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Research Article

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Neutrophil/Lymphocyte and Platelet/lymphocyte Ratios as Predictors of Patient Response to Bevacizumab in Iraqi Patients with Metastatic Colorectal Cancer

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Abstract

Background: Global clinical trials have shown that bevacizumab, along with chemotherapy, is beneficial for people with metastatic colorectal cancer (mCRC). Nevertheless, there isn't a useful biomarker to predict its effectiveness. ***Objectives***: The study's goal was to analyze and evaluate the practical pretreatment biomarker in people with metastatic colorectal cancer (mCRC) to predict bevacizumab efficacy. ***Methods***: This study, which is retrospective, includes 157 patients diagnosed with mCRC who received bevacizumab in association with chemotherapy from three centers in Iraq. The study looked at how clinical data and biomarkers relate to disease control (DC), overall survival (OS), and progression-free survival (PFS). It also looked at how well they could predict these outcomes. The cutoff values of neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) were examined with ROC analysis. ***Results***: For all patients, the median follow-up duration was 12 months. The PLR, NLR and median alkaline phosphatase (ALP) values were considerably lower in disease-control (DC) patients than in non-DC patients. The carcinoembryonic antigen (CEA) baseline level significantly correlated with shorter OS, while the ALP baseline level did not significantly correlate with shorter PFS. Among the clinical data, only multiple organ metastases showed a strong correlation with a shorter PFS and OS. ***Conclusions***: A low pretreatment N/L ratio and P/L ratio might be good predictors of bevacizumab efficacy for metastatic colorectal cancer patients, and it could be clinically useful for choosing responders.

***Keywords*:** Bevacizumab, Metastatic colorectal cancer, Neutrophil/lymphocyte ratio, Platelet/lymphocyte ratio.

نسب العدلات/الخلايا الليمفاوية والصفائح الدموية/الخلايا الليمفاوية كمنبئات للاستجابة للبيفاسيزوماب في المرضى العراقيين المصابين بسرطان القولون والمستقيم النقيلي

الخلاصة

الخلفية: أظهرت التجارب السريرية العالمية أن بيفاسيزوماب، إلى جانب العلاج الكيميائي، مفيد للأشخاص المصابين بسرطان القولون والمستقيم النقيلي ومع ذلك لا توجد علامة حيوية مفيدة للتنبؤ بفعاليته. **الأهداف**: تحليل وتقييم العلامة الحيوية العملية قبل المعالجة لدى الأشخاص المصابين بسرطان القولون والمستقيم النقيلي (mCRC) للتنبؤ بفعالية بيفاسيزوماب. **الطريقة**: تشمل هذه الدراسة بأثر رجعي 157 مريضا تم تشخيص إصابتهم ب mCRC والذين تلقوا بيفاسيزوماب بالاشتراك مع العلاج الكيميائي من ثلاثة مراكز في العراق. نظرت الدراسة في كيفية ارتباط البيانات السريرية والمؤشرات الحيوية بالسيطرة على الأمراض والبقاء على قيد الحياة بشكل عام، والبقاء على قيد الحياة بدون تقدم. كما نظرت في مدى قدرتهم على التنبؤ بهذه النتائج. تم فحص القيم الفاصلة لنسبة العدلات/الخلايا الليمفاوية (NLR) ونسبة الصفائح الدموية/الخلايا الليمفاوية (PLR)باستخدام تحليلROC. **النتائج**: بالنسبة لجميع المرضى، كان متوسط مدة المتابعة 12 شهرا. كانت قيم PLR و NLR ومتوسط الفوسفاتيز القلوي (ALP) أقل بكثير في مرضى السيطرة على الأمراض (DC) مقارنة بالمرضى غير المصابين ب DC. ارتبط مستوى خط الأساس للمستضد السرطاني المضغي (CEA) ارتباطا كبيرا بنظام التشغيل الأقصر، في حين أن مستوى خط الأساس ALP لم يرتبط بشكل كبير مع PFS الأقصر. من بين البيانات السريرية، أظهرت نقائل الأعضاء المتعددة فقط ارتباطا قويا مع PFS ونظام تشغيل أقصر. **الاستنتاجات**: قد تكون نسبة N/L المنخفضة قبل المعالجة ونسبة P/L منبئين جيدين بفعالية بيفاسيزوماب لمرضى سرطان القولون والمستقيم النقيلي، ويمكن أن تكون مفيدة سريريا لاختيار المستجيبين.

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INTRODUCTION

The World Health Organization (WHO) reports that colorectal cancer (CRC) will be the second leading cause of death globally in 2020 and the third most common type of cancer worldwide [1]. In Iraq, the CRC disease still primarily affects the elderly, and mortality rates are rising across all age groups. In 2010 and 2019, respectively, the proportion of deaths in Iraq due to the CRC increased from 1.25 to 1.77 per 100,000 individuals [2]. Tumors can originate from the walls of the colon or the rectal cavity, spread to the vascular system or lymph vessels, and eventually metastasize to other parts of the body. Over the past years, there has been a substantial advancement in the treatment of metastatic colorectal cancer (mCRC) due to the invention of new cytotoxic and molecular-targeted medications [3]. Bevacizumab is a carefully chosen drug that targets and blocks vascular endothelial growth factor A (VEGF-A), a protein involved in angiogenesis. It does this by very specifically attaching to the VEGF receptor. Clinical trials have demonstrated that bevacizumab, when used in conjunction with traditional chemotherapy treatment, can effectively extend survival in people with metastatic colorectal cancer (mCRC). [4]. In the global analysis, nine randomized studies totaling 3,914 individuals evaluated bevacizumab chemotherapy as first-line therapy for patients with mCRC. Individuals who received chemotherapy in addition to bevacizumab showed greater response rates and progression-free survival (PFS) [hazard ratio= 0.69; 95% confidence interval (CI): 0.63 to 0.75; $p<0.00001$], heterogeneity [response rate (RR)= 0.89; 95% confidence interval (CI): 0.82 to 0.96; a p-value= 0.003], and moderately variable overall survival rates (OS) [hazard ratio= 0.87; 95% confidence interval (CI): 0.80 to 0.95; a p-value= 0.002] [5]. These advanced treatments are more expensive and harmful when taken. Thus, we need reliable markers of therapy outcomes, especially in areas with limited resources, to assist patients in rationalizing their therapies [6]. There is currently no objective marker found, and nothing is known about predictive and prognostic biomarkers that are useful in bevacizumab treatment. Researchers have thoroughly examined alkaline phosphatase (ALP), hemoglobin (Hb), and carcinoembryonic antigen (CEA) levels, as well as inflammation-based scores like the leukocyte count (WBC), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR), in relation to the results of cancer treatment [7–12]. Because of their reasonable price, easy access, and simple interpretation, these markers are viewed as being helpful. The purpose of this study was to examine the predictive value in patients with mCRC receiving Bevacizumab.

METHODS

Study design and setting

In this retrospective study, we analyzed the records of 157 patients diagnosed with mCRC who received bevacizumab (7.5 mg/kg every 21 days) in association with combined standard chemotherapeutic regimens [5-fluorouracil, oxaliplatin and leucovorin (FOLFOX), 5-fluorouracil, leucovorin and irinotecan (FOLFIRI), and capecitabine and oxaliplatin (XELOX)]. The patient's records were collected from three centers in Iraq (Oncology Teaching Hospital, Baghdad, Iraq; AL-Anbar Center for Oncology; and AL-Fallujah Hospital). The study population followed from September 2022 to November 2023.

Inclusion criteria

All patients met the following enrollment criteria: 1) Patients treated with bevacizumab in addition to chemotherapy; 2) Eastern Cooperative Oncology Group (ECOG) performance scores (PS) of 0, 1, 2, or 3. There is comprehensive pretreatment complete blood cell count information, including ALP, Hb and CEA levels.

Exclusion criteria

The three exclusion criteria were as follows: 1) first-line therapy contained anti-epidermal growth factor receptor (anti-EGFR) monoclonal antibodies; 2) patients with incomplete data; and 3) participants who did not receive bevacizumab because they had warning signs for severe adverse events or who got chemotherapy plus bevacizumab for insufficient cycles.

Data collection

We recorded the pre-treatment clinicopathologic parameters of the patients. Every patient gave their informed written consent. We assessed the response using the RECIST criteria [13]. The ALP, Hb, CEA levels and WBC count were measured in the institution-owned laboratory. The pre-Bevacizumab treatment NLR and PLR were computed for every patient. PFS was calculated by month as the time from randomization to progression of the disease or any cause of death and OS was defined as the duration until death.

Ethical considerations

The study was carried out in accordance with the Declaration of Helsinki and good clinical practice recommendations, with approval from the ethics committees at each participating center: Oncology Teaching Hospital, Baghdad, Iraq; Al-Anbar Center for Oncology; and Al-Fallujah Hospital. The Mustansiriyah University Research Ethics Committee also approved the study protocol.

Statistical analysis

The Statistical Package for Social Sciences (IBM Corp., Armonk, N.Y., USA) software version 25 was used for all statistical analyses. Shapiro-Wilk's test was used to determine the sample normalcy. Visual examination of their histograms, box blots, and normal Q-Q plots revealed that none of the examined variables were normally distributed. The median and range were used

to express continuous variables. Comparisons among groups were performed using the Mann-Whitney test. Frequency and percentage were used to represent categorical variables. A chi-square test was used to compare the groups. PFS and OS were calculated by the Kaplan-Meier method, and the log-rank test was utilized to examine the variations between the two patient groups. P-values less than 0.05 were considered significant.

RESULTS

A total of 157 patients were recruited, with a median age of 60 years ranging from 18 to 84 years and a median body mass index (BMI) of 26.3 kg/m^2 and 84 (53.5%) of the patients were male. The majority, 120 (76.4%), had colon cancer, and 24 (15.3%) exhibited multiple sites of metastasis. Nine individuals (5.7%) had an ECOG PS of less than 1. The median duration from diagnosis to starting bevacizumab treatment was 3 months. The median follow-up period after bevacizumab treatment was 12 months, ranging between 4 and 28 months; no patient was lost during follow-up. Baseline measured biomarkers are illustrated in Table 1.

Table 1: Characteristics of the included patients (n=157)

Characteristic		Value
Age (year)	Median (range)	60(18-84)
Sex n(%)	Female Male	73(46.5) 84(53.5)
BMI (kg/m^2)	Median (range)	26.3(15.5-56.9)
ECOG n(%)	0 ≥1	148 (94.3) 9(5.7)
Primary site n(%)	Colon Rectum	120(76.4) 37(23.6)
Organs with met n(%)	1 ≥2	133(84.7) 24(15.3)
Time from diagnosis to Avastin treatment (month)	Median (range)	3(0-39)
Pretreatment CEA, ng/mL	Median (range)	5.9(0.08-729)
Pretreatment ALP, U/L	Median (range)	190(7.5-584.3)
Pretreatment WBC count × 10^9/L	Median (range)	7.3(1.8-18.8)
Pretreatment Hb, g/L	Median (range)	10.6(5.4-14.4)
Pretreatment NLR	Median (range)	4.9(0.29-28.5)
Pretreatment PLR	Median (range)	245(82.7-1215)

NLR: Neutrophil/Lymphocyte Ratio; PLR: Platelet/Lymphocyte Ratio; WBC: White Blood Cell; CEA: Carcinoembryonic antigen; ALP: Alkaline phosphatase; Hb: Hemoglobin; ECOG: Eastern Cooperative Oncology; BMI: Body mass index

Disease control (DC) was achieved in 89 (56.7%), 11 (7%) depicted a complete response and 53 (33.8%) had a partial response while stable disease was observed in 25 (15.9%) (Table 2). Progressive disease (PD) accounted for 68 of all cases, with a rate of 43.3%. The progression-free survival data were immature, with a mean OS of 18.8 (95% CI, 17.2-20.5) months and a 75 percentile of 7 months. The overall median OS was 20 (95% CI, 16.2-23.8) months.

Table 2: The response of patients to treatment, according to RECIST(n=157)

Response	Value n(%)
Disease control (responders)	89(56.7)
Complete response	11(7)
Partial response	53(33.8)
Stable disease	25(15.9)
Disease without control (non-responders)	
Progressed disease	68(43.3)

Values are expressed as numbers and percentages.

To investigate the parameters associated with the efficacy of bevacizumab in achieving DC, the patients were categorized into two groups: those with DC (n=89, 56.7%) and those with progressive disease (n=68, 43.3%); see Table 3. The baseline NLR in the DC group had a median value of 3.43 (range: 0.29–14.4), which was significantly lower than the PD group NLR of 7.25 (range: 0.7–28.5). Furthermore, the PLR in DC 197.62 (82.7–434) demonstrated a significantly lower level compared to PD 366.8 (182.5–1215), with a p-value of < 0.001. In addition, the median ALP value was significantly lower in DC 132 (7.5 to 522) compared to PD 207 (74 to 584.3), with a *p*-value of 0.001. There was also a significant association between multiple sites of metastasis and PD ($p<0.001$). To evaluate the utility of NLR and PLR as biomarkers for PFS and OS, receiver operating characteristic curve (ROC) analysis was utilized (Figure 1). In comparison to NLR, which had an area under the curve (AUC) of 0.853 (95% confidence interval: 0.791–0.914), PLR had a larger AUC of 0.919 (95% confidence interval: 0.919–0.983). Both were significant in their own right, with a *p*-value less than 0.001. The median NLR (4.90) had 82.4% sensitivity and 74.2% specificity. The NLR value of 4.96 had a higher specificity than the median 4.90 (75.3% *vs*. 74.2%), with the same sensitivity of 82.4%. The PLR value of 248 had higher specificity than the median 245 (86.5% *vs*. 85.4%) with the same sensitivity of 95.6%; therefore, 4.96 and 248 were selected as cutoff values for NLR and PLR, respectively, to evaluate patient survival after bevacizumab treatment. Only multiple organ metastases were significantly linked to a shorter PFS, with a mean of 9.5 months and a 95% confidence interval of 7.7–11.3 months ($p<0.001$) (Figure 2). They also had a shorter OS with a median of 15 months (95% CI: 12.2–17.8) compared to 20 (14.7–25.3) months for patients with a single site of metastasis $p=0.001$. Among biomarkers, there was a strong association between high NLR and PLR levels and shorter PFS (Figure 3 A and C). The PFS for high NLR compared to low was mean (95% CI): 13.0(10.93-15.1) *vs*. 24.7(23.0-26.4) months, whereas for high PLR compared to low, it was [9.3(8.1-10.5) *vs*. 27.2(26.3-28.1)] months, with a p-value of less than 0.001. Similarly, high NLR and PLR were related to shorter OS, with a median OS of 17 (95% CI: 15.4–18.6) months for high NLR and a 75 percentile for low NLR of 19 months (Figure 3 B and D).

Table 3: Comparison between patients with and without disease control (n=157)

Characteristic		Disease control n= 89	Progressive disease n= 68	*p*-value
Age (year)	Median (range)	57(19-84)	55(18-74)	0.561[a]
Sex n(%)	Female	43(58.9)	30(41.1)	0.631[a]
	Male	46(54.8)	38(45.2)	
BMI (kg/m^2)	Median (range)	27(15.5 -56.9)	25.9(16.8-40.1)	0.473[a]
ECOG n(%)	0	82(55.4)	66(44.6)	0.301[a]
	1	7(77.8)	2(22.2)	
Primary site n(%)	Colon	65(54.2)	55(45.8)	0.263[a]
	Rectum	24(64.9)	13(35.1)	
Organs with metastases n(%)	1	84(63.2)	49(36.8)	<0.001[a]
	≥2	5(20.8)	19(79.2)	
Time from diagnosis to bevacizumab treatment (month)	Median(range)	3(0-36)	3(0-39)	0.790[b]
Pretreatment CEA, (ng/mL)	Median(range)	5.4 (0.08-390)	6.5(0.84 -729)	0.124[b]
Pretreatment ALP (U/L)	Median(range)	132 (7.5-522)	207(74-584.3)	0.001[b]
Pretreatment WBC (count × 10^9/L)	Median(range)	7.1(1.8-15)	7.35(4-18.8)	0.302[b]
Pretreatment Hb (g/L)	Median(range)	10.5(5.4-13.6)	10.6(6.6-14.4)	0.855[b]
Pretreatment NLR	Median(range)	3.43(0.29-14.4)	7.25 (0.7-28.5)	<0.001[b]
Pretreatment PLR	Median(range)	197.6(82.7- 434)	366.8(182.5-1215)	<0.001[b]

[a] Chi-square test; [b] Mann-Whitney test. NLR: Neutrophil/Lymphocyte Ratio; PLR: Platelet/Lymphocyte Ratio; WBC: White Blood Cell; CEA: Carcinoembryonic antigen; ALP: Alkaline phosphatase; Hb: Hemoglobin; ECOG: Eastern Cooperative Oncology Group.

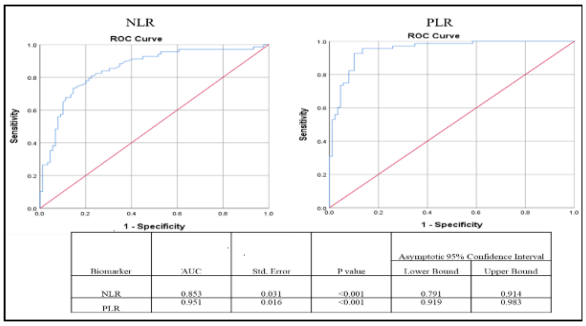

Figure 1: ROC curve for NLR and PLR with the corresponding area under the curve (AUC).

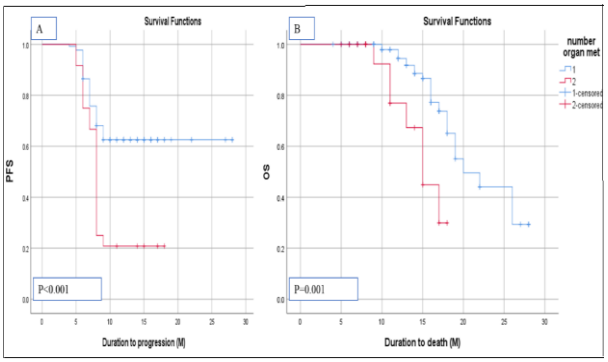

Figure 2: Kaplan Meier curve showing for A) progression-free survival (PFS); B) overall survival (OS) for number of organ metastasis.

Similarly, the median survival for high PLR was 16 months (95% CI: 14.3–17.7), but the data was not yet mature enough to estimate the median survival for low PLR. The median OS for a CEA level of ≥ 5.9 ng/mL was 18 months (95% CI: 14.6-21.4), which was much shorter than the low level of <5.9 ng/mL at 22 months (95% CI: 17.2-26.8) (Figure 4). The median PFS for an ALP level of ≥ 190 U/L was 17.1 months (14.8–19.4). None of the other variables showed a statistically significant difference (Figure 5). Table 4 provides further details.

DISCUSSION

This retrospective study revealed a significant correlation between the pretreatment PLR and NLR and both DC, PFS, and OS in individuals with mCRC who received bevacizumab plus chemotherapy. More and more data points to a link between a poor tumor prognosis and elevated systemic inflammatory markers like PLR and NLR in colorectal cancer [14,15]. However, little is known about how these markers affect bevacizumab's effectiveness. This study investigated the relationship between bevacizumab efficacy in mCRC and levels of NLR and PLR. According to this research, PLR and NLR may serve as predictive or prognostic biomarkers for bevacizumab responsiveness. To the best of our knowledge, this is the first study to look at PLR and NLR's potential as clinical biomarkers in Iraqi patients receiving bevacizumab treatment, with a median follow-up of more than a year. Systemic inflammatory responses are important during every stage of the growth of a tumor and promote the spread of cancer and induce angiogenesis, immunosuppression, the prevention of DNA damage and apoptosis [16,17]. According to numerous studies, platelets cause the transition from epithelial to mesenchymal form in circulating tumor cells and encourage extravasation to the locations of metastases [18,19]. Neutrophils release VEGF and proteases into the blood, which are examples of circulating growth factors that help cells stick to and spread to distant organs [20, 21]. In adaptive immune responses, lymphocytes are very important for protecting against tumors. They kill cancer cells and stop them from growing and migrating, which determines the host's immune response to cancer [22]. Changes brought about by inflammation promote the growth of cancer by altering the cancer microenvironment. Inflammation develops through the release of cytokines and chemokines [23]. Previous

studies have demonstrated the use of inflammatory indices (NLR and PLR) as predictive and prognostic markers in various human cancer types, particularly in mCRC or completely removed colorectal cancer. [24-27] Furthermore, a poor response to bevacizumab with chemotherapy was associated with a higher baseline NLR in mCRC patients [28]. The baseline NLR in the DC group was significantly lower than the PD group's NLR.

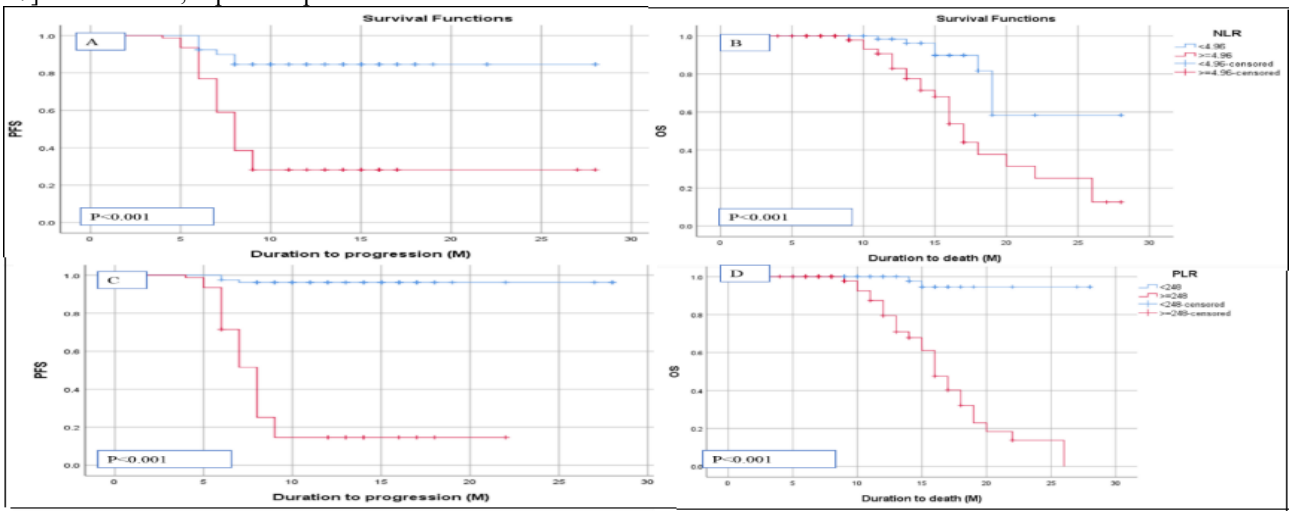

Figure 3: Kaplan Meier curve showing progression-free survival (PFS), for A) NLR; C) PLR and overall survival (OS) for B) NLR and D) PLR.

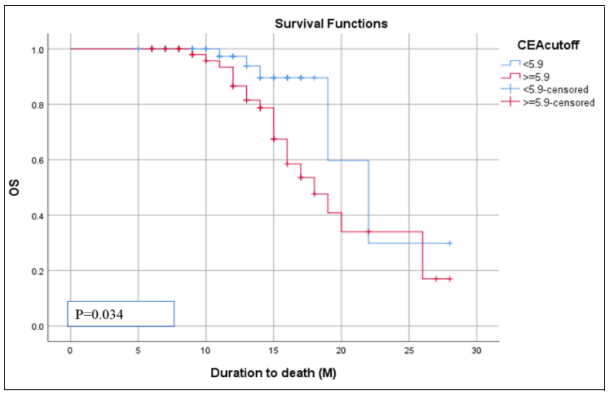

Figure 4: Kaplan Meier curve showing overall survival (OS) for CEA level.

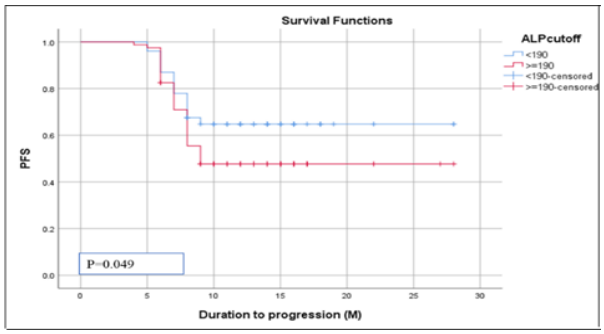

Figure 5: Kaplan Meier curve showing progression free survival (PFS) for ALP level.

Furthermore, the PLR in DC demonstrated a significantly lower level compared to PD, with a p-value of < 0.001. This phenomenon suggests that it's critical for patients' immune states and inflammation levels to be in balance. In addition, ALP in this study seemed to be a potent prognostic factor. Patients with high ALP at baseline had a poor prognosis; the median ALP value was significantly lower in DC compared to PD, with a p-value of 0.001. and these results are compatible with the previous studies [29,30]. ALP is required for several physiological functions, including bone production and liver function [31, 32]. On the other hand, an overproduction of ALP may result from tumors or aberrant growths in certain body parts, which may then flow into the blood [33]. The frequency of organ metastases is one of the many factors that have been identified in recent years as influencing survival in mCRC. Studies on this topic have produced conflicting results, with some demonstrating evidence of an association [34] and others not [35]. In this study, multiple organ metastases showed a significant association with a shorter PFS. They also had a shorter OS compared to a single site of metastasis (p=0.001), suggesting that more than one metastatic organ might counteract bevacizumab treatment. The results showed that the PLR and NLR had a big effect on how well the treatment worked and how long the patients lived, but not on the absolute numbers of platelets, neutrophils, or lymphocytes. There was a strong association between high NLR and PLR levels, as well as a shorter PFS. Based on the idea that CEA promotes angiogenesis [36], the results showed a strong link between a high level of CEA at the start of the study and a short OS. This suggests that higher CEA levels might work against bevacizumab treatment. In addition, this study showed a significant correlation between a high baseline level of ALP and a short PFS, suggesting that higher ALP might counteract the bevacizumab effect. It appeared that high ALP was a strong prognostic factor. Individuals who had

a high baseline level of ALP had a poor prognosis, which was in line with the high-risk category determined by Köhne *et al*. [37]. In this study, we found that the low NLR, low PLR, and low ALP patients had a significantly higher DC than the high NLR, high PLR, and high ALP patients treated with bevacizumab. Nevertheless, the precise link between the PLR, NLR, and CRC patient outcomes requires further research. Furthermore, we outline the pretreatment PLR, NLR, CEA, and ALP's predictive potential in patients with mCRC receiving chemotherapy in combination with bevacizumab. With the help of these easily available biomarkers, physicians might treat these patients with suitable medications regularly.

Table 4: Progression-free (PFS) and overall (OS) survival according to predictive and prognostic factors (n=157)

Characteristic		Cases (n)	Mean* PFS (95% CI) Months	*p*-value[a]	Median OS (95% CI) Months	*p*-value[a]
Age (year)	<60	94	18.0(15.9-20.2)	0.294	19(14.3-23-7)	0.306
	≥60	63	19.9(17.4-22.5)		20(11.96-28.0)	
Sex	Female	73	19.3(16.9-21.7)	0.560	22(14.5-29.5)	0.310
	Male	84	18.4(16.1-20.6)		18(16.6-19.4)	
Primary site	Colon	120	18.3(16.4-20.2)	0.317	19(14.3-23.7)	0.686
	Rectum	37	14.7(12.8-16.6)		20	
Number of organs with met	1	133	20.2(18.4-21.9)	<0.001	20(14.7-25.3)	0.001
	2	24	9.5(7.7-11.3)		15(12.2-17.8)	
Pretreatment CEA (ng/mL) (cutoff: 5.9)	<5.9	62	19.8(17.2-22.4)	0.181	22(17.2-26.8)	0.034
	≥ 5.9	62	17.1(14.4-19.7)		18(14.6-21.4)	
Pretreatment ALP (U/L) level (cutoff:190)	<190	77	20.5(18.3-22.8)	0.049	22(14.4-29.6)	0.260
	≥ 190	80	17.1(14.8-19.4)		19(17.5-20.5)	
Pretreatment WBC (count × 10^9/L) (cutoff: 7.3)	< 7.3	78	19.6(17.3-21.9)	0.415	26(18.3-33.7)	0.472
	≥7.3	79	18.1(15.7-20.4)		19(15.97-22.0)	
Pretreatment Hb (g/L) (cutoff: 10.6)	< 10.6	78	19.0(16.7-21.4)	0.738	26(10.1-41.9)	0.319
	≥10.6	79	18.1(15.9-20.3)		19(16.0-21.99)	
Pretreatment NLR (cutoff:4.96)	Low (< 4.96)	79	24.7(23.0-26.4)	<0.001	-	<0.001
	High (≥ 4.96)	78	13.0(10.93-15.1)		17(15.4-18.6)	
Pretreatment PLR (cutoff: 248)	Low (<248)	80	27.2(26.3-28.1)	<0.001	-	<0.001
	High(≥248)	77	9.3(8.1-10.5)		16(14.3-17.7)	

[a]*p*-value calculated by the log-rank test. NLR: Neutrophil/Lymphocyte Ratio; PLR: Platelet/Lymphocyte Ratio; WBC: White Blood Cell; CEA: Carcinoembryonic antigen; Hb: Hemoglobin; ALP: Alkaline phosphatase; ECOG: Eastern Cooperative Oncology Group; OS: Overall survival; CI: confidence interval PFS: progression free survival. *Progression-free survival data was immature and the median was not reached, the mean survival was reported.

Study limitations

The study only includes a small number of patients. Conditions, such as the use of steroids or non-steroidal medicines, can alter inflammation markers and lead to inflammation-related complications (we did not exclude this group). The progression-free survival data lacked maturity, and the median did not meet the protocol's target maturity of 50% for survival. The study was retrospective; there was an imbalance in the patients' characteristics. Therefore, we suggest that in the future, the number of participants will be high, excluding patients using steroids or non-steroidal medicines, increasing the duration of the patient's follow-up period and conducting more evaluations through properly planned research.

Conclusion

In this study, PLR, NLR, CEA, and ALP were all able to predict risk for PFS and OS with a sufficient level of accuracy; however, PLR and NLR were the most successful and superior to the rest. We can conclude that PLR and NLR have the potential to serve as simple, dependable, inexpensive, and repeatable CRC prognostic risk markers.

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Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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