

The Relationship of Red-Cell Distribution Width and Carotid Intima Media in Chronic Kidney Disease

Kronik Böbrek Yetmezliği Hastalarında Kırmızı Küre Dağılım Hacmi ve Karotis İntima Media Kompleks İlişkisi

ABSTRACT

OBJECTIVE: Red-cell distribution width (RDW) is a parameter routinely used for diagnosis of different anemia types. Recent studies have shown the RDW relationship with mortality in general population and patients with cardiovascular disease. However, the number of studies on RDW in chronic kidney disease (CKD) is insufficient. We evaluated the relationship between RDW and carotid intima media thickness (IMT), which is a predictor of atherosclerosis, in patients with CKD.

MATERIAL and METHODS: 30 healthy controls, 30 patients with CKD, 37 hemodialysis patients were included. IMT was measured with ultrasonography.

RESULTS: We identified statistically significant differences in CRP (p: 0.039), hemoglobin (p<0.001), IMK (p<0.001), RDW (p<0.001), urea (p<0.001), creatinine (p<0.001), albumin (p<0.001), uric acid (p<0.001) and ferritin (p<0.001) levels among three groups. In post hoc analysis, the IMK value was statistically significantly higher in the predialysis (p<0.001) and hemodialysis group than healthy controls. IMK value was not statistically different in the hemodialysis group than the predialysis group (p: 0.988). The RDW value was higher in the predialysis group than controls with a trend to statistical significance (p: 0.067). RDW value showed positive correlation with IMK (r: 0.356 P: 0.012) and CRP (r: 0.361 P: 0.004).

CONCLUSION: RDW is associated with inflammation and intima media thickness in patients with CKD.

KEY WORDS: RDW, Atherosclerosis, Chronic kidney disease

ÖZ

AMAÇ: Eritrosit dağılım genişliği (RDW) rutin olarak tam kan sayımından elde edilen bir parametredir. Son yıllarda yapılan çalışmalarda kardiyovasküler hastalığı olanlarda ve sağlıklı gönüllülerde RDW'nin kardiyovasküler hastalıklarla ilişkili olduğu gösterilmiştir. Böbrek yetmezliği hastalarında RDW ile ilgili yeterli çalışma yoktur. Biz kronik böbrek yetmezliği hastalarında RDW'nin aterosklerozun bir ön göstergesi olan karotis intima media kalınlığı (IMK) ile ilişkisini araştırdık.

GEREÇ ve YÖNTEMLER: 30 sağlıklı kontrol, 30 kronik böbrek yetmezliği hastası, 37 hemodiyaliz hastası çalışmaya alındı. Hastaların ultrasonografik yöntem ile IMK değerleri ölçüldü.

BULGULAR: CRP (p=0,039), hemoglobin (p<0,001), IMK (p<0,001), RDW(p<0,001), üre (p<0,001), kreatinin (p<0,001), albumin (p<0,001), ürik asit (p<0,001) ve ferritin (p<0,001) değerlerinde her üç grup arasında istatistiksel olarak anlamlı farklılık tespit edildi. Posthoc analizde IMK değeri prediyaliz grubunda (p<0,001) ve hemodiyaliz grubunda (p<0,001) sağlıklı kontrollere göre istatistiksel olarak anlamlı yüksek tespit edildi. Hemodiyaliz ve prediyaliz gruplarının ortalama IMK değerleri arasında istatistiksel farklılık tespit edilmedi (p:0,988). RDW değeri hemodiyaliz grubunda control grubuna (p:0,046) ve prediyaliz grubuna (p:0,03) göre yüksek saptandı. RDW değeri prediyaliz grubunda control grubuna göre istatistiksel anlamlılılık sınırına yakın yüksek tespit edildi (p: 0,067). RDW değeri IMK (r: 0,356 P: 0,012) ve CRP (r: 0,361 P: 0,004) ile pozitif korelasyon, gösterdi.

SONUÇ: Kronik böbrek yetmezliği hastalarında RDW inflamasyon ve intima media kalınlığı ile ilişkilidir.

ANAHTAR SÖZCÜKLER: RDW, Aterosklerozis, Kronik böbrek yetmezliği

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INTRODUCTION

The red blood cell distribution width (RDW) is a marker of anisocytosis of the erythrocyte (1, 2). It is performed as part of a complete blood count. Recent studies have shown that an elevated RDW may be seen in diseases such as coronary artery disease, peripheral artery disease, renal dysfunction, and inflammatory disease (3-5). Atherosclerotic cardiovascular disease is one of the leading causes of mortality in patients with chronic kidney disease (6). Latest studies have demonstrated that cardiovascular risk in hemodialysis patients is 20 times higher than that of the general population (7). It was shown that carotid intima media thickness is independently associated with atherosclerosis (8, 9). Identification of patients at risk could alert physicians to monitor cardiovascular risk and implement aggressive control of risk factors. There is a need for noninvasive cardiac markers to predict future heart diseases in CKD patients. There are very few studies on the role of RDW in predicting subclinical atherosclerosis in population of hemodialysis patients.

This study aims to evaluate the relationship between RDW and carotid intima media thickness in patients with chronic kidney disease.

MATERIAL and METHODS

The study protocol was approved by the Pamukkale University Ethical Committee. 30 healthy controls, 37 hemodialysis patients, and 30 predialysis patients were enrolled in the study. Patients who had active infections; a history of blood transfusion within the past 3 months; were taking immunosuppressive medication; malignancies; hematologic or documented cardiac diseases; history of percutaneous or surgical revascularization, systemic conditions (ankylosing spondylitis, rheumatoid arthritis) were excluded.

All of the hemodialysis patients have been receiving hemodialysis 3 times per week with bicarbonate dialysate solution at least for one year. Systolic (SBP) and diastolic blood pressure (DBP) was measured in each individual twice, following a 5-minute rest, with an Erka brand sphygmomanometer using an appropriate cuff width. Patients who were on hypertension medication were recorded.

Biochemical Analysis

The hemogram and biochemistry results of each patient, obtained after one-night fasting period, were recorded from patient files. Complete blood count measurement was performed with the flow cytometry method; fasting blood glucose, creatinine, albumin, and serum lipids measurements were performed with the enzymatic colorimetric method; C-reactive protein (CRP) measurements were performed with the immunoturbidimetric method; and sodium, potassium, and chloride measurements were performed with the ion selective electrode method. The Sysmex XT 2000I device was used for complete blood count and the other biochemical parameters were studied using the Modular P, Roche/Hitachi device.

Carotid Intima Media Thickness Measurement

Intima media thickness (IMT) of the carotid artery as an indicator of subclinical atherosclerosis was measured. Carotid artery ultrasounds of all groups were performed by a single radiologist at the Pamukkale University Department of Radiology, Medical Faculty Hospital. Toshiba aplio XY high-resolution B-mode ultrasonography with a 7.5 MHz linear probe was used for the measurements. The measurement between two echogenic lines seen between the intima lumen interface and media adventitia interface was described as the IMT measurement (10). The posterior wall was used in the measurement as performed in the axial and longitudinal plans in views. Imaging techniques were performed within 2 hours after blood was collected from patients.

Statistical Analysis

The continuous variables were expressed as mean \pm SD, whereas categorical variables were expressed as percentage values. While pre-analysis homogeneity of variance was tested with Levene's test, pre-analysis homogeneity of normality was tested with the Smirnov and Shapiro-Wilk tests. $P < 0.05$ was recognized as statistically significant. Parametric continuous variables were compared by independent Student's t test or the Mann-Whitney U test. Categorical variables were analyzed by chi-squared and Fisher's exact tests. The statistical analyses were carried out with Windows SPSS v17.0 package program.

RESULTS

The basal characteristics of the hemodialysis group, predialysis group, and healthy control group are shown in Table I. There was no difference in mean age, leukocytes, Ca, and phosphorus values ($p > 0.05$). The values of Crp ($p: 0.039$), hemoglobin ($p < 0.001$), IMT ($p < 0.001$), RDW ($p < 0.001$), urea ($p < 0.001$), creatinine ($p < 0.001$), albumin ($p < 0.001$), uric acid, ($p < 0.001$), and ferritin ($p < 0.001$) were detected to be significantly different among three groups.

When Post hoc analysis of significantly different parameters was conducted among the three groups (Table II), IMT was significantly higher in the hemodialysis ($p < 0.001$) and predialysis groups ($p < 0.001$) than the control group. IMT was not significantly different in the hemodialysis group compared to the predialysis group ($p > 0.005$). RDW was significantly higher in the hemodialysis group than the predialysis ($p: 0.013$) and control groups ($p < 0.001$). RDW was higher with a trend towards statistical significance level in the predialysis group compared to the control group ($p: 0.067$). CRP was significantly higher in the hemodialysis group than the control group ($p: 0.042$). CRP was not significantly different in the predialysis group than the hemodialysis group and control groups ($p: 0.183$). The albumin level was significantly lower in the hemodialysis group than control ($p < 0.001$) and the predialysis group ($p < 0.001$); even though it was lower in the predialysis group compared to the control group, it did not reach to statistical significance ($p: 0.628$).

Table I: Laboratory parameters of all groups.

	Control	Predialysis	Hemodialysis	p
Age	52.76±13.57	52.28±13.75	56.02±16.06	0.525
Leukocyte	7.25±3.04	7.7±2	7.71±2,82	0.746
Ca	9.50±0.48	9.02±0.81	8.95±0.89	0.064
Phosphorus	3.6±0.61	3.95±1.01	4.17±1.36	0.153
CRP	0.49±0.47	0,76±0,87	1.53±2.44	0.039
Hemoglobin	13.77±1.42	12.02± 2.25	10.97±1.24	0.000
IMK	0.65±0.12	0.85 ±0.15	0.86±0.14	0.000
RDW	14.01±1.07	15.01 ±2.12	16.23±1.73	0.000
Urea	31.07±8.43	94.96±49.28	150.63±45.10	0.000
Creatinin	0.84±0.18	3.23±1.70	8.92±2.78	0.000
Albumin	4.29±0.25	4.20±0.36	3.54±0.27	0,000
Uric acid	4.54±1.40	6.78±1.73	6.53±1.1	0.000
Ferritin	56.51±48.62	94.71±87.28	944.38±394.11	0.000

GFR: Glomerular filtration rate, **RPR:** RDW to platelet ratio, **CRF:** Chronic renal failure.

Table II: Post hoc analysis of all groups.

	Control	Predialysis	Hemodialysis	P h-k	P h-p	P p-k
Hemoglobin	13.77±1.42	12.02± 2.25	10.97±1.24	0.00	0.035	0.000
CRP	0.49±0.47	0.76±0.87	1.53±2.44	0.042	0.183	0.830
RDW	14.01±1.07	15.01 ±2.12	16.23±1.73	0.000	0.013	0.067
IMK	0.65±0.12	0.85 ±0.15	0.86±0.14	0.00	0.998	0.000
Urea	31.07±8.43	94.96±49.28	150.63±45.10	0.00	0.00	0.00
Creatinine	0.84±0.18	3.23±1.70	8.92±2.78	0.00	0.00	0.00
Albumin	4.29±0.25	4.20±0.36	3.54±0.27	00.0	0.00	0.628
Uric acid	4.54±1.40	6.78±1.73	6.53±1.1	0.000	0.762	0.000
Ferritin	56.51±48.62	94.71±87.28	944.38±394.11	0.000	0.000	0.932

P h-k: Hemodialysis versus control p< 0.05, **P h-p:** Hemodialysis versus predialysis p< 0.05, **P p-k:** Predialysis versus control.

The uric acid level was significantly higher in the predialysis group (p<0.001) and hemodialysis group (p<0.001) compared to the healthy controls. Although the uric acid level was higher in the hemodialysis group than the predialysis group, it did not reach statistical significance (p: 0.762). The ferritin level was significantly higher in the hemodialysis group compared to the control (p<0.001) and predialysis group (p<0.001). The ferritin level was not statistically significantly higher in the predialysis group than the control group (p: 0.932). We identified a positive

correlation of RDW with IMT (r: 0.356, p: 0.012) and CRP (r: 0.361, p: 0.004) (Figure1,2).

DISCUSSION

Essentially, mean RDW value was identified as significantly higher in the hemodialysis group and predialysis group than the control group in our study. Also, we showed that RDW is associated with CRP and carotid intima media in patients with chronic kidney disease.

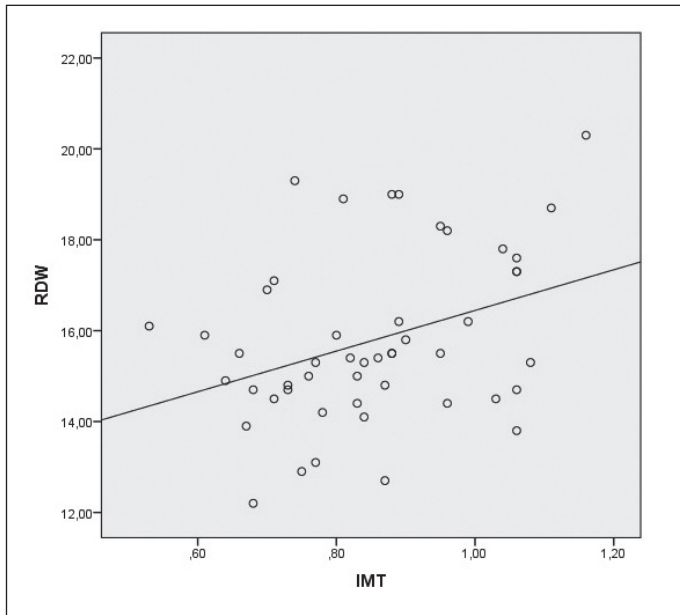


Figure 1: The relationship with RDW and IMT. $r: 0.356$ $p: 0.012$.

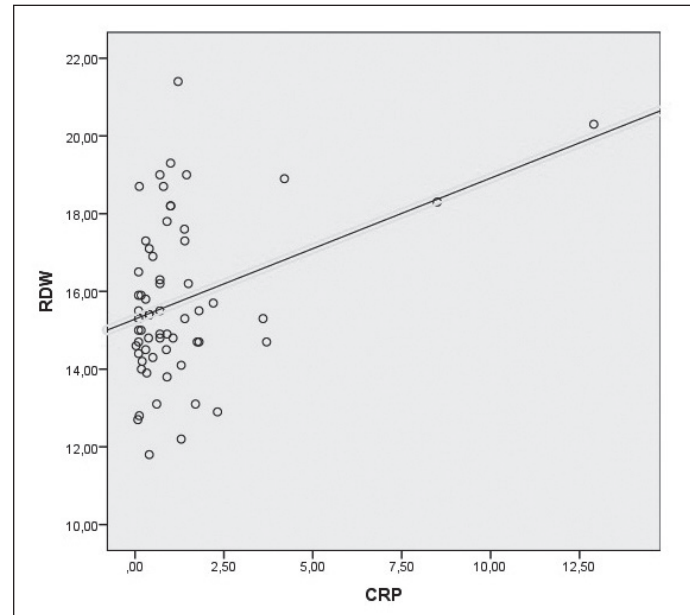


Figure 2: The relationship with RDW and CRP. $r: 0.361$ $p: 0.004$.

Early morphological and functional changes can be seen in arterial wall due to atherosclerosis before cardiovascular diseases occur. Identification of new markers related with preclinical atherosclerosis is important to lower mortality and morbidity of patients with chronic kidney disease.

RDW reflects the variability of red cell volume in circulation (11). Recent evidence shows that RDW is closely associated with atherosclerotic coronary artery disease, fatal and non-fatal cardiovascular disease. Importance of RDW in cardiovascular diseases increases further with easy access and no additional cost of RDW (12-14). The relationship between RDW and IMT was shown in several studies. Södörholm et al. showed a relationship between RDW and intima media in a population based cohort study (15). In the study of Wen, a relationship between RDW and IMT was identified in hypertensive patients (16). The study conducted by Fruer et al. suggested a relationship between RDW and IMT (17). In the study of Gunbatar et al., a relationship between RDW and IMT was found in OSAS patients (18). To the best of our knowledge, only one study investigated the relationship between RDW and intima media in patients with chronic kidney disease. In the study of Solak et al., it was suggested that RDW has a relationship with IMT and FMD in patients with chronic kidney disease (19).

Importance of inflammation in atherosclerosis has been shown (20). Although the relationship between RDW and intima media, which is a good indicator of atherosclerosis, is unclear, the most probable underlying cause is inflammation. Immature erythrocyte transition to circulation due to increased inflammation, shorter lifespan of erythrocytes due to inflammatory cytokines and deterioration of iron metabolism

might cause anisocytosis and RDW increase in chronic kidney disease (21-23).

In line with our study, Lippi et al. showed a graduated relationship between RDW and hsCRP (24). Semba et al. showed that oxidative stress and inflammation might be associated with RDW increase (25). Recently it has been shown that RDW is an essential marker of chronic inflammation and oxidative stress (26). Lippi et al. (27) showed a close relationship between RDW and kidney function tests. In their study, a low glomerular filtration rate strongly predicted RDW increase independent of the glomerular filtration rate, age, gender, MCV and hemoglobin level in logistic regression analysis. In accordance with the literature, we showed that RDW levels are higher in chronic kidney disease and hemodialysis patients compared to healthy controls in our study.

CONCLUSION

RDW was associated with subclinical atherosclerosis and inflammation in patients with chronic kidney disease in our study. Further studies are required to understand the relationship between RDW and atherosclerosis.

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