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Investigating the Relationship between Red Blood Cell Distribution Width and Early Detection of Colorectal Cancer and Colonic Polyps

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Abstract

Background: Colorectal cancer is a common cancer and has a high rate of mortality and morbidity. This can be reduced by screening tests. Some of the studies have recently referred to Red Cell Distribution Width (RDW) as a marker for early detection of various cancers. The aim of this study was to investigate the RDW and early detection of colorectal cancer and polyp.

Methods: A total of 90 patients were divided into three groups. One group included patients with colon cancer, another group with colon polyps, and the third group with normal colonoscopy as a control group. Blood samples were taken from patients and mean corpuscular volume (MCV), hemoglobin (HB), platelet (PLT), red blood cell distribution width (RDW), ferritin, serum iron, and total iron-binding capacity (TIBC) values were recorded. Transferrin saturation (Tsat) was also calculated. Statistical analysis was performed to remove the anemia effect of patients who had Tsat less than 20%, which was compared to patients who had Tsat over 20%. For the relationship between RDW and colon cancer, a receiver operating characteristic (ROC) curve was used.

Results: The area under the receiver-operating characteristic curve (AUC) of the RDW for predicting colon cancer was 0.698, with cut off >14 which had 80% sensitivity and 60% specificity.

Conclusions: RDW can be considered as a parameter for predicting colorectal cancer.

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Introduction

Colorectal cancer is the third most common cancer in both sexes (10.2%). Moreover, the second most common cause of mortality due to cancer (9.2%) and one in every 10 deaths occurs because of it (1). However, the level of mortality decreased due to advances in screening techniques and improvement in treatments (2). Polyps, especially adenomatous polyps, are one of the major causes of colorectal

cancer and its early detection and polypectomy will help to prevent colorectal cancer (3). Chronic blood loss in the stool can cause anemia in colorectal cancer, it can cause iron deficiency anemia by creating bleeding especially when the tumor is at the beginning of the large intestine (4). The red blood cell distribution width (RDW) is measured with a simple blood test as part of the complete blood count (CBC). It is a cheap laboratory method that can measure changes in size or volume of the red blood cells. This method has gained more attention recently because it can be used to evaluate prognosis in various diseases (5). The value of RDW in assessing the severity of disease and clinical outcome has been proven in various conditions including sepsis (6), heart failure (7) chronic kidney disease (8), and acute pulmonary embolism (9). Accumulated evidence indicated that RDW may be a prognostic factor for various malignancies (10) such as, hematologic malignancies (11), hepatocellular carcinoma (12), gastric cancer (13)and breast cancer (14). It has also been shown that RDW reflects the increase in cytokines such as IL6, TNFa, and CRP which in this case is characterized by an increase in inflammation (15). Some studies showed that RDW could be used as an additional parameter in the early detection of colorectal cancer (10,16-19). Only Ay et al. investigated the role of RDW in the early detection of the colorectal polyp (16).

In this study, a case-control design was used to investigate the role of RDW as a biomarker in the early diagnosis of colon cancer and polyp since previous studies were done retrospectively and because of the prevalence of colon cancer.

Materials and Methods

This was a case-control study. The target population in this study was patients referring to endoscopy department of the Imam Khomeini Hospital Complex for colonoscopy from October 2016 to December 2017. In addition, those who referred to the gastroenterology clinic in Imam Khomeini Hospital with a colonoscopy and pathology report were also included. Colonoscopy was not performed without medical indication for any of the patients. The exclusion criteria included patients with distal metastasis, infection, hematological disorder, iron supplementation therapy, recent venous thrombosis (past 6 months), recent blood transfusion (past 3 months), renal failure, diabetes mellitus, cardiovascular disease and inflammatory bowel disease. In this study, the researchers were required to implement the Helsinki Statement. All information about patients was confidential, all tests were part of the routine examination of the patients and no additional cost was imposed on the patient. The study population comprised 90 patients. Based on the sample taken of the colonoscopy, the patients were divided into three 30-person groups. One group consisted of colon cancer patients, another group included patients with colon polyps, and the third group included patients with normal colonoscopy as a control group. Blood sample was taken from patients and all tests were sent to the Imam Khomeini Hospital laboratory. The mean cell volume (MCV), hemoglobin (HB), platelet (PLT), RDW, ferritin, serum iron and total iron-binding capacity (TIBC) values were recorded. Moreover, transferrin saturation (Tsat) was calculated with the formula serum iron level ×100/TIBC. Statistical analysis was performed to remove the anemia effect of patients who had Tsat less than 20%, which was compared to patients who had Tsat over 20%. The SPSS 18 statistical software was used to analyze the obtained data. For qualitative variables, the frequency was calculated and for quantitative variables mean, range and standard deviation were calculated.

Chi-square test was used to evaluate the qualitative variables in two groups. Analysis of variance (ANOVA) was used to evaluate quantitative variables in two groups. The t-test was used to examine the relationship between RDW level in Tsat <20% and> 20%. The sensitivity, specificity and best cut-off of the RDW and other detection parameters for prediction of colon cancer and polyp were estimated by receiver operating characteristic (ROC) curve analysis. Furthermore, p <0.05 was considered statistically significant.

Results

In the normal group, 12 patients (40%) were male and 18 (60%) were female. In the cancer group 21 patients (70%) were male and 9 were female (30%). In the polyp group, 15 (50%) patients were male and 15 (50%) were female. In total, 48 (53.33%) of the patients were male and 42 (46.67%) were female. The mean age of the patients in the normal group was 54.70, in the cancer group was 53.66 and in the polyp group was 53.73. There were no statistically significant differences in the sex and age between the groups (p=0.06).

Levels of HB, Serum Iron, TIBC, and Tsat showed a significant statistical difference between the three groups (Table 1).

In polyp group, the mean RDW was 13.90 for T sat<20%, and 15.09 for T sat>20% (p = 0.04). In the cancer group, the mean RDW was 15.38 for T sat<20% and 14.56 for T sat>20% (p = 0.5) (Table2).

Table 1. Laboratory Parameters level in different groups

Parameters	Groups	Mean	Std. Deviation	P value
HB (g/dl)	Normal	13.79	0.91	
	Cancer	11.73	1.62	0.001
	Polyp	13.65	1.18	
MCV (fl)	Normal	86.97	6.48	
	Cancer	76.97	6.65	0.3
	Polyp	84.90	6.30	
PLT (1000/mm^3)	normal	255.70	45.88	
	cancer	262.47	114.63	0.7
	polyp	246.23	75.53	
RDW (%)	normal	15.63	2.89	
	cancer	14.99	3.60	0.9
	polyp	14.77	1.43	
Serum Iron (µg/dl)	normal	81.40	30.79	
	cancer	53.88	33.59	0.001
	polyp	77.64	23.73	
Ferritin (µg/l)	normal	83.61	81/53	
	cancer	111.42	46/02	0.3
	polyp	73.67	46/59	
TIBC (µg/dl)	normal	359.23	54.42	
	cancer	311.81	60/41	0.0001
	polyp	282.17	68/18	
Tsat (%)	normal	23.15	9.54	
	cancer	18.19	11.72	0.0001
	polyp	29.46	9/7	

Table 2. RDW level in different groups based on Tsat

groups	level	Mean	Std. Deviation	P value
normal patients	<20%	13.11	0.6	0.4
	>20%	13.42	1.2	
	Total	13.30	1.1	
polyp patients	<20%	13.90	1.1	0.04
	>20%	15.11	1.4	
	Total	14.77	1.4	
cancer patients	<20%	15.38	3.7	0.5
	>20%	14.56	3.7	
	Total	15.03	3.7	

According to ROC analysis, the best cut-off values for predicting colon polyps were HB<13 with 100% sensitivity and 58.3% specificity (AUC= 0.156), Serum iron<100.25 with 100% sensitivity and 80% specificity (AUC= 0.252), and T sat<16.6 with 70% sensitivity and 70% specificity (AUC=0.325). (Table 3). Additionally, the best cut-off values for predicting colon cancer were HB<12 with 70% sensitivity and 60% specificity (AUC=0 .627), RDW >14 with 80% sensitivity and 60% specificity (AUC=0 .698), Serum iron <39 with 100% sensitivity and 78% specificity (AUC=0 .272) and T sat<25.6 with 70% sensitivity and 60% specificity (AUC=0 .686) (Table 4, Figure1).

Table 3. The sensitivity, specificity and best cut-off of statistically meaningful cases in predicting the presence of colorectal polyp

Test Result Variable(s)		Area	Cut	sensitivity	specify	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
							Lower Bound	Upper Bound
polyp	HB	0.156	<13	100	58.3	0.0001	0.066	0.247
	Serum Iron	0.252	<100.25	100	80	0.0001	0.133	0.371
	T sat	0.325	<16.6	70	70	0.007	0.199	0.451

Table 4. The sensitivity, specificity and best cut-off of statistically meaningful cases in predicting the presence of colorectal cancer

Test Result Variable(s)		Area	Cut	sensitivity	specify	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
							Lower Bound	Upper Bound
cancer	HB	0.627	<12.0	70	60	0.050	0.509	0.746
	RDW	0.698	>14	80	60	0.002	0.582	0.814
	Serum Iron	0.272	<39	100	78	0.000	0.157	0.387
	Tsat	0.686	<25.6	70	60	0.007	0.564	0.808

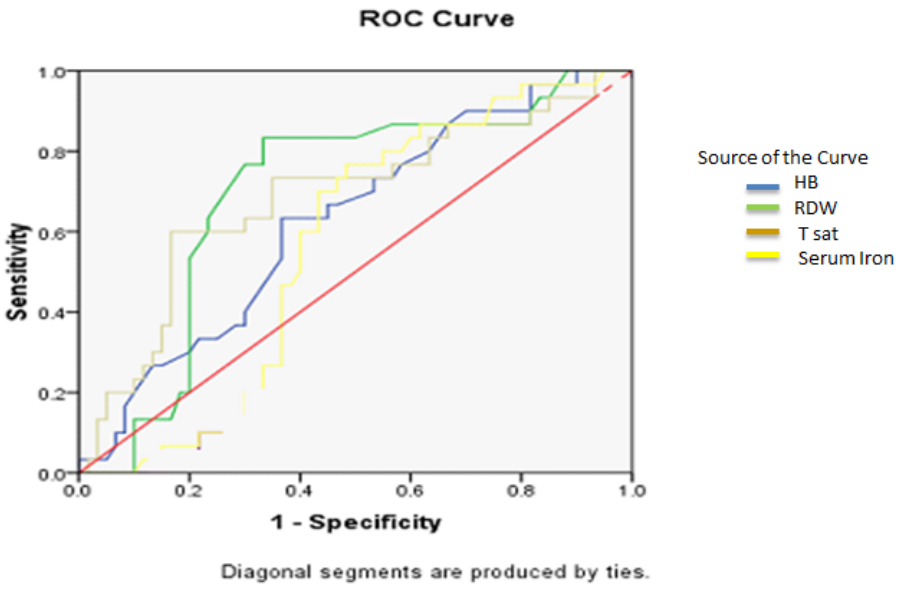

Figure 1. Receiver Operating Characteristics (ROC) Curve Analysis for RDW in the cancer group

Discussion

According to ROC analysis, it was found that RDW, HB, TIBC, and Tsat can be used together to predict the presence of colon cancer and in the polyp group HB, Serum iron, and Tsat can be used together to predict the presence of polyps. In the study conducted by Ay et al., the patients were divided into two groups of cancer patients (n=115) and polyp patients (n=30). They measured the values of MCV, HB, PLT, and RDW which showed that RDW had increased significantly in the cancer group compared to polyp group ($p<0.05$). The mean RDW was 15.5 in the polyp group and 17.7 in the cancer group. In the study by Ay et al., there was no significant difference between the two groups in MCV, HB, PLT (16). Yang et al. in a study found RDW is associated with metastatic colorectal cancer and increases in these patients. The study showed that the AUC (95% CI) for RDW was 0.721 (0.612–0.831) , optimal threshold was 13.25% with sensitivity (65.9%) and specificity (75.6%) for the diagnosis of metastatic colorectal cancer (17). In the study carried out by Spell et al., RDW had 84% sensitivity and 88% specificity in patients with right-sided colon cancer (19). Yalun Li et al. showed that a high RDW level is correlated with poor prognosis pathological features of colorectal cancer. They also indicated that higher RDW is more probable to be found in higher stages of the disease (20). Kust et al. examined the values of RDW of 90 patients with colorectal cancer before and after surgery. Optimal cut-off value for RDW preoperatively was 14% with AUC= 0.704 and after surgery was 13.6% with AUC: 0.608. Moreover, they found that the RDW before the operation had a stronger connection with the characteristics and stages of the tumor (18). Zhang et al. revealed that the high RDW can be an independent prognostic factor in patients undergoing resection for non-metastatic colorectal malignancies, and it is associated with poor prognosis in terms of survival-free disease (21). In our study, the AUC (95% CI) for RDW was 0.698 with Cut Off > 14, which had a sensitivity of 80% and 60% specificity for early detection of colorectal cancer. According to the results, the presence of colon cancer is predicted more accurately when RDW with HB, TIBC, and Tsat are used in combination. Although there is a significant difference in RDW value in

patients with polyps in Tsat <20% and> 20%, according to ROC analysis, this value does not have any significance in the prediction of polyps. It seems that more studies with more samples are needed to examine RDW level changes to predict the presence of polyp. One of the strengths of this article, compared to other similar studies is that this study was a case-control study. The patients in this study had not yet undergone any surgical procedure or systemic chemotherapy. One of the limitations of this study was the sample size, which suggested that future studies need a larger sample size. In future studies, it is suggested that the ESR be measured as a marker-inflammation to determine its effect on RDW to be more certain of the RDW value. It is also suggested to investigate the association between tumor location in the colon and RDW in future studies.

Conclusion

Regarding the results of this study, RDW along with HB, Serum Iron, and Tsat can be considered as a parameter for predicting colon cancer. It is also easy to be measured with a standard blood test, which is not a costly test. The results show that RDW may help early detection of patients with colorectal cancer for referring to colonoscopy. In order to be able to detect colon cancer more accurately with RDW, there is a need for more studies with more samples.

Conflict of interest

The authors declare no conflict of interests.

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