

# Predictors of functional capacity in younger and elderly chronic heart failure patients: an observational study

*Kronik kalp yetersizliği olan genç ve yaşlı hastalarda fonksiyonel kapasitenin bağımsız öngördürücüleri: Gözlemsel bir çalışma*

*Nihat Polat, Fahrettin Öz, Derya Baykız, Ahmet Yaşar Çizgici, İbrahim Altun, Zehra Buğra, Berrin Umman, Fatih Tufan\*, Hüseyin Oflaz*

From Departments of Cardiology and \*Internal Medicine/Geriatrics, İstanbul Faculty of Medicine, İstanbul University, İstanbul-Turkey

## ABSTRACT

**Objective:** The prevalence of chronic heart failure (CHF) in the elderly population is growing. Identification of risk factors in patients with CHF is important. Recent studies suggest that red cell distribution width (RDW) has prognostic significance in these patients. We aimed to evaluate the relationship of RDW with clinical and laboratory parameters in patients with young and elderly CHF patients.

**Methods:** We evaluated patients with CHF with an ejection fraction (EF) of <50% in this observational cross-sectional study. Exclusion criteria were decompensated CHF, malignancy and end stage renal disease. Clinical information, functional capacity (FC), hemoglobin, RDW, EF, and pro-B type natriuretic peptide (proBNP) were recorded. The younger and elderly groups were compared and correlation of RDW with clinical and laboratory parameters were analyzed in each group. Ordinal regression analysis was performed to determine independent correlates of increased FC.

**Results:** Seventy young and 47 elderly cases were enrolled. The groups were similar regarding EF, proBNP and FC. RDW showed stronger correlation with FC in the young group ( $r=0.627$ ,  $p<0.001$ ) compared to the elderly group ( $r=0.332$ ,  $p=0.023$ ). In the younger group, there was a negative correlation between RDW and EF ( $r=-0.278$ ,  $p=0.021$ ) and a positive correlation between RDW and proBNP ( $r=0.487$ ,  $p<0.001$ ). RDW (OR=16.36, 95% CI 0.33-0.96,  $p<0.001$ ), EF [OR=7.75, 95% CI (-0.16)-(-0.03),  $p=0.005$ ] and usage of RAS inhibitors (OR=6.7, 95% CI 0.57-3.36,  $p=0.007$ ) were independent predictors of increased FC.

**Conclusion:** We found a stronger correlation between RDW and EF, proBNP and FC in the younger patients compared the elderly group. RDW is a simple, inexpensive and easily accessible parameter that may be considered risk predictor especially in younger patients with CHF. (*Anadolu Kardiyol Derg 2013; 13: 778-83*)

**Key words:** Heart failure, erythrocytes, risk assessment, stroke volume, natriuretic peptides, metabolic equivalent, regression analysis

## ÖZET

**Amaç:** Kronik kalp yetersizliği (KKY) prevalansı yaşlı nüfusta giderek artmaktadır. Bu hastalarda kalp yetersizliği risk faktörlerini belirlemek önemlidir. Bu hastalarda eritrosit dağılım hacminin (EDH) prognostik önemi olduğu tespit edilmiştir. Amacımız olan genç ve yaşlı KKY hastalarında EDH ile klinik ve laboratuvar parametreleri arasındaki ilişkiyi araştırmaktır.

**Yöntemler:** Kesitsel ve gözlemsel çalışmamıza ejeksiyon fraksiyonu %50'nin altında olan 117 hasta dahil edildi. Dekompanse kalp yetersizliği, malignitesi ve son dönem böbrek yetersizliği olan hastalar çalışmadan dışlandı. Klinik bilgiler, fonksiyonel kapasite, EDH, hemoglobin, EF ve pro-B-tip natriüretik peptit (proBNP) değerleri kaydedildi. Her iki grupta EDH ile klinik ve laboratuvar parametreleri arasındaki ilişkiyi araştırmak amacıyla korelasyon analizi yapıldı. Fonksiyonel kapasiteyi öngördüren bağımsız değişkenleri belirlemek amacıyla ordinal regresyon analizi yapıldı.

**Bulgular:** Yetmiş genç ve 47 yaşlı hasta çalışmaya alındı. EF, proBNP ve fonksiyonel kapasite açısından gruplar benzerdi. Genç hastalarda ( $r=0,627$ ,  $p<0,001$ ) yaşlı hastalar ile kıyaslandığında ( $r=0,332$ ,  $p=0,023$ ) EDH ile fonksiyonel kapasite arasında güçlü bir pozitif korelasyon vardı. Genç hastalarda EDH ile EF arasında negatif korelasyon ( $r=-0,278$ ,  $p=0,021$ ) ve EDH ile proBNP arasında pozitif korelasyon ( $r=0,487$ ,  $p<0,001$ ) vardı. Regresyon analizinde, EDH (OO=16,36, %95 CI 0,33-0,96,  $p<0,001$ ), EF (OO=7,75, %95 GA (-0,16)-(-0,03),  $p=0,005$ ) ve RAS blokleri kullanımı (OO=6,7, %95 GA 0,57-3,36,  $p=0,007$ ), fonksiyonel kapasitenin bağımsız değişkenleri olarak saptandı.

**Address for Correspondence/Yazışma Adresi:** Dr. Fahrettin Öz, İstanbul Üniversitesi İstanbul Tıp Fakültesi, Kardiyoloji Anabilim Dalı, İstanbul-Türkiye Phone: +90 212 414 20 00 E-mail: fahrettin\_oz@hotmail.com

**Accepted Date/Kabul Tarihi:** 18.03.2013 **Available Online Date/Çevrimiçi Yayın Tarihi:** 25.10.2013

©Telif Hakkı 2013 AVES Yayıncılık Ltd. Şti. - Makale metnine [www.anakarder.com](http://www.anakarder.com) web sayfasından ulaşılabilir.

©Copyright 2013 by AVES Yayıncılık Ltd. - Available on-line at [www.anakarder.com](http://www.anakarder.com)

doi:10.5152/akd.2013.265



**Sonuç:** Çalışmamızın sonucunda genç hastalarda EDH, EF ve proBNP ile fonksiyonel kapasite arasında güçlü bir korelasyon bulduk. EDH özellikle KKY olan genç hastalarda, risk öngördürücüsü olarak değerlendirilebilen, basit, ucuz ve kolay elde edilebilen bir parametredir. (*Anadolu Kardiyol Derg 2013; 13: 778-83*)

**Anahtar kelimeler:** Kalp yetersizliği, eritrosit, risk değerlendirmesi, atım hacmi, natriüretik peptitler, metabolik eşdeğer, regresyon analizi

## Introduction

Among the global aging phenomenon, prevalence of CHF is increasing especially in the elderly (1, 2). Despite advances in the treatment of CHF, it is associated with a high mortality rate (3, 4). Functional capacity (FC) is an important parameter in the assessment of patients with CHF. While major determinant of FC is cardiac functions, especially elderly patients may have other causes of functional limitation like anemia, pulmonary diseases, depression, hypogonadism and sarcopenia. Determining factors associated with increased functional limitation is crucial to enhance life quality in these patients.

New markers for risk assessment in patients with CHF would enhance the treatment of these patients. Among these markers, B-type natriuretic peptides (BNP) are the most commonly used. Recent studies show that increased red cell distribution width (RDW) in patients with acute heart failure (HF) and CHF is an independent predictor of mortality (5-8). Like the natriuretic peptides, increased RDW has been shown to be an important marker for re-hospitalization and mortality in patients with CHF (5, 6). Different studies suggest that, regardless of the anemia, increased RDW is associated with higher mortality rate in patients with CHF (5, 9) and in patients with coronary heart disease (CHD) (10). Two separate population-based studies also showed that the association of RDW with mortality was independent from the presence of anemia (11, 12). In patients with CHF, increased RDW seems to be associated with malnutrition, inflammation, renal insufficiency, and ineffective erythropoiesis (6). Furthermore, increased RDW may be a finding of increased erythropoiesis related to neurohormonal activation (13). However, the exact mechanisms underlying the association of increased RDW and adverse outcomes in patients with CHF are not completely explained.

We aimed to evaluate the association of RDW with clinical and laboratory parameters in young and elderly patients with CHF.

## Methods

### Study design

This study was an observational cross-sectional cohort study.

### Study population

Patients with CHF who were seen in the Department of Cardiology, İstanbul Faculty of Medicine, İstanbul University between February 2010 and June 2010 were enrolled to this study. The term chronic heart failure (CHF) was used for patients who have had heart failure for at least 6 months. The diagnosis of CHF was done using clinical history, physical examination,

chest X-ray, electrocardiography and echocardiography according to the current European Society of Cardiology guidelines (1). Diagnosis of CHF was confirmed by a senior cardiologist.

Patients with isolated diastolic HF [ejection fraction (EF) >50%], New York Heart Association (NYHA) functional classification class 4, acute exacerbation of HF, end-stage renal disease [ESRD, a glomerular filtration rate (GFR) below 15 mL/min/1.73 m<sup>2</sup>], hematological malignancies, and significant lung disease were excluded.

The study was approved by the ethics committee of İstanbul University, İstanbul School of Medicine. All patients provided written informed consent.

### Study protocol

All patients' age, gender, height, weight, and comorbid diseases were recorded. The patients above the age of 65 years were classified as elderly. Body-mass index (BMI, kg/m<sup>2</sup>) was determined and body surface area (BSA) was calculated using the Dubois formula (14). Estimated glomerular filtration rate (eGFR) was calculated with modification of diet in renal disease (MDRD) formula (15) and was corrected for BSA. Complete blood count, cholesterol levels, C-reactive protein (CRP), creatinine values were measured. Blood counts were measured by an automated hematology analyzer (Coulter Gen-S, COULTER Corp, Miami USA). The outcome variable RDW was obtained from this automatized blood count analysis (normal reference values: 11-15%).

Amino-terminal pro-B-type natriuretic peptide (proBNP) values were measured (normal reference values: <125 pg/dL, Elecsys Roche Diagnostics, Mannheim, Germany). The proBNP levels were adjusted for eGFR and age according to following formula (16):

Normalized proBNP (NBNP) =  $k \times \log(\text{proBNP}) \times 1000/\text{eGFR}$   
(k: 0.825 for age <50 years, 0.762 for age between 50-70 years and 0.636 for age >70 years)

Echocardiography was performed using the Vivid 7 echocardiography device (General Electrics, Milwaukee, WI, USA) using a middle-range frequency (3-8 MHz) broadband transducer. EF was measured with area/length method according to the ASE guidelines (17). The biochemical tests and echocardiography were performed within the same day.

### Functional capacity

Varieties of approaches have been used to quantify the degree of functional limitation imposed by HF. The most widely used scale is the NYHA functional classification (18). Classification of FC of the patients (the predictor variable in this study) was made on the basis of clinical evaluation according to NYHA classification (18).

NYHA functional classification based on severity of symptoms and physical activity (18)

- **Class 1:** No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
- **Class 2:** Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.

- **Class 3:** Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
- **Class 4:** Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

**Table 1. Demographic features, comorbid diseases, BMI and FC of the cases**

Variables	Young (n=70)	Elderly (n=47)	Z/Chi-square	p
Gender, % males	84.3	78.7	0.591**	0.4
Age, years	56.5 (27-64)	70 (65-84)	-9.2*	<0.001
Smoking, %	57.1	48.9	0.762**	0.38
DM, %	41.4	40.4	0.012**	0.9
HT, %	57.1	74.5	3.668**	0.06
CHD, %	70	87.2	4.705**	0.030
CABG, %	14.3	34	6.350**	0.012
AF, %	14.3	27.7	3.184**	0.074
BMI, kg/m <sup>2</sup>	27.36 (18.7-43.7)	25.1 (18-44.1)	-1.857*	0.063
FC, median	2 (1-3)	2 (1-3)	-1.651*	0.099

Data are presented as mean±SD, median (range) and percentage values  
\*Mann-Whitney U test, \*\*Chi-square test  
AF - atrial fibrillation, BMI - body mass index, CABG - coronary artery bypass grafting, CHD - coronary heart disease, DM - diabetes mellitus, FC - functional capacity, HT - hypertension, NS - not significant

**Table 2. Laboratory characteristics of cases**

Variables	Young (n=70)	Elderly (n=47)	t/Z	p
Hb, g/dL	13.2±1.7	12.5±1.7	1.947*	0.54
Hct, %	39.9±5	38.3±5.1	1.645*	0.103
MCV, fL	88.0 (70.0-97.5)	88.9 (76.0-102.5)	-0.848**	0.396
MPV, fL	8.70 (6.9-11.3)	8.65 (6.4-11.8)	-0.359**	0.720
RDW, %	13.9 (10.6-20.3)	13.7 (12.2-23.6)	-0.394**	0.694
Platelets (x1000/mm <sup>3</sup> )	275.1±93.1	231.7±75.8	2.658*	0.009
Leukocyte, mm <sup>3</sup>	8100(1100-12820)	8100(3670-28900)	-0.081**	0.936
Creatinine, mg/dL	0.9 (0.5-2.9)	1.1 (0.6-2.5)	-2.385**	0.017
GFR, ml/dk	79.6(19.3-160)	67.2 (30-157.7)	2,724**	0.006
proBNP, pg/mL	930 (74-14753)	1577(103.8-18498)	-1.727**	0.084
NBNP	28.8 (14-151)	34 (11-102)	-2.1**	0.036
CRP, mg/L	3.36 (0.3-36)	5.11 (0.5-51)	-1.861**	0.063
LDLC, mg/dL	100.6±33.2	97.7±33	0.471*	0.638
HDLC, mg/dL	39.0 (12-54)	39.5 (19-63)	-1.221**	0.222
TG, mg/dL	121 (51-419)	111 (54-298)	-1.129**	0.259
EF, %	34 (19-49)	35 (20-49)	-0.896**	0.370

Data are presented as mean±SD and median (range) values  
\*Student t-test, \*\*Mann-Whitney U test  
CRP - C reactive protein, EF - ejection fraction, Hb - hemoglobin, Hct-hematocrit, GFR - glomerular filtration rate, HDLC - HDL cholesterol, LDLC - LDL cholesterol, MCV - mean corpuscular volume, MPV - mean platelet volume, NBNP - normalized proBNP, RDW - red cell distribution width, proBNP - pro-brain natriuretic peptide, TG - triglyceride

**Statistical analysis**

Statistical analysis was performed using SPSS version 13 for Windows (SPSS Inc. Chicago. Illinois, USA).

Distributions of continuous variables were determined with Kolmogorov-Smirnov test in each group. Between-group comparisons were done with Chi-square test for categorical variables, with Student’s t test for continuous variables with normal distribution, and with Mann-Whitney U test for continuous variables with abnormal distribution and ordinal variables. Correlation analyses were done with Pearson test for variables with normal distribution, and Spearman test for continuous variables with abnormal distribution and ordinal variables. Ordinal regression analysis (logistic regression analysis for ordinal dependent variable- three categories of FC) including age, gender, hemoglobin, RDW, CRP, proBNP, EF, history of diabetes, smoking status, and usage of renin angiotensin aldosterone system (RAS) inhibitors, beta blockers, diuretics and aldosterone blockers was performed to detect factors independently associated with increased FC. Strength of correlation were defined as weak for r values between 0.2-0.4, intermediate for r values between 0.4-0.7, and strong for r values over 0.7. A p value of <0.05 was considered as statistically significant.

**Results**

**Clinical characteristics**

A total of 117 patients were enrolled, 70 patients were in the younger and 47 patients were in the elderly group. Gender ratio, smoking rate, comorbid disease frequencies (other than CHD), FC and BMI were similar in both groups (Table 1). Frequency of CHD and history of coronary by-pass surgery were higher in the elderly group. Both groups had similar EF, proBNP, hemoglobin, hematocrit, mean corpuscular volume (MCV), and mean platelet volume (MPV), RDW, hsCRP values and cholesterol levels (Table 2). The elderly group had higher creatinine and NBNP levels and lower platelet counts and GFR values. The medical treatments were similar in both groups (Table 3). Although significant anemia was not an exclusion criterion, only 3 patients in the younger group and 2 patients in the elderly group had hemoglobin levels between 8.6 and 10 g/dL, all other patients had hemoglobin levels above 10 g/dL. While ESRD was an exclusion criterion, only 1 patient in the younger group had a GFR level below 30 mL/min/1.73 m<sup>2</sup> (19 mL/min/1.73 m<sup>2</sup>).

**Relationship between RDW and clinical variables**

In the younger group, RDW showed moderate and positive correlations with proBNP and FC, a weak and positive correlation with NBNP, moderate and inverse correlations with Hb and MCV, and weak and inverse correlations with BMI, EF, TG, HDL-C

**Table 3. Medical treatments of the patients**

Variables	Young (n=70)	Elderly (n=47)	Chi-square	p
Beta blockers, %	88.6	89.4	0.018	0.894
ACEI/ARB, %	82.9	70.2	2.601	0.107
Diuretic, %	61.4	48.9	1.785	0.182
Statin, %	77.1	80.9	0.230	0.631
Aspirin, %	82.9	87.2	0.414	0.520

Data are presented as percentage values, Chi-square test  
ACE-I - angiotensin-converting enzyme inhibitors, ARB - angiotensin II receptor blockers

**Table 4. The correlation between the RDW and clinical features and laboratory parameters**

Variables	All cases		Elderly group		Young group	
	r*	p	r*	p	r*	p
Age	-0.001	0.993	0.079	0.597	0.050	0.685
Hb, g/dL	-0.364	<0.001	-0.232	0.116	-0.461	<0.001
MCV, fL	-0.325	<0.001	-0.128	0.391	-0.425	<0.001
MPV, fL	0.057	0.541	-0.076	0.614	0.147	0.229
Creatinine, mg/dL	0.175	0.60	0.353	0.015	0.092	0.453
GFR, mL/min/1.73 m <sup>2</sup>	-0.175	0.60	-0.239	0.106	-0.155	0.203
proBNP, pg/mL	0.361	<0.001	0.175	0.249	0.487	<0.001
NBNP	0.253	0.007	0.256	0.089	0.259	0.034
CRP, mg/L	-0.001	0.989	0.024	0.875	0.002	0.987
EF (%)	-0.160	0.88	0.099	0.512	-0.278	0.021
FC	0.512	<0.001	0.332	0.023	0.627	<0.001
LDL-C, mg/dL	-0.206	0.026	-0.101	0.501	-0.282	0.019
HDL-C, mg/dL	-0.175	0.60	-0.033	0.828	-0.248	0.040
TG, mg/dL	-0.084	0.369	0.265	0.072	-0.286	0.017
BMI, kg/m <sup>2</sup>	-0.129	0.169	0.021	0.890	-0.260	0.031

\*Spearman correlation test  
BMI - body mass index, CRP - C reactive protein, EF - ejection fraction, FC - functional capacity, GFR - glomerular filtration rate calculated by modification of diet in renal disease formula, Hb - hemoglobin, HDLC - HDL cholesterol, LDLC - LDL cholesterol, MCV - mean corpuscular volume, MPV - mean platelet volume, NBNP - normalized proBNP, proBNP - pro-brain natriuretic peptide, RDW - red cell distribution width, TG - triglyceride

and LDL-C (Table 4). In the elderly group, RDW did not have a significant correlation with proBNP or EF. A statistically significant weak and positive correlation was found between RDW and creatinine and FC in the elderly group.

The correlations between other important markers of heart failure are shown in Table 5. While proBNP showed a moderate and inverse correlation with EF in the young group, this correlation was not seen in the elderly. NBNP showed a weak and inverse correlation with EF in the young group and there was no correlation between NBNP and EF in the elderly. While proBNP showed moderate and positive correlations with FC in both groups, NBNP had a weak and positive correlation with FC only in the elderly group. C-reactive protein showed a positive and weak correlation with proBNP in both groups and a positive and weak correlation with NBNP in the younger group. While EF showed a moderate

**Table 5. Correlations between biomarkers of heart failure**

Variables	All cases		Elderly group		Young group	
	r*	p	r*	p	r*	p
proBNP-EF	-0.458	<0.001	-0.295	0.052	-0.587	<0.001
proBNP-FC	0.492	<0.001	0.479	0.001	0.487	<0.001
proBNP-CRP	0.387	<0.001	0.376	0.011	0.360	0.003
BNP-GFR	-0.425	<0.001	-0.435	0.003	-0.335	0.005
NBNP-EF	-0.227	0.016	-0.14	0.365	-0.347	0.004
NBNP-FC	0.262	0.005	0.386	0.009	0.170	0.166
NBNP-CRP	0.302	0.001	0.197	0.195	0.315	0.009
EF-FC	-0.343	<0.001	0.066	0.663	-0.532	<0.001
CRP-FC	0.118	0.209	0.171	0.249	0.016	0.898

\*Spearman correlation test  
BNP - B type natriuretic peptide, CRP - C reactive protein, EF - ejection fraction, FC - functional capacity, GFR - glomerular filtration rate, NBNP - normalized proBNP

**Table 6. Ordinal regression analysis for independent correlates of increased functional capacity**

Variables	Wald	95% CI	p
Gender	0.28	-0.9-1.6	0.6
Age	3.9	0.001-0.11	0.05
Diabetes mellitus	0.18	-1.1-0.7	0.7
RAASB use	7.4	0.57-3.36	0.007
Beta blocker use	0.006	-1.6-1.5	0.9
Diuretic use	2.7	-2-0.2	0.1
Spironolactone use	0.9	-0.52-1.5	0.3
Hemoglobin	0.01	-0.3-0.3	0.9
C reactive protein	1.1	-0.024-0.08	0.3
RDW	16.2	0.33-0.96	<0.001
Ejection fraction	8	(-0.16)-(-0.03)	0.005
Estimated-GFR	2.2	-0.004-0.03	0.14
proBNP	3.5	-0.001-0.001	0.06

CI - confidence interval, BNP - B-type natriuretic peptide, GFR - glomerular filtration rate, RAASB - renin angiotensin aldosterone system blocker, RDW - red cell distribution width RDW (OR=16.36, 95% CI 0.33-0.96, p<0.001), EF [OR=7.75, 95% CI (-0.16)-(-0.03), p=0.005] and usage of RAS inhibitors (OR=6.7, 95% CI 0.57-3.36, p=0.007)

and negative correlation with FC in the young group, it did not have a significant correlation with FC in the elderly.

#### Factors associated with increased FC

Ordinal regression analysis revealed that only RDW (OR=16.36, 95% CI 0.33-0.96, p<0.001), EF [OR=7.75, 95% CI (-0.16)-(-0.03), p=0.005] and usage of RAS inhibitors (OR=6.7, 95% CI 0.57-3.36, p=0.007) were independent correlates of increased FC (Table 6).

#### Discussion

In the present study, we observed that independent determinants of FC were RDW, EF and RAS blocker use. In addition, we

also found strong correlations between RDW and EF, proBNP and FC. FC is an important parameter, since lower FC translates into independence in daily activities and improved quality of life. Especially in the elderly population, frailty and sarcopenia currently draw significant attention and are important predictors of multiple adverse health outcomes including death (19-21). Although cardiac functions are the primary determinants of FC in the CHF patients, especially elderly patients may have additional causes of functional limitation like anemia, depression, hypogonadism and sarcopenia, which are rather common in this population. Regarding anemia, only 3 patients in the younger group and 2 patients in the elderly group had hemoglobin levels below 10 g/dL. A recently published study which aimed to determine transfusion threshold in a large group of high-risk patients, suggested that a target hemoglobin level of >8 g/dL rather than >10 g/dL is safe (22). Furthermore, hemoglobin was not an independent correlate of FC in our study. Thus, functional limitation due to significant anemia does not seem likely. However, we did not assess the presence of depression, hypogonadism or sarcopenia in our patients and we cannot rule out their contribution to functional limitation. Particularly, screening for depression in patients with CHF is important. Study of Bisschop et al. (23), suggested that cardiac disease and arthritis are the most common predisposing factors for medical illness related depression.

RDW is a readily available parameter of complete blood count analysis. The term anisocytosis is used for increased RDW values and denotes increased diversity of red cell volume. Normal RDW values are between 11% and 14.5% (24, 25). Iron, vitamin B12 and folic acid deficiency may cause increased RDW values. Other underlying factors of increased RDW values include hemolysis, malnutrition, inflammation, renal insufficiency and ineffective erythropoiesis (6). In patients with CHF, increased RDW might especially be associated with nutritional anemia, inflammation, renal insufficiency, ineffective erythropoiesis and oxidative stress (26, 27). In addition, neurohormonal activation seems to be associated with increased erythropoiesis, thus increasing the RDW values (13). In a recent study, a strong and independent association between RDW and inflammatory markers was demonstrated in a large cohort (28). We found a significant correlation between RDW and important parameters of heart failure like FC and proBNP. The correlation between RDW and FC were stronger in younger compared to elderly cases. RDW was also correlated with EF in younger patients. In the elderly patients, RDW was correlated only with NBNP and FC. There was no correlation between CRP and RDW in our study. This suggests that the increase in RDW in these patients was not associated with inflammation. These findings suggest that increased RDW may be considered as a risk factor, especially in younger patients. Furthermore, since RDW is a readily available parameter, which is included in the routine blood count analysis, it does not cause additional cost.

Some recent studies indicate that NT-proBNP but not BNP is influenced from kidney insufficiency (29). Some authors suggest utilization of NBNP levels instead of proBNP in patients with

impaired renal functions, especially if the patient is old (16). Although elderly patients were included in our study, proBNP showed stronger correlation with FC and EF compared to NBNP. However, end-stage renal disease was an exclusion criterion and our patients had below-normal but relatively preserved GFR levels (mean 79.6 and 68.6 mL/dk/1.73 m<sup>2</sup> in young and elderly groups, respectively).

Interestingly, EF was correlated with FC and proBNP in the younger group but not in the elderly group. However, proBNP and FC had moderate correlations in both the younger and the elderly groups. Although we did not assess diastolic functions in our study, we speculate that diastolic functions may have been worse in the elderly group, thus attenuating the clinical importance of the EF value. These findings suggest that, the clinical relevance of EF may be diminished and natriuretic peptides and RDW may be better clinical predictors in the elderly.

Interestingly, usage of RAS blockers but no other drugs was independently associated with a better FC. Although usage of RAS blockers may be associated with a better FC by preserving cardiac functions, cross-sectional design of our study does not allow us make conclusions in this subject. Moreover, there is data indicating that usage of RAS inhibitors may be associated with improvement in functional limitation even in patients without CHF (30).

### Study limitations

Limitations of our study include the small number of patients and the cross-sectional design. Exclusion of patients with class 4 functional classification further limits extrapolation of our results to this subgroup of CHF patients.

### Conclusion

In our study, independent determinants of FC were RDW, EF and RAS blocker use. We also found strong correlations between RDW and EF, proBNP and FC. These correlations were more pronounced in the younger patients. RDW is an easily accessible parameter which does not require additional cost. We suggest utilization of RDW in the routine evaluation of CHF patients.

**Conflict of interest:** None declared.

**Peer-review:** Externally peer-reviewed.

**Authorship contributions:** Concept - N.P, H.O., F.T.; Design - F.Ö., N.P.; Supervision - H.O.; Resource- A.Y.Ç., İ.A., D.B.; Data collection&/or Processing - A.Y.Ç., N.P., D.B., F.Ö.; Analysis &/or interpretation - H.O., Z.B., B.U.; Literature search - D.B., A.Y.Ç., İ.A., F.Ö.; Writing - N.P, F.T., F.Ö.; Critical review - B.U., Z.B., H.O.

### References

1. Hunt SA American College of Cardiology; American Heart Association Task Force on Practice Guidelines (Writing Committee

- to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol* 2005; 46: e1-82.
2. Swedberg K, Cleland J, Dargie H, Drexler H, Follath F, Komajda M, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *Eur Heart J* 2005; 26: 1115-40. [\[CrossRef\]](#)
  3. Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KK, et al. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002; 347: 1397-402. [\[CrossRef\]](#)
  4. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001; 345: 1435-43. [\[CrossRef\]](#)
  5. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. *J Am Coll Cardiol* 2007; 50: 40-7. [\[CrossRef\]](#)
  6. Forhecz Z, Gombos T, Borgulya G, Pozsonyi Z, Prohaszka Z, Janoskuti L. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. *Am Heart J* 2009; 158: 659-66. [\[CrossRef\]](#)
  7. Al-Najjar Y, Goode KM, Zhang J, Cleland JG, Clark AL. Red cell distribution width: an inexpensive and powerful prognostic marker in heart failure. *Eur J Heart Fail* 2009; 11: 1155-62. [\[CrossRef\]](#)
  8. van Kimmenade RR, Mohammed AA, Uthamalingam S, van der Meer P, Felker GM, Januzzi JL, Jr. Red blood cell distribution width and 1-year mortality in acute heart failure. *Eur J Heart Fail* 2010; 12: 129-36. [\[CrossRef\]](#)
  9. Pascual-Figal DA, Bonaque JC, Redondo B, Caro C, Manzano-Fernandez S, Sanchez-Mas J, et al. Red blood cell distribution width predicts long-term outcome regardless of anaemia status in acute heart failure patients. *Eur J Heart Fail* 2009; 11: 840-6. [\[CrossRef\]](#)
  10. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M. Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People With Coronary Disease. *Circulation* 2008; 117: 163-8. [\[CrossRef\]](#)
  11. Patel KV, Ferrucci L, Ershler WB, Longo DL, Guralnik JM. Red blood cell distribution width and the risk of death in middle-aged and older adults. *Arch Intern Med* 2009; 169: 515-23. [\[CrossRef\]](#)
  12. Patel KV, Semba RD, Ferrucci L, Newman AB, Fried LP, Wallace RB, et al. Red cell distribution width and mortality in older adults: a meta-analysis. *J Gerontol A Biol Sci Med Sci* 2010; 65: 258-65. [\[CrossRef\]](#)
  13. Kato H, Ishida J, Imagawa S, Saito T, Suzuki N, Matsuoka T, et al. Enhanced erythropoiesis mediated by activation of the renin-angiotensin system via angiotensin II type 1a receptor. *FASEB J* 2005; 19: 2023-5.
  14. Wang Y, Moss J, Thisted R. Predictors of body surface area. *J Clin Anesth* 1992; 4: 4-10. [\[CrossRef\]](#)
  15. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999; 130: 461-70. [\[CrossRef\]](#)
  16. Bernstein LH, Zions MY, Haq SA, Zarich S, Rucinski J, Seamonds B, et al. Effect of renal function loss on NT-proBNP level variations. *Clin Biochem* 2009; 42: 1091-8. [\[CrossRef\]](#)
  17. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr* 1989; 2: 358-67.
  18. The Criteria Committee of the New York Heart Association Nomenclature and criteria for diagnosis of diseases of the heart and blood vessels. Boston: Little Brown, 1964.
  19. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; 39: 412-23. [\[CrossRef\]](#)
  20. Evans WJ, Paolisso G, Abbatecola AM, Corsonello A, Bustacchini S, Strollo F, et al. Frailty and muscle metabolism dysregulation in the elderly. *Biogerontology* 2010; 11: 527-36. [\[CrossRef\]](#)
  21. Visser M, Schaap LA. Consequences of sarcopenia. *Clin Geriatr Med* 2011; 27: 387-99. [\[CrossRef\]](#)
  22. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, Rhoads GG, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011; 365: 2453-62. [\[CrossRef\]](#)
  23. Bisschop MI, Kriegsman DM, Deeg DJ, Beekman AT, van Tilburg W. The longitudinal relation between chronic diseases and depression in older persons in the community: the Longitudinal Aging Study Amsterdam. *J Clin Epidemiol* 2004; 57: 187-94. [\[CrossRef\]](#)
  24. Marsh WL Jr, Bishop JW, Darcy TP. Evaluation of red cell volume distribution width (RDW). *Hematol Pathol* 1987; 1: 117-23.
  25. Bessman JD, Gilmer PR Jr, Gardner FH. Improved classification of anemias by MCV and RDW. *Am J Clin Pathol* 1983; 80: 322-6.
  26. Douglas SW, Adamson JW. The anemia of chronic disorders: studies of marrow regulation and iron metabolism. *Blood* 1975; 45: 55-65.
  27. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med* 2005; 352: 1011-23. [\[CrossRef\]](#)
  28. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relationship between red blood cell distribution width and kidney function tests in a large cohort of unselected outpatients. *Scand J Clin Lab Invest* 2008; 68: 745-8. [\[CrossRef\]](#)
  29. Tagore R, Ling LH, Yang H, Daw HY, Chan YH, Sethi SK. Natriuretic peptides in chronic kidney disease. *Clin J Am Soc Nephrol* 2008; 3: 1644-51. [\[CrossRef\]](#)
  30. Sumukadas D, Witham MD, Struthers AD, McMurdo ME. Effect of perindopril on physical function in elderly people with functional impairment: a randomized controlled trial. *CMAJ* 2007; 177: 867-74. [\[CrossRef\]](#)