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The value of red blood cell distribution width in diagnosis of patients with colorectal cancer

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ABSTRACT

Background: Red blood cell distribution width (RDW) is a parameter of standard full blood count tests that reflects the size variability of erythrocytes In recent studies, RDW levels have been associated with ischemic heart disease, acute and chronic heart failure, hypertension, and inflammatory bowel disease. However, it is unclear whether RDW is associated with colorectal cancer.

Methods: Eighty-five patients were diagnosed with colorectal cancer. Fifty-four other patients each diagnosed with colon polyps during the same period served as the control group. The patients were classified according to the seventh edition of the AJCC Cancer Staging Manual of 2009 into groups of different cancer stages, and simultaneously divided into groups with or without metastasis. The multigroup metering data was tested by a non-parametric Kruskal-Wallis *H* test, and the two subsets of patients formed above were compared using a Mann-Whitney *U* test. The association between continuous variables was assessed by Spearman correlation analysis while the association between RDW and colorectal cancer metastasis was estimated by receiver operating characteristic (ROC) curve analysis.

Results: Increased RDW was observed in patients with colorectal cancer. The RDW was significantly different for each subgroup of colorectal cancer as follows: stage III + IV > stage III, T3 + T4 > T1 + T2, N1 + N2 > N0, and M1 > M0 ($P < 0.05$). The area under the receiver-operating characteristic curve of the RDW in the diagnosis of colorectal cancer metastasis was 0.721 (95% confidence interval of 0.612–0.831).

Conclusions: The value of RDW is closely related to colorectal cancer metastasis.

1. Introduction

Spurred on by a growing aging population and unhealthy lifestyles, colorectal cancer (CRC) has become one of the most commonly diagnosed cancers and the leading cause of cancer deaths worldwide [1]. Regardless of the high incidence, treatment options for CRC remain limited and unsuccessful; the current 5-year survival rates for advanced cancer are inherently unsatisfactory, mainly due to a very poor early diagnosis [2]. Blood-borne biomarkers for early detection of CRC could markedly increase screening uptake. However, current tumor markers, such as the carcinoembryonic antigen (CEA) and carbohydrate antigen 199 (CA199), are frequently ineffective for early CRC detection, inevitably resulting in a delayed diagnosis for CRC [3]. Therefore, novel accurate and early diagnostic biomarkers are urgently needed to detect early stage CRC and to identify the most effective treatments for CRC patients.

The red blood cell distribution width (RDW) measures the heterogeneity of the distribution of red blood cell size [4], which can primarily reflect impaired erythropoiesis and abnormal red blood cell survival [5]. Previously, the clinical use of RDW was limited to the diagnosis of anemia-related disease. However, recent studies found that a high RDW is strongly associated with the risk of atherosclerosis, ischemic heart disease, acute and chronic heart failure, hypertension, and inflammatory bowel disease [6, 7]. The use of the RDW in diagnosis of malignant tumors and judgment of tumor metastasis has recently attracted much attention. Related studies mainly focused on endometrial cancer, liver cancer, and ovarian cancer [8–10]. A recent report found that an increased RDW was associated with breast cancer metastasis [11]. Meanwhile, it was reported that the RDW values were associated with cancer stage in patients as well [12]. However, the relationship between RDW and clinical characteristics in metastatic colorectal cancer has not yet been reported.

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In the present study, we analyzed the correlation between the RDW and colorectal cancer incidence to explore whether RDW could be a potential marker for the diagnosis of colorectal cancer with metastasis.

2. Patients and methods

2.1. Patients

Medical records of all newly diagnosed and pathologically proven patients with colorectal cancer admitted to Shanghai Tongji Hospital between July 2014 and June 2017 were retrospectively reviewed. Patients who met any of the following criteria were excluded: cardiovascular diseases, kidney diseases, blood diseases, other malignant diseases, or blood transfusion 3 months prior to admission. A final number of 85 eligible patients were all included for analysis. These patients were classified according to the seventh edition of the AJCC Cancer Staging Manual in 2009 into groups of different cancer stages, and categorized in parallel into groups with or without metastasis. 19 patients (22.4%) had stage I cancer, 22 patients (25.9%) had stage II, 39 patients (45.9%) had stage III, and 5 patients (5.9%) had stage IV. Forty-four patients had metastasized and 41 patients had no metastases. Fifty-four patients diagnosed with colon polyps in our hospital during the same period comprised the control group, and these patients were diagnosed as benign in pathology.

3. Methods

The following clinical and laboratory data of all subjects in admission were extracted: age, gender, hematological parameters, and tumor markers. The RDW, Mean corpuscular volume (MCV), hemoglobin (Hb) concentration, total number of platelets, absolute neutrophil count (N), and absolute lymphocyte count (L) were directly detected using a Sysmex XN-9000 analyzer (Sysmex Corp., Kobe, Japan). The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated as follows: absolute neutrophil count/absolute lymphocyte count, and total number of platelets/absolute lymphocyte count, respectively. The RDW ranged from 11.9% to 14.5% in our study. The serum tumor markers CEA and CA19-9 were measured using a Roche E601 analyzer (Roche Diagnostics, Basel, Switzerland).

3.1. Statistical analysis

Continuous variables were presented as median values (min-max) and compared using a Mann-Whitney *U* or Kruskal-Wallis *H* test as appropriate. The association between continuous variables was assessed by Spearman correlation analysis. The diagnostic value of the RDW and other detection parameters was estimated by receiver operating characteristic (ROC) curve analysis, obtaining the area under the curve (AUC) and its confidence interval (CI). AUCs were compared with the Z test. The optimal cut-off for each test was determined when the Youden index achieved the highest value. All the analyses were performed using SPSS 19.0 software (IBM Corp., Armonk, NY). The level of statistical significance was set at $P < 0.05$.

4. Results

4.1. Clinical characteristic of the subjects

As shown in Table 1, the RDW, platelet, CA19-9 and CEA values were significantly higher in the colorectal cancer group than in the control group ($P < 0.05$). The hemoglobin value was significantly lower in the colorectal cancer group than in the control group ($P < 0.05$). The age, neutrophil, lymphocyte, PLR, and NLR values were not significantly different between the colorectal cancer group and control group ($P > 0.05$).

Table 1
Clinical characteristics of the subjects.

Characteristics	Colorectal cancer group (n = 85)		Control group (n = 54)		
	Median	Min-max	Median	Min-max	*P* value
Age, years	65.00	17.00–93.00	62.00	34.00–84.00	0.079
RDW, %	13.20	11.70–27.40	12.55	11.70–14.70	0.000
Hb, g/L	122.00	47.00–170.00	131.50	81.00–155.00	0.004
Platelet, ×109/L	219.00	75.00–586.00	201.00	103.00–366.00	0.021
Neutrophil, ×109/L	3.60	1.50–12.90	3.20	1.80–8.70	0.136
Lymphocyte, ×109/L	1.60	0.40–3.70	1.70	0.30–3.80	0.526
PLR	124.48	69.39–732.50	113.19	53.79–676.67	0.059
NLR	2.08	0.88–32.25	1.87	0.75–29.00	0.091
CA19-9, U/ml	12.34	0.60–130.30	7.79	0.60–80.18	0.014
CEA, ng/ml	3.02	0.83–139.20	1.83	0.21–7.93	0.000

Values are presented as median (minimum to maximum) for continuous variables, and absolute numbers for categorical data.
RDW: red blood cell width distribution, Hb: hemoglobin, PLR: platelet to lymphocyte ratio, NLR: neutrophil to lymphocyte ratio, CA19-9: carbohydrate antigen 19-9, CEA: carcinoembryonic antigen.

Table 2
Comparison of median RDW levels in different TNM staging.

Group	N	RDW (%) = (median (min-max))
Stage		
I + II	41	12.90 (11.90–19.50)
III + IV	44	13.65 (11.70–27.40)[a]
Tumor		
T1 + T2	23	12.70 (11.90–14.80)
T3 + T4	62	13.40 (11.70–27.40)[b]
Node		
N0	41	12.90 (11.90–19.50)
N1 + N2	44	13.60 (11.70–27.40)[c]
Metastasis		
M0	80	13.20 (11.70–27.40)
M1	5	19.30 (12.70–21.70)[d]

[a] $P < 0.01$ when compared with stage I + II.
[b] $P < 0.01$ when compared with T1 + T2.
[c] $P < 0.01$ when compared with N0.
[d] $P < 0.05$ when compared with M0.

4.2. Association between RDW and colorectal cancer stage and metastasis

As shown in Table 2, the RDW was significantly different in each subgroup of colorectal cancer as follows: stage III + IV > stage I + II, T3 + T4 > T1 + T2, N1 + N2 > N0 and M1 > M0 ($P < 0.05$). Correlation analysis shows that the RDW has a certain correlation with cancer stage and metastasis ($P < 0.05$) (Fig. 1).

4.3. Analysis of each marker on the diagnosis of metastatic colorectal cancer

As shown in Fig. 2, the AUC (95% CI) for RDW, CA19-9 and CEA, as parameters in the diagnosis of metastatic colorectal cancer (lymph node and distant metastasis), were 0.721 (0.612–0.831), 0.568 (0.445–0.691), and 0.644 (0.526–0.763), respectively. There were no statistically significant differences between the AUC of RDW and those of CA19-9 and CEA ($P > 0.05$). However, diagnostic performance can be improved when RDW and two other indicators are combined for detection. The optimal cut-off and corresponding sensitivity and specificity for the parameters mentioned above are shown in Table 3. Furthermore, RDW also has a good sensitivity (65.9%) and specificity (75.6%).