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Predictive value of pretreatment hematological biomarkers for tumor grade and stage in renal cell carcinoma; a retrospective study with multivariate analysis

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ABSTRACT

Introduction: Hematological biomarkers are potential cost-effective tools to gauge systemic inflammation. The cut off values of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have not been standardized in renal cell carcinoma (RCC). The utility of hemoglobin-to-platelet ratio (HPR) has not been thoroughly explored.

Objectives: This study determined the predictive value of NLR, PLR and HPR in the grading and staging of RCC.

Patients and Methods: In this cross-sectional study, the clinicopathological data with NLR, PLR and HPR of 122 RCC cases were analysed retrospectively. Receiver operating characteristic (ROC) curve analysis for each hematological parameter was achieved with respect to the WHO/ISUP (World Health Organization/ International Society of Urological Pathology) grade and T-stage. Univariate and subsequently multivariate analyses were performed. The odds ratio was also calculated.

Results: There was a statistically significant association between the NLR and high grade ($P=0.001$), high T-stage ($P<0.001$), PLR and high grade ($P=0.044$), high T-stage ($P=0.023$), HPR and low grade ($P=0.005$), and low T-stage ($P=0.007$). Multivariate analysis revealed that high NLR, low HPR, lymphovascular invasion and large tumor size were independent predictors of high grade and high T-stage.

Conclusion: A high preoperative NLR, PLR and low HPR are modest but statistically significant predictors of high WHO/ISUP grade and high pathological T-stage in RCC.

Implication for health policy/practice/research/medical education:

In this study, we found the statistically significant associations between high neutrophil-to-lymphocyte ratio (NLR), high platelet-to-lymphocyte ratio (PLR) and low hemoglobin-to-platelet ratio (HPR) and high grade and stage of renal cell carcinoma (RCC). Multivariate analysis revealed that high NLR, low HPR, lymphovascular invasion and large tumor size were independent predictors of high grade and high T-stage. Hematological biomarkers can be effectively incorporated into preoperative scoring systems to predict the plausible prognosis in RCC patients.

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Introduction

Renal malignancy accounts for 2.2% of all cancers and is the 14th most common cancer, with 434,419 new cases as per cancer statistics projected in GLOBOCAN 2022 (1). Renal cell carcinoma (RCC) is the commonest renal malignancy in adult population (2). With increasing public awareness about cancer detection, as well as an

ample number of advanced diagnostic techniques, the incidental detection of these cases has risen substantially. RCC is proposed to be metabolically driven, with potential risk factors such as obesity, hypertension, cigarette smoking, occupational hazards, alcohol and diet (3,4). The recurrence rate post-nephrectomy is estimated to be approximately 12–20% (5–7).

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Inflammation and immunopathology in RCC are interlinked, and they form a basis for novel targeted therapy with immune checkpoint inhibitors in locally advanced/metastatic tumors (8-10). Immune dysregulation mediated by various cytokines and chemical mediators occurs in response to increase in neutrophils and platelets and decrease in lymphocytes in the tumor. This imbalance between neutrophils and lymphocytes aids in tumor progression, invasion and metastasis (11-13). These leucocyte, platelet, and erythrocyte parameters and their ratios in peripheral blood act as potential biomarkers for assessing tumor grade and stage (14-16).

While neutrophils are the primary line of defence in acute inflammation, lymphocytes are mediators of cell-mediated immunity (16). The cytotoxic substances produced by neutrophils, such as arginase, free radicals such as nitric oxide and reactive oxygen species, accentuate the systemic inflammatory response (17,18). Impaired cell-mediated immunity due to a decrease in CD4 and CD8 lymphocytes promotes cancer progression. Furthermore, elevated platelets release mediators like Vascular endothelial growth factor, platelet activating factor and platelet-derived growth factor, thereby promoting angiogenesis and metastasis (7,9,11).

Red cell distribution width is a measure of variation in erythrocyte size. It has been proposed that inflammation can trigger maturation disorders in RBCs through effects on their membrane (19). Oxidative stress, in addition to inflammation-induced erythropoiesis, results in variations in red blood cell distribution width (RDW) (20). Concurrent thrombocytosis and anemia lead to hypoxic damage in cancer patients, resulting in a low hemoglobin-to-platelet ratio (HPR). Recently, HPR is yet another biomarker under investigation in solid malignancies such as nasopharyngeal and urothelial carcinoma, and data regarding its utility in RCC are sparse (10,18,21). The role of the RDW-to-platelet ratio in benign pathologies such as acute kidney injury has been evaluated but not explored in RCC. Therefore, we intend to evaluate these markers in RCC, as they are cost effective, reliable, rapid diagnostic tools and potential biomarkers of systemic inflammation in cancer.

Objectives

To determine the predictive value of hematological biomarkers, like neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), HPR, RDW and RDW-to-platelet ratio (RPR), in the grading and staging of RCC.

Materials and Methods

In this cross-sectional study, after seeking institutional ethics committee clearance, this retrospective analysis

was conducted from 2014 to 2019. Among 155 nephrectomy specimens, 33 did not have pre-treatment hematological biomarkers and were excluded. Overall, about 122 cases were analysed. Complete blood count reports were retrieved from electronic data storage. Data collection included patient demographics, WHO grading, tumor-node-metastasis staging, and estimation of the preoperative NLR, PLR, HPR, RDW and RPR. Complete blood count data comprising the neutrophil, lymphocyte and platelet counts, and hemoglobin percentage, were retrieved. Biomarkers such as the NLR, PLR and HPR were calculated. As this was a retrospective study, RDW was available only in 20/122 cases. Hence, we made a preliminary investigation of RDW and RPR and their association with RCC.

The cases were dichotomously divided based on their WHO/ISUP grade into high-grade (G3, G4) and low-grade (G1, G2). Similarly, they were divided into high-stage (pT3, pT4) and low-stage (pT1, pT2) groups on the basis of T-stage (8).

Statistical analysis

The receiver operating characteristic (ROC) curve analysis was achieved to derive the optimal cut-off values for each hematological parameter with respect to the WHO/ISUP grade and T-stages. The cut-off values were determined using the highest Youden index.

The data collected were recorded in Microsoft Excel and subjected to analysis by DataTab software. Descriptive statistics are presented as the mean, standard deviation (SD) and percentages. Chi-square tests were performed to evaluate the associations between WHO/ISUP grade and T-stage and their respective hematological parameters. When the *P* value was <0.05, the association was considered significant, with a 95% confidence interval. Multivariate analysis using binary logistic regression was accomplished to identify independent predictors of WHO/ISUP grade and T-stage. The biomarkers (NLR, PLR, and HPR), age, sex, tumor size, lymphovascular invasion status, histologic type, tumor grade, tumor stage and necrosis status were subjected to univariate analysis. The NLR, PLR, and HPR were subjected to multivariate logistic regression as dichotomized variables based on the ROC cut-offs. The significant variables (*P*<0.05) in the univariate analysis were incorporated in the multivariate analysis. The odds ratios with 95% confidence intervals were calculated.

Results

A total of 122 patients were included, of which 101 (82.79%) were males and 21 (17.21%) were females. The M: F (male to female) ratio was 4.8:1. The age distribution ranged from 24–83 years, with a mean of 57.22 ± 12.15

years. The size of the tumor ranged from 0.5 to 25 cm, with a mean of 6.71 ± 3.97 cm. The majority of the tumors (95.08%) were unifocal. The commonest histological subtype was clear-cell RCC (85.25%). Among the 122 cases, 39 (31.96%) were high grade (G3, G4), and 83 (68.03%) were low grade (G1, G2). High T-stage (pT3, pT4) was found in 45 (36.88%) patients, and low T-stage (pT1, pT2) was found in 77 (63.11%) patients. The baseline features of the tumors are depicted in Table 1.

The mean hemoglobin level, total leucocyte count and platelet count were 12.38 ± 2.24 g/dL, $8.50 \times 10^9/L$, and $265.16 \times 10^9/L$, respectively. The optimal cut-off values

for NLR, PLR, HPR, RDW and RPR were 3.12, 132.46, 0.338, 15.4%, and 0.05, respectively with respect to WHO/ISUP grade. For T-stages, the cut-off values for the NLR, PLR, HPR, RDW and RPR were 2.86, 151.34, 0.505, 16.3% and 0.07, respectively.

The NLR was high in high-grade (median-3.06) and high-T-stage (median-3.11) tumors in comparison to low-grade (median-2.57) and low-T-stage (median-2.56) tumors. Similarly, the PLR was high in high-grade (median: 151.34) and high-T-stage (median: 157.13) tumors compared with low-grade (median: 129.55) and low-T-stage (median: 128.27) tumors. The HPR was

Table 1. Baseline characteristics of the study participants

Characteristics		n (%) or Mean $\pm$ SD
Age (years)		57.22 $\pm$ 12.15
Gender	Male	101 (82.79%)
	Female	21 (17.21%)
Procedure	Radical nephrectomy	105 (86.07%)
	Partial nephrectomy	17 (13.93%)
Laterality	Right	68 (55.74%)
	Left	54 (44.26%)
Site	Upper pole	37 (30%)
	Lower pole	34 (27.8%)
	Mid pole	27 (22.1%)
	Others (e.g., upper+ mid-pole, lower+ mid-pole, entire kidney, renal pelvis, renal hilum)	24 (19.67%)
Size (cm)		6.71 $\pm$ 3.97
Tumor focality	Unifocal	116 (95.08%)
	Multifocal	5 (4.1%)
	Bifocal	1 (0.82%)
Histological type	Clear-cell RCC	104 (85.25%)
	Papillary RCC	9 (7.37%)
	Chromophobe RCC	3 (2.46%)
	Others (unclassified, mucinous tubular and spindle RCC, clear cell papillary tumor)	6 (4.91%)
Sarcomatoid features	Not identified	113 (92.62%)
	Present	9 (7.37%)
Rhabdoid features	Not identified	115 (94.26%)
	Present	7 (5.73%)
Tumor necrosis	Not identified	73 (59.84%)
	Present	49 (40.16%)
Tumor extension	Limited to kidney	77 (63.11%)
	Extension into renal sinus/pelvic/lyceal system/perinephric fat/renal capsule/renal vein/Gerota's fascia/adrenal gland	45 (36.88%)
Margins	Uninvolved	108 (88.52%)
	Involved	14 (11.47%)
Lymphovascular invasion	Not identified	97 (79.51%)
	Present	25 (20.49%)
WHO/ISUP grade	High (G3, G4)	39 (31.96%)
	Low (G1, G2)	83 (68.03%)
T-stage	High (pT3, pT4)	45 (36.88%)
	Low (pT1, pT2)	77 (63.11%)

RCC: Renal cell carcinoma.

inversely related to high grade and stage; i.e., it was low in high-grade (median-0.45) and high-T-stage (median-0.45) tumors and high in low-grade (median-0.51) and low-T-stage (median-0.53) tumors. RDW values were directly proportional to T-stage. High RDWs (median: 17) were seen in high-T-stage tumors, and low RDWs (median: 15.4) were seen in low-T-stage tumors. However, RDW values did not correlate with higher grade. RPR did not correlate with grade or stage. The sensitivity, specificity and area under the curve for the NLR, PLR, HPR, RDW and RPR with respect to WHO/ISUP grade and T-stage are depicted in Tables 2 and 3.

There was a statistically significant association between the NLR and high grade ($P=0.001$), high T-stage ($P<0.001$), PLR and high grade ($P=0.044$), high T-stage ($P=0.023$), HPR and low grade ($P=0.005$), and low T-stage ($P=0.007$). A significant association between RDW and high T-stage ($P=0.006$) but not between RDW and WHO/ISUP grade ($P=0.16$) was detected. No significant correlation was found between the RPR and grade or stage. The box plot charts and ROC curves of the NLR, PLR, HPR, RDW and RPR with respect to histologic grade and T-stage are depicted in Figures 1 and 2, respectively.

Univariate analysis revealed statistically significant associations between lymphovascular invasion and high tumor grade ($P=0.001$) and high T-stage ($P<0.001$), tumor size and high tumor grade ($P=0.002$), and high T-stage ($P=0.001$), necrosis and high T-stage ($P=0.025$), while age, sex, and histologic subtype did not significantly differ.

Multivariate analysis revealed that the NLR, HPR,

lymphovascular invasion and tumor size were independent predictors of high grade, whereas the PLR and tumor stage were not statistically significant. Multivariate analysis for high stage with the variables such as tumor size, lymphovascular invasion, necrosis, histological grade and biomarkers (NLR, PLR, and HPR) revealed that high NLR, low HPR, presence of lymphovascular invasion and large tumor size consistently emerged as independent predictors of high T-stage, whereas PLR, necrosis and grade were not significant. The odds ratios with 95% confidence intervals and p values of the multivariate analysis are depicted in Tables 4–9.

Discussion

Well-known prognostic factors for RCC are tumor size, WHO/ISUP grade, tumor-node-metastasis stage, histological subtype, the presence of sarcomatoid and rhabdoid features, necrosis and lymphovascular invasion, the overall clinical performance status of the patient and the presence of anemia (9,14). Preoperative prognostic scoring systems such as the UISS (UCLA Integrated Staging System), MSKCC (Memorial Sloan-Kettering Cancer Center) and IMDC (International Metastatic Renal Cell Carcinoma Database Consortium) are commonly used for metastatic RCC (6,8,17,20). Hematological biomarkers such as the NLR, PLR and HPR are currently not included. A growing body of evidence suggests that these biomarkers of inflammation are potential predictive factors of higher grade and tumor stage.

Inflammation in the tumor microenvironment of RCC is secondary to intrinsic genetic alterations as well as extrinsic inflammation due to risk factors such as obesity,

Table 2. ROC analysis of hematological parameters and WHO/ISUP grade

Ratios	Cut-off	Sensitivity (%)	Specificity (%)	AUC
NLR	3.125	48.7	20.5	0.618
PLR	132.468	64.1	44.6	0.615
HPR	0.338	89.2	66.7	0.606
RDW	15.4%	80	50	0.665
RPR	0.05	70	40	0.67

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, HPR: Hemoglobin-to-platelet ratio, RDW: Red cell distribution width, RPR: RDW-to-platelet ratio.

Table 3. ROC analysis of hematological parameters and T-stage

Ratios	Cut-off	Sensitivity (%)	Specificity (%)	AUC
NLR	2.858	64.4	29.9	0.672
PLR	151.34	53.3	32.5	0.597
HPR	0.505	61	35.6	0.603
RDW	16.3%	72.7	11.1	0.763
RPR	0.071	36.4	11.1	0.576

NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, HPR: Hemoglobin-to-platelet ratio, RDW: Red cell distribution width, RPR: RDW-to-platelet ratio.

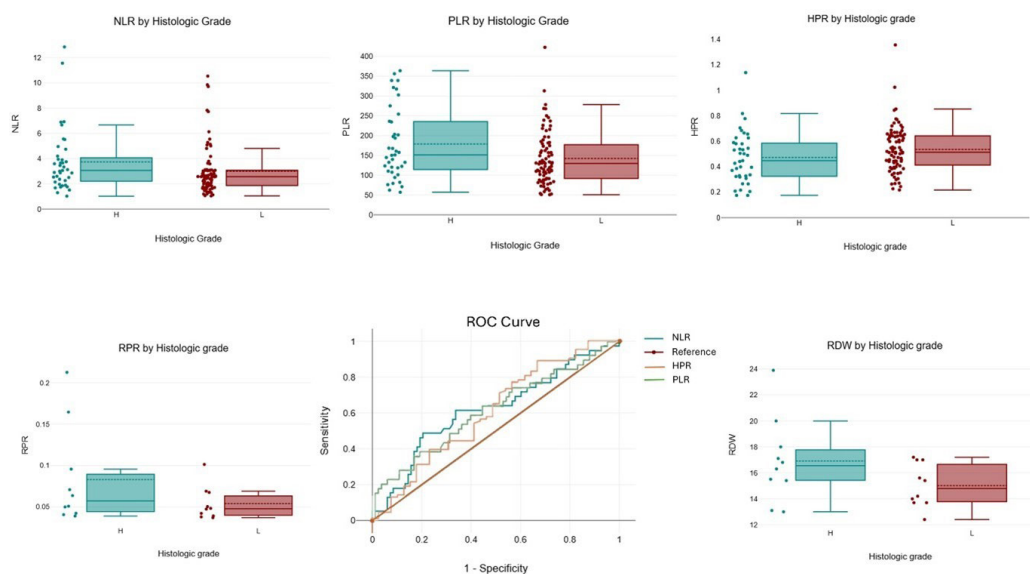


Figure 1. The box plot charts (NLR, PLR, HPR, RPR and RDW) and ROC curves (NLR, PLR, HPR) with respect to histologic grade.

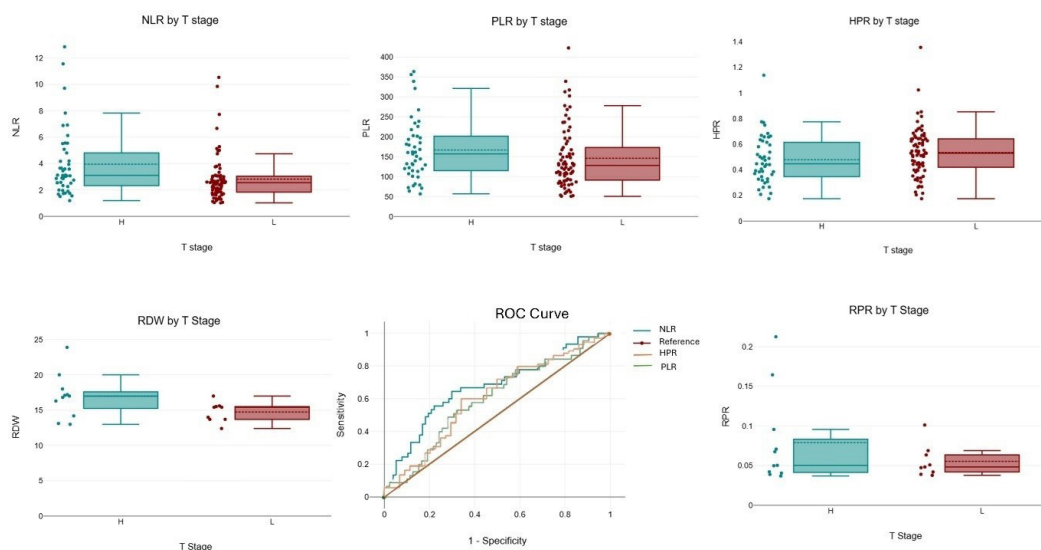


Figure 2. The box plot charts (NLR, PLR, HPR, RPR and RDW) and ROC curves (NLR, PLR, HPR) with respect to histologic stage.

infection and smoking. Genomic alterations in RCC include mutations in the *VHL*, *CDKN2A*, *SMARCB1*, *TFEB*, *TFE3*, *PTEN*, *TP53*, and *NRF2* genes in addition to mitochondrial dysfunctions. These alterations are responsible for the formation and release of neoantigens, thus triggering an adaptive immune response (13).

Signalling pathways that are activated in RCC include VHL-HIF α , STAT3, Hippo-Yap/TAZ, NF κ B, cGAS-STING and epigenetic modifications. Epithelial-mesenchymal transition, tumor cell proliferation, immune evasion, angiogenesis, invasion and metastasis are subsequently mediated by chemical mediators such as interferons (IFN γ and IFN α), interleukins (IL-1 β , IL-

6, IL-2, IL-23, and IL-12), TNF α , and TGF β and the activation of chemokine receptors (CXCR1, 2, and 4) (13).

High vascularity in RCC acts as a niche for inflammation through the recruitment of immune cells to the tumor microenvironment. RCC can thus be divided into inflamed and noninflamed subtypes. Histopathologically, noninflamed RCC is characterized by increased angiogenesis and infiltration by mast cells and plasmacytoid dendritic cells, whereas inflamed RCC is characterized by the presence of neutrophils, eosinophils, Tregs, Th cells, CD8 cells, activated dendritic cells, B cells, natural killer (NK) cells and macrophages. Notably,

Table 4. Multivariate logistic regression analysis including the NLR for predicting high-grade tumors (WHO/ISUP grade)

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
NLR	0.97	0.47	2.05	0.04	2.64	1.04 - 6.69
T-stage	0.06	0.50	0.12	0.905	1.06	0.39 - 2.86
Size	0.14	0.06	2.37	0.018	1.15	1.03 - 1.30
Lymphovascular invasion (Present)	1.22	0.54	2.27	0.023	3.39	1.18 - 9.70

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; CI, confidence interval.

Table 5. Multivariate logistic regression analysis including the PLR for predicting high-grade tumors (WHO/ISUP grade)

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
PLR	0.52	0.44	1.19	0.234	1.69	0.71 - 3.99
T-stage	0.27	0.48	0.56	0.574	1.31	0.51 - 3.35
Size	0.14	0.06	2.29	0.022	1.15	1.02 - 1.30
Lymphovascular invasion (Present)	1.22	0.52	2.34	0.019	3.38	1.22 - 9.41

Abbreviations: PLR, Platelet-to-lymphocyte ratio; CI, Confidence interval.

Table 6. Multivariate logistic regression analysis including the HPR for predicting high-grade tumors (WHO/ISUP grade)

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
Low HPR	1.23	0.53	2.30	0.022	3.41	1.20 - 9.68
T-stage	0.24	0.49	0.49	0.624	1.27	0.48 - 3.35
Size	0.14	0.06	2.16	0.03	1.15	1.01 - 1.30
Lymphovascular invasion (Present)	1.36	0.54	2.53	0.011	3.91	1.36 - 11.24

Abbreviations: HPR, Hemoglobin-to-platelet ratio; CI, Confidence interval.

Table 7. Multivariate logistic regression analysis including the NLR as a predictor of advanced T-stage

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
NLR	1.12	0.45	2.50	0.012	3.07	1.28 - 7.37
Histologic grade	0.15	0.49	0.31	0.76	1.16	0.45 - 3.01
Size	0.15	0.07	2.22	0.026	1.16	1.02 - 1.33
Lymphovascular invasion (Present)	1.63	0.56	2.93	0.003	5.09	1.71 - 15.11
Tumor necrosis	0.33	0.46	0.72	0.47	1.40	0.56 - 3.45

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; CI, confidence interval.

Table 8. Multivariate logistic regression analysis including the PLR as a predictor of advanced T-stage

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
PLR	0.73	0.45	1.64	0.1	2.08	0.87 - 4.98
Histologic grade	0.25	0.48	0.52	0.603	1.28	0.50 - 3.28
Size	0.15	0.07	2.20	0.028	1.17	1.02 - 1.34
Lymphovascular invasion (Present)	1.70	0.55	3.12	0.002	5.49	1.89 - 15.98
Tumor necrosis	0.36	0.46	0.80	0.425	1.44	0.59 - 3.51

Abbreviations: PLR, Platelet-to-lymphocyte ratio; CI, Confidence interval.

Table 9. Multivariate logistic regression analysis including the HPR as a predictor of advanced T-stage

Variables	Coefficient B	Std. Error	z	P	Odds ratio	95% CI
Low HPR	0.89	0.45	2.00	0.046	2.44	1.02 - 5.86
Histologic grade	0.26	0.49	0.53	0.593	1.30	0.50 - 3.36
Size	0.15	0.07	2.17	0.03	1.17	1.01 - 1.34
Lymphovascular invasion (Present)	1.69	0.55	3.08	0.002	5.44	1.85 - 16.00
Tumor necrosis	0.30	0.46	0.65	0.515	1.35	0.55 - 3.35

Abbreviations: HPR, Hemoglobin-to-platelet ratio; CI, Confidence interval.

as inflammation increases, clinical manifestations such as anemia and thrombocytosis also increase, thus decreasing overall survival rates in patients with RCC (13).

In response to inflammation, the CRP level, neutrophil count, NLR, PLR and RDW increase. An elevated neutrophil count could also be secondary to paraneoplastic production of granulocyte-colony stimulating factor and granulocyte-macrophage colony stimulating factor by cancer cells (14,22). Neutrophilia hinders the activity of CD4 and CD8 lymphocytes, further worsening protective cell-mediated immunity (14).

Our study confirms the associations between high NLR and PLR and high grade and stage. The cut-off values used for the NLR were 3.12 and 2.86 for grade and stage, respectively. An NLR of ≥ 3 is associated with poor outcomes (6,14,23). Moreover, Keiner et al reported that a high NLR (≥ 2.27) and a De Ritis ratio (≥ 2.72) were associated with worse all-cause mortality and non-cancer mortality (3). Likewise, Parosanu et al reported that an NLR ≥ 3 is a predictor of poor outcome in patients treated with tyrosine kinase inhibitors or immune checkpoint inhibitors for advanced RCC (6).

We demonstrated a positive correlation between high PLR and high grade (cut-off of 132.46) and high stage (cut-off of 151.34). According to the study by Caliskan, both the NLR and the PLR are greater in advanced-stage and high-grade tumors (7). Additionally, Chandrasekaran et al evaluated the pre-treatment NLR and PLR in 150 patients and reported that elevated NLR and PLR are associated with high grade and stage, as in the present study (8). However, Ergin et al reported that the preoperative PLR did not sequentially increase with grade but that the NLR increased with grade (9).

Recently, Young et al reported that an NLR ≥ 3 , low hemoglobin levels and elevated platelet counts at 12 weeks after treatment with immune checkpoint inhibitor therapy indicated poor overall survival in patients with metastatic RCC (10). Similarly, Kim et al evaluated the role of pre- and postoperative NLR and PLR in non-metastatic RCC and reported that high NLR and PLR were significant predictive factors for recurrence-free survival and proposed that an NLR ≥ 1.9 on follow-up with unfavourable clinicopathological factors could indicate possible metastasis (11). In addition, Aktepe et al evaluated 150 patients treated with tyrosine kinase inhibitors and reported that patients with a PLR ≥ 204 had poor overall survival. Additionally, compared with the NLR, the PLR is a better predictor of overall survival in patients with metastatic RCC (12).

The cut-off values used for HPRs in our study were 0.338 and 0.505 for grade and stage, respectively. We demonstrated the association of HPR with WHO/ISUP grade and stage, with sensitivities of 89.2% and 66.7%,

respectively. Recently, Albisinni et al assessed the utility of the NLR, PLR and HPR in RCC and concluded that although high NLR, PLR and low HPR suggested poor overall survival according to univariate analysis, only low HPR was a predictor of overall survival according to multivariate analysis (18). Zapala et al reported that a higher NLR, PLR, systemic inflammatory response index (SIRI), and systemic immune-inflammation index (SII) and a lower HPR were associated with worse cancer-specific survival (5).

Multivariate analysis in the present study consistently revealed that high NLR, low HPR, the presence of lymphovascular invasion and large tumor size were independent predictors of high grade and high stage RCC.

We used cut-off values of 15.4% and 16.3% for RDW with respect to grade and stage, respectively. Zyczkowski et al reported that a RDW $\geq 13.9\%$ was a predictor of poor cancer-specific survival in patients with RCC and that a high RDW was associated with tumor necrosis, a large tumor size, low hemoglobin levels and RBC counts (19). Similarly, Wei et al reported that high RDW was associated with poor overall survival in RCC patients (20).

Wu et al evaluated the role of the RPR in acute kidney injury and reported that an increased RPR was associated with increased hospital mortality in terminally ill patients (24). The utility of RPR is evaluated in inflammatory conditions such as acute pancreatitis, neonatal sepsis and breast cancer (24,25). However, its role in RCC has not been explored. Our study did not show a significant correlation between RPR and grade or stage, potentially because of the small sample size. Hence, follow-up studies with larger cohorts are needed to establish its use as a biomarker for predicting outcomes.

Conclusion

In conclusion, we have demonstrated that higher preoperative NLR and PLR and low HPR are modest but statistically significant predictors of high WHO/ISUP grade and higher pathological T-staging in RCC. Multivariate analysis revealed that large tumor size, presence of lymphovascular invasion, high NLR, and low HPR were independent predictors of high tumor grade and T-stage. Thus, hematological biomarkers can be effectively incorporated into preoperative scoring systems to predict the prognosis of patients with RCC.

Limitations of the study

The limitations of our study include its single-center, retrospective nature. Survival analysis was not performed. Given that the analyses of RDW and the RPR were conducted as pilot studies, a large sample load is necessary to evaluate the associations between the RPR and RCC stage and grade.

Authors' contribution

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Investigation: Riya Kurmude, Sridevi Hanaganahalli Basavaiah, Sneha Rao Adoor Ramakrishna.

Methodology: Riya Kurmude, Sridevi Hanaganahalli Basavaiah, Sneha Rao Adoor Ramakrishna.

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Resources: Riya Kurmude, Sridevi Hanaganahalli Basavaiah, Sneha Rao Adoor Ramakrishna.

Software: Sneha Rao Adoor Ramakrishna, Riya Kurmude.

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Writing—review & editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This study was conducted in accordance with the principles of the Declaration of Helsinki, and approved by the Institutional Ethics Committee, Kasturba Medical College, Mangaluru (IEC KMC MLR 01-2020/14). Prior to any intervention, all participants provided written informed consent. The authors declare that no data fabrication, plagiarism, or duplicate publication was involved in this study.

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