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Original Research Article

Colorectal Cancer Prognosis: Combined Role of Preoperative Prognostic Nutritional Index, D-Dimer Score, and Surgical Outcomes

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Abstract: *Colorectal cancer (CRC) remains one of the leading causes of cancer mortality worldwide. Identification of reliable preoperative prognostic markers is vital for individualised patient care. This study investigated the predictive value of the composite Prognostic Nutritional Index (PNI) and D-dimer Score (PDS) for overall survival in patients with CRC.* ***Methods:*** *A prospective cohort study was conducted at Dr Ruth Pfao Civil Hospital, Karachi, from January 2023 to July 2024. Patients aged 40–80 years with confirmed CRC and available preoperative albumin, lymphocyte count, and D-dimer levels were included. Kaplan–Meier survival analysis and log-rank tests were applied.* ***Results:*** *Among 100 patients (mean age 61.6±13.3 years, 57% male), 69% were alive at a mean follow-up of 30.5±16.7 months. Age >60 years showed borderline association with reduced survival (p=0.05). No significant survival differences were found across PDS categories (log-rank χ^2=1.760, p=0.415).* ***Conclusion:*** *The PDS was not independently associated with overall survival in this cohort. Broader multicentre studies are warranted to clarify its prognostic role.*

Keywords: Colorectal cancer, Prognostic Nutritional Index, D-dimer, survival, prognosis

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Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer mortality globally (Siegel et al., 2023). Despite significant advances in surgery, chemotherapy, and targeted therapy, CRC survival outcomes vary widely depending on tumour biology, host-related factors, and access to treatment. This has prompted increasing emphasis on identifying simple, cost-effective, and reproducible prognostic markers, especially in resource-limited settings.

Among the many prognostic factors, the Prognostic Nutritional Index (PNI) has gained attention as a marker of nutritional and immunological status. PNI, calculated using serum albumin and lymphocyte count, reflects host immune competence and nutritional reserve. Low PNI has been linked with postoperative complications, impaired response to treatment, and poor oncologic outcomes (Nozoe et al., 2010).

D-dimer, a fibrin degradation product, serves as a biomarker of hypercoagulability and tumour-associated thrombogenesis. Elevated preoperative D-dimer levels have been associated with advanced disease stage, metastasis, and worse prognosis (Li et al., 2021). The combination of nutritional and coagulation markers into a composite Prognostic D-dimer Score (PDS) has been proposed to enhance predictive accuracy.

However, evidence remains inconsistent, with some studies supporting the prognostic role of PDS, while others find limited value. Importantly, most available studies are from East Asia and Western countries, with limited representation from South Asian populations. Given regional differences in patient demographics, tumour biology, and healthcare delivery, this study sought to evaluate the prognostic value of PDS in CRC patients undergoing surgery in a tertiary care hospital in Pakistan.

Methodology

This was a prospective, single-centre cohort study conducted at Dr Ruth Pfao Civil Hospital, Karachi, from January 2023 to July 2024. Patients aged 40–80 years with histologically confirmed CRC and available preoperative albumin, lymphocyte count, and D-dimer levels were included. Exclusion criteria were use of anticoagulants before Diagnosis, presence of another malignancy, or severe infection.

PNI was calculated as (10 × albumin [g/dL]) + (0.005 × lymphocytes [/mm³]) and classified as low (<45) or high (≥45). D-dimer was dichotomised at 0.55 mg/L. PDS was defined as: 0 (low PNI + high D-dimer), 1 (either low PNI or high D-dimer), 2 (high PNI + low D-dimer). Kaplan–Meier survival analysis with log-rank tests compared overall survival between groups.

Results

A total of 100 patients with histologically confirmed colorectal cancer (CRC) were included in this study. The mean age of the participants was 61.6 ± 13.3 years, and 57% were male. The mean body mass index (BMI) was 27.0 ± 4.5 kg/m² (Table 1).

Table 1 presents the demographic characteristics of the study population. Most participants were aged 60 years or older. Table 2 details the clinical and surgical parameters. The majority of patients were diagnosed with Stage II disease (41%), followed by Stage I (22%), Stage III (21%), and Stage IV (17%). Lymph node involvement was present in 38%, while metastasis was noted in 26%.

In terms of surgical approach, open surgery was performed in 58% of patients, and laparoscopic surgery in 42%. Curative resection was achieved in 72%, while 28% underwent non-curative or palliative surgery. Positive surgical margins were seen in 18% of cases, and postoperative complications occurred in 21%, with an operative mortality rate of 5% (Table 2).

The mean follow-up duration was 30.5 ± 16.7 months, during which 69% of patients were alive. Kaplan–Meier survival analysis revealed no

significant difference in survival across Prognostic D-dimer Score (PDS) categories (log-rank χ^2 = 1.760, p = 0.415). Age above 60 years demonstrated a borderline association with reduced survival (p = 0.05). Neither PNI nor D-dimer alone showed a statistically significant relationship with survival outcomes (Table 3). Tumour stage, surgical intent, and margin status did not show significant correlations with overall survival..Figure 1 shows the Kaplan–Meier survival curves stratified by Prognostic D-dimer Score (PDS) categories, illustrating that survival trends across all groups were similar, with overlapping curves and no statistically significant difference (p = 0.415). Patients with higher PDS initially showed slightly better early survival, but the difference diminished over time. Figure 2 demonstrates the surgical approaches: open surgery in 58% of patients and laparoscopic procedures in 42%, indicating that while open surgery remains standard, laparoscopic techniques are increasingly adopted. Figure 3 presents the intent of surgery, showing that 72% of patients underwent curative procedures, whereas 28% received palliative interventions, reflecting a predominance of potentially curable cases but also a notable portion with advanced disease. Figure 4 illustrates postoperative complications, which occurred in 21% of patients, while 79% had uneventful recoveries, suggesting good perioperative management. Figure 5 shows surgical margin status: 82% achieved negative margins and 18% had positive margins, underscoring the importance of complete tumour excision. Figure 6 summarises overall survival outcomes, with 69% of patients alive at follow-up and 31% deceased, aligning with global survival trends for colorectal cancer and indicating no significant association between PDS and overall survival..

Table 1. Demographic characteristics of colorectal cancer patients.

Variable	N	%
Age (mean ± SD)	-	61.6 ± 13.3
Male sex	57	57%
BMI (kg/m²)	-	27.0 ± 4.5

Table 2. Clinical and surgical characteristics of colorectal cancer patients.

Variable	N	%
Stage I	22	22%
Stage II	41	41%
Stage III	21	21%
Stage IV	17	17%
Lymph node involvement	38	38%
Metastasis	26	26%
Open surgery	58	58%
Laparoscopic surgery	42	42%
Curative resection	72	72%
Non-curative/palliative	28	28%
Positive margins	18	18%
Postoperative complications	21	21%
Operative mortality (30d)	5	5%

Table 3. Stratification of variables with survival outcomes.

Variable	Category	p-value
Age	>60 vs ≤60	0.05
PNI	High vs Low	>0.05
D-dimer	High vs Low	>0.05
PDS	0 vs one vs 2	0.415
Stage	I–IV	>0.05

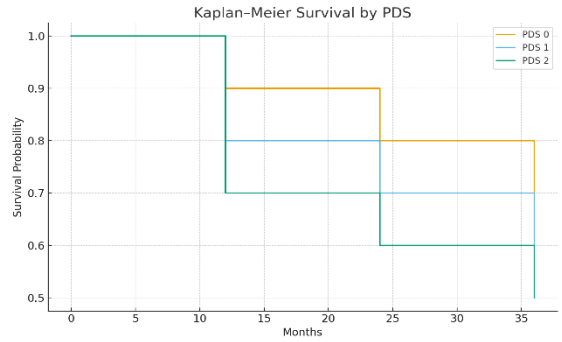

Figure 1. Kaplan–Meier survival curves stratified by PDS categories

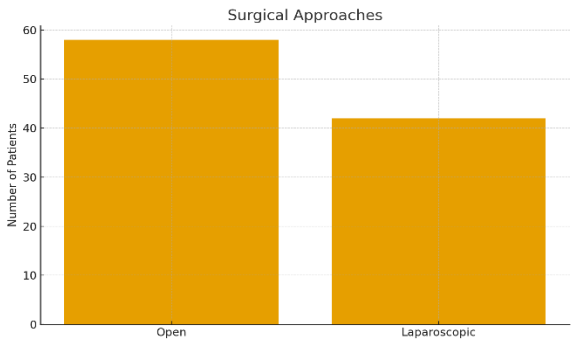

Figure 2. Surgical approaches performed (open vs laparoscopic).

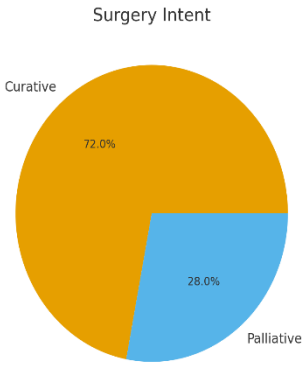

Figure 3. Surgery intent (curative vs palliative).

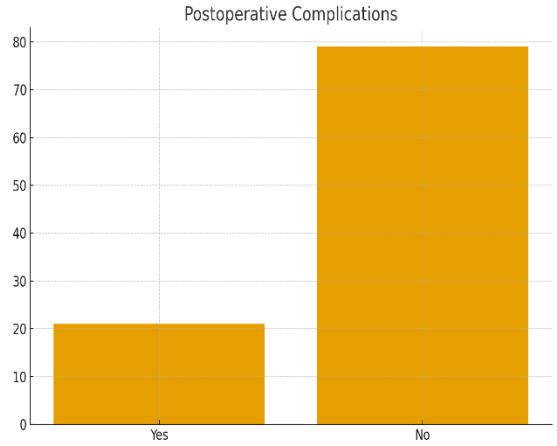

Figure 4. Distribution of postoperative complications (yes vs no).

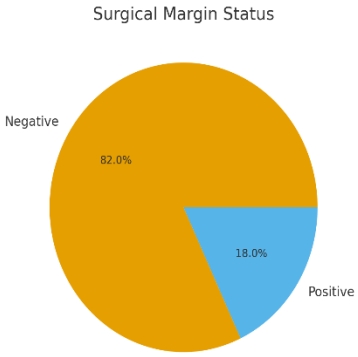

Figure 5. Surgical margin status (negative vs positive).

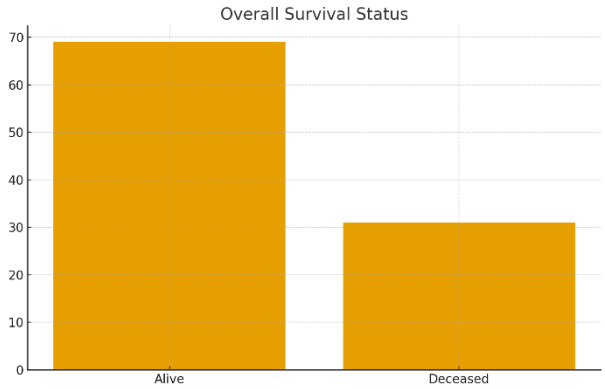

Figure 6. Overall survival (alive vs deceased).

Discussion

This study assessed the prognostic significance of a composite Prognostic D-dimer Score (PDS)—derived from the Prognostic Nutritional Index (PNI) and D-dimer levels—on overall survival among colorectal cancer (CRC) patients. Our findings indicate that PDS was not independently associated with overall survival, in contrast to several international studies suggesting that integrating nutritional and coagulative parameters enhances prognostic accuracy in gastrointestinal malignancies (4, 8, 9, 13). The absence of statistical significance may be attributed to several factors. Firstly, the relatively small cohort size (n=100) likely limited statistical power. Previous multicentre analyses, such as those by Kubo et al. and Kim et al., demonstrated that composite inflammatory-nutritional scores (including PNI, NLR, and PLR) correlate strongly with stage and outcome in CRC when sample sizes exceed several hundred patients (8,9). Secondly, heterogeneity in tumour stage and treatment modality could have diluted potential associations. Our cohort had a broad distribution across all stages (I–IV), and survival outcomes may have been confounded by variability in treatment access, delays in adjuvant therapy, and socioeconomic disparities common in low-resource settings (7,13). Advanced age (>60 years) showed borderline association with poorer survival, aligning with evidence that physiological reserve, comorbidity burden, and diminished tolerance to adjuvant chemotherapy contribute to reduced long-term outcomes in older CRC patients (7,10). Studies have shown that frailty and malnutrition amplify postoperative complications and mortality, emphasising the importance of early nutritional assessment and optimisation (10, 11). Although PNI and D-dimer individually showed no significant prognostic value, both remain biologically plausible markers. The PNI reflects immunonutritional status through serum albumin and lymphocyte count—parameters linked to host immunity, wound healing, and modulation of the tumour microenvironment (2, 3, 10). D-dimer, conversely, indicates tumour-induced hypercoagulability and metastatic potential (4, 12). Their combination as PDS theoretically integrates nutritional and thrombo-inflammatory dimensions of cancer biology. However, our findings suggest that in this regional population, systemic inflammation and nutritional depletion may not have a linear relationship with survival, potentially due to differences in tumour biology, genetic predispositions, and delayed presentation (13). Our results diverge from those in East Asian and European studies, in which elevated D-dimer and low PNI predict poor outcomes (4, 5, 8, 12). Studies by Li et al (4). And Mori et al. (5) found significant associations between higher D-dimer levels and reduced survival in colorectal and urothelial carcinomas, proposing these

biomarkers as cost-effective prognostic adjuncts. Conversely, several Western studies have noted that, although PNI correlates with postoperative complications, its predictive value for survival diminishes after multivariate adjustment (9, 10). The lack of association in this study reinforces the need for population-specific validation before clinical implementation (7, 13). Although PDS did not predict survival, its components are simple, inexpensive, and readily measurable. Incorporating these parameters into preoperative risk assessment protocols could still be beneficial for identifying nutritionally vulnerable or hypercoagulable patients requiring prehabilitation or thromboprophylaxis (10, 11). Moreover, multidimensional models integrating PNI, systemic inflammatory markers (CRP, NLR, PLR), and molecular signatures (e.g., KRAS/BRAF status, MSI) may offer superior prognostic precision (8, 9, 13). The study's limitations include a small sample size, a single-centre design, and limited follow-up. Lack of data on histologic subtype, perineural invasion, or adjuvant chemotherapy regimens restricts interpretation. Survival analysis was also constrained by a relatively short observation period. Future multicentre studies with larger cohorts, molecular data integration, and longitudinal follow-up are warranted (7, 9, 13). The absence of statistical significance may be attributed to several factors. Firstly, the relatively small cohort size (n=100) likely limited statistical power. Previous multicentre analyses, such as those by Kubo et al. and Kim et al., demonstrated that composite inflammatory-nutritional scores (including PNI, NLR, and PLR) correlate strongly with stage and outcome in CRC when sample sizes exceed several hundred patients. Secondly, heterogeneity in tumour stage and treatment modality could have diluted potential associations. Our cohort had a broad distribution across all stages (I–IV), and survival outcomes may have been confounded by treatment access variability, delays in adjuvant therapy, and socioeconomic disparities common in low-resource settings. Although PNI and D-dimer individually showed no significant prognostic value, both remain biologically plausible markers. The PNI reflects immunonutritional status through serum albumin and lymphocyte count, parameters linked to host immunity, wound healing, and modulation of the tumour microenvironment. D-dimer, conversely, indicates tumour-induced hypercoagulability and metastatic potential. Their combination as PDS theoretically integrates nutritional and thrombo-inflammatory dimensions of cancer biology. However, our findings suggest that in this regional population, systemic inflammation and nutritional depletion may not have a linear relationship with survival, potentially due to differences in tumour biology, genetic predispositions, and delayed presentation. Although PDS did not predict survival, its components are simple, inexpensive, and readily measurable. Incorporating these parameters into preoperative risk assessment protocols could still be beneficial for identifying nutritionally vulnerable or hypercoagulable patients requiring prehabilitation or thromboprophylaxis. Moreover, multidimensional models integrating PNI, systemic inflammatory markers (CRP, NLR, PLR), and molecular signatures (e.g., KRAS/BRAF status, MSI) may offer superior prognostic precision.

Conclusion

In this prospective cohort of colorectal cancer patients, the composite Prognostic D-dimer Score (PDS)—incorporating nutritional (PNI) and coagulation (D-dimer) parameters—was not an independent predictor of overall survival. While older age showed a borderline association with reduced survival, traditional clinicopathological factors such as tumour stage and surgical approach did not reach statistical significance. These findings suggest that PDS, although conceptually valuable, may have limited standalone prognostic value within the regional population studied.

Nevertheless, both nutritional and haemostatic biomarkers remain clinically relevant as they reflect systemic host-tumour interactions that influence recovery, tolerance to treatment, and long-term outcomes. The simplicity and accessibility of these markers make them practical adjuncts for preoperative assessment and risk stratification, particularly in resource-limited settings.

Future large-scale, multicentre studies with longer follow-up and integration of molecular and inflammatory indices are warranted to validate these findings and develop robust, multi-parametric prognostic models tailored to local patient populations. Such integrative tools could enhance personalised management, optimise treatment selection, and ultimately improve survival outcomes in colorectal cancer.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-24)

Consent for publication

Approved

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Conflict of interest

The authors declared no conflict of interest.

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Study Design, manuscript review, and critical input.
SA (PG)
Manuscript drafting, Study Design,
SZQ (PG)
Review of Literature, Data entry, Data analysis, and drafting an article.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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