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Prognostic impact of the Controlling Nutritional Status score following curative nephrectomy for patients with renal cell carcinoma

Yangqin Zheng, MD[a], Lianmin Bao, MD[b], Wenhan Wang[c], Qinquan Wang, MD[d], Yue Pan, MD[d], Xiaomin Gao, PhD[e,*]

Abstract

We aimed to evaluate the prognostic significance of the preoperative Controlling Nutritional Status (CONUT) score in patients with renal cell carcinoma (RCC), and then compared its accuracy of the prognostic nutritional index (PNI), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) as predictors of survival.

We included 635 patients who underwent nephrectomy for RCC from January 2004 to July 2014. The X-tile program was used to determine the optimal cut-off values for CONUT score, PNI, NLR, and PLR.

The median follow-up duration after surgery was 48.40 (29.30–80.10) months. The optimal cutoff values were 2 for CONUT score, 48 for PNI, 3.5 for NLR and 204.7 for PLR by X-tile program with cancer-specific survival (CSS) as end-point. Higher CONUT score, NLR and PLR, and lower PNI were statistically associated with worse OS and CSS in the univariate analysis. Multivariate analysis showed that higher CONUT score was an independent predictor for OS (HR = 3.012; 95% CI, 1.525–5.948; $P = .001$) and CSS (HR = 3.001; 95% CI, 1.290–6.984; $P = .011$), and CONUT score was superior to PNI, NLR, and PLR according to the HR.

Therefore, preoperative CONUT score can be a strong independent predictor in RCC patients after nephrectomy.

Abbreviations: CONUT = Controlling Nutritional Status, PNI = prognostic nutritional index, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio, CSS = cancer-specific survival, OS = overall survival, RCC = renal cell carcinoma.

Keywords: inflammation, nephrectomy, nutrition, renal cell carcinoma, survival

1. Introduction

Renal cell carcinoma (RCC) is the seventh most common tumor, representing 2% to 3% of all cancers.[1,2] Although nephron-sparing surgery, active surveillance, and minimally invasive techniques (e.g., cryotherapy and radiofrequency ablation) have been introduced into daily clinical practice in order to limit invasive procedures, iatrogenic renal function impairment, and overtreatment, surgery remains the standard of care for localized RCC.[2] However, the clinical outcome of RCC is still poor, as approximately 30% patients will develop local or distant disease recurrence after surgery for localized RCC.[1] Moreover, 20% of newly diagnosed RCC patients will have advanced-stage disease.[1] RCC survival outcomes could be significantly improved if RCC patients can be detected at an early stage in patients. Therefore, it is crucial for patients with RCC to seek useful predictors for risk and prognostic stratification.

Despite evidence from other malignancies that the nutrition and inflammation status may affect patient morbidity and mortality, these prognostic biomarkers, including the prognostic nutritional index (PNI), neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), Glasgow prognostic score (GPS), and systemic immune-inflammation index, have been identified as independent predictors of survival in patients with RCC.[3–5] Peng et al reported that a low PNI, which was based on serum albumin levels and lymphocyte count, was an independent predictor of the progression-free survival (PFS) and overall survival (OS) in a multivariate analysis[5] and was superior to the NLR, PLR, and LMR as a predictor. Recently, the controlling nutritional status (CONUT) score has been reported to be a predictive biomarker of survival in several cancers.[6–10] The CONUT score is an index calculated using the serum albumin concentration, total lymphocyte count and total cholesterol concentration. A more accurate result can be obtained by including the total cholesterol concentration and reducing the importance of the serum albumin concentration in the evaluation criteria.[11] Actually previous studies had demonstrated that the total cholesterol concentration was correlated with the prognosis of cancers.[12–14] However, the significance of the CONUT score in the prognosis of RCC patients is still unknown.

Therefore, the aims of this study were to evaluate the impact of the preoperative CONUT score on survival, compare the

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YZ, LB, and QW contributed equally to this manuscript.

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[a] Department of Hematology, The Third Clinical Institute Affiliated to Wenzhou Medical University, The People's Hospital of Wenzhou, [b] Department of Respiratory, [c] Department of Endocrinology, Rui'an People's Hospital, The Third Affiliated Hospital of the Wenzhou Medical University, [d] Department of Urology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, [e] Department of Urology, Changhai Hospital, Second Military Medical University, China.

[*] Correspondence: Xiaomin Gao, Department of Urology, Changhai Hospital, Second Military Medical University, China (e-mail: doctorgaoxiaomin@163.com).

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accuracy of the CONUT score with the PNI, NLR, and PLR in patients with RCC who underwent curative nephrectomy.

2. Materials and methods

2.1. Patients

This study has been approved by the ethics committee of The First Affiliated Hospital of Wenzhou Medical University. The medical records of all newly diagnosed non-metastatic RCC patients (>20 years old) between January 2004 and July 2014 in the First Affiliated Hospital of Wenzhou Medical University were collected and retrospectively analyzed in the present study. In our department, 803 patients underwent radical or partial nephrectomy for non-metastatic RCC. Among these patients, we consecutively excluded patients with kidney transplantation before surgery (n = 6), only 1 kidney (n = 3), hemodialysis therapy (n = 20), those with any history of other cancers (n = 32), bilateral RCC (n = 7), prior surgery for RCC (n = 12), those with relevant comorbidity affecting systemic inflammatory response markers (i.e., chronic liver disease, immunosuppression, cytotoxic medications, leukemia, lymphoma, autoimmune diseases, and chronic inflammatory diseases), (n = 61), and those with incomplete clinical data (n = 27) (Fig. 1). The remaining 635 patients were included in this study.

2.2. Management

Before surgery, we performed a physical examination and conducted the blood tests in patients. Patients who had evidence of distant metastasis on computed tomography (CT) scan of the abdomen and chest or the X-ray of chest were excluded. Lymph node dissection was performed if palpably enlarged lymph nodes were found on preoperative imaging or during surgery. No 1 received systemic therapy, local radiotherapy, or embolization. The T stage and histologic subtype of the tumor were classified according to the Union for International Cancer Control seventh TNM classification, the American Joint Committee on Cancer guidelines, and the Heidelberg recommendations. Tumor grading was assessed according to the Fuhrman's grading system. Tumor size was defined as the largest diameter based on the pathological report. Anemia was defined as hemoglobin <13 g/dL in men and <12 g/dL in women, according to the World Health Organization (WHO) criteria.[15] The CONUT scores, as calculated using the serum albumin concentration, total lymphocyte count, and total cholesterol concentration, are shown in Table 1. Hypoalbuminemia was defined as albumin <3.5 g/dL. The low total cholesterol concentration was defined as total cholesterol <180 mg/dL. The PNI was calculated as the serum albumin level (g/L) + 5 × lymphocyte count (10^9/L), the NLR was the neutrophil count divided by the lymphocyte count, the PLR as the platelet count divided by the lymphocyte count. Follow-up care consisted of blood and urine tests, and chest and abdominal CT or magnetic resonance imaging every 3 to 6 months for the first 2 years and annually after that. Information on the death of patients was obtained from outpatient medical records, telephone interviews, or the patient's social security death index. The follow-up cutoff was September 1, 2016. The OS and cancer-specific survival (CSS) were calculated from the date of surgery to the date of death from any cause and cancer-specific death, respectively, or the date of the last follow-up visit. The primary endpoint of this

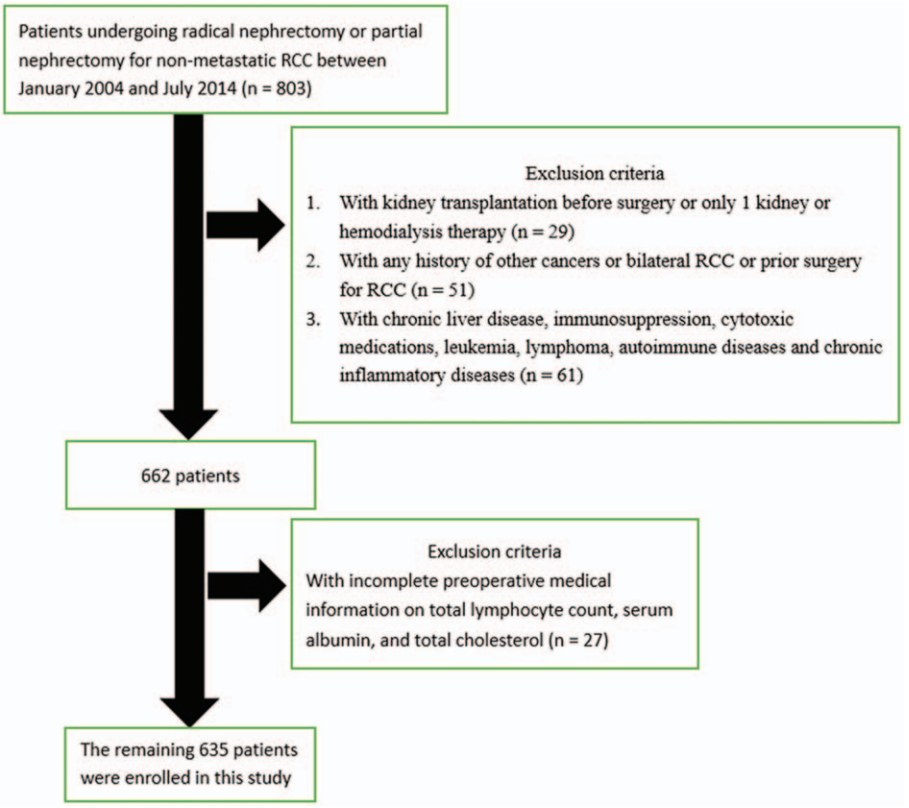

Figure 1. Flowchart showing patient selection.

Table 1

Scoring system for the CONUT.

Parameter	Undernutrition degree			
	None	Light	Moderate	Severe
Serum albumin, g/dL	3.5–4.5	3.00–3.49	2.50–2.99	<2.50
Score	1	2	4	6
Total lymphocyte count, /mm^3	≥1600	1200–1599	800–1199	<800
Score	0	1	2	3
Total cholesterol, mg/dL	≥180	140–179	100–139	<100
Score	0	1	2	3
Total score	0–1	2–4	5–8	9–12
Classification (total score)	<2 low CONUT group ≥2 high CONUT group			

CONUT = Controlling Nutritional Status.

study was the CSS because previous studies used the CSS as the endpoint to calculate the optimal cutoff values.[7,16]

2.3. Statistical analysis

Continuous variables are presented as the mean ± standard deviation, and categorical variables are presented as counts and percentages. The optimal cutoff values of the CONUT score, PNI, NLR, and PLR were determined using the X-tile program (Version 3.6.1, Yale University, New Haven, CT). This method has been previously applied in the literature to determine the threshold value of the continuous covariables, NLR and LMR, (increased mortality with NLR >5.7 or LMR ≤1.1).[17] We analyzed the association of the CONUT score, with the PNI, NLR, PLR and clinicopathological variables using the Student *t* test. The Kaplan–Meier survival curves were plotted to estimate the OS and CSS, and the significance was compared using the log-rank test. The predictors of the OS and CSS as determined by univariate analysis were evaluated in a multivariate analysis (forward stepwise method) using a Cox's proportional hazards model. Variables with $P < .05$ in the univariate analysis were included in the subsequent multivariate analysis. All tests were 2-sided, and the differences were considered statistically significant at $P < .05$. Statistical analyses were performed using the SPSS software package version 22.0 (IBM, Armonk, NY) and R software (Version 3.4.1; Institute for Statistics and Mathematics, Vienna, VIC, Austria).

Table 2

Components of the CONUT score.

	Low CONUT (n = 286)	High CONUT (n = 349)
CONUT score		
0	93 (32.52%)	
1	193 (67.48%)	
2		154 (44.13%)
3		114 (32.66%)
4		41 (11.75%)
5		20 (5.73%)
6		13 (3.72%)
7		4 (1.15%)
8		1 (0.29%)
9		2 (0.57%)
Albumin score		
0	123 (43.01%)	44 (12.61%)
1	163 (56.99%)	271 (77.65%)
2		25 (7.16%)
4		9 (2.58%)
6		0
Total lymphocyte score		
0	263 (91.96%)	119 (34.10%)
1	23 (8.04%)	132 (37.82%)
2		79 (22.64%)
3		19 (5.44%)
Total cholesterol score		
0	232 (81.12%)	88 (25.21%)
1	54 (18.88%)	173 (49.57%)
2		84 (24.07%)
3		4 (1.15%)

CONUT = Controlling Nutritional Status.

3. Results

3.1. Optimal cutoff values for the CONUT score, PNI, NLR, and PLR

To determine the cutoff values for the CONUT score, PNI, NLR and PLR, the X-tile program was applied with CSS as the endpoints, which were 2, 48, 3.5, and 204.7, respectively (Figure S1-S4, http://links.lww.com/MD/C665). The χ^2 log-rank value of the CONUT score, PNI, NLR, and PLR were 21.10, 30.41, 21.46, and 18.47, respectively. Therefore, patients were divided into 2 groups according to these cutoff values (CONUT score <2 and CONUT score ≥2; PNI <48 and PNI ≥48; NLR <3.5 and NLR ≥3.5; and PLR <204.7 and PLR ≥204.7). In addition, Table 2 shows the individual CONUT score components for the low and high CONUT score groups.

3.2. Baseline characteristics of patients

The baseline clinicopathologic characteristics of the 635 non-metastatic RCC patients are summarized in Table 3. Of the 635 patients, 400 (62.99%) were male and 235 (37.01%) were female, 27 (4.25%) patients underwent regional lymph node dissection. The mean age at surgery was 61.71 ± 12.51 years, and the mean tumor size was 4.87 ± 3.33 cm. The mean follow-up duration was 56.83 ± 32.37 (median: 48.40; range: 29.30–80.10) months. During 10 years follow-up, a total of 60 (9.45%) patients died and 41 (6.46%) patients died from cancer-specific causes. The 5-year OS rate was 90.00%, and the 5-year CSS rate was 92.40%.

The association of the baseline characteristics with the CONUT score, PNI, NLR, and PLR is shown in Table 3. The ASA grade, anemia, and hypoalbuminemia were significantly

Table 3

Association of baseline clinicopathologic characteristics and CONUT score, PNI, NLR, and PLR.

Factors	N	CONUT	*P* value	PNI	*P* value	NLR	*P* value	PLR	*P* value
Sex			.110		.995		.191		.353
female	235	1.83±1.39		51.54±5.79		2.54±1.88		137.99±62.92	
male	400	2.03±1.59		51.53±6.07		2.75±1.95		133.25±61.57	
Age, years			.034		<.001		.259		.570
<65	368	1.84±1.43		52.54±5.66		2.60±1.96		133.81±59.77	
≥65	267	2.10±1.63		50.15±6.11		2.78±1.88		136.65±65.19	
ASA grade			<.001		.002		.025		.026
1–2	595	1.89±1.48		51.73±5.75		2.63±1.87		133.59±60.84	
3–4	40	2.80±1.87		48.69±8.15		3.33±2.61		156.07±75.98	
BMI, Kg/m^2			<.001		<.001		.706		.001
<25	484	2.10±1.56		51.03±6.09		2.69±1.85		139.73±63.35	
≥25	151	1.48±1.28		53.14±5..24		2.62±2.18		119.87±55.30	
Anemia			<.001		<.001		<.001		<.001
No	470	1.66±1.24		52.80±5.04		2.46±1.59		125.06±50.22	
Yes	165	2.79±1.89		47.92±6.86		3.29±2.58		163.33±81.19	
Diabetes mellitus			.286		.100		<.001		.089
No	479	1.91±1.49		51.76±6.03		2.52±1.64		132.62±60.48	
Yes	156	2.06±1.61		50.85±5.72		3.16±2.56		142.34±66.38	
Hypertension			.966		.531		.042		.208
No	365	1.95±1.52		51.66±5.93		2.54±1.88		132.33±61.18	
Yes	270	1.95±1.53		51.36±6.01		2.86±1.97		138.62±63.19	
Hypoalbuminemia			<.001		<.001		.001		<.001
No	601	1.78±1.30		52.27±5.16		2.62±1.85		131.66±58.11	
Yes	34	4.91±1.98		38.46±3.69		3.72±2.81		194.19±93.90	
Lower total cholesterol			<.001		<.001		.003		.115
No	319	1.12±1.03		52.61±5.43		2.45±1.49		131.14±57.27	
Yes	316	2.79±1.47		50.45±6.28		2.90±2.27		138.91±66.43	
Mean tumor size			.050		.167		.359		.002
<7	525	1.90±1.49		51.68±5.85		2.64±1.98		131.58±58.99	
≥7	110	2.21±1.63		50.82±6.45		2.83±1.64		151.37±73.17	
Pathological T stage			.051		.030		.014		.027
1 and 2	565	1.91±1.50		51.72±5.87		2.63±1.93		133.09±61.89	
3 and 4	70	2.29±1.63		50.07±6.53		3.02±1.87		150.43±61.76	
Regional lymph node involvement			.414		.171		216		.004
pNX-0	608	2.19±1.42		51.60±5.95		2.65±1.92		133.50±60.28	
pN1	27	1.94±1.52		50.00±6.21		3.12±2.07		168.93±88.64	
Fuhrman grade			.064		.027		.019		.005
1 and 2	472	1.89±1.46		51.84±5.81		2.57±1.86		130.97±58.09	
3 and 4	163	2.14±1.67		50.64±6.32		2.98±2.10		146.69±71.30	
Histologic subtype			.505		.793		.328		.324
Clear cell	559	1.97±1.52		51.56±5.96		2.70±2.00		134.11±62.44	
No-clear cell	76	1.84±1.55		51.37±6.06		2.47±1.21		141.60±59.24	

CONUT = Controlling Nutritional Status, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio, PNI = prognostic nutritional index.

correlated with the CONUT score, PNI, NLR, and PLR. Moreover, the PNI, NLR, and PLR significantly differed by pathological T stage and tumor grade; CONUT score, PNI, and PLR statistically differed by BMI; the CONUT score, PNI, and NLR significantly differed by lower total cholesterol; the age of the patients was associated with the CONUT score and PNI, diabetes mellitus and hypertension were correlated with NLR, and mean tumor size and regional lymph node involvement were closely associated with PLR. None of the 4 indexes differed by sex and histologic subtype.

3.3. Predictive factors for OS

In the univariate analysis, the age, ASA grade, BMI, anemia, hypoalbuminemia, low total cholesterol, high CONUT score, low PNI, high NLR and PLR, regional lymph node involvement, mean tumor size, pathological T stage, and Fuhrman grade were associated with reduced OS (Fig. 2). In the multivariate analysis, the CONUT score (HR = 3.012; 95% CI, 1.525–5.948; *P* = .001), age, anemia, regional lymph involvement, tumor grade, and pathological T stage were independent risk predictors of OS (Table 4).

3.4. Predictive factors for CSS

In the univariate analysis, the age, ASA grade, BMI, anemia, low total cholesterol, high CONUT score, low PNI, high NLR, and PLR, regional lymph node involvement, mean tumor size, pathological T stage, and Fuhrman grade were associated with reduced CSS (Fig. 3). In the multivariate analysis, the CONUT score (HR = 3.001; 95% CI, 1.290–6.984; *P* = .011), the age, NLR, regional lymph involvement, mean tumor size, pathological T stage, and Fuhrman grade were independent risk predictors of CSS (Table 4).

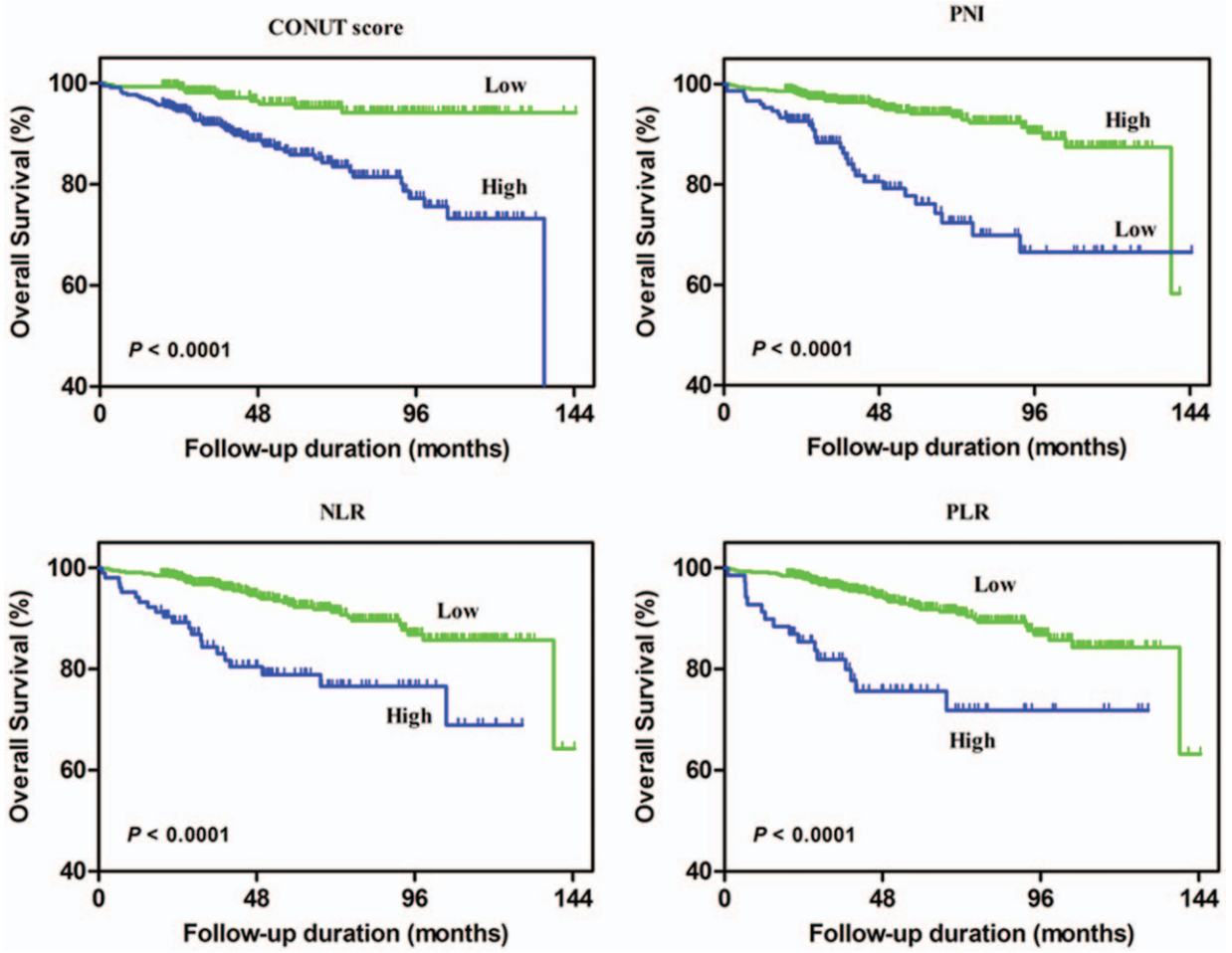

Figure 2. Overall survival stratified by (A) CONUT score, (B) PNI, (C) NLR, and (D) PLR. CONUT = Controlling Nutritional Status, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte Ratio, PNI = Prognostic Nutritional Index.

3.5. The comparison between the CONUT score and factors that comprise the CONUT score

We examined the influence of the factors that comprise the CONUT score (albumin, total cholesterol, and total lymphocyte count) on the OS and CSS. In the univariate analysis for OS, the albumin, total cholesterol, and total lymphocyte count were found to be predictive factors (Table 5). In the univariate analysis for CSS, the total cholesterol, and total lymphocyte count were found to be predictive factors (Table 5). The multivariate analysis for OS showed that the CONUT score was a more useful factor than serum albumin concentration and total lymphocyte count (Tables 6–8). The multivariate analysis for the CSS demonstrated that the CONUT score was a stronger factor than the serum albumin and total cholesterol concentrations (Tables 6–8). Therefore, these results indicated that the CONUT score was superior to its individual components for predicting survival (Tables 6–8).

4. Discussion

The prediction of the tumor response is important in the treatment of RCC. Previous studies have declared that PNI, NLR, and PLR are statistically correlated with prognosis of patients with RCC treated with nephrectomy. In addition, the CONUT score has received focus as a predictor of survival in patients with several cancers.[6,7,9,10,18] In the present study, we evaluated the predictive value of the CONUT score and further compared the accuracy of this biomarker with PNI, NLR, and PLR in RCC patients. In the present study, each of these 4 indexes were associated with the OS and CSS in the univariate analysis. In the multivariate analysis, the CONUT score was identified as the independent risk factor both for the OS and CSS rather than the other 3 factors. Although NLR was also shown to be an independent predictor for CSS, the CONUT score more accurately predicted the survival than NLR. Therefore, the CONUT score might be superior to the PNI, NLR, and PLR in the prognosis. Moreover, our results also suggested that the CONUT score was a better factor than its individual components for predicting survival. In a short, these results suggested that the CONUT score may serve as a risk predictor for RCC after surgery compared with other markers.

The CONUT score was proposed to correlate with the length of hospitalization and chronic diseases (e.g., end-stage liver disease and chronic heart failure) in the beginning.[19,20] Studies subsequently demonstrated that the CONUT score is generally correlated with poor survival in patients with cancer. Iseki et al reported that the CONUT score was a strong independent predictor of the survival among patients with colorectal cancer, and superior to PNI.[7] In addition, the prognostic significance of the CONUT score was identified in thoracic esophageal

Table 4

Univariate and multivariate analysis of the prognostic factors for the OS and CSS.

OS	Univariate analysis HR (95% CI), *P* value	Multivariate analysis HR (95% CI), *P* value
Sex (male)	1.528 (0.870–2.685), .140	
Age (≥65)	3.974 (2.180–7.247), <.001	3.709 (1.996–6.891), <.001
ASA grade (≥III)	3.573 (1.848–6.908), <.001	
BMI (≥25)	0.271 (0.108–0.677), .005	
Anemia (yes)	3.867 (2.306–6.482), <.001	2.200 (1.280–3.780), .004
Diabetes mellitus (yes)	1.275 (0.719–2.263), .406	
Hypertension (yes)	1.157 (0.693–1.931), .578	
Hypoalbuminemia (yes)	3.260 (1.546–6.874), .002	
Lower total cholesterol (yes)	2.999 (1.648–5.460), <.001	
CONUT score (≥2)	4.146 (2.151–7.993), <.001	3.012 (1.525–5.948), .001
PNI (<48)	3.856 (2.322–6.404), <.001	
NLR (≥3.5)	3.034 (1.780–5.170), <.001	
PLR (≥204.7)	3.519 (1.981–6.250), .001	
Regional lymph node involvement (yes)	3.709 (1.682–8.179), .001	3.311 (1.445–7.587), .005
Mean tumor size (≥7)	2.945 (1.741–4.983), <.001	
Pathological T stage (≥3)	4.797 (2.719–8.463), <.001	3.661 (2.015–6.651), <.001
Fuhrman grade (≥3)	2.769 (1.664–4.608), <.001	1.941 (1.141–3.301), .014
Histologic subtype (Clear cell)	1.641 (0.829–3.246), .155	
CSS	**Univariate analysis HR (95% CI), *P* value**	**Multivariate analysis HR (95% CI), *P* value**
Sex (male)	0.967 (0.516–1.813), .918	
Age (≥65)	3.877 (1.899–7.915), <.001	3.999 (1.875–8.530), <.001
ASA grade (≥III)	4.050 (1.869–8.773), <.001	
BMI (≥25)	0.330 (0.118–0.925), .035	
Anemia (yes)	3.625 (1.956–6.719), <.001	
Diabetes mellitus (yes)	1.294 (0.648–2.586), .465	
Hypertension (yes)	1.454 (0.786–2.688), .233	
Hypoalbuminemia (yes)	1.638 (0.505–5.311), .411	
Lower total cholesterol (yes)	2.213 (1.128–4.341), .021	
CONUT score (≥2)	4.416 (1.957–9.966), <.001	3.001 (1.290–6.984), .011
PNI (<48)	4.470 (2.416–8.269), <.001	
NLR (≥3.5)	3.904 (2.097–7.268), <.001	2.189 (1.153–4.156), .017
PLR (≥204.7)	3.930 (2.004–7.705), <.001	
Regional lymph node involvement (yes)	4.632 (1.945–11.033), .001	3.332 (1.262–8.793), .015
Mean tumor size (≥7)	4.436 (2.400–8.202), <.001	2.585 (1.327–5.035), .005
Pathological T stage (≥3)	3.756 (2.012–7.009), <.001	3.478 (1.712–7.064), .001
Fuhrman grade (≥3)	5.487 (2.829–10.642), <.001	2.174 (1.122–4.212), .021
Histologic subtype (Clear cell)	1.723 (0.762–3.895), .191	

CONUT = Controlling Nutritional Status, CSS = cancer-specific survival, NLR = neutrophil-to-lymphocyte ratio, OS = overall survival, PLR = platelet-to-lymphocyte ratio, PNI = prognostic nutritional index.

squamous, hepatocellular carcinoma, and gastric cancer.[6,8,10] However, there have been no studies previously reported the relationship between the preoperative immune-nutritional status and the survival after curative nephrectomy for RCC using the CONUT score. Therefore, this is the first report to demonstrate the significant association between the preoperative CONUT score and RCC patients' survival after surgery.

The CONUT score is a newly proposed scoring system to assess patients' immune and nutrition status.[11] It is calculated from the serum albumin concentration, total lymphocyte count and total cholesterol concentration, which are easily obtained in a blood examination. With regard to the 3 components of the CONUT, the serum albumin concentration is a reliable nutritional screening tool and has been reported to correlate with the prognosis patients with RCC.[21] A lower albumin level is not only caused by nutritional status, but also by many other factors, including liver function, inflammation, and changes in body fluid volume.[22] The decreased level of albumin may be due to the production of pro-inflammatory cytokines, such as interleukin-6, which modulate the production of albumin by hepatocytes.[23] In addition, the systemic and chronic inflammatory response to RCC is also correlated with lower albumin level and a reduction in the survival of RCC patients.[21] The total lymphocyte count is an index of systemic immunity.[24] Lymphocytes, such as CD4+ T cells and natural killer cells, is crucial in innate cellular immunity against caners.[25] Therefore, RCC patients with lymphopenia are more likely to have poor survival because they lack an adequate immune response to cancer.[24] Finally, a low serum cholesterol concentration was also reported as a risk factor for the prognosis of various malignancies, including RCC. Cholesterol is supposed as an essential structural component of healthy cells and a crucial part of lipid metabolism; it affects membrane structure and function, such as membrane protein activity and membrane fluidity.[26,27] Therefore, a decrease in the serum cholesterol means a loss of cholesterol from the membrane of cells, which affects the ability of immunocompetent cells to fight against cancer cells.[28] This finding might explain why a low serum cholesterol concentration is associated with a poor prognosis in RCC.

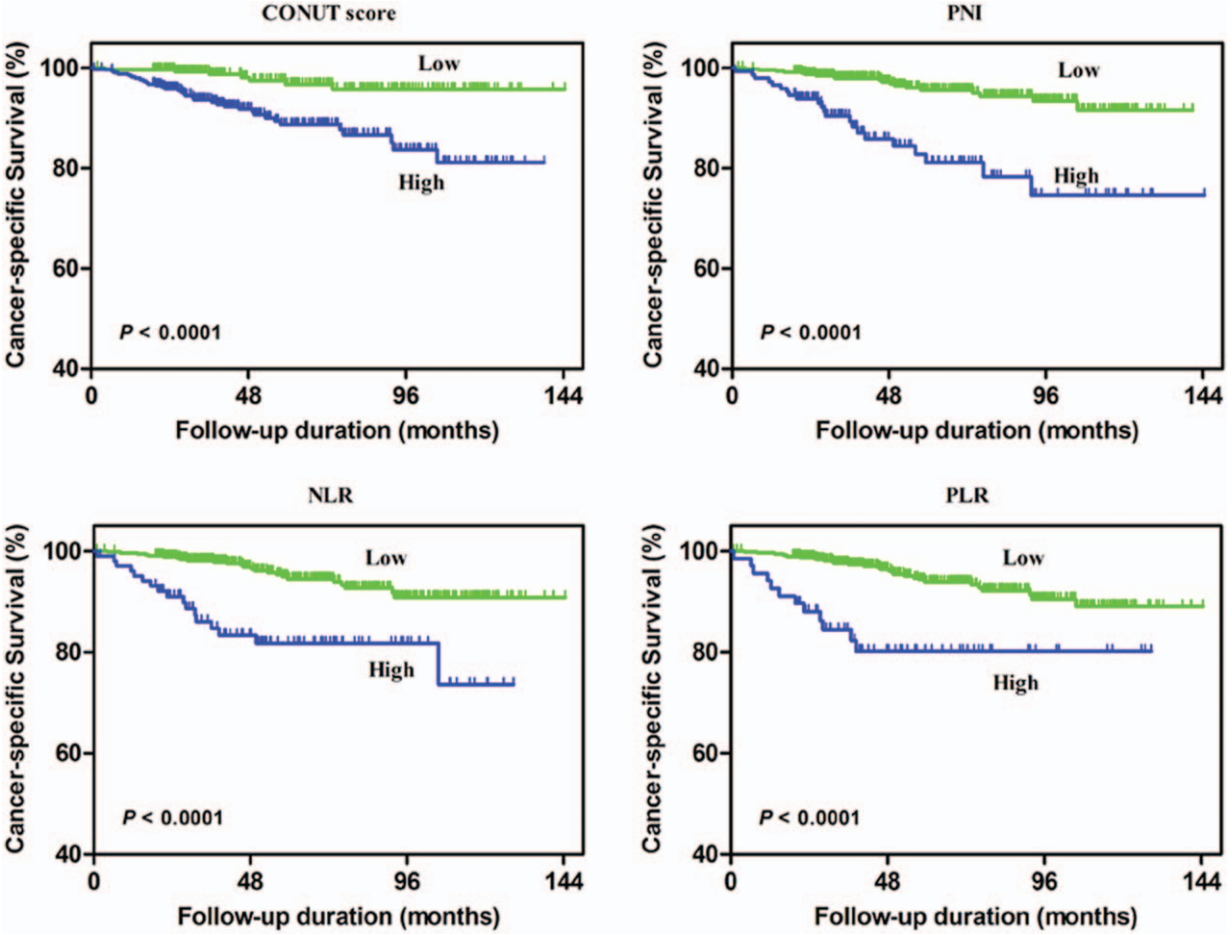

Figure 3. Cancer-specific survival stratified by (A) CONUT score, (B) PNI, (C) NLR, and (D) PLR. CONUT = Controlling Nutritional Status, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-to-lymphocyte ratio, PNI = Prognostic Nutritional Index.

In the present study, the optimal cutoff values to predict survival were determined from the maximal χ^2 log-rank values using the X-tile program. It was observed that optimal cutoff value of 2 for CONUT score was a superior prognostic level based on HR. However, the cutoff level of CONUT score in this study was inconsistent with the results of previous studies,[6,8,10] which may attribute to the differences in sample size, follow-up periods, survival end-point, and assays measuring serum albumin concentration, total lymphocyte count and total cholesterol concentration. In addition, there is still no best method to determine optimal cutoff values. Further studies are needed to determine an adequate cutoff value to predict prognosis of RCC patients. In addition, the proportion of patients in pathological T3 and T4 stage in our study was 10.71%, which was relatively lower compared with other studies,[4,5] and this may explain why the all-cause mortality and cancer-specific mortality of RCC in the present study (9.45% and 6.46%, respectively) were lower than those in previous studies.

This study has several limitations. First, this was a retrospective design in a single institution. However, our data were representative and reliable because our department is the largest urologic cancer center with the largest sample size for RCC patients in the south of Zhejiang Province. Second, other inflammatory factors, such as C-reactive protein and LMR, were not examined in our study. Finally, we failed to include other screening systems, such as the Nutrition Risk Index (NRI), Nutritional Risk Screening (NRS-2002), and Malnutrition

Table 5

Univariate analysis of albumin, total cholesterol, and total lymphocyte count for OS and CSS.

Factors	OS HR (95% CI), *P* value	CSS HR (95% CI), *P* value
Albumin (<3.5 g/dL)	3.260 (1.546–6.874), .002	1.638 (0.505–5.311), .411
Total cholesterol, (<180mg/dL)	2.999 (1.648–5.460), <.001	2.213 (1.128–4.341), .021
Total lymphocyte count, (<1600/mm^3)	2.210 (1.321–3.699), .003	2.630 (1.409–4.912), .002

CSS = cancer-specific survival, OS = overall survival.

Table 6

Multivariate analysis of the association between the CONUT score and the albumin with OS and CSS.

Factors	OS HR (95% CI), *P* value	CSS HR (95% CI), *P* value
CONUT score (>0.50)	3.802 (1.950–7.415), <.001	4.414 (1.943–10.028), <.001
Albumin (<3.5 g/dL)	2.064 (0.967–4.408), .061	1.006 (0.307–3.294), .992

CONUT = Controlling Nutritional Status, CSS = cancer-specific survival, OS = overall survival.

Table 7

Multivariate analysis of the association between the CONUT score and the total cholesterol with OS and CSS.

Factors	OS HR (95% CI), *P* value	CSS HR (95% CI), *P* value
CONUT score (>0.50)	3.135 (1.481–6.638), .003	4.208 (1.681–10.534), .002
Total cholesterol, (<180mg/dL)	1.662 (0.838–3.297), .146	1.090 (0.510–2.332), .824

CONUT = Controlling Nutritional Status, CSS = cancer-specific survival, OS = overall survival.

Table 8

Multivariate analysis of the association between the CONUT score and the total lymphocyte count with OS and CSS.

Factors	OS HR (95% CI), *P* value	CSS HR (95% CI), *P* value
CONUT score (>0.50)	3.780 (1.832–7.801), <.001	3.610 (1.454–8.964), .006
Total lymphocyte count, (<1600/mm^3)	1.193 (0.676–2.106), .543	1.437 (0.715–2.889), .308

CONUT = Controlling Nutritional Status, CSS = cancer-specific survival, OS = overall survival.

Universal Screening Tool (MUST), because these screening systems needed to be assessed prospectively. However, the result of the comparison between the CONUT score and PNI indicated that the CONUT score was superior at predicting the statistical outcomes.[7] Further studies are needed to assess the efficiency of these screening systems to evaluate the status of patients.

5. Conclusions

In the present study, we compared the prognostic significance of CONUT score, PNI, NLR, and PLR in RCC patients after curative nephrectomy and found CONUT score might be a better predictor than other factors for OS and CSS.

Author contributions

Conceptualization: Xiaomin Gao.
Data curation: Yangqin Zheng, Yue Pan.
Formal analysis: Xiaomin Gao.
Investigation: Yangqin Zheng, Qinquan Wang.
Methodology: Yue Pan.
Resources: Yue Pan, Qinquan Wang.
Software: Yangqin Zheng.
Supervision: Xiaomin Gao and Lianmin Bao.
Writing - original draft: Yangqin Zheng.
Writing – review and editing: Xiaomin Gao and Wenhan Wang.

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