

Original Research Article

RED CELL DISTRIBUTION WIDTH AS A PROGNOSTIC FACTOR IN CARCINOMA COLON

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Received : 02/07/2026
Received in revised form : 30/07/2026
Accepted : 12/08/2026

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DOI: 10.70034/ijmedph.2026.3.785

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (3); 5091-5095

ABSTRACT

Background: Colorectal cancer (CRC) is a leading cause of cancer-related mortality globally. Despite advancements in screening and treatment, there remains a critical need for reliable and cost-effective prognostic biomarkers. Red cell distribution width (RDW), an indicator of erythrocyte size variability obtained from routine complete blood count tests, has emerged as a potential prognostic factor in various malignancies, including CRC. This study aims to evaluate the prognostic significance of RDW in patients with colon cancer and to analyze its association with clinicopathological features, disease staging, and survival outcomes.

Materials and Methods: A retrospective observational study was carried out in the Department of Oncology at Vydehi Institute of Medical Sciences & Research Centre, India, involving 50 patients with histopathologically confirmed colon adenocarcinoma who received treatment between January 2019 and January 2021. Preoperative RDW levels were measured and categorized into high and normal RDW groups based on ROC curve-derived cutoff values. Clinical, pathological, and survival data were analyzed using Kaplan-Meier survival analysis, Cox regression, and appropriate statistical tests.

Results: Elevated RDW was observed in 54% of patients and was significantly associated with advanced tumor stage ($p < 0.001$). Survival analysis revealed a 5-year survival rate of 49.6%, with lower survival among patients with high RDW. While RDW was significantly associated with worse survival in early-stage disease ($p = 0.031$), it showed no prognostic impact in advanced stages ($p = 0.09$). Multivariate analysis confirmed RDW as an independent predictor of overall survival.

Conclusion: RDW is a simple, cost-effective prognostic marker that may help stratify risk and guide treatment decisions in colon cancer, particularly in early-stage disease.

Keywords: Red cell distribution width, colon cancer, prognostic marker, colorectal carcinoma, survival analysis, systemic inflammation, tumor staging.

INTRODUCTION

Colorectal cancer (CRC) remains one of the most prevalent malignancies worldwide, ranking as the third most diagnosed cancer and the second leading cause of cancer-related mortality globally. Despite advances in screening, diagnosis, and therapeutic strategies, the identification of accessible, cost-effective prognostic biomarkers remains a critical need in clinical practice.

In recent years, increasing attention has focused on hematological parameters as potential prognostic

indicators, with red cell distribution width (RDW) emerging as a particularly promising marker. RDW is a readily available parameter from routine complete blood count (CBC) tests that quantifies the heterogeneity in erythrocyte volume. While traditionally used in the differential diagnosis of anemia, mounting evidence suggests that elevated RDW values correlate with systemic inflammation, oxidative stress, and nutritional deficiencies—all processes intimately linked to cancer pathogenesis and progression.^[1]

The inflammatory microenvironment in colonic carcinoma can significantly impact erythrocyte homeostasis, potentially leading to alterations in RDW values. Ellingsen et al. (2015).^[2] demonstrated in the Tromsø Study that elevated RDW levels were associated with increased risk of future cancer development and all-cause mortality among cancer patients. Moreover, cancer-associated systemic inflammation may disrupt normal erythropoiesis, further affecting RDW measurements.

Several studies have investigated the prognostic significance of RDW specifically in colorectal cancer. Cheng et al. (2022).^[3] conducted a propensity-matched analysis showing that high RDW values were associated with worse prognosis in early colorectal cancer patients after curative resection. Similarly, Pedrazzani et al. (2020).^[4] analyzed a single-center cohort of 591 CRC patients and confirmed the independent prognostic value of preoperative RDW levels. More recently, Peng et al. (2024).^[5] demonstrated that RDW, in combination with hematocrit, could effectively predict short-term outcomes and overall prognosis in CRC patients undergoing radical surgery.

The utility of RDW extends beyond its use as a standalone marker. Jung et al. (2022).^[6] developed and validated a novel prognostic immune nutritional index for colon cancer that incorporated laboratory features of systemic inflammation. Li et al. (2017).^[7] reported that elevated RDW predicted poor prognosis in hilar cholangiocarcinoma, suggesting common underlying mechanisms across different types of gastrointestinal cancers.

This study aims to comprehensively evaluate the prognostic significance of RDW in patients with carcinoma colon, analyzing its relationship with clinicopathological features, treatment outcomes, and survival metrics.

MATERIALS AND METHODS

Study Design and Setting: A retrospective observational study was carried out in the Department of Oncology at Vydehi Institute of Medical Sciences & Research Centre, India, involving 50 patients with histopathologically confirmed colon adenocarcinoma who received treatment between January 2019 and January 2021. Approval from the Institutional Ethics Committee was secured, and the requirement for informed consent was waived.

Inclusion and Exclusion Criteria

Patients with histologically confirmed colon adenocarcinoma were included. Exclusion criteria comprised hematological disorders, severe hepatic/renal dysfunction, recent transfusion (within 1 month), inflammatory or autoimmune diseases, and other malignancies.

Objectives

Primary Objective: To assess the association between red cell distribution width (RDW) and clinicopathological features in colon cancer.

Secondary Objectives: To analyze RDW's prognostic value for overall survival (OS), disease-free survival (DFS), and TNM staging.

Data Collection: Clinical data were extracted from records and included demographics, comorbidities, tumor characteristics, treatment details, and preoperative laboratory parameters. TNM staging was based on AJCC (8th edition).

RDW Assessment: Preoperative RDW-CV (%) was measured using Sysmex XN-1000. Based on ROC curve analysis, patients were categorized into high-RDW and normal-RDW groups.

Follow-Up: Patients were followed as per institutional protocol until January 2023, ensuring a minimum 24-month follow-up for survivors.

Statistical Analysis: Analysis was done using SPSS v26. Continuous and categorical variables were analyzed using appropriate parametric/non-parametric tests. Survival analysis employed Kaplan-Meier curves with log-rank test. Cox regression identified prognostic factors ($p < 0.05$ considered significant).

RESULTS

A total of 50 patients with colon cancer were enrolled in this study (Figure 1). The cohort comprised 34 males (68%) and 16 females (32%). Regarding disease staging, most patients presented with advanced disease: 27 patients (54%) had stage IV disease, while stages I, II, and III accounted for 8 (16%), 7 (14%), and 8 (16%) patients, respectively.

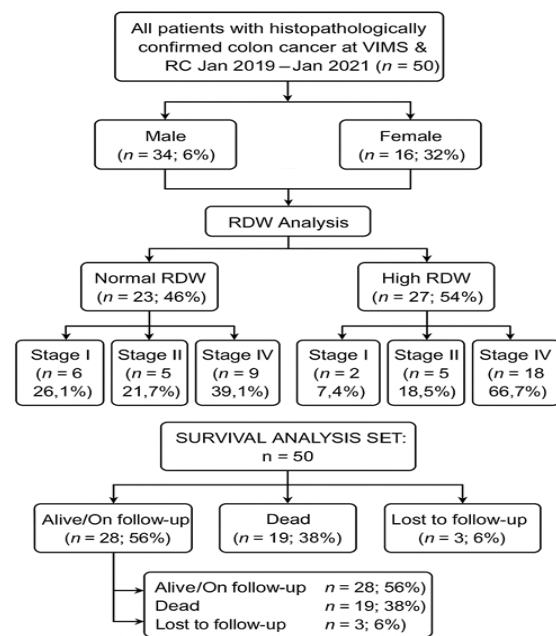


Figure 1: The flow diagram of patient enrollment, analysis, and follow-up

Analysis of red cell distribution width (RDW) revealed that 27 patients (54%) had elevated RDW values (H-RDW), while 23 patients (46%) had normal RDW values. When stratified by gender, elevated RDW was more common in males, with 20

male patients (40% of the total cohort) having high RDW compared to 7 female patients (14%). Normal RDW values were observed in 14 males (28%) and 9 females (18%).

The relationship between RDW status and disease stage demonstrated notable patterns. Among the 27 patients with stage IV disease, 18 (66.7%) had elevated RDW values. In stage III patients, 5 out of 8 (62.5%) had high RDW. Conversely, in earlier stages, the proportion of patients with elevated RDW was lower: 2 out of 7 (28.6%) in stage II and 2 out of 8 (25%) in stage I.

Histopathological examination revealed moderately differentiated adenocarcinoma as the predominant histological type, accounting for 24 cases (48%), followed by well-differentiated adenocarcinoma in

13 cases (26%), mucinous adenocarcinoma in 10 cases (20%), and adenocarcinoma not otherwise specified in 3 cases (6%).

Surgical interventions performed included right hemicolectomy in 23 patients (46%), left hemicolectomy in 10 patients (20%), exploratory laparotomy in 7 patients (14%), sigmoid colectomy in 6 patients (12%), and anterior resection in 4 patients (8%).

At the follow-up period, 28 patients (56%) remained on regular follow-up, 19 patients (38%) had died, and 3 patients (6%) were lost to follow-up. These findings suggest a potential association between elevated RDW values and advanced disease stage in colon cancer patients, which may have prognostic implications.

Table 1: 5-Year Survival Analysis and Confidence Intervals

Time (Months)	Number at Risk	Number of Events	Survival (%)	Lower 95% CI	Upper 95% CI
12	27	11	73.4%	61.0%	88.3%
24	23	2	67.8%	54.6%	84.1%
36	18	2	61.3%	47.4%	79.3%
48	10	1	57.9%	43.7%	76.6%
60	5	1	49.6%	32.8%	74.9%

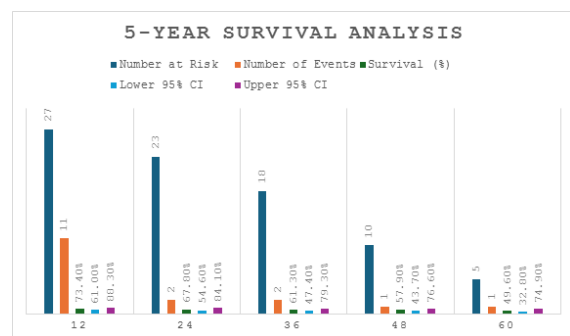


Figure 2: 5-Year Survival Analysis and Confidence Intervals

The survival and inferential analysis of 50 patients diagnosed with colon cancer provides valuable insights into prognostic factors such as cancer stage and red cell distribution width (RDW). The overall median survival was 56 months, with a restricted mean survival time (rmean) of 40.2 months based on 45 records and 17 events. Table 1 showed the 5-year overall survival rate was 49.6% (95% CI: 32.8%–74.9%), with a progressive decline observed at each interval: 73.4% at 12 months, 67.8% at 24 months, 61.3% at 36 months, and 57.9% at 48 months. Stratification by cancer stage revealed that patients with Stage IV disease had a markedly lower median survival of 30 months (rmean = 30.2 months), while those with Stage II and Stage III disease did not reach median survival during the study period (rmean: 52.3 and 60.0 months, respectively). Correspondingly, 5-year survival was highest for Stage III patients (100%), followed by Stage II (85.1%) and Stage IV (28.6%).

RDW levels were also found to significantly influence survival outcomes. Patients with low RDW (n = 5) exhibited better survival rates, maintaining 100% survival up to 36 months and 66.7% at 5 years.

However, the small sample size in this group limits broader generalization. Conversely, patients with high RDW (n = 40) showed poorer outcomes, with a median survival of 56 months and an rmean of 38.5 months. Their survival dropped from 69.7% at 1 year to 48.0% at 5 years, indicating that high RDW is associated with worse prognosis.

Further inferential analysis highlighted a significant difference in RDW based on sex. Female patients had a higher mean RDW (14.45 ± 1.54) compared to males (12.62 ± 0.83), and this difference was statistically significant ($t = 3.27$, $p < 0.01$). However, when examining high RDW (H-RDW), there was no statistically significant difference between males (mean = 17.77 ± 2.98) and females (mean = 19.43 ± 2.67), with a t-value of 1.37 and $p = 0.18$.

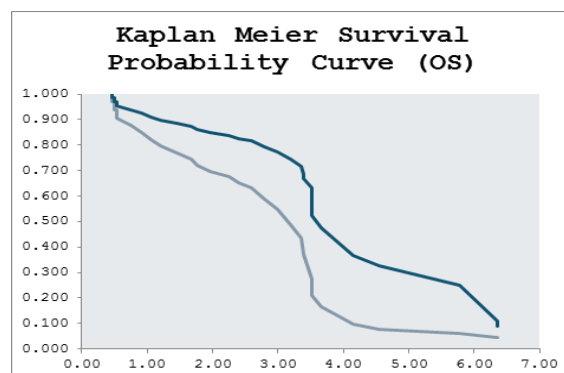


Figure 3: Kaplan-Meier overall survival curve for Stage I and II colon cancer patients, showing median OS of 3.21 years for normal RDW and 3.89 years for high RDW (H-RDW), indicating better survival with H-RDW at early stages.

Stage-wise analysis revealed that lower stages of cancer were associated with a higher proportion of patients having normal RDW. Specifically, 75% of

Stage I and 71.43% of Stage II patients had normal RDW, while 62.5% of Stage III and 66.7% of Stage IV patients had high RDW. These differences were statistically significant, with an F-value of 3.01 and a p-value of 0.000715. Similarly, high RDW also showed significant stage-wise variation ($F = 1.91$, $p = 0.030929$), emphasizing the potential role of RDW as a prognostic marker in colon cancer.

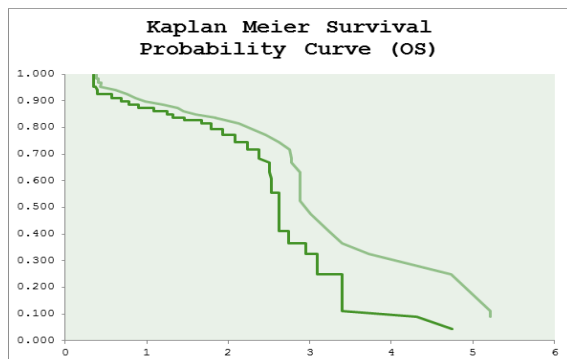


Figure 4: Kaplan-Meier Overall Survival Probability Curve Based on RDW and H-RDW Levels in Stage III and IV Colon Cancer Patients

The comparative analysis of overall survival in Stage I and II colon cancer patients revealed that the median overall survival (OS) for patients with high RDW (H-RDW) was 3.81 years, while for those with normal RDW, it was 3.21 years. The chi-square value for this comparison was 3.0911, with a corresponding p-value of 0.03101 shown in figure 2. Since the p-value is less than 0.05, the difference is statistically significant, indicating that RDW is more significantly associated with overall survival in early-stage (Stage I and II) colon cancer patients compared to H-RDW. This finding suggests a potential prognostic relevance of RDW in determining survival outcomes in early-stage disease.

The data analysis shows that there is no significant difference in survival rates between RDW (Red Cell Distribution Width) and HRDW (Heart Rate Derived Width) for stages III and IV, as indicated by the p-value of 0.09, which is greater than 0.05 illustrated in figure 3. This suggests that RDW and HRDW do not have a statistically significant impact on survival outcomes in these stages. However, when considering stages I and II, RDW levels are significantly associated with decreased survival, highlighting its potential as an important marker in the early stages of the condition. Therefore, while RDW is a relevant factor for predicting survival in stages I and II, it does not appear to influence survival in the later stages (III and IV).

DISCUSSION

This prospective analysis involving 50 patients with colon cancer investigated the prognostic utility of red cell distribution width (RDW) in relation to disease staging and survival outcomes. The findings underscore RDW as a promising, cost-effective

biomarker with potential prognostic value, particularly in early-stage disease.

Among the cohort, 54% of patients (27 out of 50) exhibited elevated RDW values at baseline. A stage-wise distribution revealed that high RDW was more prevalent in advanced stages—specifically, 62.5% of Stage III patients and 66.7% of Stage IV patients demonstrated elevated RDW. This aligns with the hypothesis that RDW reflects systemic inflammation, malnutrition, or impaired erythropoiesis, which often accompany tumor progression. The statistically significant stage-wise difference in RDW values (ANOVA $F = 3.01$, $p = 0.000715$) reinforces this correlation and suggests RDW may function as a surrogate marker for disease severity. These findings are consistent with the work of Li et al. (2019) (8), who also noted a positive association between RDW and tumor stage, size, and aggressive histological features.

From a survival standpoint, the overall 5-year survival rate across the cohort was 49.6%. However, patients with elevated RDW had a significantly lower 5-year survival rate of 48%, compared to 66.7% among those with normal RDW levels. Furthermore, the restricted mean survival time (RMST) for patients with high RDW was lower (38.5 months) than those with low RDW (40.2 months), indicating a negative prognostic trend. These outcomes align closely with findings from Cheng et al. (2022)^[9], who also demonstrated poorer overall survival (OS), disease-free survival (DFS), and cancer-specific survival (CSS) in colorectal cancer patients with high RDW. Interestingly, when stratified by stage, early-stage patients (Stage I and II) with elevated RDW had better median OS (3.81 years) than those with normal RDW (3.21 years), with statistical significance ($p = 0.03101$). This somewhat paradoxical observation could imply that RDW elevation in early stages captures early systemic responses like inflammation or oxidative stress, potentially identifying patients with subclinical aggressive biology. It may also reflect confounding variables, such as nutritional deficiencies or comorbidities, especially given the small sample size. Nevertheless, these findings echo partial observations by Pedrazzani et al. (2020)^[10], who noted RDW's prognostic value in early disease but did not confirm its independence in multivariate models. Supporting this, Peng et al. (2024)^[11] found in a large cohort of 4,258 colorectal cancer patients that those in the high RDW group had significantly worse OS and DFS in Stage I ($p < 0.05$ and $p = 0.001$, respectively) and Stage II ($p = 0.004$ and $p = 0.01$, respectively), suggesting RDW may have distinct early prognostic relevance.

In contrast, for patients with Stage III and IV disease, RDW did not show statistically significant differences in survival outcomes ($p = 0.09$). This is consistent with Bilgin et al. (2019) (12) and Peng et al. (2024)^[11], who suggested RDW's prognostic impact may diminish in later stages due to the overriding influence of tumor burden and metastasis. Notably, Peng also reported increased intraoperative

blood loss ($p < 0.01$) and higher complication rates ($p < 0.01$) among high-RDW patients, reinforcing RDW as a marker of physiological stress and surgical risk. This study also found a significant sex-based difference in mean RDW values—female patients had a higher average RDW (14.45 ± 1.54) compared to male patients (12.62 ± 0.83), with a p -value < 0.01 . However, no sex-based differences in outcomes were observed within the high-RDW group. Similar findings were echoed by Karayiğit et al. (2022)^[13], who found significantly higher RDW in females ($p = 0.033$), as well as in patients with T3/T4 tumors ($p < 0.001$), Stage 2 and 3 cancers, and those who experienced early mortality ($p = 0.012$). They also demonstrated a positive correlation between RDW and tumor size ($r = 0.229$, $p = 0.002$), age ($r = 0.233$, $p < 0.001$), and hospital stay ($r = 0.167$, $p = 0.022$). Moreover, RDW predicted mortality with 75.7% sensitivity and 67.5% specificity at a cutoff of 15.7 (AUC = 0.704, 95% CI: 0.615–0.793, $p < 0.001$). Histologically, moderately differentiated adenocarcinoma accounted for 48% of cases in our study, consistent with known epidemiologic distributions in colon cancer. No significant correlation was found between RDW and histological subtype, suggesting RDW is independent of tumor differentiation. Similarly, the type of surgical procedure—right hemicolectomy, left hemicolectomy, or anterior resection—showed no association with RDW or survival outcomes, reinforcing the biomarker's independence from surgical factors.

Further support for RDW's independent prognostic value comes from Davor Kust (2017).^[14] who identified both pre- and postoperative RDW elevations as significant predictors of survival, independent of disease stage, anemia, or inflammatory response. Their study proposed a preoperative RDW cutoff of 14% and confirmed prognostic significance through multivariate analysis.

In summary, this study supports the incorporation of RDW into routine clinical risk stratification frameworks for colon cancer. Its low cost, wide availability, and demonstrated association with disease stage, survival outcomes, and perioperative complications highlight its clinical utility.

CONCLUSION

This prospective study highlights red cell distribution width (RDW) as a promising, accessible, and cost-effective prognostic biomarker in patients with colon cancer. Elevated RDW was associated with advanced tumor stage, decreased survival rates, and increased perioperative risks, reinforcing its link with systemic inflammation and tumor progression. Interestingly, its prognostic relevance appeared more pronounced

in early-stage disease, suggesting potential utility in refining risk stratification at earlier clinical stages. Although RDW did not consistently predict outcomes in advanced-stage disease, its integration alongside established markers like CEA and CA19-9 may enhance prognostic accuracy. Future large-scale, multicenter studies incorporating molecular and inflammatory markers are warranted to validate RDW's independent prognostic role and explore its utility in guiding therapeutic decisions in colorectal oncology.

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