Original Article

Prognostic nomogram for patients with lung metastatic renal cell carcinoma: a SEER-based study

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Background: Our study aimed to establish a clinically practical and reliable prognostic nomogram based on the important prognostic factors to predict the prognosis of patients with lung metastatic renal cell carcinoma (RCC).

Methods: Clinical data of patients with lung metastatic RCC between 2010 and 2015 were collected from the SEER database. Prognostic nomogram was established using R software to predict the OS and CSS probability for individual patients. Consistency index (C-index), calibration curve and decision curve analysis (DCA) were used to assess the predictive performance of the nomogram, and to calibrated the nomogram for 1-, 2-, and 3-year cancer-specific survival (CSS) and overall survival (OS).

Results: 1,563 patients were enrolled in this study. All patients were randomly divided into the primary cohort (937) and the validation cohort (626). Multivariate Cox regression showed that age, histology, N-stage, T-stage, surgery and radiotherapy were independent risk factor of OS, and histology, N-stage, T-stage, surgery were CSS related factors in patients with lung metastatic RCC in the primary cohort. The C-index of the nomogram OS was 0.662 and the C-index of CSS was 0.658 in the primary cohort. In the validation cohort, the C-index of the nomogram CSS and OS were 0.685 and 0.694, respectively. Moreover, the calibration curves showed good consistency between nomogram predictions and actual 1-, 2-, and 3-year OS and CSS rates in the primary and external verification cohorts.

Conclusions: The prognostic nomogram constructed in this study can provide an individualized treatment and risk assessment for survival in patients with lung metastatic RCC.

Keywords: Renal cell carcinoma (RCC); lung metastatic; prognostic nomogram; SEER

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Introduction

Renal cell carcinoma (RCC) was the most common renal parenchyma malignant that originated from the kidney, accounting for 80–85% of renal tumors and 2–3% of systemic malignant malignancies (1). According to statistics, the number of newly diagnosed cases of RCC worldwide in 2018 was 403,262, and the number of deaths were approximately 175,100 (2). Due to the lack of reliable diagnostic biomarkers and concealed early clinical symptoms of RCC, 20–30% of patients were in the advanced stage at the first visit (3,4). Even after surgical treatment with early-stage RCC, 30% of the patients progressed to metastatic RCC eventually (5,6).

RCC with distant metastasis at the time of diagnosis or metastasis after operation was collectively referred to as metastatic RCC (RCC). Cytoreductive nephrectomy (CN) was an aggressive treatment modality for patients with metastatic RCC. Metastatic RCC had a high mortality rate with a 5-year survival rate of approximately 10% and a median survival time of 13.9 months among patients treated with CN (7,8). In RCC organ metastasis, lung metastasis were common, followed by bone, but liver and brain metastasis remained relatively rare (9). Abdel-Rahman analysis of 5,992 patients with organ metastatic RCC found that the prognosis of bone metastasis was the best and while liver metastasis had the worst prognosis (10). The treatment of metastatic RCC was still a major clinical challenge. Therefore, it is necessary to further study the predictors of long-term survival in patients with metastatic RCC

At present, some studies had shown that sex, age, tumor size and other clinicopathological factors may affect the prognosis of patients with RCC. But there were still few studies on independent prognostic factors of lung metastatic RCC (11,12). Therefore, a comprehensive prognostic assessment model incorporating a variety of important demographic and clinicopathological variables was necessary. The nomogram based on the regression coefficients of each variable, combines many important prognostic correlates to more accurately predict individual patient survival rates (13).

In this study, we obtained prognostic factors and demographic features of patients with lung metastatic RCC from the Surveillance, Epidemiology, and End Results (SEER) database. We first used multivariate Cox regression analysis to identify independent prognostic risk factors, and then further constructed and verified the prognostic nomogram for patients with lung metastatic RCC based on the above results.

We present the following article in accordance with the TRIPOD reporting checklist (available at http://dx.doi.org/10.21037/apm-20-1488).

Methods

Patients selection

In this study, all patients were extracted from the National Cancer Institute-funded SEER database. The SEER database contains approximately 28% US population, including patient demographic and clinical information, such as diagnosis year, sex, age, race, marital status, insurance, primary site, tumor grade, Tumor-Node-Metastasis (TNM) stage, histological type, treatment methods, cause of death and survival time (14). In addition, SEER database information on lung, liver, bone, and brain organ metastases is presented only for data from 2010 onwards. This study used the SEER*Stat software (version 8.3.6). Using the "Primary Site-labeled" variable, we identified 100,813 RCC patients between January 1, 2010 and December 31, 2016.

Exclusion criteria in our study were as follows (*Figure 1*): (I) not only one primary tumor (n=29,398); (II) unknown survival time (n=848); (III) diagnosed at 2016 (n=11,250); (IV) without or with unknown lung metastases (n=53,560); (V) with bone metastases (n=1,954); (VI) with brain metastases (n=428); (VII) with liver metastases (n=684); (VIII) T0 or T stage unknown (n=508); (IX) N stage unknown (n=141); (X) not systemic therapy (n=459); (XI) tumor size unknown; (XII) patients under 18 years (n=1).

Cases, which were diagnosed after January 1, 2016 were excluded to make sure that all cases had a longer than 1-year survival status observation at the last follow-up in December 2016. Finally, we confirmed the data of 1,563 eligible patients diagnosed with lung metastatic RCC. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Study variables

Specific information on age, year of diagnosis, race, sex, tumor T-stage, N-stage, histology, tumor size, chemotherapy, surgery, radiotherapy, survival time and causes of death can be found in the SEER database. The overall survival (OS) time was defined as the time from the date of diagnosis of RCC to the date of death from any cause or the last follow-up visit in December 2016. Deaths from other causes were excluded from the analysis of

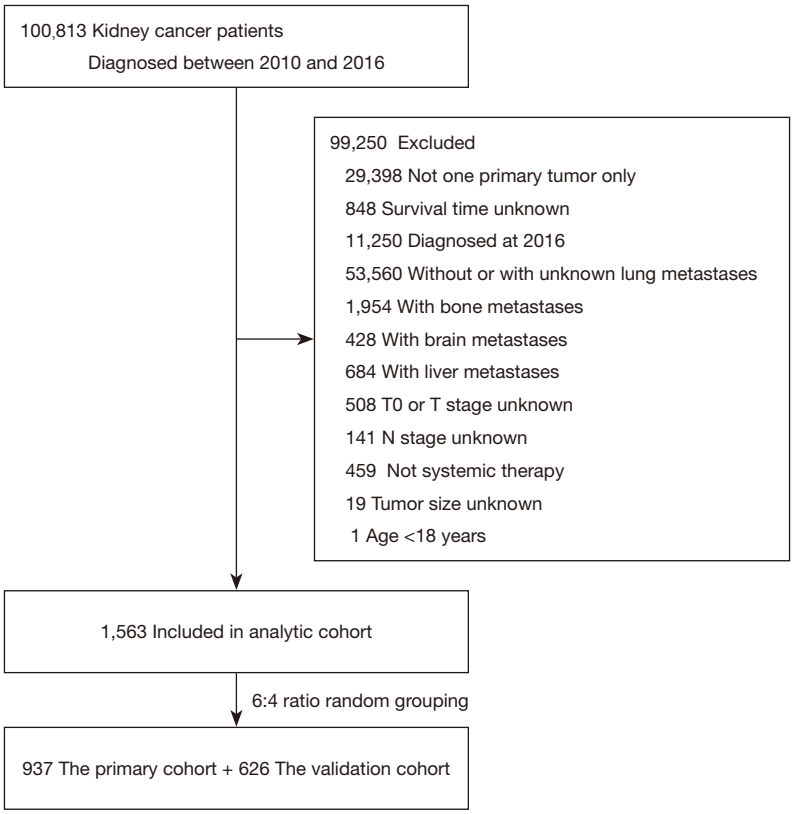

Figure 1 Schematic flowchart of the inclusion and exclusion criteria for this study.

cancer-specific survival (CSS).

Statistical analysis

According to the optimal cutoff value generated by the X-tile software (Version 3.6.1), the age was trivially stratified (<65 years, 65–74 years and >74 years; Figure S1). By RStudio software, all patients were randomized in a ratio of 6:4 into a primary cohort and validation cohort. In the entire cohort, Kaplan-Meier curves were used to detect variables related to OS and CSS of lung metastatic RCC and differences between the curves were analyzed by the log-rank test. We used univariate and multivariate Cox models to analyze prognostic factors associated with lung metastasis RCC and to measure hazard ratios (HR) and 95% confidence intervals (CI).

Based on the results of the multivariate Cox proportional hazard regression model, the RStudio software was used to construct prognostic nomograms of RCC patients with lung metastasis to predict the OS and CSS probability of each patient. In addition, the calibration curves and consistency index (C-index) were used to evaluate the predictive performance of the nomograms, and to calibrate the predictive ability of the nomograms for 1-, 2- and 3-year OS and CSS. The value of C-index statistic ranged from 0.5 (non-discrimination) to 1 (perfect discrimination), and a higher value means a better prognostic model. All these assessments were performed by bootstrap with 1,000 resamples. Since there is no direct clinical explanation for the C-index, we analyzed the decision curve analysis (DCA), a new method for evaluating predictive models for net benefit assessment in terms of clinical outcomes (15). SPSS software (version 20.0) and RStudio software (Version 1.2.5033) were used for all statistical analyses. A P value of <0.05 (two-sided) was considered statistically significant.

Results

Demographic and clinicopathologic characteristics

From 2010 to 2015, a total of 1,563 eligible lung metastatic RCC patients were included in our study cohort, of which the primary cohort included 937 patients and the validation cohort included 626 patients. *Table 1* showed the clinical

Table 1 Demographic and clinicopathologic characteristics in patients with lung metastatic RCC

Characteristic	Total, No. (%)	The primary cohort, No. (%)	The validation cohort, No. (%)	P
Total	1,563	937 (59.9)	626 (40.1)	
Year of diagnosis				0.156
2010	211 (13.5)	130 (13.9)	81 (12.9)	
2011	260 (16.6)	172 (18.4)	88 (14.1)	
2012	259 (16.6)	141 (15.0)	118 (18.8)	
2013	265 (17.0)	155 (16.5)	110 (17.6)	
2014	284 (18.2)	168 (17.9)	116 (18.5)	
2015	284 (18.2)	171 (18.2)	113 (18.1)	
Age, years				0.688
<65	938 (60.0)	569 (60.7)	369 (58.9)	
65–74	421 (26.9)	245 (26.1)	176 (28.1)	
>74	204 (13.1)	123 (13.1)	81 (12.9)	
Sex				0.304
Male	1,121 (71.7)	681 (72.7)	440 (70.3)	
Female	442 (28.3)	256 (27.3)	186 (29.7)	
Race				0.765
White	1,294 (82.8)	773 (82.5)	521 (83.2)	
Black	114 (7.3)	72 (7.7)	42 (6.7)	
Others	155 (9.9)	92 (9.8)	63 (10.1)	
Histology				0.336
Clear cell adenocarcinoma	927 (59.3)	560 (59.8)	367 (58.6)	
Renal cell carcinoma	432 (27.6)	246 (26.3)	186 (29.7)	
Papillary adenocarcinoma	61 (3.9)	38 (4.1)	23 (3.7)	
Others	143 (9.1)	93 (9.9)	50 (8.0)	
T stage				0.056
T1	166 (10.6)	84 (9.0)	82 (13.1)	
T2	292 (18.7)	185 (19.7)	107 (17.1)	
T3	975 (62.4)	589 (62.9)	386 (61.7)	
T4	130 (8.3)	79 (8.4)	51 (8.1)	
N stage				0.134
N0	1,053 (67.4)	632 (67.4)	421 (67.3)	
N1	266 (17.0)	148 (15.8)	118 (18.8)	
N2	244 (15.6)	157 (16.8)	87 (13.9)	
Tumor size, cm				0.254
≤7	332 (21.2)	190 (20.3)	142 (22.7)	

Table 1 *(continued)*

Table 1 *(continued)*

Characteristic	Total, No. (%)	The primary cohort, No. (%)	The validation cohort, No. (%)	P
>7	1,231 (78.8)	747 (79.7)	484 (77.3)	
Surgery				0.302
Yes	1,126 (72.0)	684 (73.0)	442 (70.6)	
No/Unknown	437 (28.0)	253 (27.0)	184 (29.4)	
Chemotherapy				0.101
Yes	1,054 (67.4)	627 (66.9)	427 (68.2)	
No/Unknown	509 (32.6)	310 (33.1)	199 (31.8)	
Radiotherapy				0.592
Yes	105 (6.7)	55 (5.9)	50 (8.0)	
No/Unknown	1,458 (93.3)	882 (94.1)	576 (92.0)	
Follow-up data (median, months)	15.00	16.00	14.00	
Number of events (OS)	580	342	238	
Number of events (CSS)	453	269	184	
1-year OS rate	60.6%	61.3%	57.2%	
2-year OS rate	39.6%	40.0%	39.0%	
3-year OS rate	26.7%	26.0%	27.6%	
1-year CSS rate	62.3%	63.0%	61.3%	
2-year CSS rate	44.2%	44.7%	43.6%	
3-year CSS rate	30.9%	29.7%	32.7%	

Percentages may not total 100 because of rounding.

and demographic characteristics of RCC patients with lung metastases. There were 1,121 (71.7%) males and 442 (28.3%) females in the entire cohort. The majority of patients were <65 years and white in both cohorts. The most common tumors were clear cell adenocarcinoma, T3 stage, N0 stage and tumor size <7 cm. In the whole cohort, the median follow-up data was 15.00 months, of which 580 patients died and 453 died of RCC. The OS rates of 1-, 2-, and 3-year were 60.6%, 39.6%, and 26.7% (Figure S2A), respectively, and the CSS rates of 1-, 2-, and 3-year were 62.3%, 44.2% and 30.9% (Figure S2B).

Identification of prognostic factors of OS and CSS in lung metastatic RCC patients

Univariate and multivariate Cox regression were used to analyze the prognostic factors associated with OS and CSS in patients with lung metastatic RCC. Univariate Cox regression analysis showed that histology, age at diagnosis, T-stage, N-stage, surgery, chemotherapy and radiotherapy were related factors of OS in patients with lung metastatic RCC in the primary cohort. After multivariate Cox regression analysis, only chemotherapy was not an independent risk factor for OS in patients with lung metastatic RCC (*Table 2*).

And in terms of CSS, in univariate Cox regression analysis the demographic and clinicopathological factors, which were significantly correlated with CSS were diagnostic age, histology, N-stage, T-stage, surgery, chemotherapy and radiotherapy. All the factors identified above were included in the multivariate Cox proportional hazard regression analysis, indicating that histology, N-stage, T-stage and surgery were independent prognostic factors of RCC with lung metastasis RCC, while age,

Table 2 Univariate and multivariate analysis of overall survival (OS) rates in the primary cohort

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age, years				
<65	Reference		Reference	
65–74	1.14 (0.95–1.37)	0.162	1.14 (0.96–1.37)	0.145
>74	1.37 (1.08–1.72)	0.009	1.36 (1.08–1.71)	0.009
Sex				
Male	Reference			
Female	1.08 (0.91–1.28)	0.402		
Race				
White	Reference			
Black	1.17 (0.89–1.55)	0.266		
Others	0.83 (0.64–1.08)	0.161		
Histology				
Clear cell adenocarcinoma	Reference		Reference	
Renal cell carcinoma	1.34 (1.11–1.62)	0.002	1.32 (1.10–1.60)	0.004
Papillary adenocarcinoma	1.59 (1.08–2.35)	0.020	1.63 (1.11–2.40)	0.012
Others	1.83 (1.42–2.37)	<0.001	1.89 (1.47–2.43)	<0.001
T stage				
T1	Reference		Reference	
T2	1.30 (0.87–1.95)	0.255	1.33 (0.97–1.83)	0.080
T3	1.44 (1.00–2.06)	0.049	1.44 (1.07–1.94)	0.015
T4	1.79 (1.16–2.75)	0.008	1.79 (1.24–2.57)	0.002
N stage				
N0	Reference		Reference	
N1	1.56 (1.27–1.93)	<0.001	1.30 (1.04–1.62)	0.019
N2	2.31 (1.90–2.80)	<0.001	1.81 (1.48–2.23)	<0.001
Tumor size, cm				
≤7	Reference			
>7	1.09 (0.90–1.33)	0.367		
Surgery				
Yes	Reference		Reference	
No/Unknown	2.08 (1.77–2.45)	<0.001	1.67 (1.37–2.05)	<0.001
Chemotherapy				
Yes	Reference		Reference	

Table 2 *(continued)*

Table 2 *(continued)*

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
No/Unknown	0.75 (0.64–0.89)	0.001	–	0.985
Radiotherapy				
Yes	Reference		Reference	
No/Unknown	0.65 (0.48–0.88)	0.005	0.71 (0.52–0.95)	0.023

OS, overall survival; [a]Model was adjusted by age at diagnosis, histology, T stage, N stage, surgery, chemotherapy and radiotherapy.

Table 3 Univariate and multivariate analysis of cancer-specific survival (CSS) rates in the primary cohort

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age, years				
<65	Reference		Reference	
65–74	1.25 (1.04–1.50)	0.019	–	0.270
>74	1.27 (1.00–1.62)	0.055	–	0.179
Sex				
Male	Reference			
Female	0.98 (0.90–1.07)	0.679		
Race				
White	Reference			
Black	1.33 (0.99–1.78)	0.055		
Others	0.92 (0.71–1.21)	0.567		
Histology				
Clear cell adenocarcinoma	Reference		Reference	
Renal cell carcinoma	1.70 (1.41–2.04)	<0.001	1.29 (1.06–1.58)	0.012
Papillary adenocarcinoma	1.91 (1.29–2.83)	0.001	1.70 (1.14–2.53)	0.010
Others	2.10 (1.61–2.75)	<0.001	1.69 (1.28–2.23)	<0.001
T stage				
T1	Reference		Reference	
T2	1.20 (0.87–1.67)	0.275	1.28 (0.91–1.78)	0.153
T3	1.08 (0.81–1.45)	0.594	1.37 (1.01–1.87)	0.047
T4	1.92 (1.32–2.80)	0.001	1.77 (1.20–2.60)	0.004
N stage				
N0	Reference		Reference	

Table 3 *(continued)*

Table 3 *(continued)*

Characteristic	OS			
	Univariate analysis		Multivariate analysis[a]	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
N1	1.57 (1.26–1.96)	<0.001	1.29 (1.03–1.63)	0.030
N2	2.43 (1.99–2.97)	<0.001	1.90 (1.54–2.35)	<0.001
Tumor size, cm				
≤7	Reference			
>7	1.09 (0.89–1.33)	0.408		
Surgery				
Yes	Reference		Reference	
No/Unknown	2.08 (1.75–2.47)	<0.001	1.73 (1.40–2.13)	<0.001
Chemotherapy				
Yes	Reference		Reference	
No/Unknown	0.72 (0.60–0.86)	<0.001	–	0.692
Radiotherapy				
Yes	Reference		Reference	
No/Unknown	0.70 (0.51–0.97)	0.033	–	0.131

CSS, cancer-specific survival. [a]Model was adjusted by age at diagnosis, histology, T stage, N stage, surgery, chemotherapy and radiotherapy.

chemotherapy and radiotherapy were not (*Table 3*).

Prognostic nomograms for OS and CSS in patients with lung metastatic RCC

In the primary cohort, combined with the results of multivariate Cox regression analysis of OS and CSS in patients with lung metastatic RCC, we developed and established nomograms of OS and CSS that included all independent variables. *Figure 2* shows the nomogram of the prognosis of 1-, 2- and 3-year OS and CSS.

In the nomogram, the length of the line corresponding to each predictive variable represented its degree of effect on the survival outcome. No matter of the OS or CSS nomograms, surgery scores made the greatest contribution to the survival outcome, followed by chemotherapy, and marital status contributed the least to survival outcomes.

Validation and calibration of the nomograms

We used C-index and DCA curves to compare whether the survival times predicted by the nomograms were consistent with the actual survival times. In the primary cohort, the C-index of the nomogram OS was 0.662 (95% CI: 0.640–0.684) and the C-index of CSS was 0.658 (95% CI: 0.634–0.682). The C-index of the nomogram OS and CSS were 0.694 (95% CI: 0.670–0.719) and 0.685 (95% CI: 0.659–0.711), respectively in the validation cohort. Moreover, DCA curves also showed better clinical utility of the nomogram in both cohorts (*Figure 3*). This result indicated that the prognostic nomogram models we constructed was quite accurate.

Moreover, we calibrated the 1-, 2- and 3-year OS and CSS nomogram of the primary and validation cohorts. In *Figure 4* and *Figure 5*, the calibration curves were close to the perfect curves, which predicts a good consistency between nomogram predictions and the actual observation in the primary and validation cohorts.

Discussion

RCC was one of the common malignant tumors of the

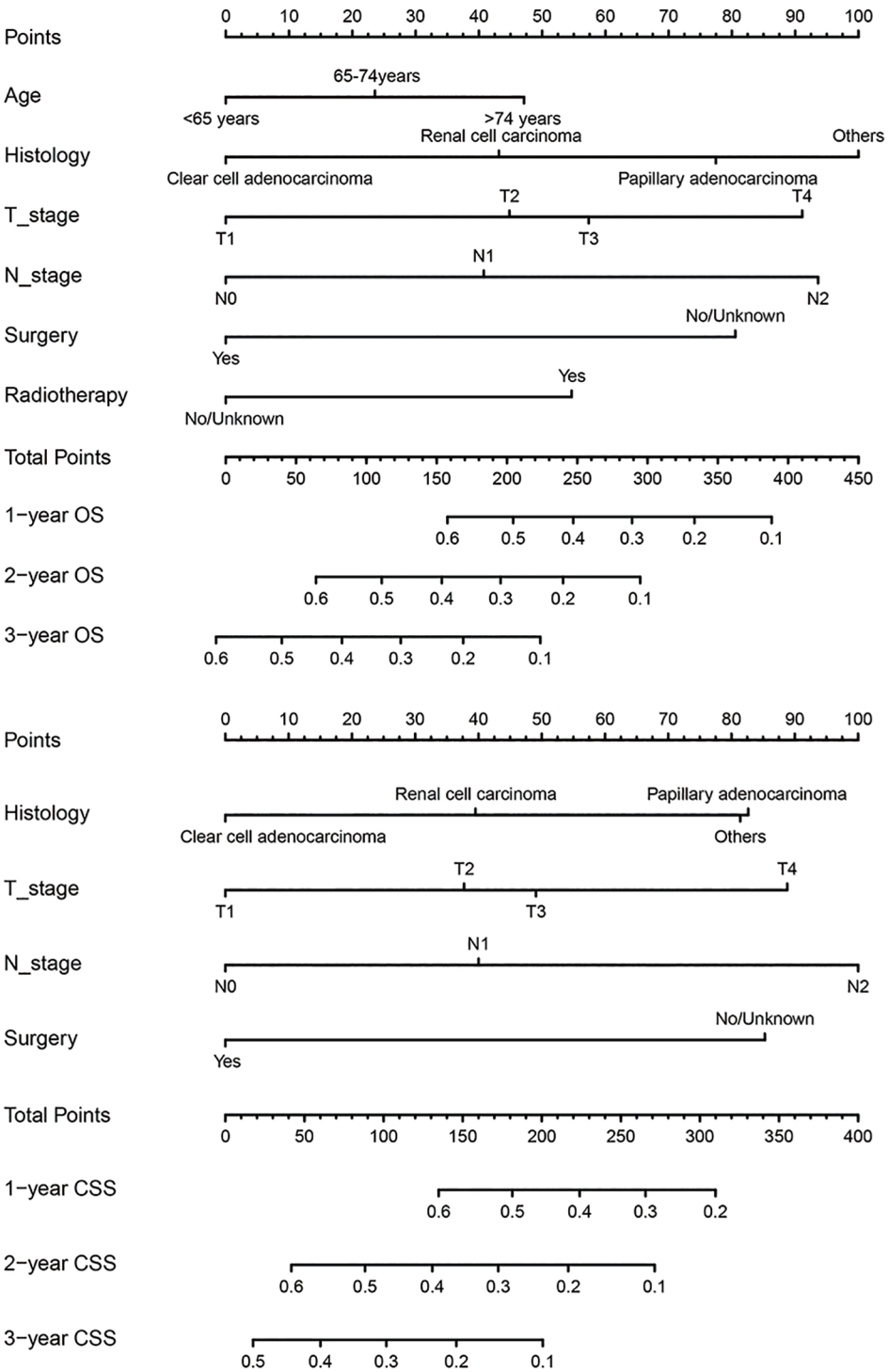

Figure 2 Prognostic nomogram predicting 1-, 2-, and 3-year overall survival and cancer-specific survival rate in patients with lung metastatic RCC. (A) Overall survival rate; (B) cancer-specific survival rate.

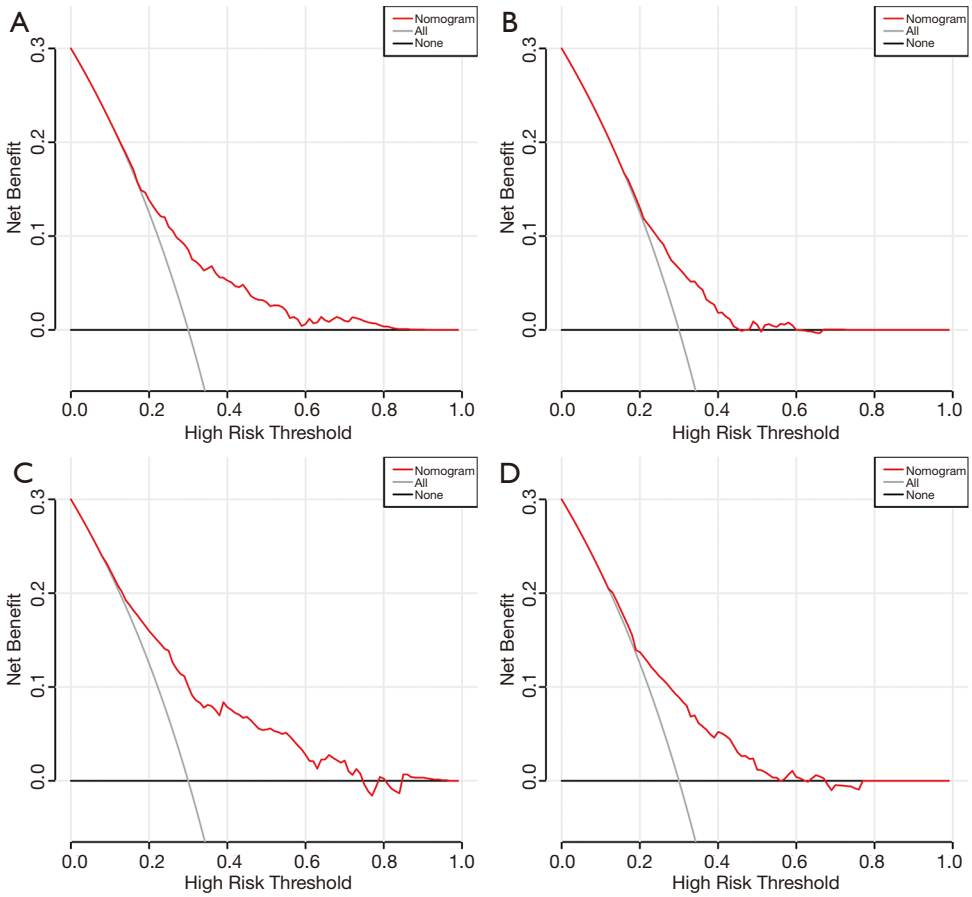

Figure 3 Decision curve analysis curves detects the predictive value of the nomogram in lung metastatic RCC patients. (A) Decision curve analysis curve of overall survival in primary cohort. (B) Decision curve analysis curve of cancer-specific survival in primary cohort. (C) Decision curve analysis curve of overall survival in validation cohort. (D) Decision curve analysis curve of cancer-specific survival in validation cohort.

urinary system. In China, the incidence of RCC in 2015 was 66.8/100,000, and the mortality rate was 23.4/100,000 (16). In recent years, the incidence of RCC had been increasing. Compared with ten years ago, the incidence of RCC had increased by 2–3% (17). A considerable number of RCC patients had distant metastatic at the time of consultation, and their prognosis was poor. Among RCC organ metastatic, lung metastatic was the most common. However, the independent factors of lung metastasis RCC were still unknown. The purpose of our study was to determine independent prognostic indicators in patients with lung metastatic RCC.

In our study, Cox regression analysis was performed on a large number of patients with lung metastatic RCC from the SEER database. It was found that age at diagnosis, histology, N-stage, T-stage, surgery and chemotherapy were independent risk factors for OS and while histology, N-stage, T-stage and surgery were independent risk factors for CSS in patients with lung metastatic RCC. Based on the above result, we developed and established a prognostic nomogram of lung metastatic RCC patients. In addition, we calibrated and verified the above-constructed prognostic nomograms and evaluated the accuracy of the OS and CSS prognostic nomograms for 1-, 2- and 3-year. The results showed good agreement between nomogram predictions and the actual observations, and good reliability in both primary and external validation cohorts.

The nomogram was an image representation based on the results of multivariate survival regression analysis, which makes various prognostic factors more intuitive (18,19). The model integrates multiple independent prognostic survival factors, allowing for a more focused evaluation

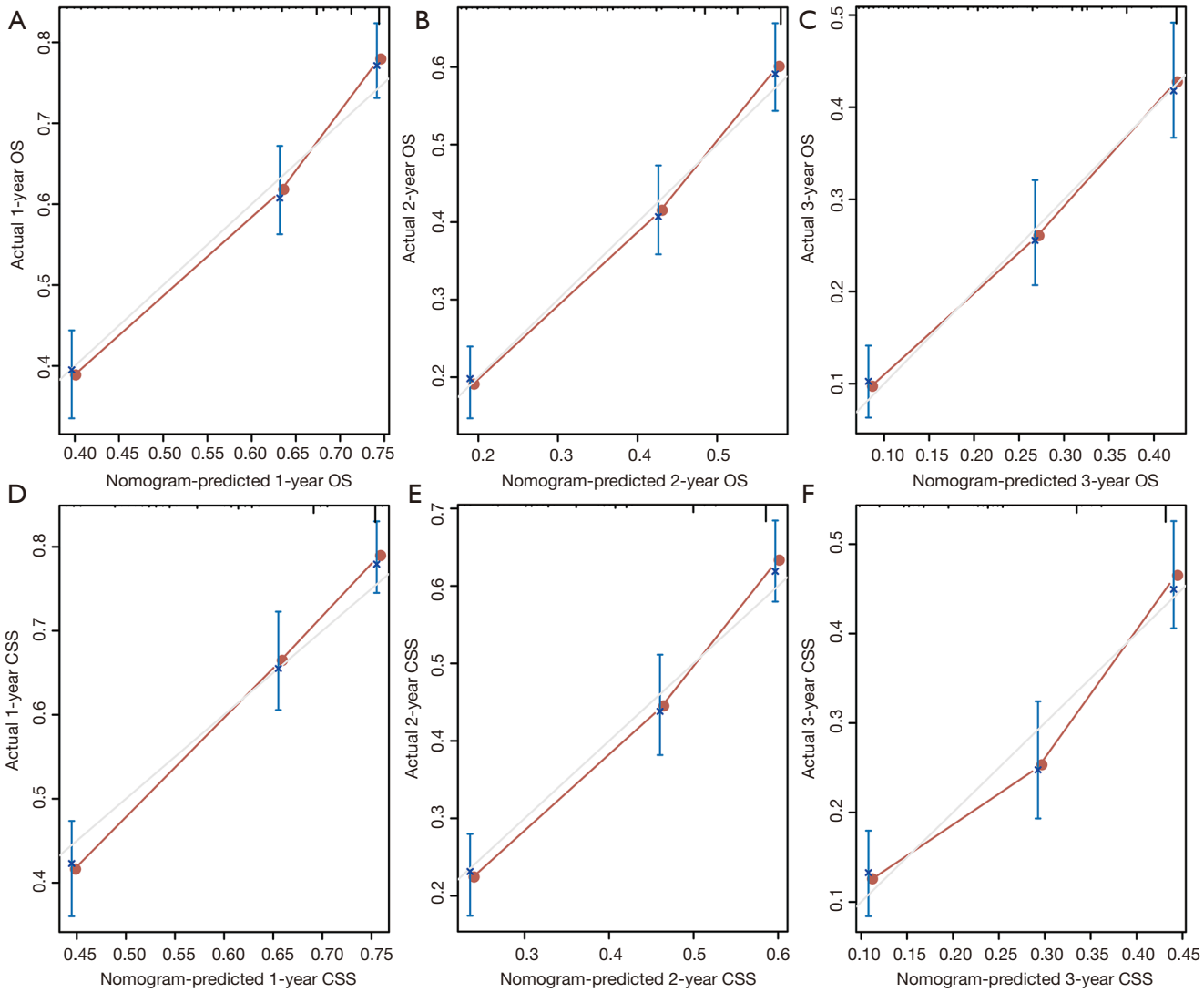

Figure 4 Calibration plot of the nomogram for predicting 1-, 2-, and 3-year overall survival and cancer-specific survival in primary cohort. (A) 1-year overall survival; (B) 2-year overall survival; (C) 3-year overall survival; (D) 1-year cancer-specific survival; (E) 2-year cancer-specific survival; (F) 3-year cancer-specific survival.

of individual patient survival probabilities (20). To date, prognostic nomograms have been developed for many cancer types and showed a more accurate ability to predict the prognosis than the traditional TNM systems (21). In addition, nomograms allowed clinicians to assess patients' physical condition more intuitively to provide personalized predictions. Therefore, the establishment of a reliable and effective prognostic nomogram is of great significance for the prognosis of patients with lung metastatic RCC and to provide individualized treatment.

The nomogram has been widely used in various tumors of the urinary system, and is important for accurate prognosis prediction and individualized treatment (22). Some studies have found that the bladder cancer nomogram was better than the prognostic model using standard pathological grouping, which can better predict the risk of recurrence after radical cystectomy (23). Similarly, Graefen *et al*. (24) also found the accuracy of the preoperative prostate nomogram prediction for prostate cancer. Zhang *et al*. (13) developed a nomogram for patients with clear cell renal cell carcinoma, which could accurately predict the incidence of 3-, 5-, and 10-year of OS and disease-specific

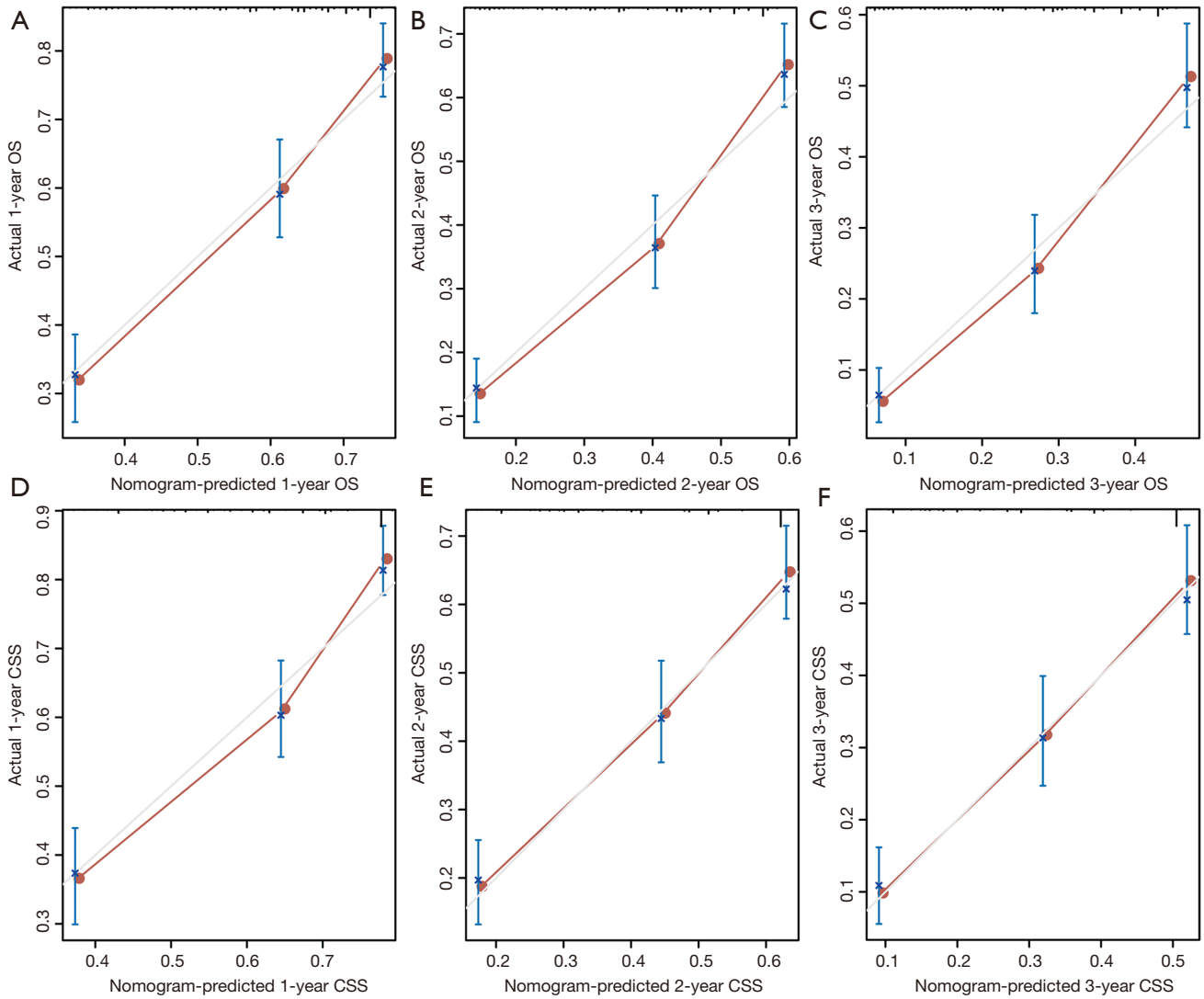

Figure 5 Calibration plot of the nomogram for predicting 1-, 2-, and 3-year overall survival and cancer-specific survival in validation cohort. (A) 1-year overall survival; (B) 2-year overall survival; (C) 3-year overall survival; (D) 1-year cancer-specific survival; (E) 2-year cancer-specific survival; (F) 3-year cancer-specific survival.

survival (DSS) in these patients.

There were more and more studies on the nomogram of patients with distant organ metastatic. The most common was the study of bone metastatic tumors, but there were few studies on lung metastatic tumors. Hu *et al.* (25) studied 194 colorectal cancer patients with indeterminate pulmonary nodules and found that the clinical-radiomics nomogram based on radiological characteristics and clinical risk factors showed good discriminant ability and accuracy in predicting lung metastatic. To our knowledge, this was the first study of prognostic factors in patients with lung metastatic RCC, and reliable nomograms have been established. Using these nomograms, urologists could evaluate patients with lung metastatic RCC, enabling personalized treatment and monitoring possible.

There were some limitations to be recognized in the present study. First, the SEER database published information on liver, lung, bone, and brain-related organ metastases in 2010, follow-up was not long enough, and the degree and amount of lung metastasis were not available from the database. Second, the SEER database was a retrospective analysis and requires prospective studies

for further validation. In addition, details of the type and duration of other adjuvant immunotherapies, targeted therapies, or systemic therapies were unclear. Moreover, information on patient complications or performance of metastasectomy was unclear.

Conclusions

Our study constructed a nomogram prognostic evaluation model for patients with lung metastatic RCC. The nomogram accurately and reliably predicted the 1-, 2- and 3-year OS and CSS of lung metastatic RCC.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-20-1488). The authors have no conflicts of interest to declare.

Ethical Statement: The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This article does not contain any studies with animals performed by any of the authors. The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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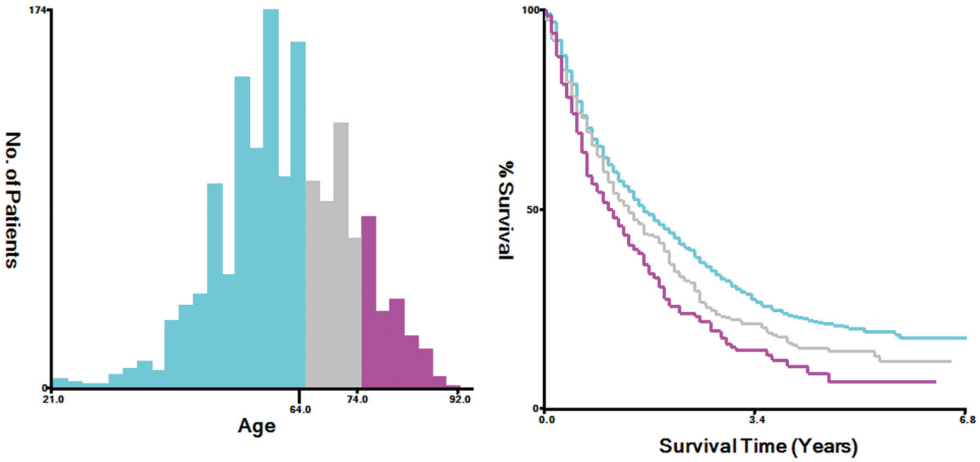

Figure S1 Using X-tile software to group the age of patients with lung metastatic RCC.

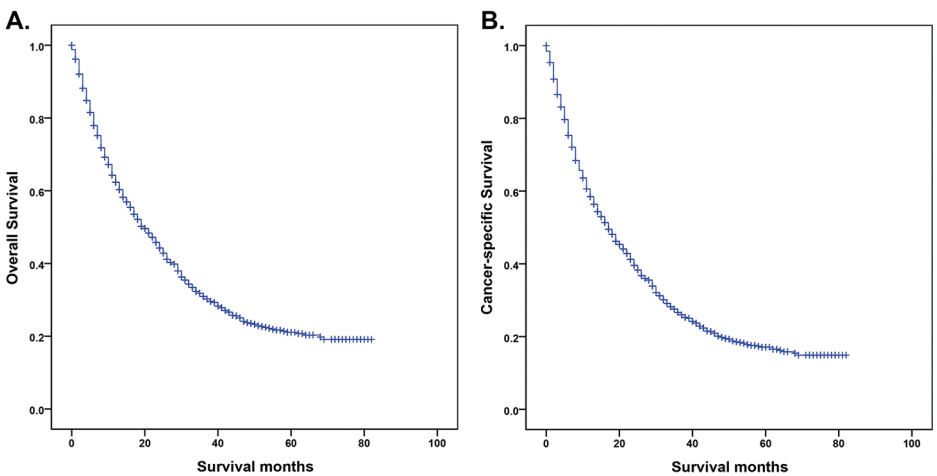

Figure S2 Kaplan-Meier curve estimate the overall survival and cancer-specific survival of lung metastatic RCC. (A) Overall survival; (B) cancer-specific survival.

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