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ORIGINAL ARTICLE

Relationship between red cell distribution width and echocardiographic parameters in patients with diastolic heart failure

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Abstract Red cell distribution width (RDW) was found to be a prognostic marker in heart failure patients. The aim of the study was to investigate the relationship between RDW and echocardiographic parameters in diastolic heart failure (DHF). Seventy-one consecutive DHF patients (26 men) and 50 controls (21 men) were included in the study. All of the study population underwent echocardiographic evaluation, and blood samples were obtained. RDW and N-terminal pro-B-type natriuretic peptide (NT-proBNP) values were significantly higher, whereas there was an increasing trend for high-sensitivity C-reactive protein levels in DHF patients than those in controls ($p < 0.001$, $p < 0.001$, and $p = 0.064$, respectively). All of the echocardiographic parameters evaluating diastolic function were more deteriorated in the DHF group. Patients who had an RDW value greater than the cutoff point also had higher NT-proBNP levels, an elevated ratio of mitral peak velocity of early diastolic filling to early diastolic mitral annular velocity, and increased estimated pulmonary capillary wedge pressures by tissue Doppler parameters, but lower creatinine clearance ($p < 0.05$ for all). According to the cutoff values calculated using receiver operating characteristic analysis, RDW > 13.6% and NT-proBNP > 125 pg/mL have high diagnostic accuracy for predicting DHF. RDW values were increased in the DHF population. Our results suggest that the high RDW levels in patients with DHF may be related to increased neurohormonal activity, impaired renal functions, and elevated filling pressure, but not to increased inflammation.

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Introduction

Diastolic heart failure (DHF) is a clinical syndrome characterized by the symptoms and signs of heart failure, a preserved ejection fraction, and abnormal diastolic function [1]. Various definitions, such as "heart failure with preserved systolic function" or "heart failure with normal or near normal ejection fraction" have also been used [2]. The proportion of patients with DHF in epidemiological studies ranges from 40% to 71% (mean, 56%), but in hospital-based cohort studies, it is slightly lower, ranging from 24% to 55% (mean, 41%) [3]. Older age; hypertension with left ventricular hypertrophy; pathologies, such as diabetes, obesity, coronary artery disease (CAD), and new onset atrial fibrillation are commonly associated with DHF [2,3].

Red cell distribution width (RDW) is a quantitative measure of anisocytosis, the variability in size of the circulating erythrocytes, and is routinely reported by automated laboratory equipment used to perform complete blood counts [4]. Higher RDW values indicate that a greater variety of cell sizes is present. In clinical practice, RDW is generally used to narrow the differential diagnosis of anemia, especially to differentiate iron deficiency anemia and thalassemia [5,6]. Recently, there has been growing attention given to the relationship between RDW and cardiovascular disorders, such as heart failure and CAD. This interest was spurred by the report from Felker et al. [7], which showed that there is a strong, independent association between RDW and the risk of adverse outcomes in heart failure patients, and the study by Tonelli et al. [8], which predicted a graded independent relationship between RDW and the risk of death and cardiovascular events in patients with CAD.

Although the prognostic importance of RDW in various cardiovascular diseases, including systolic heart failure, is well known, there are no data about RDW in the DHF population. The purpose of the present study was to determine if RDW levels are significantly different in DHF patients compared with those of controls and to investigate the relationship between RDW and echocardiographic parameters.

Design and methods

Study population

Seventy-one consecutive patients [mean age, 57 ± 7 years; 26 (37%) men] diagnosed with DHF in our clinic and 50 controls [mean age, 56 ± 7 years; 21 (42%) men] were included in the study. DHF was diagnosed when symptoms (dyspnea not associated with any other cause) and signs (rales or peripheral edema) of heart failure were observed along with a preserved left ventricular ejection fraction (LVEF $\geq$ 50%) and evidence of diastolic dysfunction. The control group was formed from voluntary individuals admitted to our clinic who did not have heart failure symptoms and signs and who had a preserved LVEF. Patients with systolic heart failure; hemodynamically unstable valvular heart disease; congenital heart disease; atrial fibrillation; chronic obstructive pulmonary disease; malignancy; known hematological diseases, such as hemolytic anemia, neoplastic metastases in the bone marrow; pregnancy; severe arthritis and inflammatory bowel diseases that can increase plasma RDW levels and other extracellular fluid increasing diseases, such as hypothyroidism and liver cirrhosis, were excluded from the study. The patient group was divided into two according to the most appropriate cutoff point of RDW calculated for predicting DHF (RDW $\leq$ 13.6%, RDW $>$ 13.6%).

The present study was a single-center study. All examinations were performed by the cardiology clinic of our hospital. All participants gave their informed consent before inclusion in the study. The study protocol was approved by the local committee at our institution.

Echocardiographic measurements

All of the study population underwent echocardiographic evaluation individually on the day of their admission (2.5-mHz transducer; Philips EnVisor C, Bothell, WA, USA). Standardized projections and measurements were performed for the evaluation of cardiac anatomy, ventricular function, and valve competence. LVEF was measured by Simpson's method [9]. Left ventricular mass was calculated by the formula described by Devereux et al., and left ventricular mass index was obtained by dividing the left ventricular mass by the body surface area [10]. The following conventional mitral inflow pulse wave Doppler parameters were measured: peak velocity of early diastolic filling and late filling, and deceleration time of the E-wave velocity. These parameters were obtained from the apical four-chamber view with a 1-mm to 3-mm sample volume placed between the mitral leaflet tips during diastole. Pulmonary venous flow parameters were also measured: peak systolic velocity (Ps), peak antegrade diastolic velocity (Pd), and the Ps/Pd ratio. These parameters were obtained from the apical four-chamber view with a 2-mm to 3-mm sample volume placed 1 cm into the pulmonary vein. Tissue Doppler parameters were measured: peak systolic mitral annular velocity, early diastolic mitral annular velocity (Em), and late diastolic mitral annular velocity (Am). These parameters were obtained from the apical four-chamber view with a 2-mm to 5-mm sample volume placed 1 cm within the septal and lateral insertions of the mitral leaflets. The mean of three or more measurements was used for analysis of the Doppler data. The ratio of mitral peak velocity of early diastolic filling to early diastolic mitral annular velocity (E/Em) was calculated for the lateral and septal annulus, and the mean of the lateral and septal E/Em were also determined. As previously described, the formula $(1.24 \times (E/\text{Em}) + 1.9)$ was used to estimate pulmonary capillary wedge pressure (PCWP) [11]. Diastolic dysfunction is defined as Em $<$ Am if Em is less than 10 cm/s in lateral mitral annulus or less than 8 cm/s in septal mitral annulus [12].

Biochemical measurements

Blood samples were obtained during admission for routine chemistry, including N-terminal pro-B-type natriuretic peptide (NT-proBNP) and high-sensitivity C-reactive protein (hs-CRP) after an overnight fast. RDW values were measured