced or advanced renal cancer[42, 43]. Further research on chemoradiotherapy is needed for renal cancer.

There were some limitations to this study. First, although the SEER database is a large public database, some patients' data is still missing or unknown. The study was retrospective and lacked external validation. In addition, the clinical trial organization collected prospectively should be considered the best source of validation, and the hierarchy of validation cohorts should be established.

5. Conclusion

In summary, we collected multiple factors that may affect prognosis through the SEER database and included them in the analysis, selected 9 prognostic factors and constructed a new nmRCC prognostic nomogram model. The results of this study showed that the nomogram model has good discrimination, accurate prediction, and clinical benefits.

References

[1] A.M. Saad, M.M. Gad, M.J. Al-Husseini, et al.: Trends in Renal-Cell Carcinoma Incidence and Mortality in the United States in the Last 2 Decades: A SEER-Based Study. Clin Genitourin Cancer,Vol. 17(2019).No. 1, p. 46-57 e5.

[2] U. Capitanio and F. Montorsi: Renal cancer. Lancet,Vol. 387(2016).No. 10021, p. 894-906.

[3] R.L. Siegel, K.D. Miller, N.S. Wagle, et al.: Cancer statistics, 2023. CA Cancer J Clin,Vol. 73(2023).No. 1, p. 17-48.

[4] P. De, M.C. Otterstatter, R. Semenciw, et al.: Trends in incidence, mortality, and survival for kidney cancer in Canada, 1986-2007. Cancer Causes Control,Vol. 25(2014).No. 10, p. 1271-81.

[5] M. Mohammadian, R. Pakzad, F. Towhidi, et al.: Incidence and mortality of kidney cancer and its relationship with HDI (Human Development Index) in the world in 2012. Clujul Med,Vol. 90(2017).No. 3, p. 286-293.

[6] I. Frank, M. Blute, J. Cheville, et al.: An outcome prediction model for patients with clear cell renal cell carcinoma treated with radical nephrectomy based on tumor stage, size, grade and necrosis: the SSIGN score. Vol. 168(2002).No. 6, p. 2395-400.

[7] A. Kutikov, B.L. Egleston, Y.N. Wong, et al.: Evaluating overall survival and competing risks of death in patients with localized renal cell carcinoma using a comprehensive nomogram. J Clin Oncol,Vol. 28(2010).No. 2, p. 311-7.

[8] H.J. Cho, S.J. Kim, U.S. Ha, et al.: Prognostic value of capsular invasion for localized clear-cell renal cell carcinoma. Eur Urol,Vol. 56(2009).No. 6, p. 1006-12.

[9] M. Sun, S.F. Shariat, C. Cheng, et al.: Prognostic factors and predictive models in renal cell carcinoma: a contemporary review. Eur Urol,Vol. 60(2011).No. 4, p. 644-61.

[10] Z. Liao, D. Wang, N. Song, et al.: Prognosis of clear cell renal cell carcinoma patients stratified by age: A research relied on SEER database. Front Oncol,Vol. 12(2022).No., p. 975779.

[11] B.I. Chung, J.J. Leow, F. Gelpi-Hammerschmidt, et al.: Racial Disparities in Postoperative Complications After Radical Nephrectomy: A Population-based Analysis. Urology,Vol. 85(2015).No. 6, p. 1411-6.

[12] N.H. Patel, K.M. Attwood, M. Hanzly, et al.: Comparative Analysis of Smoking as a Risk Factor among Renal Cell Carcinoma Histological Subtypes. J Urol,Vol. 194(2015).No. 3, p. 640-6.

[13] L. Feng, Y.J. Yang, J. Du, et al.: Marital status and survival of patients with colorectal signet ring cell carcinoma: a population-based study. Sci Rep,Vol. 10(2020).No. 1, p. 17881.

[14] S. Guo, K. Yao, X. He, et al.: Prognostic significance of laterality in renal cell carcinoma: A population-based study from the surveillance, epidemiology, and end results (SEER) database. Cancer Med,Vol. 8(2019).No. 12, p. 5629-5637.

[15] H.D. Patel, M. Kates, P.M. Pierorazio, et al.: Survival after diagnosis of localized T1a kidney cancer: current population-based practice of surgery and nonsurgical management. Urology,Vol. 83(2014).No. 1, p. 126-32.

[16] W.R. Grubb, L. Ponsky, S.S. Lo, et al.: Final results of a dose escalation protocol of stereotactic body radiotherapy for poor surgical candidates with localized renal cell carcinoma. Radiother Oncol,Vol. 155(2021).No., p. 138-143.

[17] E. Wood, N. Donin, and B. Shuch: Adjuvant Therapy for Localized High-Risk Renal Cell Carcinoma. Urologic Clinics of North America,Vol. 47(2020).No. 3, p. 345-358.

[18] E. Jonasch, J. Gao, and W.K. Rathmell: Renal cell carcinoma. BMJ,Vol. 349(2014).No., p. g4797.

[19] A.M. Molina and R.J. Motzer: Clinical Practice Guidelines for the Treatment of Metastatic Renal Cell Carcinoma: Today and Tomorrow. The Oncologist,Vol. 16(2011).No. S2, p. 45-50.

[20] W.M. Linehan, G. Bratslavsky, P.A. Pinto, et al.: Molecular diagnosis and therapy of kidney cancer. Annu Rev Med,Vol. 61(2010).No., p. 329-43.

[21] V. Ficarra, G. Martignoni, C. Lohse, et al.: External validation of the Mayo Clinic Stage, Size, Grade and Necrosis (SSIGN) score to predict cancer specific survival using a European series of conventional renal cell carcinoma. J Urol,Vol. 175(2006).No. 4, p. 1235-9.

[22] B. Escudier, C. Porta, M. Schmidinger, et al.: Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol,Vol. 27(2016).No. suppl 5, p. v58-v68.

[23]M.D. Galsky: A prognostic model for metastatic renal-cell carcinoma. Lancet Oncol,Vol. 14(2013).No. 2, p. 102-3.

[24] E. Scosyrev, J. Messing, K. Noyes, et al.: Surveillance Epidemiology and End Results (SEER) program and population-based research in urologic oncology: An overview. Urologic Oncology: Seminars and Original Investigations,Vol. 30(2012).No. 2, p. 126-132.

[25] C. Chen, X. Geng, R. Liang, et al.: Nomograms-based prediction of overall and cancer-specific survivals for patients with chromophobe renal cell carcinoma. Exp Biol Med (Maywood),Vol. 246(2021).No. 6, p. 729-739.

[26] P. Tai, E. Yu, R. Shiels, et al.: Short- and long-term cause-specific survival of patients with inflammatory breast cancer. BMC Cancer,Vol. 5(2005).No., p. 137.

[27] G. Huang, J. Liao, S. Cai, et al.: Development and validation of a prognostic nomogram for predicting cancer-specific survival in patients with metastatic clear cell renal carcinoma: A study based on SEER database. Front Oncol,Vol. 12(2022).No., p. 949058.

[28] M.C. Cakici, E. Kisa, M.Y. Yalcin, et al.: Influence of border-age on survival of sporadic renal cell carcinoma: young adults versus octogenarians. Int Urol Nephrol,Vol. 52(2020).No. 11, p. 2087-2095.

[29] N. Wagener, D. Edelmann, A. Benner, et al.: Outcome of papillary versus clear cell renal cell carcinoma varies significantly in non-metastatic disease. PLoS One,Vol. 12(2017).No. 9, p. e0184173.

[30] J. Huang, D. Huang, J. Yan, et al.: Comprehensive subgroup analyses of survival outcomes between clear cell renal cell adenocarcinoma and papillary renal cell adenocarcinoma. Cancer Medicine,Vol. 9(2020).No. 24, p. 9409-9418.

[31] Y. Xie, X. Ma, H. Li, et al.: Prognostic Value of Clinical and Pathological Features in Chinese Patients with Chromophobe Renal Cell Carcinoma: A 10-Year Single-Center Study. Journal of Cancer,Vol. 8(2017).No. 17, p. 3474-3479.

[32] J. Li, X. Li, Z. Jiang, et al.: Predicting the probability of malignant pathological type of kidney cancer based on mass size: A retrospective study. Prog Urol,Vol. 32(2022).No. 12, p. 849-855.

[33] T. Steiner, R. Knels, and J. Schubert: Prognostic significance of tumour size in patients after tumour nephrectomy for localised renal cell carcinoma. Eur Urol,Vol. 46(2004).No. 3, p. 327-30.

[34] J.J. Oh, S.S. Byun, S.E. Lee, et al.: Partial nephrectomy versus radical nephrectomy for non-metastatic pathological T3a renal cell carcinoma: a multi-institutional comparative analysis. Int J Urol,Vol. 21(2014).No. 4, p. 352-7.

[35] J. Muhlbauer, K.F. Kowalewski, M.T. Walach, et al.: Partial nephrectomy preserves renal function without increasing the risk of complications compared with radical nephrectomy for renal cell carcinomas of stages pT2-3a. Int J Urol,Vol. 27(2020).No. 10, p. 906-913.

[36] R.J. Ellis, V.M. White, D.M. Bolton, et al.: Tumor size and postoperative kidney function following radical nephrectomy. Clin Epidemiol,Vol. 11(2019).No., p. 333-348.

[37] R.A. Ghandour, M.R. Danzig, and J.M. McKiernan: Renal cell carcinoma: risks and benefits of nephron-sparing surgery for T1 tumors. Adv Chronic Kidney Dis,Vol. 22(2015).No. 4, p. 258-65.

[38] H.J. Tan, C.P. Filson, and M.S. Litwin: Contemporary, age-based trends in the incidence and management of patients with early-stage kidney cancer. Urol Oncol,Vol. 33(2015).No. 1, p. 21 e19-21 e26.

[39] P. Sosa-Fajardo, J.M. Blanco-Suarez, A. Pineda-Munguia, et al.: Stereotactic body radiation therapy for kidney cancer. Where do we stand? Int J Urol,(2023).No.

[40] S.R. Grant, X. Lei, K.R. Hess, et al.: Stereotactic Body Radiation Therapy for the Definitive Treatment of Early Stage Kidney Cancer: A Survival Comparison With Surgery, Tumor Ablation, and Observation. Adv Radiat Oncol,Vol. 5(2020).No. 3, p. 495-502.

[41] F. de Vathaire, B. Scwhartz, C. El-Fayech, et al.: Risk of a Second Kidney Carcinoma Following Childhood Cancer: Role of Chemotherapy and Radiation Dose to Kidneys. J Urol,Vol. 194(2015).No. 5, p. 1390-5.

[42] K. Kawai, D. Ichioka, H. Inai, et al.: Assessment and management of renal impairment in chemotherapy for urogenital cancer. Jpn J Clin Oncol,Vol. 43(2013).No. 11, p. 1055-63.

[43] J. Kala and K.W. Finkel: Onconephrology. Crit Care Clin,Vol. 37(2021).No. 2, p. 365-384.