Red cell distribution width as a novel prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction

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Objectives **Red cell distribution width (RDW), a measure of red blood cell size heterogeneity, was evaluated in patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI).**

Background **Higher RDW is associated with mortality in patients with symptomatic cardiovascular disease, heart failure, and also in the general population. We hypothesized that admission RDW would be predictive of adverse outcomes in patients after primary PCI.**

Methods **Two thousand five hundred and six consecutive STEMI patients (mean age 56.6 ± 11.8 years; 2075 males, 431 females) undergoing primary PCI were retrospectively enrolled into this study. Admission RDW was measured as part of the automated complete blood count. Patients were grouped as elevated or nonelevated RDW using the upper limit of normal value of 14.8% and were followed for in-hospital and long-term outcomes for a mean period of 1.8 ± 1.3 years (median 21 months).**

Results **A higher in-hospital mortality rate was observed among patients with elevated admission RDW (mean 16.1 ± 1.6%) compared with those with nonelevated RDW (mean 13.4 ± 0.8%) (7.6 vs. 3.6%, $P < 0.001$). The long-term cardiovascular prognosis was worse for patients with elevated admission RDW (Kaplan–Meier, log-rank $P < 0.001$). We used Cox proportional hazard models to examine the association between RDW and adverse clinical outcomes. After discharge, there were 129 deaths during follow-up. A significant association was noted between elevated admission RDW level and the adjusted risk of cardiovascular mortality (hazard ratio: 1.831, 95% confidence interval: 1.034–3.24, $P = 0.03$). In addition, elevated admission RDW was also an independent predictor of cardiovascular mortality in the nonanemic subpopulation of patients (hazard ratio: 2.703, 95% confidence interval: 1.208–6.048, $P = 0.016$).**

Conclusion **A high admission RDW level in patients with STEMI undergoing primary PCI was associated with increased risk for in-hospital and long-term cardiovascular mortality.** *Coron Artery Dis* **22:138–144 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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Introduction

Red cell distribution width (RDW) is a measure of variation in the size of circulating erythrocytes [1]. RDW is routinely used by physicians in clinical practice as part of the automated complete blood count (CBC); in particular it is mainly used for the differential diagnosis of anemia [2].

Recent studies have reported a strong independent association between high RDW and the risk of adverse outcomes in patients with heart failure [3,4], cardiovascular disease [5,6], acute coronary syndrome [7], acute myocardial infarction (MI) [8], and also in the general population [9,10]. However, to the best of our knowledge, no study regarding the prognostic effect of RDW after primary percutaneous coronary intervention (PCI) exists in the literature.

The aim of this study was to test, in a large population, the hypothesis that elevated RDW levels are associated with increased risk of in-hospital and long-term cardiovascular mortality after primary PCI for ST-segment elevation MI (STEMI).

Methods

Patient population

We retrospectively evaluated 2825 consecutive patients with acute STEMI who were admitted to the emergency department of our hospital and underwent urgent cardiac

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catheterization procedures in our catheter laboratory between October 2003 and March 2008. Patients were enrolled in the study if they fulfilled the following criteria: (i) if they presented within 12 h (18 h for cardiogenic shock) from the onset of symptoms (typical chest pain lasting for > 30 min), (ii) if there was ST-segment elevation of at least 2 mm in at least two contiguous electrocardiography (ECG) leads or new onset of complete left bundle-branch block, (iii) patients with primary PCI (angioplasty and/or stent deployment). Three hundred and nineteen patients were excluded because of no indication for PCI ($n = 96$), coronary bypass surgery was not suitable for PCI ($n = 85$), missing or unavailable RDW ($n = 92$), and no follow-up ($n = 46$). Therefore, the final study population consisted of 2506 patients. The study protocol was approved by the hospital's ethics committee.

Analysis of patient data

A clinical history of risk factors such as age, sex, diabetes mellitus (DM), hypertension, hypercholesterolemia, smoking, family history of cardiovascular disease, MI history, PCI, or bypass history was determined from medical records. Angina-to-reperfusion time and door-to-balloon time were also determined.

Blood values (including hemoglobin and RDW) that were determined at hospital admission (before catheterization procedures) were recorded from medical reports. Hemoglobin and RDW were measured as part of the automated CBC using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland Inc., Mervue, Galway, Ireland) (normal range: 11.6–14.8%).

A 12-lead ECG was recorded in each patient immediately after hospital admission. In addition, MI type was recorded from the ECGs.

The glomerular filtration rate was estimated by the simplified Modification of Diet in Renal Disease equation [11,12].

We obtained echocardiographic data from patients' records. A transthoracic echocardiography was performed using a system V (Vingmed, GE, Horten, Norway) with a 2.5 MHz phased-array transducer. Recordings were taken with patients positioned in the left lateral decubitus position. The left ventricular ejection fraction was measured using the modified Simpson's rule [13].

Coronary angiography, primary angioplasty, and stenting

All patients received chewable aspirin (300 mg, unless contraindicated) and oral clopidogrel (300 mg loading dose) before coronary angiography. The patients' angiographic data were evaluated from catheter laboratory records. Emergency coronary angiography was performed by the percutaneous femoral approach. In all cases, a nonionic low-osmolality contrast media was used. First, the contralateral artery was injected. The infarct-related artery (IRA) was graded according to thrombolysis in MI classification [14]. Heparin (10 000 U) was administered when coronary anatomy was first defined. Coronary artery stenosis greater than 50% was considered clinically significant. Occlusion of the IRA was crossed by using a 0.014-inch guide wire. Primary coronary interventions, including balloon angioplasty and/or stent implantation, were performed only on the IRA. For each procedure, procedural success during the acute phase was defined as an obstruction and stenosis of the IRA having been reduced to less than 50% stenosis with thrombolysis in MI 2 or 3 flow after primary PCI. After angioplasty, all patients were admitted to the coronary care unit, where 500 U/h of intravenous heparin or 1 mg/kg/day of subcutaneous low-molecular weight heparin was administered; 100 mg aspirin and 75 mg clopidogrel were continued in all patients. The use of tirofiban was left to the discretion of the operator.

Definitions

Reperfusion time was defined as the time from onset of chest pain to first balloon inflation. Door-to-balloon time was defined as the time between hospital admission and balloon inflation. Admission anemia was defined as a baseline hemoglobin concentration less than 13 mg/dl in men and less than 12 mg/dl in women (WHO definition). Cardiogenic shock was defined as marked and persistent (> 30 min) hypotension with systolic arterial pressure of less than 80 mmHg with signs of hypoperfusion because of left ventricular dysfunction, right ventricular infarction, and mechanical complications. Patients were also evaluated according to the Killip clinical examination classification [15]. Advanced heart failure was defined as a New York Heart Association classification of at least 3. Multivessel disease was defined by a stenosis of greater than 50% in three major epicardial coronary arteries. DM was defined by treatment with oral hypoglycemic agents or insulin. Hypercholesterolemia was defined as total cholesterol of at least 200 mg/dl. Acute stent thrombosis was defined as the abrupt onset of cardiac symptoms (i.e. an acute coronary syndrome) along with an elevation in the levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment in the first 24 h, which was accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent.

Cardiovascular mortality was defined as unexplained sudden death, death as a result of acute MI, heart failure, and arrhythmia. Reinfarction was defined as an elevation of serum CK-MB enzyme levels by twice the upper limit of normal and ST-segment reelevations.

Follow-up

Follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their personal physicians. Major adverse cardiac events (MACE) were defined as cardiovascular

mortality, reinfarction, repeat target-vessel revascularization (percutaneous or surgical). Only cardiovascular mortality was recorded. Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), stroke, cardiopulmonary resuscitation, advanced heart failure, atrioventricular block, transient pace intervention, intra-aortic balloon pump, atrial fibrillation, major bleeding requiring at least 2 U of blood, dialysis, acute stent thrombosis, and MACE were also recorded during the in-hospital period.

Statistical analysis

Patients were grouped as either an elevated or a nonelevated RDW using the upper limit of normal value of 14.8%. Quantitative variables were expressed as mean value ± standard deviation, and qualitative variables were expressed as a percentage. A comparison of the parametric values between the two groups was performed by a two-tailed Student's *t*-test. Categorical variables were compared by the likelihood ratio χ^2 test or Fisher's exact test. A backward stepwise multivariate Cox regression analysis, which included variables with *P* value less than 0.1 was performed to identify independent predictors of cardiovascular mortality. Sex, age, time-to-reperfusion greater than 6 h, DM, hypertension, smoking habit, glomerular filtration rate less than 60 ml/min/1.73 m^2, multivessel disease, unsuccessful procedure, anterior MI, admission anemia, blood transfusion, killip greater than 1, RDW greater than 14.8 were entered into the model. The cumulative survival curve for cardiovascular mortality was constructed using the Kaplan–Meier method with differences assessed by the log-rank test. A *P* value less than 0.05 was considered statistically significant. All statistical studies were carried out with the SPSS program (version 15.0, SPSS, Chicago, Illinois, USA).

Results

Patient characteristics

The baseline characteristics of the two groups are summarized in Table 1. Among the 2506 study patients (mean age 56.6 ± 11.8 years; 2075 males, 431 females), RDW ranged from 9.7 to 28.4% (median 13.6%, mean 13.8 ± 1.36%); and 422 patients (16.8%) had RDW levels outside the normal range of 11.6–14.8% with RDW less than 11.6 [*n* = 52 (2.1%)] and greater than 14.8 [*n* = 370 (14.8%)].

Patients with elevated RDW were more likely to be female, significantly older, and more commonly had hypertension, PCI, MI history, and a more advanced Killip class. However, smoking and hypercholesterolemia were less in the elevated RDW group (Table 1).

Laboratory findings

Table 2 lists the patients' laboratory data. Basal renal failure and anemia were more frequent in the elevated RDW group. Surprisingly, hypercholesterolemia and dyslipidemia were more common in patients with nonelevated RDW. A similar enzymatic peak was observed in the two groups (Table 2).

Angiographic and procedural characteristics

Angiographic and procedural characteristics are depicted in Table 3. The mean left ventricular ejection fraction and the rate of successful procedures were less in patients with elevated RDW (Table 3). The other angiographic and procedural data were the same between the groups.

In-hospital outcomes

Table 4 presents the in-hospital adverse outcomes after primary PCI. The in-hospital mortality rate was double in patients with elevated RDW than in those with nonelevated RDW (7.6 vs. 3.6%, $P < 0.001$). MACE were more frequent (10.8 vs. 7.6%, $P = 0.04$) and the length of hospital stay longer (8.2 vs. 7.1 days, $P = 0.003$) in patients with elevated RDW than in those with nonelevated RDW. There were more complicated in-hospital outcomes in patients with elevated RDW, with a higher

Table 1 Baseline characteristics of study patients

	Nonelevated RDW (≤ 14.8%) (*n*=2136)	Elevated RDW (>14.8%) (*n*=370)	*P* value
Age (years)	55.8 (11.5)	61.1 (12.4)	<0.001
Age ≥ 75 (years)	147 (6.9)	54 (14.6)	<0.001
Male	1794 (84)	281 (75.9)	<0.001
Anterior myocardial infarction	1043 (48.8)	184 (49.7)	0.75
Hypertension	823 (38.5)	162 (43.8)	0.04
Hypercholesterolemia	741 (34.7)	108 (29.2)	0.05
Diabetes mellitus	514 (24.1)	102 (27.6)	0.14
Current smoker	1264 (59.2)	185 (50)	0.02
Family history for cardiovascular disease	359 (16.8)	47 (12.7)	0.06
By pass	57 (2.7)	15 (4.1)	0.14
Percutaneous coronary intervention	155 (7.3)	46 (12.4)	0.001
Myocardial infarction history	201 (9.4)	67 (18.1)	<0.001
Admission cardiogenic shock	58 (2.7)	14 (3.8)	0.2
Killip >1	128 (6)	37 (10)	0.001
Reperfusion time (h)	3.2 (2.4)	3.4 (2.4)	0.3
Door-to-balloon time (min)	34 (23)	30 (21)	0.56

Mean values (standard deviation) and % (*n*) are reported for continuous and categorical variables, respectively.
RDW, red cell distribution width.

Table 2 Laboratory findings of patients

	Nonelevated RDW (≤ 14.8%) ($n=2136$)	Elevated RDW (>14.8%) ($n=370$)	*P* value
Creatinine concentration at admission (mg/dl)	0.97 (0.3)	1.13 (0.8)	<0.001
Admission GFR (MDRD) <60 ml/min/1.73 m^2	229 (10.7)	79 (21.4)	<0.001
RDW (%)	13.4 (0.8)	16.1 (1.6)	<0.001
Hemoglobin (g/dl)	13.8 (1.6)	12.7 (2.3)	<0.001
Peak CK-MB (U/l)	216.5 (181.9)	231.5 (186.9)	0.15
Total cholesterol (mg/dl)	189.4 (42.2)	182.1 (43.9)	0.008
LDL cholesterol (mg/dl)	118.4 (35.3)	110.9 (34.3)	0.002
HDL cholesterol (mg/dl)	40.6 (9.1)	41.8 (9.1)	0.05
Triglycerides (mg/dl)	153.3 (105)	139.4 (125.3)	0.06
Admission blood glucose concentration (mg/dl)	156.4 (77.4)	157.6 (70.5)	0.8
Anemia at admission	462 (21.6)	163 (44.1)	<0.001

Mean values (standard deviation) and % (*n*) are reported for continuous and categorical variables, respectively.
GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MDRD, modification of diet in renal disease; RDW, red cell distribution width.

Table 3 Angiographic and procedural characteristics of patients

	Nonelevated RDW (≤ 14.8%) ($n=2136$)	Elevated RDW (>14.8%) ($n=370$)	*P* value
Culprit lesion			0.75
Left main coronary artery	2 (0.1)	0 (0)	
Left anterior descending coronary artery	1051 (49.2)	185 (50)	
Circumflex coronary artery	271 (12.7)	50 (13.5)	
Right coronary artery	790 (37)	134 (36.2)	
Bypass graft	18 (0.8)	1 (0.3)	
Intermedier artery	4 (0.2)	0 (0)	
Number of diseased vessels			0.1
1	914 (42.8)	137 (37)	
2	688 (32.2)	130 (35.1)	
3	534 (25)	103 (27.8)	
Pre-TIMI grade			0.74
0/1	1878 (87.9)	322 (87)	
2	167 (7.8)	33 (8.9)	
3	91 (4.3)	15 (4.1)	
Post-TIMI grade			0.29
0/1	189 (8.8)	43 (11.6)	
2	110 (5.2)	22 (5.9)	
3	1837 (86)	305 (82.5)	
Stent	1772 (83)	298 (80.5)	0.33
Stent length (mm)	19.2 (6.7)	19.7 (7.1)	0.3
Stent diameter (mm)	3.11 (0.35)	3.13 (0.36)	0.55
Stent type			0.73
Bare metal stent	1721 (97.1)	286 (96)	
Paclitaxel eluting stent	22 (1.2)	5 (1.7)	
Sirolimus eluting stent	29 (1.6)	7 (2.3)	
Proximal location of the lesion	1138 (53.3)	193 (52.2)	0.63
Left ventricular ejection fraction (%)	47.9 (11.1)	45 (11.5)	0.001
Tirofiban	1026 (48)	185 (50)	0.52
Success of the procedure	1940 (90.8)	325 (87.8)	0.07

Mean values (standard deviation) and % (*n*) are reported for continuous and categorical variables, respectively.
RDW, red cell distribution width; TIMI, thrombolysis in myocardial infarction.

incidence of advanced heart failure, higher percentage of cardiopulmonary resuscitation, intra-aortic balloon pump, dialysis, and blood transfusion (Table 4).

Long-term prognosis

The median follow-up time was 21 months. Table 5 presents the long-term adverse outcomes. The Kaplan–Meier survival plot for cardiovascular death is presented in Fig. 1. Cardiovascular mortality, MACE, and advanced heart failure were significantly higher in patients with elevated RDW. The elevated RDW group had a trend toward a higher incidence of reinfarction. Independent predictors of cardiovascular mortality were determined by Cox proportional hazards analysis. Elevated RDW was independently associated with an 83% increase in the hazard of long-term cardiovascular mortality [hazard ratio: 1.831, 95% confidence interval: 1.034–3.24, $P = 0.03$] (Table 6).

The nonanemic subpopulation

In the elevated RDW group, hemoglobin levels were low and anemia was more frequent. As far as anemia has been an independent risk factor associated with mortality in patients with acute coronary syndromes [16], additional analyses were therefore performed in the subpopulation of patients who were not anemic on presentation. A total of 1881 (75.1%) patients were classified as nonanemic. In this subgroup of patients, there were a total of 73 deaths

Table 4 In-hospital cardiac events and complications

	Nonelevated RDW (≤ 14.8%) (n=2136)	Elevated RDW (>14.8%) (n=370)	P value
In-hospital mortality	76 (3.6)	28 (7.6)	<0.001
Reinfarction	46 (2.2)	5 (1.4)	0.31
Target-vessel revascularization	97 (4.5)	15 (4.1)	0.68
MACE	163 (7.6)	40 (10.8)	0.04
Stroke	13 (0.6)	4 (1.1)	0.31
Serious ventricular arrhythmia	99 (4.6)	21 (5.7)	0.39
Cardiopulmonary resuscitation	91 (4.3)	31 (8.4)	0.001
Advanced heart failure	261 (12.2)	79 (21.4)	<0.001
Intra-aortic balloon pump	91 (4.3)	27 (7.3)	0.01
Renal failure requiring dialysis	9 (0.4)	9 (2.4)	<0.001
New atrial fibrillation	30 (1.4)	7 (1.9)	0.47
Complete atrioventricular block requiring transient pacemaker	80 (3.7)	15 (4.1)	0.77
Major bleeding requiring blood transfusion	71 (3.3)	30 (8.1)	<0.001
Acute stent thrombosis	20 (0.9)	2 (0.5)	0.45
Time of hospital stay (days)	7.1 (4.4)	8.2 (5.5)	0.003

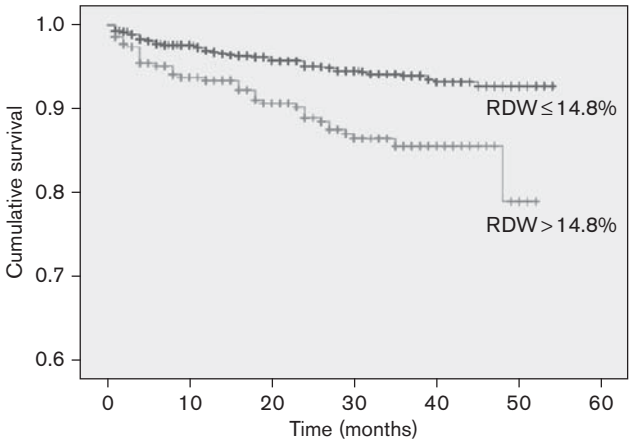
Mean values (standard deviation) and % (n) are reported for continuous and categorical variables, respectively.
MACE, major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization); RDW, red cell distribution width.

Table 5 Long-term cardiac events

	Nonelevated RDW (≤ 14.8%) (n=2060)[a]	Elevated RDW (>14.8%) (n=342)[b]	P value
Cardiovascular mortality	90 (4.4)	39 (11.4)	<0.001
Reinfarction	161 (7.8)	35 (10.2)	0.08
Target-vessel revascularization	332 (16.1)	50 (13.5)	0.81
MACE	436 (21.2)	90 (26.3)	0.01
Advanced heart failure	144 (7)	38 (11.1)	0.003

% (n) are reported for categorical variables.
MACE, major adverse cardiac events (cardiovascular death, reinfarction, target-vessel revascularization); RDW, red cell distribution width.
[a]n=2060 for low RDW (76 patients died in-hospital).
[b]n=342 for high RDW (28 patients died in-hospital).

Fig. 1



Kaplan–Meier curve for long-term survival according to red cell distribution width (RDW) groups in the entire cohort of patients (P<0.001 by log-rank test).

during follow-up. After adjustment for covariates that were the same for the entire group, elevated RDW remained independently associated with a 2.7-fold increase in the risk of long-term cardiovascular mortality (hazard ratio: 2.703, 95% confidence interval: 1.208–6.048, P = 0.016) (Table 7). Similar to the entire group, the Kaplan–Meier survival plot for cardiovascular death for the nonanemic subpopulation showed a significantly reduced survival rate in patients with elevated RDW (Fig. 2).

Table 6 Multivariate predictors of long-term cardiovascular mortality in the entire cohort of patients

Variables	Wald	HR	95% CI	P value
Age	28.4	1.073	1.045–1.101	<0.001
Diabetes mellitus	14.4	2.74	1.626–4.599	<0.001
Killip >1	19.7	4.284	2.253–8.145	<0.001
Admission anemia	7.7	2.14	1.25–3.666	0.006
RDW >14.8%	4.3	1.831	1.034–3.24	0.03

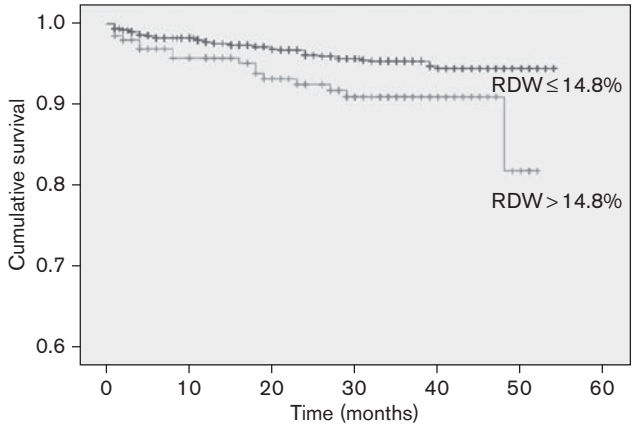
Sex, time-to-reperfusion >6 h, hypertension, smoking habit, glomerular filtration rate <60 ml/min/1.73 m^2, multivessel disease, unsuccessful of the procedure, anterior myocardial infarction, blood transfusion were also entered into the Cox model.
CI, confidence interval; HR, hazard ratio; RDW, red cell distribution width.

Table 7 Multivariate predictors of long-term cardiovascular mortality in the nonanemic subpopulation of patients

Variables	Wald	HR	95% CI	P value
Age	11.9	1.065	1.028–1.104	0.001
Diabetes mellitus	11.7	3.616	1.73–7.557	0.001
Killip >1	11.8	4.502	1.907–10.628	0.001
RDW >14.8%	5.9	2.703	1.208–6.048	0.016

Sex, time-to-reperfusion >6 h, hypertension, smoking habit, glomerular filtration rate <60 ml/min/1.73 m^2, multivessel disease, unsuccessful of the procedure, anterior myocardial infarction, blood transfusion were also entered into the Cox model.
HR, hazard ratio; CI, confidence interval; RDW, red cell distribution width.

Fig. 2



Kaplan–Meier curve for long-term survival according to red cell distribution width (RDW) groups in the non-anemic subpopulation of patients ($P=0.009$ by log-rank test).

Discussion

This is the first study to evaluate the impact of admission RDW levels in patients undergoing primary PCI for STEMI. Elevated RDW was independently associated with an increase in in-hospital, long-term mortality, and longer hospital stay. Elevated RDW was one of the strongest independent predictors of diminished survival.

RDW is a marker of variation in the size of circulating red cells (anisocytosis) and is routinely reported by analyzers as part of the routine CBC [1]. The formula for RDW is standard deviation of red cell volume/mean cell volume $\times$ 100. So elevated RDW means that there is heterogeneity of cell sizes in the peripheral blood smear [17,18]. Elevated RDW levels can be seen in hemolysis, nutritional deficiencies such as iron, vitamin B12, and folate, or after blood transfusion [6]. In thrombotic thrombocytopenic purpura, inflammatory bowel diseases, and pregnancy, RDW levels can be high [19]. Only hemoglobin levels were measured in this study, and other factors including, iron, vitamin B12, and folate were not measured. In this study, some of the underlying pathologic processes may have been present, but elevated RDW remained an independent risk factor after adjusting for anemia and blood transfusions. Thus, heterogeneity of red blood cell sizes is associated with worse clinical outcomes even in the absence of anemia.

Over the last few years, studies on the association of RDW with cardiovascular mortality and morbidity have been carried out in different populations. In 2007, for the first time, in two large heart failure populations (CHARM and DUKE Databank), RDW was found to be a very strong independent predictor of morbidity and mortality [3]. Tonelli *et al.* [5] performed an analysis of the data from the CARE study. They found an independent relation between higher RDW levels and the risk of death and cardiovascular events in people with prior MI. In another study, Cavusoglu *et al.* [7] showed that elevated RDW was a strong independent predictor of all-cause mortality in an unselected population of male patients referred for coronary angiography. Patel *et al.* [9] measured RDW in a healthy sample of 8175 adults aged 45 years and older, and found that for every 1% increment in RDW, the all-cause mortality risk increased by 22%. Recently, Dabbah *et al.* [8] reported that there was a graded, independent association between increased RDW and mortality after STEMI. Their results indicated that an increase in RDW during hospitalization was predictive of adverse clinical outcome. There was heterogeneity in the treatment of patients; reperfusion therapy was administered in 24.5% of patients and primary angioplasty was performed in 28.6% of patients. However, in our study, primary angioplasty was performed in all patients.

The precise mechanism is not clear. Elevated RDW levels may reflect the production of humoral mediators by the bone marrow. In acute STEMI, infarction-related inflammatory cytokines and neurohumoral mediators are activated. In experimental studies, inflammatory cytokines have been found to suppress the maturation of erythrocytes, so immature erythrocytes enter into the circulation [20]. Neurohumoral states may accelerate erythropoiesis [21,22]. In addition, the plasma erythropoietin level increases in STEMI [23]. These conditions lead to an increase in the heterogeneity of circulating erythrocytes [24]. There is evidence that humoral mediators contribute to adverse clinical outcomes [25,26]. For example, angiotensin II may affect erythropoiesis by regulating erythropoietin levels and through a direct stimulation of erythroid progenitor cells [21]. Adrenergic activation may also affect bone marrow response in patients with STEMI [27,28]. There could be a genetic contribution to red cell size in the general population that can also be important in disease states [29].

Not surprisingly, RDW levels were high in older patients. This was because older patients more commonly had a higher inflammatory burden, hypertension, anemia, bad nutritional status, and age-associated diseases. Genetic contribution may explain elevated RDW levels in females. Hypertension was observed more in the elevated RDW group, but DM frequency was not different between the groups. We could not accurately estimate DM prevalence because approximately 4% of patients admitted with STEMI were newly diagnosed with DM. Surprisingly, total cholesterol, LDL cholesterol and triglyceride levels were low, and HDL cholesterol levels were high in the elevated RDW group. However, we have no meaningful explanation for this contradiction.

Study limitations

This study is subject to the usual limitations of retrospective design. We were able to show the independent

adverse effects of elevated RDW, but we could not determine the exact mechanism for the association between RDW and clinical outcomes. We did not look at high sensitive C-reactive protein, B-type natriuretic peptide, other proinflammatory cytokines, plasma levels of angiotensin II, erythropoietin, or markers of oxidative stress. Despite adjusting for multiple risk factors, it is possible that there may have been residual confounding conditions and medications; for example, iron, folate, and vitamin B_{12}. In addition, RDW was assessed only once. We have no data on any changes in RDW levels during the course of hospital stay.

Conclusion

This study shows that elevated RDW is associated with worse clinical outcomes, longer hospital stays, and higher mortality, both in-hospital and post-discharge, than patients with nonelevated RDW. In summary, RDW is an inexpensive and powerful prognostic factor in patients undergoing primary angioplasty for STEMI. We hope this study will stimulate a prospective investigation, including the potential role of confounding factors, in patients with STEMI.

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