Research article
Araştırma makalesi

RED CELL DISTRIBUTION WIDTH (RDW) AS A DIAGNOSTIC TOOL FOR CHRONIC VENOUS INSUFFICIENCY

ERİTROSİT DAĞILIM GENİŞLİĞİ (RDW)'NİN KRONİK VENÖZ YETMEZLİKTE TANI ARACI OLARAK KULLANIMI

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Öz

Giriş: Kronik venöz yetmezlik (KVY) kronik bir enflamatuar hastalıktır ve yayınlanan çalışmalarda bazı biyobelirteçlerin KVY hastaları için prediktif değeri olduğu gösterilmiştir. Eritrosit dağılım genişliği (RDW), dolaşımdaki eritrositlerin heterojenliğinin bir ölçüsüdür. Biz bu çalışma ile RDW ve KVY sınıflandırması arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntemler: Bu çalışmada alt ekstremite venöz Doppler ultrasonu çekilmiş 102 hasta değerlendirildi. Doppler ultrason sonuçları, hematolojik ve biyokimyasal laboratuvar sonuçları retrospektif olarak hastane tıbbi kayıtlarından elde edildi.

Çalışma popülasyonu Doppler ultrason sonuçlarına göre kronik venöz yetmezlik grubu ve kontrol grubuna ayrıldı. Kronik venöz yetmezlik grubu CEAP sınıflandırmasının klinik bulgularına göre sınıflandırıldı.

Bulgular: Toplam 102 hasta çalışmaya dahil edildi. Çalışma popülasyonunun ortalama yaşı 52.3±14.6 ve 54'ü (%52,9) erkekti. Hastaların%25,5'i CVI grubuna, %74,5'i kontrol grubuna alındı. Çalışma popülasyonunun CEAP sınıflandırmasının klinik bulgularına göre %21,6'sı (n=26) Sınıf 1, %44,1'i (n=45) Sınıf 2 ve %8,8'i (n=9) Sınıf 3 olarak sınıflandırıldı. RDW, venöz yetmezlik grubunda kontrol grubuna göre anlamlı derecede yüksekti (p = 0.02). İkili karşılaştırmada; Sınıf 1 ile Sınıf 2 arasında p= 0,150; Sınıf 1 ile Sınıf 3 arasında p = 0,125 ve Sınıf 2 ile Sınıf 3 arasında p= 0,05 saptandı.

Sonuç: Sonuçlarımız RDW'nin CVI için bir tanı aracı olarak kullanılabileceğini, ancak CVI'nın şiddetinin RDW tarafından belirlenemeyeceğini göstermektedir.

Anahtar kelimeler: Eritrosit Dağılım Genişliği, RDW, Kronik Venöz Yetmezlik, Kronik Venöz Yetmezlik Sınıflaması

Abstract

Introduction: Chronic venous insufficiency (CVI) is a chronic inflammatory disease and biomarkers are defined to be used as predictive biomarkers for CVI patients. Red cell distribution width (RDW) is a measure of heterogeneity of erythrocytes in circulation. With this study we aim to investigate the relationship between RDW and CVI classification

Materials and Methods: 102 consecutive patients with lower extremity venous Doppler ultrasound were evaluated for the study. The Doppler ultrasound results, hematological and biochemical laboratory results were obtained retrospectively from hospital medical records.

The study population was divided to chronic venous insufficiency group and control group according to Doppler ultrasound results. Chronic venous insufficiency group also classified according to clinical findings of CEAP classification

Results: A total of 102 patients were included in the study. Mean age of the study population was 52.3 ± 14.6 and 54 (52.9%) was male. 25.5% of the patients were included in CVI group and 74.5% of the patients were included in the control group. 21.6% (n=26) of the study population was classified as Class 1, 44.1% (n=45) was classified as Class 2 and 8.8% (n=9) of the patients were classified as Class3 according to the clinical findings of the CEAP classification. RDW was significantly higher in venous insufficiency group compared to control group (p=0.02). The pairwise comparison of Class 1 to Class 2 was 0.150, Class 1 to Class 3 was p=0.125 and Class 2 to Class 3 was 0.05.

Conclusion: Our results propose that RDW may be used as a diagnostic tool for CVI but severity of CVI cannot be determined by RDW.

Keywords: Red cell distribution width, RDW, Chronic venous insufficiency, Chronic venous insufficiency classification

Introduction

Chronic venous insufficiency (CVI) is a very common problem with a prevalence of 25-33% in adult female and 10-20% in adult male populaion[1]. CVI can be asymptomatic and cause cosmetic problems or can be symptomatic and may cause many complaints. This disorder can be seen in a wide spectrum and the clinical problem may be venous ulceration, atrophie blanche, lipodermatosclerosis, hyperpigmentation, venous eczema, edema, varicose veins, reticular veins and telangiectases[2]. CVI can be seen at superficial veins and/or deep venous system. The level or the location of the venous insufficiency can be determined by venous Doppler ultrasound[3]. Many etiological, anatomical and pathophysiological mechanisms play various roles at varying degrees in the development of CVI. For this reason, Clinical, Etiologic, Anatomic and Pathophysiologic (CEAP) classification has been developed to make a complete definition[4].

Red cell distribution width (RDW) is a routinely checked parameter for it is a component of total blood count in medical practice. It is a measure of the heterogeneity of erythrocytes in circulation. High RDW can generally occur as a result of increased hemolysis, nutritional deficiency or blood transfusion[5]. In addition, RDW elevation is observed as a result of ineffective erythropoiesis due to chronic inflammation and neurohumoral activation. During inflammation, inflammatory cytokines suppress erythrocyte maturation and cause increased erythrocyte heterogeneity by

causing juvenile erythrocyte entry into the circulation[6-9].There are several studies that shows the relationship between cardiovascular diseases, peripheral vascular diseases, atrial fibrillation, heart failure, stroke and RDW[10]. In this study we aim to investigate the relationship between RDW and chronic venous insufficiency.

Materials and Methods

The study population was consisted of 102 consecutive patients who had lower extremity venous Doppler ultrasound at cardiology clinic. The population was divided to chronic venous insufficiency group and control group according to Doppler ultrasound results. Chronic venous insufficiency group also classified according to clinical findings of CEAP classification. According to the clinical classification; C_0 represents no visible sign of venous disease, C_1 represents telangiectasia or reticular veins, C_2 represents varicose veins, C3 represents edema, C_4 represents changes in skin and subcutaneous tissue (4A for pigmentation or eczema, 4B for lipodermatosclerosis or atrophe blanche), C_5 represents healed ulcer and C_6 represents active ulcer[11].

Data are presented as mean ± standard deviation (SD). The t-test or Chi-square test was used for comparisons of continuous and categorical variables, respectively. Distribution of the data for normality was tested by the Shapiro–Wilk test and homogeneity of group variances were tested by the Levene test. For the parameters which are not normally distributed, Mann Whithey U test was used. The data were analyzed using SPSS 22.0 (IBM SPSS Ver. 20.0, IBM Corp, Armonk NY, USA). The study was approved by the local ethics committee.

Results

Mean age of the study population was 52.3 ± 14.6 and 54 (52.9%) was male. 76 patients were diagnosed as venous insufficiency and 26 patients had normal Doppler results. RDW was significantly higher in venous insufficiency group compared to control group (p=0.02). (Table 1)

22 patients were classified as Class 1, 45 patients as Class 2 and 9 patients as Class 3 according to clinical findings of CEAP classification. RDW values was significantly different according to comparison results among venous insufficiency classes 1,2 and 3 (p=0.016). The pairwise comparison of RDW values among venous insufficiency classes are as follows; Class 1 to Class 2, p = 0.150; Class 1 to Class 3, p=0.125; Class 2 to Class 3, p = 0.05 (Figure 1).

Discussion

Our study showed that RDW may be a diagnostic tool to differentiate venous insufficiency patients from normal population but classification according to RDW levels should not be done according to our results.

RDW is an indicator of variability in the measure of circulating red blood cells. RDW is routinely checked parameter in complete blood count, and elevated RDW is a measure of increase in the heterogeneity of reticulocytes in peripheral blood[5]. In humans, the physiologic volume of erythrocytes may range between 80 to 100 fL. But under particular circumstances erythrocyte volume may increase or decrease remarkably. Plasticity of cell membrane and relative modest content of intracellular molecules like hemoglobin may allow

expansion or contraction of erythrocyte volume and size.

Table 1. Comparison of the baseline characteristics and laboratory results of the study groups.

Variables	Chronic Venous Insufficiency Group (n=76) Mean ± SD	Control Group (n=26) Mean ± SD	p
Men, %	41 (53.9%)	7 (26.9%)	0.017
Age, years	52.3 ± 15.2	52.1 ± 13.0	0.940
FBG, mg/dL	116.4 ± 58.7	119.0 ± 86.0	0.900
Creatinine, mg/dL	0.8 ± 0.2	0.9 ± 0.5	0.152
HDL-C, mg/dL	42.3 ± 8.5	34.4 ± 5.2	0.009
LDL-C, mg/dL	129.4 ± 41.2	109.6 ± 25.5	0.160
Triglyceride, mg/dL	179.8 ± 108.2	313.1 ± 216.0	0.026
Hb, g/dL	13.7 ± 1.9	14.7 ± 1.6	0.037
Leukocyte, x10³/mm³	8.3 ± 2.5	8.1 ± 2.1	0.778
Neutrophils, x10³/mm³	5.0 ± 2.3	5.0 ± 1.6	0.996
Lymphocytes, x10³/mm³	2.4 ± 0.8	2.4 ± 0.7	0.965
Platelets, x10³/mm³	234.7 ± 57.8	248.8 ± 70.5	0.377
RDW, fL	42.0 ± 6.2	35.6 ± 10.6	0.002
MPV, fL	10.5 ± 0.9	10.4 ± 0.9	0.540
PDW, fL	12.8 ± 2.5	13.3 ± 2.0	0.402

Abbreviations: BUN, blood urea nitrogen; FBG, fasting plasma glucose; Hb, hemoglobin; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MPV, mean platelet volume; PDW, platelet distribution width; RDW, red cell distribution width.

Erythrocytes can increase its' volume up to 150 fL or decrease to 60 fL and less without damaging the cell. The degree of heterogeneity is calculated by an equation in which the standard deviation of erythrocyte volume is divided by erythrocyte mean corpuscular volume and then multiplied for 100 which gives us RDW[12]. Along with anemia, sex, genetic factors, age, dyslipidemia and renal functions also affects RDW. There are many studies investigating the relationship between RDW and coronary artery disease. In these studies, RDW was stated to be an anemia-independent prognostic factor and its relationship with mortality was shown[13,14]. RDW also shown to be associated with peripheral arterial disease, myocardial infarction and stroke[15-17]. Atherosclerosis is the main disturbance behind these disorders but whether or not atherosclerosis is behind the erythrocyte fragmentation and heterogeneity of erythrocyte size causing increased RDW is not known[18-20]. Also inflammatory processes plays major role in pathophysiology of chronic venous insufficiency. Fluid shear stress causes venous distension and causes increase in cellular responses. These changes trigger inflammatory mediators[21-23].

Karahan et al.[24] evaluated the relationship between inflammatory markers and clinical severity of chronic venous insufficiency. In this study they studied white blood cell count, neutrophil, lymphocyte, platelet counts, mean platelet volume, albumin, d-dimer, fibrinogen, fibrinogen to albumin ratio, neutrophil to

lymphocyte ratio and reported that serum fibrinogen and albumin levels shows disease severity and clinical class in chronic venous insufficiency patients. Our study evaluated the relationship between RDW and chronic venous insufficiency. We found out that RDW is higher in chronic venous insufficiency patients. Chronic inflammation and oxidative stress may be the cause of increased RDW in chronic venous insufficiency patients.

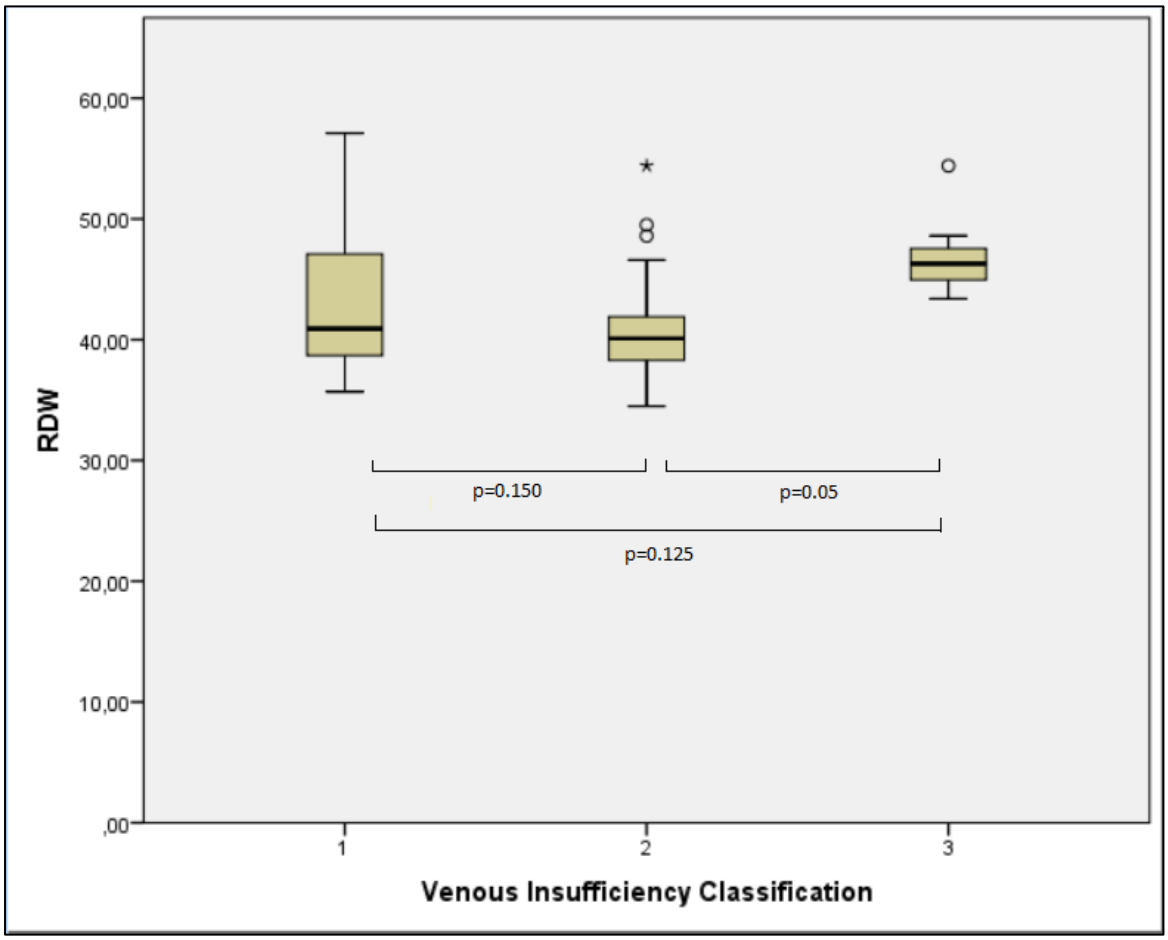

Figure 1 Venous insufficiency classification

Conclusion

RDW is an easily accessible and inexpensive parameter and many publications evaluate its role in various diseases. The literature search showed that this is the first study that shows the relationship of RDW with chronic venous insufficiency. In this study we showed that RDW may be used as a parameter for detection of venous insufficiency. Also RDW did not increase as the severity of venous insufficiency increased according to our study. This means RDW cannot be used for classification of the disease. This study has many limitations. We do not know the ejection fraction of the patients or coronary artery disease history. Further

studies should be made with higher number of patients and also it would be better to include severe venous insufficiency patients like Class 4, 5 and 6 to reach more significant results.

Conflict of Interest

The authors declare that they have no conflict of interest

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