Assessment of the association between red blood cell distribution width and disease activity in patients with systemic vasculitis

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Abstract. The present study aimed to investigate whether red blood cell distribution width (RDW) could serve as a marker for estimating disease activity in patients with systemic vasculitis (SV). A total of 287 patients with SV and 64 age- and sex-matched healthy controls (HCs) were included in the present study. Biochemical indicators and hematologic parameters were evaluated in patients with SV and the HCs. Disease activity was assessed on the basis of the Birmingham Vasculitis Activity Score (BVAS). RDW was significantly elevated in patients with SV compared with HCs ($P<0.05$). A similar result was obtained for the comparison of patients with various disease states, active vs. inactive ($P<0.05$). RDW was significantly increased in patients with kidney injury compared with patients without kidney injury ($P<0.05$). The correlation analysis indicated that there were positive correlations between RDW and BVAS, erythrocyte sedimentation rate, high-sensitivity C-reactive protein, white blood cells and serum creatinine (Scr; all $P<0.05$). In addition, there was a significant negative correlation between RDW and hemoglobin levels ($P<0.05$). Multivariate logistic regression analysis indicated that RDW was independently correlated with patients with active SV. The combined diagnosis of RDW and Scr indicated that the sensitivity and specificity were 68.6 and 88.9%, respectively, in terms of assessing disease activity in patients with SV. Therefore, the present study suggested that RDW may serve as a useful index for estimating disease activity and kidney injury in patients with SV. Moreover, the combination of RDW and Scr may be more effective than RDW alone when assessing the risk of disease activity in patients with SV.

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Introduction

Systemic vasculitis (SV) is an autoimmune disease involving various types of vessels and its primary characteristics are vascular wall injury and necrosis as a result of inflammation (1). However, the pathogenesis behind SV is not fully understood. Although SV has received increasing attention, as SV can occur in patients of all ages, the clinical manifestations are complex and diverse, and there is a lack of specific markers (2). Therefore, diagnosing and estimating the disease activity of SV is difficult. If left untreated, SV progresses to permanent organ damage, resulting in poor health, poor quality of life, premature death and other manifestations, which ultimately result in a heavy socio-economic burden (3). Therefore, identifying novel markers for estimating the disease activity in patients with SV is important (4,5).

Red blood cell distribution width (RDW), routinely reported as a parameter of the standard automated complete blood count, is a reflection of the variability in the erythrocyte size in the circulation (6). In the past few decades, RDW has been widely used in clinical practice as a tool for analyzing and identifying types of anemia (7). In recent years, the value of RDW has attracted increasing attention and its application scope has become increasingly extensive (8). RDW is considered as an inflammatory related index and research has revealed that it has a potential for predicting the overall mortality in a variety of human inflammatory diseases (9,10). It has also been indicated that increased RDW is associated with autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus (10-13). However, the role of RDW in assessing the disease activity, especially in polyarteritis nodosa (PAN), is not completely understood. Therefore, the present study aimed to investigate whether RDW was increased in patients with SV and could serve as a reliable marker to evaluate disease activity.

Patients and methods

Study subjects. A total of 287 patients with SV who received diagnosis and treatment at the People's Hospital of Xinjiang

Uygur Autonomous Region (Urumqi, China) between January 2010 and December 2016 were included as the disease group (Female, n=147, Male, n=140; Age, 49.02±16.52 years). Patients were diagnosed with SV according to the 2012 revised International Chapel Hill Consensus Conference classification criteria or the 1990 American College of Rheumatology (14-18). Inclusion criteria for the classification of Churg-Strauss syndrome (CSS) (14): i) Asthma (history of wheezing or diffuse high-pitched rales on expiration); ii) Eosinophilia (Eosinophils >10% on white blood cell differential count); iii) mononeuropathy or polyneuropathy [development of mononeuropathy, multiple mononeuropathies or polyneuropathy (i.e. glove/stocking distribution) attributable to a systemic vasculitis]; iv) non-fixed pulmonary infiltrates [migratory or transitory pulmonary non-fixed infiltrates on radiographs (not pulmonary infiltrates, including fixed infiltrates, attributable to systemic vasculitis)]; v) paranasal sinus abnormality (history of acute or chronic paranasal sinus pain or tenderness or radiographic opacification of the paranasal sinuses); and vi) extravascular eosinophils (biopsy, including artery, arteriole or venule, showing accumulations of eosinophils in extravascular areas). For purposes of classification, a patient should have CSS ≥ four of these six criteria. Criteria for the classification of Wegener's granulomatosis (WG) (15): i) Nasal or oral inflammation (development of painful or painless oral ulcers, purulent or bloody nasal discharge); ii) abnormal chest radiograph (chest radiograph showing the presence of nodules, fixed infiltrates or cavities); iii) urinary sediment [Microhematuria (>5 red blood cells per high power field) or red cell casts in urine sediment]; iv) granulomatous inflammation on biopsy [histological changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (artery or arteriole)]; For purposes of classification, a patient should have WG ≥ two of these four criteria are present. There is no uniform standard for the diagnosis of microscopic polyangiitis (MPA), which must be distinguished from PAN and WG before diagnosis. The following conditions contribute to the diagnosis of MPA (16): i) Middle-aged and elderly (≥45 years), but more commonly seen in men; ii) renal involvement (proteinuria, hematuria or/and acute renal insufficiency); iii) pulmonary involvement (cough, hemoptysis, dyspnea, pulmonary inflammation and pulmonary renal syndrome); iv) with gastrointestinal (including nausea, vomiting, gastrointestinal bleeding, ischemic abdominal pain, ulcer, intestinal perforation, vascular infarction, intestinal obstruction, melena, hematochezia and peritonitis), heart (including chest pain, heart murmur, palpitation, valve disease, angina pectoris, myocardial infarction, congestive heart failure, hypertension, pericarditis, pericardial effusion and cardiomyopathy), eyes (including exophthalmos, eye pain, optic nerve and eye muscle damage, blurred vision, vision loss, conjunctivitis, corneal ulcer, episcleritis, iritis, retinal vasculitis, visual impairment, ischemic retinopathy or hypertensive retinopathy), ears (including conductive deafness and sensorineural deafness), joints (including joint pain, myalgia, muscle pain, arthritis, intermittent movement disorder of upper and lower limbs) and other organs involved in the performance of the whole body; v) ANCA (indirect fluorescence immunoassay was used for detection) positive; and vi) renal and lung biopsy is helpful in diagnosis for MPA. Criteria for the classification of PAN (17): i) Weight loss ≥4 kg (loss of ≥4 kg body weight since illness began, not due to dieting or other factors); ii) Livedo reticularis (mottled reticular pattern over the skin of portions of the extremities or torso); iii) testicular pain or tenderness (pain or tenderness of the testicles not due to infection, trauma or other causes); iv) myalgias, weakness or leg tenderness [diffuse myalgias (excluding shoulder and hip girdle) or weakness of muscles or tenderness of leg muscles]; v) mononeuropathy or polyneuropathy (development of mononeuropathy, multiple mononeuropathies or polyneuropathy); vi) diastolic blood pressure (BP) >90 mm Hg (development of hypertension with the diastolic BP >90 mm Hg); vii) Elevated blood urea nitrogen (BUN) creatinine (elevation of BUN >40 mg/dl or creatinine >1.5 mg/dl not due to dehydration or obstruction); viii) hepatitis B viral infection (Presence of hepatitis B surface antigen or antibody in serum); ix) arteriographic abnormality (arteriogram showing aneurysms or occlusions of the visceral arteries, not due to arteriosclerosis, fibromuscular dysplasia, or other noninflammatory causes); and x) biopsy of the small or medium-sized artery containing PAN (histological changes showing the presence of granulocytes or mononuclear granulocytes). For classification purposes, a patient should have PAN ≥ three of these 10 criteria. Criteria for the classification of Takayasu arteritis (TA) (18): i) Age at disease onset ≤40 years (development of symptoms or findings related to TA at age ≤40 years); ii) claudication of extremities (development and worsening of fatigue and discomfort in muscles of ≥ one extremity whilst in use, especially the upper extremities); iii) Decreased brachial artery pulse (decreased pulsation of one or both of the brachial arteries); iv) BP difference >10 mm Hg (Difference of >10 mm Hg in systolic blood pressure between arms); v) Bruit over subclavian arteries or aorta (bruit audible on auscultation over one or both of the subclavian arteries or abdominal aorta); vi) arteriogram abnormality (arteriographic narrowing or occlusion of the entire aorta, its primary branches or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental). For purposes of classification, a patient would be diagnosed with Takayasu arteritis if ≥ three of these six criteria are present. Exclusion criterion: Patients with secondary vasculitis, systemic lupus erythematosus, rheumatoid arthritis, malignancy, infection or with any other coexisting renal disease, including anti-glomerular basement membrane nephritis, IgA nephropathy, diabetic nephropathy or lupus nephritis.

A further 64 age- and sex-matched healthy controls (HC) were included as the control group (female, n=34, male, n=30; age, 48.13±11.03 years). All participants signed informed consent and the study protocol was approved by the Ethics Committee of Xinjiang People's Hospital (Urumqi, China).

Data collection and measurements. All clinical data were obtained from the medical records of patients with SV during hospitalization. The following laboratory parameters were assessed: Hematological parameters, high-sensitivity C-reactive protein (Hs-CRP), serum creatinine (Scr), erythrocyte sedimentation rate (ESR). RDW, white blood cell (WBC), red blood cell (RBC), hemoglobin (HB) and platelet counts were measured by electrical impedance testing method, products of Sysmex diagnostic and using a Sysmex XN 9000

Table I. Demographic and clinical characteristics in systemic vasculitis patients and healthy controls.

Parameters	SV, n=287	HC, n=64	P-value[c]	AAV (n=170)	PAN (n=73)	TA (n=44)	P-value[d]
Age, years	49.02±16.52	48.13±11.03	0.597	56.29±15.52[a]	41.36±10.89[a,b]	34.00±11.85	<0.001
Female, n (%)	147 (51.2)	34 (53.1)	0.783	82 (48.2)[a]	34 (46.6)[a]	31 (70.5)	0.021
WBC, x10^9/l	8.36±3.21	6.25±1.43	<0.001	8.90±3.48	7.31±2.21[b]	7.95±3.04	0.001
RBC, x10^9/l	4.21±0.88	4.78±0.50	<0.001	3.87±0.93[a]	4.73±0.53[b]	4.67±0.65	<0.001
HB, g/l	122.13±27.88	144.73±12.45	<0.001	113.40±28.67[a]	138.31±18.41[b]	132.79±14.56	<0.001
PLT, x10^9/l	238.23±89.56	251.33±66.80	0.189	231.29±91.02	237.10±69.54	262.45±105.88	0.154
RDW, %	14.13±1.73	12.67±0.66	<0.001	14.50±1.82[a]	13.52±1.57[b]	13.87±1.26	<0.001
ESR, mm/h	31.52±25.49	11.13±8.11	<0.001	39.27±27.79[a]	18.60±11.89[b]	25.63±23.55	<0.001
Hs-CRP, mg/l	23.76±46.10	1.82±2.61	<0.001	36.41±56.22[a]	4.31±5.91[b]	8.13±14.18	<0.001
Scr, mg/dl	204.28±240.26	63.50±17.27	<0.001	276.96±287.90[a]	100.55±43.87[b]	91.62±41.90	<0.001
BVAS	9.54±6.68	-	-	10.82±6.88[a]	8.11±5.67[b]	7.00±6.34	<0.001

Data are presented as the mean ± SD or as the count (percentage). SV vs. HC: Age, WBC, RBC, HB, PLT and RDW were compared using the independent sample Student's t-test. The female % was compared using the χ^2 test. ESR, Hs-CRP and Scr were compared using the Kruskal-Wallis test. [c]Independent sample Student's t-test, χ^2 test or Kruskal Wallis test. AAV vs. PAN vs. TA: Age, WBC, RBC, HB, PLT and RDW were compared using one-way ANOVAs and post hoc Student-Newman-Keuls. The female % was compared using the χ^2 test. ESR, Hs-CRP, Scr and BVAS were compared using the Kruskal-Wallis tests and post hoc Dunn's tests. [a]P<0.05 vs. TA; [b]P<0.05 vs. AAV. [d]One-way ANOVA, χ^2 test or Kruskal Wallis test. AAV, anti-neutrophil cytoplasmic antibody associated vasculitis; BVAS, Birmingham Vasculitis Activity Score; ESR, erythrocyte sedimentation rate; HB, hemoglobin; HC, healthy controls; Hs-CRP, high-sensitivity C-reactive protein; PAN, polyarteritis nodosa; PLT, platelets; RBC, red blood cell; RDW, red blood cell distribution width; Scr, serum creatinine; SV, systemic vasculitis; TA, takayasu arteritis; WBC, white blood cell.

Hematology analyzer (Sysmex GmbH). ESR was measured by using a Model Minitor-100 (light emitting diodes and photocells were used to detect the change of light transmittance at the interface between red blood cells and plasma, where the ESR value was obtained). Hs-CRP was performed using a turbid metric method and diagnostic products of Olympus diagnostic, using an Olympus AU-2700 Chemistry Analyzer (Olympus Corporation). Scr was measured by enzyme colorimetry method, products of Olympus diagnostic and using an Olympus AU-2700 Chemistry Analyzer (Olympus Corporation).

Definitions of disease activity. Disease activity was measured using the third version of the Birmingham Vasculitis Activity Score (BVAS) (19). Active disease was defined as a BVAS ≥1, whereas inactive disease was defined as BVAS=0.

Definitions of kidney injury. The presence of increased Scr, proteinuria and/or hematuria was taken to indicate kidney injury. Increased Scr was defined as Scr >84 μmol/l or >104 μmol/l for female and male patients, respectively. Proteinuria was defined as >1+ in the routine urine collection or in a 24-h urine collection, containing ≥150 mg protein. Hematuria was defined as ≥ five red blood cells per high-power field (light microscopy; magnification, x400; Olympus Corporation) in urine sediment (20,21).

Statistical analysis. Statistical analyses were performed using SPSS software (version 20.0; IBM Corp). Continuous variables are presented as the mean ± SD or median (interquartile range). Categorical variables are presented as the number (%). Comparisons among groups were analyzed using an independent sample Student's t-test or one-way ANOVA. Multiple comparison tests were performed using the Student-Newman-Keuls test. The Kruskal-Wallis test was used to test data that was not normally distributed. Multiple comparison tests were performed using the Dunn's post hoc test. Categorical variables were evaluated using the χ^2 test. Binary logistic regression was used to identify independent factors of disease activity in patients with SV. Correlation between numerical data was calculated using Spearman's or Pearson's correlation coefficient. A receiver-operating characteristic (ROC) curve was used to determine a cut-off value with the highest sensibility and specificity for estimating the disease activity in patients with SV. In addition, to further improve sensitivity or specificity, multiple biomarkers were used for combined diagnosis, and binary logistic regression analysis and ROC curves were established (22). P<0.05 was considered to indicate a statistically significant difference.

Results

Characteristics of patients with SV and HC. A total of 287 patients with SV and 64 HCs were recruited. Among the patients with SV, 170 were diagnosed as anti-neutrophil cytoplasmic antibody associated vasculitis (AAV), 73 were diagnosed with PAN and 44 were diagnosed with TA) Among them, 193 patients had active SV and 94 had inactive SV. Moreover, 149 patients displayed kidney injury and 138 patients did not display kidney injury. Demographic and clinical characteristics of patients and HCs are presented in Tables I and II. There were no significant differences in the age and sex distribution of patients with SV and HCs (all P>0.05).

RDW in patients with SV and HC. RDW in the SV group was significantly increased compared with matched HCs (14.13±1.73 vs. 12.67±0.66; P<0.05; Fig. 1A). RDW was higher in the active stage group compared with the inactive

Table II. Demographic and clinical characteristics of patients with active stage, inactive stage and healthy controls.

Parameters	Active, n=193	Inactive, n=94	HC, n=64	P-value[c]
Age, years	51.91±16.31	43.15±15.57[a,b]	48.13±11.03	<0.001
Female, n (%)	92 (47.7)	55 (58.5)	34 (53.1)	0.217
WBC, x10^9/l	8.79±3.32[b]	7.45±2.76[a,b]	6.25±1.43[a]	<0.001
RBC, x10^9/l	4.06±0.96[b]	4.50±0.61[a,b]	4.78±0.50[a]	<0.001
HB, g/l	117.01±29.56[b]	132.93±20.17[a,b]	144.73±12.45[a]	<0.001
PLT, x10^9/l	235.44±93.82	244.03±80.18	251.33±66.80	0.402
RDW, %	14.45±1.82[b]	13.48±1.30[a,b]	12.67±0.66[a]	<0.001
ESR, mm/h	36.53±26.69[b]	20.83±18.78[a,b]	11.13±8.11[a]	<0.001
Hs-CRP, mg/l	28.85±50.59[b]	13.52±33.35[a,b]	1.82±2.61[a]	<0.001
Scr, mg/dl	265.21±271.04[b]	76.39±31.12[a]	63.50±17.27[a]	<0.001

Data are presented as mean ± SD or as the count (percentage). Age, WBC, RBC, HB, PLT and RDW were compared using one-way ANOVAs with post hoc Student-Newman-Keuls tests. The female % was compared using the χ^2 test. ESR, Hs-CRP and Scr were compared using the Kruskal-Wallis test and post hoc Dunn's tests. [a]P<0.05 vs. Active; [b]P<0.05 vs. HC. [c]one-way ANOVA or χ^2 test or Kruskal Wallis test. ESR, erythrocyte sedimentation rate; HB, hemoglobin; Hs-CRP, high-sensitivity C-reactive protein; PLT, platelets; RBC, red blood cell; RDW, red blood cell distribution width; Scr, serum creatinine; WBC, white blood cell.

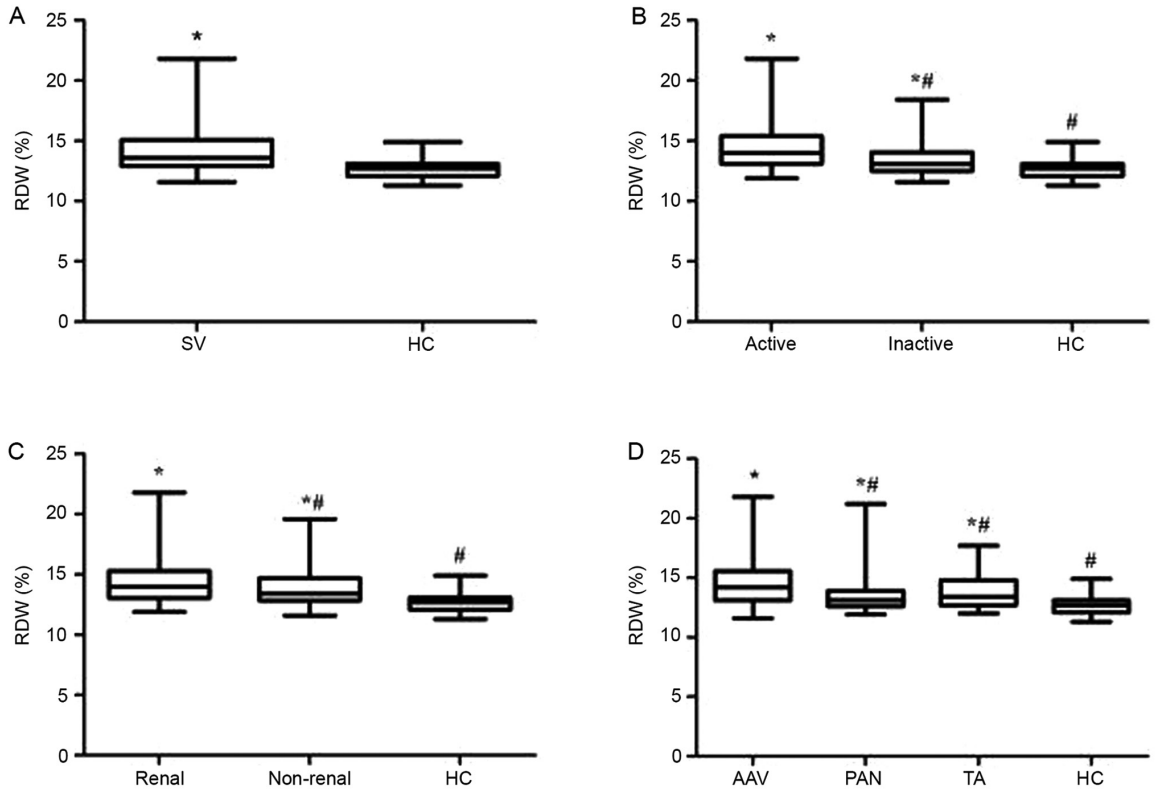

Figure 1. RDW in the various groups. (A) RDW in patients with SV and HCs. *P<0.05 vs. HC. (B) RDW in patients with active and inactive SV. *P<0.05 vs. HC; #P<0.05 vs. active. (C) RDW in patients with SV with kidney injury and non-kidney injury. *P<0.05 vs. HC; #P<0.05 vs. kidney injury. (D) RDW in SV subsets. *P<0.05 vs. HC; #P<0.05 vs. AAV. AAV, antineutrophil cytoplasmic antibody associated vasculitis; HC, healthy control; PAN, polyarteritis nodosa; RDW, red blood cell distribution width; SV, systemic vasculitis; TA, takayasu arteritis.

stage group (14.45±1.82 vs. 13.48±1.30; P<0.05; Fig. 1B). In addition, the RDW was significantly different between patients with kidney injury and patients without kidney injury (14.35±1.84 vs. 13.89±1.56; P<0.05; Fig. 1C). In the subgroup analysis, the RDW of each subgroup, including TA, PAN and AAV, was higher compared with the HC group (AAV vs. HC, 14.50±1.82 vs. 12.67±0.66, P<0.05; PAN vs. HC, 13.52±1.57 vs. 12.67±0.66, P<0.05; TA vs. HC, 13.87±1.26 vs. 12.67±0.66, P<0.05). Moreover, RDW was increased in patients with AAV compared with patients with PAN or TA (AAV vs. PAN, 14.50±1.82 vs. 13.52±1.57, P<0.05; AAV vs. TA, 14.50±1.82 vs. 13.87±1.26, P<0.05; Fig. 1D). RDW was not

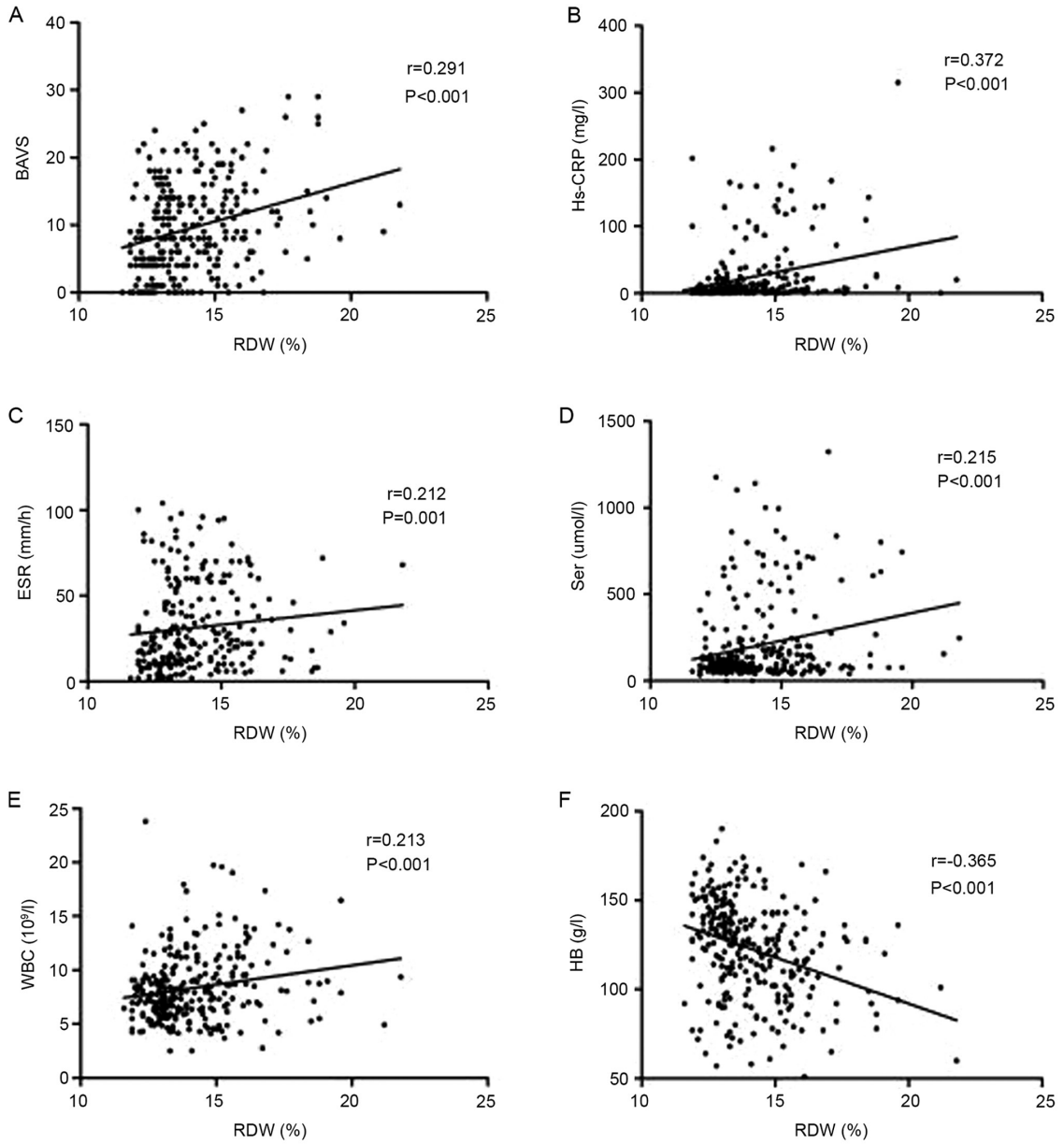

Figure 2. Correlations of RDW with BVAS, Hs-CRP, ESR, Scr, WBC and HB. The correlations between RDW and (A) BVAS, (B) Hs-CRP, (C) ESR, (D) Scr, (E) WBC and (F) HB were analyzed in patients with systemic vasculitis. BVAS, Birmingham Vasculitis Activity Score; ESR, erythrocyte sedimentation rate; HB, hemoglobin; Hs-CRP, high-sensitivity C-reactive protein; RDW, red blood cell distribution width; Scr, serum creatinine; WBC, white blood cell.

significantly different between the patients with PAN and patients with TA (13.52±1.57 vs. 13.87±1.26; P>0.05; Fig. 1D).

Correlation between RDW and other parameters in patients with SV. The relationship between RDW and laboratory parameters in patients with SV was assessed. The results indicated that there was positive correlation between RDW and BVAS (r=0.291; P<0.001), Hs-CRP (r=0.372; P<0.001), ESR (r=0.212; P=0.001), Scr (r=0.215; P<0.001) and WBC (r=0.213; P<0.001) (Fig. 2A-E). By contrast, the opposite result was obtained between RDW and HB (r=-0.365; P<0.001; Fig. 2F). Multivariate logistic regression analysis suggested that RDW [odds ratio (OR) =1.500; 95% confidence interval (CI)=1.101-2.042; P=0.010] and Scr [OR=1.024; 95% CI=1.013-1.045; P<0.001] were independently associated with patients with active SV (Table III).

ROC curve analysis to identify optimal cutoff values of RDW. When assessing the presence of disease activity with RDW in patients with SV, a cut-off value of 13.65, with 57.3% sensitivity and 67.0% specificity was observed according to ROC curve analysis [area under the curve (AUC)=0.68; 95% CI=0.61-0.74; Fig. 3A]. Furthermore, binary logistic regression and ROC curves assessed the combined diagnostic efficiency of multiple parameters. The combination of RDW and Scr, after adjusting by the regression coefficient of the binary logistic regression, had 68.6% sensitivity and 88.9% specificity for diagnosing patients with active SV (AUC=0.84; 95% CI=0.80-0.89; Fig. 3B).

Discussion

The extent of disease activity or relapse serves an important role in the early individualized therapy and prognostic

Table III. Multivariate logistic regression analysis of patients with active stage versus inactive stage.

	Univariate analysis			Multivariate analysis		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.035	1.018-1.052	<0.001	0.984	0.957-1.012	0.261
Female	0.639	0.388-1.052	0.078	0.599	0.255-1.406	0.239
WBC	1.167	1.062-1.283	0.001	1.136	0.959-1.346	0.140
HB	0.977	0.966-0.987	<0.001	1.009	0.986-1.033	0.435
PLT	0.999	0.996-1.002	<0.001	0.998	0.993-1.004	0.536
RDW	1.533	1.260-1.865	<0.001	1.500	1.101-2.042	0.010
ESR	1.031	1.017-1.046	<0.001	1.018	0.991-1.045	0.190
Hs-CRP	1.010	1.002-1.018	0.018	0.994	0.979-1.009	0.413
Scr	1.022	1.014-1.031	<0.001	1.024	1.013-1.045	<0.001

CI, confidence interval; ESR, erythrocyte sedimentation rate; HB, hemoglobin; Hs-CRP, high-sensitivity C-reactive protein; OR, odds ratio; PLT, platelets; RDW, red blood cell distribution width; Scr, serum creatinine; WBC, white blood cell.

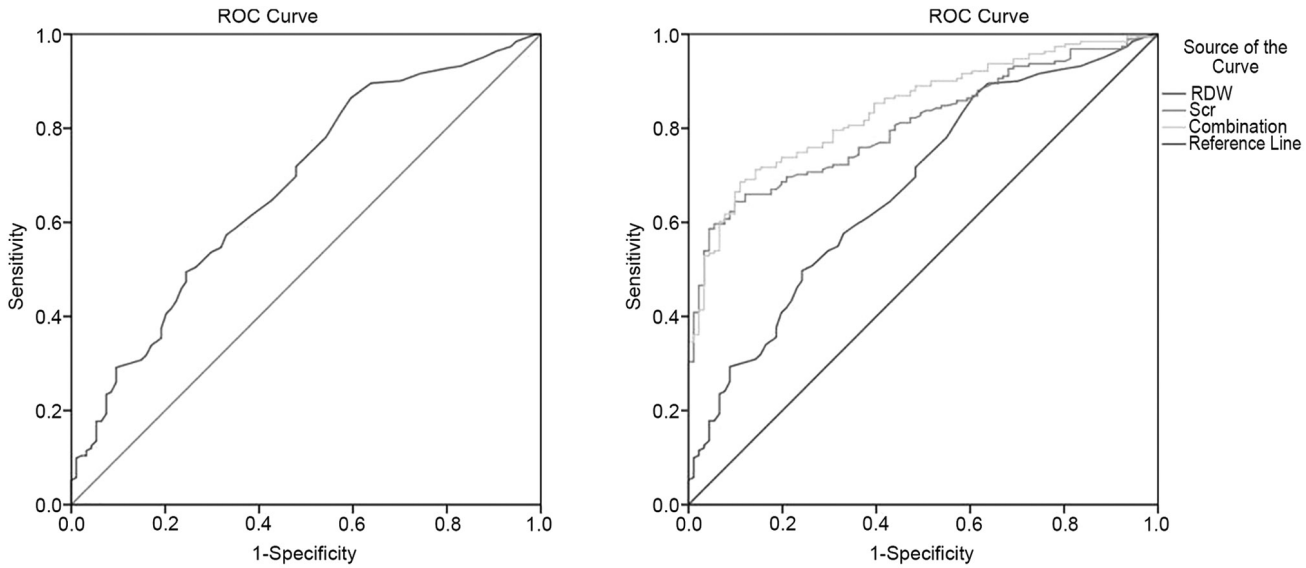

Figure 3. ROC curves in patients with SV. ROC curve of RDW for identifying patients with active SV. ROC curve of the combination of the RDW and Scr for identifying patients with active SV. RDW, red blood cell distribution width; ROC, receiver operating characteristic; Scr, serum creatinine; SV, systemic vasculitis.

assessment of SV (23). However, the assessment of disease activity and relapses in patients with SV is difficult (24). Although angiography and biopsies are used to assess disease activity and relapses in patients with SV, both strategies display imperfect sensitivity due to sampling error and often contain inconclusive findings (25). Furthermore, the strategies are expensive, invasive, clinically risky and not easily tolerated by all patients (26). Therefore, improved tests and useful markers are required to assess disease activity and relapses in patients with SV. RDW is an indicator of inflammation that has feasibility as a prognostic parameter in various diseases (7). In the clinic, RDW is easily obtained as part of a routine blood examination and provides valuable information in a number of diseases without adding additional financial burden on the patients (8). Recent studies have discovered a relationship between subsets of SV and RDW (27,28); therefore, the present study investigated whether RDW could serve a role as a marker for estimating the disease activity of SV.

The results of the present study suggested that RDW was significantly elevated in patients with active SV compared with patients with inactive SV or HCs. The correlation analysis indicated that there was positive correlation between RDW and BVAS, Hs-CRP, ESR and WBC. As the P-value was low and the correlation coefficient was <0.4, it is unlikely that there was a strong correlation. A potential explanation for this is that the present study was retrospective; therefore, further longitudinal studies are required to verify the results of the present study. In addition, RDW was found to be an independent factor for patients with active SV, which was indicated by multivariate logistic regression analysis. The results suggested that RDW could be a reflection of disease activity in patients with SV. As aforementioned, there was a connection between RDW and SV subsets. RDW has been reported to be

a potential marker to evaluate disease activity in other forms of vasculitis, including Behçet disease, TA and granulomatosis with polyangiitis (29-31), which was consistent with the results of the present study. In addition, RDW in patients with inactive SV was raised compared with the HCs. The results indicated a potential persistent state of hidden inflammation or tissue/vascular wall injury, but further investigation is required to verify this finding.

Several studies have assessed renal function and extent of renal damage with RDW in various diseases (32-34). The present study investigated whether RDW was related to kidney injury in SV. The results indicated that RDW was elevated in patients with SV with kidney injury compared with patients with SV without kidney injury. The correlation analysis suggested that there was a positive correlation between RDW and Scr, as well as a negative correlation between RDW and HB. Zhu *et al* (27) indicated that RDW was increased in patients with TA with anemia compared with patients with TA without anemia and control subjects, which was consistent with the present study. However, Kim *et al* (30) indicated that RDW was not significantly associated with HB, which may be related to the sex and age variations between the enrolled cohorts.

Subgroup analysis of the type of SV was also performed in the present study. The results indicated that RDW was significantly higher in patients with AAV, PAN and TA compared with HCs, which suggested that RDW may participate in the pathogenesis behind SV subsets. However, the exact role of RDW requires further investigation. Additionally, RDW was higher in patients with AAV compared with patients with PAN and TA. A potential explanation may be due to the relatively higher disease activity of patients with AAV. To further assess the disease activity in patients with SV, ROC analysis was conducted. The results suggested that the optimal cut-off value of RDW was 13.65 with 57.3% sensitivity and 67.0% specificity. To improve the accuracy and efficiency of diagnosis, identification of patients with active SV is important. Using RDW and Scr as combinatorial markers to construct ROC curves using binary logistic regression indicated that RDW combined with Scr had an advantage compared with RDW alone, with 68.6% sensitivity and 88.9% specificity. Therefore, the combination achieved higher values for assessing patients with active SV.

At present, the exact pathogenesis behind the relationship between RDW and SV is not completely understood. A previous study indicated that RDW levels might be affected by inflammatory cytokines, such as IL-1, IL-6 and TNF-α (12). Inflammatory cytokines may affect the function of bone marrow, inhibit the maturation of erythrocytes and increase the RDW (35). Therefore, higher RDW levels may reflect the underlying inflammatory state caused by chronic inflammation, thereby transforming the intracellular homeostasis of red blood cells and impairing the maturation of red blood cells (36). Collectively, the aforementioned findings suggested that cytokines and RDW serve an important role in the pathogenesis of SV.

The results of the present study suggested that RDW may serve as a suitable biomarker for assessing the disease activity of patients with SV and its subgroups. However, the present study had a number of limitations. Firstly, due to the limitations of cross-sectional research, the present study was unable to derive the causal relationship between RDW and SV. Therefore, prospective studies are required to investigate whether RDW predicts the prognosis of SV. Secondly, the present study included patients with anemia, but serum iron, vitamin B12 and folic acid levels were not recorded. Therefore, some of the patients may have had anemia due to vitamin B12 and mineral deficiencies, thus affecting RDW levels. Finally, the relationship between RDW and other sensitive inflammatory markers, such as TNF-α, IL-1 and IL-6, was not evaluated.

In conclusion, the results of the present study suggested that RDW might serve as a potential marker for disease activity and kidney injury in patients with SV. Moreover, the combination of RDW and Scr may have a higher value when assessing the risk of disease activity in patients with SV. However, further studies are required to investigate the exact role of RDW in the pathogenesis of SV.

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Availability of data and materials

All data generated and/or analyzed during this study are included in this published article.

Authors' contributions

JH and BZ analyzed the data and wrote the manuscript. XC, ShanL and ShasL performed the data collection from medical records and participated in the data analysis. QZ, XC and TW participated in the study design and revised the manuscript. XC, TW, XA and AA performed the data collection from medical records. XC and TW revised the manuscript critically for important intellectual content. QZ and TW confirm the authenticity of all the raw data. NL conceived and helped design the study, revised the manuscript and approved the final version of the manuscript. JH and BZ contributed equally to this study, and should be regarded as co-first authors. All authors reviewed and approved the final manuscript.

Ethics approval and consent to participate

All participants have signed an informed consent form the study protocol was approved by the ethics committee of Xinjiang People's Hospital (Urumqi, China).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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