



## PREOPERATIVE PROGNOSTICATION OF RENAL CELL CARCINOMA BY BASIC BLOOD PARAMETERS

**W. Harry Santhaseelan**

Assistant Professor, Institute of Urology, Madras Medical College

**K. Niranj\***

Junior Resident, Institute of Urology, RGGGH, Madras Medical College, Chennai-3  
\*Corresponding Author

**ABSTRACT** The study aimed to answer whether preoperative determination of basic blood cell count can be used to predict prognosis of non-metastatic RCC with respect to risk of metastasis, recurrence, cancer specific mortality. We retrospectively analyzed 292 patients with non-metastatic renal cell carcinoma who underwent surgery between 2012 and 2017. Data with respect to tumour characteristics, patient characteristics and blood parameters based on RBCs and platelets were analyzed. The best predictor among the analyzed preoperative laboratory parameters is the platelet count and volume. However individual blood parameters have low predictive value than stage and grade of tumour.

**KEYWORDS :** Renal Cell Carcinoma, Prognosis, Platelet

### INTRODUCTION

Renal Cell Carcinoma is one of the deadliest urologic malignancies and about two to three percent of all adult cancers. About 50% of cases are diagnosed incidentally. But still twenty to thirty percent of the cases present to the urologist with advanced disease. Renal Cell Carcinoma has a very unpredictable nature as even tumours small in size can present with metastases and large tumours can remain indolent. Surgery is the mainstay of treatment for Renal Cell Carcinoma and therefore patients with advanced disease stand a little chance of cure. Early detection is of great advantage for the patient in order to achieve cure. Prognostic indicators in Renal Cell Carcinoma include clinical features, laboratory investigations and factors related to the tumour such as nuclear grade, size, stage and histologic subtype. These have a high influence on the nature of the disease and have a great value in detecting the cancer specific survival in patients with Renal Cell Carcinoma. Molecular prognostic factors are listed among the prognostic factors; however, their major drawbacks are cost and low availability. The following study aims to answer whether preoperative determination of basic blood cell count can be used as a popular and inexpensive prognostic factor in the treatment of renal cell carcinoma limited to the organ.

### MATERIALS AND METHODS

The medical records of 292 patients who underwent surgery for renal tumors in our center in the years 2012–2017 were analysed retrospectively. During the five-year follow-up period of all 292 patients operated on, 210 patients with the postoperative diagnosis of non-metastatic renal cell carcinoma were enrolled in the study. The median follow-up was 3.8 years. Patients with coexisting conditions that may have an impact on the blood morphology parameters were excluded. On the basis of the information gathered, routinely collected blood count parameters namely RBC Count, Hemoglobin HCT [%], MCV [fL], MCHC [g/dL], MCH[pg], RDW [%], Platelet Count], MPV [fL] at the time of admission to the ward were analyzed. We analyzed the data on histopathological material, TNM, size and location of the tumor removed, and the positive margin in the case of the nephron sparing surgery (NSS). Histopathologic tumor grade was rated according to the three-degree Fuhrman scale. In order to determine the clinical stage, given data were analyzed according to the TNM classification.

All the data gathered was analyzed in relation to the local recurrence, metastasis, and tumor-specific deaths. Statistical analysis was performed using IPSS software. For determining the risk of metastasis, tumor recurrence, or death within five years, Cox proportional hazards model was used. To assess the quality of the classifier and the search for the optimal cut-off point, ROC (Receiver Operating Characteristic) curve was used as a tool to describe the overall sensitivity and specificity for the variability characteristics of the classifier.

### RESULTS

The study group included 103 men and 107 women. The average age was 62 years. Tumor size was 6.2 cm. 59 patients underwent nephron sparing surgery (NSS) (mean tumor size was 3.5 cm), and 141 patients underwent radical nephrectomy (mean tumor size was 7.2 cm). Local recurrence during follow-up occurred in 32 patients and distant

metastases were found in 16 patients. Tumor-specific death was reported in 8 cases after the NSS and in 28 after radical nephrectomy. 101 patients had tumour in the right kidney and 109 in the left kidney. The most frequently observed tumors were located on the lower pole, followed by upper pole. In the interpole 12 tumors were detected.

98 patients had T1 disease, 56 patients had T2 and T3 was seen in 46 patients. T4 was found in 10 patients.

**TABLE 1**

Blood Parameters	Average Values
RBC Count [ $10^6/\mu\text{L}$ ]	4.0± 0.4
Hb[g/dl]	12.5 ± 1.2
MCV [fL]	80.02± 4.8
MCH [pg]	28.6±2
MCHC [gm/dl]	28±1.8
HCT [%]	38±3.8
RDW [%]	12±2
Platelets [ $103/\mu\text{L}$ ]	237± 67
MPV[fL]	10±1

For determining the risk of metastasis, tumor recurrence, or death, Cox proportional hazards model was used. Statistically significant results in the univariate model are summarized in Table 2.

Similar results were shown in the multivariate analysis which also showed a low predictive value for individual blood parameters with the best predictor being platelet count and MPV. Using the ROC curve it was found that the most likely event is predicting the case of tumor recurrence using the platelet count (PLT). For the cut-off point of 2,46,000 platelet count (specificity 64%, sensitivity 90%), the likelihood of correctly predicting an event is up to 84% (AUC). Similarly the best predictor of death was again platelet counts with a cut-off point of 3,68,000 having 77% probability.

**TABLE 2**

Adverse Event	Parameters	Regression coefficient	P value
Metastasis	Platelet	0.004	0.003
Recurrence	Hb	-2.260	0.02
	MCV	-2.002	0.01
	MCH	-3.146	0.04
	HCT	-2.224	0.02
	Platelet	0.006	0.001
Death	Hb	-1.324	0.04
	MCV	-1.897	0.03
	MCH	-1.444	0.05
	MCHC	-1.254	0.04
	RDW	0.134	0.05
	HCT	-1.144	0.02
	Platelet	0.008	0.001
	MPV	-2.465	0.01

## DISCUSSION

Despite advances in medicine, an increase in morbidity and mortality due to kidney cancer is still observed. The diversity of kidney cancers does not enable unambiguous determination of prognosis. Given that 30% of patients with disease confined to the organ will develop generalized disease after surgical treatment, it is important to search for prognostic factors. Numerous reports of treatment of erythropoietin (EPO) level elevation in patients with renal cancer prompted us to search the potential prognostic factors among blood counts<sup>2</sup>. The study was an attempt to determine whether any of the tested parameters can be used to assess the prognosis of kidney cancer, so that a group of patients that require special oncological surveillance can be selected. Among the preoperative parameters associated with the red blood cells system, the erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin concentration were analyzed in the study. It has been proven that lowering the value of all the above-mentioned parameters below a specified cut-off point results in an increased risk of tumor-specific death within the five years of follow-up. Reduced preoperative values of HGB, HCT, MCV, and MCH also predispose patients to early recurrence of cancer. Similar results were also obtained by other authors<sup>3</sup>. To date, there are no reports in the literature on the prognostic value of the parameters relating to the construction of red blood cells.

Thrombocytosis as a paraneoplastic syndrome is widely described in the literature<sup>4</sup>. In research studies so far, many authors have confirmed that preoperative thrombocytosis is an unfavorable prognostic factor for renal cell carcinoma<sup>5</sup>. Our analyses have shown that the increase in platelet count is a negative prognostic factor in patients undergoing surgery for renal cell carcinoma. Statistical significance was confirmed in the single and multidimensional analyses. In addition, the predictive value of the volume of platelets was confirmed to have statistical significance. The combination of high platelet counts with their small volume is characteristic for cancer diseases<sup>6</sup>. To date, no reports on the predictive value of MPV in renal cancer have been published.

Previous studies looking for new, readily available prognostic factors do not constitute a breakthrough and only improve the predictive value of factors related to tumor stage and anatomy. It is estimated that the parameters of blood count and biochemical parameters may constitute independent prognostic factors for renal cell carcinoma, but they are not qualitatively superior to the TNM classification<sup>7</sup>. It should also be remembered that all the evaluated morphological and biochemical parameters of blood are characterized by low repeatability and are dependent on many factors.

## CONCLUSION

Low preoperative hemoglobin concentration, hematocrit, mean volume, and mean hemoglobin concentration may be considered in the category of risk factors for recurrence and progression of renal cell carcinoma after surgical treatment. The best predictor among the analyzed preoperative laboratory parameters is the platelet count and volume. However individual blood parameters have low predictive value than stage and grade of tumour.

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