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Red cell distribution width (RDW) correlates with markers of diastolic dysfunction in patients with impaired left ventricular systolic function

Fadi T. Alattar [a], Nashat B. Imran [b,*], Pooja Patel [c], Saad Usmani [c], Fayez E. Shamoon [a]

[a] Cardiology department, Saint Michael's Medical Center, Newark, NJ, USA
[b] Nephrology Division, Internal Medicine Department, Wayne State University, Detroit, Michigan, USA
[c] Internal medicine department, Trinitas Regional Medical Center, Elizabeth, NJ, USA

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ABSTRACT

Objective: Red-cell distribution width (RDW) has been identified as a novel prognostic marker in a heterogeneous group of heart failure patients. In this group, diastolic dysfunction is associated with worse outcome. As the evidence is limited, the aim of the present study was to assess the relationship of RDW to diastolic markers in patients with left ventricular dysfunction (LVD) diagnosed during cardiac catheterization.
Methods: Clinical and angiographic data were collected retrospectively on a total of 291 stable patients (mean age 62 years, 199 males) with systolic dysfunction documented during cardiac catheterization in a regional medical center between January 2006 and December 2010.
Results: Positive association was seen between RDW and Left ventricular end diastolic pressure (LVEDP), estimated systolic pulmonary arterial pressure(sPAP), and left atrial dimension (LAD) (r: 0.18, 0.24, 0.28, respectively; p:<0.05).Three year retrospective survival analysis for 108 patients admitted in the first 2 years showed a statistically significant decrease in survival patients with high RDW(>14.5) vs. normal RDW (73%vs.88%;log rank p:0.03). This was seen even in the asymptomatic subgroup (71% vs. 94%; log rank p: 0.01).
Conclusion: RDW correlates with markers of diastolic dysfunction in patients with LVD. Additionally, in patients asymptomatic LVD, high RDW is still associated with lower survival.

1. Introduction

Red cell distribution width (RDW) is a readily available test from a standard full blood count, and is a measure of variation in red blood cell size. It has been shown in many studies to be a powerful predictor of outcome in heart failure patients [1–3]. Most of these studies enrolled patients with congestive symptoms and some included patients with preserved systolic function. Among other predictors of worse outcome in heart failure population is the presence of diastolic dysfunction [4,5]. In this work, we sought to study the correlation between RDW and markers of diastolic dysfunction in patients with symptomatic and asymptomatic LVD.

2. Methods

Medical and angiographic records of patients who underwent elective cardiac catheterization in a 500-bed teaching community hospital in urban New Jersey from January 2006 to December 2010 were retrospectively reviewed. Patients with normal EF on left ventriculogram, iron deficiency anemia, positive hemoccult blood, Hemoglobin <10 g/dL, cancer, AIDS, elevated tropinins, or stage III-V chronic kidney disease were excluded. Data regarding estimated ejection fraction (EF), number of diseased vessels, and Left ventricular end diastolic pressure (LVEDP) were retrieved from cardiac catheterization reports. If right heart catheterization was not performed, systolic pulmonary artery pressure was estimated using tricuspid regurgitation velocity, in addition to estimated right atrial pressure from transthoracic echocardiography in the same admission. Echocardiography reports were also used to assess chamber dimension and size. Other demographic and clinical data were collected from the electronic medical records of those patients. All-cause mortality data were obtained from social security death index for patients in the first 2 years of the study to calculate the 3 year retrospective survival analysis. The study was conducted in Trinitas Regional Medical Center, where it was approved by the Institutional Review Board.

Highest RDW and brain natriuretic peptide (BNP) results during the index admission were recorded. Patients were considered to have symptomatic LVD if they were known to have symptoms and signs of heart failure at, or before the time of catheterization. Non-ischemic cardiomyopathy (NICD) was defined as the presence of LVD with no

* Corresponding author.
E-mail address: nimran@med.wayne.edu (N.B. Imran).

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obstructive lesion (stenosis >50%) in any of the three coronary arteries or their major branches.

3. Statistical analysis

Interval variables were tested for normality using the D'Agostino-Pearson omnibus normality test. Groupwise comparisons for normally distributed variables were made using Student's t test; variables that were not normally distributed were subjected to a nonparametric (Mann–Whitney) test. For non-normally distributed data, medians and interquartile ranges (IRs) are provided; for normally distributed variables, data are expressed as means and standard deviations (SDs). Categorical data were compared using Fisher's exact test. Odds Ratios (OR) and 95% confidence intervals (CIs) are provided. Spearman's rank correlation coefficient was used to measure the statistical association between two non-normally distributed variables. Logistic regression was used to adjust ORs for differences in baseline characteristics if the P value for the difference between the groups was less than 0.05. For the present study, α was set at 0.05; thus, $P < 0.05$ (two-sided) was considered to be statistically significant. Data were analyzed using Prism software (GraphPad Corp, USA), except for logistic regression, which was performed using an online routine (available at www.stat-pages.org/logistic.html; accessed on July, 14, 2011). Retrospective survival analysis was done using Kaplan–Meier curve with log rank test.

4. Results

We reviewed the angiographic reports of 2150 patients, of them 291 patients were included (199 men, mean age 61.9 ± 13.5 yr). This cohort was divided into 2 groups, Group 1 (patients with high RDW) included 117 patients, and Group 2 (normal RDW group) included 174 patients (Table 1). Ischemic cardiomyopathy (ICD) was found in 169 patients, and non-ischemic cardiomyopathy (NICD) was found in the remaining 122 patients. Symptomatic LVD was found in 41% of the group. Patients with high RDW were more likely to be symptomatic (OR 4.5 (2.7–7.4; p: <0.0001)), more likely to have non- ischemic cardiomyopathy (OR: 2.9 (1.8–4.7; p: <0.0001)).They were more likely to have lower EF (median EF 35% (IR: 25–40%) vs. normal RDW median EF 40% (IR 30–45%); p:0.0007), higher BNP (median BNP: 907 pg/ml (IR: 253–1923) vs.347 pg/ml (IR: 127–676); p: <0.0001), larger LAD (median LAD 4.17 cm (3.65–4.80) vs. normal RDW median LAD 3.78 cm (IR: 3.38–4.2); p: <0.0001).There was also a trend toward having more atrial fibrillation in group 1 vs. group 2 (OR: 1.9 (1.01–3.06); p: 0.08), and larger left ventricular end diastolic volume index(LVEDVI) (68 ml/m^2 in group 1 vs. 61 ml/m^2 in group 2; p: 0.05). Differences in LVEDP did not reach statistical significance (group 1 LVEDP 18 vs. 16 mm Hg in group 2, p: 0.09) (Table 2). In the symptomatic group, patients who had high RDW were more likely to have abnormal maximum left ventricular dP/dt (OR: 6 (1.3–28); p: 0.04). NICD patients were more likely to have abnormal RDW in comparison to ICD patients (OR: 2.9 (1.783–4.715); p: <0.001). This was independent of the presence of symptoms, or severe LVD (EF < 30%) (p value for interaction >0.05).In this study, Hypertension was the presumed etiology in 67% of NICD patients. The latter group were relatively younger than ICD patients (median age 57 yr. (47–68) vs ICD 65 yr. (54–75)),they were less likely to be on statins(OR: 0.4 (0.24–0.68); p: 0.005), and they were found to have larger ventricles(median LVEDVI 74 ml/m^2 vs. 64 ml/m^2; p: 0.006).

In addition to the well-established correlation between RDW and MCV, creatinine, BUN, EF, we found a modest but statistically significant correlations between RDW and LAD (r: 0.28; p: <0.0001), sPAP(r: 0.24; p: 0.0028), LVEDP (r: 0.18; p: 0.039), and BNP (r: 0.3; p: <0.0001) (Table 3, Figs. 1, 2, and 3).

Data for 108 patients (52 patients asymptomatic) from the period (Jan 2006 to Dec. 2007) were included in 3-year retrospective survival analysis, and they were divided according to RDW into 2 groups. Three year survival was higher in the patients with LVD and normal RDW vs. high RDW (88% vs. 73%; log rank p: 0.03) (Fig. 4).This was also seen even in the asymptomatic patients (normal RDW group 94% vs. high RDW group 71%; log rank p: 0.01) (Fig. 5).Survival curves were not different in the symptomatic group between high and normal RDW group (log rank p: >0.05).

5. Discussion

High RDW values have been shown to be independently related to increased mortality and cardiovascular events in people with congestive heart failure [1–3], acute coronary syndrome [6,7], and in patients referred for coronary angiography [8]. This study extends the prognostic value of RDW to all patients with systolic LVD even the asymptomatic group, a group that is less presented in other studies.

As this correlation was independent of hemoglobin level in most of the studies [1–4,9], RDW is presumed to reflect the degree of neurohormonal activation in HF patients [10,11]. Not surprising was our finding that RDW correlates with BUN and BNP, two other markers of neurohormonal activation [12].

Table 1
Abbreviations: ACEi/ABR blockers: angiotensin converting enzyme inhibitors/angiotensin receptor blockers; BMI: body mass index; BNP: brain natriuretic peptide; BUN: blood urea nitrogen; Cr: creatinine; Hb: hemoglobin, Na: serum sodium.

	Group 1 (RDW > 14.5%) 117 patients	Group 2 (RDW ≤ 14.5%) 174 patients	P value
Age (mean)	61 ± 13 years	62 ± 14 years	0.6
Male gender	79	120	0.8
Race			<0.0001
Caucasians	38 (33%)	75(43%)	
Hispanics	23 (20%)	60 (35%)	
Blacks	56 (47%)	39(22%)	
Diabetes	49	71	0.9
Hypertension	94	122	0.06
Dyslipidemia	55	80	0.9
Smoking	57	70	0.16
BMI (kg/m^2)	28 (25–32)	28 (25–32)	0.4
Symptoms of CHF	73	47	<0.0001
Atrial fibrillation	25	22	0.08
Cr (mg/dl)	0.9 (0.8–1.1) mg/dl	1.1 (0.9–1.3) mg/dl	<0.0001
BUN (mg/dl)	14 (11–18)	16 (12–24)	0.005
Na (meq/dl)	137 (136–140) meq/dl	137(136–140)	0.38
BNP (pg/ml)	907 (252–1923)	348 (128–676)	<0.0001
Hb (gm/dl)	13.3 (12.3–14.2)	14 (12.7–14.9)	0.003
Medications			
Beta blockers	52	76	0.9
ACEi./ARB Blockers	70	75	0.006
Statins	41	65	0.7
Diuretics	41	48	0.07
Digoxin	17	9	0.005
warfarin	11	11	0.3

Table 2
Abbreviations: L. A.: left atrium; LVEDP: left ventricular end diastolic volume; LVEDVI: left ventricular end diastolic volume index; LVIDd: left ventricular internal dimension in diastole, LVIDs: left ventricular internal dimension in sytole; sPAP: systolic pulmonary artery pressure.

	Group1	Group 2	P value
Ejection fraction	35%(25–40)	40% (30–45)	0.0007
Diseased vessels			<0.0001
None	67(57%)	55 (31%)	
Single vessel	15 (13%)	39 (22%)	
Two vessels	20 (17%)	31 (18%)	
Three vessels	15 (13%)	49 (29%)	
LVEDP (mm Hg)	18 (12–25)	16 (11–21)	0.09
Maximum LV dP/dt (mm Hg/s)	1171 (965–1471)	1340 (1109–1564)	0.2
L.A. Dimension(cm)	3.8 (3.4–4.2)	4.2 (3.7–4.8)	<0.0001
LVEDVI (ml/m^2)	68 (53–86)	62 (50–77)	0.05
LVIDd (cm)	5.4 (4.9–6.3)	5.6 (4.9–6.3)	0.7
LVIDs(cm)	4.1(3.6–5)	3.9(3.5–4.8)	0.4
Estimated sPAP (mm Hg)	27 (16–46)	21(15–29)	0.009