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Original article

Elevation of red blood cell distribution width during hospitalization predicts mortality in patients with acute decompensated heart failure

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ABSTRACT

Background: Increased red blood cell distribution width (RDW) is associated with adverse outcomes in heart failure. In the present study, we assessed the association between changes in RDW values during hospitalization and long-term prognosis in patients with acute decompensated heart failure (ADHF).
Methods: We measured the RDW value in 229 consecutive patients with ADHF. Blood samples were obtained at the time of hospital admission and at discharge. Changes in RDW were calculated as the mean difference between RDW values on admission and those at the time of hospital discharge.
Results: Patients were followed up for a median of 692 days. A Kaplan–Meier survival analysis demonstrated that patients whose RDW levels increased during hospitalization had significantly higher all-cause and cardiac-based mortality following heart failure than did patients whose RDW levels decreased during hospitalization. A multivariate Cox regression analysis revealed that change in RDW values during hospitalization, but not the values of RDW and hemoglobin on admission, was independently correlated with all-cause and cardiac-based mortality after adjusting for other risk factors in patients with ADHF.
Conclusions: These data document that the change in RDW values during hospitalization independently predicts poor outcomes in patients with ADHF. Continuous follow-up of RDW values could provide useful information for long-term prognosis after heart failure.

Introduction

Acute decompensated heart failure (ADHF) is a major cause of death and disability in industrialized countries [1,2]. It would therefore be clinically valuable to discover a useful marker to predict which patients with heart failure would have the best outcomes.

Red blood cell distribution width (RDW) is one of the parameters reported in a complete blood count. RDW represents the variability of sizes of circulating erythrocytes and has been used in combination with the mean corpuscular volume (MCV) for the classification of anemia, such as thalassemia, iron deficiency, and chronic disease-related anemia [3,4]. Recently, the clinical significance of RDW in inflammatory-related disorders has been extensively investigated. High RDW values are strongly associated with poor clinical outcomes in patients with acute coronary heart disease, pancreatitis, and rheumatoid arthritis [5–8].

In regard to the relationship between RDW and heart failure, numerous studies have reported that RDW predicts mortality in heart failure [8–12]. Higher RDW values at admission are associated with worse short- and long-term outcomes in patients with acute or chronic heart failure. However, these results have been inconsistent [13]. These findings suggest that RDW values in patients with heart failure do not have sufficient predictive value for long-term prognosis. Therefore, in order to identify a prognostic biomarker that better predicts outcomes after ADHF, we assessed the association between changes in RDW values during hospitalization and long-term prognosis in patients with ADHF.

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Methods

Study population

We retrospectively assessed 265 consecutive patients who were admitted to Anjo Kosei Hospital for the treatment of ADHF between April 2010 and March 2011. All diagnoses were based on the Framingham criteria [14]. We excluded patients with hemodialysis. A medical history was obtained to document etiology, medications, and co-morbid disease. Hypertension was defined as a systolic blood pressure (BP) of ≥140 mmHg or a diastolic BP of ≥90 mmHg on repeated measurements, or receiving antihypertensive treatment. Diabetes mellitus was defined according to the World Health Organization criteria [15]. Dyslipidemia was defined as total cholesterol of ≥220 mg/dL, triglycerides of ≥150 mg/dL, low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol <40 mg/dL, or receiving lipid-lowering therapy.

Biomarker analysis

Complete blood counts for RDW values were performed utilizing a Sysmex XE-5000 analyzer (Sysmex, Kobe, Japan). The normal range of RDW in this system is 11.5–14.5%. Blood samples were obtained at the time of hospital admission and at discharge. Changes in RDW were calculated as the mean difference between RDW values on admission and those at the time of hospital discharge. In some analyses, we divided the patients into two groups according to whether they had higher or lower than the normal range of RDW levels on admission. Plasma B-type natriuretic peptide (BNP) was measured with the AIA-2000 enzymatic immunoassay analyzer (TOSOH, Tokyo, Japan). Other biomarkers were measured using a LABOSPECT 008 autoanalyzer (Hitachi Co., Tokyo, Japan). Estimated glomerular filtration rate (eGFR) was calculated by the Modification of Diet in Renal Disease (MDRD) formula [16].

Echocardiography

Echocardiographic examination was performed by an experienced sonographer using Vivid E9 with XD clear (GE Healthcare, Tokyo, Japan). The images were recorded in console and analyzed offline. Left ventricular ejection fraction (LVEF) was calculated using a modified Simpson's rule.

Follow-up and assessment of clinical outcomes

All patients underwent regular follow-up (typically every month) by means of outpatient clinical visits. All-cause mortality and cardiac-based mortality were determined by Anjo Kosei Hospital staff cardiologists. Cardiac-based mortality was a composite of cardiac death attributed to heart failure, myocardial infarction, or sudden death coronary heart disease.

Statistical analysis

All analyses were performed using PASW Statistics 18 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as means ± standard deviation (SD). All-cause mortality and cardiac-based mortality were determined by Kaplan–Meier analysis with the log-rank test. Categorical variables are presented as counts and/or percentages. Cox proportional hazard models were applied to determine independent predictors of all-cause mortality and cardiac-based mortality. Variables with $p < 0.10$ in the univariate analysis were incorporated into the multivariable model. Hazard ratios (HRs) with 95% confidence intervals (CIs) were determined. In all analyses, $p < 0.05$ was considered statistically significant.

Results

Baseline characteristics

A total of 229 patients with ADHF were enrolled in this study. Their baseline clinical characteristics are shown in Table 1. Patients were 76.8 ± 11.9 years of age and 56.8% male, predominantly classified as New York Heart Association (NYHA) functional classes III and IV. The mean length of hospital stay was 12.0 days. Patients had preserved ejection fraction (mean LVEF, 48.0 ± 29.0%; LVEF ≥50%, 53.7%). The median BNP level was 813.2 pg/mL (range, 503.5–1622.2 pg/mL). The etiology of heart failure in 26.2% of patients was ischemic heart disease. Seventy-two percent of the 229 patients had hypertension, and 25% had diabetes mellitus (DM). Thirty-two percent had dyslipidemia. The usage of angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers, beta-blockers, calcium channel blockers, and diuretics at admission was 49.8%, 39.7%, 31.4%, and 47.2%, respectively.

Influence of ADHF on RDW values

RDW values in patients with ADHF are shown in Table 2. The mean RDW level measured on admission was 15.0 ± 1.9% (RDW at

Table 1
Patient characteristics at baseline ($n = 229$).

Baseline variables	
Age (years), mean ± SD	76.8 ± 11.9
Male sex (%)	130 (56.8%)
Length of hospital stay (days), median (IQR)	12.0 (8.0–18.0)
History of heart failure (%)	81 (35.4%)
History of coronary artery disease (%)	60 (26.2%)
Hypertension (%)	165 (72.1%)
Diabetic mellitus (%)	58 (25.3%)
Atrial fibrillation (%)	76 (33.2%)
RDW at admission (%), mean ± SD	15.0 ± 1.9
Hb (g/dL), mean ± SD	11.8 ± 2.5
CRP (mg/dL), median (IQR)	0.75 (0.20–2.70)
Alb (g/dL), mean ± SD	3.4 ± 0.6
eGFR (mL/min/1.73 m^2), mean ± SD	48.0 ± 29.0
BNP (pg/mL), median (IQR)	813.2 (503.5–1622.2)
LV ejection fraction (%), mean ± SD	48.0 ± 29.0
Ejection fraction ≥50% (%)	123 (53.7%)
Medications	
ACE inhibitors/ARBs (%)	114 (49.8%)
Beta blockers (%)	91 (39.7%)
Calcium channel blockers (%)	72 (31.4%)
Diuretics (%)	109 (47.2%)

SD, standard deviation; RDW, red blood cell distribution width; Hb, hemoglobin; CRP, C-reactive protein; IQR, interquartile range; Alb, albumin; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic protein; LV, left ventricular; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers.

Table 2
Changes in red blood cell distribution width during hospitalization.

Variables	
RDW at admission (%), mean ± SD	15.0 ± 1.9
RDW at admission ≥14.5 (%)	120 (52.4%)
RDW (%), mean ± SD	16.0 ± 2.0
RDW at admission <14.5 (%)	109 (47.6%)
RDW (%), mean ± SD	13.7 ± 0.5
RDW at discharge (%), mean ± SD	15.4 ± 2.5
Changes in RDW	0.0 ± 1.2
Positive change of RDW (%)	82 (35.8%)
RDW change, mean ± SD	1.08 ± 0.13
Negative or static change of RDW (%)	147 (64.2%)
RDW change, mean ± SD	−0.60 ± 0.63

RDW, red blood cell distribution width; SD, standard deviation.