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Original Article

Combined Diagnostic Efficacy of Red Blood Cell Distribution Width (RDW), Prealbumin (PA), Platelet-to-Lymphocyte Ratio (PLR), and Carcinoembryonic Antigen (CEA) as Biomarkers in the Diagnosis of Colorectal Cancer

Xiaolei Li[1, 2], Mohammad Reza Mohammadi[3,*]

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ABSTRACT

This study was designed to investigate the value of red blood cell distribution width (RDW), prealbumin (PA), platelet to lymphocyte ratio (PLR), and carcinoembryonic antigen (CEA) in the diagnosis of colorectal cancer. There was 500 colorectal cancer (CRC) patients, 250 polyps of colorectal patients, and 250 healthy volunteers performed to complete blood counts with automated differential counts. The differences in RDW, PA, PLR, and CEA among the three groups were statistically significant (P<0.05). RDW, PA, PLR, CEA, and RDW+PA+PLR+CEA all had a high accuracy rate for the diagnosis of colorectal cancer. RDW, PA, PLR, CEA, and RDW+PA+PLR+CEA were divided into high-expression groups and low-expression groups according to ROC cut-off values. Age was statistically different between the high and low groups in RDW, PA, and CEA. M staging was statistically different between high and low groups in CEA, and PLR. T staging was statistically different between high and low groups in PA, CEA, PLR, and RDW+PA+CEA+ PLR. N staging and blood vessel invasion were statistically different between the high and low groups in CEA. TNM staging was statistically different between high and low groups in PA, CEA, PLR, and RDW+PA+CEA+PLR. Perineural invasion was statistically different between the high and low groups in PA and CEA. The number of lymph node metastases was significantly and positively correlated with CEA. CEA and PLR were independent risk factors for the TNM staging. And they had good diagnostic efficacy for the TNM staging of colorectal cancer.

1. Introduction

Colorectal cancer (CRC) is the third most common cancer in the global [1]. Since most patients are diagnosed at an advanced stage, there is an urgent need for an early diagnosis of colorectal cancer. Early diagnosis can reduce the incidence and mortality of colorectal cancer [2]. Colonoscopy remains the most effective method for detecting colorectal cancer, but up to a quarter of colonoscopies have inadequate intestinal preparation, which contributes to the slower recovery of polyps and adenomas [3]. Fecal occult blood testing (FOBT) and fecal immunochemical testing (FIT) can be used to assess for occult blood in the feces and are commonly used in the diagnosis of colorectal cancer [4]. However, they are influenced by many factors in the daily diet [5].

[1]*Department of Oncology, the First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China*
[2]*Department of Bio-Therapeutic, the First Medical Centre, Chinese People's Liberation Army General Hospital, Beijing, China*
[3]*Department of Bacteriology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran*
***Corresponding Author**: Mohammad Reza Mohammadi (mreza_mohammadi@modares.ac.ir)*

Carcinoembryonic antigen (CEA) and glycoantigen (CA) 199 are used to detect the response of colorectal cancer to treatment, but low sensitivity and specificity make them less suitable as diagnostic markers [6]. Therefore, there is an urgent to search for a new diagnostic marker.

It has been shown that inflammation is closely associated with the development of cancer [7]. Inflammation promotes genetic aberrations in a variety of pathogens, and these alterations may be critical for early diagnosis and prevention of cancer in liquid biopsies [8]. It has been shown that tumors can lead to inflammation and inflammation is positively associated with RDW [9]. Tumor growth can lead to malnutrition, which can lead to changes in red blood cell production. Furthermore, CRC patients have a tendency to bleed, which reduces iron stores. All of these causes can lead to changes in red blood cell size and an increase in RDW.

Inflammation can lead to decreased levels of prealbumin in the blood, increasing the risk of colorectal cancer [10, 11]. It has been shown that PLR can identify the different stages of colorectal cancer at an early stage and imply poor prognosis [12]. These findings suggest that RDW, PA, CEA, and PLR may be of great value in the diagnosis of colorectal cancer. Previous studies have shown that the combination of different markers has a very high diagnostic accuracy for colorectal cancer.

In this study, we conducted a retrospective analysis to examine the diagnostic value of preoperative RDW, PA, PLR, CEA, and combined markers for colorectal cancer. To our knowledge, this is the first study to examine the value of RDW, PA, PLR, CEA, and combined markers in the diagnosis of colorectal cancer.

2. Materials and methods

Study sample this paper used retrospective analysis. The medical records of 500 patients with a confirmed diagnosis of colorectal cancer were analyzed. The diagnosis of colorectal cancer was obtained from colonoscopy reports and confirmed after surgical treatment. Five hundred patients with colorectal cancer who underwent surgical treatment at the Department of Gastroenterology, The First Affiliated Hospital of Anhui Medical University between July 2017 and October 2020 were selected as the study group. During hospitalization, enrolled patients underwent CT plain + enhancement of the thoracoabdominal pelvis and MRI of the pelvis. Patients were staged according to the American Joint Committee on Cancer (AJCC) 8th edition staging system.

The established exclusion criteria for the study were (a) a 5-year history of recurrent colorectal cancer or other malignancies; (b) previous chemotherapy or radiotherapy treatment; (c) other gastrointestinal, inflammatory, hematological, hepatobiliary, pulmonary, and cardiovascular diseases; and (d) anti-aggregation or anticoagulation therapy, lipid-lowering therapy, non-steroidal anti-inflammatory drugs, and recent blood transfusion therapy.As a comparison, we analyzed the medical records of 250 colorectal polyps and 250 healthy volunteers examined at the First Affiliated Hospital of Anhui Medical University during the same period. There were no statistically significant differences between the polyp of the colorectal group and the healthy volunteer's group compared with the colorectal cancer group in gender and age ($P>0.05$). This study had reviewed and approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University (Code of ethics: 230031).

Fasting venous blood was collected in the early morning. Serum concentrations of carcinoembryonic antigen (CEA), glycoantigen 199 (CA199), alpha-fetoprotein (AFP), and glycoantigen 125 (CA125) were measured using a chemiluminescent immunoassay analyzer and supporting reagents. Absolute neutrophil count (ANC), absolute lymphocyte count (ALC), absolute monocyte count (MONO), red blood cell distribution width (RDW), platelet count (PLT), platelet distribution width (PDW), mean platelet volume (MPV), albumin concentration (ALB), lactate dehydrogenase (LDH), platelet mean volume (MPV) and prealbumin concentration (PA) in venous blood were measured using a fully automated hematology analyzer. NLR was calculated by dividing the absolute

neutrophil count by the absolute lymphocyte count. PLR was calculated by dividing the absolute platelet count by the absolute lymphocyte count. MLR was calculated by dividing the monocyte count by the lymphocyte count.

Statistical analysis was performed using SPSS 25.0 software. Measurement data were expressed as mean ± standard deviation (SD) and compared by the Mann-Whitney U test. Count data were expressed as [n (%)] and compared using the chi-square test. Receiver operating characteristic (ROC) curve analysis was performed to calculate the area under the curve (AUC) to determine the diagnostic efficacy of each index. The sensitivity, specificity, and cut-off value of each index were determined according to the maximum Youden index. The Spearman method was used for correlation analysis. Multivariate logistic regression was used to analyze independent risk factors for CRC. Results were considered statistically significant when $p<0.05$.

3. Results

The clinic pathological characteristics of the colorectal cancer group, polyp of the colorectal group, and healthy volunteer group are summarized. Among the 500 colorectal cancer patients, there were 250 (50%) rectal cancer patients and 250 (50%) colon cancer patients with a mean age of (60.99±12.14) years, 331 (66.20%) males and 169 (33.80%) females. There were TNM stagings I in 34 (6.80%) patients, TNM stagings II in 93 (18.60%) patients, TNM stagings III in 75(15.00%) patients, and TNM stagings IV in 298(59.60%) patients. Pathology was suggestive of cancerous nodules in 51 (10.20%), nerve invasion in 254 (50.80%), and vascular cancerous thrombosis in 222 (44.40%) patients. There were 250 patients with polyp colorectal, the mean age was (59.12 ± 15.82) years, 162 (65.32%) were male, and 86 (34.68%) were female. There were 250 healthy volunteers; the mean age was (58.89±16.16) years, 148 (59.20%) males, and 102 (40.80%) females.

The diagnostic value of biomarkers for colorectal cancer; As shown in (Table 1), there are differences among the three groups were statistically significant in ANC, ALC, MONO, RDW, PDW, MPV, ALB, PA, CEA, NLR, PLR, and MLR($P<0.05$). There were no significant differences among the three groups in PLT, LDH, CA199, and AFP ($P>0.05$). Multivariate logistic regression of the above markers showed that the four markers (RDW, PA, CEA, and PLR) were independent risk factors (Table 2). It was greater the likelihood of developing colorectal cancer if the RDW, CEA, and PLR values were higher or the PA value was lower.

The results of ROC analysis in RDW, PA, CEA, PLR, and RDW+PA+CEA+PLR had been shown (Table 3 and Figure 1). Among the above indicators, RDW+PA+CEA+PLR were highest in AUC, sensitivity, and specificity. There was AUC of 0.957, sensitivity of 0.894, and specificity of 0.867.

If the cut-off value for RDW+PA+CEA+ PLR in the ROC is greater than the cut-off value obtained from the formula Logit(P), patients are more likely to be diagnosed with colorectal cancer.

The value of biomarkers to predict prognosis, metastasis, and staging of colorectal cancer: Based on the cut-off values obtained in Table 3, patients with colorectal cancer were divided into high and low groups in RDW, PA, CEA, PLR, and RDW+PA+CEA+PLR. The results (Table 4) showed that age was statistically different between the high and low groups in RDW, PA, and CEA. M staging was statistically different between the high and low groups in CEA and PLR. T staging was statistically different between the high and low groups in PA, CEA, PLR, and RDW+PA+CEA+PLR. N staging and vascular cancer embolism were statistically different between the high and low groups in CEA. TNM staging was statistically different between the high and low groups in PA, CEA, PLR, and RDW+PA+CEA+PLR. Perineural invasion was statistically different between the high and low groups in PA and CEA. The rest of the indicators were not statistically different in RDW, PA, CEA, PLR, and RDW+PA+CEA+PLR ($P>0.05$).

Table 1. Comparison of indicators between the three groups

	Healthy volunteers	Polyp of Colorectal	Colorecta Cancer	Z	P
ANC	3.41±1.25	3.37±1.37	3.86±2.28[ab]	13.026	0.001
ALC	1.96±0.64	1.85±0.58	1.60±0.56[ab]	70.220	0.000
MONO	0.34±0.11	0.35±0.13	0.38±0.16[ab]	19.606	0.000
RDW	42.44±2.95	43.35±3.69[a]	45.03±6.05[ab]	40.497	0.000
PLT	198.28±61.12	225.33±64.04[a]	237.57±92.46[b]	47.759	0.000
PDW	14.19±3.44	14.43±2.74	13.85±6.27[ab]	18.287	0.000
MPV	12.37±9.74	11.47±1.16	11.06±1.20[ab]	26.745	0.000
ALB	45.89±2.79	42.83±3.51[a]	40.81±4.31[ab]	262.258	0.000
LDH	194.38±133.79	179.86±36.05	192.18±77.32	2.389	0.303
PA	285.26±65.58	276.34±55.51	236.14±70.23[ab]	90.890	0.000
CA199	13.09±8.75	11.28±11.26[a]	36.14±113.47[b]	19.332	0.000
CEA	1.41±1.01	2.42±1.91[a]	15.95±72.06[ab]	274.537	0.000
AFP	2.74±1.82	3.31±1.81[a]	3.48±3.92[a]	23.284	0.000
NLR	1.87±0.85	1.95±0.91	2.80±2.50[ab]	83.281	0.000
PLR	114.63±41.24	122.74±42.38[a]	168.47±96.90[ab]	106.745	0.000
MLR	0.18±0.09	0.20±0.08[a]	0.27±0.15[ab]	120.464	0.000

Table 2. Multivariate logistic regression

	B	SE	Wald	P	OR	OR 95% CI	
						Upper limit	Lower limit
RDW	0.062	0.026	5.704	0.017	1.064	1.011	1.120
PA	-0.006	0.002	14.062	0.000	0.994	0.990	0.997
CEA	0.307	0.052	34.200	0.000	1.359	1.226	1.506
PLR	0.013	0.002	32.737	0.000	1.013	1.009	1.018
Constant	-3.290	1.317	6.245	0.012	0.037		

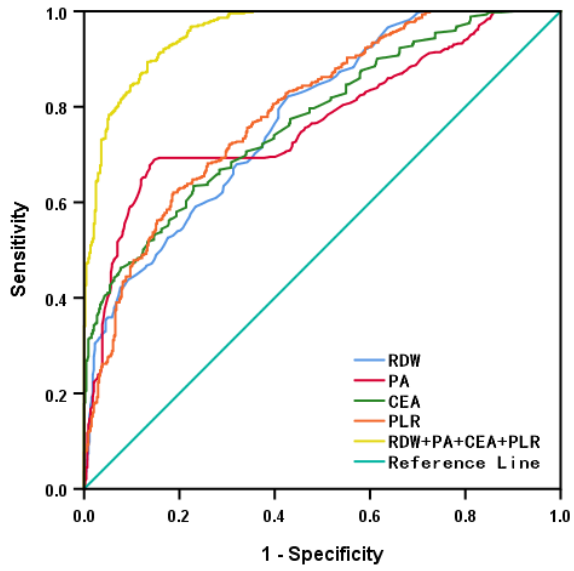

Fig. 1. ROC analysis of individual and combined indicators for the diagnosis of colorectal cancer

Table 3. ROC analysis of diagnostic markers for colorectal cancer

Indicator	AUC	SE	Sensitivity	Specificity	Jorden Index	cut-off values	95%CI
RDW	0.778	0.015	0.822	0.572	0.394	43.150	0.748~0.807
PA	0.772	0.016	0.688	0.855	0.542	228.500	0.741~0.804
CEA	0.774	0.015	0.634	0.770	0.405	2.510	0.744~0.804
PLR	0.793	0.015	0.621	0.813	0.434	147.494	0.764~0.822
RDW+PA+CEA+PLR	0.957	0.006	0.894	0.867	0.761	-0.011	0.945~0.968

(the formula: Logit(P)=RDW cut-off value*0.062+PA cut-off value*(-0.006) +CEA cut-off value*0.07+PLR cut-off value*0.013-3.290)

Table 4. Differences in indicators at high and low levels of RDW, PA, CEA, PLR and RDW+PA+CEA+PLR

		RDW		X^2	P	PA		X^2	P	CEA		X^2	P
		< 43.15	≥ 43.15			< 228.50	≥ 228.50			< 2.510	≥ 2.51		
age	< 60	180(83%)	36(16%)	5.06	*0.02*	97(44.9%)	119(55%)	6.82	*0.00*	127(58.8%)	89(41.2%)	5.85	0.01
	≥60	213(75%)	71(25%)			161(56.6%)	123(43%)			136(47.8%)	148(52.1%)		
Cancerous nodules	NO	350(77%)	99(22%)	1.10	*0.29*	231(51.4%)	218(48%)	0.04	*0.84*	242(53.9%)	207(46.1%)	2.97	0.08
	Yes	43(84.3%)	8(15.6%)			27(52.9%)	24(47.0%)			21(41.1%)	30(58.8%)		
M	M0	349(79%)	89(20%)	2.45	*0.11*	219(50.0%)	219(50%)	3.6	*0.05*	244(55.7%)	194(44.2%)	13.68	0.00
	M1	44(70.9%)	18(29%)			39(62.9%)	23(37.1%)			19(30.6%)	43(69.3%)		
T	T1	36(90.0%)	4(10.0%)	4.73	*0.19*	12(30.0%)	28(70%)	1 5.5	*0.00*	31(77.5%)	9(22.5%)	19.03	0.00
	T2	76(76.0%)	24(24%)			42(42.0%)	58(58.0%)			63(63.0%)	37(37.0%)		
	T3	62(73.8%)	22(26.1%)			51(60.7%)	33(39.2%)			38(45.2%)	46(54.76%)		
	T4	219(79%)	57(20%)			153(55.4%)	123(44%)			131(47.4%)	145(52.5%)		
N	N0	237(77%)	69(22%)	0.61	*0.43*	155(50.6%)	151(49%)	0.23	*0.59*	173(56.5%)	133(43.4%)	4.90	0.02
	N1+N2	156(80%)	38(19%)			103(53.0%)	91(46.9%)			90(46.3%)	104(53.6%)		
TNM	I	81(80.2%)	20(19%)	1.21	*0.74*	38(37.6%)	63(62.3%)	16.0	*0.00*	76(75.2%)	25(24.7%)	34.4	0.00
	II	128(76%)	39(23%)			90(53.89%)	77(46%)			87(52.10%)	80(47.90%)		
	III	137(80%)	33(19%)			87(51.18%)	83(48%)			81(47.65%)	89(52.35%)		
	IV	47(75.8%)	15(24%)			43(69.35%)	19(30%)			19(30.65%)	43(69.35%)		
Perineural invasion	NO	194(78%)	52(21%)	0.020	*0.888*	112(45.5%)	134(54%)	7.148	*0.008*	144(58.5%)	102(41%)	6.845	0.009
	Yes	199(78%)	55(21%)			146(57.4%)	108(42%)			119(46.8%)	135(53.1%)		
blood vessel invasion	NO	217(78%)	61(21%)	0.110	*0.741*	135(48.5%)	143(51%)	2.315	*0.128*	160(57.55%)	118(42.4%)	6.163	0.013
	Yes	176(79%)	46(20%)			123(55.4%)	99(44%)			103(46.4%)	119(53.6%)		

Continuation of **Table 4.**

		PLR		X^2	P	RDW+PA+CEA+PLR		X^2	P
		< 147.494	≥ 147.494			<- 0.011	≥ -0.011		
age	< 60	104(48.15%)	112(51.85%)	1.610	*0.205*	92(42.59%)	124(57.41%)	1.623	*0.203*
	≥60	153(53.87%)	131(46.13%)			105(36.97%)	179(63.03%)		
Cancerous nodules	NO	230(51.22%)	219(48.78%)	0.054	*0.816*	178(39.64%)	271(60.36%)	0.109	*0.741*
	Yes	27(52.94%)	24(47.06%)			19(37.25%)	32(62.75%)		
M	M0	234(53.42%)	204(46.58%)	5.796	*0.016*	179(40.87%)	259(59.13%)	3.186	*0.074*
	M1	23(37.10%)	39(62.90%)			18(29.03%)	44(70.97%)		
T	T1	23(57.50%)	17(42.50%)	10.82	*0.013*	24(60.00%)	16(40.00%)	15.111	*0.002*
	T2	64(64.00%)	36(36.00%)			47(47.00%)	53(53.00%)		
	T3	35(41.67%)	49(58.33%)			23(27.38%)	61(72.62%)		
	T4	135(48.91%)	141(51.09%)			103(37.32%)	173(62.68%)		
N	N0	152(49.67%)	154(50.33%)	0.941	*0.332*	116(37.91%)	190(62.09%)	0.735	*0.391*
	N1+2	105(54.12%)	89(45.88%)			81(41.75%)	113(58.25%)		
TNM	I	67(66.34%)	34(33.66%)	20.626	*0.000*	49(48.51%)	52(51.49%)	11.801	*0.008*
	II	73(43.71%)	94(56.29%)			54(32.34%)	113(67.66%)		
	III	95(55.88%)	75(44.12%)			76(44.71%)	94(55.29%)		
	IV	22(35.48%)	40(64.52%)			18(29.03%)	44(70.97%)		
Perineural invasion	NO	134(54.47%)	112(45.53%)	1.829	*0.176*	100(40.65%)	146(59.35%)	0.317	*0.573*
	Yes	123(48.43%)	131(51.57%)			97(38.19%)	157(61.81%)		
blood vessel invasion	NO	145(52.16%)	133(47.84%)	0.144	*0.704*	108(38.85%)	170(61.15%)	0.080	*0.778*
	Yes	112(50.45%)	110(49.55%)			89(40.09%)	133(59.91%)		

Based on these results, we further analyzed the relationship between CEA and the number of lymph node metastases. It was found that CEA was significantly and positively correlated with the number of lymph node metastases (r=0.146, *p<0.05*). In other words, it was more in the number of lymph node metastases, if the CEA value was higher in colorectal cancer.

Multivariate logistic regression showed that CEA had a significant effect on clinical

staging (*P=0.000<0.05*), with higher CEA values associated with higher clinical staging (Table 5). PLR had a significant effect on clinical staging (*P=0.046<0.05*), with higher PLR values associated with higher clinical staging. RDW was not associated with clinical staging (Table 4), while PA did not have a significant effect on clinical staging (*P > 0.05*).

Table 5. Multivariate logistic regression of TNM staging

		Estimate	Std. Error	Wald	P.	95% Confidence Interval	
						Lower Bound	Upper Bound
Threshold	I	-1.116	0.411	7.36	0.00	-1.923	-0.310
	II	0.495	0.407	1.48	0.224	-0.302	1.292
	III	2.690	0.439	37.62	0.000	1.831	3.550
Location	PA	-0.001	0.001	1.03	0.310	-0.004	0.001
	CEA	0.017	0.005	13.21	0.000	0.008	0.027
	PLR	0.002	0.001	3.97	0.046	0.000	0.004

4. Discussion

Inflammation is closely related to the occurrence and development of cancer [13]. The tumor microenvironment plays an important role in the formation of tumors, and the inflammatory cells participate in it, which can not only promote the proliferation of tumors but also promote the metastasis of tumors [14]. Carcinoembryonic antigen (CEA) is a commonly used prognostic marker in colorectal cancer (CRC) diagnosis. It can monitor response to treatment. The high level of CEA is closely associated with CRC progression [15]. However, there is a high level of CEA not only in colorectal cancer but also in other types of cancer and non-cancerous diseases [16]. CEA has limitations as a diagnostic marker for colorectal cancer. There is an urgent to find a new diagnostic marker for colorectal cancer. It has found that CEA combined with inflammatory cells is superior to either method alone in the diagnosis of colorectal cancer [17]. This was also confirmed in our study.

It has shown that the level of inflammation caused by tumors was significantly positively correlated with RDW [18, 19]. This may be related to malnutrition caused by tumor growth, which can lead to changes in red blood cell production. Colorectal cancer patients have a tendency to bleed, which reduces iron storage, leading to changes in red blood cell size and an increase in RDW. This is consistent with the result that the RDW value of colorectal cancer patients is significantly higher than that of non-colorectal cancer patients, as shown in (Table 2). It has shown that serum albumin and prealbumin can evaluate the nutritional status of the body and are important predictors of the recovery and survival of colorectal cancer patients [20]. It has found that the common inflammatory cytokine interleukin-6 may inhibit protein synthesis, leading to the development of hypoproteinemia in cancer patients [21]. The finding revealed that PA values in patients with colorectal cancer were significantly lower than in non-colorectal cancer, as shown in (Table 2). It has found that PLR could be used as a biomarker for the early diagnosis of colorectal cancer [22]. The result of the study found that PLR values were significantly higher in patients with colorectal cancer than in controls (Table 2). PLRs also were associated with the TNM staging of colorectal cancer. If PLR values were higher, TNM staging in patients with colorectal cancer was later.

Most previously published studies have studied either inflammatory markers or tumor markers independently, with only a few of them combining two different markers. To our knowledge, this is the first study to combine RDW, PA, PLR, and CEA. It has high sensitivity and specificity. The result of the study found that RDW, PA, CEA, and PLR had high diagnostic validity in patients with colorectal cancer. RDW+PA+CEA+PLR had the highest sensitivity and specificity, with a sensitivity of 0.894 and a specificity of 0.867. The result of the study found that CEA was significantly and positively correlated with the number of lymph node metastases in colorectal cancer. Higher CEA values suggest a higher number of lymph node metastases in

colorectal cancer. The number of lymph node metastases was more if the CEA value was higher. Meanwhile, multivariate logistic regression showed that CEA and PLR values were related to the TNM staging of the patients. There were higher the CEA and PLR values, the higher the TNM staging of the patients. Based on these results, we concluded a preliminary diagnosis of colorectal cancer.

5. Conclusion

RDW, PA, PLR, and CEA can be used for the diagnosis of colorectal cancer as well as for the prediction of the TNM staging of colorectal cancer. When the critical value of RDW+PA+CEA+PLR in serum is greater than -0.011, colorectal cancer can be diagnosed. RDW+PA+CEA+PLR can improve the sensitivity and specificity of colorectal cancer diagnosis in routine physical examination. And it was easy to perform and cost-effective. However, as the number of patients with colorectal cancer in this cohort is limited and all samples are from the same hospital, further confirmation is needed using more samples from more hospitals.

Conflict of Interest

All authors state that they are free of any conflicts of interest related to this paper.

Author's contributions

All authors confirm that they have read and approved this manuscript.

Consent for publications

All authors have read and approved the final manuscript for publication.

Availability of data and material

The authors have embedded all data in the manuscript.

Ethics approval and consent to participate

The authors did not use human or animals in the research.

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References

1. Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ (2017) Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. International journal of molecular sciences 18 (1): 197. doi:https://doi.org/10.3390/ijms18010197
2. Biller LH, Schrag D (2021) Diagnosis and treatment of metastatic colorectal cancer: a review. Jama 325 (7): 669-685. doi:https://doi.org/10.1001/jama.2021.0106
3. Kim SY, Kim H-S, Park HJ (2019) Adverse events related to colonoscopy: Global trends and future challenges. World journal of gastroenterology 25 (2): 190. doi:https://doi.org/10.3748%2Fwjg.v25.i2.190
4. Jain S, Maque J, Galoosian A, Osuna-Garcia A, May FP (2022) Optimal strategies for colorectal cancer screening. Current treatment options in oncology 23 (4): 474-493. doi:https://doi.org/10.1007/s11864-022-00962-4
5. Song L-L, Li Y-M (2016) Current noninvasive tests for colorectal cancer screening: An overview of colorectal cancer screening tests. World journal of gastrointestinal oncology 8 (11): 793. doi:https://doi.org/10.4251%2Fwjgo.v8.i11.793
6. Young GP, Pedersen SK, Mansfield S, Murray DH, Baker RT, Rabbitt P, Byrne S, Bambacas L, Hollington P, Symonds EL (2016) A cross-sectional study comparing a blood test for methylated *BCAT 1* and *IKZF 1* tumor-derived DNA with CEA for detection of recurrent colorectal cancer. Cancer medicine 5 (10): 2763-2772. doi:https://doi.org/10.1002/cam4.868
7. Singh N, Baby D, Rajguru JP, Patil PB, Thakkannavar SS, Pujari VB (2019) Inflammation and cancer. Annals of African medicine 18 (3): 121. doi:https://doi.org/10.4103%2Faam.aam_56_18
8. Murata M (2018) Inflammation and cancer. Environmental health and preventive medicine 23 (1): 1-8. doi:https://doi.org/10.1186/s12199-018-0740-1

9. Song Y, Huang Z, Kang Y, Lin Z, Lu P, Lin Q, Cai Z, Cao Y, Zhu X (2018) Clinical usefulness and prognostic value of red cell distribution width in colorectal cancer. BioMed Research International 2018): Article ID: 9858943. doi:https://doi.org/10.1155/2018/9858943
10. Ghuman S, Van Hemelrijck M, Garmo H, Holmberg L, Malmström H, Lambe M, Hammar N, Walldius G, Jungner I, Wulaningsih W (2017) Serum inflammatory markers and colorectal cancer risk and survival. British journal of cancer 116 (10): 1358-1365. doi:https://doi.org/10.1038/bjc.2017.96
11. Yang F, Wei L, Huo X, Ding Y, Zhou X, Liu D (2018) Effects of early postoperative enteral nutrition versus usual care on serum albumin, prealbumin, transferrin, time to first flatus and postoperative hospital stay for patients with colorectal cancer: a systematic review and meta-analysis. Contemporary nurse 54 (6): 561-577. doi:https://doi.org/10.1080/10376178.2018.1513809
12. Stojkovic Lalosevic M, Pavlovic Markovic A, Stankovic S, Stojkovic M, Dimitrijevic I, Radoman Vujacic I, Lalic D, Milovanovic T, Dumic I, Krivokapic Z (2019) Combined diagnostic efficacy of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) as biomarkers of systemic inflammation in the diagnosis of colorectal cancer. Disease markers 2019): Article ID: 6036979. doi:https://doi.org/10.1155/2019/6036979
13. Khandia R, Munjal A (2020) Chapter Six - Interplay between inflammation and cancer. In: Donev R (ed) Advances in Protein Chemistry and Structural Biology, vol 119. Academic Press, pp 199-245. doi:https://doi.org/10.1016/bs.apcsb.2019.09.004
14. Mantovani A, Allavena P, Sica A, Balkwill F (2008) Cancer-related inflammation. nature 454 (7203): 436-444. doi:https://doi.org/10.1038/nature07205
15. Campos-da-Paz M, Dórea JG, Galdino AS, Lacava ZG, de Fatima Menezes Almeida Santos M (2018) Carcinoembryonic antigen (CEA) and hepatic metastasis in colorectal cancer: update on biomarker for clinical and biotechnological approaches. Recent patents on biotechnology 12 (4): 269-279. doi:https://doi.org/10.2174/1872208312666180731104244
16. Hao C, Zhang G, Zhang L (2019) Chapter Eleven - Serum CEA levels in 49 different types of cancer and noncancer diseases. In: Zhang L (ed) Progress in Molecular Biology and Translational Science, vol 162. Academic Press, pp 213-227. doi:https://doi.org/10.1016/bs.pmbts.2018.12.011
17. Li X, Guo D, Chu L, Huang Y, Zhang F, Li W, Chen J (2019) Potential diagnostic value of combining inflammatory cell ratios with carcinoembryonic antigen for colorectal cancer. Cancer Management and Research 11): 9631. doi:https://doi.org/10.2147%2FCMAR.S222756
18. de Gonzalo-Calvo D, de Luxán-Delgado B, Rodríguez-González S, García-Macia M, Suárez FM, Solano JJ, Rodríguez-Colunga MJ, Coto-Montes A (2012) Interleukin 6, soluble tumor necrosis factor receptor I and red blood cell distribution width as biological markers of functional dependence in an elderly population: A translational approach. Cytokine 58 (2): 193-198. doi:https://doi.org/10.1016/j.cyto.2012.01.005
19. Ephrem G (2013) Red blood cell distribution width should indeed be assessed with other inflammatory markers in daily clinical practice. Cardiology 124 (1): 61-61. doi:https://doi.org/10.1159/000345925
20. Fujii T, Sutoh T, Morita H, Katoh T, Yajima R, Tsutsumi S, Asao T, Kuwano H (2012) Serum albumin is superior to prealbumin for predicting short-term recurrence in patients with operable colorectal cancer. Nutrition and cancer 64 (8): 1169-1173. doi:https://doi.org/10.1080/01635581.2012.718034
21. Sun F, Tan YA, Gao QF, Li SQ, Zhang J, Chen QG, Jiang YH, Zhang L, Ying HQ, Wang XZ (2019) Circulating fibrinogen to pre-albumin ratio is a promising biomarker for diagnosis of colorectal cancer. Journal

of Clinical Laboratory Analysis 33 (1): e22635. doi:https://doi.org/10.1002/jcla.22635

22. Kilincalp S, Çoban S, Akinci H, Hamamcı M, Karaahmet F, Coşkun Y, Üstün Y, Şimşek Z, Erarslan E, Yüksel İ (2015) Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as potential biomarkers for early detection and monitoring of colorectal adenocarcinoma. European journal of cancer prevention 24 (4): 328-333. doi:https://doi.org/10.1097/CEJ.0000000000000092

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