RESEARCH ARTICLE

Editorial Process: Submission:04/11/2025 Acceptance:10/12/2025 Published:10/19/2025

Validation of Platelet-index based Score (PIBS) for Early Prediction of the Pathological Stage in Colorectal Cancer

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Abstract

Introduction: Accurate staging is essential in colorectal cancer (CRC) management. Platelet indices have emerged as promising biomarkers of tumor burden and progression. This study aimed to validate the Platelet Index-Based Score (PIBS-CRC), a machine learning-based model using platelet parameters, for predicting the pathological TNM stage of CRC. **Materials and Methods:** A cross-sectional study was conducted involving 116 patients with histologically confirmed CRC. Preoperative platelet indices platelet count (PLT), platelet distribution width (PDW), mean platelet volume (MPV), and plateletcrit (PCT) were input into the PIBS-CRC model. The model's prediction was then compared with the final pathological TNM stage (AJCC 8th edition). Diagnostic performance was assessed using confusion matrix and classification metrics. **Results:** The PIBS-CRC score showed strong performance, with an overall accuracy of 87%, precision of 87%, F1-score of 88%, and Matthews Correlation Coefficient (MCC) of 0.81. The model accurately predicted stages I, III, and IV, though some misclassification occurred between stages II and III. PLT and PCT were significantly associated with advancing TNM stage ($p < 0.001$). **Conclusion:** The PIBS-CRC model is a reliable, non-invasive tool for predicting pathological CRC stages using routine blood tests. It is particularly useful for early-stage detection and may serve as a practical adjunct in clinical settings with limited diagnostic resources.

Keywords: colorectal cancer- platelet indices- staging prediction- PIBS-CRC score- TNM classification

Asian Pac J Cancer Prev, **26 (10)**, 3743-3748

Introduction

Colorectal cancer ranks second in global cancer-related deaths and third in overall incidence. Its incidence is increasing, especially in developing nations, and is expected to reach 3.2 million cases by 2040 [1, 2]. In Indonesia, colorectal cancer ranks fourth in incidence, with 35,676 new cases and 19,255 deaths reported in 2022 [3]. In 2023, 293 cases were recorded at Dr. Wahidin Sudirohusodo Hospital in Makassar, mostly in male patients with a mean age of 54 years, and most diagnosed at stage III [4]. CRC staging typically follows the TNM system, based on pre-treatment clinical assessment or post-surgical pathology [5]. The association between platelets and cancer has been recognized since the 19th century. Cancer cells and platelets interact bidirectionally, promoting tumor progression, metastasis, immune evasion, and angiogenesis [6–9].

Recent data from Dr. Wahidin Sudirohusodo Hospital revealed that platelet indices PC, PDW, PCT, and MPV are significantly associated with CRC staging [4]. The Platelet Index-Based Scoring for Colorectal Cancer (PIBS-CRC) is a machine learning tool that uses platelet indices to predict cancer stage in a non-invasive, affordable, and accessible manner. This study aimed to validate the PIBS-CRC model for predicting pathological TNM stages of CRC using platelet indices, conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar.

Materials and Methods

Study Design and Setting

This observational study employed a cross-sectional design to evaluate the preoperative Platelet Index-Based Score for Colorectal Cancer (PIBS-CRC) as a predictor of pathological staging (pTNM, AJCC 8th edition) among colorectal cancer patients. The study was conducted from August 2024 to January 2025 at the Digestive

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Surgery Division, Dr. Wahidin Sudirohusodo General Hospital, Makassar an Eastern Indonesia referral center with diverse CRC cases. This study was approved by the Ethics Committee of the Faculty of Medicine, Hasanuddin University (ID: UH24110918).

Population and Sampling

Subjects were enrolled via consecutive sampling. Inclusion criteria were: (1) histopathologically confirmed adenocarcinoma; (2) available clinical data (age, sex, tumor site, platelet indices); (3) scheduled for curative-intent surgery; (4) signed informed consent. Exclusion criteria were: incomplete records, hematologic or immunologic disease, prior platelet transfusion, or history of chemotherapy/radiotherapy for other malignancies. Sample size was calculated using a single-population diagnostic test formula, requiring a minimum of 97 subjects.

Variables and Operational Definitions

The dependent variable was pathological TNM stage (AJCC 8th ed). The independent variable was the predicted stage based on PIBS-CRC, a machine learning model incorporating platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT). Each index was inputted into a custom Python web-based calculator (developed using Streamlit) to produce stage predictions (link).[4] The pathological stage was determined by intraoperative findings and histopathology based on the TNM classification.

Data Collection and Laboratory Analysis

Blood samples were collected preoperatively in EDTA tubes, processed within 2 hours (or stored at 4°C up to 24 hours), and analyzed using a Mindray BC-1800 hematology analyzer. Reagents used included M-18 CFL LISE, RINSE, and E-2 probe cleaner. Values for PC, MPV, PDW, and PCT were recorded. Histopathologic data were collected post-surgery and staged according to pTNM classification.

Statistical Analysis

All data were entered into Microsoft Excel, cleaned, and analyzed using SPSS v25.0 and Python. Descriptive statistics (mean ± SD, frequency) were used. A confusion matrix assessed model performance across stages. Diagnostic metrics (accuracy, sensitivity, specificity, precision, F1-score, and Matthews Correlation Coefficient/MCC) were computed. Group comparisons used Chi-square tests, ANOVA, and Tukey HSD post hoc test as appropriate. Statistical significance was set at $p < 0.05$.

Results

A total of 116 colorectal cancer (CRC) patients were included in this study, all of whom were treated at the Digestive Surgery Department of Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia. The average patient age was 56.06 ± 12.00 years, with 53.45% being male. The most common tumor site was the rectum (59.48%), and most patients underwent definitive surgical treatment (74.14%). Table 1 summarizes the demographic and clinical characteristics. Platelet indices were: platelet count (PLT) 395.01 ± 140.17 ×10⁹/L, platelet distribution width (PDW) 8.90 ± 1.68 fL, mean platelet

Table 1. Study Characteristic Include in This Study

Variable	N	%
Sex		
Male	62	53.45
Female	54	46.55
Location		
Caecum	5	4.31
Ascending colon	9	7.76
Transversum colon	6	5.17
Descendens colon	5	4.31
Sigmoid	22	18.97
Rectum	69	59.48
PIBS CRC Stage		
I	9	7.76
II	30	25.86
III	63	54.31
IV	14	12.07
Management		
Definitive	86	74.14
Divertion	30	25.86
Tumor (pT)		
T1	2	1.72
T2	15	12.93
T3	38	32.76
T4	61	52.59
Node (pN)		
N0	47	40.52
N1	68	58.62
N2	1	0.86
Metastasis (M)		
M0	100	86.21
M1	16	13.79
Stage (pTNM)		
I	7	6.1
II	34	29.3
III	59	50.8
IV	16	13.8
Survival		
Alive	104	86.21
Dead	12	13.79
Variable	Mean	SD
Age	56,06	12.00
Platelet Index		
PLT	395,01	140.17
PDW	8,90	1.68
MPV	8,84	1.20
PCT	0,31	0.11

volume (MPV) 8.84 ± 1.20 fL, and plateletcrit (PCT) 0.31 ± 0.11%. The distributions of PIBS-CRC predicted stages and pathological TNM stages are also provided in Table 1.

Table 2 displays the distribution of platelet indices across TNM stages. PLT and PCT values increased with advancing cancer stage and showed statistically significant differences ($p < 0.001$, One-Way ANOVA). PDW and MPV values did not differ significantly among stages ($p = 0.226$ and $p = 0.482$, respectively). Post-hoc Tukey HSD analysis (Table 3) showed that PLT and PCT differed significantly between all stage comparisons ($p < 0.001$), reinforcing the link between higher platelet indices and more advanced stages.

Figure 1 illustrates the confusion matrix comparing PIBS-CRC predicted stages and actual pathological TNM stages. The model showed strong classification performance: 100% of stage I cases were correctly predicted, 76.5% for stage II (with some misclassified into stages I and III), 93.2% for stage III, and 87.5% for stage IV. Overall diagnostic performance is summarized in Figure 2, with an accuracy of 87.93%, sensitivity of 89.3%, and specificity of 94.8%, indicating robust staging discrimination.

The ROC curves are shown in Figure 3. The model's overall AUC-ROC was 89.63%, indicating excellent predictive ability. Stage-specific AUCs were 0.99 (stage I), 0.86 (stage II), 0.90 (stage III), and 0.94 (stage IV), demonstrating high accuracy across stages, with slightly lower performance for stage II.

Table 4 summarizes the model's statistical validation.

Table 2. Distribution of Platelet Index Variables by TNM Stage

Variable	Stage I	Stage II	Stage III	Stage IV	p-value
PLT	206,22 ± 34,50	312,13 ± 45,60	402,90 ± 100,15	658,43 ± 74,03	<0.001*
PDW	8,74 ± 1,83	8,51 ± 1,59	8,93 ± 1,41	9,08 ± 2,68	0.226
MPV	8,62 ± 1,15	8,66 ± 0,94	8,77 ± 0,73	9,14 ± 2,66	0.482
PCT	0,18 ± 0,03	0,25 ± 0,06	0,34 ± 0,09	0,38 ± 0,16	<0.001*

Table 3. Post Hoc Test (Turkey HSD) for Significant Variables

Stage-PLT				Stage-PCT			
Grup 1	Grup 2	Meandiff	p-value	Grup 1	Grup 2	Meandiff	p-value
I	II	105.91	0.001	I	II	0.07	0.001
	III	196.68	0.001		III	0.16	0.001
	IV	452.21	0.001		IV	0.2	0.001
II	III	90.77	0.001	II	III	0.09	0.001
	IV	346.3	0.001		IV	0.13	0.001
III	IV	255.52	0.001	III	IV	0.04	0.001

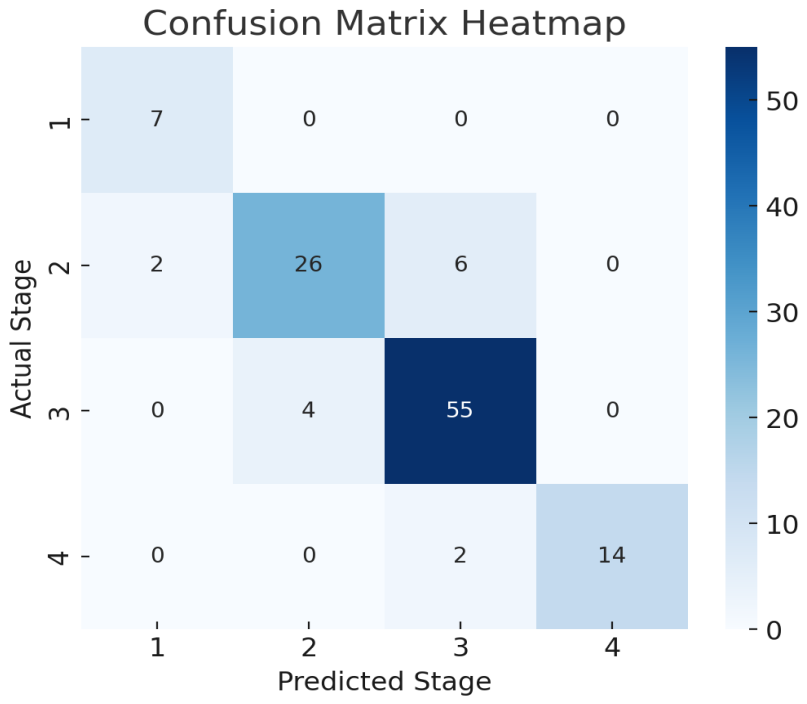

Figure 1. Confusion Matrix Comparing Stage Prediction with pTNM Stage

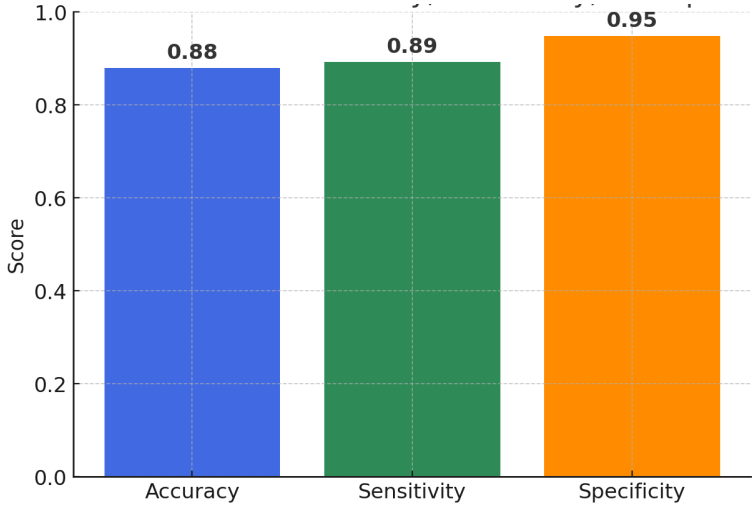

Figure 2. Accuracy, Sensitivity and Specificity of PIBS-CRC Scoring in Predicting TNM Pathological Stage

Table 4. Statistical Test of PIBS CRC Stage Prediction with TNM Pathology Stage

Statistical test methods	Results
Chi square	<0.001
Cohen's kappa	0.8074
Precision	87.4%
F1-score	88.06%
Matthews correlation coefficient	0.8095
Misclassification analysis	12.07%

The Chi-square test confirmed a significant correlation between predicted and actual staging ($p < 0.001$). Cohen's kappa coefficient was 0.8074, indicating substantial agreement. The model also showed high precision (87.4%), F1-score (88.06%), and Matthews Correlation Coefficient (MCC) of 0.8095. The overall misclassification rate was 12.07%, mainly between stages II and III, likely due to overlapping clinical features.

Discussion

The pathological TNM staging system remains the gold standard for assessing prognosis and determining adjuvant therapy in colorectal cancer (CRC). It is determined after surgical resection and pathological examination, allowing for more precise staging. However, the advent of predictive models, such as the Platelet Index-Based Scoring for Colorectal Cancer (PIBS-CRC), offers promising non-invasive alternatives that may assist in early stratification of disease severity [4]. PIBS-CRC is a scoring system derived from machine learning analysis using four platelet indices platelet count (PC), plateletcrit (PCT), platelet distribution width (PDW), and mean platelet volume (MPV) which are converted

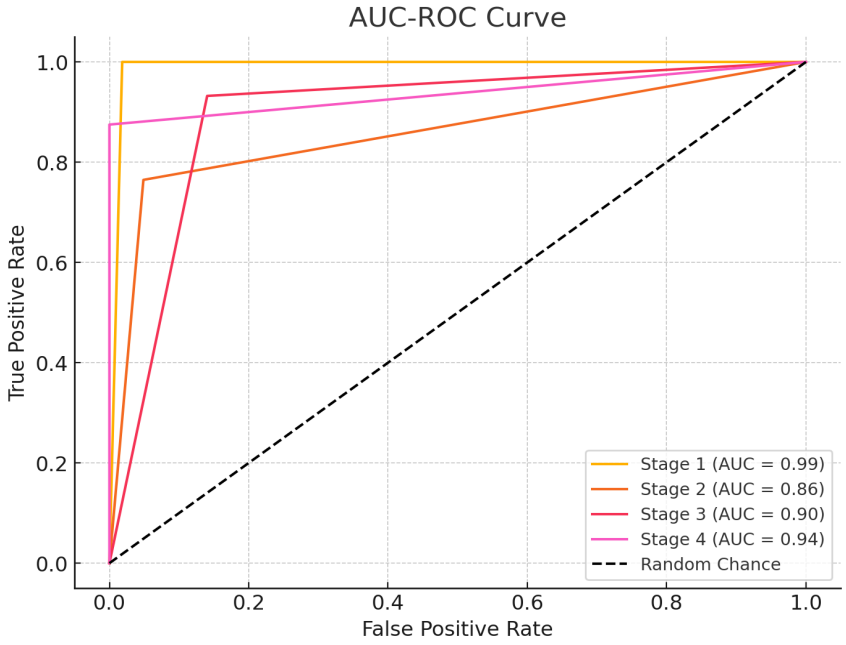

Figure 3. AUC-ROC Graph Prediction of PIBS CRC Stage against pTNM Pathology Stage

into a categorical stage prediction based on their values processed through an online platform. This offers a non-invasive alternative for estimating disease stage at diagnosis.

Emerging evidence supports the role of platelets in tumor progression. CRC cells may stimulate thrombopoiesis and platelet activation, thereby contributing to epithelial-mesenchymal transition, angiogenesis, immune evasion, and metastasis [10]. Among platelet parameters, PC has the strongest association with tumor staging, followed by PCT, PDW, and MPV [4]. Elevated PC levels often reflect a tumor-induced inflammatory response, mainly mediated by interleukin-6 (IL-6) which enhances megakaryocyte activity and thrombopoiesis [11]. These elevated platelets form a "cloak" that shields cancer cells from immune surveillance, especially natural killer (NK) cells, thus facilitating metastasis [10]. Clinical data support this: patients with stage III–IV CRC exhibit significantly higher PC than those with earlier stages [12,13].

Mean platelet volume (MPV) indicates platelet activation and correlates with increased thrombogenic potential. Larger, more reactive platelets release growth factors that contribute to tumor invasion and metastasis [14,15]. PDW, a marker of platelet size heterogeneity, is considered a surrogate of platelet activation. Higher PDW values have been correlated with lymph node metastasis and reduced survival in CRC [16,17]. Retrospective studies have identified PDW as an independent predictor for recurrence and survival in non-metastatic CRC patients. [17] PCT reflects the total volume of circulating platelets and is associated with tumor size, vascular invasion, and advanced TNM stage [18,19]. These findings suggest that changes in platelet dynamics are closely linked with tumor biology.

In this study, the PIBS-CRC model demonstrated high classification accuracy (87.93%) against pathological TNM staging. It accurately predicted all stage I cases, most stage III and IV cases, and showed some misclassification between stages II and III likely due to overlapping clinical features. Confusion matrix analysis confirmed strong agreement (Cohen's kappa = 0.8074), and performance metrics such as precision (87.94%), F1-score (88.06%), and MCC (0.8094) supported its reliability in clinical settings. The AUC-ROC (89.63%) indicated high overall discriminatory power, with stage-specific AUCs ranging from 0.86 to 0.99.

These results align with previous efforts using hematological biomarkers (e.g., NLR, PLR) or AI-assisted models for CRC staging [10,13,20]. While deep learning models may reach up to 92% accuracy, they often require extensive datasets and infrastructure. By contrast, PIBS-CRC provides a cost-effective and accessible solution, particularly for resource-limited settings [18,21]. External validation remains essential to ensure generalizability across diverse populations.

Notably, this model performed best for early-stage CRC, likely due to subtler inflammatory and hematologic changes in stages I and II [22]. Conversely, inflammation-driven cytokine production and platelet activation intensify in stages II and III, but the gradual progression may hinder model differentiation between these stages. The PIBS-CRC model's diagnostic performance was reinforced by a high MCC (0.81), precision (87%), and F1-score (88%), supporting its reliability in class-imbalanced datasets [23]. Despite these barriers, platelet-based models present a pragmatic approach to CRC staging, especially in resource-limited settings. They may complement, rather than replace, more advanced diagnostic tools. Importantly, model performance must be monitored over time through continual learning strategies to ensure sustained clinical relevance [24].

This study offers a novel validation of the PIBS-CRC scoring model against pathological TNM staging, using readily available platelet indices from routine blood tests. Its strengths include a relatively large sample size, robust internal validation with machine learning metrics, and potential applicability in resource-limited settings. However, being a single-center study limits generalizability, and the lack of external validation may affect reproducibility. Platelet indices can be influenced by confounding factors such as infections or medications, and the model does not integrate other biomarkers like CEA or imaging data. Thus, PIBS-CRC should be considered a complementary tool for early risk stratification rather than a replacement for standard staging methods.

In conclusion, the PIBS-CRC scoring model exhibited robust predictive performance, particularly for stages I, III, and IV of colorectal cancer, albeit with some misclassification observed between stages II and III. With an accuracy of 87%, precision of 87%, F1-score of 88%, and a Matthews Correlation Coefficient (MCC) of 0.81, the model demonstrated a balanced diagnostic capability and was particularly effective in identifying early-stage disease. These findings support the potential clinical utility of platelet indices as non-invasive, accessible biomarkers for tumor staging.

To enhance the model's clinical relevance, future studies should prioritize external validation across multiple centers with diverse patient populations. Integrating additional biomarkers, such as inflammatory markers or genetic data, and employing artificial intelligence approaches may enhance prediction accuracy. Furthermore, real-world implementation through clinical decision support tools or AI-powered applications should be explored through prospective trials to assess the practical impact of the PIBS-CRC model in routine oncologic care.

Author Contribution Statement

AA conceptualized the study, led the data collection, and wrote the manuscript. LM supervised the research process and provided input on methodology and discussion. MS contributed to statistical analysis and interpretation of results. All authors have read and approved the final version of the manuscript.

Acknowledgements

Availability of Data

The datasets generated and/or analyzed during this study are available from the corresponding author on

reasonable request.

Study Registration

This study is not a clinical trial and was therefore not registered in any clinical trial registry.

Scientific Approval

This study is part of an approved student thesis submitted to the Department of Surgery, Faculty of Medicine, Universitas Hasanuddin.

Ethical Approval

The study protocol was reviewed and approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Hasanuddin, under approval number UH24110918.

Conflict of Interest

The authors declare no conflict of interest.

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