

Relationship between red cell distribution with levels and severity of coronary artery ectasia

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Abstract. – OBJECTIVE: Coronary artery ectasia (CAE) is defined as abnormal dilatation of coronary arteries. Inflammation is thought to be important in the pathogenesis of CAE. Red blood cell distribution width (RDW) is also an inflammatory marker. In this study, we examined the association between RDW levels and CAE severity.

PATIENTS AND METHODS: A total of 6737 patients who were admitted to the Cardiology Clinic of our hospital between January 2010 and December 2015 and diagnosed with coronary artery disease (CAD) were evaluated for inclusion. Of them, 126 patients who had CAE as a result of retrospective scanning, 104 randomly selected patients with CAD, and 76 patients who had normal coronary arteries were included in the study (n = 306).

RESULTS: The severity and prevalence of CAE were evaluated according to the Markis ectasia classification, and the RDW value for type 1 CAE was significantly higher than that of other types of CAE. The RDW values for types 1-4 were 19.48 ± 11.81 , 15.26 ± 9.17 , 15.51 ± 8.07 , and 15.33 ± 7.26 , respectively ($p = 0.098$; $r = 0.114$).

CONCLUSIONS: High RDW values are associated with CAE and CAD, and correlate with the severity of CAE. These findings indicate that RDW values can be used to estimate the severity of CAE disease.

Key Words:

Coronary artery ectasia, Coronary artery disease, Red blood cell distribution width, Markis, Coronary angiography.

Introduction

Coronary artery ectasia (CAE) is defined as abnormal regional or diffuse dilatation (≥ 1.5 times) of the normal coronary artery lumen^{1,2}. Previous studies have reported that 0.3-5% of patients have CAE based on coronary angiography (CAG)²⁻⁶. Although atherosclerosis is the most commonly

observed etiological factor in patients with CAE (50%)⁵⁻⁹, other factors include congenital coronary anomalies and inflammatory and connective tissue diseases¹⁰. Furthermore, infectious diseases, toxicity, and trauma may also play roles in the etiology of CAE¹¹.

Markis et al² showed that histopathological changes in the coronary artery wall are similar to those seen in atherosclerosis and recommended classifying different types of CAE to determine better the severity and prevalence of the disease. Accordingly, CAE types are grouped based on the Markis et al² ectasia classification, as follows: type 1: diffuse vascular ectasia in two or three vessels; type 2: diffuse vascular ectasia in one vessel and localized disease in other vessels; type 3: diffuse ectasia in one vessel; and type 4: localized or segmental involvement. CAE can occur with occlusive coronary artery disease (CAD), depending on the severity of atherosclerosis. Some studies have concluded that intense inflammation is a factor in the etiology of CAE. These studies indicate that CAE is related to various factors such as interleukin-6, C-reactive protein, tumor necrosis factor alpha, matrix metalloproteinases, white blood cell count, neutrophil count, monocyte count, and the neutrophil-lymphocyte ratio, albeit at different rates¹²⁻¹⁷.

Red cell distribution width (RDW) is a numerical measure of the variability in the size of circulating erythrocytes. Factors that contribute to increased erythrocyte size include iron and vitamin B12/folate deficiency, decreased erythrocyte life span, and impaired erythropoiesis. Factors that contribute to lysis of erythrocytes include increased brittleness and decreased red cell destruction¹⁸. RDW has been associated with CAE¹⁹. Some studies have reported that RDW is a strong predictor of various cardiovascular diseases and their undesirable results²⁰⁻²⁴.

No study has examined the relationship between RDW values and the severity and preva-

lence of CAE. Thus, in this study, we examined the association between RDW values and CAE severity.

Patients and Methods

Patients and Procedure

A total of 6737 patients who were admitted to the cardiology clinic of our hospital between January 2010 and December 2015 due to angina or equivalent symptoms and/or had signs of ischemia after CAG were initially considered for the study. Of them, 126 patients who had CAE as a result of retrospective scanning, 104 randomly selected patients with CAD, and 76 patients who had normal coronary arteries were included in the study ($n = 306$).

We excluded patients who had no blood count or biochemical data. Additionally, patients who had acute coronary syndrome, decompensated heart failure, inflammatory disease, an active infection, severe native valvular disease, a prosthetic valve, cancer, kidney or liver dysfunction, anemia, B12 or folic acid deficiency, or hematological diseases were also excluded from the study. Age, sex, hypertension (HT), hyperlipidemia, diabetes mellitus (DM), and cigarette smoking history were also determined.

Blood samples were obtained from the antecubital fossa, and a blood count was performed using an automatic blood cell counting instrument (K-X-21N auto analyzer; Sysmex Corp, Kobe, Japan) prior to CAG.

The CAG results were evaluated by two experienced cardiologists who were blinded to the study and who were selected according to the aims of the study and patient characteristics. CAE was defined as abnormal dilatation of an artery (≥ 1.5 times that of normal size) when adjacent coronary vessels and the coronary arteries were compared. The CAE types

were grouped according to the Markis ectasia classification². CAD was diagnosed when the patient had $\geq 50\%$ dilatation in at least one vessel. Patients were divided into CAE, CAD, and control groups. Participants were considered to have HT when they were using antihypertensive medications, when their systolic blood pressure was ≥ 140 mmHg or more, and when their diastolic blood pressure was ≥ 90 mmHg according to their medical records. Participants were considered to have as DM if they were using antidiabetic medications, their glycated hemoglobin level was $\geq 6.5\%$, and when their fasting blood glucose level was ≥ 126 mg/dl. Patients who were smoking ≥ 10 cigarettes/day were considered smokers.

Statistical Analysis

SPSS 15.0 software for Windows (SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Continuous variables are presented as the mean $\pm$ standard deviation, and categorical variables are presented as percentages. The Kolmogorov-Smirnov test was performed to determine the normality of data distribution. Continuous variables were not normally distributed; therefore, the Kruskal-Wallis test was used to compare these groups. The Mann-Whitney test and the relevant post-hoc analysis were used to detect differences between groups. The correlation between continuous variables was detected by Spearman's correlation analysis. A p -value < 0.05 was considered significant.

Results

Baseline characteristics and laboratory parameters of patients with coronary artery ectasia, coronary artery disease and normal coronary angiogram summarized in Table I and Table II. No differences in demographics, complete blood count,

Table I. Baseline characteristics of patients with coronary artery ectasia, coronary artery disease and normal coronary angiogram.

	CAE (n=126)	CAD (n=104)	Normal (n=76)	p-value
Age (years)	64 $\pm$ 10	64 $\pm$ 11	65 $\pm$ 11	0.97
Sex, Female (n, %)	58 (45)	45 (45)	33 (43)	0.97
Smoking n (%)	20 (16)	18 (18)	14 (19)	0.81
Hypertension n (%)	84 (67)	69 (70)	53 (73)	0.66
Hyperlipidemia n (%)	42 (33)	33(34)	28 (38)	0.75
Diabetes mellitus (n, %)	26 (21)	23 (24)	19 (26)	0.67
Family history n (%)	38 (30)	27 (28)	18 (25)	0.70
BMI (kg/m ²)	25.8 $\pm$ 2.6	25.6 $\pm$ 2.5	25.7 $\pm$ 2.4	0.770

BMI: body mass index; Family history: for coronary artery disease.

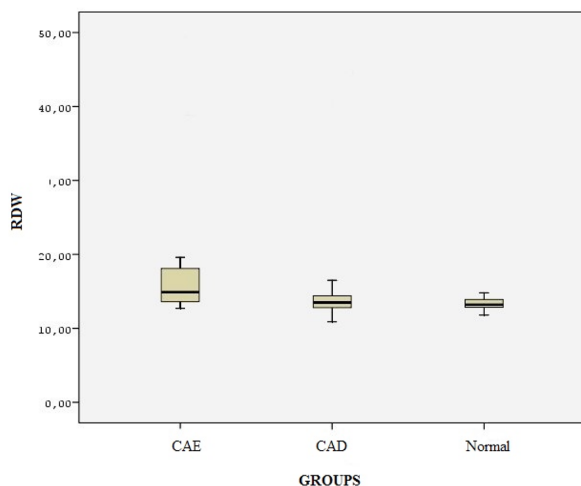
Table II. Laboratory parameters of patients with coronary artery ectasia, coronary artery disease and normal coronary angiogram.

	CAE (n=126)	CAD (n=104)	Normal (n=76)	p-value
Glucose (mg/dl)	109 (71-296)	106 (64-287)	105 (65-277)	0.933
BUN (mg/dl)	17 (7-69)	18 (8-59)	17 (8-58)	0.980
Creatinine (mg/dl)	0.8 (0.4-6.5)	0.8 (0.5-6.5)	0.8 (0.5-6.5)	0.406
Total cholesterol (mg/dl)	190.0 (102-333)	183.0 (109-328)	182 (113-294)	0.501
Triglyceride (mg/dl)	146.5 (58-673)	145 (64-663)	138 (57-677)	0.968
LDL (mg/dl)	113.35 (43-222)	110.5 (44-218)	111 (45-220)	0.375
HDL (mg/dl)	41.5 (19-71)	42 (21-77)	42 (22-69)	0.431
ALT (U/L)	19.0 (5-71)	19 (5-73)	19 (6-63)	0.657
AST (U/L)	19.0 (7-53)	19.0 (8-57)	19.0 (5-75)	0.443
WBC (x1000 μ L)	8.0 $\pm$ 2.2	8.0 $\pm$ 2.1	8.0 $\pm$ 2.2	0.986
Hb (g/dl)	14.0 $\pm$ 1.5	14.1 $\pm$ 1.5	14.1 $\pm$ 1.5	0.821
Platelet (x1000 μ L)	231.3 $\pm$ 62.8	239.3 $\pm$ 70.8	237.7 $\pm$ 64.5	0.366
MPV (fL)	9.8 $\pm$ 1.2	9.9 $\pm$ 1.1	10.0 $\pm$ 1.1	0.681
RDW (%)	20.6 $\pm$ 11.4	15.2 $\pm$ 6.7	13.4 $\pm$ 0.7	0.0003

BUN: Blood urea nitrogen; LDL: Low density lipoprotein; AST: aspartate amino transferase; ALT: alanine amino transferase; WBC: white blood cell; RBC: Red blood cell; MPV: Mean platelet volume; RDW: Red cell distribution width; SD: standard deviation; Bolded data indicate significance.

or biochemical parameters were detected between the CAE, CAD, and control groups.

The RDW values were significantly higher in the CAE (16.88 ± 9.40) and CAD (15.54 ± 7.87) groups than in the control (13.59 ± 5.78) group ($p < 0.05$). However, no difference was observed between the CAE and CAD groups. The severity and prevalence of CAE were evaluated according to the Markis et al² ectasia classification. The RDW value of type 1 CAE (19.48 ± 11.81) was significantly higher than that of types 2 (15.26 ± 9.17), 3 (15.51 ± 8.07), and 4 (15.33 ± 7.26) ($p = 0.098$; $r = 0.114$) (Figure 1).

**Figure 1.** Boxplot of RDW and groups.

Discussion

Intense inflammation has been associated with the etiology of CAE, along with a variety of other biochemical factors¹²⁻¹⁷. Markis et al² reported that histopathological changes in the coronary artery wall are similar to those in atherosclerosis and classified different types of CAE to determine better the severity and prevalence of CAE.

The RDW value is a numerical measure of the variability in the size of erythrocytes in blood circulation. Factors that contribute to lysis of erythrocytes include increased brittleness and decreased red cell destruction¹⁸. RDW has been associated with CAE¹⁹. Some studies²⁰⁻²⁴ have reported that RDW is a strong predictor of various cardiovascular diseases and their undesirable results.

RDW values are higher in patients with CAD and particularly in patients with CAE compared to individuals whose vessels are normal on CAG. Furthermore, we found a significant relationship between RDW values and CAE severity.

Some limitations of our study should be mentioned. The sample size was comparatively low, and the data were collected retrospectively from one center. Furthermore, we did not examine inflammatory markers or vitamin deficiencies that may affect the RDW value. Therefore, further studies should verify our findings.

Conclusions

We show that high RDW values are associated with CAE and CAD. Furthermore, this is the first study to show that high RDW values are correlated with CAE severity. These findings can be used to estimate CAE disease severity.

Conflicts of interest

The authors declare no conflicts of interest.

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