

Relation Between Red Cell Distribution Width and Serum Lipoprotein (a) in Healthy Adult Men

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Abstract

Objective: The aim of this study was to investigate the relationship between the serum lipoprotein(a) (Lp(a)) levels and red cell distribution width (RDW) in healthy adult men.

Method: For this purpose, 116 healthy, drug-free adult men with normal physical examination and laboratory findings were included in the study. Serum Lp(a) levels and RDW were measured by auto analyzers and commercial kits.

Results: The mean age of the subjects was 27.2 years, mean body mass index was 24.2, and mean serum Lp(a) level was 0.21 mg/dL. There was a significant positive correlation between the serum Lp(a) and RDW ($r=0.267$; $p=0.004$).

Conclusions: Of late, RDW is a commonly used marker for some diseases. High Lp(a) predicts the risk of cerebrovascular disease, atherosclerosis, thrombosis, and stroke. Evaluation of both Lp(a) and RDW may be useful to predict the risk for coronary heart disease, heart failure, hypertension, arrhythmias, and stroke in healthy subjects in the future.

Keywords: Lipoprotein(a); Red cell distribution width; Adult men

Introduction

Coronary Artery Disease (CAD), cancer, stroke, pulmonary diseases, obesity, and other pathologies related metabolic syndrome are the leading causes of mortality and morbidity in the modern world. Some biologic markers are associated with increased risk for these diseases. Insulin resistance, dyslipidemia, increased activation of the coagulation cascade, elevations in cell adhesion molecules and in molecules associated with inflammation play important role in pathogenesis of these diseases [1-4]. High blood levels of Lipoprotein (a) [Lp(a)] has been identified as a risk factor for cerebrovascular disease (CVD), atherosclerosis, thrombosis, and stroke [3-8].

Red cell distribution width (RDW) is a measure of the variability in size of circulating erythrocytes. An increased RDW can result from conditions that modify the shape of red blood cells due to the premature release of immature cells into the bloodstream [9]. Recently, it has showed that RDW may be used as a marker for some diseases [9-11]. Although the association between RDW and the risk of heart events in patients with CAD is yet to be fully elucidated, it has been found to be a novel prognostic biomarker in patients with CAD [12].

We aimed to investigate the possible relation between the serum Lp(a) and RDW in healthy adult men in this study.

Material and Methods

This study was designed in Departments of Medical Biochemistry in Medical Faculty, Kahramanmaras Sutcu Imam University in Turkey. Randomly selected 116 healthy adult men were included to this study. All subjects gave informed consent and the study protocol was approved by the local ethics committee. Patients with acute infection, neoplasia, previous stroke and Myocardial Infarctus (MI) history, diabetes mellitus, hypertension, thyroid disorders, taking drugs such as vitamins, anti-inflammatory agents or antibiotics were excluded from the study. All subjects were examined physically. Age, height, weight, alcohol intake and smoking status were recorded.

After the 8-hour overnight fast in the morning 08:00-09:00, 10 mL of peripheral venous blood samples were taken from each individual.

The blood samples were distributed into EDTA and gel tubes in volumes appropriate. To obtain serum, gel tubes were incubated for 30 min at room temperature and after coagulation they were centrifuged +4 degrees and at 2500 g, for 10 minutes. Serum samples were stored at -20 degrees until runtime inflammatory markers after to study routine laboratory tests. Complete blood Count (CBC) was studied with cytometric method by using commercial kit and hematologic analyzer (Siemens, Germany). RDW-SD values were obtained from CBC results.

SPSS 17.0 (Statistical Package for the Social Sciences, Inc., Chicago, IL) software was used for statistical analysis. Parametric variables are expressed as mean \pm standard deviation. Pearson correlation analysis was applied to test the relationships between the parametric variables. If p value was <0.05 , it was accepted as statistically significant.

Results

The mean of the age of the persons was 27.2 years; body mass index was 24.2; RDW-SD was 48.54 and serum Lp(a) level was 0.21 mg/dL (Table 1). There was significantly positive correlation between the Lp(a) and RDW-SD ($r=0.267$; $p=0.004$) (Table 2, Figure 1).

Discussion

Our results indicate that there is positive significant correlation between blood Lp(a) and RDW-SD levels. To the best of our knowledge this study is the first to demonstrate a correlation between Lp(a) and RDW in healthy adult men.

High Lp(a) predicts the risk of early atherosclerosis, independent

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Parameters	Mean ± SD
Age, year	27.2 ± 7.9
BMI, kg/m ²	24.5 ± 4.2
WBC, K/ μ L	6.76 ± 1.56
RBC, K/ μ L	5.09 ± 1.12
RDW-SD	48.54 ± 3.25
PLT, K/ μ L	224.4 ± 53.3
Lipo(a), mg/dL	0.21 ± 0.17

BMI: Body Mass Index; Lipo(a): Lipoprotein(a); PLT: Platelet; RBC: Red Blood Cell; RDW-SD: Red Cell Distribution Width-Standard Deviation

Table 1: Characteristics of study population.

Parameters		WBC	RBC	RDW-SD	PLT	Lipo(a)
Age, year	r	0.059	-0.001	0.078	-0.123	0.05
	p	0.529	0.989	0.413	0.187	0.594
BMI, kg/m ²	r	0.227*	0.032	-0.105	0.041	-0.055
	p	0.015	0.733	0.272	0.665	0.556
WBC, K/ μ L	r		-0.017	0.108	0.271**	-0.042
	p		0.857	0.258	0.003	0.653
RBC, K/ μ L	r			0.026	0.156	-0.02
	p			0.787	0.094	0.83
RDW-SD	r				0.089	0.267**
	p				0.351	0.004
PLT, K/ μ L	r					0.086
	p					0.36

BMI: Body Mass Index; Lipo(a): Lipoprotein(a); PLT: Platelet; RBC: Red Blood Cell; RDW-SD: Red Cell Distribution Width-Standard Deviation

Table 2: Correlations between Lipo(a) and hematologic parameters.

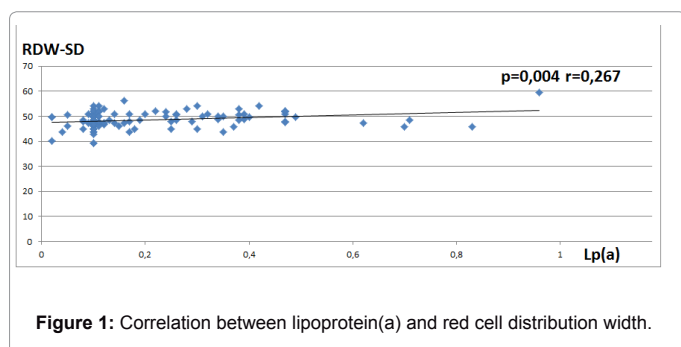


Figure 1: Correlation between lipoprotein(a) and red cell distribution width.

of other cardiac risk factors, including LDL. In patients with advanced cardiovascular disease, Lp(a) indicates a coagulant risk of plaque thrombosis. Lp(a) accumulates in the vessel wall and increases the clotting tendency by inhibiting plasmin production and inhibiting plasminogen (PLG) binding to the cell surface. This inhibition of PLG by Lp(a) also promotes proliferation of smooth muscle cells. These features of Lp(a) suggest that Lp(a) causes generation of clots and atherosclerosis [7]. Lp(a) carries cholesterol and transports the more atherogenic proinflammatory oxidized phospholipids, which attract inflammatory cells to vessel walls and leads to smooth muscle cell proliferation, thus contributes to atherosclerosis [4,5,8].

RDW is one of the commonly used markers recently. Skjelbakken et al. [10] investigated whether RDW was associated with risk of first-ever MI in a large cohort study with 1779 participants recruited from a general population. They have reported that RDW is associated with incident MI in a general population independent of anemia and cardiovascular risk factors. Wang et al. [11] have found that elevated RDW was associated with a heavier intracoronary thrombotic burden and a higher incidence of three-branch vascular lesions. In addition, they have reported that a high RDW might be associated with the sever-

ity and instability of acute myocardial infarction in their retrospective study.

The increased RDW value is associated with the acceleration of RBC proliferation. Some pathophysiological conditions such as B12 and Folate deficiency leading to macrocytic anemia accelerate the production of RBC leads to the release of larger reticulocytes to circulation. Furthermore, increased RDW needs to be evaluated even in the absence of anemia, as it may be the first clue to an underlying pathology [13]. Oxidative stress and inflammation increase RDW by impairing iron metabolism, reducing red cell life span, and modulating the response to erythropoietin by the bone marrow. So, RDW is suggested to be a biomarker reflecting a proinflammatory condition [12,14]. On the other hand, it has been demonstrated that there is no association between RDW and inflammatory parameters fibrinogen, C-reactive protein, plasma viscosity and neutrophil count [15].

In recent studies, it has been pointed that risk scores in several cardiovascular diseases should include RDW. The erythrocyte membrane promotes cardiovascular events by deposition of free cholesterol to atherosclerotic plaques, thereby providing lipid rich membranes to foam cell formation, and by propagation of the inflammatory cascade. Accumulation of erythrocytes promotes plaque instability in cardiovascular events [16-19]. The erythrocytes contain large amounts of free cholesterol. Cholesterol content of erythrocytes membrane (CEM) levels is positively associated with RDW values independently from possible confounders (inflammatory, nutritional renal or hemathological) and severity of coronary artery disease [20-22]. The erythrocyte membrane stiffness and shape influence deformability and blood flow in the microcirculation [23]. Hypoxia and iron accumulation cause the most important cardiovascular events in congenital chronic hemolytic anaemia [24].

It has been reported that genetic variants associated with Lp(a) lipoprotein level and coronary disease and some studies show that the LPA variants are strongly associated with increased Lp(a) levels [25,26]. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme produced by inflammatory cells and hydrolyzes oxidized phospholipids in LDL [27,28]. Plasma Lp-PLA2 concentrations and RDW have been found higher in patients with CAD and RDW-CV and LP-PLA2 were significantly correlated with the Gensini score [29]. Plasma Lp-PLA2 concentrations were positively associated with all LDL sub-fractions and small HDL subtraction in CAD patients [30]. RDW may increase caused by CEM contents of erythrocytes, genetic variations of blood Lp(a) levels, oxidative stress, inflammation, and anemia. Increased Lp(a) levels may facilitate our understanding why RDW is associated with increased morbidity and mortality in coronary heart disease, heart failure, hypertension, arrhythmias, stroke, and thromboembolism.

Our data shows only a weakly positive correlation, but does not show the temporal aspects or dynamic interplay between the two parameters. We have only studied the association of RDW with Lp(a), but not with other lipid parameters. Thus, only a significant correlation with Lp(a) was noted.

Conclusion

In conclusion, data from the present study showed a relation between serum Lp(a) level and anisocytosis. CBC and hematological parameters such as RDW are useful, inexpensive, widely available tools for the evaluation of patients with coronary heart disease, heart failure, hypertension, arrhythmias, and stroke. Evaluation of both serum Lp(a) level and RDW may predict the risk for these diseases in healthy subjects in future. Measuring both of them could add little additive

prognostic value. The relationship between them may be different in high-risk patients.

Author's Contributions

Ahmet Celik contributed Study Design, Data Collection, Statistical Analysis, Data Interpretation Manuscript Preparation, Literature Search, Funds Collection and Metin Kilinc contributed Data Collection, Manuscript Preparation, Literature Search, Funds Collection.

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