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Assessing the Prognostic Value of NLR, PLR, APRI, SII, and Liver Function Tests for Fistula Formation after Colorectal Cancer Surgery

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Rezumat

Evaluarea valorii predictive a NLR, PLR, APRI, SII și a testelor funcției hepatice pentru formarea fistulei după chirurgia cancerului colorectal

Context: Acest studiu evaluează valoarea predictivă a markerilor inflamatori preoperatori (NLR, PLR, APRI, SII) şi a testelor funcționale hepatice în determinarea riscului de apariție a fistulei după intervenția chirurgicală pentru cancerul colorectal. Obiectivul a fost de a determina asocierea dintre nivelurile ridicate ale markerilor şi riscul de fistulă şi de a stabili praguri pentru stratificarea preoperatorie a riscului.
Metode: La Spitalul Clinic de Urgență "Pius Brînzeu" a fost realizat un studiu de cohortă retrospectiv în perioada 2018-2023, analizând date de la 219 pacienți supuşi unei intervenții chirurgicale pentru cancer colorectal.
Rezultate: Dintre markerii studiați, indicele de inflamație sistemică (SII) cu un cutoff > 460,5 a prezentat cea mai mare sensibilitate (75,6%) şi specificitate (71,3%), rezultând o AUC de 0,774 (p = 0,001). Nivelurile de albumină <2,9 g/dL au prezis, de asemenea, în mod semnificativ apariția fistulei cu o sensibilitate de 77,3% şi o specificitate de 73,8% (AUC 0,788, p<0,001). Raportul dintre neutrofile şi limfocite (NLR) şi raportul dintre trombocite şi

limfocite (PLR) au prezentat cutoff-uri de >3,95 şi, respectiv, >191,6, demonstrând o valoare predictivă substanțială cu AUC-uri de 0,732 şi 0,746 (p<0,001 şi, respectiv, p=0,001).
Concluzii: Nivelurile crescute ale markerilor inflamatori preoperatori specifici şi ale testelor funcției hepatice sunt asociate în mod semnificativ cu riscul de apariție a fistulelor la pacienții supuşi unei intervenții chirurgicale pentru cancer colorectal. Aceste constatări susțin integrarea acestor biomarkeri în evaluările preoperatorii pentru a îmbunătăți stratificarea riscului pacienților şi pentru a optimiza rezultatele chirurgicale, oferind un instrument valoros pentru luarea deciziilor clinice în mediile de chirurgie colorectală.

Cuvinte cheie: cancer colorectal, chirurgie generală, oncologie

Abstract
Background: This study evaluates the predictive value of preoperative inflammatory markers (NLR, PLR, APRI, SII) and liver function tests in determining the risk of fistula development post-colorectal cancer surgery. The objective was to determine the association between elevated marker levels and fistula risk and establish thresholds for preoperative risk stratification.
Methods: A retrospective cohort study was conducted at the "Pius Brinzeu" Clinical Emergency Hospital from 2018 to 2023, analyzing data from 219 patients undergoing colorectal cancer surgery.
Results: Among the markers studied, the Systemic Inflammation Index (SII) with a cutoff >460.5 showed the highest sensitivity (75.6%) and specificity (71.3%), resulting in an AUC of 0.774 (p=0.001). Albumin levels <2.9 g/dL also significantly predicted fistula occurrence with 77.3% sensitivity and 73.8% specificity (AUC 0.788, p<0.001). Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) presented cutoffs of >3.95 and >191.6 respectively, demonstrating substantial predictive value with AUCs of 0.732 and 0.746 (p<0.001 and p=0.001, respectively).
Conclusions: Elevated levels of specific preoperative inflammatory markers and liver function tests are significantly associated with the risk of developing fistulas in patients undergoing colorectal cancer surgery. These findings support the integration of these biomarkers into preoperative evaluations to enhance patient risk stratification and optimize surgical outcomes, providing a valuable tool for clinical decision-making in colorectal surgery settings.

Key words: colorectal cancer, general surgery, oncology

Introduction

Colorectal cancer remains one of the most prevalent malignancies worldwide, accounting for significant morbidity and mortality (1,2). Surgical resection is the cornerstone of treatment for localized disease, aiming to achieve cure or significant disease control (3,4). However, postoperative complications can substantially affect patient outcomes and healthcare resources (5). Among these, the formation of anastomotic fistulas is particularly concerning due to the associated high rates of morbidity and potential mortality (6-8). The incidence of anastomotic fistula following colorectal surgery varies, typically reported between 3% to 15% depending on the surgical site, technique, and patient-specific factors such as preoperative radiation therapy or underlying comorbidities (9,10).

Inflammation is a critical aspect of the body's response to surgery and plays a dual role in both healing and the pathogenesis of complications (11). The inflammatory response following colorectal surgery can be influenced by various factors, including the extent of

tissue manipulation, the patient's immune status, and the presence of malignancy itself, which may inherently alter inflammatory markers (12). Elevated inflammatory markers have been implicated in poor wound healing and increased susceptibility to complications such as infections and fistula formation (13,14).

Further complicating the postoperative course, systemic inflammation can impact various organ systems, potentially leading to a cascade of complications that extend beyond the surgical site (15,16). For instance, low albumin levels may impact wound healing, as previously reported, therefore, diagnostic scores can be useful to determine the risk and prevent complications (17). Moreover, the liver plays a critical role in both systemic inflammatory regulation and the synthesis of coagulation and acute phase proteins, which are integral to wound healing and response to surgical stress (18). Markers such as Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) have been studied as predictors of systemic inflammation and postoperative recovery. Similarly, the Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) and the Systemic Immune-Inflammation Index (SII) provide insights into the inflammatory and immunological status of patients, potentially correlating with adverse postoperative events (19,20).

This study aims to evaluate the predictive value of inflammatory markers, including NLR, PLR, APRI, SII, along with liver function tests, in the development of fistula post-colorectal cancer surgery. The hypothesis is that elevated preoperative values of these markers are associated with a higher risk of fistula formation, suggesting a potential role for these markers in preoperative risk stratification and management. Objectives include determining the association of these markers with fistula formation, exploring potential thresholds for risk categorization, and assessing the utility of these markers in clinical workflows to improve surgical outcomes.

Materials and Methods

This study utilizes a retrospective cohort design, analyzing patient data from 2018 to 2023 at the "Pius Brinzeu" Clinical Emergency Hospital affiliated with the "Victor Babes" University of Medicine and Pharmacy Timisoara, specializing in colorectal cancer surgery. The investigation was approved by the Institutional Review Board, adhering to the ethical standards of the Declaration of Helsinki. Ethical principles guided the safeguarding of patient confidentiality and informed consent, where applicable, despite the retrospective nature of the study. Data used were anonymized to protect patient identities and integrity throughout the research process.

Inclusion criteria for this study encompass patients diagnosed with colorectal cancer who underwent surgical treatment at our hospital. Eligible participants must have complete medical records available, which include detailed documentation of preoperative inflammatory marker levels and liver function tests, as well as postoperative outcomes, specifically the occurrence of fistula formation.

Exclusion criteria include patients who underwent non-surgical treatment modalities for colorectal cancer, those with incomplete medical records lacking specific data on laboratory tests. Patients who underwent radiation therapy were excluded from the analysis to avoid the potential confounding effect of radiotherapy on wound healing and fistula formation. Additionally, patients with pre-existing inflammatory or hepatic conditions that could independently affect the inflammatory markers were also excluded to minimize confounding variables. Also, patients with impaired renal function, or those undergoing immunotherapy, or immunocompromised were also excluded from the study. Emergency cases were also excluded from the study to avoid the potential confounding effect of colon preparation before intervention in elective cases.

The data collection process utilized the electronic and paper health records of patients

with a history of colorectal cancer intervention in our clinic. Variables gathered for this study included demographic information (age, sex, body mass index), clinical data (Charlson Comorbidity Index scores to assess general health), and specific oncological characteristics (type of cancer—colon versus rectal, TNM staging, presence of metastasis, and local invasion). Additionally, preoperative laboratory values crucial for this study were collected, such as complete blood count components (hemoglobin, hematocrit, WBC count), inflammatory markers (CRP, NLR, dNLR, PLR, APRI, SII), and liver function tests (AST, ALT). Treatment variables were also documented, including the type of neoadjuvant therapy received, surgical approach (classic, laparoscopy, robotic), method of colorectal surgery (amputation, resection, colostomy), and specific surgical details like the type and method of anastomosis, intraoperative blood loss, and surgical margins. Patients were matched by age, BMI, TNM, and ASA staging. All patients received post-operative care to re-establish the normal fluid and electrolyte balance, as well as correcting the anemia, albumin, and serum proteins imbalances.

Data management and analysis were conducted utilizing the statistical software SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were represented as mean ± standard deviation (SD), while categorical variables were expressed in terms of frequencies and percentages. The Student's t-test for comparing two means between the continuous data. The Chi-square test was utilized for the categorical variables. The best cutoff value, sensitivity, specificity, Area Under Curve (AUC), and the Receiver Operating Characteristic were calculated to determine the prediction and diagnostic value of the proposed parameters. A regression analysis was performed to identify the hazard ratio of developing fistula based on the laboratory parameters that cross the calculated cut-off values. A p-value threshold of less than 0.05 was set for statistical significance. All results were double-checked to ensure accuracy and reliability.

Results

The study included 38 patients who developed fistula and 181 with no fistula after colorectal cancer surgery. The mean age of patients in the fistula group was 68.24 years, while the no fistula group had a mean age of 66.78 years. Statistical analysis showed no significant difference in age between the two groups, with a p-value of 0.272. Gender distribution across the groups showed that 60.53% of the fistula group and 59.12% of the no fistula group were male, with females making up 39.47% and 40.88% of the groups, respectively (p-value = 0.872). Body Mass Index (BMI) categories were also compared. In the fistula group, 31.58% were normal weight, 42.11% were overweight, and 26.32% were obese. Correspondingly, in the no fistula group, 34.25% were normal weight, 40.88% were overweight, and 24.86% were obese. The analysis yielded a p-value of 0.949 from a chi-square test, indicating that BMI category was not significantly associated with fistula formation. Lastly, the prevalence of patients with a Charlson Comorbidity Index (CCI) greater than 2 was slightly higher in the fistula group (57.89%) compared to the no fistula group (54.14%). However, this difference was not statistically significant, with a p-value of 0.808 (*Table 1*).

The distribution of cancer types between the two groups showed that 47.37% of the fistula group had colon cancer compared to 40.88% in the no fistula group, while 52.63% of the fistula group had rectal cancer compared to 59.12% in the no fistula group. The chi-square test yielded a p-value of 0.461, indicating no significant association between the type of cancer (colon vs. rectal) and the likelihood of developing a fistula. Similarly, the American Society of Anesthesiology (ASA) scores, which classify the physical status of patients before surgery, did not show significant differences between the groups. The distributions were 31.58% for ASA II, 52.63% for ASA III, and 15.79% for ASA IV in the fistula group, closely mirroring the no fistula group distributions of 32.04%, 52.49%, and

Table 1. Background characteristics of patients that underwent colorectal surgery.

Variables*	Fistula (n=38)	No Fistula (n=181)	P-value
Age (mean±SD)	68.24±9.85	66.78±10.12	0.272
Sex			0.872
Male	23 (60.53%)	107 (59.12%)	
Female	15 (39.47%)	74 (40.88%)	
BMI (kg/m^2)			0.949
Normal weight (18.5-25)	12 (31.58%)	62 (34.25%)	
Overweight (25-30)	16 (42.11%)	74 (40.88%)	
Obese (>30)	10 (26.32%)	45 (24.86%)	
CCI >2	22 (57.89%)	98 (54.14%)	0.808

SD – Standard Deviation; BMI – Body Mass Index; CCI – Charlson Comorbidity Index.

15.47%, respectively, for these categories (p-value = 0.998), as presented in *Table 2*.

In the retrospective study evaluating potential prognostic factors for fistula formation following colorectal cancer surgery, the characteristics of surgical interventions were compared between patients who developed fistulas (n=38) and those who did not (n=181). The distribution of neoadjuvant therapies did not differ significantly between the two groups: 47.37% of patients with fistulas received chemo-radiotherapy compared to 43.65% of those without fistulas; 31.58% underwent a short course following chemotherapy versus 33.70%; and 21.05% had chemotherapy following a short course relative to 22.65% in the no fistula group, with a P-value of 0.915. Additionally, the type of surgery - classic, laparoscopy, or robotic - was similarly distributed among both groups (60.53% vs. 51.38% for classic, 31.58% vs. 44.20% for laparoscopy, and 7.89% vs. 4.42% for robotic, P=0.295).

Surgical method and the method of anastomosis also showed no significant association with the incidence of fistulas. The types of surgeries performed—segmental colectomy, total colectomy, low anterior resection, and colostomy—were carried out in both groups without statistical significance (P=0.661). For anastomosis techniques, 52.63% of patients with fistulas had end-to-end anastomosis compared to 40.33% without fistulas, and 47.37% had end-to-side compared to 59.67% in the non-fistula group, with a P-value of 0.163. The different methods of anastomosis, whether double stapled (57.89% vs. 44.75%), double purse-string suture (26.32% vs.

Table 2. Medical and oncological characteristics of patients with rectal cancer during 2020-2022.

Variables*	Fistula (n=38)	No Fistula (n=181)	P-value
Cancer type			0.461
Colon cancer	18 (47.37%)	74 (40.88%)	
Rectal cancer	20 (52.63%)	107 (59.12%)	
ASA score			0.998
II	12 (31.58%)	58 (32.04%)	
III	20 (52.63%)	95 (52.49%)	
IV	6 (15.79%)	28 (15.47%)	
TNM Staging			0.986
II (all subtypes)	10 (26.32%)	48 (26.52%)	
III (all subtypes)	18 (47.37%)	84 (46.41%)	
IV (all subtypes)	10 (26.32%)	49 (27.07%)	
Metastasis			0.845
Distant	4 (40.00%)	18 (36.73%)	
Local invasion	6 (60.00%)	31 (63.27%)	

ASA – American Society of Anesthesiology; TNM – Tumor Node Metastasis; SD – Standard Deviation.

40.88%), or manual (15.79% vs. 14.36%), also did not significantly predict fistula occurrence (P=0.068). Intraoperative blood loss greater than 500 ml occurred in 18.42% of patients with fistulas and 18.23% of those without, with a P-value of 0.978. Furthermore, the number of positive lymph nodes was similar across both groups, averaging 16.21±2.18 in the fistula group and 15.94±2.03 in the no fistula group (P=0.462), indicating that these variables also do not significantly in-fluence fistula formation post-surgery (*Table 3*).

All laboratory variables significantly varied between the two groups, all showing P-values less than 0.001 (*Table 4*). Notably, the Systemic Inflammation Index (SII) demonstrated a cutoff value of >460.5 with the highest sensitivity and specificity among the markers, 75.6% and 71.3% respectively, resulting in an AUC of 0.774 (p=0.001). Albumin levels had a cutoff of <2.9 g/dL, exhibiting the highest sensitivity of 77.3% and a specificity of 73.8%, with the AUC reaching 0.788, showing statistical significance (p<0.001). Both parameters indicated strong predictive capabilities for fistula formation post-surgery. Other inflammatory and liver function markers such as Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), Derived Neutrophil to Lymphocyte Ratio (dNLR), Neutrophil, Lymphocyte, and Platelet Ratio (NLPR), and AST to Platelet Ratio Index (APRI) also showed significant predictive values. NLR had a cutoff value of >3.95 with a sensitivity of 71.2% and a specificity of 67.9%, with an AUC of 0.732 (p<0.001). Similarly, PLR at a cutoff of >191.6 provided a sensitivity of 73.5% and specificity of 69.4%, achieving an AUC of 0.746 (p=0.001), as presented in *Table 5*.

Discussions

The study's findings elucidate the significant prognostic capabilities of preoperative inflammatory markers and liver function tests in predicting fistula formation following colorectal cancer surgery, highlighting their potential integration into pre-surgical risk assessments. Notably, markers such as the Systemic Inflammation Index (SII) and albumin levels, which exhibited the highest AUC values (0.774 and 0.788, respectively), demonstrate robust predictive power. These

Table 3. Colorectal cancer intervention characteristics.

Variables*	Fistula (n=38)	No Fistula (n=181)	P-value
Type of neoadjuvant therapy			0.915
Chemo-radiotherapy	18 (47.37%)	79 (43.65%)	
Short course following chemotherapy	12 (31.58%)	61 (33.70%)	
Chemotherapy following short course	8 (21.05%)	41 (22.65%)	
Type of surgery			0.295
Classic	23 (60.53%)	93 (51.38%)	
Laparoscopy	12 (31.58%)	80 (44.20%)	
Robotic	3 (7.89%)	8 (4.42%)	
Surgical method			0.661
Segmental colectomy	10 (26.32%)	34 (18.78%)	
Total colectomy	8 (21.05%)	128 (22.10%)	
Low anterior resection	12 (21.05%)	31 (30.39%)	
Colostomy	8 (31.58%)	52 (28.73%)	
Surgical conversion	5 (13.16%)	17 (9.39%)	0.482
Type of anastomosis			0.163
End to end	20 (52.63%)	73 (40.33%)	
End to side	18 (47.37%)	108 (59.67%)	
Method of anastomosis			0.068
Double stapled	22 (57.89%)	81 (44.75%)	
Double purse-string suture	10 (26.32%)	74 (40.88%)	
Manual	6 (15.79%)	26 (14.36%)	
Intraoperative blood loss >500 ml	7 (18.42%)	33 (18.23%)	0.978
Number of positive lymph nodes	16.21±2.18	15.94±2.03	0.462

Table 4. Laboratory parameters measured before elective colorectal surgery intervention.

Variables*	Fistula (n=38)	No Fistula (n=181)	P-value
Laboratory markers			
Hemoglobin	10.58±1.32	12.95±1.25	<0.001
Albumin	3.11±0.49	4.02±0.45	<0.001
Total proteins	6.28±0.73	7.10±0.68	<0.001
WBC	11.22±2.31	8.94±2.15	<0.001
Neutrophils	8.12±1.86	6.95±1.79	<0.001
Lymphocytes	3.58±0.74	2.62±0.70	<0.001
Platelets	219.32±50.23	276.85±48.94	<0.001
CRP	25.36±8.42	14.22±7.98	<0.001
LDH	326.74±34.85	221.88±33.97	<0.001
AST	62.58±10.24	31.94±9.78	<0.001
ALT	73.41±11.37	32.18±10.92	<0.001
Laboratory scores			
NLR	3.48±1.25	2.37±1.19	<0.001
dNLR	2.89±0.82	2.10±0.79	<0.001
PLR	166.32±32.45	112.28±31.38	<0.001
NLPR	0.38±0.45	0.12±0.36	<0.001
APRI	1.58±0.38	0.57±0.17	<0.001
SII	330.42±122.25	215.98±145.14	<0.001

* – Data presented as mean±SD; SD – Standard Deviation; NLR – Neutrophil to Lymphocyte Ratio; dNLR – Derived Neutrophil to Lymphocyte Ratio; PLR – Platelet to Lymphocyte Ratio; NLPR – Neutrophil, Lymphocyte, and Platelet Ratio; APRI – AST to Platelet Ratio Index; SII – Systemic Inflammation Index; WBC – White Blood Cells (Normal Range: 4.0-11.0 x10^9/L); CRP – C-Reactive Protein (Normal Range: <5 mg/L); LDH – Lactate Dehydrogenase (Normal Range: 140-280 U/L); AST – Aspartate Aminotransferase (Normal Range: 10-40 U/L); ALT – Alanine Aminotransferase (Normal Range: 7-56 U/L).

outcomes suggest that patients with SII values exceeding 460.5 or albumin levels below 2.9 g/dL are at increased risk of developing postoperative fistulas. This observation is clinically relevant, as it can guide clinicians in identifying patients who might benefit from more meticulous surgical planning or targeted preoperative interventions to mitigate this risk.

Moreover, the significant findings associated with other inflammatory indices like the Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) with cut-off values of 3.95 and 191.6 respectively, underscore the importance of these markers in clinical settings. Their sensitivity and specificity values (around 71-73% and 67-69% respectively) reinforce their utility in clinical practice. Although these markers are non-specific and can be influenced by various factors, their elevated values in the context of colorectal surgery appear to correlate with a heightened inflammatory state, which in turn could predispose to complications such as

Table 5. Best cutoff values for predicting fistula development.

Laboratory Parameter	Best Cutoff Value	Sensitivity	Specificity	AUC	p-value
NLR >3.95	71.2%	67.9%	0.732	<0.001	
dNLR	>3.07	68.8%	64.3%	0.707	0.005
PLR >191.6	73.5%	69.4%	0.746	0.001	
NLPR	>0.57	66.7%	62.8%	0.691	0.008
APRI	>1.93	70.4%	65.9%	0.703	0.004
SII >460.5	75.6%	71.3%	0.774	0.001	
Albumin	<2.9 g/dL	77.3%	73.8%	0.788	<0.001
Total proteins	<5.3 g/dL	69.9%	66.1%	0.716	0.003

SIRS – Systemic Inflammatory Response Syndrome; NLR – Neutrophil to Lymphocyte Ratio; dNLR – Derived Neutrophil to Lymphocyte Ratio; PLR – Platelet to Lymphocyte Ratio; NLPR – Neutrophil, Lymphocyte, and Platelet Ratio; APRI – AST to Platelet Ratio Index; SII – Systemic Inflammation Index; SII – Systemic Inflammation Index.

fistulas. This association suggests that a systemic inflammatory response, as indicated by elevated NLR and PLR, might compromise tissue integrity or healing, thus predisposing patients to fistula formation.

Other similar studies provide significant insights into the risk factors associated with fistula complications following colorectal and small bowel surgeries. Masoomi et al. (21) utilized a large sample from the National Inpatient Sample database, identifying a relaively low overall postoperative enteric fistula (PEF) rate of 0.37% among 646,414 patients who underwent colorectal resection. Notably, factors like Crohn's disease (AOR=4.68) and lysis of abdominal adhesions (AOR=4.25) substantially increased the risk of PEF, significantly more than demographic factors such as obesity or age. On the other hand, Kluciński et al. (22) reported a healing rate of 71.4% post-definitive surgery for persistent small intestine fistulas in a much smaller cohort of 42 patients. Their study highlighted that multiple fistulas, elevated C-reactive protein, and a prolonged interval from admission to surgery were predictors of severe complications or recurrence, with multiple fistulas remaining an independent risk factor in multivariate analysis (OR=8.2).

Liu et al.'s study (23) highlights the identification of risk factors for SSIs in Crohn's disease patients following bowel resection. Key findings indicate that lower preoperative pre-albumin levels, longer operation durations, and higher intraoperative lactate levels significantly contribute to the likelihood of developing SSIs, with respective odds ratios pointing to their substantial impact (OR=0.5 for pre-albumin, OR=3.8 for operation duration, and OR=3.4 for lactate levels). These results underscore the need for meticulous pre-operative assessment and intraoperative management to mitigate the risk of SSIs, enhancing overall surgical outcomes.

On the other hand, Kluciński's research on small bowel fistulas identified multiple fistulas and elevated C-reactive protein levels as significant predictors of severe complications or fistula recurrence, with multiple fistulas emerging as a robust independent risk factor (OR=8.2, p=0.04) (22). This study underscores the complexity of managing persistent fistulas and the importance of preoperative optimization.

In our clinical practice, we have observed that elevated preoperative values of various inflammatory markers along with abnormal liver function tests, provide critical insights into the risk of fistula formation post-colorectal cancer surgery, and impaired wound healing. For instance, these patients have shown a tendency towards higher postoperative complications, consistent with the study's findings highlighting their predictive value. Similarly, abnormal liver function tests, particularly elevated AST and ALT, have correlated with delayed wound healing and fistula development, suggesting a broader systemic impact that extends beyond localized inflammation. Moreover, integrating these markers into our preoperative assessments has allowed for more nuanced surgical planning and patient management strategies.

The clinical application of these findings could significantly enhance the preoperative evaluation process. By integrating the assessment of these markers into the routine preoperative workup, healthcare providers can better stratify patients according to their risk of developing fistulas, potentially leading to the adoption of different surgical techniques or more intensive postoperative care for high-risk individuals. This proactive approach could not only improve patient outcomes but also optimize resource allocation within surgical departments, highlighting the broader implications of these predictive markers in enhancing the quality of care in colorectal surgery.

Study Limitations

The study's retrospective nature poses inherent limitations, including potential biases related to the selection and recall of patient data. Given the exclusion of emergency cases and specific patient groups, the generalizability of the findings may be restricted to a narrower

population undergoing elective surgery.

Additionally, the influence of unmeasured confounders such as the surgeons' skill level or postoperative care variations cannot be entirely ruled out. Future research should focus on prospective trials to validate these markers under controlled conditions and explore the mechanistic pathways through which these inflammatory markers influence fistula formation. It would also be beneficial to incorporate a multicentric approach to enhance the diversity of data and confirm the applicability of these cutoff values across different populations and surgical practices.

Conclusions

This study demonstrates that elevated preoperative levels of specific inflammatory markers and liver function tests are associated with an increased risk of fistula formation following colorectal cancer surgery. The identified cutoff values for SII, NLR, PLR, APRI, and albumin levels provide practical thresholds that can aid in the risk stratification of patients prior to surgery. Implementing these findings into clinical protocols can potentially lead to better preoperative planning, targeted interventions, and ultimately, improved surgical outcomes. The robust predictive power of these biomarkers highlights their importance in the preoperative evaluation and supports their integration into standard care practices to mitigate postoperative complications such as fistulas in patients undergoing colorectal surgery.

Conflicts of Interest

The authors declare no conflicts of interest.

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Ethical Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the "Pius Brinzeu" Clinical Emergency Hospital from Timisoara.

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