Original Research

Nomograms-based prediction of overall and cancer-specific survivals for patients with chromophobe renal cell carcinoma

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Impact statement

Chromophobe renal cell carcinoma (chRCC) make up of approximately 5% of all the renal cell carcinoma cases. However, currently we still lack a standardized treatment for the management of advanced chRCC, which also points to the necessity of identifying significant prognostic parameters for improving the survival of early staged chRCC patients. Nomogram is an effective and reliable graphic prediction tool covering important factors more than tumor node metastasis (TNM) variables, and can be applied to predict cancer prognosis. Moreover, nomograms could also facilitate the determination of the practical stage of a patient before treatments. This study mainly focused on developing two nomograms for the prognostic prediction of CSS and OS for three and five years, hoping to contribute to the advancement of chRCC treatment.

Abstract

This study built and tested two effective nomograms for the purpose of predicting cancer-specific survival and overall survival of chromophobe renal cell carcinoma (chRCC) patients. Multivariate Cox regression analysis was employed to filter independent prognostic factors predictive of cancer-specific survival and overall survival, and the nomograms were built based on a training set incorporating 2901 chRCC patients in a retrospective study (from 2004 to 2015) downloaded from the surveillance, epidemiology, and end results (SEER) database. The nomograms were verified on a validation cohort of 1934 patients, subsequently the performances of the nomograms were examined according to the receiver operating characteristic curve, calibration curves, the concordance (C-index), and decision curve analysis. The results showed that tumor grade, AJCC and N stages, race, marital status, age, histories of chemotherapy, radiotherapy and surgery were the individual prognostic factors for overall survival, and that AJCC, N and SEER stages, histories of surgery, radiotherapy and chemotherapy, age, tumor grade were individual prognostic factors for cancer-specific survival. According to C-indexes, receiver operating characteristic curves, and decision curve analysis outcomes, the nomograms showed a higher accuracy in predicting overall survival and OSS when compared with TNM stage and SEER stage. All the calibration curves were significantly consistent between predictive and validation sets. In this study, the nomograms, which were validated to be highly accurate and applicable, were built to facilitate individualized predictions of the cancer-specific survival and overall survival to patients diagnosed with chRCC between 2004 and 2015.

Keywords: Nomogram, chromophobe renal cell carcinoma, SEER, prognosis, overall survival, cancer-specific survival

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Introduction

It has been found that approximately 5% of all the cases of renal cell carcinoma are made up by chromophobe renal cell carcinoma (chRCC), an incidence secondary to papillary renal cell carcinoma (pRCC, 15%) and clear cell ranal cell carcinoma (ccRCC, 70%–80%).[1] Normally, chRCC is assigned into classic subtype or eosinophilic subtype. Despite its slow growth, 5–10% of chRCC patients have developed metastasis by the time of diagnosis.[2] As a cancer with a low degree of malignancy, five-year survival rate of chRCC ranging from 78% to 100%,[3] is more favorable than the prognosis of clear cell renal cell carcinoma (ccRCC) and similar to that of papillary renal cell carcinoma (pRCC).[4,5] Surgical resection is widely adopted for chRCC management at a localized stage, followed by the use of antiangiogenics treatment, immunotherapy, and mTOR pathway inhibitors when ccRCC is at a metastatic stage.[6] Noticeably, many clinical trials have been developed for other types of renal cell carcinoma, and little attention has been paid to chRCC for its low incidence.[7] Cancer

metastasis accounts for a majority of cancer-related mortality, also from previous studies, factors decisive to survival outcome also vary greatly.[8,9] Therefore, developing effective prognostic factors to improve clinical treatment strategies for managing chRCC patients has a high clinical significance.

At present, American Joint Committee on Cancer (AJCC) staging system is a widely recognized and employed staging system applicable to the prognosis prediction of RCC patients under most circumstances.[10] Patients with the same clinical pathological features of RCC may develop different prognoses, potentially due to individual differences in the factors such as age, gender, race, tumor site, and treatment that are all closely associated with the prognosis of chRCC.[11] Therefore, an effective and reliable prognosis model should be developed for the evaluation of the prognosis of patients with chRCC.

Though the prognosis of chRCC is commonly evaluated on the basis of the TNM staging system at present, cancer prognosis is also dependent on many nonanatomic factors as well, such as gender, age, race, surgery, radiotherapy, and/or other characteristics.[12] Nomogram is a data-based graphic calculating tool in estimating the risk of developing a certain disease based on the AJCC staging system and other critical risk factors correlated with prognosis.[13,14] Various nomogram models have been proposed for RCC, but most are for ccRCC or pRCC.[15–18] For chRCC prognosis prediction, Xie *et al.* analyzed the relation between the clinical and pathological features of Chinese patients and patients' prognosis, and Luzzago *et al.* explored the effect of tumor stage and grade on CSS of ccRCC and non-ccRCC patients.[19,20] However, there are no effective and reliable nomograms available to the prognostic prediction of chRCC patients.

The current study adopted the data of chRCC patients diagnosed between 2004 and 2015 from SEER database, aiming to develop and test the performance of the nomograms in prognostic performance of OS and CSS.

Materials and methods

Patient population and the source of data

We searched SEER database, which is a population-based cancer database whose population consists of 67% of Hawaiian/Pacific Islanders, half of Asians, 44% of both Alaska Natives and American Indians, 38% of Hispanics, and 26% of African-Americans. In our study, the data of 6933 chRCC patients recorded from 2004 to 2015 in SEER were included in this research. The inclusion criteria were specifically described as follows: those patients with only kidney malignancy; patients at least 18 years old; patients with known survival time; patients with known AJCC, T, or N stage. Patients who failed to meet one of these criteria were excluded. A final 4835 chRCC patients were included for OS and CSS analyses, resulting in 60% (2901 chRCC patients) of the subjects in the training group and 40% (1934 chRCC patients) in the validation group.

Statistical analysis

To identify the significant characteristics and OS- and CSS-related independent prognostic factors, the information of gender, race, marital status, age, grade, stage (T/N/M), AJCC and SEER stages, histories of chemotherapy, radiotherapy, and surgery of the subjects in the training group were extracted for multivariate and univariate Cox regression analyses. To further evaluate the effects of each factor on survival risks, we applied the hazard ratios (HR) and 95% confidence interval (CI). The significant variables of $P < 0.05$ were determined for developing the nomograms. $HR > 1$, $HR < 1$, and $HR = 1$ indicated increased degree of risk, decreased degree of risk, and no effect, respectively, as compared with the reference group.

In this research, two nomograms were developed by R software. The nomogram for OS included the variables of marital status, race, age, tumor grade, AJCC and N stages, surgery, radiotherapy and chemotherapy histories, while another nomogram with the variables of age, grade, N and SEER stages, surgery, radiotherapy, and chemotherapy histories was developed for CSS. The receiver operating characteristic (ROC) curves of the two nomograms were drawn by the MedCalc software (version 15.2.0) and the areas under the curves, which refer to AUC, were calculated. Calibration curves and concordance (C-index) were also employed to evaluate the performance of the nomograms in the prognostic prediction of patients' survival time. We calibrated the nomograms for three-year and five-year CSS and OS with data from the validation cohort. Statistically, value of the C-index varied between 0.5 (defined as "non-discrimination") to 1 (defined as "perfect discrimination"), with a higher value of C-index correlating with a higher accuracy of the prognostic model.

In addition, based on the clinical outcome, the accuracy of the nomogram models in prognostic prediction was examined by the decision curve analysis (DCA) for net benefit assessment.

The data were processed by SPSS 16.0 (Chicago, USA), R version 3.5.3 (http://www.r-project.org/), and R packages ("rms"), formula, ggplot2, survival, and also Remote Direct Memory Access (RDMA). A $P < 0.05$ (two-sided) signified that the statistics showed significant difference.

Results

Baseline characteristics of patients

In this study, a total of 4835 eligible chRCC patients recorded between 2004 and 2015 in the SEER were recruited into a primary cohort, with 2901 patients in training group and 1934 patients in validation group (see Table 1). By analysis, number of female chRCC patients nearly equaled to the number of male patients (2236 vs. 2599). And almost 50% of the 4835 subjects aged younger than 58 years old (2398, 49.6%) and 80.1% of the patients was white population. The most patients both in the two cohorts had AJCC stage I, T1N0M0 stage, and localized SEER stage. Among the eligible patients, 2969 (61.4%) of the patients received total nephrectomy, 0.6% of them received radiotherapy, and 1.7% were treated by chemotherapy. In addition, the best

Table 1. Baseline demographic and clinical characteristics.

Variables	All patients *n* (%)	Training set *n* (%)	Validation set *n* (%)
Total	4835	2901 (60.0)	1934 (40.0)
Gender			
Female	2236 (46.2)	1352 (46.6)	884 (45.7)
Male	2599 (53.8)	1549 (53.4)	1050 (54.3)
Age, years			
<58	2398 (49.6)	148 (49.2)	970 (50.2)
58–75	1924 (39.8)	1153 (39.7)	771 (39.9)
>75	513 (10.6)	320 (11.0)	193 (10.0)
Marital status			
Married	3014 (62.3)	1817 (62.6)	1197 (61.9)
Unmarried	1563 (32.3)	937 (32.3)	626 (32.4)
Unknown	258 (5.3)	147 (5.1)	111 (5.7)
Race			
White	3872 (80.1)	2326 (80.2)	1546 (79.9)
Black	603 (12.5)	363 (12.5)	240 (12.4)
Others	360 (7.4)	212 (7.3)	148 (7.7)
Grade			
Grade I	244 (5.0)	145 (5.0)	99 (5.1)
Grade II	1719 (35.6)	1030 (35.5)	689 (35.6)
Grade III	1007 (20.8)	598 (20.6)	409 (21.1)
Grade IV	187 (3.9)	123 (4.2)	64 (3.3)
Unknown	1678 (34.7)	1005 (34.6)	673 (34.8)
AJCC stage			
I	3157 (65.3)	1866 (64.3)	1303 (67.4)
II	953 (19.7)	615 (21.2)	364 (18.8)
III	608 (12.6)	404 (13.9)	228 (11.8)
IV	117 (2.4)	16 (0.6)	39 (2.0)
T stage			
T1	3179 (65.7)	1866 (64.3)	1313 (67.9)
T2	989 (20.5)	615 (21.2)	374 (19.3)
T3	644 (13.3)	404 (13.9)	240 (12.4)
T4	23 (0.5)	16 (0.6)	7 (0.4)
N stage			
N0	4751 (98.3)	2850 (98.2)	1901 (98.3)
N1	48 (1.0)	31 (1.1)	17 (0.9)
N2	36 (0.7)	20 (0.7)	16 (0.8)
M stage			
M0	4753 (98.3)	2845 (98.1)	1908 (98.7)
M1	82 (1.7)	56 (1.9)	26 (1.3)
SEER stage			
Localized	4110 (85.0)	2443 (84.2)	1667 (86.2)
Regional	637 (13.2)	399 (13.8)	238 (12.3)
Distant	88 (1.8)	59 (2.0)	29 (1.5)
Surgery			
No/unknown	93 (1.9)	65 (2.2)	28 (1.4)
Partial nephrectomy	1773 (36.7)	1026 (35.4)	747 (38.6)
Total nephrectomy	2969 (61.4)	1810 (62.4)	1159 (59.9)
Radiotherapy			
Yes	31 (0.6)	15 (0.5)	16 (0.8)
No/unknown	4804 (99.4)	2886 (99.5)	1918 (99.2)
Chemotherapy			
Yes	81 (1.7)	48 (1.7)	33 (1.7)
No/unknown	4754 (98.3)	2853 (98.3)	1901 (98.3)

AJCC: American Joint Committee on Cancer; SEER: surveillance, epidemiology, and end results.

cut-off age was estimated to be 58 years old by X-tile software (Supplementary Figure 1).

Univariate and multivariate Cox regression in the training set

This study conducted univariate Cox regression for determining the characteristics significantly correlated with patients' OS and CSS. From Table 2, it could be observed that all the characteristics were significant for OS except for gender, whereas age, tumor grade, AJCC, T/N/M, and SEER stages, histories of chemotherapy, radiotherapy, and surgery were significant factors for CSS (see Table 3). Next, the analysis of multivariate Cox regression demonstrated that the independent parameters for OS were histories of

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

Variables	No. of patients	Univariate analysis *P* value	Multivariate analysis[a] HR (95% CI)	*P* value
Gender		0.883		
Female	1352			
Male	1549			
Age, years		<0.001		
<58	148		Reference	
58–75	1153		3.069 (2.297–4.102)	<0.001
>75	320		6.545 (4.758–9.003)	<0.001
Marital status		<0.001		
Married	1817		Reference	
Unmarried	937		1.619 (1.283–2.042)	<0.001
Unknown	147		1.060 (0.601–1.869)	0.840
Race		0.003		
White	2326		Reference	
Black	363		1.594 (1.180–2.154)	0.002
Others	212		0.582 (0.324–1.044)	0.069
Grade		<0.001		
Grade I	145		Reference	
Grade II	1030		0.737 (0.440–1.234)	0.245
Grade III	598		0.713 (0.415–1.226)	0.222
Grade IV	123		1.534 (0.833–2.824)	0.169
Unknown	1005		0.823 (0.490–1.382)	0.462
AJCC stage		<0.001		
I	1866		Reference	
II	615		0.713 (0.491–1.035)	0.076
III	404		1.820 (1.351–2.451)	<0.001
IV	16		4.313 (2.692–6.909)	<0.001
T stage		<0.001		
T1	1866		Reference	
T2	615		–	0.743
T3	404		–	0.471
T4	16		–	0.723
N stage		<0.001		
N0	2850		Reference	
N1	31		2.248 (1.271–3.976)	0.005
N2	20		2.579 (1.359–4.895)	0.004
M stage		<0.001		
M0	2845		Reference	
M1	56		–	0.498
SEER stage		<0.001		
Localized	2443		Reference	
Regional	399		–	0.668
Distant	59		–	0.668
Surgery		<0.001		
No/unknown	65		Reference	
Partial nephrectomy	1026		0.215 (0.124–0.371)	<0.001
Total nephrectomy	1810		0.382 (0.235–0.619)	<0.001
Radiotherapy		<0.001		
Yes	15		Reference	
No/unknown	2886		0.327 (0.168–0.639)	0.001
Chemotherapy		<0.001		
Yes	48		Reference	
No/unknown	2853		0.450 (0.272–0.744)	0.002

[a]Model was adjusted by age, marital status, race, grade, AJCC stage, TNM stage, SEER stage, surgery, radiotherapy, and chemotherapy. OS: overall survival; HR: hazard ratio; CI: confidence intervals; AJCC: American Joint Committee on Cancer; SEER: surveillance, epidemiology, and end results.

chemotherapy, radiotherapy, and surgery, age, marital status, race, grade, AJCC and N stages, while the individual factors for CSS were histories of chemotherapy, radiotherapy, and surgery, age, grade, and N and SEER stages (Tables 2 and 3).

Prognostic nomograms for predicting CSS and OS

To evaluate the OS and CSS for three and five years, we developed two nomograms in terms of the independent characteristics screened from the multivariate Cox

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

Variables	No. of patients	Univariate analysis *P* value	Multivariate analysis[a]	
			HR (95% CI)	*P* value
Gender		0.273		
Female	1352			
Male	1549			
Age, years		<0.001		
<58	148		Reference	
58–75	1153		2.111 (1.336–3.337)	0.001
>75	320		2.949 (1.717–5.03)	<0.001
Marital status		0.186		
Married	1817			
Unmarried	937			
Unknown	147			
Race		0.643		
White	2326			
Black	363			
Others	212			
Grade		<0.001		
Grade I	145		Reference	
Grade II	1030		0.743 (0.257–2.143)	0.582
Grade III	598		0.981 (0.340–2.828)	0.971
Grade IV	123		1.852 (0.611–5.609)	0.276
Unknown	1005		0.689 (0.239–1.989)	0.491
AJCC stage		<0.001		
I	1866		Reference	
II	615		–	0.784
III	404		–	0.862
IV	16		–	0.862
T stage		<0.001		
T1	1866		Reference	
T2	615		–	0.342
T3	404		–	0.902
T4	16		–	0.689
N stage		<0.001		
N0	2850		Reference	
N1	31		3.146 (1.675–5.907)	<0.001
N2	20		3.032 (1.454–6.323)	0.003
M stage		<0.001		
M0	2845		Reference	
M1	56		–	0.635
SEER stage		<0.001		
Localized	2443		Reference	
Regional	399		5.762 (3.572–9.295)	<0.001
Distant	59		15.166 (8.065–28.516)	<0.001
Surgery		<0.001		
No/unknown	65		Reference	
Partial nephrectomy	1026		0.033 (0.010–0.111)	<0.001
Total nephrectomy	1810		0.191 (0.095–0.387)	<0.001
Radiotherapy		<0.001		
Yes	15		Reference	
No/unknown	2886		0.459 (0.219–0.962)	0.039
Chemotherapy		<0.001		
Yes	48		Reference	
No/unknown	2853		0.413 (0.228–0.747)	0.003

[a]Model was adjusted by age, grade, AJCC stage, TNM stage, SEER stage, surgery, radiotherapy, and chemotherapy.
CSS: cancer-specific survival; HR: hazard ratio; CI: confidence intervals; AJCC: American Joint Committee on Cancer; SEER: surveillance, epidemiology, and end results.

regression analysis (Figure 1). A criterion was set for each variable. Then, we obtained the three-year and five-year CSS and OS by calculating the scores of each variable overlapping with the total point model.

ROC curves for prognosis and calibration of the nomograms

The three-year and five-year AUCs of OS were 0.854 and 0.828 in the training group, and 0.805 and 0.797 in the

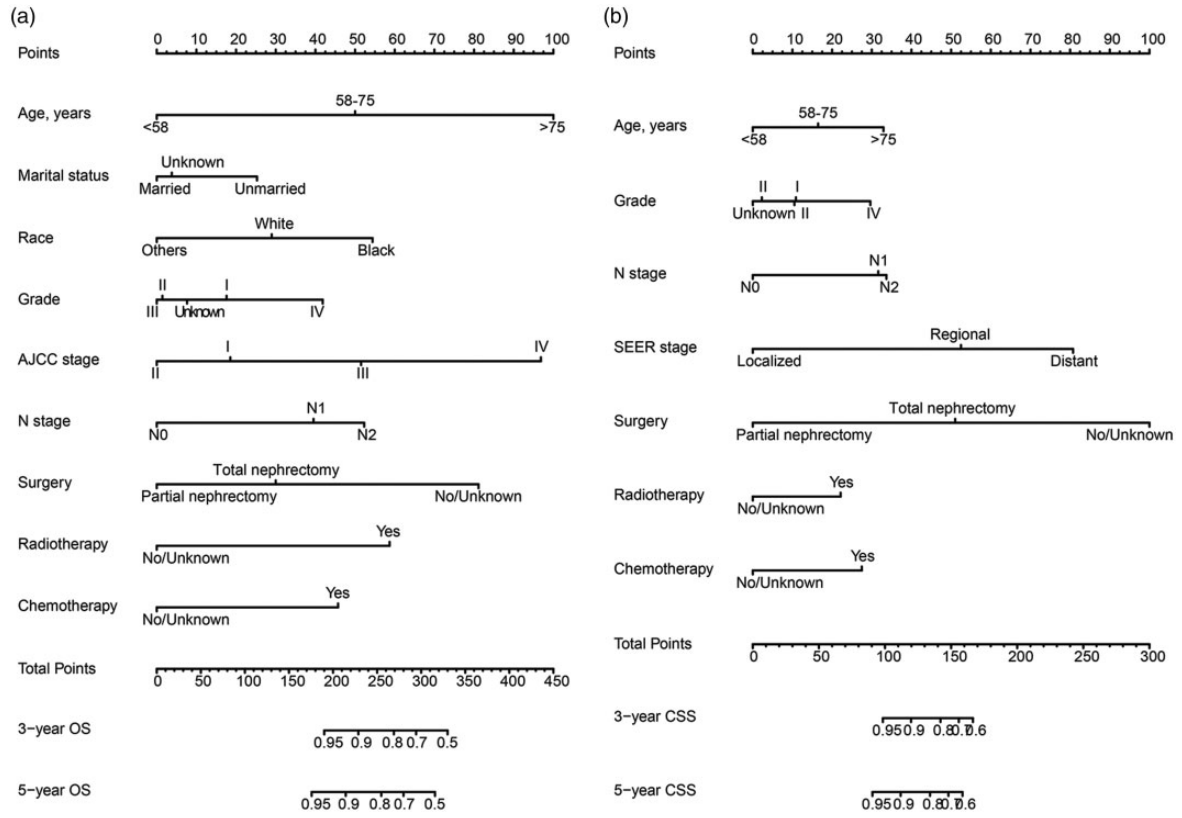

Figure 1. Two nomograms for the prognostic prediction of three-year and five-year overall survival (OS) and cancer-specific survival (CSS) rate of chRCC. (a) OS rate; (b) CSS rate.

validation group. The three-year and five-year AUCs of CSS were 0.900 and 0.878 in the validation group, and 0.920 and 0.912 in the training group (Figure 2). In addition, the three-year and five-year OS and CSS nomograms of the two cohorts were calibrated. The data revealed that the calibration curves closely fitted the AUC curves, indicating a high uniformity between the actual observation model and the prediction model in the training and validation group (Figures 5 and 6).

Comparison of AJCC TNM and SEER staging system with the two nomograms

The prognosis prediction of the two nomograms was compared with SEER and AJCC TNM staging system. For OS, the C-index of the nomograms in the validation group and training group was 0.790 and 0.821, showing a greater predictive performance compared with AJCC TNM stage (0.663; 0.636) and SEER stage (0.644; 0.637). For CSS, the C-index values for the nomogram were 0.902 in the training group and 0.868 in the validation group, showing a similar trend to OS. In comparison with AJCC TNM and SEER staging system, the C-indexes were 0.831 and 0.840 in the training set, and 0.817 and 0.805 in the validation set (Table 4). As for OS, the AUCs of the nomogram, TNM stage, and SEER stage were 0.818, 0.649, and 0.626 in the training cohort, and 0.807, 0.613, and 0.606 in the validation cohort. As for CSS, the AUCs of the nomogram, TNM stage, and SEER stage were 0.895, 0.822, and 0.807 in the training cohort, and 0.853, 0.822, and 0.781 in the validation cohort (Figure 3 and Table 5).

The clinical validity of the two nomograms developed in this study was assessed by applying decision curve analysis (DCA). From the plotted DCA curves, it can be seen that the nomograms showed more clinical net benefits than the classic AJCC TNM and SEER stage (Figure 4), indicating that the nomograms were applicable to the prognosis prediction of three-year and five-year CSS and OS.

Discussion

Chromophobe renal cell carcinoma (chRCC), a subtype of RCC,[21] is derived from the distal nephron, with the third highest incidence, and is histologically and molecularly different from the other two main subtypes papillary renal cell carcinoma (pRCC) and clear cell ranal cell carcinoma (ccRCC), which arise from proximal nephron.[22] Currently, there have been no publically agreed independent prognostic factors of chRCC. The number of studies associated with the prognostic factors for chRCC is limited, due to small sample size and low incidence of cancer-specific clinical events.[19] Here, we applied the data recorded between 2004 and 2015 from SEER database to identify the individual characteristics for chRCC. A total of 4835 chRCC patients were enrolled, which composed a sample size relatively large enough for developing and validating the performance of the nomograms in the prognostic prediction of CSS and OS to the patients.

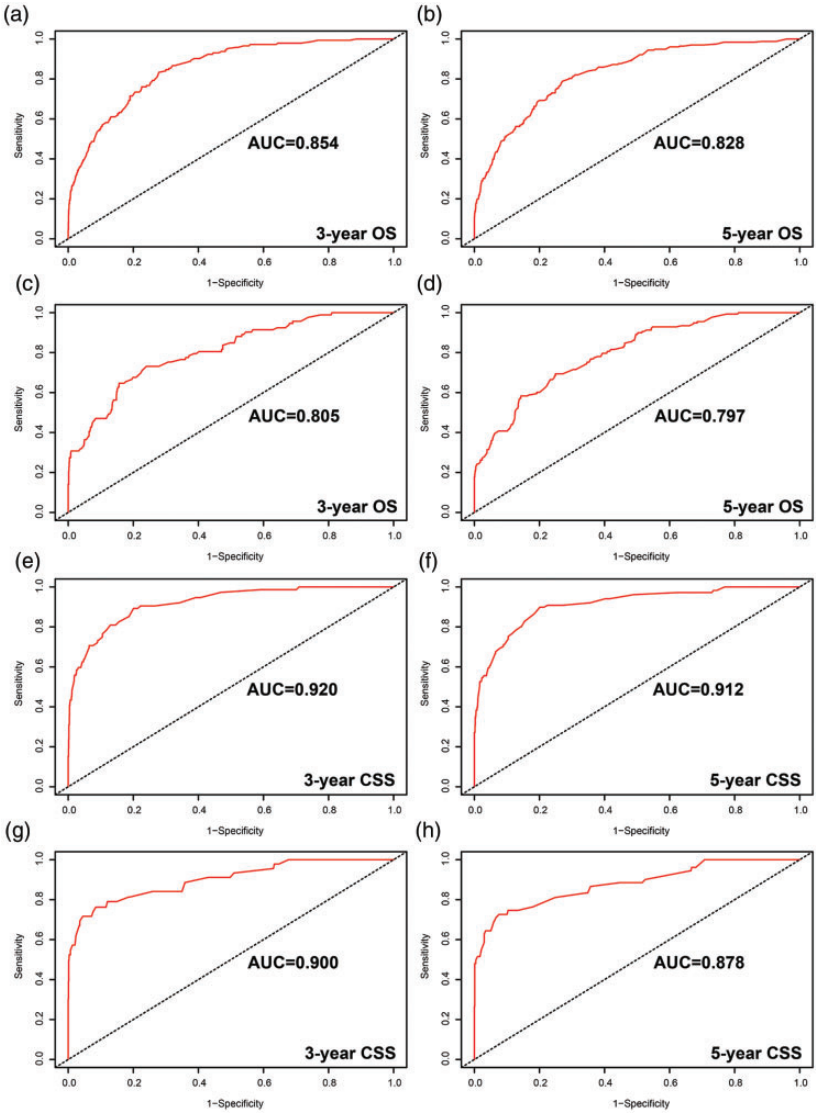

Figure 2. Receiver operating characteristic (ROC) curves of the two nomograms in the training group and validation group. (a, b, e, f), three-year and five-year OS and CSS in the training group; (c, d, g, h), three-year and five-year OS and CSS in the validation group. (A color version of this figure is available in the online journal.)

Table 4. Comparison of C-indexes between the nomogram, TNM, and SEER stages in chromophobe renal cell carcinoma patients.

	Training set		Validation set	
Characteristics	**HR**	**95% CI**	**HR**	**95% CI**
OS				
Nomogram	0.821	0.797–0.845	0.790	0.756–0.824
TNM stage	0.663	0.630–0.696	0.636	0.589–0.683
SEER stage	0.644	0.614–0.674	0.637	0.598–0.676
CSS				
Nomogram	0.902	0.873–0.931	0.868	0.817–0.919
TNM stage	0.831	0.784–0.878	0.840	0.778–0.902
SEER stage	0.817	0.772–0.862	0.805	0.742–0.868

HR: hazard ratio; CI: confidence interval; SEER: surveillance, epidemiology, and end results.

Xie *et al.* have previously demonstrated that N stage and grade are significant factors in the survival risks of chRCC patients, which are similar to our findings.[19] In this study, we observed that patients aged older than 58 years old seemed to develop a worse OS and CSS rate with the increase of age. For OS, the prognosis of white and single patients was worse compared with the married and black ones. For both OS and CSS, histories of chemotherapy and

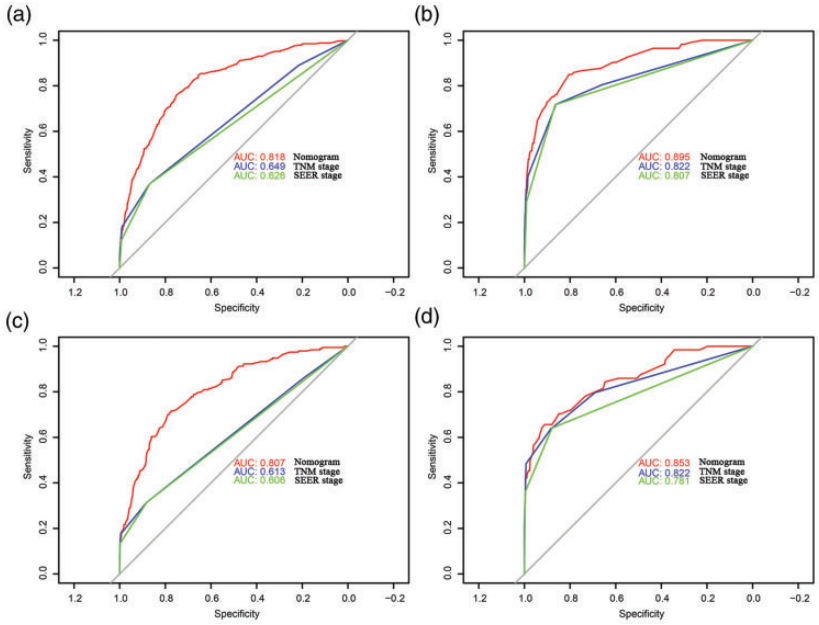

Figure 3. Comparisons of the area under the curve (AUC) between the nomograms, TNM and SEER stage in predicting the OS and CSS of chRCC patients. (a–b), OS in the training group; (c–d), CSS in the validation group. (A color version of this figure is available in the online journal.)

Table 5. Comparison of area under the curve (AUC) between the nomogram, TNM, and SEER stages in chromophobe renal cell carcinoma patients.

	Training set		Validation set	
Characteristics	**AUC**	**95% CI**	**AUC**	**95% CI**
OS				
Nomogram	0.818	0.794–0.843	0.807	0.775–0.840
TNM stage	0.649	0.615–0.684	0.613	0.566–0.659
SEER stage	0.626	0.590–0.661	0.606	0.559–0.652
CSS				
Nomogram	0.895	0.863–0.927	0.853	0.800–0.906
TNM stage	0.822	0.773–0.872	0.822	0.756–0.889
SEER stage	0.807	0.757–0.858	0.781	0.707–0.854

AUC: area under the curve; CI: confidence interval; SEER: surveillance, epidemiology, and end results.

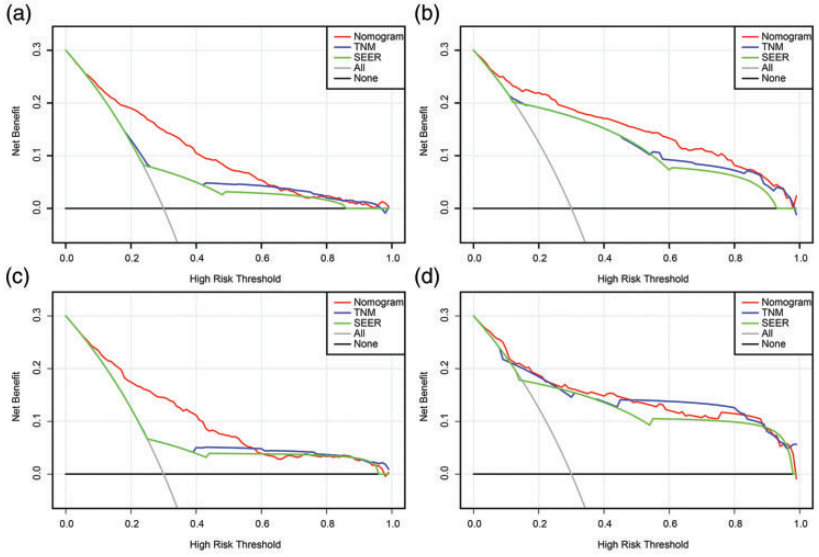

Figure 4. Decision curve analysis (DCA) for the predictive performance of the two developed nomograms in chRCC. (a–b), OS and CSS in the training group; (c–d), OS and CSS in the validation group. (A color version of this figure is available in the online journal.)

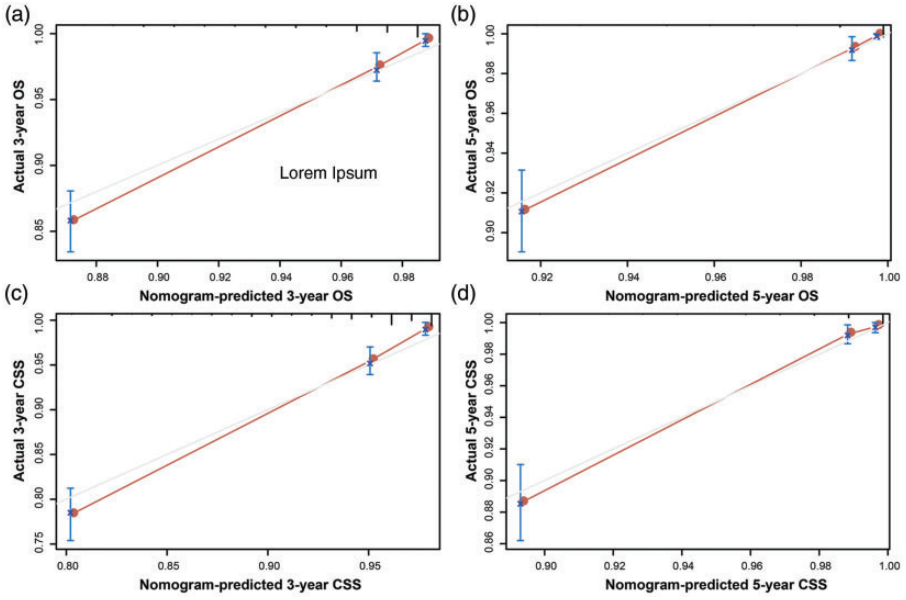

Figure 5. Calibration curves for examining the effects of nomograms for predicting the three-year and five-year OS and CSS in the training group. (a–b), calibration curve of three-year and five-year OS in the training group; (c–d), calibration curve of three-year and five-year CSS in the training group. (A color version of this figure is available in the online journal.)

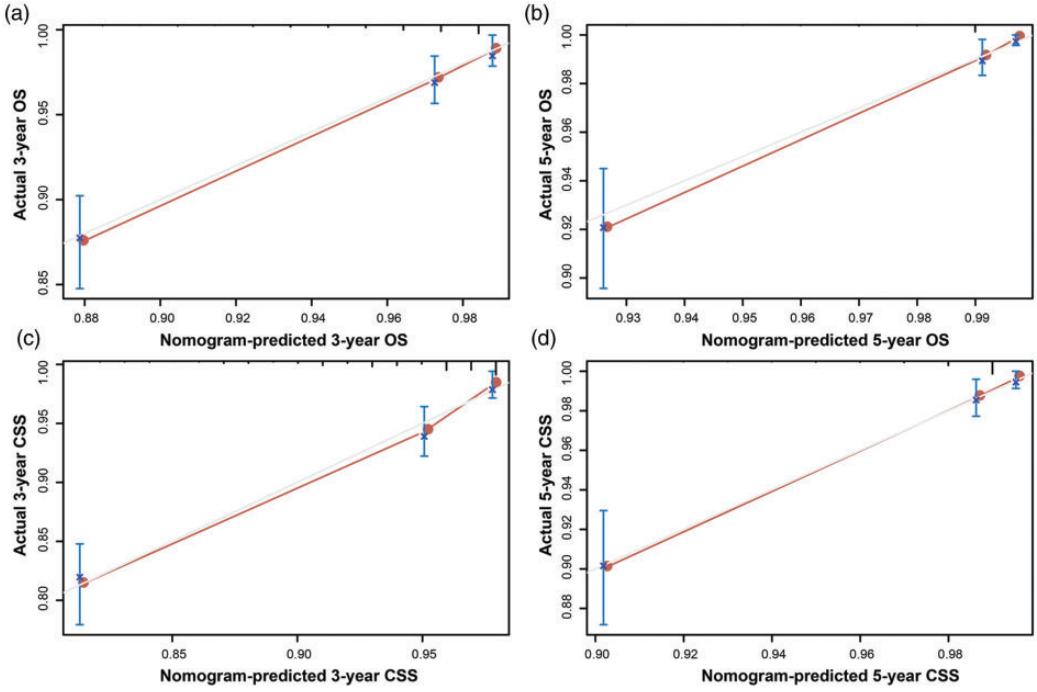

Figure 6. Calibration curves for analyzing the effects of nomograms for predicting the three-year and five-year OS and CSS in the validation group. (a–b), calibration curve of three-year and five-year OS in the validation group; (c–d), calibration curve of three-year and five-year CSS in the validation cohort. (A color version of this figure is available in the online journal.)

radiotherapy were protective factors to patients with metastatic or advanced chRCC.

This study applied American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system, which is regarded as the most frequently used and widely recognized worldwide staging system for various cancers.[23] In RCC staging, TNM staging system covers some important anatomic prognostic parameters, such as distant sites (M), metastasis to regional lymph nodes (N), or Gerota's fascia (T), tumor size, invasion into ipsilateral adrenal gland, extension into veins or perinephric tissues.[24] Nowadays, in the newest eighth edition, the AJCC has enrolled nonanatomic prognostic parameters and biomarkers in identifying the prognostic stage.[25]

Nomogram is a graphic tool mainly covering social, biological, and clinical variables to predict individual risks of

particular events.[26,27] The data from our Cox regression analysis revealed that the independent parameters for OS were histories of surgery chemotherapy and radiotherapy, age, marital status, race, grade, AJCC and N stages, while the individual factors for CSS were histories of surgery chemotherapy and radiotherapy, N and SEER stages, age and tumor grade. Subsequently, the independent factors were enrolled to build nomograms to predict the three-year and five-year CSS and OS of chRCC patients. Here, we observed that the nomograms showed significantly high performance in the validation and training groups.

According to the ROC curves and calibration curves, the nomograms demonstrated a high performance in predicting OS and CSS in both the training and validation groups. When compared with the AJCC TNM and SEER, the nomograms were more accurate in analyzing OS and CSS, according to the C-indexes and DCA curves. These results were consistent by the evaluation of the nomograms and practical observation.

In the prediction of total incidence and OS of RCC patients, studies have increasingly recruited more useful characteristics such as ethnicity, surgery, lymph node density, and marital status.[28–31] This study first established and validated two reliable nomograms to predict the CSS and OS of chRCC patients recorded between 2004 and 2015. A total of 4835 patients, which far exceeded the sample size of the most previous studies conducted on identifying the prognostic factors, for example, Xie's study [19] and Silafy's study.[32] The nomograms constructed in this study showed its accuracy, effectiveness, and potentials for replacing the traditional AJCC TNM staging system in the prognostic prediction of the CSS and OS to chRCC patients.

There are still some limitations in this study. For example, SEER database lacked the laboratory test indicators. Also, the patients mainly came from a retrospective cohort without detailed information on their radiotherapy and chemotherapy. Moreover, the patient race was limited to black and white populations.

Conclusions

This study is the first research that developed and validated the performance of two nomograms for the prognostic prediction of the three-year and five-year CSS and OS to chRCC patients based on independent prognostic parameters, according to the data recorded from 2004 to 2015 in SEER database. The predictive model could be included in the standardized evaluation of individual survival of a chRCC patient.

AUTHORS' CONTRIBUTIONS

All authors participated equally in the design, interpretation of the studies, data analyses as well as in the review of the manuscript; CYC, XYG, RL, DZZ, and MYS conducted the experiments, CYC and XYG, GBZ analyzed the data, CYC wrote the manuscript, and JQH contributed to the conception of the present research and was responsible for approving the version before publication. The final manuscript was carefully read and approved by all the authors.

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DATA AVAILABILITY

The analyzed data sets of this research are available from the corresponding author of this research on reasonable demand.

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SUPPLEMENTAL MATERIAL

Supplementary material for this article is available online.

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