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ORIGINAL ARTICLE

Red Blood Cell Distribution Width is Associated with Poor Clinical Outcome After Subarachnoid Hemorrhage: A Pilot Study

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Abstract

Introduction The red cell distribution width (RDW) is a biomarker strongly associated with poor outcome in inflammatory and thrombotic diseases. Subarachnoid hemorrhage (SAH) is both an inflammatory and thrombotic state in which many biomarkers have been studied. In this exploratory pilot study, we sought to determine whether RDW predicts poor outcome in patients with SAH.

Methods Patients with moderate-to-severe SAH were prospectively enrolled in an observational study of biomarkers and outcome. CBC, ESR, high sensitivity CRP, D-dimer, and fibrinogen were obtained on post-bleed days (PBD) 1, 3, 5, 7, and 10. Poor outcome was defined as a modified Rankin score of 3–6 at 90-days.

Results Of 40 patients, 5 (12.5 %) died and 19 (47.5 %) had a poor outcome. RDW ($p = 0.046$) when measured serially over the study period, was significantly higher among patients with poor outcome. Maximum RDW (OR 2.3 95 % CI 1.2–3.6; $p = 0.014$) and maximum WBC count (OR 1.29 95 % CI 1.04–1.60; $p = 0.018$) were associated with poor outcome. Stepwise addition of maximum ESR, CRP, D-dimer, and fibrinogen yielded a model with RDW (OR 2.54 95 % CI 1.21–5.35; $p = 0.014$) and fibrinogen (OR 1.01 95 % CI 1.002–1.01; $p = 0.004$) predicting outcome. With addition of age and Hunt and Hess grade, RDW, fibrinogen, and high-grade status remained significantly associated with poor outcome. Use of PBD1 RDW in lieu of maximum RDW, resulted in a similar model.

Conclusions An elevated RDW is associated with poor outcome in SAH patients. RDW may be a useful predictor of outcomes after SAH.

Keywords RDW · SAH · Biomarker · Outcomes · Aneurysm stroke

Introduction

The ideal biomarker permits accurate risk stratification, measures response to treatment, identifies patients for targeted therapies, and correlates with long-term outcomes. The red cell distribution width (RDW), a biomarker strongly associated with mortality and poor outcomes in inflammatory [1–3] and thrombotic [4, 5] disease states, has the added advantage of being routinely and serially obtained in the hospital setting. Subarachnoid hemorrhage (SAH) is both an inflammatory and thrombotic disease

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state in which many biomarkers have been studied [6–9]. However, little attention has been paid to the RDW.

The RDW, a parameter of red cell size, measures the variability in size of circulating erythrocytes [10]. Although primarily used in conjunction with mean corpuscular volume (MCV) to diagnose different types of anemias, the RDW is also associated with poor outcome in critically ill patients [2, 11–15]. An increased RDW is an independent risk factor for poor outcome in heart failure and cardiac disease [16, 17]. Similarly, in patients with acute cerebral infarction, RDW is associated not only with short- and long-term mortality, but also with functional outcome [18]. RDW elevations are also associated with incidence of deep vein thrombosis [19] and survival in patients with acute pulmonary embolism [4].

Patients with SAH are at risk for thrombotic and inflammatory complications [20]. The major morbidity of SAH is delayed cerebral ischemia (DCI), which is thought to be due, in part, to micro- and macro-vascular thrombosis [21, 22] possibly incited by a marked inflammatory response. Cardiac complications, including heart failure due to stress cardiomyopathy and other cardiac problems are common after SAH [23, 24]. Given that SAH is an inflammatory and hypercoagulable state, and that its associated comorbidities have been associated with an increased RDW [4, 16–18, 25, 26], we hypothesized that RDW may serve as a predictor of outcome in patients with SAH. In this pilot study, we sought to determine whether: (1) RDW independently predicts functional outcome and mortality in patients with SAH and (2) RDW is more closely associated with functional outcome than other established biomarkers of SAH.

Methods

Forty consecutive patients with moderate-to-severe SAH (defined as Fisher group III) were prospectively enrolled in a study of inflammatory biomarkers at the University of Pennsylvania, a tertiary care academic hospital. IRB approval was obtained according to institutional guidelines. Criteria for inclusion were diffuse thick subarachnoid clot on admission head CT (Fisher group III), hospital admission within 24 h of ictus, and projected ICU care of greater than 24 h. Patients who received treatment using investigational drugs were excluded from analysis. Patients with SAH from antecedent head trauma, ischemic or hemorrhagic stroke, vascular malformation, or other secondary causes were excluded, as were patients with perimesencephalic SAH.

Demographic data, including age, sex, and race, as well as clinical and laboratory data were recorded. Hunt and Hess classifications were determined by the admitting physician and based on the clinical examination obtained in the Emergency Department. Fisher group was recorded on the basis of the initial head CT. Aneurysm size and location were recorded based on information from catheter angiography or operative reports.

All patients were treated according to a local standard protocol [27] that included aggressive pre-hospital and preoperative resuscitation, early aneurysm occlusion, and aggressive prevention, and treatment of intracranial hypertension and delayed cerebral ischemia according to published recommendations [28, 29]. Transcranial Doppler ultrasound studies were performed daily from admission to hospital day 21 for all patients with adequate temporal bone windows. Mean velocities of >200 cm/s in the middle cerebral arteries and Lindegaard ratios of >3 were recorded as evidence of TCD vasospasm. Continuous EEG for alpha variability was performed for all patients between post-bleed days (PBD) 2 and 10. Patients experiencing delayed cerebral ischemia received hypertensive euvolemic therapy. Intra-arterial vasodilator therapy, balloon angioplasty, and/or intraventricular nicardipine administration were considered if TCD elevations persisted despite-induced hypertension, EEG demonstrated worsening alpha variability, or neurological state declined. Intracranial hypertension was treated according to a step-wise protocol. Patients were treated for hypovolemia to a goal of normal volume status. Sodium levels were monitored serially and maintained >135 g/dL.

Recorded laboratory parameters included baseline complete blood count (CBC), erythrocyte sedimentation rate (ESR), fibrinogen (FIB), D-dimer (DD), high sensitivity C-reactive protein (CRP), coagulation profile, and chemistry panel. Blood samples for CBC were obtained on PBD 1, 3, 5, 7 and 10. Admission, mean, maximum, and minimum RDW, HGB, WBC, MCV, MCH, MCHC, PLT, ESR, CRP, and DD values were recorded. Binary measures (i.e., high RDW, low PLT) were also determined for each parameter, based on normative values determined by the hospital's central and coagulation laboratory. For example, an elevated RDW was defined as the presence of one value >14.5 % during the study period. The definition of an elevated WBC count was defined as $>11.0 \times 10^9$/L; elevated MCV $>$ 100 f/L; low MCV $<$ 80 f/L; elevated MCH $>$ 33 ρg; MCHC $>$ 36 g/dL; PLT $< 150 \times 10^6$/L; RBC $<$ 3.8 mil/μL; HGB $<$ 12 g/dL; D-dimer $>$ 0.5 μg/mL; FIB level $>$ 410 mg/dL.

The primary outcome measure was poor functional outcome defined as a 3-months modified Rankin scores (mRS) between 3 and 6. Secondary endpoints included mortality upon hospital discharge and at 3-months. If 3-months mRS was not available, discharge mRS (adjudicated by a blinded reviewer) was carried forward.

All data were analyzed using STATA/SE 11.2 software (College Station, TX). Continuous variables are reported as mean ± SD. Univariate analyses of continuous variables were analyzed using the student's t test, while univariate analysis of non-normally distributed data were performed using the Wilcoxon rank-sum test. Categorical variables were compared using Fisher's exact test for significance. Assessments of all serial values (e.g., RDW) over time were assessed by repeated measures ANOVA. Logistic regression was used to determine whether serum biomarkers predicted outcome at 3 months. Multivariable models were built sequentially using stepwise logistic regression of poor outcome and included (1) CBC parameters; (2) CBC parameters associated with outcome in the prior model, FIB, DD, ESR, and CRP; and (3) CBC parameters and blood biomarkers significantly associated with outcome in prior models, and age and Hunt Hess grade. These models were built using the maximum and PBD1 values. Receiver operator characteristics (ROC curves) were performed to assess the goodness-of-fit for each of the multivariable models.

Results

Demographic characteristics of the entire cohort are described in Table 1. Of 40 patients, 7 (17.5 %) died. Four (10 %) had evidence of a stress cardiomyopathy by 2D-echocardiography and 15 (39 %) were transfused packed RBCs. Twenty-seven (67.5 %) had a poor functional outcome (mRS 3–6) at hospital discharge and 19 (47.5 %) had poor functional outcome at 3 months.

Mean RDW was higher over the study period in those with poor outcome ($p = 0.046$) (Fig. 1). Hemoglobin and platelet counts were not significantly different between those with and without poor outcome. The only other CBC parameter that was significantly higher in patients with poor outcome was the WBC count ($p = 0.02$) (Fig. 2). Mean ESR ($p = 0.002$), FIB ($p = 0.028$), and CRP ($p = 0.010$) were significantly higher among patients with poor outcome (Supplementary Table). RDW was significantly associated with poor outcome on PBD 1, 3, 5, and 7 (Table 2). ESR was significantly associated with outcome on PBD 3, 5, 7, and 10. Other parameters significantly associated with poor

Table 1 Demographic information of the cohort

	Total cohort $n = 40$ (%)	RDW low $n = 28$	RDW high n = 12	p value
Age	52.8 ± 10.2	51.0 ± 10.0	57.1 ± 9.6	0.09
Women	30 (75)	19 (68)	11 (92)	0.23
Hypertension	25 (63)	18 (64)	7 (58)	0.74
Diabetes mellitus	4 (10)	3 (11)	1 (8)	1.00
Coronary artery disease	5 (12)	4 (14)	1 (8)	1.00
Tobacco use	27 (67.5)	21 (75)	8 (67)	0.70
Alcohol use	15 (37.5)	13 (46)	2 (20)	0.38
Hunt and Hess				
1	6 (15)	5 (18)	1 (8)	0.44
2	12 (30)	10 (36)	2 (17)	
3	10 (25)	6 (21)	4 (33)	
4	7 (17.5)	5 (18)	2 (17)	
5	5 (12.5)	2 (7)	3 (25)	
High grade (4–5)	12 (30)	7 (25)	5 (42)	0.45
Surgical clip	12 (30)	9 (32)	3 (25)	1.00
Endovascular coil	25 (63)	18 (64)	7 (58)	1.00
Angiogram negative	3 (7.5)	1 (4)	2 (17)	0.21
Anterior aneurysm location	26 (65)	17 (61)	9 (75)	0.48
Stress cardiomyopathy	4 (10)	3 (11)	1 (8)	1.00
RBC transfusion	15 (39)	8 (31)	7 (58)	0.16
Delayed cerebral ischemia	26 (65)	18 (64)	8 (67)	1.00
TCD elevation (mean > 200 cm/s)	10 (25)	8 (20)	2 (5)	0.45

RDW high was defined as a value >14.5 % at any point during the study period

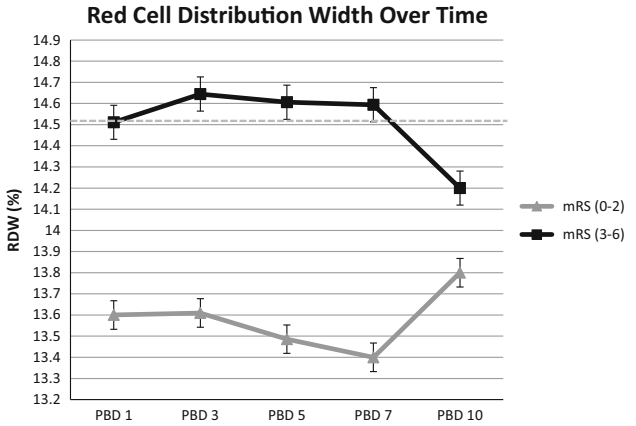

Fig. 1 Red blood cell distribution width (RDW) over time stratified by outcome (modified Rankin score). The *dashed line* represents top normal percentile for RDW (14.5 %). Study period was 10 days from ictus. RDW associated with poor outcome was significantly different than RDW levels for those with good outcome when assessed by repeated measures ANOVA ($p = 0.046$)

outcome in logistic regression analysis included WBC, HGB, FIB, and CRP. Mean D-dimer levels were not significantly associated with poor outcome. Factors associated with RDW, including RBC transfusion and incidence of stress cardiomyopathy, were not associated with an elevated RDW.

In the multivariable logistic regression analysis of CBC parameters, maximum RDW over the first 10 days was associated with poor functional outcome (OR 2.3 95 % CI 1.2–4.6; $p = 0.01$). Maximum WBC count was also associated with poor outcome (OR 1.29 95 % CI 1.04–1.60; $p = 0.018$). Neither HGB nor MCV was associated with functional outcome or mortality in multivariable analysis of CBC parameters. RDW was also associated with 90-days mortality (OR 3.04 95 % CI 1.04–8.80; $p = 0.041$) independent of WBC, PLT, HGB, MCV, MCH, and MCHC.

In hierarchical models including other coagulation biomarkers, specifically DD, and FIB, maximum RDW (OR 2.54 95 % CI 1.21–5.35; $p = 0.014$) and maximum FIB (OR 1.01 95 % CI 1.002–1.01; $p = 0.004$) were associated with poor outcome. Addition of ESR and CRP did not change the model. In the final prediction model (Table 3) incorporating age and high Hunt and Hess grade, a widely acknowledged measure of disease severity significantly associated with outcome, RDW was still strongly associated with poor outcome. The receiver operating curve statistic for this model was 0.91.

Similar models were built in the same sequential manner using RDW values obtained on PBD1. Using these values, RDW remained the only CBC parameter associated with

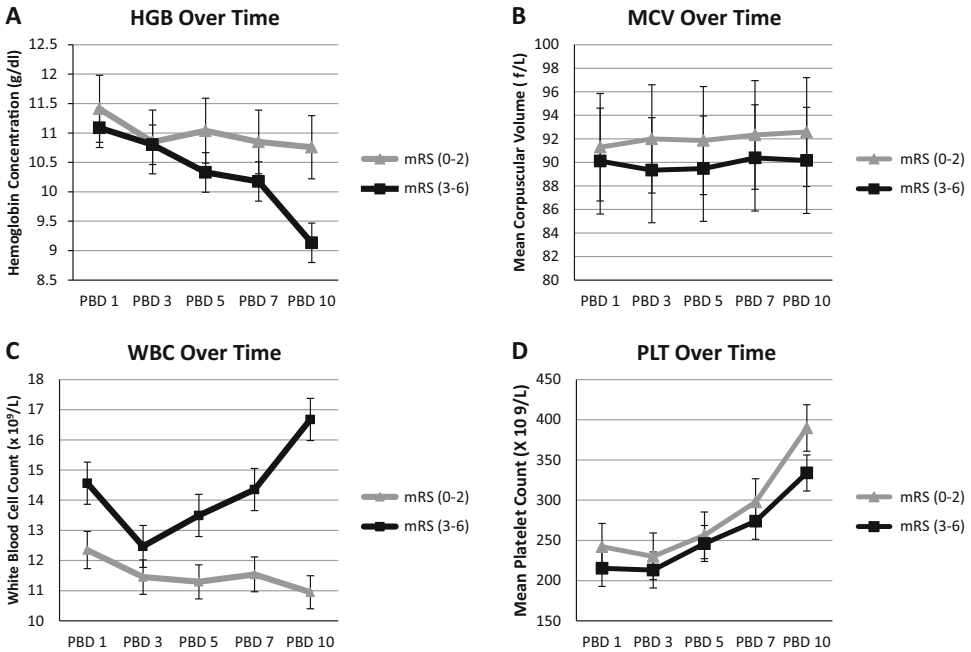

Fig. 2 The relationship between other CBC parameters stratified by outcome. **a** Hemoglobin concentration over time. Hemoglobin concentration in patients with poor outcome was not significantly different from values for those with good outcome when assessed by repeated measures ANOVA ($p = 0.16$). **b** MCV over time. MCV in patients with poor outcome was not significantly different from values for those with good outcome when assessed by repeated measures ANOVA ($p = 0.30$). **c** WBC count over time. WBC count in the poor outcome was significantly different than WBC count for those with good outcome when assessed by repeated measures ANOVA ($p = 0.026$). **d** Platelet count over time. There was no identified relationship between platelet count and outcome by repeated measures ANOVA ($p = 0.27$)

Table 2 The relationship between CBC parameters and other biomarkers on 90-days modified Rankin Scores

	PBD 1	PBD 3	PBD 5	PBD 7	PBD 10
WBC	OR 1.16 (0.98–1.39) $p = 0.089$	OR 1.09 (0.91–1.32) $p = 0.349$	OR 1.19 (0.98–1.39) $p = 0.089$	**OR 1.16 (0.98–1.47) p = 0.039**	**OR 1.39 (1.04–1.86) p = 0.026**
HGB	OR 0.84 (0.54–1.30) $p = 0.429$	OR 0.96 (0.64–1.46) $p = 0.844$	OR 0.72 (0.46–1.11) $p = 0.136$	OR 0.71 (0.44–1.14) $p = 0.153$	**OR 0.42 (0.21–0.85) p = 0.016**
RDW	**OR 1.81 (1.02–3.20) p = 0.042**	**OR 1.73 (1.03–2.90) p = 0.039**	**OR 1.84 (1.06–3.20) p = 0.030**	**OR 1.65 (1.02–2.70) p = 0.042**	OR 1.20 (0.70–2.60) $p = 0.502$
MCV	OR 0.97 (0.87–1.08) $p = 0.594$	OR 0.93 (0.83–1.04) $p = 0.196$	OR 0.93 (0.83–1.05) $p = 0.250$	OR 0.95 (0.84–1.06) $p = 0.346$	OR 0.94 (0.84–1.07) $p = 0.350$
MCH	OR 0.85 (0.64–1.13) $p = 0.269$	OR 0.85 (0.65–1.12) $p = 0.246$	OR 0.83 (0.62–1.10) $p = 0.199$	OR 0.87 (0.66–1.14) $p = 0.302$	OR 0.88 (0.66–1.17) $p = 0.393$
MCHC	OR 0.48 (0.91–1.21) $p = 0.120$	OR 0.62 (0.27–1.43) $p = 0.262$	OR 0.60 (0.28–1.29) $p = 0.190$	OR 0.81 (0.37–1.81) $p = 0.615$	OR 0.81 (0.33–1.98) $p = 0.641$
PLT	OR 0.99 (0.99–1.00) $p = 0.226$	OR 1.00 (0.99–1.00) $p = 0.369$	OR 0.99 (0.99–1.01) $p = 0.711$	OR 1.00 (0.99–1.01) $p = 0.538$	OR 1.00 (0.99–1.01) $p = 0.214$
RBC	OR 1.06 (0.83–1.35) $p = 0.658$	OR 1.48 (0.42–5.23) $p = 0.540$	OR 0.63(0.17–2.31) $p = 0.481$	OR 0.46 (0.10–2.17) $p = 0.327$	OR 1.02 (0.95–1.08) $p = 0.603$
FIB	OR 1.00 (1.00–1.01) $p = 0.490$	**OR 1.01 (1.00–1.01) p = 0.039**	OR 1.00 (1.00–1.01) $p = 0.094$	**OR 1.01 (1.00–1.01) p = 0.004**	OR 1.00 (1.00–1.01) $p = 0.075$
ESR	OR 1.03 (0.99–1.07) $p = 0.206$	**OR 1.03 (1.00–1.06) p = 0.031**	**OR 1.04 (1.01–1.06) p = 0.005**	**OR 1.04 (1.02–1.07) p = 0.003**	**OR 1.06 (1.02–1.10) p = 0.004**
CRP	OR 1.01 (1.00–1.02) $p = 0.092$	OR 1.01 (1.00–1.02) $p = 0.091$	**OR 1.02 (1.01–1.04) p = 0.019**	**OR 1.03 (1.01–1.05) p = 0.009**	OR 1.03 (1.00–1.05) $p = 0.061$
D-dimer	OR 1.33 (0.78–2.29) $p = 0.293$	OR 1.34 (0.74–2.42) $p = 0.333$	OR 1.27 (0.62–2.58) $p = 0.515$	OR 1.16 (0.66–2.04) $p = 0.600$	OR 0.96 (0.85–1.09) $p = 0.564$

Values listed represent the mean ± SD. Control patients are listed first

Bold text denotes $p < 0.05$ by logistic regression

Table 3 Hierarchical multivariate logistic regression model including all laboratory parameters, as well as age and high Hunt and Hess grade to predict 3-months functional outcome (mRS 3–6)

	OR	95 % CI	*p* value
Max RDW	2.06	1.01–4.19	0.025
Max fibrinogen	1.01	1.00–1.01	0.011
Hunt Hess 4–5	13.0	1.25–133.9	0.038

The ROC for the model is 0.91

outcome (OR 1.80 95 % CI 1.02–3.19; $p = 0.044$). The addition of DD, FIB, ESR, and CRP did not change the model. In the final prediction model, including age and Hunt and Hess grade, RDW was associated with poor outcome with a similar point estimate (OR 1.82 95 % CI 0.98–3.38; $p = 0.058$). The odds ratio for poor outcome with a high-grade SAH was 30.2 (95 % CI 3.03–300 $p = 0.004$).

Given the possibility that transfusion might alter RDW, we performed a set of sensitivity analyses evaluating patients who did not receive RBC transfusions during the study period. RDW remained associated with poor outcome (increasing the odds of poor outcome 14-fold) accounting for Hunt and Hess grade, with a ROC for the model of 0.91.

To determine the mechanism by which RDW affects outcome, univariate analyses were performed between RDW and measures of delayed cerebral ischemia. There was no relationship between RDW and elevated mean TCD velocities, defined as any recording >200 cm/s over the 10 days study period. Similarly, there was no identified relationship between RDW and concern for arterial vasospasm prompting angiography or presence of arterial narrowing on angiography.

Discussion

In this exploratory pilot study, elevated RDW appears to be independently associated with poor clinical outcome in patients with SAH. Our findings demonstrate a more robust association between RDW and functional outcomes than with any other parameters of the CBC, including HGB. Moreover, RDW was more strongly associated with outcome than other inflammatory markers, such as the ESR and CRP. In multivariable analysis including Hunt and Hess grade, RDW remained associated with poor outcome and purported SAH biomarkers such as WBC count, platelet count, D-dimer, and MCV did not.

The RDW is typically elevated in conditions of ineffective red cell production (such as iron deficiency, B12 or

folate deficiency, and hemoglobinopathies), increased red cell destruction (such as hemolysis), or after blood transfusion [30, 31]. Other disease states in which RDW may be elevated are liver disease, malnutrition, occult colon cancer, inflammatory bowel disease, and neoplastic metastases to marrow [32, 33]. Although the mechanism through which RDW may affect the clinical outcome is not clear, certain hypotheses do exist.

RDW elevation may be a surrogate measure of premorbid inflammation, as has been suggested in other disease processes [16, 34]. Chronic inflammation, such as in diabetes mellitus, can lead to ineffective erythropoiesis by a variety of mechanisms and may lead to poor outcome in critically ill patients. The mechanisms by which chronic inflammation may influence mortality include direct myelosuppression of erythroid precursors, reducing renal erythropoietin production and the bioavailability of iron, increasing erythropoietin resistance in erythroid precursor cell lines, and by promoting cell apoptosis [35, 36]. This may result in the release of immature red blood cells into the circulation leading to higher RDW. In the general population, higher RDW has been independently associated with decreased life expectancy [34, 37–39]. Tobacco use, a common comorbidity in SAH patients, is associated with chronic inflammation; however, no such relationship was identified in our cohort.

It is more likely that an elevated RDW in our study represents an acute pathological hyper-inflammatory response. Increased RDW is associated with high oxidative stress and low antioxidant levels [40]. Oxidative stress reduces red cell survival leading to increase in the number of immature red cells in the circulation, and therefore an increased RDW. High oxidative stress and low antioxidant levels may promote thrombosis via impaired RBC deformability and increased RBC-endothelium adhesion [18]. In addition to the production of reactive oxygen species, inflammation may be deleterious in SAH due to production of deleterious cyto- and chemo-kines, activation of endogenous macrophages, rupture of the blood–brain barrier, and expression of selectins by endothelial cells [41]. If unchecked, these pro-inflammatory processes may incite secondary injury, and the observed relationship between elevated RDW and poor outcome may be representative of pathological inflammation. This hypothesis is supported by the fact that RDW has been associated with pro-inflammatory cytokines [25, 34, 42], oxidative stress 18, and endothelial dysfunction [43].

Increased RDW may also represent a procoagulant state of red cells independent of inflammation. The elevated RDW may reflect in increased complement of immature reticulocytes; these circulating erythrocyte precursors may be procoagulant [44]. Immature reticulocytes may be less deformable than mature RBCs and have been implicated in the mechanisms underlying thrombosis in sickle cell disease and in association with erythropoiesis-stimulating agents [45]. Furthermore, deformed RBCs may accelerate platelet aggregation, leading to vascular compromise, and decreased blood flow [46]. Variable cell size, decreased deformability, and increased red cell adhesion may lead to slow flow and consequent thrombosis [19, 47, 48]. Such changes have been observed in pathogenesis of stroke and myocardial infarction [46, 49] and venous thromboembolism [4, 5].

Another plausible explanation of the association between elevated RDW and poor outcomes may be that it reflects bone marrow dysfunction, which in turn may predispose to infections from leukocyte dysfunction [50] and thrombotic events from platelet dysfunction [11].

Not only may RDW be a useful predictor of long-term outcome, but also it may help guide diagnostic testing and response to treatment. In an observational study of patients with chest pain admitted to an observation unit, an RDW value of <13.0 % obviated the need for stress echocardiography [51]. The RDW better predicted results of stress echocardiography better than the high sensitivity cardiac troponin-1 [51]. Moreover, in a study of beta-blockers on newly diagnosed hypertension, RDW was used to define treatment effects and to establish the increased efficacy of one medication over another [52]. A similar marker in patients with SAH would be welcome to define the end of ICU course or for those patients with perimesencephalic or angionegative SAH who may not require prolonged ICU or hospital stays.

This is the first description of RDW and poor outcome in SAH to the authors' knowledge and supports the concept that the aforementioned mechanisms may play a role in patients with SAH. In the present pilot study, RDW was more strongly associated with poor outcomes, than was hemoglobin concentration, a widely acknowledged risk factor for poor prognosis after SAH [53]. Although we hypothesized that the effect of RDW on outcome would be mediated through a hypercoagulable mechanism; no relationship was identified between RDW and surrogates for delayed cerebral ischemia. However, the small sample size may have obscured a possible association. The mechanism by which RDW exerts its influence on outcome remains unknown.

Predictive biomarkers are often assessed early in hospital course to predict discharge or long-term outcomes. Given the complexities and complications of SAH, it was unclear a priori which time point to include in the predictive models. Given the exploratory nature of this pilot study, we decided that it was reasonable to assess the various biomarkers over multiple time points. We suspected that the admission RDW may not be as predictive of outcome in SAH as it is in other disease processes, such as

heart failure, due to the fact that outcomes in SAH may be less influenced by premorbid health (presumably reflected in the admission RDW) than the multifactorial complications endured during the delayed cerebral ischemia (DCI) window. Additionally, admission RDW data, when available, did not differ significantly between those with good or poor outcome, again reinforcing the notion that pre-ictus health may not be the determinant of an elevated RDW. We hypothesized that the multi-factorial changes that occur during the DCI window impacts the RDW, and perhaps this would correlate with outcome. For those reasons, we chose the maximum RDW parameter.

The main limitation of this study is that it represents a secondary analysis of pilot data from a small sample size at a single tertiary care center. Therefore, attempts to determine the cause of the increased RDW in the study were not made and measures, such as the reticulocyte counts, were not routinely obtained. Although data regarding the demographics and comorbidities of the patient population were collected, the effects of the individual factors on clinical outcome or RDW could not be assessed given the small sample size. Similarly, RDW may be influenced by medications, nutritional state, blood transfusion, inflammation, oxidative stress, and other factors; due to the retrospective nature of this study, these potential confounders were unable to be assessed.

Conclusions

The data suggest that RDW may be used as a biomarker for predicting outcomes in patients with aneurysmal subarachnoid hemorrhage. Higher values may be associated with increased mortality and poor functional outcome in these patients. Given the ability of this readily available index to discriminate functional status at 3-months, RDW may prove to be a reasonable biomarker of outcome after SAH. Further studies in larger cohorts are required to confirm the observed association.

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