Journal of Geriatric Cardiology (2020) 17: 486–494
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Research Article · Open Access ·

Relationship between red blood cell distribution width levels and atrial fibrillation in hypertensive patients

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Abstract

Background Information on the relationship between red blood cell distribution width (RDW) and atrial fibrillation (AF) in patients with essential hypertension are scarce. The study aimed to assess the relationship between AF and RDW in hypertensive patients. **Methods** We enrolled 432 hypertensive patients, including 350 AF patients and 82 patients as controls. Patients' demographic, clinical, laboratory and echocardiographic characteristics were recorded. The AF patients were further divided into the persistent and paroxysmal AF subgroups. Electrocardiograms were monitored to identify the cardiac rhythm during blood sampling, and based on the rhythm, the paroxysmal AF group was categorized into the presence (with AF rhythm during blood sampling) and absence (with sinus rhythm during blood sampling) groups. **Results** The AF group had elevated RDW levels than the controls (12.7% ± 0.8% *vs.* 12.4% ± 0.7%, $P = 0.002$), and the persistent AF subgroup had higher RDW levels than the paroxysmal AF subgroup (12.9% ± 0.8% *vs.* 12.6% ± 0.8%, $P = 0.007$). Furthermore, in the paroxysmal AF group, the presence group had higher RDW levels than the absence group (13.0% ± 0.6% *vs.* 12.5% ± 0.9%, $P = 0.001$). There was no significant difference in RDW levels between the persistent AF subgroup and presence group of the paroxysmal AF subgroup ($P = 0.533$) and between the absence group of the paroxysmal AF subgroup and control group ($P = 0.262$). In multivariate regression analysis, in hypertensive patients, the presence of AF rhythm is an independent predictor for increased RDW concentration ($P = 0.001$). **Conclusions** The RDW may be associated with the presence of AF rhythm, which implies the importance of maintaining the sinus rhythm in hypertensive patients.

J Geriatr Cardiol 2020; 17: 486–494. doi:10.11909/j.issn.1671-5411.2020.08.006

Keywords: Atrial fibrillation; Hypertension; Inflammation; Red blood cell distribution width

1 Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with considerable morbidity and mortality.[1,2] Hypertension is very common in AF patients. Evidence points towards a significant contribution of high blood pressure to AF incidence. In the Framingham Heart Study, hypertension and diabetes were demonstrated as the independent predictors for AF, and hypertension induced a 1.7-fold higher risk of AF in the population-based estimates.[3] Recent studies have demonstrated that inflammation plays a crucial role in the pathophysiology of AF.[4–7] Inflammation has also been implicated to be associated with hypertension.[8,9]

Red blood cell distribution width (RDW) is a measurement of the variability in the size of circulating erythrocytes and is obtained routinely in standard complete blood cell counts. The RDW has emerged as an independent and strong marker of adverse outcomes in patients with various cardiovascular disease states.[10–14] Increased RDW has been clearly associated with activated inflammatory state and oxidative stress in several pathological conditions.[15,16]

Data on the relationship between RDW and AF in patients with essential hypertension are very limited.[17] This study aimed to investigate this association in hypertensive patients without significant comorbidities and associated cardiovascular conditions that may affect the RDW levels.

2 Methods

2.1 Study population

This case-control study enrolled consecutive patients who were admitted to our department from August 2015 to

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Received: April 18, 2020 **Revised:** June 30, 2020
Accepted: July 20, 2020 **Published online:** August 28, 2020

September 2019. All hypertensive patients with AF were included, and hypertensive patients with paroxysmal supraventricular tachycardia (PSVT) were randomly enrolled in this study as controls.

No subjects had any heart abnormalities other than AF or PSVT. Hypertension was diagnosed as a systolic pressure of > 140 mmHg and/or a diastolic pressure > 90 mmHg or if the individual was taking antihypertensive medications. Paroxysmal AF was defined as having paroxysms of AF that terminated within 30 days of onset. Persistent AF was defined as AF lasting for > 30 days.[18]

The exclusion criteria were as follows: coronary artery disease, valvular heart disease, congenital heart disease, cardiomyopathy, left ventricular systolic dysfunction, previous cardiac surgery, hepatic or renal dysfunction, acute or chronic pulmonary embolism, chronic obstructive pulmonary disease, thyroid dysfunction, and established diagnosis of diabetes mellitus or sleep apnea. In addition, none of the participants had any history of inflammatory or infectious disease or recent (within the last four weeks) trauma or surgery; none was receiving treatment with nonsteroidal anti-inflammatory or corticosteroids drugs.

To explore the relationship between inflammation and AF, all the participants were divided into the AF and control groups. The AF group was further divided into the following two subgroups: paroxysmal and persistent AF subgroups. Moreover, the paroxysmal AF subgroup was further categorized into the presence (AF was present at the time of blood sampling) and absence (sinus rhythm was present at the time of blood sampling) groups.

All AF patients discontinued treatment of all anti-arrhythmic drugs at least for five half-lives prior to the enrollment in the study. Informed written consent was obtained from all patients, and this study was approved by the Ethics Committee of Fuwai Hospital (No.2015-ZX51) and clinical investigations are conducted according to the principles stipulated in the Declaration of Helsinki.

2.2 Study protocol

The flowchart of the study protocol and study groups has been shown in Figure 1. All participants provided a detailed medical history and underwent physical examinations, and laboratory and transthoracic echocardiographic examinations were performed.

The body mass index (BMI) was calculated as body weight (kg) divided by the square of the height (m) at the time of the admission. The thyroid function test, exercise stress test, nuclear cardiac imaging, and coronary CT/angiography were performed. Echocardiography was performed to evaluate the left atrial diameter (LAD), left ventricular end diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), interventricular septal thickness

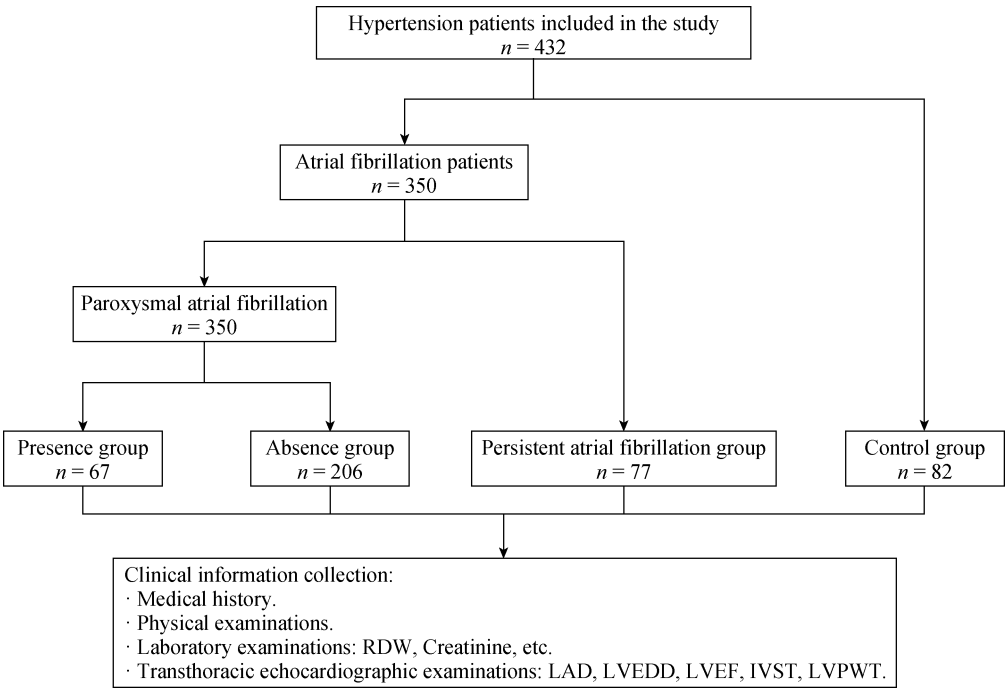

Figure 1. The flowchart of the study and study subgroups. IVST: interventricular septum thickness; LAD: left atrial diameter; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVPWT: left ventricular posterior wall thickness; RDW: red cell distribution width.

(IVST) and left ventricular posterior wall thickness (LVPWT).

Fasting venous blood samples were collected from the antecubital vein of the participants from 5: 00 a.m. to 6: 00 a.m. on the morning or on the second day of admission. All patients were monitored by electrocardiography at the time of blood sampling. The sinus rhythm was shown in all controls at the time of sampling. Blood samples were collected in tubes containing EDTA-treated or plain tubes. The complete blood count, including the total white blood cell (WBC) count, hemoglobin levels and RDW levels, was measured using an automated hematological analyzer (ST-1800i, Sysmex Corporation, Japan). The reference range for RDW level was 11.0%–11.5%. The inter-run coefficient of variation of the RDW assay during the study period was routinely < 1%.

2.3 Statistical analysis

Continuous data are reported as mean ± SD and categorical variables as percentage. The Kolmogorov-Smirnov statistic was used to test for normality of the distribution, and the variables with non-normally distributed scores were presented as median and interquartile range. With the continuous variables, group mean values were compared using the Student's *t*-test and the Mann-Whitney *U* test if otherwise. Categorical variables were compared using the Pearson's chi-square test.

Univariate and multivariate linear correlation test was used to analyze the relationship between the plasma RDW level and continuous variables. The covariates entered into the analyse model were age, gender, duration of hypertension, AF rhythm, BMI, smoking, aspirin, anticoagulation drugs, angiotensin-converting enzyme inhibitors (ACEIs)/ angiotensin receptor blockers (ARBs), beta-blocker, diuretics, calcium channel blockers, statins, office systolic blood pressure, office diastolic blood pressure, office heart rate, serum creatinine, LAD, LVEDD, LVEF, IVST and LVPWT. All statistical analyses were performed using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided, and *P*-value < 0.05 was considered to be statistically significant.

3 Results

3.1 Clinical characteristics

A total of 432 patients with hypertension were included in the study, including 350 patients with AF and 82 patients as controls. In the 350 patients with AF, 273 patients had paroxysmal AF and 77 patients had persistent AF. Based on the cardiac rhythm at the time of blood sampling, the paroxysmal AF subgroup included 67 patients with AF rhythm (presence group) and 206 patients with a sinus rhythm (absence group).

Between the AF groups and controls, there were no significant differences in sex, BMI, office systolic/diastolic blood pressure, fasting blood glucose, potassium level and smoking history. There were also no significant differences between AF group and the controls in the ACEIs/ARBs, beta-blockers, diuretics, statins and calcium channels blockers used. Compared to the control group, the AF group was older and had increased LAD, IVST and LVPWT, respectively (Table 1).

Among the paroxysmal AF subgroup, the presence group had a larger LAD and higher level of office heart rate than the absence group, and there were no significant differences in the other indexes between the two groups.

The clinical and echocardiographic characteristics of the study populations are presented in Table 1.

3.2 RDW levels

3.2.1 AF groups compared to the control group

The RDW levels were significantly higher in the AF group than in the control group (12.7% ± 0.8% *vs.* 12.4% ± 0.7%, $P = 0.002$). Both the WBC count and hemoglobin level were also higher in the AF group than those of in the control group.

3.2.2 Paroxysmal and persistent AF subgroups compared to the control group

The persistent AF subgroup had a higher RDW level than the paroxysmal AF subgroup (12.9% ± 0.8% *vs.* 12.6% ± 0.8%, $P = 0.007$) and control group (12.9% ± 0.8% *vs.* 12.4% ± 0.7%, $P = 0.001$). The RDW level is higher in the paroxysmal AF subgroup than that in the control group (12.6% ± 0.8% *vs.* 12.4% ± 0.7%, $P = 0.018$). The WBC count was higher in the paroxysmal AF subgroup and persistent AF subgroup, compared to control group ($P > 0.05$) (Table 1).

3.2.3 Persistent AF group, presence and absence groups of the paroxysmal AF subgroup, and control group

The persistent AF subgroup had an elevated RDW level, which is similar to that of the presence group of the paroxysmal AF subgroup (12.9% ± 0.8% *vs.* 13.0% ± 0.6%, $P = 0.07$). Moreover, there was no significant difference in the RDW level between the absence group of the paroxysmal AF subgroup and control group (12.5% ± 0.9% *vs.* 12.4% ± 0.7%, $P = 0.262$) (Figure 2).

Table 1. Baseline characteristics of study populations.

Characteristic	Control group	AF		Persistent AF		Paroxysmal AF	
	(*n* = 82)	(*n* = 350)	*P*-value*	(*n* = 77)	*P*-value*	(*n* = 273)	*P*-value*
Age, yrs	54.1 ± 11.3	60.7 ± 10.4	0.001	60.8 ± 9.5	0.001	60.7 ± 10.7	0.001
Male	55 (67.1%)	240 (68.6%)	0.793	63 (81.8%)	0.034	177 (64.8%)	0.709
Smoking	32 (39.0%)	123 (35.1%)	0.510	26 (33.8%)	0.491	97 (35.5%)	0.564
Duration of hypertension, yrs	6 (4–9)[&]	8 (6–11)[&]	0.001	8 (6–12)[&]	0.001	8 (6–11)[&]	0.001
BMI, kg/m^2	24.2 ± 2.6	24.7 ± 2.4	0.167	25.2 ± 2.6	0.023	24.5 ± 2.3	0.422
Office heart rate, beats/min	74.5 ± 14.9	79.0 ± 16.3	0.02	85.5 ± 11.6	0.001	77.2 ± 17.0	0.184
Office SBP, mmHg	146.1 ± 10.4	145.1 ± 5.8	0.215	146.5 ± 5.2	0.786	144.7 ± 5.9	0.110
Office DBP, mmHg	88.5 ± 10.2	90.2 ± 9.5	0.152	92.0 ± 8.1	0.019	89.7 ± 9.9	0.338
WBC, ×10^9/L	5.4 ± 1.3	5.7 ± 1.8	0.001	6.2 ± 2.0	0.002	5.5 ± 1.7	0.001
Hb, g/L	139.8 ± 16.2	143.5 ± 16.3	0.063	149.7 ± 15.4	0.001	141.7 ± 16.2	0.334
RDW, %	12.4 ± 0.7	12.7 ± 0.8	0.002	12.9 ± 0.8	0.001	12.6 ± 0.8	0.018
Creatinine, μmol/L	77.5 ± 12.4	80.6 ± 16.7	0.108	86.5 ± 18.0	0.001	79.0 ± 16.0	0.436
TG, mmol/L	4.8 ± 0.4	4.9 ± 0.5	0.076	5.0 ± 0.4	0.023	4.9 ± 0.5	0.141
HDL-c, mmol/L	1.4 ± 0.1	1.4 ± 0.2	0.018	1.3 ± 0.1	0.696	1.4 ± 0.2	0.003
LDL-c, mmol/L	3.0 ± 0.5	3.1 ± 0.4	0.509	3.0 ± 0.5	0.632	3.0 ± 0.4	0.515
Triglycerides, mmol/L	1.8 ± 0.4	1.8 ± 0.4	0.654	1.8 ± 0.4	0.253	1.8 ± 0.4	0.883
Fasting glucose, mmol/L	4.9 ± 0.7	4.8 ± 0.6	0.209	4.7 ± 0.6	0.097	4.8 ± 0.6	0.334
Na^+, mmol/L	141.9 ± 2.2	141.2 ± 2.5	0.037	140.9 ± 2.6	0.016	141.3 ± 2.4	0.074
K^+, mmol/L	4.0 ± 0.3	4.0 ± 0.3	0.746	4.1 ± 0.4	0.009	4.0 ± 0.3	0.578
LAD, mm	33.9 ± 4.4	39.5 ± 5.7	0.001	43.0 ± 5.6	0.001	38.2 ± 5.3	0.001
LVEDD, mm	46.8 ± 4.3	48.0 ± 4.6	0.041	48.5 ± 4.0	0.014	47.2 ± 4.7	0.090
LVPWT, mm	9.2 ± 1.3	11.4 ± 1.4	0.001	11.7 ± 1.4	0.001	11.3 ± 1.3	0.001
IVST, mm	9.3 ± 1.6	11.6 ± 1.6	0.001	12.0 ± 1.7	0.001	11.5 ± 1.6	0.001
LVEF, %	63.0 ± 6.5	62.3 ± 4.8	0.23	60.5 ± 5.9	0.012	62.7 ± 4.3	0.664
ACEIs/ARBs	55 (67.1%)	203 (58.0%)	0.132	37 (48.1%)	0.015	166 (60.8%)	0.305
Statins	20 (24.4%)	108 (30.9%)	0.248	33 (42.9%)	0.014	75 (27.5%)	0.661
Beta-blockers	23 (28.0%)	140 (40.0%)	0.06	32 (41.6%)	0.073	108 (39.6%)	0.058
Diuretics	10 (12.2%)	50 (14.3%)	0.662	10 (13.0%)	0.880	40 (14.7%)	0.575
CCBs	33 (40.2%)	130 (37.1%)	0.602	14 (18.2%)	0.002	116 (42.5%)	0.718
Propafenone	-	100 (28.6%)	-	25 (32.5%)	-	75 (27.5%)	-
Amiodarone	-	103 (29.4%)	-	28 (36.4%)	-	80 (29.3%)	-
Digoxin	-	51 (14.6%)	-	11 (14.3%)	-	40 (14.7%)	-
Aspirin	35 (42.7%)	175 (50.0%)	0.233	37 (48.1%)	0.497	138 (50.5%)	0.211
Anticoagulation drugs	-	55 (15.7%)	-	17 (22.1%)	-	39 (14.3%)	-
Warfarin	-	39 (11.1%)	-	10 (13.0%)	-	29 (10.6%)	-
Dabigatran/Rivaroxaban	-	17 (5.0%)	-	7 (9.1%)	-	10 (3.7%)	-

Data are presented as means ± SD or *n* (%). [&]Presented as median (interquartile range). *Refers to versus control group. ACEIs: angiotensin-converting enzyme inhibitors; AF: atrial fibrillation; ARBs: angiotensin receptor blocking agents; BMI: body mass index; CCBs: calcium channel blockers; DBP: diastolic blood pressure; Hb: hemoglobin; HDL-c: high-density lipoprotein cholesterol; IVST: interventricular septum thickness; LAD: left atrial diameter; LDL-c: low-density lipoprotein cholesterol; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVPWT: left ventricular posterior wall thickness; RDW: red cell distribution width; SBP: systolic blood pressure; TG: total cholesterol; WBC: white blood cell.

Furthermore, the RDW concentrations in the persistent AF subgroup and presence group of the paroxysmal AF subgroup were higher than those of the control group ($P = 0.001$, $P = 0.001$, respectively) and the absence group of the paroxysmal AF subgroup ($P = 0.001$, $P = 0.001$, respectively). The presence group of the paroxysmal AF subgroup had a similar WBC count with the absence group of the paroxysmal AF subgroup (5.9 ± 1.4 *vs.* $5.4 \pm 1.8 \times 10^9$/L, $P = 0.189$) (Table 2).

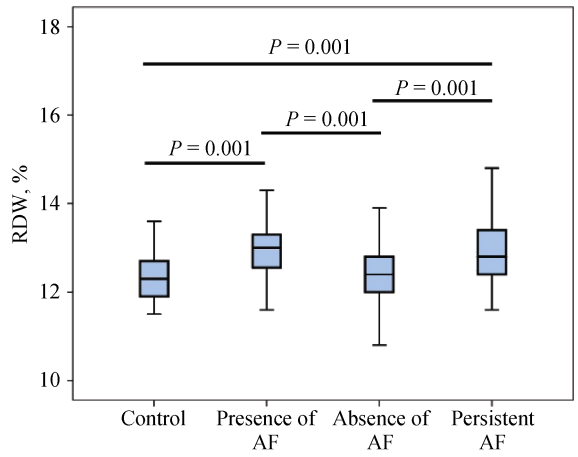

Figure 2. The RDW level in the control, presence of AF, absence of AF and persistent AF group. AF: atrial fibrillation; RDW: red cell distribution width.

There was no significant difference in the WBC count between the absence group of the paroxysmal AF subgroup and control group ($P = 0.189$).

3.3 Predictors of increased RDW concentration in hypertensive AF patients

In the univariate analysis, including age, sex, BMI, smoking, antihypertensive drugs, statin, duration of hypertension, AF rhythm, LAD, LVEDD, LVEF, IVST and LVPWT of all AF patients were analyzed. It demonstrated that LAD, statin, LVPWT and AF rhythm were associated with the RDW level.

In the multivariate analysis, the AF rhythm ($t = 4.448$, $P = 0.001$) and LVPWT ($t = –2.778$, $P = 0.006$) was independently associated with high RDW levels, respectively (Table 3).

4 Discussion

The present study demonstrated the independent association between AF rhythm and RDW in hypertensive patients. Among patients with essential hypertension, those with AF had elevated RDW levels compared to controls. Furthermore, the RDW levels in patients with persistent AF was similar to those of paroxysmal AF patients with AF rhythm at the time of blood sampling, both of which were higher than those of the controls and paroxysmal AF patients with a sinus rhythm at the time of blood sampling. Presence of AF rhythm was independently associated with an elevated RDW level after adjusting for other variables.

Recently, a growing body of evidence demonstrated that inflammation is implicated in the pathophysiology of atrial remodeling in AF.[4–7] The mechanisms link atrial remodeling and inflammation are complex; while diverse underlying diseases and conditions, including hypertension, may partipate in the pathway. Inflammation indexes, including C-reactive protein, tumor necrosis factor-α, interleukin-1 and interleukin-6, have been associated with AF initiation and perpetuation, recurrence post-catheter ablation, and even with prothrombotic states. It has been demonstrated that oxidant stress and inflammatory activation may be involved as the inter-related pathways, promoting atrial electrical and structural remodeling and leading to atrial fibrosis and increased stroke risk.

The RDW reflects the variability in the size of circulating red blood cells provided by an automatic blood count instrument that measures, in more than ten seconds, a hundred thousand red blood cell volume changes to the size of the coefficient of variation and that can accurately and timely reflect the extent of the changes in the red blood cell size. Recently, evidence suggests that high levels of RDW may reflect an activated inflammatory state. Specifically, inflammation and oxidative stress may inhibit erythrocyte maturation. Thus, immature red blood cells enter into the blood circulation and increase their relative proportion to mature red blood cells leading to the observed heterogeneity in the size. Some studies have demonstrated an association between increased RDW levels and adverse cardiovascular events in patients with heart failure, coronary artery disease, stroke and cardiovascular disease as well as the general population.[10–14] Recently, several published works explored the potential relationship between AF and RDW.[19–22] They suggested that an enhanced RDW level is not only a predictive factor and a marker of AF, but also a helpful predictor of the risk of developing adverse complications in patients with AF, such as recurrence and prolonged duration of AF, hospitalization for heart failure, bleeding, left atrial thrombosis and stasis, thromboembolic events and mortality.

The present study included the patients with essential hypertension. Previous studies have shown that inflammation plays an important role in the development of hypertension.[8,9] In the setting of hypertension, accumulating data demonstrated that low grade inflammation with endothelial dysfunction and activation of reni-anigotensin-aldosterone axis are implicated to the development of hypertensive target organ damage, including left atrial and ventricular myocardium. Furthermore, angiotensin II promotes persistent activation of the sympathetic nervous system, oxidant production via NADPH oxidases, cardiac hypertrophy, systematic inflammatory activation and atrial inflammatory cell infiltration, development of atrial fibrosis, gap junction uncoupling, impaired atrial Ca^{2+}-handling and atrial ion channel remodeling.[23]

Table 2. Baseline characteristics: presence versus absence of paroxysmal atrial fibrillation.

Characteristic	Presence of paroxysmal AF				Absence of paroxysmal AF		
	(*n* = 67)	*P*-value*	*P*-value**	*P*-value#	(*n* = 206)	*P*-value*	*P*-value**
Age, yrs	57.1 ± 10.3	0.105	0.024	0.001	61.8 ± 10.6	0.001	0.468
Male	58 (86.6%)	0.006	0.438	0.001	119 (57.8%)	0.145	0.001
Smoking	22 (32.8%)	0.434	0.906	0.596	75 (36.4%)	0.678	0.680
Duration of hypertension, yrs	8 (5–10)&	0.067	0.157	0.317	7 (6–11)&	0.001	0.471
BMI, kg/m^2	24.7 ± 1.9	0.217	0.219	0.372	24.4 ± 2.4	0.559	0.021
Office heart rate, beats/min	88.4 ± 15.4	0.001	0.212	0.001	73.6 ± 15.9	0.675	0.001
Office SBP, mmHg	144.3 ± 7.0	0.860	0.033	0.533	144.8 ± 5.5	0.163	0.021
Office DBP, mmHg	88.2 ± 9.2	0.860	0.010	0.156	90.2 ± 10.0	0.202	0.161
WBC, ×10^9/L	5.9 ± 1.4	0.032	0.208	0.189	5.4 ± 1.8	0.001	0.854
Hb, g/L	145.1 ± 15.8	0.045	0.080	0.048	140.6 ± 16.2	0.681	0.001
RDW, %	13.0 ± 0.6	0.001	0.533	0.001	12.5 ± 0.9	0.262	0.001
Creatinine, μmol/L	82.1 ± 13.4	0.029	0.102	0.061	78.0 ± 16.7	0.820	0.001
TG, mmol/L	4.9 ± 0.5	0.180	0.503	0.881	4.9 ± 0.5	0.170	0.355
HDL-c, mmol/L	1.4 ± 0.2	0.016	0.007	0.677	1.4 ± 0.2	0.003	0.001
LDL-c, mmol/L	3.0 ± 0.4	0.714	0.386	0.169	3.1 ± 0.4	0.339	0.735
Triglycerides, mmol/L	1.9 ± 0.4	0.002	0.001	0.001	1.7 ± 0.3	0.093	0.868
Fasting glucose, mmol/L	4.8 ± 0.7	0.673	0.246	0.633	4.8 ± 0.6	0.288	0.335
Na^+, mmol/L	141.2 ± 2.5	0.075	0.579	0.532	141.4 ± 2.4	0.114	0.168
K^+, mmol/L	4.0 ± 0.3	0.884	0.012	0.669	4.0 ± 0.3	0.510	0.001
LAD, mm	40.1 ± 4.7	0.001	0.001	0.004	38.0 ± 5.4	0.001	0.001
LVEDD, mm	48.6 ± 4.6	0.015	0.839	0.107	47.6 ± 4.7	0.227	0.130
LVPWT, mm	11.4 ± 1.0	0.001	0.223	0.230	11.2 ± 1.4	0.001	0.012
IVST, mm	11.4 ± 1.8	0.001	0.035	0.777	11.5 ± 1.5	0.001	0.008
LVEF, %	62.4 ± 4.6	0.530	0.034	0.479	62.9 ± 4.2	0.802	0.001
ACEIs/ARBs	46 (68.7%)	0.837	0.013	0.130	120 (58.3%)	0.167	0.124
Statins	20 (29.9%)	0.001	0.106	0.543	55 (26.7%)	0.768	0.009
Beta-blockers	28 (41.8%)	0.079	0.977	0.234	80 (38.8%)	0.085	0.677
Diuretics	11 (16.4%)	0.484	0.586	0.638	29 (14.1%)	0.673	0.813
CCBs	31 (46.3%)	0.460	0.001	0.471	85 (41.3%)	0.874	0.001
Propafenone	20 (29.9%)	-	0.735	0.616	55 (26.7%)	-	0.276
Amiodarone	25 (37.3%)	-	0.906	0.097	55 (26.7%)	-	0.112
Digoxin	11 (16.4%)	-	0.723	0.638	29 (14.1%)	-	0.964
Aspirin	34 (50.7%)	0.326	0.747	0.970	104 (50.5%)	0.232	0.716
Anticoagulation drugs	7 (10.4%)	-	0.091	0.301	32 (15.5%)	-	0.295
Warfarin	4 (6.0%)	-	0.156	0.155	25 (12.1%)	-	0.847
Dabigatran/Rivaroxaban	3 (4.5%)	-	0.277	0.683	7 (3.4%)	-	0.049

Data are presented as means ± SD or *n* (%). &Presented as median (interquartile range). *Refers to versus control group. **Refers to versus persistent AF. #Refers to versus absence of AF group. ACEIs: angiotensin-converting enzyme inhibitors; AF: atrial fibrillation; ARBs: angiotensin receptor blocking agents; BMI: body mass index; CCBs: calcium channel blockers; DBP: diastolic blood pressure; Hb: hemoglobin; HDL-c: high-density lipoprotein cholesterol; IVST: interventricular septum thickness; LAD: left atrial diameter; LDL-c: low-density lipoprotein cholesterol; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVPWT: left ventricular posterior wall thickness; RDW: red cell distribution width; SBP: systolic blood pressure; TG: total cholesterol; WBC: white blood cell.

Table 3. Univariate and multivariate analysis results for elevated RDW levels in patients with atrial fibrillation with hypertension.

Variable	Univariate analysis			Multivariate analysis		
	β	*t*	*P*-value	β	*t*	*P*-value
Age, yrs	–0.059	–1.095	0.274	–0.018	–0.323	0.747
Male	0.017	0.208	0.745	0.019	0.291	0.772
Smoking	0.095	1.691	0.092	0.087	0.585	0.114
BMI, kg/m^2	0.048	0.893	0.373	–0.014	–0.270	0.787
Duration of hypertension, yrs	0.027	0.505	0.614	0.011	0.198	0.843
Office heart rate, beats/min	0.076	1.425	0.155	–0.026	–0.460	0.646
Office SBP, mmHg	0.039	0.728	0.467	0.039	0.739	0.460
Office DBP, mmHg	0.061	1.144	0.253	0.057	1.083	0.280
AF rhythm	0.262	5.061	0.001	0.276	4.448	0.001
Creatinine, μmol/L	–0.062	–1.165	0.245	–0.091	1.443	0.150
LAD, mm	0.134	2.520	0.012	0.106	1.809	0.071
LVEDD, mm	0.041	0.770	0.442	0.011	0.212	0.833
LVEF, %	–0.080	–1.499	0.138	–0.017	–0.312	0.755
IVST, mm	–0.096	–1.802	0.072	–0.094	–1.693	0.091
LVPWT, mm	–0.147	–2.770	0.006	–0.156	–2.778	0.006
Statins	0.108	2.026	0.043	0.065	1.191	0.234
ACEIs/ARBs	0.014	0.263	0.793	–0.005	–0.085	0.933
Beta-blockers	–0.009	–0.165	0.869	–0.043	–0.803	0.423
Diuretics	–0.011	–0.196	0.844	0.039	0.621	0.535
CCBs	–0.065	–1.223	0.222	–0.037	–0.601	–0.548
Aspirin	0.047	0.883	0.378	0.053	0.890	0.374
Anticoagulation drugs	0.004	0.082	0.935	–0.008	–0.137	0.891

ACEIs: angiotensin-converting enzyme inhibitors; AF: atrial fibrillation; ARBs: angiotensin receptor blocking agents; BMI: body mass index; CCBs: calcium channel blockers; DBP: diastolic blood pressure; IVST: interventricular septum thickness; LAD: left atrial diameter; LVEDD: left ventricular end diastolic diameter; LVEF: left ventricular ejection fraction; LVPWT: left ventricular posterior wall thickness; RDW: red cell distribution width; SBP: systolic blood pressure.

The RDW level is increased in hypertensive patients, especially in those with non-dipper hypertension.[15,24] Anisocytosis, mainly resulting from the ongoing vascular inflammation, is correlated with complications of essential hypertension, especially with an abnormal left ventricular geometric pattern. Hypertension is major risk factor for AF and is often accompanied by underlying cardiovascular disease or other metabolic abnormalities, such as diabetes or metabolic syndrome.[2,3] Thus, to avoid the potential effects of these abnormal situations on the RDW level, the patients with other cardiovascular disorders were excluded.

The present study further explored the relationship between AF and RDW in hypertensive patients. Patients with paroxysmal AF had transient elevation of RDW levels, which returned to baseline level after the reversion to sinus rhythm. Moreover, in the multivariate logistic regression, the AF rhythm was independently related to the elevated RDW level. Previous studies have shown that the presence of anisocytic erythrocytes was involved in the mechanisms underlying adverse cardiac remodeling,[25] thus leading to atrial fibrosis and predisposing the patients to a higher risk of developing AF.[26] Combined with our study, the relatively increased RDW concentrations during the AF rhythm may demonstrate the involvement of RDW in the inflammatory reaction of the atrial myocardium and the myocardial tissue damage. In this sense, in hypertensive AF patients, effective treatment of the maintenance of sinus rhythm may be of great importance for the attenuation of the atrial remodeling.

There is limited information about the relationship between RDW and AF in hypertension.[17] Our study confirms that the RDW levels were higher in hypertensive patients with AF than in those without AF, which is consistent with the finding of the previous study.[17] More importantly, our

work further explored the different RDW levels of the controls, persistent AF patients and paroxysmal AF patients with and without AF rhythm at the time of blood sampling. It is believed that these results further improve the knowledge of the association between RDW and AF in hypertension patients.[27]

4.1 Limitations

Although our results indicate a possible association between RDW and AF in hypertensive patients, it still had a limitation. The present study did not have a prospective cohort design, which hindered the determination of the cause-effect relationship between inflammation and AF. Thus, it remains controversial whether inflammation was the cause or the consequence of AF. Further studies on this matter is warranted in the future.

4.2 Conclusions

This study demonstrated that, in patients with hypertension, the inflammation indexed by RDW is significantly related to AF. Moreover, the prensence of AF rhythm is independently associated with elevated RDW levels.

Acknowledgments

This study was supported by the National Natural Scientific Foundation of China (No.81600275). All authors had no conflicts of interest to disclose.

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