Clinica Chimica Acta 438 (2015) 205–209

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

The association of red blood cell distribution width with anemia and inflammation in patients with Takayasu arteritis

Qing Liu, Ai-min Dang *, Bing-wei Chen, Na-qiang Lv, Xu Wang, De-yu Zheng

Department of Special Care Center, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China

ARTICLE INFO

Article history:
Received 7 June 2014
Received in revised form 12 August 2014
Accepted 21 August 2014
Available online 27 August 2014

Keywords:
Takayasu arteritis
Red blood cell distribution width
Anemia
Inflammation
Disease activity

ABSTRACT

Background: Red blood cell distribution width (RDW) has been shown to be related to both anemia and inflammation in various diseases. However, the role of RDW in patients with Takayasu arteritis (TA) is unknown. Therefore, we investigated the association of RDW with anemia, inflammation, and disease activity in TA.
Methods: RDW was determined in 156 patients with TA and in 156 control subjects. Anemia status and disease activity were defined according to the World Health Organization and National Institutes of Health criteria, respectively.
Results: RDW was significantly increased in patients with anemia (14.6 ± 2.2) compared with those without anemia (13.6 ± 1.3, $p < 0.001$) and control subjects (12.7 ± 0.6, $p < 0.001$). Regardless of the presence of anemia, RDW showed correlation with high-sensitivity C-reactive protein (hs-CRP) (both $p < 0.05$). RDW was higher in active TA than inactive TA in patients without anemia (14.1 ± 1.5 vs. 13.3 ± 1.1, $p = 0.001$). Moreover, multiple regression analysis showed that hs-CRP and mean corpuscular volume were independently associated with RDW.
Conclusions: RDW is influenced by both anemia and inflammation, and RDW may be a useful marker to assess disease activity in patients without anemia.

1. Introduction

Red blood cell distribution width (RDW) is a parameter routinely measured to quantify the heterogeneity of circulating erythrocytes. RDW has been traditionally used as a marker to discriminate between different types of anemia [1]. Recently, increased RDW has shown to be associated with mortality in the general population [2,3], heart failure [4,5], coronary artery disease [6,7], pulmonary hypertension [8,9], stroke [10,11], diabetes mellitus [12], and infectious diseases [13]. Although the exact mechanisms underlying these findings remain unclear, chronic inflammation has been proposed as a key point in the association of RDW with these adverse outcomes [5,7,14]. In this sense, it has been found that RDW increases in several inflammatory diseases, such as rheumatoid arthritis (RA) [15], systemic lupus erythematosus (SLE) [16,17], and inflammatory bowel disease (IBD) [18,19]. Moreover, RDW has been strongly associated with inflammatory markers and disease activity in patients with SLE [17] and IBD [18,19].

Takayasu arteritis (TA) is a chronic non-specific inflammatory disease, which primarily involves large vessels including the aorta and its main branches, and pulmonary and coronary arteries. Vessel wall inflammation may cause luminal stenosis, occlusion, dilation, or aneurysm formation [20]. As TA is often associated with anemia [21], it is possible that both anemia and inflammation may influence RDW values in these patients. The natural course of TA consists of active and quiescent phases, and accurate assessment of disease activity is essential for the management of TA. Erythrocyte sedimentation rate (ESR) and C-reactive protein are commonly used inflammatory markers to evaluate disease activity in TA, despite being shown to be neither sensitive nor specific enough [22,23]. As a novel indicator for inflammation, RDW may be also useful for disease activity assessment in TA. However, no studies evaluating the association of RDW with TA have been published.

2. Materials and methods

2.1. Patients and control subjects

A total of 156 consecutive Chinese patients with TA in Fuwai Hospital from 2011 to 2013 were included in this study. All patients fulfilled the American College of Rheumatology classification criteria for TA [24]. The control group included 156 age-, sex-, and body mass

* Corresponding author at: Department of Special Care Center, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, 167 Beilishi Road, Beijing 100037, China. Tel.: +86 10 88398040; fax: +86 10 88396323.
E-mail address: amdang@fuwaihospital.org (A. Dang).

http://dx.doi.org/10.1016/j.cca.2014.08.025
0009-8981/

index (BMI)-matched healthy individuals who had routine checkup over the same period. The study protocol was approved by the Ethics Committee of the Fuwai Hospital, and informed consent was obtained from all participants.

2.2. Classification criteria

TA is classified into 4 types according to Lupi-Herrera's criteria: type I, involvement of the aortic arch and its major branches; type II, involvement of the thoracic and abdominal aorta; type III, involvement of the whole aorta; and type IV, involvement of the pulmonary artery [25].

2.3. Disease activity and anemia status assessment

The disease activity in patients with TA was evaluated according to the National Institutes of Health criteria [22]. Active disease in TA was considered if a patient presented new onset or worsening of at least two of the following features: (1) systemic symptoms not attributable to other clinical conditions; (2) characteristics of vascular insufficiency, such as claudication, vascular pain, bruit, or asymmetry in pulses or blood pressure; (3) elevated ESR without infection or malignancy; and (4) typical angiographic characteristics.

Anemic status in patients with TA was defined as a hemoglobin concentration lower than 130 g/l for males and 120 g/l for women according to World Health Organization criteria [26].

2.4. Laboratory tests

A 12-h fasting blood sample was collected for laboratory measurements that included hematological parameters, ESR, high-sensitivity C-reactive protein (hs-CRP), and other biochemical indexes. Hematological parameters, including hemoglobin, mean corpuscular volume (MCV), RDW, white blood cell (WBC), red blood cell (RBC), and platelets (PLT) counts, were analyzed by standard methods. ESR and hs-CRP were determined by Westergren method and immunonephelometry, respectively.

2.5. Statistical analysis

All variables were tested for normality of distribution using the Kolmogorov–Smirnov test. Continuous variables were displayed as mean ± SD, and categorical variables were presented as total number (percentage). ESR, hs-CRP and RDW were log-transformed to improve normality for statistical testing. Differences between the groups were assessed using one-way ANOVA and post-hoc LSD tests, independent *t* test, or Mann–Whitney *U* test for continuous variables, and chi-square test or Fisher's exact test for categorical variables. The Spearman approach was used to analyze the correlation between RDW and other continuous variables. Multiple linear regression analysis was performed to determine the factors independently associated with RDW. $p < 0.05$ was accepted as statistically significant (SPSS 17.0).

3. Results

3.1. Participant characteristics

The clinical characteristics of 156 patients with TA and 156 healthy controls are shown in Table 1 and Table 2. The mean age of patients with TA was 40.0 ± 13.3 y and 86.5% were female. There were 69 patients (44.2%) in the active phase of the disease and anemia was observed in 55 patients (35.3%) at the outset of the study. Based on the classification criteria, 39.7% had type III TA, while 31.4%, 16.7%, and 10.3% had types I, II, and IV, respectively. One hundred and twelve patients (71.8%) received prednisone therapy, and the mean daily dosage was 20.0 ± 10.2 mg.

3.2. RDW and anemia status

RDW values were significantly higher in patients with anemia (a-TA) (14.6 ± 2.2) and patients without anemia (na-TA) (13.6 ± 1.3)

Table 1
Demographic and clinical characteristics of 55 patients with anemia, 101 patients without anemia and 156 healthy controls.

	All TA (N = 156)	a-TA (N = 55)	na-TA (N = 101)	Controls (N = 156)	P value
Age, yrs	40.0 ± 13.3	37.8 ± 13.1	41.2 ± 13.2	40.2 ± 7.2	NS
Female, n (%)	135 (86.5%)	51 (92.7%)	84 (83.2%)	135 (86.5%)	NS
BMI, kg/m^2	23.1 ± 3.3	23.5 ± 3.2	23.0 ± 3.4	23.1 ± 1.7	NS
Disease duration, y	10.3 ± 10.3	8.5 ± 9.3	11.3 ± 10.7	–	NS
Hypertension, n (%)	90 (57.7%)	33 (60.0%)	57 (56.4%)	–	NS
Diabetes mellitus, n (%)	9 (5.8%)	2 (3.6%)	7 (6.9%)	–	NS
Hyperlipidemia, n (%)	44 (28.2%)	14 (25.5%)	30 (29.7%)	–	NS
WBC counts, $\times 10^9$/l	7.9 ± 2.8	7.6 ± 2.6 *	8.1 ± 3.0 *	5.9 ± 1.5	<0.001
RBC counts, $\times 10^{12}$/l	4.4 ± 0.6	4.0 ± 0.4 *,**	4.7 ± 0.5	4.6 ± 0.4	<0.001
Hemoglobin, g/l	129.0 ± 21.2	107.6 ± 11.2 *,**	140.7 ± 15.4	138.9 ± 11.6	<0.001
MCV, fl	87.6 ± 7.2	84.0 ± 8.7 *,**	89.6 ± 5.4	90.1 ± 3.7	<0.001
PLT, $\times 10^9$/l	232.7 ± 86.0	257.4 ± 97.5 *,**	219.3 ± 76.2	231.9 ± 44.8	0.004
RDW, %	14.0 ± 1.7	14.6 ± 2.2 *,**	13.6 ± 1.3 *	12.7 ± 0.6	<0.001
Creatine, umol/l	66.2 ± 18.8	65.6 ± 21.9	66.6 ± 16.9	64.3 ± 10.6	NS
ESR, mm/h	16.7 ± 18.0	23.9 ± 21.3 **	12.7 ± 14.7	–	<0.001
Hs-CRP, mg/l	5.0 ± 4.7	5.9 ± 5.4 *	4.5 ± 4.2 *	1.1 ± 0.9	<0.001
Clinical classification, n (%)					NS
No vascular impairment	3 (1.9%)	1 (1.8%)	2 (2.0%)	–	
Type I	49 (31.4%)	18 (32.7%)	31 (30.7%)	–	
Type II	26 (16.7%)	10 (18.2%)	16 (15.8%)	–	
Type III	62 (39.7%)	25 (45.5%)	37 (36.6%)	–	
Type IV	16 (10.3%)	1 (1.8%)	15 (14.9%)	–	
Prednisone, n (%)	112 (71.8%)	42 (76.4%)	70 (69.3%)	–	NS
Daily prednisone dose, mg	20.0 ± 10.2	20.8 ± 10.6	19.5 ± 10.0	–	NS

Data are presented as mean ± standard deviation or as number (percentage).
TA: Takayasu arteritis; a-TA: TA with anemia; na-TA: TA without anemia; BMI: body mass index; WBC: white blood cell; RBC: red blood cell; MCV: mean corpuscular volume; PLT: platelets; RDW: red blood cell distribution width; ESR: erythrocyte sedimentation rate; Hs-CRP, high-sensitivity C-reactive protein.
* $p < 0.05$ vs controls.
** $p < 0.05$ vs inactive TA.