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ORIGINAL RESEARCH

# Validation of the Prognostic Value of Preoperative Albumin-to-Alkaline Phosphatase Ratio in Patients with Surgically Treated Non-Metastatic Renal Cell Carcinoma

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**Purpose:** Several studies have revealed that albumin-to-alkaline phosphatase ratio (AAPR) was correlated to the survival of several cancers. To explore the impact of AAPR on the survival of non-metastatic renal cell carcinoma (RCC) patients following nephrectomy, the present study was conducted.

**Patients and Methods:** A total of 648 patients were enrolled in the present study. The cut-off value of AAPR was determined based on the receiver-operating characteristic (ROC) analysis. Univariate and multivariate analyses were applied to identify prognostic factors. The discrimination and calibration of models for survival outcomes were evaluated based on the concordance index (C-index), ROC analysis and calibration curve.

**Results:** The low AAPR (≤0.5) was associated with older age (P<0.001), higher T stage (P=0.002), larger tumor size (P=0.014) and tumor necrosis (P=0.003). A high AAPR was significantly correlated to better OS (hazard ratio, HR=0.61; P=0.038) and CSS (HR=0.52; P=0.013) based on multivariate analysis. Integrating AAPR with UISS or SSIGN, the C-indexes of nomogram for OS (UISS: 0.790 vs 0.765; SSIGN: 0.861 vs 0.850) and CSS (UISS: 0.832 vs 0.805; SSIGN: 0.905 vs 0.896) increased. Moreover, the nomogram for OS and CSS was established based on the multivariate analysis. The C-indexes of nomogram for OS and CSS were 0.834 (95% CI 0.794–0.874) and 0.867 (95% CI 0.830–0.904), respectively.

**Conclusion:** In conclusion, the high preoperative AAPR was a favorable prognostic factor for surgically treated non-metastatic RCC patients. AAPR also could improve the predictive value of well-established models. The nomogram that incorporates AAPR had a good performance. More prospective studies with a large scale are essential to validate our findings.

**Keywords:** albumin-to-alkaline phosphatase ratio, non-metastatic renal cell carcinoma, prognostic impact, nephrectomy

## Introduction

Renal cell carcinoma (RCC) is one of the common urological cancers, taking up 2–3% of all cancers.[1] During the last two decades, the occurrence of RCC is increasing by approximately 2% annually, leading to approximately 403,200 new cases and 175,100 cancer-related deaths.[1,2] For localized diseases, surgical resection with curative intent is the standard treatment.[2] However, local or distant

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recurrence would occur in about 20–30% of patients after surgical resection of localized RCC.[3,4] Furthermore, about 16% of patients harbor distant metastasis at the first diagnosis.[5] The survival of patients who have distant metastasis is discouraging and the 5-year survival rate is about 12%.[5] Therefore, the recognition of prognostic factors is critical to improving the management of patients.

Tumor, node, metastasis (TNM) classification system, tumor grade, tumor subtype, presence of sarcomatoid component and tumor necrosis are well-established prognostic factors. Several models have been proposed which enroll several prognostic factors, such as the Mayo Clinic Stage Size Grade Necrosis (SSIGN) score and the University of California, Los Angeles (UCLA) Integrated Staging System (UISS), which are commonly used and well validated.[6,7] But the performance of these models could be potentially improved because these models mostly focused on the pathological information which only could be obtained after surgery and did not consider clinical factors.

Various serum markers have been proposed for predicting survival in RCC patients, such as C-reactive protein-to-albumin ratio (CAR), albumin-to-globulin ratio, platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR).[8–10] Recently, a novel marker, albumin-to-alkaline phosphatase ratio (AAPR) was proposed and reported to be correlated to the survival of various malignancies, including non-small-cell lung cancer (NSCLC), breast cancer and hepatocellular carcinoma (HCC),[11–13] while the prognostic value of preoperative AAPR is not been well explored in the RCC. Therefore, the present study was designed to explore the impact of AAPR on the survival of non-metastatic RCC patients following nephrectomy.

# Patients and Methods

## Patients Selection and Evaluation

The present study retrospectively reviewed the patients with non-metastatic RCC who underwent nephrectomy in Sichuan University West China Hospital from January 2010 to December 2013. Exclusion criteria were as listed: 1) incomplete clinicopathological information; 2) bilateral or multiple RCC; 3) with diseases that might influence albumin (ALB) or alkaline phosphatase (ALP), for instance: bone diseases, liver diseases, and active infection; 4) pathological N+ or distant metastasis; 5) without available follow-up data. Finally, a total of 648 patients were enrolled in the present study. The Ethics Committee of Sichuan University West China Hospital approved the present study.

The laboratory tests are performed within 1 week before surgery. All patients underwent the chest computed tomography (CT) scan or X-ray and abdominal magnetic resonance imaging (MRI) or CT scan to stage cancer. The pathological stages were defined in accordance with the 8th version of the TNM staging system.[14] Histological diagnoses, including RCC type, nuclear grade, sarcomatoid features, and tumor necrosis, were made according to the 2016 World Health Organization (WHO) classification.[15]

## Data Collection

All patients' information was reviewed and extracted from medical records, including gender, age, diabetes mellitus, hypertension, tumor laterality, surgical type and approach, tumor size, pathological T stage, RCC subtype, tumor grade, tumor necrosis, and sarcomatoid features. The patients were divided into normal and abnormal ALP group based on the normal ALP range (female: 50–135U/L); (male: 45–125U/L), which is commonly utilized in routine clinical practice. Preoperative AAPR was calculated based on the formula: preoperative serum ALB level (g/L)/ALP (U/L).

## Follow-Up

Postoperative surveillance was conducted routinely based on the recommendations, including physical and laboratory examinations, radiological examinations of the chest and abdomen. All patients were regularly followed up every 3 months for the first 2 years, every 6 months for 3–5 years, and then once a year afterward. The primary outcomes were overall survival (OS) and cancer-specific survival (CSS). OS was calculated from the time of operation to the time of death or the end of follow-up. CSS was calculated as the time interval between the time of operation and the time of RCC-related death or the end of follow-up.

## Statistical Analysis

Mean (standard derivation, SD) or median (interquartile range, IQR) was presented for continuous variables. Frequency (proportion) was presented for categorized variables. Comparing differences of continuous and categorized variables between groups were conducted by Student's $t$ test and Chi-square test. By setting CSS as the endpoint, the receiver-operating characteristic (ROC) curve was carried out to identify the optimal cut-off value

of AAPR with the maximum Youden index (sensitivity +specificity-1).[16] The Kaplan–Meier curve analysis and Log rank test were applied to compare survival rates between groups. Univariate and multivariate Cox proportional hazards regression analyses were conducted to identify prognostic factors.

Furthermore, the nomograms for predicting OS and CSS were built in accordance with the multivariate analysis. The discrimination and calibration of models for OS and CSS were evaluated in accordance with the ROC analysis, concordance index (C-index), and calibration curve. A two-sided P value<0.05 was regarded statistically significant. The R software version 3.6.2 (http://www.r-project.org/) and SPSS version 23.0 (IBM Corp, Armonk, NY, USA) were applied for all statistical analyses.

**Table 1** Clinicopathological Characteristics of Non-Metastatic Renal Cell Carcinoma Patients

| | **Total** | **AAPR** | | |
|---|---|---|---|---|
| | | **≤0.5** | **>0.5** | **P-value** |
| No. of patients | 648 | 197 | 451 | |
| Age (years) | 54.84±12.64 | 57.45±11.79 | 53.70±12.85 | <0.001 |
| Gender | | | | |
| Male | 394 (60.80%) | 116 (58.88%) | 278 (61.64%) | 0.508 |
| Female | 254 (39.20%) | 81 (41.12%) | 173 (38.36%) | |
| Hypertension | 168 (25.93%) | 57 (28.93%) | 111 (24.61%) | 0.248 |
| Diabetes mellitus | 78 (12.04%) | 25 (12.69%) | 53 (11.75%) | 0.736 |
| Laterality | | | | |
| Left | 316 (48.77%) | 99 (50.25%) | 217 (48.12%) | 0.616 |
| Right | 332 (51.23%) | 98 (49.75%) | 234 (51.88%) | |
| Tumor size (cm) | 4.5 (3.1–6) | 5 (3.4–6.7) | 4.41 (3.05–5.7) | 0.014 |
| Operative approach | | | | |
| Open | 453 (69.91%) | 144 (73.10%) | 309 (68.51%) | 0.242 |
| Laparoscopic | 195 (30.09%) | 53 (26.90%) | 142 (31.49%) | |
| Nephrectomy | | | | |
| Radical | 437 (67.44%) | 139 (70.56%) | 298 (66.08%) | 0.263 |
| Partial | 211 (32.56%) | 58 (29.44%) | 153 (33.92%) | |
| Pathological T stage | | | | |
| T1 | 522 (80.56%) | 145 (73.60%) | 377 (83.59%) | 0.002 |
| T2 | 55 (8.49%) | 18 (9.14%) | 37 (8.20%) | |
| T3 | 63 (9.72%) | 28 (14.21%) | 35 (7.76%) | |
| T4 | 8 (1.23%) | 6 (3.05%) | 2 (0.44%) | |
| Histologic subtype | | | | |
| Clear cell | 545 (84.10%) | 169 (85.79%) | 376 (83.37%) | 0.546 |
| Non-clear cell | 103 (15.90%) | 28 (14.21%) | 75 (16.63%) | |
| Tumor grade | | | | |
| G1 | 24 (3.70%) | 6 (3.05%) | 18 (3.99%) | 0.065 |
| G2 | 339 (52.31%) | 101 (51.27%) | 238 (52.77%) | |
| G3 | 266 (41.05%) | 79 (40.10%) | 187 (41.46%) | |
| G4 | 19 (2.93%) | 11 (5.58%) | 8 (1.77%) | |
| Tumor necrosis | 72 (11.11%) | 33 (16.75%) | 39 (8.65%) | 0.003 |
| Sarcomatoid features | 7 (1.08%) | 3 (1.52%) | 4 (0.89%) | 0.440 |

**Abbreviation:** AAPR, albumin-to-alkaline phosphatase ratio.

# Results

## Clinicopathological Characteristics

Overall, 648 patients were included in the present study, and the clinicopathological characteristics were presented in Table 1. The whole cohort comprised 394 males (60.80%) and 254 females (39.20%), with a mean age of 54.84 years (±12.64). Among them, 195 patients underwent laparoscopic surgery and 453 patients had open surgery. Besides, most patients (n=437, 67.44%) underwent radical nephrectomy. As for tumor characteristics, the median tumor size was 4.5 cm (IQR, 3.1–6). Most patients (n=522, 80.56%) had pathological T1 stage disease. Clear cell RCC was diagnosed in 545 patients (84.10%), followed by non-clear cell RCC in 103 patients (15.90%). Tumor necrosis and sarcomatoid features were found in 72 patients (11.11%) and 7 patients (1.08%), respectively. The median duration of follow-up was 84 months.

## Relation Between Clinicopathological Characteristics and AAPR

Based on ROC curve analysis, the optimal cut–off value of AAPR was 0.5 with the sensitivity of 52.1%, specificity of 74.5% and the maximum Youden index of 0.266 (Figure 1). Thus, the patients were divided into low (≤0.5) and high (>0.5) AAPR group. Tumor necrosis (P=0.003) and higher pathological T stage (P=0.002) were commonly observed in the low AAPR groups. Furthermore, the low AAPR was associated with older age (P<0.001). Additionally, the low AAPR was significantly associated with a larger tumor size (P=0.014). No significant discrepancies in other characteristics between the low and high AAPR groups were observed (Table 1).

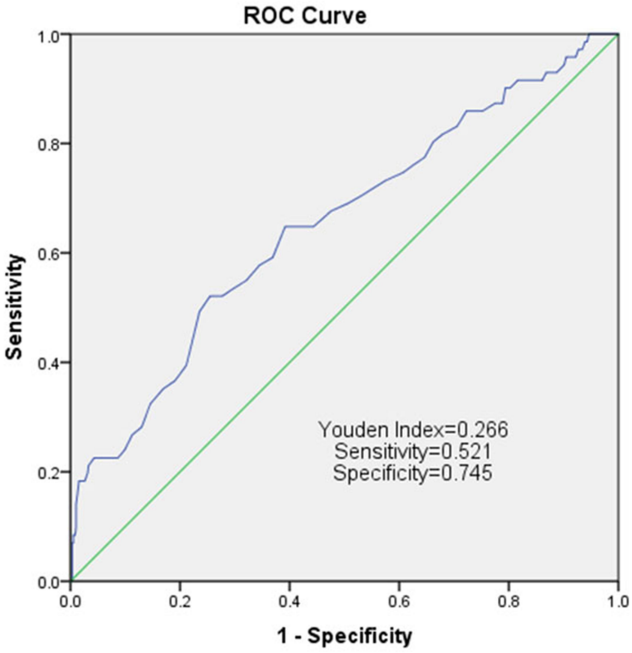


**Figure 1** ROC curve analysis of CSS for RCC patients.
**Abbreviations:** CSS, cancer-specific survival; RCC, renal cell carcinoma; ROC, receiver operating characteristic.

## Survival Analysis

At the last follow-up, 85 patients (13.12%) had died, among which 71 patients died of RCC-related cause. The 5-year OS rate (81.7% vs 92.9%) and CSS rate (82.6% vs 94.2%) of the patients with low AAPR were worse than those with the high AAPR. Kaplan–Meier curve and Log rank test also revealed that the patients with the low AAPR had an inferior OS (Figure 2A) and CSS (Figure 2B) than those with the high AAPR. Subset analysis also showed that the low AAPR was associated with worse OS (Figure 3A) and CSS (Figure 3B) for clear cell RCC patients. In the univariate analysis, age, sarcomatoid feature, tumor grade, T stage, tumor necrosis, ALB, and AAPR were related to OS and CSS (all P-value <0.5, Table 2). Multivariate analysis also revealed that higher AAPR (>0.5) was a favorable factor of OS (HR=0.61; 95% CI 0.38–0.97; P=0.038) and CSS (HR=0.52; 95% CI 0.31–0.87; P=0.013). Furthermore, age, sarcomatoid feature, tumor grade, T stage, and tumor necrosis were also associated with survival based on multivariate analysis (Table 2).

## The Performance of AAPR and Nomogram for OS and CSS

The two commonly used models, including UISS and SSIGN, were validated in the present study. SSIGN was only validated for clear cell RCC patients. The C-indexes of UISS for OS and CSS predictions were 0.765 (95% CI 0.719–0.810) and 0.805 (95% CI 0.763–0.847), respectively. The C-indexes of SSIGN for OS and CSS predictions were 0.850 (95% CI 0.811–0.890) and 0.896 (95CI 0.870–0.922), respectively. By integrating AAPR with UISS or SSIGN, the C-indexes of the nomogram for OS (UISS: 0.790 vs 0.765; SSIGN: 0.861 vs 0.850) and CSS (UISS: 0.832 vs 0.805; SSIGN: 0.905 vs 0.896; Table 3) predictions increased. Furthermore, after incorporating AAPR in UISS and SSIGN, the area under ROC curve (AUC) for OS (UISS: 0.823 vs 0.798; SSIGN: 0.893 VS 0.883) and CSS (UISS: 0.856 vs 0.827; SSIGN: 0.924 vs 0.915; Table 3) were also improved. Moreover, the present

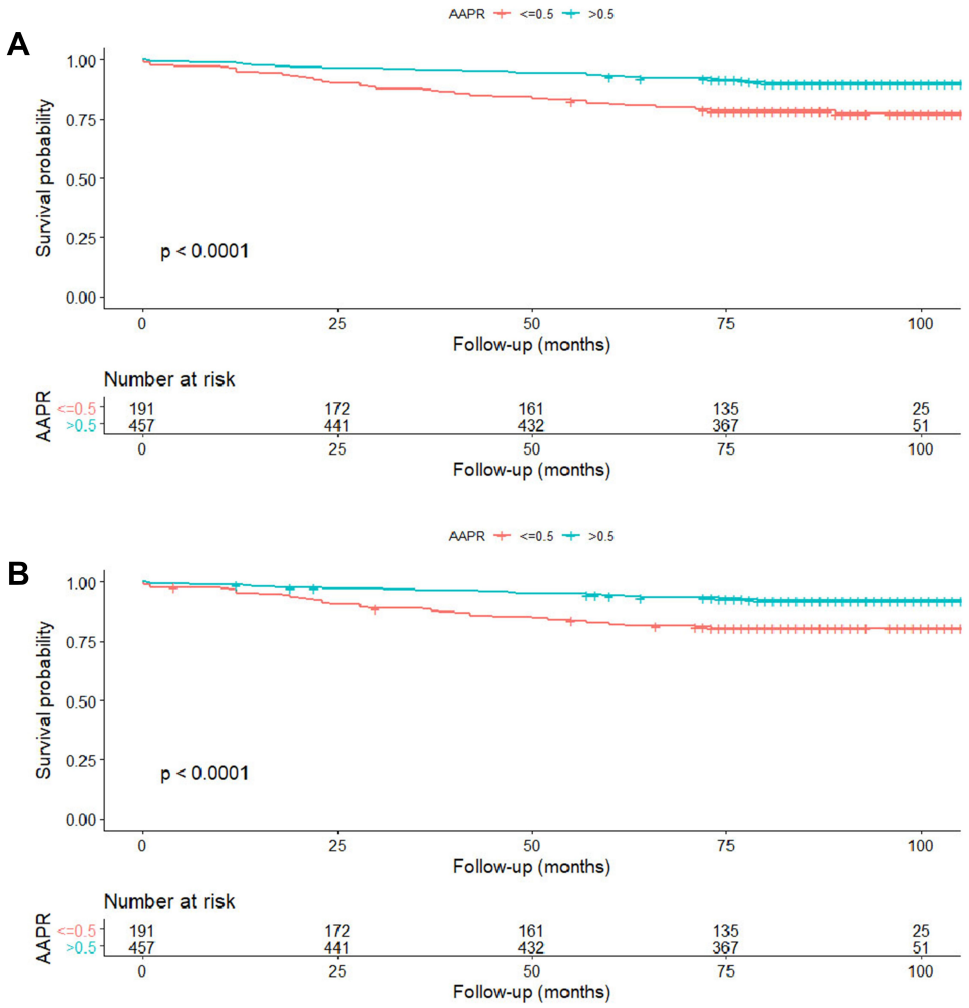


**Figure 2** Kaplan–Meier survival analysis of (**A**) OS and (**B**) CSS in non-metastatic RCC patients who underwent nephrectomy.
**Abbreviations:** AAPR, albumin-to-alkaline phosphatase ratio; CSS, cancer-specific survival; OS, overall survival; RCC, renal cell carcinoma.

study also established the nomogram for OS (Figure 4A) and CSS (Figure 4B) based on the multivariate analysis, which also included AAPR. The C-indexes of nomogram for OS and CSS predictions were 0.834 (95% CI 0.794–0.874) and 0.867 (95% CI 0.830–0.904), respectively. The AUC of the nomogram for predicting OS and CSS were 0.874 (95% CI 0.833–0.915) and 0.901 (95% CI 0.865–0.937), respectively. The calibration plots for predicting OS (Figure 5A) and CSS (Figure 5B) fitted very well between the nomogram-predicted probability and actual observation at 5 years after operation.

## Discussion

The present study was designed to explore the impact of AAPR on the survival of non-metastatic RCC patients following nephrectomy. The low AAPR (≤0.5) was significantly associated with older age, higher T stage, more proportion of tumor necrosis, and larger tumor size, which are all well-known adverse factors. Besides, lower preoperative AAPR was significantly related to inferior OS and CSS. We also validated the performance of two commonly used models, UISS and SSIGN, and found the predictable ability improved after incorporating AAPR. Furthermore, we also established the nomogram based on our data, which also incorporates AAPR, and the discriminatory capability is not inferior to UISS and SSIGN.

Chan et al firstly introduced the AAPR and found AAPR was associated with OS and disease-free survival (DFS) for HCC patients who receive curative treatment.[12] They also observed that AAPR had the highest C-index and chi-square compared with other liver parameters. Cai et al demonstrated that AAPR > 0.38 was correlated to favorable factors in advanced HCC patients, such as less portal vein tumor thrombus and ascites.[17] AAPR was regarded as a prognostic factor

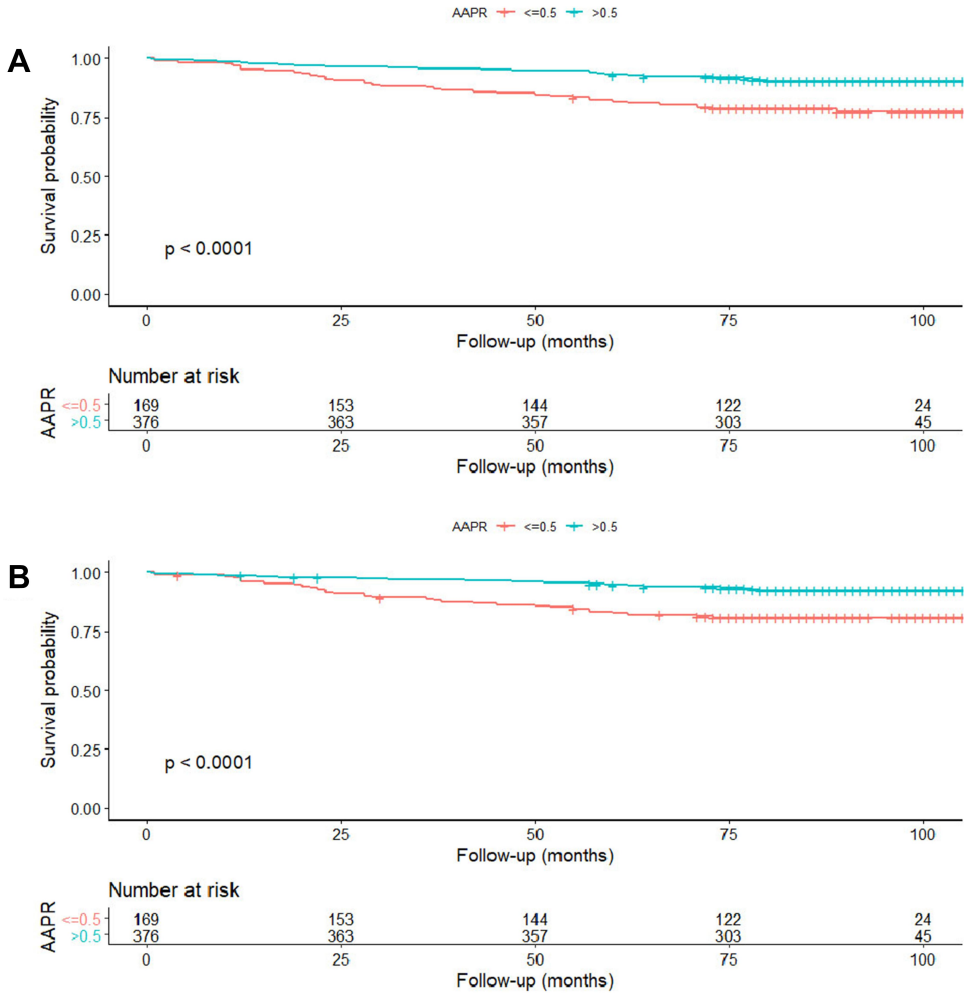


**Figure 3** Kaplan–Meier survival analysis of (**A**) OS and (**B**) CSS in clear cell RCC patients who underwent nephrectomy.
**Abbreviations:** AAPR, albumin-to-alkaline phosphatase ratio; CSS, cancer-specific survival; OS, overall survival; RCC, renal cell carcinoma.

and could enhance the predictive ability of the TNM system, which is similar to our findings. Besides, Pu et al demonstrated that AAPR was connected with OS for pancreatic ductal adenocarcinoma patients following curative resection.[18] They also suggested that the predictive model would be more accurate and advanced by the incorporation of AAPR. Zhang et al revealed the patients with higher AAPR (≥0.68) had a better OS and DFS compared with lower AAPR (<0.68) for patients with cervical cancer following radical hysterectomy.[19] Long et al included 746 non-metastatic breast cancer and observed increased pretreatment AAPR (≥0.525) was related to tumor size, age and other factors, which is consistent with our results.[11] Multivariate analysis showed AAPR was related to OS. Li et al determined 0.57 as optimal cut-off value and demonstrated low preoperative AAPR was linked with poor OS and DFS for resected NSCLC.[13] After performing propensity score-matching analysis to balance characteristics, the AAPR was also associated with OS and DFS. Regarding urological cancers, Tang et al found that lower AAPR (<0.58) was an unfavorable factor of OS, CSS and recurrence-free survival for patients with upper tract urothelial carcinoma following radical nephroureterectomy.[20] AAPR was found to be associated with adverse factors such as higher pT stage, grade, and larger tumor size. Xia et al firstly introduced AAPR in RCC, revealing low AAPR (<0.39) was correlated to OS and CSS.[21] They also established nomograms for OS (C-index:0.821) and CSS (C-index:0.839) with moderate discriminative ability. However, they only evaluated the added predictive ability of AAPR in their nomograms, while they did not observe significant discrepancies in tumor characteristics between low and high AAPR, which is different from other studies. We also evaluated whether AAPR could improve the predictive ability of well-established models, and thus established nomograms of OS (C-index)0.834 and CSS

**Table 2** Univariate and Multivariate Analyses of Prognostic Factors for OS, CSS and PFS in Patients with Non-Metastatic RCC (n=648)

| | OS | | CSS | |
|---|---|---|---|---|
| | Univariate | Multivariate | Univariate | Multivariate |
| | HR (95% CI) P-value | HR (95% CI) P-value | HR (95% CI) P-value | HR (95% CI) P-value |
| Age (≧55 vs<55) | 3.29 (1.99–5.43) <0.001 | 2.09 (1.25–3.52) 0.005 | 2.74 (1.62–4.64) <0.001 | 1.52 (0.87–2.63) 0.139 |
| Gender (male vs female) | 1.2 (0.77–1.88) 0.418 | | 1.29 (0.79–2.1) 0.317 | |
| Laterality (right vs left) | 0.92 (0.6–1.4) 0.686 | | 0.82 (0.51–1.3) 0.394 | |
| Histology (non-clear cell vs clear cell) | 0.97 (0.54–1.74) 0.908 | | 1.09 (0.58–2.02) 0.795 | |
| T stage (3–4 vs 1–2) | 8.92 (5.8–13.74) <0.001 | 4.87 (3.05–7.77) <0.001 | 12.45 (7.8–19.9) <0.001 | 6.66 (4–11.05) <0.001 |
| Tumor grade (G3-4 vs G1-2) | 4.33 (2.65–7.1) <0.001 | 2.19 (1.27–3.76) 0.005 | 5.75 (3.2–10.32) <0.001 | 2.63 (1.39–4.98) 0.003 |
| Tumor necrosis (yes vs no) | 5.19 (3.32–8.1) <0.001 | 2.46 (1.5–4.02) <0.001 | 6.08 (3.77–9.79) <0.001 | 2.92 (1.73–4.93) <0.001 |
| Sarcomatoid feature (yes vs no) | 10.8 (4.35–26.8) <0.001 | 4.35 (1.7–11.11) 0.002 | 12.8 (5.1–31.96) <0.001 | 5.63 (2.17–14.6) <0.001 |
| Albumin, g/L (≥35 vs <35) | 0.18 (0.09–0.33) <0.001 | 0.84 (0.4–1.74) 0.635 | 0.19 (0.09–0.37) <0.001 | 1.21 (0.54–2.7) 0.647 |
| ALP, U/L (normal vs abnormal) | 0.81 (0.41–1.62) 0.552 | | 0.87 (0.4–1.91) 0.737 | |
| AAPR (>0.5 vs ≤0.5) | 0.41 (0.27–0.63) <0.001 | 0.61 (0.38–0.97) 0.038 | 0.37 (0.23–0.59) <0.001 | 0.52 (0.31–0.87) 0.013 |

**Abbreviations:** AAPR, albumin-to-alkaline phosphatase ratio; ALP, alkaline phosphatase; CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; OS, overall survival.

**Table 3** Comparison of Discriminatory Capabilities of Models for OS and CSS in Patients with Non-Metastatic RCC

| Model | OS | | | | CSS | | | |
|---|---|---|---|---|---|---|---|---|
| | C-Index | 95% CI | AUC | 95% CI | C-Index | 95% CI | AUC | 95% CI |
| UISS | 0.765 | 0.719–0.810 | 0.798 | 0.746–0.850 | 0.805 | 0.763–0.847 | 0.827 | 0.778–0.876 |
| UISS+AAPR | 0.790 | 0.743–0.837 | 0.823 | 0.770–0.877 | 0.832 | 0.789–0.876 | 0.856 | 0.807–0.906 |
| SSIGN[a] | 0.850 | 0.811–0.890 | 0.883 | 0.841–0.926 | 0.896 | 0.870–0.922 | 0.915 | 0.885–0.944 |
| SSIGN+AAPR | 0.861 | 0.825–0.898 | 0.893 | 0.853–0.933 | 0.905 | 0.881–0.928 | 0.924 | 0.898–0.950 |
| Nomogram (exclude AAPR) | 0.833 | 0.793–0.874 | 0.870 | 0.828–0.913 | 0.860 | 0.819–0.900 | 0.891 | 0.850–0.932 |
| Nomogram[b] | 0.834 | 0.794–0.874 | 0.874 | 0.833–0.915 | 0.867 | 0.830–0.904 | 0.901 | 0.865–0.937 |

**Notes:** [a]Validation of the SSIGN for clear cell renal cell carcinoma patients. [b]pT+tumor grade+necrosis+sarcomatoid feature+age+AAPR for predicting OS; pT+tumor grade + necrosis+sarcomatoid feature+AAPR for CSS.

**Abbreviations:** AAPR, albumin-to-alkaline phosphatase ratio; AUC, area under receiver-operating characteristic curve; C-index, concordance index; CI, confidence interval; CSS, cancer-specific survival; OS, overall survival; SSIGN, stage size grade and necrosis; UISS, University of California Los Angeles Integrated Staging System.

(C-index=0.867), which may have better discrimination than theirs. Among reported studies, the optimal cut-off value is different, ranging from 0.38 to 0.68.[11–13,17–21] Several factors might cause different cut-off values, such as different types of cancers, stage, sample sizes, duration of follow-up, assay methods for ALB and ALP, as well as different methods to select a cut-off value. Hence, more well-designed studies are further required.

Increasing evidence suggested that nutritional deficiency and systemic inflammatory response were related to the development and progression of cancers.[22] Tumor growth and aggression need the nutrient and cause the immunological response. ALB, the most abundant protein in serum, reflects patients' nutritional status. ALB is also related to systemic immune reaction to inflammation or tumor.[23] Furthermore, ALB could stabilize cell growth and proliferation, exert antioxidants agents against carcinogens.[23,24] Tumor could directly inhibit the generation of ALB through secreting proinflammatory cytokine, ALB also could penetrate interstitial space because of inflammation-induced increased vascular permeability.[25] Also, low ALB or hypoalbuminemia was reported to be associated with an immunosuppressed status, reflecting a poor anti-cancer response.[26] ALB was reported to be correlated to the survival of several cancers, including RCC.[25]

ALP is a hydrolytic enzyme, mainly synthesized in the bile duct, liver, kidney, bone, and several other organs. The ALP level will increase under some pathological conditions of corresponding tissues, such as HCC, kidney and bone diseases.[20] ALP can be synthesized and excreted into the serum directly by cancer cells and regulates tumor development.[27] Besides, elevated ALP was reported to be

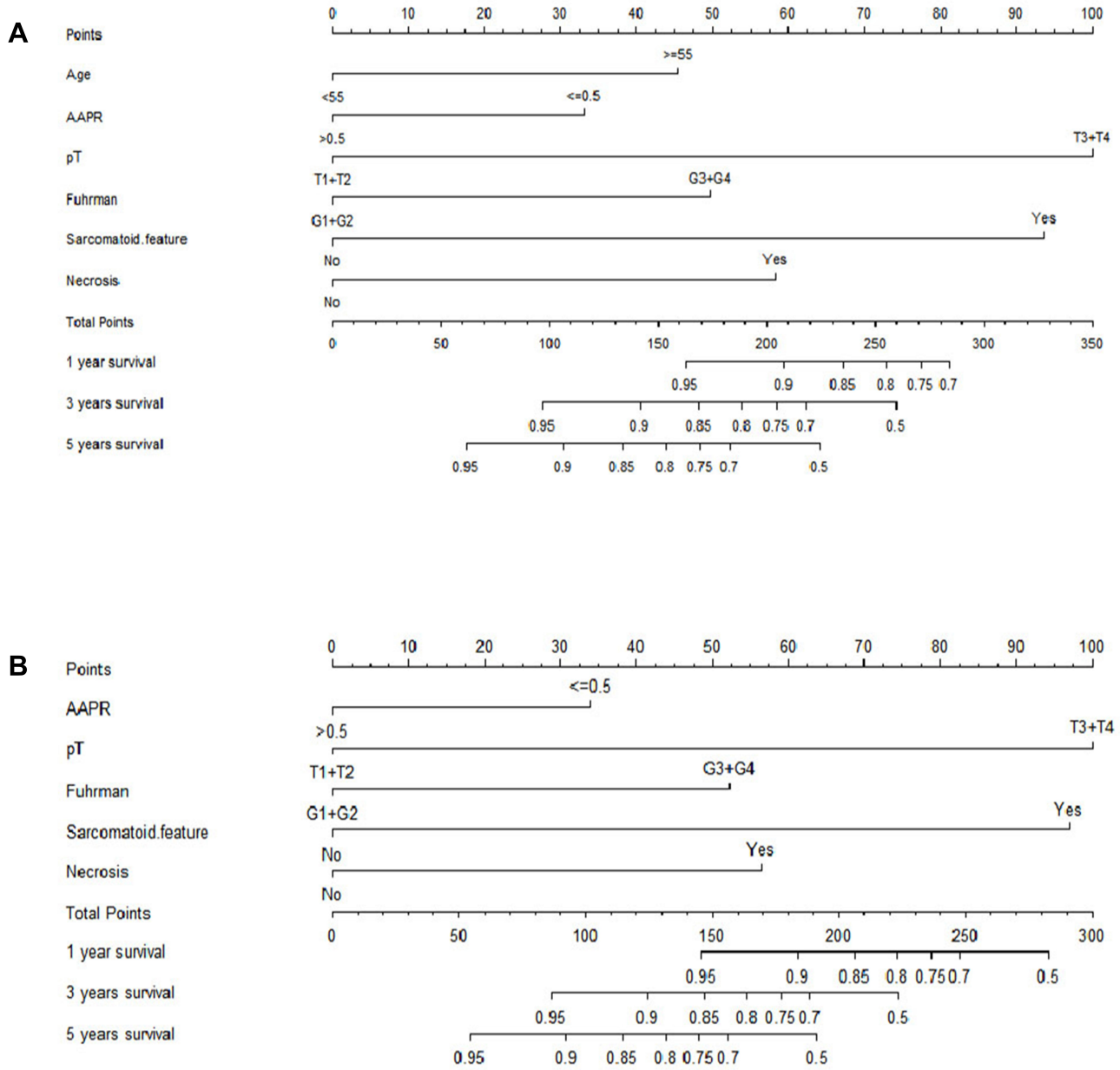


**Figure 4** Nomogram for predicting (**A**) OS and (**B**) CSS in non-metastatic RCC patients.
**Abbreviations:** CSS, cancer-specific survival; OS, overall survival; RCC, renal cell carcinoma.

a potential indicator of oxidative stress, which plays an important role in tumorgenesis.[28] Moreover, ALP was reported to be associated with the survival of HCC, gastric cancer, and RCC.[28–31]

AAPR, calculated based on the ALB and ALP, may reflect the nutritional status, and immunological response in patients with cancers, which could predict the survival of cancer patients. AAPR is low-cost, non-invasive and easily obtained, which could stratify the patients and be beneficial for patients' management. Low AAPR was related to poor survival outcomes, thus the patients with low AAPR could improve the nutritional status and received relevant therapies. Besides, for these patients, adjuvant therapy and more closed follow-up could be provided.

However, our study is not devoid of limitations. Firstly, the present study is retrospective which may lead to a selection bias. Next, the present study extracted data from one center, the sample size is moderate. The optimal cut-off value of AAPR still needs to be validated. Thus, the multicenter studies with large scale are necessary. Thirdly, we centered on the preoperative AAPR; however, dynamic change of AAPR was not evaluated. At last, the

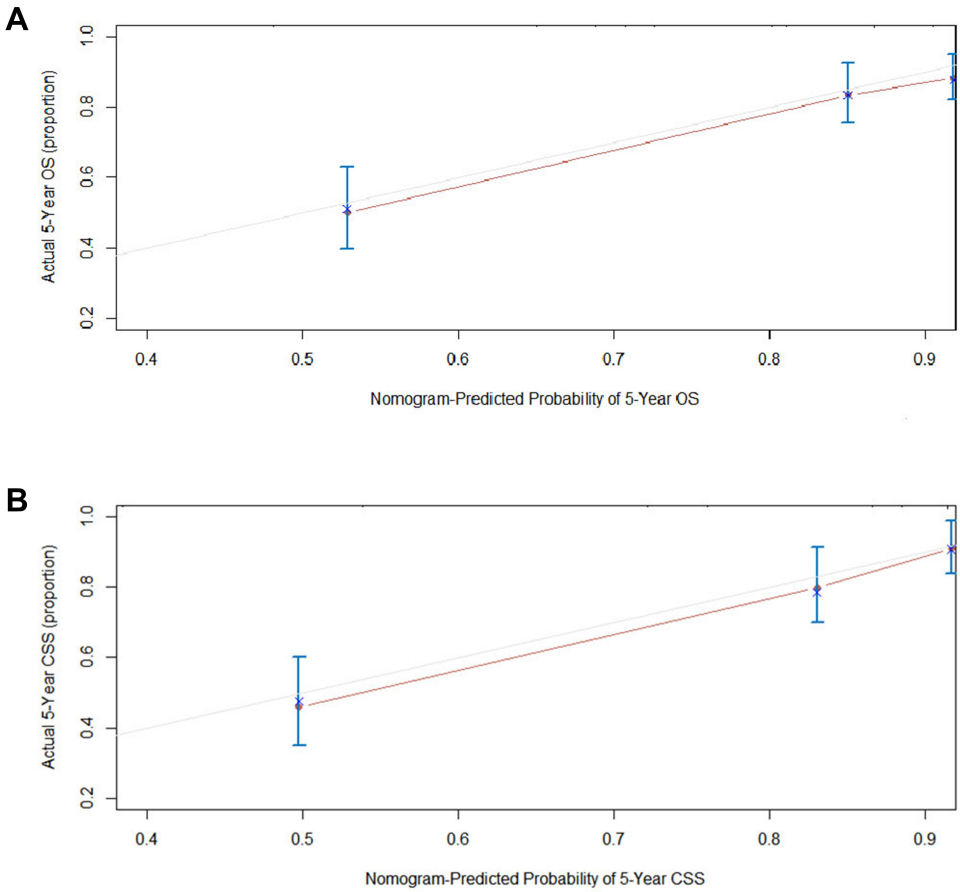


**Figure 5** The calibration curve predicts (**A**) OS and (**B**) CSS at 5 years after nephrectomy in non-metastatic RCC patients.
**Abbreviations:** CSS, cancer-specific survival; OS, overall survival; RCC, renal cell carcinoma.

exact mechanism of AAPR between the survival of cancer patients is needed to be further explored in basic research.

## Conclusion

In conclusion, the high preoperative AAPR was a favorable prognostic factor for surgically treated non-metastatic RCC patients. AAPR also could improve the predictive value of well-established models. The nomogram incorporating AAPR had a good performance. More prospective studies with a large scale are essential to validate our findings.

## Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request.

## Ethical Approval and Informed Consent

All procedures performed in studies involving human participants were according to the ethical standards of the ethics committee of Sichuan University West China Hospital and Declaration of Helsinki. The ethics committee of Sichuan University West China Hospital approved this study, and informed consent was waived by the board due to the nature of retrospective design. The patients' data were anonymized and analyzed with confidentiality.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

All authors report no conflicts of interest in this work.

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