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# Preoperative Mean Corpuscular Hemoglobin Concentration (MCHC) as Indicators of Patients' Poor Prognosis for Renal Clear Cell Carcinoma

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## Abstract

**Introduction:** Low Mean Erythrocyte Hemoglobin Concentrations (MCHC) has been linked to tumor oxygenation issues and anemia connected to cancer, according to studies. It is unknown, though, what role MCHC plays in renal cell cancer patients. In this study, Clear Cell Renal Cell Carcinoma (CCRCC) patients had their preoperative MCHC evaluated for its predictive usefulness.

**Materials and Methods:** Patients diagnosed with CCRCC and undergoing nephrectomy at our institution between 2003 and 2012 were included in the retrospective analysis. Preoperative MCHC was correlated with clinicopathological characteristics and survival rate using the Cox proportional hazards regression model and the Kaplan-Meier method.

**Results:** Overall Survival (OS, P<0.001) and Cancer-Specific Survival (CSS, P<0.001) were favorably linked with MCHC levels in patients with CCRCC, as depicted by the Kaplan-Meier method. Univariate analysis showed that MCHC was substantially linked with OS [Hazard Ratio (HR)=0.278; 95% Confidence Interval (CI) (0.146-0.530); P<0.001] and CSS [HR=0.244; 95% CI (0.125-0.476); P<0.001] in patients with CCRCC. In multivariate analysis, higher MCHC was linked to better OS [HR=0.296; 95% CI (0.144-0.609); P<0.001] and CSS [HR=0.249; 95% CI (0.116-0.533)); P<0.001], suggesting that preoperative MCHC level is an independent predictor of CCRCC.

**Conclusion:** Our data imply that in patients with CCRCC, preoperative MCHC is a more accurate predictor of OS and CSS.

**Keywords: Mean erythrocyte hemoglobin concentration; CCRCC; Preoperative; Prognosis**

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## Abbreviations

HR: Hazard Ratio; LVI: Lymphovascular Invasion; CI: Confidence Interval; AKP: Alkaline Phosphatase; CCRCC: Clear Cell Renal Cell Carcinoma; MCHC: Mean Erythrocyte Hemoglobin Concentrations

## Introduction

One of the most frequent malignant tumors of the genitourinary system, Renal Cell Carcinoma (RCC), makes up roughly 2% to 3% of all malignant tumors [1]. RCC originates from renal epithelial cells, and the primary pathological subtype is Clear Cell Renal Cell Carcinoma (CCRCC) [2]. It has been reported that most patients have no obvious clinical symptoms in the early stage. Still, about 25% of patients have advanced manifestations of locally invasive or metastatic RCC with a poor prognosis [3]. Surgery is a reliable treatment option, but one-third of patients tend to relapse [4]. To assess therapy response and prognosis, it is necessary to investigate a straightforward and precise new biomarker.

Anemia and the onset of cancer are tightly associated [5]. In recent years, more and more evidence has shown that Mean Erythrocyte Hemoglobin Concentration (MCHC) is closely related to a variety of cancers, including laryngeal cancer [6], non-small cell lung cancer [7], rectal cancer [8], breast cancer [9], hepatocellular carcinoma [10], cervical cancer [11], etc. According to Kong [10], low MCHC was significantly linked to a poor prognosis for hepatocellular carcinoma after hepatectomy [Hazard Ratio (HR)=0.372; 95% Confidence Interval (CI) (0.206-0.672); P=0.001], and the lower the MCHC value, the worse the prognosis after hepatectomy. Low hemoglobin levels

were reported by Lee et al. [12] to predict a poor outcome in 451 patients with advanced head and neck cancer. Similarly, Xiao [9] also found that MCHC could predict the behavior and biological activity of tumors, which might be employed as a novel metric to assess the prognosis of breast cancer. However, it has also been reported that in patients with gastric cancer, high levels of MCHC predict poor Overall Survival (OS) and Disease-Free Survival (DFS). In addition, MCHC also significantly increases with tumor enlargement in oral tumors [13]. Cumulative evidence shows that the poor prognosis of cancer patients is closely correlated with preoperative MCHC levels, including liver cancer [10], head and neck cancer [14], breast cancer [9], colorectal cancer [8], cervical cancer [11], bronchial cancer [15], esophageal cancer [16] and bladder cancer [17], etc.

The prognostic significance of preoperative MCHC in CCRCC patients has not, as far as we are aware, been studied. We identified a link between preoperative MCHC, clinicopathological variables, and patient survival in this investigation. Additionally, we sought to assess the potential of preoperative MCHC as a novel predictive biomarker in CCRCC patients.

## Methods

### Patients

Each patient provided their written informed consent, and the research ethics committee of the nearby institute approved the investigation. Three hundred ninety-eight CCRCC patients who underwent surgery at the Third Affiliated Hospital of Soochow University between 2003 and 2012 were the subject of a retrospective investigation. The following criteria were used for inclusion: Patients with CCRCC pathological subtype, patients who underwent radical nephrectomy, patients who did not receive preoperative neoadjuvant therapy, patients with no history of other cancers, and patients who underwent comprehensive preoperative laboratory tests. Among the 398 patients, 8 patients lacked preoperative MCHC data, 4 patients had incomplete clinicopathological parameters, and 9 patients were unfollowable. The remaining 377 patients were finally assessed after 21 patients were eliminated. The Third Affiliated Hospital of Soochow University's medical record inquiry system was used to gather the clinical data.

### Data collection

Each patient's clinical information, including age, gender, lymph node stage, T stage, Fuhrman grade, tumor size, and tumor necrosis, was gathered from the medical record query system of the Third Affiliated Hospital of Soochow University. At the same time, LVI and AKP data were collected. The renal TNM staging system was performed using the AJCC 2010 version [18]. Fuhrman's classification was based on the 1997 World Health Organization version. In this study, lymphatic invasion referred to the invasion of the blood vessels or lymphatic system by cancer cells without invading the underlying muscle wall [19].

### Operation and follow-up assessment

Of the eligible patients, 207 patients underwent laparoscopic nephrectomy, while the remaining 170 patients underwent open nephrectomy. All patients underwent surgical removal of the kidney, ureter, perirenal adipose tissue, adrenal gland, and nearby lymph nodes following the standards of radical nephrectomy. Postoperative follow-up was conducted by telephone and medical records inquiry system. Overall Survival (OS) was defined as the time from the date of resection until the date of the last follow-up or death. The CSS secondary endpoint measured the interval from the date of resection to CCRCC-related mortality or the last follow-up. In the first year, patients with localized CCRCC underwent two physical examinations and laboratory tests. For the first three years, patients with locally progressed CCRCC underwent physical examinations and laboratory tests every six months. Both groups had annual physical examinations and laboratory tests.

### Statistical analysis

Categorical data were provided as numbers and percentages, while continuous variables were presented as means and standard deviations to reflect the clinicopathological traits of patients. To assess the statistical connection between MCHC and clinicopathological characteristics, Fisher exact and Chi-square tests were performed. The survival curve was created using the Kaplan-Meier method and the Log-rank test. The best cut-off point was chosen using Receiver Operating Characteristic (ROC) analysis. The Youden index's maximum value, which is equal to sensitivity + specificity -1, can be found at the ideal cut-off point [20]. The predictive power of the constructed model was assessed using the area under the ROC curve. Finally, independent possible prognostic markers in CCRCC patients were examined using univariate and multivariate Cox proportional hazards regression models. $P<0.05$ was regarded as statistically significant. All tests using the SPSS 22.0 statistical analysis program (IBM Corporation, Armonk, NY, USA).

## Results

### Characteristics of patients

The filtering process and details are shown in Figure 1. Table 1 displays the clinicopathological information about the patients. This study included 377 CCRCC patients who underwent radical nephrectomy. There were 141 women and 236 men. The ages of the patients at the time of surgery ranged from 27 to 79 years (mean: 59 years). One-forty-two patients were over 60 years old, and 235 patients were under 60 years old. Surgical follow-up lasted somewhere between 1 and 149 months (mean, 60 months). Thirty-nine patients had passed away, and 338 patients had survived at the most recent check-up.

### ROC curve analysis

The predictive usefulness of MCHC in CCRCC patients was revealed by the ROC curve. According to Figure 2, the area under the ROC curve is 0.658 (0.564-0.752; $P<0.001$). The best cut-off point had a sensitivity and specificity of 77.3% and 53.7%, respectively, while the cut-off value for MCHC was 332.5 g/L. The entire population of CCRCC patients was split into "high MCHC group" and "low MCHC group" groups based on the cut-off value.

### Relationship between MCHC and other clinicopathological parameters

The correlation between preoperative MCHC and clinicopathological parameters is shown in Table 1. There were 98 cases (26.0%) in the low MCHC group and 279 cases (74.0%) in the high MCHC group. Fisher exact test and $\chi^2$ test showed that preoperative MCHC was closely correlated with tumor size (P=0.029) and T stage (P=0.021). There was no correlation with age (P=0.983), N stage (P=0.770), sex (P=0.291), Fuhrman grade (P=0.907), tumor necrosis (P=0.092), LVI (P=0.624), and AKP (P=0.297) (Table 1).

### Predictive value of MCHC and clinicopathological parameters for OS in CCRCC patients

The retrospective analysis covered 377 patients, 13 (13.3%) of

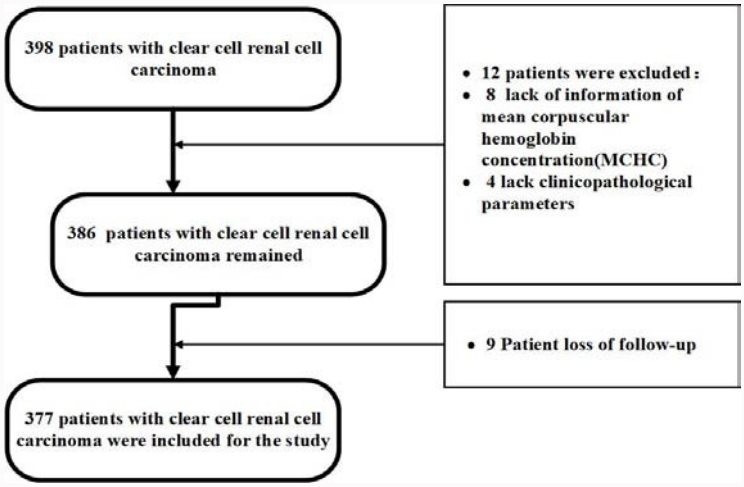


**Figure 1:** A flowchart describing the multiple stages of selection.

**Table 1:** Analysis of the relationship between preoperative MCHC levels and the clinicopathological features of CCRCC patients.

| Variable | No. of Patients (%) | | | *P* value |
|---|---|---|---|---|
| | Total | MCHC (g/L) | | |
| | (n=377) | ≤ 332.5 (n=98) | >332.5 (n=279) | |
| Age (years) | | | | 0.983 |
| ≤ 60 | 235 (62.3) | 61 (62.2) | 174 (62.4) | |
| > 60 | 142 (37.7) | 37 (37.8) | 105 (37.6) | |
| Sex | | | | 0.291 |
| Male | 236 (62.6) | 57 (58.2) | 179 (64.2) | |
| Female | 141 (37.4) | 41 (41.8) | 100 (35.8) | |
| T stage | | | | 0.021* |
| 1 | 310 (82.2) | 75 (76.5) | 235 (84.2) | |
| 2 | 43 (11.4) | 11 (11.2) | 32 (11.5) | |
| 3 | 24 (6.4) | 12 (12.2) | 12 (4.3) | |
| N stage | | | | 0.77 |
| 0 | 367 (97.3) | 95 (96.9) | 272 (97.5) | |
| 1 | 10 (2.7) | 3 (3.1) | 7 (2.5) | |
| Fuhrman grade | | | | 0.907 |
| 1+2 | 271 (71.9) | 70 (71.4) | 201 (72.0) | |
| 3+4 | 106 (28.1) | 28 (28.6) | 78 (28.0) | |
| Tumor size (cm) | | | | 0.029* |
| ≦ 5 cm | 242 (64.2) | 54 (55.1) | 188 (67.4) | |
| >5 cm | 135 (35.8) | 44 (44.9) | 91 (32.6) | |
| Tumor necrosis | | | | 0.092 |
| Absent | 346 (91.8) | 86 (87.8) | 260 (93.2) | |
| Present | 31 (8.2) | 12 (12.2) | 19 (6.8) | |
| LVI | | | | 0.624 |
| Absent | 361 (95.8) | 93 (94.9) | 268 (96.1) | |
| Present | 16 (4.2) | 5 (5.1) | 11 (3.9) | |
| AKP (U/L) | | | | 0.297 |
| ≤ 130 | 364 (96.6) | 93 (94.9) | 271 (97.1) | |
| >130 | 13 (3.4) | 5 (5.1) | 8 (2.9) | |

*Demonstrates that the two groups' differences were statistically different.
HR: Hazard Ratio; LVI: Lymphovascular Invasion; CI: Confidence Interval; AKP: Alkaline Phosphatase

98 patients with MCHC ≤ 332.5 g/L died of CCRCC, and 26 (9.3%) of 279 patients with MCHC>332.5 g/L died of CCRCC. Kaplan-Meier diagram showed that preoperative MCHC exhibited a strong correlation with OS in CCRCC patients (P<0.001), and patients with low preoperative MCHC had an OS rate that was considerably lower than patients with high preoperative MCHC (Figure 3). Cox proportional hazards regression model was used for univariate analysis. In CCRCC patients, OS is closely related to T stage (P<0.001), age (P=0.001), lymph node stage (P<0.001), tumor size (P<0.001), Fuhrman grade (P=0.006), LVI (P<0.001), tumor necrosis (P=0.002) and high AKP level (>130 U/L, P<0.001), and the lower the MCHC were all associated with poor OS [HR=0.278; 95% CI (0.146-0.530); P<0.001]. Preoperative MCHC was found to be an independent predictor in CCRCC patients after further multivariate analysis, with higher preoperative MCHC patients having a better prognosis [HR=0.296; 95% CI (0.144-0.609); P<0.001]. Age (P=0.002), T stage (P=0.001), and lymph node stage (P=0.035) were all found to be substantially linked with OS (Table 2).

## Predictive value of MCHC and clinicopathological parameters for CSS in CCRCC patients

The retrospective analysis covered 377 patients, 11 (11.2%) of 98 patients with MCHC ≤ 332.5 g/L died of CCRCC, and 26 (9.3%) of 279 patients with MCHC>332.5 g/L died of CCRCC. Regarding CSS, the bigger the MCHC, the better the CSS. Kaplan-Meier diagram showed that preoperative MCHC was significantly correlated with CSS in CCRCC patients (P<0.001), and patients with low preoperative MCHC had a CSS rate that was considerably lower than patients with high preoperative MCHC (Figure 4). Cox proportional hazards regression model was used for univariate analysis. In CCRCC patients, CSS is closely related to Age (P=0.001), lymph node stage (P<0.001), T stage (P<0.001), Fuhrman grade (P=0.003), tumor necrosis (P=0.001), LVI (P<0.001), tumor size (P<0.001) and high AKP level in CCRCC patients (>130 U/L, P<0.001), and the lower the MCHC were all linked with poor CSS [HR=0.244; 95% CI (0.125, 0.476); P<0.001]. Preoperative MCHC was identified as an independent predictive factor in CCRCC patients by further multivariate analysis, as evidenced by the better prognosis of patients with high preoperative MCHC [HR=0.249; 95% CI (0.116-0.533); P<0.001]. Additionally, there was a strong correlation between CSS and age (P=0.003), T stage (P<0.001), and lymph node stage (P=0.029) (Table 3).

**Table 2:** Univariate and multivariate analysis of overall survival in CCRCC patients.

| Variable | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95% CI) | *p* value | HR (95% CI) | *p* value |
| Age (years) | | 0.001* | | 0.002* |
| >60 *vs.* ≤ 60 | 2.917 (1.519-5.601) | | 2.971 (1.479-5.969) | |
| Sex | | 0.155 | | 0.245 |
| Male *vs.* female | 0.592 (0.288-1.219) | | 0.631 (0.290-1.373) | |
| T stage | | <0.001* | | 0.001* |
| 1 | | | | |
| 2 | 4.424 (1.970-9.937) | <0.001* | 2.478 (0.925-6.639) | 0.071 |
| 3 | 17.953 (8.489-37.97) | <0.001* | 6.633 (2.459-17.894) | <0.001* |
| N stage | | <0.001* | | 0.035* |
| 1*vs.*0 | 10.198 (4.221-24.642) | | 3.037 (1.080-8.542) | |
| Fuhrman grade | | 0.006* | | 0.902 |
| 1+2 *vs.* 3+4 | 2.464 (1.300-4.672) | | 1.047 (0.501-2.189) | |
| Tumor size (cm) | | <0.001* | | 0.203 |
| > 5 *vs.* ≤ 5 | 5.189 (2.520-10.687) | | 1.858 (0.716-4.820) | |
| Tumor necrosis | | 0.002* | | 0.67 |
| Present *vs.* absent | 3.299 (1.550-7.023) | | 1.197 (0.523-2.739) | |
| LVI | | <0.001* | | 0.205 |
| Present *vs.* absent | 8.254 (3.601-18.920) | | 2.089 (0.669-6.524) | |
| AKP (U/L) | | <0.001* | | 0.617 |
| >130 *vs.* ≤ 130 | 5.592 (2.157-14.493) | | 1.358 (0.408-4.517) | |
| MCHC (g/L) | | <0.001* | | 0.001* |
| ≤ 332.5 *vs.* >332.5 | 0.278 (0.146-0.530) | | 0.296 (0.144-0.609) | |

*Demonstrates that the two groups' differences were statistically different
HR: Hazard Ratio; LVI: Lymphovascular Invasion; CI: Confidence Interval; AKP: Alkaline Phosphatase

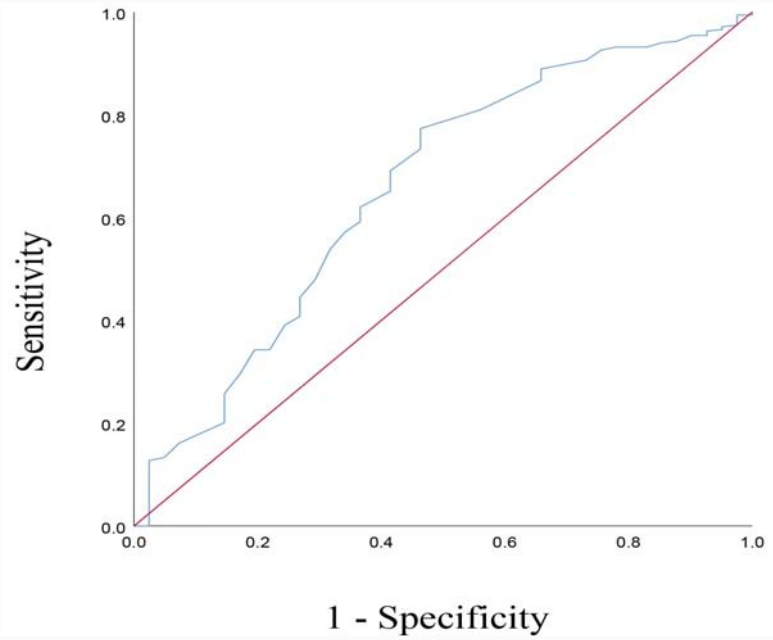


**Figure 2:** ROC curve for patients with CCRCC.

## Discussion

So far, various predictors and models have been used to evaluate the prognosis of CCRCC patients, mainly including TNM stage, Fuhrman grade, the neutrophil to lymphocyte ratio [21], the albumin to C-reactive protein ratio [22], and other ways. Still, sometimes the prediction results are not as good as expected. Therefore, it is still necessary to explore new prognostic biomarkers. Zhou found

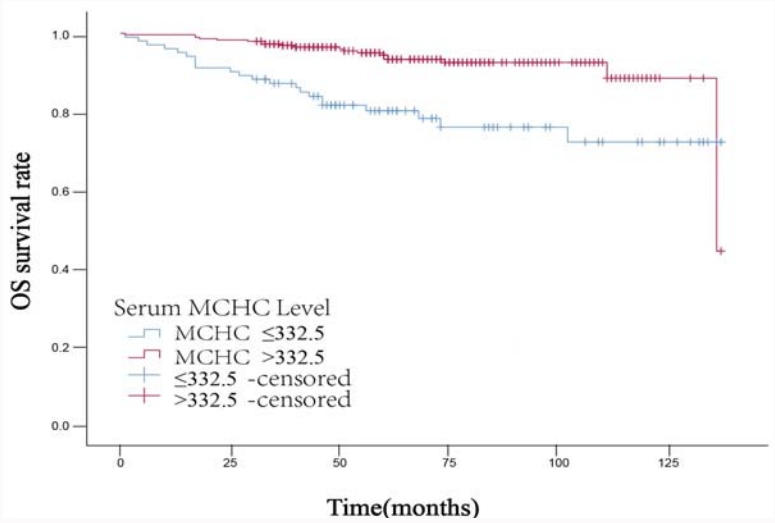


**Figure 3:** A Kaplan-Meier curve comparing high MCHC levels to low MCHC levels in terms of overall survival. Patients with low MCHC level had a worse prognosis.

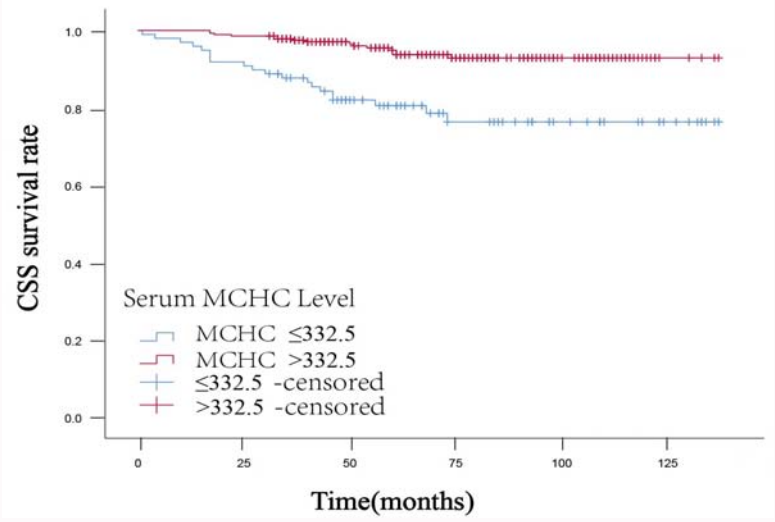


**Figure 4:** A Kaplan-Meier curve comparing high MCHC levels to low MCHC levels in terms of cancer-specific survival. Patients with low MCHC level had a worse prognosis.

in a study of 31 patients with multiple myeloma that the higher the MCHC before treatment, the better the effect, and concluded that the MCHC could be used as an independent factor in judging the prognosis of multiple myeloma. A large number of evidence also show that preoperative MCHC level is significantly correlated with the prognosis of various cancers, including liver cancer [10], head and neck cancer [14], breast cancer [9], colorectal cancer [8], cervical cancer [11], bronchial cancer [15], esophageal cancer [16] and bladder cancer [17], etc.

In this study, to better comprehend how MCHC and clinicopathological traits interact and the possible prognostic value of MCHC on OS and CSS in patients with CCRCC, we gathered pertinent clinical data. Using the Fisher exact probability test and $\chi^2$ test, we discovered that MCHC was highly linked with the T stage (P=0.021) and tumor size (P=0.029). We subsequently discovered that lower MCHC was linked to shorter OS and CSS (P<0.001) using the log-rank test and Kaplan-Meier plot. Cox proportional hazards regression models were used in univariate and multivariate studies to demonstrate the association between greater levels of MCHC and improved OS. In patients with CCRCC, a high level of MCHC is also a good indicator of CSS. As a result, MCHC is a standalone prognostic factor for those with CCRCC. Consistent with our study, the independent prognostic importance of MCHC has also been shown in some other cancers, such as head and neck cancer [14], colorectal cancer [8], cervical cancer [11], bronchial cancer [15], esophageal cancer [16], etc.

Blood is a substance that is directly exposed to cancer cells and the microenvironment of malignant tumors and responds to pathological conditions such as infection, inflammation, and cancer [23, 24]. Studies have found that the poor prognosis of tumor patients with low MCHC may be caused by oxygenation disorder caused by Cancer-Associated Anemia (CRA), which is a common indicator of poor prognosis in a variety of solid cancers [25]. Cancer-related anemia is thought to be a symptom of more advanced or aggressive disease. Statistics show that 25% of kidney cancer patients undergoing nephrectomy are anemic [26]. Studies have found that blood flow and blood viscosity can be affected by mean erythrocyte hemoglobin concentration, indirectly leading to hypoxia of tumor cells, which will

**Table 3:** Univariate and multivariate analysis of cancer-specific survival in CCRCC patients.

| Variable | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95% CI) | *p* value | HR (95% CI) | *p* value |
| Age (years) | | 0.001* | | 0.003* |
| >60 *vs.* ≤ 60 | 3.120 (1.571-6.197) | | 2.949 (1.427-6.092) | |
| Sex | | 0.155 | | 0.296 |
| Male *vs.* female | 0.577 (0.270-1.231) | | 0.645 (0.283-1.467) | |
| T stage | | <0.001* | | <0.001* |
| 1 | | | | |
| 2 | 5.983 (2.584-13.850) | <0.001* | 3.428 (1.226-9.589) | 0.019* |
| 3 | 22.426 (10.176-49.423) | <0.001* | 8.096 (2.907-22.547) | <0.001* |
| N stage | | <0.001* | | 0.029* |
| 1 *vs.* 0 | 10.198 (4.221-24.642) | | 3.200 (1.129-9.068) | |
| Fuhrman grade | | 0.003* | | 0.864 |
| 1+2 *vs.* 3+4 | 2.757 (1.421-5.351) | | 1.070 (0.495-2.313) | |
| Tumor size (cm) | | <0.001* | | 0.263 |
| > 5 *vs.* ≤ 5 | 6.346 (2.883-13.969) | | 1.808 (0.641-5.105) | |
| Tumor necrosis | | 0.001* | | 0.556 |
| Present *vs.* absent | 3.748 (1.754-8.007) | | 1.288 (0.555-2.990) | |
| LVI | | <0.001* | | 0.171 |
| Present *vs.* absent | 8.893 (3.855-20.514) | | 2.222 (0.709-6.961) | |
| AKP (U/L) | | <0.001* | | 0.829 |
| >130 *vs.* ≤ 130 | 5.592 (2.157-14.493) | | 1.143 (0.340-3.840) | |
| MCHC (g/L) | | <0.001* | | <0.001* |
| ≤ 332.5 *vs.* > 332.5 | 0.244 (0.125-0.476) | | 0.249 (0.116-0.533) | |

*Demonstrates that the two groups' differences were statistically different
HR: Hazard Ratio; LVI: Lymphovascular Invasion; CI: Confidence Interval; AKP: Alkaline Phosphatase

further affect the oxygenation process [27]. Bush et al. [28] discovered that anemia correction by blood transfusion could increase the cure rate and decrease recurrence in patients who had a low hemoglobin level during treatment. Similarly, Umar Imran Hamid [28] reported in lung cancer that patients with reduced hemoglobin levels also had worse long-term survival (P=0.07). Several clinical studies also support the idea that low MCHC is an important poor prognostic factor [29-31].

The mechanism of MCHC leading to poor prognosis remains unclear. However, accumulating evidence suggests that low MCHC levels are indeed closely associated with cancer-related anemia and tumor oxygenation disorders, and rising MCHC is associated with higher PO2 values and lower hypoxic tissue fractions [32]. Cancer-related anemia is usually caused by multiple factors, and the possible explanations are as follows: First, tumor cells can secrete a variety of soluble cytokines, such as Interferon-γ (IFN-γ), Tumor Necrosis Factor-α (TNF-α), Interleukin-6 (IL-6), and IL-1, etc., [33]. These soluble compounds may impact erythropoiesis and erythroid progenitor cell function, thereby reducing hemoglobin levels and affecting tumor oxygenation function [34]. In addition, anemia in patients with malignant tumors may be related to tumor-related bleeding, nutritional deficiency, tumor bone marrow infiltration, and iron metabolism disorders [35]. In cell culture experiments, it was found that the Vascular Endothelial Growth Factor (VEGF) expression was significantly up-regulated during hypoxia. The results indicated that there was a correlation between low hemoglobin levels and elevated VEGF [36]. Some scholars have proposed that tumor-associated anemia can lead to a hypoxic microenvironment of tumor cells, and hypoxia can induce changes in the expression pattern of Hypoxia-Inducible Factor-1α (HIF-1α) and VEGF, thereby increasing the expression of mitogenic and pro-angiogenic factors [37]. Graham also discovered that hypoxia boosted cells' capacity to colonize extracellular matrix and spread [38]. In animal experiments, hypoxia increases the likelihood of tumor metastasis in mouse models. Clinical studies have also shown a correlation between tumor oxygenation and the probability of distant metastasis in cancer patients [39]. Cumulative evidence suggests that hypoxia in the tumor microenvironment may provide selective pressure for tumor cells with a high mutation rate to weaken their response to apoptotic signals, ultimately leading to increased metastatic potential [40,41].

MCHC is a modifiable factor that can be ameliorated by drugs, blood transfusion, EPO and other methods [42]. Sun et al. reported that Erythropoietin (EPO) can increase the level of MCHC, enhance radiosensitivity, improve tissue oxygen supply, and improve local control rate. However, how to improve MCHC needs to be further studied, which also provides new ideas for future treatment direction. Of course, this study has some limitations. First of all, we are a retrospective study in a single center, and lack of training and validation sets to verify the accuracy of the study results. Secondly, we only studied the prognostic impact of MCHC in patients with CCRCC. In the future, we'll investigate the predictive efficacy of MCHC in other renal cell carcinoma subtypes.

## Conclusion

In conclusion, preoperative MCHC has significant clinical value in predicting the prognosis and the survival for patients who have CCRCC.

## Acknowledgement

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## Authors' Contributions

Kongbo Ou, Yifan Shao, Zhen Chen, and Qianfeng Zhuang conceived and designed the study. Yifan Shao analyzed and interpreted the data. KongboOu wrote the manuscript. Zhen Chen and Qianfeng Zhuang made a revised version. All authors reviewed and approved the manuscript.

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