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ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Preoperative controlling nutritional status (CONUT) score as a novel immune-nutritional predictor of survival in non-metastatic clear cell renal cell carcinoma of ≤ 7 cm on preoperative imaging

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Abstract

Purpose This study aimed at investigating the prognostic value of Preoperative controlling nutritional status (CONUT) score in non-metastatic clear-cell renal cell carcinoma of ≤ 7 cm on preoperative imaging.

Methods We retrospectively included 1046 among 1637 patients who underwent radical or partial nephrectomy for solid renal masses ≤ 7 cm (2005–2014) after excluding other pathology, conditions affecting CONUT score components, metastasis, regional lymphadenopathy, positive margin, and follow-up < 12 months. We defined high and low CONUT according to cut-off of (2). Multivariate Cox-regression analysis was used to predict factors affecting recurrence and survival. Kaplan–Meier curve was used for survival analysis.

Results The median age and follow-up were 56 years and 63 months, respectively. 41 patients had recurrence (3.9%). CONUT was a predictor for recurrence-free, cancer-specific, and overall survival (HR 3.09, $P = 0.003$ and HR 4.66, $P = 0.004$ and HR 2.81, $P = 0.003$, respectively). A higher CONUT was significantly associated with worse 5 years recurrence-free (88.2% vs. 97.1%), cancer-specific (96.2% vs. 98.8%) and overall (90.9% vs. 96.5%) survival (log-rank, $P = < 0.001$, $P = 0.006$ and $P = < 0.001$, respectively).

Conclusions The preoperative CONUT is an independent prognostic marker for survival after curative surgery for non-metastatic clear-cell renal cell carcinoma of ≤ 7 cm on preoperative imaging.

Keywords Non-metastatic clear cell renal cell carcinoma · Nutrition · Nephrectomy · Immunity

Introduction

The clear-cell (ccRCC) is the commonest variant of renal cell carcinoma (RCC) which is the third most popular urogenital tumor (Shuch et al. 2015). After surgery with curative intent for RCC, 10–20% of cases show recurrence (Park et al. 2012). The well-known prognostic factors in RCC are Pathological T stage, Fuhrman grade, sarcomatoid differentiation, lymph node metastasis, and distant metastasis (Jeon et al. 2016). Most of studies that already handled the predictors of survival in RCC notably included the nonmodifiable characteristics of both patient and the tumor itself (e.g. age, race, stage, and tumor size) (Kutikov et al. 2010). Therefore, it is important to develop readily available biomarkers that can predict and even modify the tumor outcome based on the risk stratifications. The preoperative immune-nutritional status has been addressed in various malignancies as a predictor of patient morbidity

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and mortality (Liang et al. 2017; Mimatsu et al. 2017). Obviously, RCC is widely considered as a metabolic disease (Linehan and Ricketts 2013). Besides, it is related to nutritional status and cachexia as a part of its paraneoplastic findings (e.g. hypoalbuminemia, weight loss, anorexia, and malaise) that were found to be independently associated with survival outcome (Kim et al. 2004). Moreover, nutritional deficiency (ND) in cancer patient is related to inadequate intake as well, as it is aggravated by the cancer-induced hapercatabolic state and inflammatory response (Prado et al. 2012; Karl et al. 2009). On the other hand, there is growing evidence that the host inflammatory response shares in both oncogenesis and cancer progression (Mantovani et al. 2008). Recently, the potential prognostic value of preoperative immune-nutritional status has gained a lot of concern with RCC and it has been reported to correlate with the patient survival (Jeon et al. 2016; Kim et al. 2004; Morgan et al. 2011; Ko et al. 2013; Saroha et al. 2013). Preoperative nutritional deficiency was associated with 2.4- and 2.7-fold decrease in both OS and CSS, respectively (Morgan et al. 2011). Ignacio et al. first described the Controlling Nutritional Status (CONUT) score to assess the nutritional status of patients. This score is calculated based on three variables, including serum albumin concentration, total lymphocyte count (TLC), and total cholesterol concentration (TC) in peripheral blood (Ignacio de Ulíbarri et al. 2005). In our study, we evaluated the prognostic value of preoperative CONUT score on the oncologic outcome in surgically resected non-metastatic ccRCC of tumor size ≤ 7 m on preoperative imaging from a large single center cohort.

Methods

Patient

Based on our Review Board guidelines, and in accordance with the ethical standards of Declaration of Helsinki (1964), we retrospectively reviewed 1637 adult patients with solid renal masses ≤ 7 cm on preoperative computed tomography (CT) who underwent radical or partial nephrectomy (2005–2014). We included 1046 cases with localized unilateral ccRCC. The three components of CONUT score (i.e. serum albumin concentration, peripheral TLC and TC concentration) were obtained from the same blood sample within one month prior to surgery. We excluded benign pathology, non-clear cell type, conditions affecting TC (i.e. liver disease, thyroid diseases, nephrotic syndrome, and statins intake), conditions affecting TLC (i.e. immunosuppression, hematologic and non-hematologic malignancies, autoimmune diseases, and chronic inflammatory diseases), metastasis, lymphadenopathy, positive margin, adjuvant treatment, short follow-up < 12 months, and those with missed data. Lymphadenopathy and metastasis were preoperatively diagnosed by CT, chest radiographs, and bone scans. Pathological data were collected from the same genitourinary pathology division at our institute. Tumors were classified based on TNM system of 2010—American Joint Committee on Cancer (AJCC) (Edge and Compton 2010) and Fuhrman grading (Fuhrman et al. 1982).

Follow-up

Physical examination, serum chemistry, chest radiography, and abdominal-pelvic CT were performed semi-annually for the first 3-years and annually thereafter. Recurrence equals the first detection of either local or distant recurrence. Data regarding death were investigated using our medical records.

Study endpoints

Recurrence-free survival (RFS) is the time interval from surgery to radiological detection of recurrence, Cancer-specific survival (CSS) is the time interval from surgery to cancer-related death or last follow-up and finally, Overall survival (OS) is the time interval from surgery to overall death or last follow-up.

Statistics

Preoperative CONUT score was evaluated as dichotomized variables (high and low) by obtaining the best cutoff value. Using Shapiro–Wilk test, we rejected the hypothesis that continuously coded variables were normally distributed ($P < 0.001$). Thus, they were presented as the median and interquartile range (IQR). Mann–Whitney U and χ^2 tests were used to compare with continuous and dichotomized variables, respectively.

For survival analysis, Kaplan–Meier with the log-rank test was used. The relative risk was assessed by 95% confidence intervals (CI) of hazard risk (HR). All variables with

Table 1 Definition of CONUT score (Ignacio de Ulíbarri 2005)

Parameter	None	Light	Moderate	Severe
Serum albumin, g/dl	≥ 3.50	3.00–3.49	2.50–2.99	< 2.50
Score	0	2	4	6
TLC/mm^3	≥ 1600	1200–1599	800–1199	< 800
Score	0	1	2	3
TC, mg/dl	≥ 180	140–179	100–139	< 100
Score	0	1	2	3

CONUT Controlling nutritional status, *TLC* total lymphocyte count, *TC* total serum cholesterol

a P-value < 0.05) in the univariate analysis were included in multivariate Cox regression analysis with stepwise backward elimination. All tests were two-sided, with statistical significance set at ($P < 0.05$). Statistical analysis was performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA).

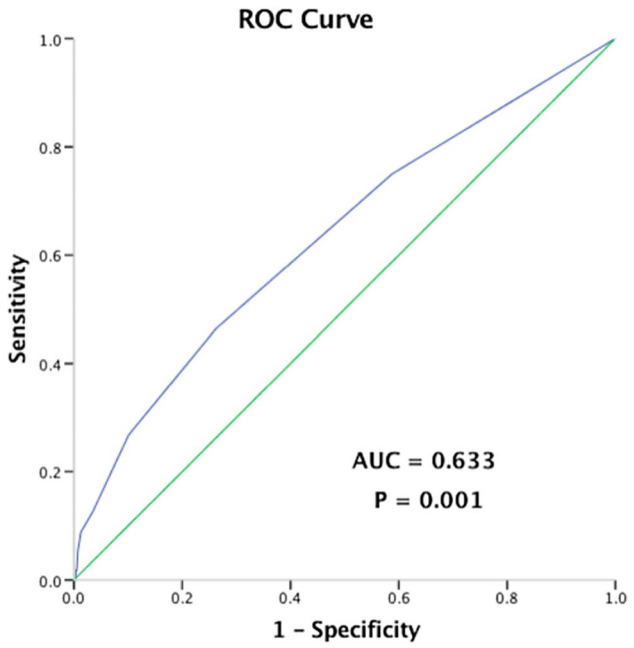

Fig. 1 Receiver operating characteristic (ROC) curve showed the most appropriate cut-off value for CONUT score to be (2) using overall death as a state variable (Area under the curve AUC 0.633, 95% CI 0.554–0.713, $P = 0.001$, the sensitivity was 46.4% and the specificity was 73.7%)

Results

Defining the CONUT score and its cutoff value

CONUT score was calculated using the serum albumin concentration, peripheral TLC and the TC concentration, as described in Table 1 (Ignacio de Ulíbarri 2005) in which patients were grouped into four ND categories: normal, light, moderate, and severe ND. The optimal cut-off value of CONUT score was determined as (2) by the receiver operating curve (ROC) analysis and using the maximum Youden Index. The areas under the curve (AUC) based on end-point of the overall death were 0.633 (sensitivity = 46.4%, specificity = 73.7%, $P = 0.001$), (Fig. 1). CONUT score was evaluated as dichotomized variables (low: ≤ 2 and high: > 2).

CONUT score components

Table 2 shows comparison between high and low CONUT score groups as regards CONUT score components. Unsurprisingly, patients in high CONUT group had higher scores for the three components than those in the low CONUT group (Table 3).

Table 2 CONUT score components

CONUT score components	Total ($n = 1046$)	CONUT ≤ 2 ($n = 931$)	CONUT > 2 ($n = 115$)	P*
Albumin score				0.000
0	1017 (97.2%)	928 (99.7%)	89 (77.4%)	
2	19 (1.8%)	3 (0.3%)	16 (13.9%)	
4	6 (0.6%)	0 (0.0%)	6 (5.2%)	
6	4 (0.4%)	0 (0.0%)	4 (3.5%)	
TLC score				0.000
0	790 (75.5%)	773 (83.0%)	17 (14.8%)	
1	162 (15.5%)	129 (13.9%)	33 (28.7%)	
2	79 (7.6%)	29 (3.1%)	50 (43.5%)	
3	15 (1.4%)	0 (0.0%)	15 (13.0%)	
TC score				
0	536 (51.2%)	528 (56.7%)	8 (7.0%)	0.000
1	374 (35.8%)	319 (34.3%)	55 (47.8%)	
2	123 (11.8%)	84 (9.0%)	39 (33.9%)	
3	13 (1.2%)	0 (0.0%)	13 (11.3%)	

CONUT Controlling nutritional status, *TLC* total lymphocyte count, *TC* total serum cholesterol

*P value from comparison between CONUT ≤ 2 and > 2

Table 3 Patient and tumor characteristics

	Total ($n=1046$)	Group A CONUT ≤ 2 ($n=931$)	Group B CONUT > 2 ($n=115$)	P*
Follow-up (months)	63 (43–87)	64 (43–88)	59 (42–82)	0.098**
Age (years)	56 (46–64)	55 (46–64)	61 (50–68)	0.001**
Gender				0.192
Male	745 (71.2%)	657 (70.6%)	88 (76.5%)	
Female	301 (28.8%)	274 (29.4%)	27 (23.5%)	
BMI	24.3 (22.5–26. 5)	24. 5 (22.6–26.5)	23.4 (21.6–25.2)	0.001**
PNI	55.0 (51.9–58.4)	55.4 (52.8–58.9)	47.9 (42.6–51.9)	< 0.001**
MLR	0.19 (0.15–0.25)	0.18 (0.15–0.24)	0.29 (0.22–40)	< 0.001**
NLR	1.83 (1.39–2.47)	1.74 (1.35–2.24)	3.16 (2.22–4.51)	< 0.001**
PLR	119.44 (97.54–151.95)	115.18 (95.58–143.12)	197.96 (150–264.94)	< 0.001**
CCI				0.010***
≤ 2	659 (63.0%)	601 (64.6%)	58 (50.4%)	
3–4	260 (24.9%)	220 (23.6%)	40 (34.8%)	
≥ 5	127 (12.1%)	110 (11.8%)	17 (14.8%)	
Pathological T stage				0.255
T1	940 (89.9%)	840 (90.2%)	100 (87.0%)	
T2	7 (0.7%)	7 (0.8%)	0 (0.0%)	
T3	99 (9.5%)	84 (9.0%)	15 (13.0%)	
Fuhrman grade				0.479***
G1–2	638 (61.0%)	564 (60.6%)	74 (64.3%)	
G3–4	408 (39.0%)	367 (39.4%)	41 (35.7%)	
PADUA score sum				0.289***
6–7	246 (23.5%)	222 (23.8%)	24 (20.9%)	
8–9	427 (40.8%)	372 (40.0%)	55 (47.8%)	
≥ 10	373 (35.7%)	337 (36.2%)	36 (31.3%)	
Radical or partial				0.229***
Radical	434 (41.5%)	380 (40.8%)	54 (47.0%)	
Partial	612 (58.5%)	551 (59.2%)	61 (53.0%)	

Data are presented as number (%) or median (interquartile range)

CONUT Controlling nutritional status, *BMI* Body mass index, *PNI* Prognostic nutritional index, *MLR* monocyte–lymphocyte ratio, *NLR* neutrophil–lymphocyte ratio, *PLR* platelet–lymphocyte ratio, *CCI* Charlson comorbidity index, *PADUA* preoperative aspects and dimensions used for anatomic classification

*P value from comparison between groups A and B

**Mann–Whitney U test for the continuous data

***Fisher's exact test

Clinicopathological features

A total of 1046 patients had median age at surgery of 56 years (IQR 46–64). The median TC, TLC, and serum albumin were 181 mg/dl (IQR 158–206), 2×10^9/l (IQR 1.6–2.4), 4.5 g/dl (4.3–4.7), respectively. Total of 115 (11%) had high CONUT score and 931 (89%) had low CONUT score. High CONUT score was significantly more common among older patients with lower BMI ($P < 0.001$) and had a higher monocyte–lymphocyte ratio (MLR) ($P = 0.003$), neutrophil–lymphocyte ratio (NLR), as well as platelet–lymphocyte ratio (PLR) ($P < 0.001$). Low CONUT score patients had a better Charlson comorbidity indexes (CCI) score of ≤ 2 ($P = 0.010$) and a higher prognostic nutritional index (PNI) ($P < 0.001$). There were no significant differences in pathological features between groups (Table 1).

Survival outcome

At median 63 months post-surgery (IQR 43–87), 41 patients experienced disease recurrence, and 56 died (18 of RCC) during median 63 months (IQR 43–87) for OS and 64 months (IQR 44–88) for CSS. The 3- and 5-year RFS rates were significantly lower in high CONUT score (92.1%

and 88.2%) vs. (98.1% and 97.1%) in low CONUT score (log-rank, $P < 0.001$).

High CONUT score had significantly lower 3- and 5-year CSS rates (96% and 96%) vs. (100% and 99%) in low CONUT score (log-rank, $P = 0.006$). Last, the 3- and 10-years for OS rates were significantly lower in low TC (95% and 91%) vs. (99% and 97%) (log-rank, $P < 0.001$) (Fig. 2a–c).

In multivariate analyses (Table 4), High CONUT score was an independent predictor of RFS (HR 3.09, $P = 0.003$), among other predictors such as CCI score, greater clinical tumor size, and greater pathological T stage. Also, high CONUT score was an independent predictor of CSS (HR 4.66, $P = 0.004$) besides greater CCI, pathologic T stage, and Fuhrman nuclear grade (Table 5). High CONUT score was an independent predictor of OS (HR 2.81, $P = 0.003$) together with greater CCI, and pathologic T stage (Table 6).

Discussion

The present study concluded that preoperative CONUT score is an independent prognostic factor for the oncologic outcome after surgery for curative intent with higher CONUT score is associated with higher recurrence as well as, worse RFS, CSS, and OS. To our knowledge, this study is the first designed to evaluate the prognostic value of CONUT score on survival and oncologic outcome in patients with RCC. Ishihara et al. proved that higher CONUT score was associated with worse survival and had a significant predictive value in patients with localized urothelial carcinoma of the upper urinary tract treated with radical nephroureterectomy (Ishihara et al. 2017).

Despite the scanty studies in genitourinary cancers, our conclusion was adopted with many of non-genitourinary cancers (Liang et al. 2017). For example, Iseki et al. showed a significant higher CSS with low CONUT group in patients with localized stage colorectal cancer undergoing curative surgery (Iseki et al. 2015). Toyokawa et al. (2016) studied the resectable thoracic esophageal cancer and showed that high CONUT score was an independent predictor of worse survival even much better than other inflammation-based markers, such as the PLR, NLR, and modified Glasgow prognostic score. Similar conclusions were reported in malignant pleural mesothelioma and non-small cell lung cancer after curative surgery (Takamori et al. 2017; Shoji et al. 2017).

On the contrary, Mimatsu et al. (2017) suggested that CONUT score did not have a predictive value in patients with stage IV gastric cancer who had undergone palliative surgery. As a complex marker, the predictive value can be correlated with CONUT score as regards each component. It was documented that a severe grade of ND has been found

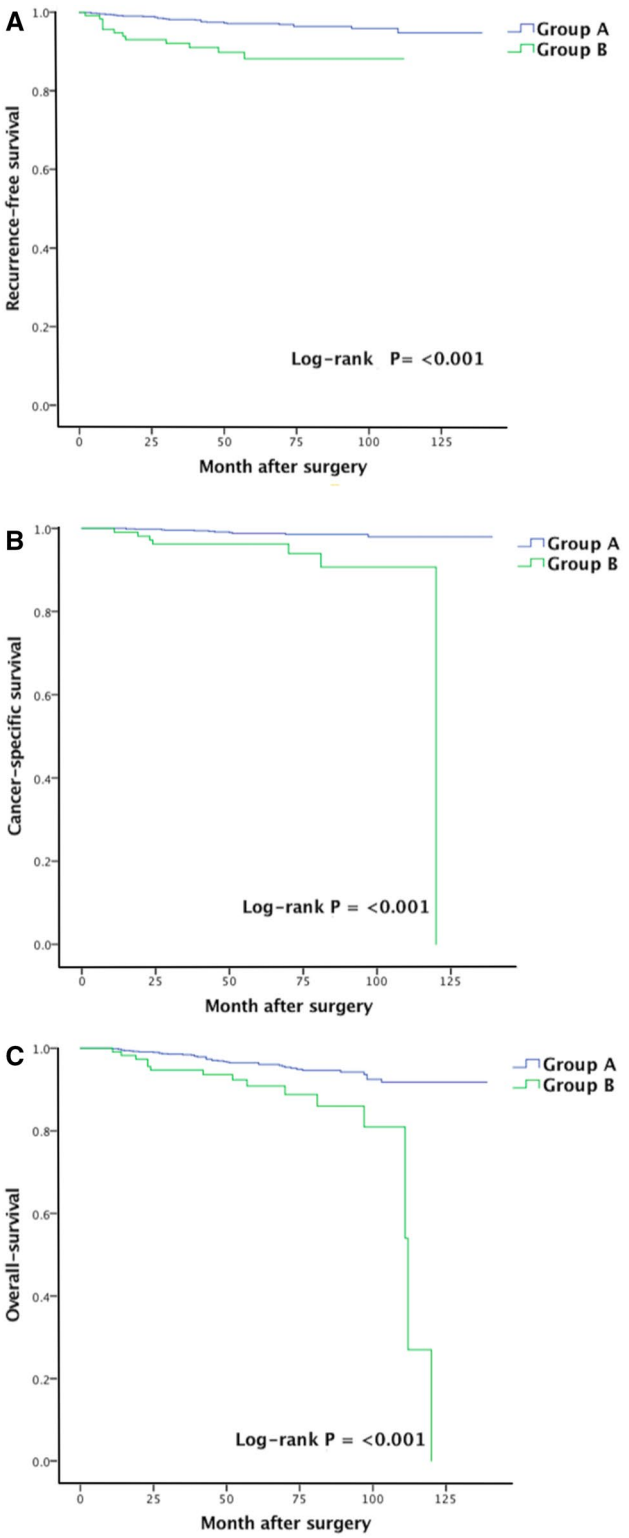

Fig. 2 Kaplan–Meier curves for RFS (**a**), CSS (**b**) and OS (**c**) according to preoperative CONUT score

Table 4 Univariate and multivariate cox regression analyses for factors predicting RFS

	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	1.041 (1.014–1.068)	0.003		
Gender				
Male	Ref.			
Female	0.698 (0.333–1.462)	0.340		
BMI	1.032 (0.938–1.134)	0.519		
CCI				
≤2	Ref.		Ref.	
3–4	3.277 (1.665–6.449)	0.001	2.887 (1.393–5.985)	0.004
>5	2.414 (0.984–5.921)	0.054	1.902 (0.719–5.030)	0.195
Clinical tumor size				
<4	Ref.		Ref.	
4–7	4.215 (2.183–8.139)	<0.001	2.872 (1.403–5.880)	0.004
Pathological T stage				
T1	Ref.		Ref.	
T2	5.031 (0.677–37.369)	0.114	5.776 (0.618–53.983)	0.124
T3	8.235 (4.395–15.432)	<0.001	5.702 (2.791–11.651)	<0.001
Fuhrman grade				
G1–2	Ref.			
G3–4	2.832 (1.499–5.350)	0.001		
PADUA score sum				
6–7	Ref.			
8–9	0.919 (0.334–2.531)	0.871		
≥10	2.527 (1.035–6.173)	0.042		
CONUT groups				
≤2	Ref.		Ref.	
>2	3.666 (1.867–7.196)	<0.001	3.092 (1.450–6.593)	0.003

RFS recurrence-free survival, *HR* hazard ratio, *CI* confidence interval, *BMI* Body mass index, *CCI* Charlson comorbidity index, *PADUA* preoperative aspects and dimensions used for anatomic classification, *CONUT* Controlling nutritional status

in about 16% of patients admitted for urologic cancers (Karl et al. 2009). Sarcopenia as a component of cancer cachexia predicts poor prognosis and indicates ND in cancer patient (Ishihara et al. 2016). Additionally, Serum albumin accurately reflects protein-energy malnutrion even in patients who still have normal BMI and body weight (Lipschitz 1988; Llop et al. 2001).

Above all, Hypoalbuminemia is not only a reflection of ND but also correlates with excess inflammatory cytokines released by the tumor cells which in turn inhibit hepatic albumin production (Ignacio de Ulíbarri et al. 2005; Cengiz et al. 2006). This correlation has been previously utilized to incorporate inflammatory markers (i.e. C-reactive protein) with albumin in prediction models (Ishihara et al. 2016). As regards serum cholesterol, the RCC-associated hypocholesterolemia is a marker reflecting poor RFS, CSS and OS (Kang et al. 2018). The tumor cells have higher activity of low-density lipoproteins (LDL) receptor-mediated endocytosis. Hence, the more the engulfing of cholesterol by tumor cells, the more the hypocholesteremia (Ishihara et al. 2017). However, it could not be confirmed whether RCC-associated hypocholesterolemia is due to change in lipid metabolism by tumor cells reflecting neoplastic aggressiveness or is a result of depletion of calories by the developing cancer cachexia (Toyokawa et al. 2016).

The last variable in the CONUT score is peripheral TLC which has antitumor effect via induction of apoptosis and suppressing tumor growth (Mantovani et al. 2008). In the tumor microenvironment, the high lymphocyte density reflects an imunnologic reaction against tumor. Therefore, peripheral leucopenia indicates a worse outcome in ccRCC (Saroha et al. 2013). We observed that the high CONUT group had a lower PNI and the latter was previously proved to have a worse survival in resectable RCC (Jeon et al. 2016). Also, we noticed that other pretreatment inflammatory markers (i.e. NLR, MLR, and PLR) are found to be higher with high CONUT score group and having worse both recurrence and survival. The previous data were

Table 5 Univariate and multivariate cox regression analyses for factors predicting CSS

	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	1.058 (1.014–1.104)	0.009		
Gender				
Male	Ref.			
Female	0.308 (0.071–1.341)	0.117		
BMI	0.916 (0.780–1.076)	0.285		
CCI				
≤2	Ref.		Ref.	
3–4	3.079 (1.034–9.167)	0.043	2.202 (0.692–7.006)	0.181
>5	4.978 (1.518–16.324)	0.008	4.710 (1.303–17.021)	0.018
Clinical tumor size				
<4	Ref.			
4–7	2.904 (1.124–7.499)	0.028		
Pathological T stage				
T1	Ref.		Ref.	
T2	0.000 (0.000–0.000)	0.982	0.000 (0.000–0.000)	0.999
T3	13.815 (5.446–35.048)	<0.001	9.115 (3.305–25.136)	<0.001
Fuhrman grade				
G1–2	Ref.		Ref.	
G3–4	4.302 (1.532–12.083)	0.006	2.880 (0.956–8.680)	0.060
PADUA score sum				
6–7	Ref.			
8–9	1.585 (0.320–7.860)	0.573		
≥10	2.662 (0.580–12.221)	0.208		
CONUT groups				
≤2	Ref.		Ref.	
>2	6.102 (2.342–15.900)	<0.001	4.664 (1.625–13.391)	0.004

CSS cancer-specific survival, *HR* hazard ratio, *CI* confidence interval, *BMI* Body mass Index, *CCI* Charlson comorbidity index, *PADUA* preoperative aspects and dimensions used for anatomic classification, *CONUT* Controlling nutritional status

previously confirmed in a comparison study between pretreatment inflammatory markers in ccRCC by Lucca et al. (2015).

The strength points in our study are that the CONUT score is a readily available and cost-effective biomarker which can be added to already valid or upcoming stratification scores, hence assisting decision making based on its prognostic value. Moreover, immune-nutritional status is a modifiable factor with promising data on a targeted preoperative nutritional supplementation that may decrease morbidity and improve survival of cancer patients, especially those with severe degree of nutritional deficiency (Morgan et al. 2011; Arends et al. 2017). This is the first study for the CONUT score in RCC and the first to have the largest sample size of patients among studies of other malignancies giving more statistical power (Liang et al. 2017; Ishihara et al. 2017; Iseki et al. 2015; Toyokawa et al. 2016; Takamori et al. 2017; Shoji et al. 2017). Another strength point that all cases were derived from a single center and subjected to the same standardized protocol of blood sampling, laboratory techniques, surgical procedure, pathological evaluation and follow-up strategy.

To establish the homogeneity of our cohort, we applied strict group of inclusion and exclusion criteria. Mainly, we only included clinical tumor size ≤7 cm and excluded any preoperative drugs or conditions that may influence the variables of CONUT score. Our study is retrospective with the limitation of selection bias; therefore, a prospective validation is needed. Another limitation is that there may be other factors which may be a competing risk, especially the cardiovascular diseases that may need further consideration (Kunimura et al. 2017).

Table 6 Univariate and multivariate cox regression analyses for factors predicting OS

	Univariate		Multivariate	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age (years)	1.091 (1.063–1.120)	< 0.001	1.045 (0.996–1.096)	0.073
Gender				
Male	Ref.			
Female	0.542 (0.273–1.074)	0.079		
BMI	1.003 (0.921–1.093)	0.941		
CCI				
≤ 2	Ref.		Ref.	
3–4	3.782 (1.867–7.659)	< 0.001	1.829 (0.672–4.983)	0.238
> 5	9.477 (4.825–18.614)	< 0.001	4.069 (1.140–14.529)	0.031
Clinical tumor size				
< 4	Ref.			
4–7	1.121 (0.652–1.927)	0.679		
Pathological T stage				
T1	Ref.		Ref.	
T2	2.197 (0.301–16.059)	0.438	7.631 (0.829–70.245)	0.073
T3	3.815 (2.078–7.005)	< 0.001	3.053 (1.537–6.062)	0.001
Fuhrman grade				
G1–2	Ref.			
G3–4	1.565 (0.926–2.646)	0.094		
PADUA score sum				
6–7	Ref.			
8–9	0.865 (0.423–1.772)	0.692		
≥ 10	1.028 (0.512–2.065)	0.938		
CONUT groups				
≤ 2	Ref.		Ref.	
> 2	3.344 (1.844–6.062)	< 0.001	2.812 (1.437–5.502)	0.003

OA overall survival, *HR* hazard ratio, *CI* confidence interval, *BMI* Body mass index, *CCI* Charlson comorbidity index, *PADUA* preoperative aspects and dimensions used for anatomic classification, *CONUT* Controlling nutritional status

Conclusion

In conclusion, CONUT score can help preoperative evaluation and predict outcome based on modifiable risk factors for patients with non-metastatic clear cell renal cell carcinoma of ≤ 7 cm on preoperative computed tomography after partial or radical nephrectomy.

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Compliance with ethical standards

Conflict of interest No conflict exists.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was not required for the purposes of this study, as the study was based on retrospective anonymous patient data and did not involve patient intervention or the use of human tissue samples.

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