Research Article

Association Between Platelet Indices and Distant Metastasis in Colorectal Cancer Patients: A Cross-Sectional Study

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ABSTRACT

Background

Distant metastasis is the leading cause of death in colorectal cancer (CRC). Platelet activation may facilitate metastasis by protecting circulating tumor cells from immune elimination, promoting angiogenesis, and supporting tumor-cell migration. However, the relationships of platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) with distant metastasis remain unclear.

Objective

To investigate associations between platelet indices and distant metastasis in CRC and assess their diagnostic performance.

Methods

This retrospective cross-sectional study included 80 adults with confirmed CRC treated at Dr. Soetomo General Academic Hospital, Indonesia, between January 1, 2020, and January 1, 2025. Pretreatment platelet indices and metastatic status were obtained at initial admission. Comparative analyses and multivariable logistic regression were performed to assess associations between platelet indices and metastasis. Receiver operating characteristic (ROC) curve analysis evaluated their ability to discriminate metastatic from nonmetastatic CRC.

Results

Distant metastasis was identified in 33 patients (41.3%). Patients with metastasis had significantly higher PLT ($p=0.021$), lower MPV ($p<0.001$), and lower PDW ($p<0.001$), while PCT did not differ significantly ($p=0.280$). In multivariable analysis, PDW was the only platelet index independently associated with distant metastasis (adjusted OR=0.164; $p=0.005$). PDW had the best ability to tell the difference between groups (AUC=0.880), with a cutoff of <8.75%, a sensitivity of 81.8%, and a specificity of 82.9%.

Conclusions

Lower PDW independently indicated a greater likelihood of distant metastasis in CRC and showed a high level of diagnostic accuracy. As an inexpensive, noninvasive, routinely available biomarker, PDW may help identify high-risk patients and support early clinical decision-making.

Keywords Biomarker; Colorectal cancer; Metastasis; Mean platelet volume; Platelet distribution width; Platelet indices.

INTRODUCTION

Worldwide, CRC represents the third most commonly diagnosed cancer and the second leading cause of cancer-related mortality [1,2]. Global cancer estimate for 2022 recorded over 1.9 M newly diagnosed CRC case and roughly 935,000 deaths worldwide [1–3], making CRC a major public health challenge despite advances in screening and treatment. Despite advances in combined treatment strategies that have improved outcomes for localized CRC, metastatic spread continues to be the strongest indicator of an unfavorable prognosis and is responsible for approximately 90% of CRC-associated fatalities [3–6]. The liver represents the predominant destination for distant tumor spread, occurring in roughly 20% of patients when CRC is first diagnosed, whereas metastatic progression develops in nearly 50% of patients over the disease trajectory [7–9]. The metastatic cascade represents a multifaceted cellular process in which malignant cells penetrate surrounding structures, enter the vascular system, withstand circulatory conditions, migrate out of blood vessels, and establish secondary tumors in distant organs [10–12]. During hematogenous dissemination, circulating tumor cells encounter considerable mechanical stress and immune surveillance [11–14]. Platelets have emerged as critical mediators of this process by forming protective aggregates around circulating tumor cells, which helps malignant cells evade natural killer cell–induced destruction while promoting interaction with the vascular endothelium, epithelial–mesenchymal transition, angiogenesis, and establishment of metastatic niches [15–20]. Consequently, platelet activation has become increasingly recognized as an important hallmark of cancer progression and metastatic potential [20–23]. Routine complete blood count provides several platelet-related parameters that may indirectly reflect platelet activation, such as circulating platelet number, MPV, PDW, and PCT [24]. Earlier investigations have reported that elevated platelet count and MPV may reflect increased platelet reactivity linked to malignant progression, while PDW has been considered an indicator of platelet variability that may shift in

responses to platelet activation and utilization [24,25]. Nevertheless, the biological significance and clinical implications of these indices remain incompletely understood, particularly in colorectal cancer. Therefore, this study aim to investigate the association between platelet indices (platelet count, MPV, PDW, & PCT) and distant metastasis among patients with colorectal cancer.

MATERIALS AND METHODS

Study Population

This retrospective, cross-sectional study was conducted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. The electronic medical records of patients diagnosed with colorectal cancer between January 2020 and January 2025 were reviewed. A total of 80 adult patients (aged ≥ 18 years) with histopathologically confirmed colorectal adenocarcinoma were included, comprising 33 patients with distant metastasis and 47 without metastasis. Metastatic status was determined based on computed tomography findings and documented in the patients' medical records. Patients with radiologically confirmed distant metastases were categorized as metastatic, while those without distant-organ involvement were classified as nonmetastatic. Platelet indices, including PLT, MPV, PDW, and PCT, were obtained from complete blood counts performed at the initial hospital admission before the initiation of surgery, chemotherapy, radiotherapy, or other oncological treatment. The platelet parameters were assessed by means of the Sysmex XN-1000 automatic hematology analyzer manufactured by Sysmex Corporation, Japan. Patients were excluded if they had platelet disorders, coronary artery disease, chronic liver failure, chronic kidney disease, diabetes mellitus, or a history of antiplatelet or anticoagulant medication use. Cases with insufficient clinical, laboratory, or radiological documentation were similarly deemed ineligible.

The study protocol was approved by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (Protocol No: 4354/101/4/IV/2026). Patient confidentiality was maintained throughout the study. All procedures were conducted in accordance with the Declaration of Helsinki and applicable national ethical regulations.

Statistical Analysis

The statistical evaluation was undertaken in SPSS 27.0 for Windows (IBM Corp., Armonk). Normally distributed variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median (interquartile range). Categorical variables were summarized as frequencies and percentages. Comparisons between metastatic and non-metastatic groups were performed using independent t-test (for normally distributed continuous variables) and Mann–Whitney U test (for non-normally distributed variables. A binary logistic model incorporating multiple covariates was constructed to determine whether platelet-related parameters were independently linked to the presence of distant metastatic disease. Metastatic status served as the outcome measure, with affected patients assigned a value of 1 and those without distant spread assigned a value of 0. Candidate platelet variables were selected for multivariable modeling based on their significance during the initial bivariable assessment. Model estimates were presented as regression coefficients the model outputs included adjusted odds estimates, 95% uncertainty intervals, and exact probability values. ROC analysis was used to determine how effectively each platelet parameter distinguished patients with distant metastatic CRC from those without metastasis. ROC-based diagnostic accuracy was expressed through the area under the curved (AUC), accompanied by its 95% confidence interval and exact p-value. For each parameter, the threshold providing the greatest Youden index was selected as the optimal cutoff, with sensitivity and specificity subsequently calculated at that point. Statistical significanced was established at $p < 0.05$ using two-tailed testing.

RESULTS

Patient Characteristics

Between January 2020 and January 2025, a total of 80 patients with colorectal cancer (CRC) were enrolled in this study. The demographics and pathological profiles of the study populations are presented in Table 1. Of the 80 CRC patients enrolled, 58.8% were male, and the mean age was 55.6 years, with the majority falling within the 18–59 age group (57.5%). Primary tumors were more frequently located in the colon (53.8%) than in the rectum or rectosigmoid (46.2%). Most patients had stage III disease (51.3%), while 33 patients (41.3%) presented with distant metastasis (stage IV). Among the patients with metastatic disease, the liver was the most frequent metastatic site (78.8%), followed by the lungs (45.4%) and other distant organs (15.1%).

Table 1. Baseline Characteristics of the Study Population

Baseline Characteristics	Value
Sex	
Male	47 (58.8%)
Female	33 (41.3%)
Age (years)	mean 55.6
<18–59 years	46 (57.5%)
≥60 years	34 (42.5%)
Primary tumor	
Colon	43 (53.8%)
Rectum/Rectosigmoid	37 (46.2%)
Cancer stage	
Stage I	4 (5.0%)
Stage II	2 (2.5%)
Stage III	41 (51.3%)
Stage IV	33 (41.3%)
Metastatic sites*	
Liver	26 (78.8%)
Lung	15 (45.4%)
Other organs	5 (15.1%)

*Percentages are calculated among metastatic patients.

Comparison of Platelet Indices Between Metastatic and Non-metastatic Patients

The platelet indices of the patients with CRC are summarized in Table 2. Patients in the metastatic group exhibited significantly higher platelet counts than those in the non-metastatic group (median 414,000 [IQR 322,000–505,000] vs. 345,000 [IQR 299,000–406,000]; p = 0.021). Furthermore, the metastatic group demonstrated a significantly lower mean platelet volume (MPV) (8.57 ± 0.54 fL vs. 9.47 ± 0.73 fL; p = 0.008) and a significantly lower platelet distribution width (PDW) (median 8.30% [IQR 7.60–8.60%] vs. 9.60% [IQR 8.85–10.80%]; p < 0.001) compared to the non-metastatic group. In contrast, plateletcrit (PCT) values showed no significant difference between the two groups (median 0.36% [IQR 0.280–0.430%] vs. 0.33% [IQR 0.275–0.385%]; p = 0.280).

Table 2. Comparison of Platelet Indices According to Metastatic Status

Platelet indices	Non-metastasis (n = 47)	Metastasis (n = 33)	p-value
PLT count (/µL)	345.000 (299.000–406.000)	414.000 (322.000–505.000)	0,021
MPV (fL)	9,47 ± 0,73	8,57 ± 0,54	<0,001
PDW (%)	9.60 (8,85–10,80)	8.30 (7,60–8,60)	<0,001
Plateletcrit (%)	0,33 (0,275–0,385)	0,36 (0,280–0,430)	0,277

Association Between Platelet Indices and Distant Metastasis

Variables significantly associated with metastatic status in the bivariate analysis were entered into a multivariable logistic regression model (Table 3). After adjusting for other platelet indices, PDW remained the only independent predictor of distant metastasis (adjusted OR: 0.164; 95% CI 0.046–0.580; p=0.005). In contrast, platelet count (p=0.360) and MPV (p=0.933) were not independently associated with metastatic disease after multivariable adjustment (Figure 1).

Table 3. Risk of distant metastasis in CRC patients associated with platelet indices

Variable	B	p-value	Adjusted OR	95% CI
PLT count	0.001	0.360	1.397	0.410–4,720
MPV value	0.083	0.933	1.086	0.160–7.382
PDW value	-1.810	**0.005**	**0.164**	0.046–0.580

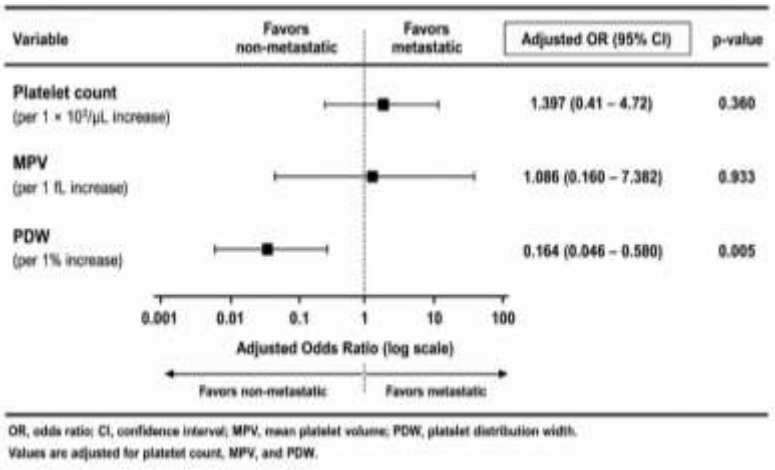


Figure 1. Forest plot of multivariable logistic regression analysis showing adjusted odds ratios for platelet count, MPV, and PDW.

Diagnostic Performance of Platelet Indices

ROC curve analyses was perform to evaluate the diagnostic performance of platelet indices for predicting distant metastasis (Table 4). PDW provided the most favorable discrimination among the platelet measurements examined (Figure 2), with an AUC value of 0.880, consistent with excellent diagnostic performance. A cutoff point of ≤8.75% resulted in 81.8% sensitivity and 82.98% specificity in distinguishing patients with distant metastases. The MPV measurement showed considerable accuracy in differentiating metastatic status, reflected by an AUC of 0.839. Its best-performing threshold was 8.95 fL, corresponding to sensitivity and specificity values of 81.8% and 76.6%, respectively. In comparison, platelet count showed only moderate discriminative ability with an AUC of 0.653. A cutoff score of 361500/μL provided a sensitivity of 63.63% and a specificity of 61.70%. Overall, ROC analysis demonstrated that PDW had the greatest diagnostic accuracy among all platelet indices evaluated, followed by MPV, whereas platelet count showed considerably lower predictive performance.

Table 4. Diagnostic performance of platelet Indices including area under the curve, optimal cut-off value, sensitivity, specificity, and Youden index (J)

Variable	AUC	Cut-off	Sensitivity (%)	Specificity (%)	J
PLT count	0.653	361500 /μL	63.63	61.70	0.253
MPV	0.839	8.95 fL	81.82	76.59	0.584
PDW	0.880	8.75%	81.82	82.98	0.648

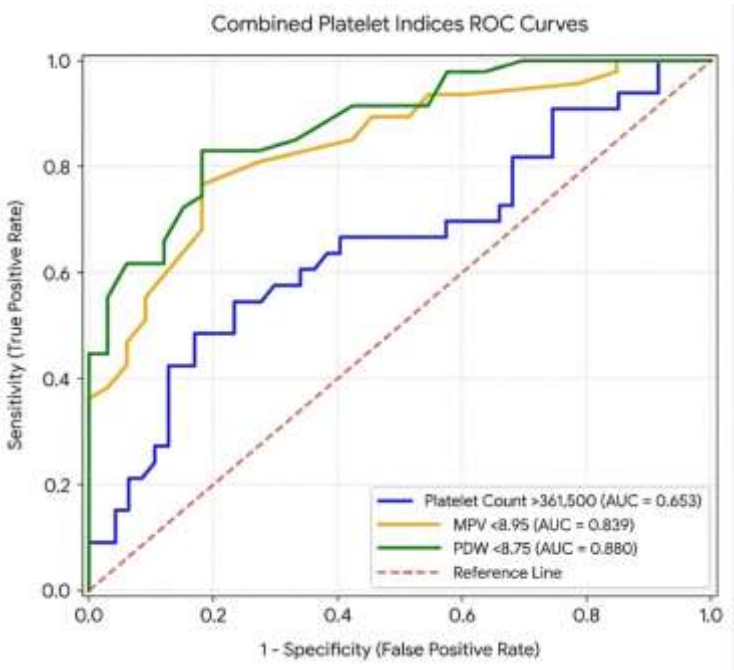


Figure 2. Receiver operating characteristic (ROC) curves comparing the diagnostic performance of platelet count, MPV, and PDW for predicting distant metastasis in colorectal cancer.

DISCUSSION

The findings of this study point to a close relationship between platelet characteristics and metastatic colorectal cancer (CRC). Among the four platelet indices examined, PDW showed the most consistent association with distant metastasis, even after platelet count and MPV were considered in the same model. PDW also distinguished metastatic from nonmetastatic disease better than the other indices. These findings do not establish PDW as a diagnostic test, but they suggest that changes in platelet-size variability may reflect biological processes accompanying metastatic spread. The contribution of platelets to cancer biology extends beyond their traditional involvement in hemostatic processes. Circulating tumor cells are capable of stimulating platelet activation and clustering after gaining access to the vascular compartment, a phenomenon known as tumor cell-induced platelet aggregation. The platelet layer surrounding these cells may shield them from circulatory mechanical forces and immune system–dependent killing. Platelets also support their attachment to the vascular endothelium, migration into distant tissues, and formation of new blood vessels through the release of cytokines, growth factors, and proangiogenic mediators [15–23,26,27]. Changes in circulating platelet indices may therefore reflect the combined effects of tumor activity, systemic inflammation, platelet production, and platelet consumption during metastatic progression.

The higher platelet count found in patients with metastasis is consistent with cancer-associated thrombocytosis. Inflammatory cytokines released in response to tumor activity, particularly interleukin-6, stimulate hepatic thrombopoietin production and increase megakaryocyte activity in the bone marrow [20–23]. Previous studies have similarly linked thrombocytosis with advanced tumor stage, lymphovascular invasion, distant metastasis, and poor survival in CRC [28,29]. In the present analysis, however, platelet count was no longer associated with metastasis after adjustment for MPV and PDW. This finding suggests that platelet count alone may not specifically reflect metastatic involvement. Platelet count is influenced by many other conditions, including infection, inflammation, anemia, bleeding, and nutritional disorders. Its initial association with metastasis may therefore reflect the broader inflammatory and hematological changes associated with advanced cancer.

A similar pattern was observed for MPV. Although metastatic patients had lower MPV values, the association disappeared in the multivariable analysis. Previous studies have reported inconsistent findings regarding MPV in cancer. Some studies found higher MPV in advanced malignancy, whereas others associated lower MPV with metastatic disease and poorer survival [30–32]. One possible explanation for the lower MPV is that larger and more active platelets are preferentially recruited and consumed during tumor–platelet interactions. This would leave a greater proportion of smaller platelets in circulation. Persistent inflammation may also alter platelet production and megakaryocyte maturation [33,34]. These explanations remain hypothetical because platelet turnover and activation were not measured directly. The loss of significance after adjustment also suggests that MPV may capture some of the same biological variation represented more clearly by PDW.

PDW was the only platelet index that remained associated with distant metastasis after mutual adjustment. Unlike MPV, which represents average platelet size, PDW reflects the degree of variation in platelet size. It may therefore be more sensitive to changes in platelet production, maturation, activation, and consumption [24,25]. A reduction in PDW could occur when heterogeneous and highly active platelets are continuously consumed while the bone marrow releases a more uniform population of circulating platelets [33]. This interpretation agrees with previous reports linking lower PDW to unfavorable outcomes in resectable CRC and to advanced clinicopathological features in gastrointestinal malignancies [24,35–37]. Nevertheless, studies in other cancer populations have not always shown the same direction of association [38,39]. Differences in tumor biology, disease stage, inflammatory burden, patient characteristics, and laboratory procedures may account for these conflicting results.

PCT was not associated with metastatic status. Because PCT represents total platelet mass and is derived from platelet count and MPV, the absence of an association is understandable [25]. In patients with metastasis, the higher platelet count was accompanied by a lower MPV. These opposing changes may have offset one another, resulting in relatively stable PCT values. This finding also suggests that changes in platelet size and size distribution may be more informative than total circulating platelet mass in metastatic CRC. PDW showed the largest area under the ROC curve among the platelet indices evaluated.

The interpretation of these findings also requires consideration of laboratory and clinical factors. MPV and PDW can vary according to the type of hematology analyzer, anticoagulant, storage conditions, and interval between blood collection and analysis. These preanalytical differences may partly explain the inconsistent findings across studies. In addition, the regression analysis adjusted the platelet indices for one another but did not account for

several relevant clinical factors, including age, sex, anemia, infection, systemic inflammation, nutritional status, primary tumor location, and tumor burden. Therefore, the association between PDW and metastasis cannot be considered fully independent of clinical confounding.

This study has several other limitations. Its retrospective cross-sectional design does not allow conclusions about whether lower PDW preceded metastasis or developed as a consequence of advanced disease. The sample was relatively small and was drawn from a single tertiary referral hospital, with most patients having stage III or IV disease. This distribution may limit the applicability of the findings to patients with earlier-stage CRC or those treated in other settings. Platelet indices were measured only once, preventing evaluation of changes over time. Inflammatory biomarkers and specific platelet-activation markers were also unavailable, so the biological mechanisms proposed in this discussion could not be tested directly.

Despite these limitations, this study provides a direct comparison of four routinely available platelet indices in relation to metastatic CRC. Examining their associations and discriminatory performance within the same patient population helped identify PDW as the index deserving further investigation. Its low cost and widespread availability make it an attractive candidate for future research. Prospective multicenter studies should include larger and more diverse populations, standardized blood-sampling procedures, relevant clinical and inflammatory covariates, serial platelet measurements, and independent validation cohorts. These steps are necessary to determine whether PDW adds meaningful information beyond established clinical, pathological, and radiological assessments.

CONCLUSION

The present study demonstrates that among routinely available platelet indices, PDW possesses the strongest association with distant metastasis and the highest diagnostic accuracy for predicting metastatic colorectal cancer. These findings further support the growing evidence that platelet activation is closely involved in the metastatic cascade and highlight PDW as a promising, inexpensive, and readily accessible biomarker for metastatic risk stratification in clinical practice.

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