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Clinical characteristics of adult patients with systemic vasculitis: Data of 1348 patients from a single center

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Abstract

Objective: To investigate the clinical characteristics of patients with systemic vasculitis in China by analyzing the data from a nationwide registry database, the Chinese Registry for Systemic Vasculitis (CRSV).
Methods: The demographic data, clinical presentations, image and laboratory test results, disease activity assessment, treatment, and outcome of patients enrolled with the confirmed diagnosis of systemic vasculitis, including Takayasu's arteritis (TAK), ANCA-associated vasculitis (AAV), Behcet's syndrome (BD), Polyangitis nodosa (PAN), and unclassified systemic vasculitis (USV), were collected since July 2013 in the CRSV. The data during July 2013 and February 28 of 2020 were retrieved and analyzed.
Results: Up to February 2020, 3852 patients in total were registered in the CRSV. In Peking Union Medical College Hospital (PUMCH), 1348 patients were registered, including 730 patients with TAK, 343 with Behcet's disease (BD), 191 with AAV, 53 with USV, and 31 with PAN. More male patients were found in PAN (64.5%), BD (59.8%), and AAV (52.4%), while TAK was more prevalent in female patients (85.9%). The average age at disease diagnosis was 29.6 in TAK, 33.2 in BD, 28.6 in PAN, 39.4 in USV, and 48.1 in AAV. A significant difference was found between age at diagnosis of TAK and AAV. Gender comparisons revealed that the age at diagnosis of male patients with AAV was older than female patients. Hypertension (57.3%) and stroke (17.5%) were found to be more common in male patients with TAK, vascular involvement (27.3%) was found to be more common in male patients with BD, while neurological involvement (29.0%) was found to be more common in male patients with AAV than in females.
Conclusion: This registry is the first in China and provides rich information about the clinical characteristics of Chinese patients with systemic vasculitis. There are significant differences in clinical presentations between different categories of systemic vasculitis.

Keywords

ANCA-associated vasculitis • Behcet's disease • clinical characteristics • polyarteritis nodosa • registry study • Takayasu arteritis • unclassified systemic vasculitis

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Introduction

Systemic vasculitis is a group of uncommon rheumatic diseases characterized by multiple system involvement and complicated clinical manifestations. The diagnosis and treatment of systemic vasculitis has been one of the biggest challenges in rheumatology. Better understanding of the clinical characteristics, patients' response to treatment, and factors related to short- and long-term prognosis is important to provide the basis for future research. Therefore, building up a national prospective cohort of patients with systemic vasculitis is an important way to understand in-depth the clinical profiles and outcome features of patients with systemic vasculitis. In this study, we introduce the development of a nationwide registry database, the Chinese Registry for Systemic Vasculitis (CRSV), and summarize the clinical features of Chinese patients with systemic vasculitis.

In order to understand the disease characteristics of systemic vasculitis in China, we developed a nationwide registry platform, called the CRSV, which is based on the Chinese Rheumatism Data Center (CRDC) platform. The CRDC was established originally by Peking Union Medical College Hospital (PUMCH) in 2011 supported by the National Health and Family Planning Commission.[1] CRDC is a platform for patient cohort development and clinical research. More than half of the Chinese rheumatologists affiliated to 282 medical institutions participated in the registry. The CRSV registry was initiated in July 2013. Twenty-one tertiary medical centers participated in the registry. The goal of this registry is to better understand the epidemiology, clinical characteristics, and the short- and long-term outcomes of Chinese patients with systemic vasculitis. Patients with 5 types of systemic vasculitis were registered in the CRSV, including Takayasu's arteritis (TAK), Behcet's disease (BD), ANCA-associated vasculitis (AAV), polyarteritis nodosa (PAN), and unclassified systemic vasculitis (USV). After being registered, patients are followed up regularly.

Methods

Data Collection

Patients in the CRSV must meet the classification criteria for each individual type of vasculitis. The data collected include demographic information, related medical histories, clinical manifestations, laboratory test results, imaging findings, disease activity assessment, treatment regimen, intervention or surgical procedures, adverse events related to medications, and complications associated with procedures and interventions as well as the outcomes. The core dataset of TAK is shown in Table 1 as an example. Scheduled visits

Table 1: The clinical characteristics of patients with Takayasu's arteritis registered by PUMCH in CRSV

	Total	Male	Female	*P*-value
Number of Patients	**730**	**103 (14.1%)**	**627 (85.9%)**	
Age at diagnosis	29.6±10.8 (3.3, 73.8)	31.1±12.6 (3.3, 73.8)	29.3±10.4 (11.1, 66.1)	0.18
Age at registry	32.3±10.8 (13.0, 74.0)	33.6±12.1(14.4, 74.0)	32.1±10.6 (13.0, 66.1)	0.63
Disease duration on registry(years)	2.5±4.8 (0, 41.0)	2.3±5.4 (0, 27.7)	2.6±4.7 (0, 41.0)	0.18
Laboratory findings				
White blood cells ($\times10^9$/L)	8.7±3.4	8.8±3.0	8.7±3.4	0.68
Hemoglobin (g/L)	123.3±18.1	141.5±16.1	120.4±16.7	<0.001***
Platelet ($\times10^9$/L)	327.5±839.0	271.5±97.4	336.4±901.8	0.50
ESR (1sthour)	25.2±27.9	21.3±27.9	25.8±27.9	0.55
CRP (mg/L)	18.2±31.0	20.1±30.1	17.9±31.2	0.15
Clinical evaluations				
BVAS	9.6±5.4	8.4±5.2	9.8±5.4	0.02*
VDI	3.0±1.7	3.0±1.7	3.0±1.8	0.95
Clinical features				
Hypertension	331 (45.3%)	59 (57.3%)	272 (43.4%)	<0.01**
Fatigue	307 (42.0%)	33 (42.3%)	249 (48,8%)	0.14
Fever (>38 centigrade)	185 (25.3%)	20 (25.6%)	146 (28.6%)	0.39
Arthralgia or arthritis	142 (19.5%)	10 (12.8%)	98 (19.2%)	0.12
Weight loss	128 (17.5%)	19 (24.4%)	99 (19.4%)	0.50
Sign and symptoms of peripheral vessels				
Vessel bruits in neck area	534 (73.2%)	55 (53.4%)	479 (76.4%)	<0.001***
Asymmetric blood pressure in bilateral limbs	452 (61.9%)	52 (50.5%)	400 (63.8%)	0.01*

(*continued*)

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Table 1: Continued

	Total	Male	Female	*P*-value
Decreased limb arterial pulsation	437 (59.8%)	57 (55.3%)	380 (60.6%)	0.31
Decreased radial artery pulsation	388 (53.2%)	47 (45.6%)	341 (54.4%)	0.10
Intermittent claudication of limbs	336 (46.0%)	36 (35.0%)	300 (47.8%)	0.02*
Intermittent claudication of tongue or mandible	58 (7.9%)	6 (5.8%)	52 (8.3%)	0.39
Carotidynia	195 (26.7%)	18 (17.5%)	177 (28.2%)	0.02*
Cardiac abnormalities	391 (53.6%)	52 (50.5%)	339 (54.1%)	0.50
Aortic insufficiency	250 (34.2%)	27 (26.2%)	223 (35.6%)	0.06
Heart murmur	107 (14.7%)	15 (14.6%)	92 (14.7%)	0.98
Pericardial effusion	103 (14.1%)	9 (8.7%)	94 (15.0%)	0.09
Angina	52 (7.1%)	10 (9.7%)	42 (6.7%)	0.27
Congestive heart failure	49 (6.7%)	7 (6.8%)	42 (6.7%)	0.97
Myocardial infarct	18 (2.5%)	4 (3.9%)	14 (2.2%)	0.30[F]
Cardiomyopathy	16 (2.2%)	1 (1.0%)	15 (2.4%)	0.71[F]
Neurological involvement				
Headache	257 (35.2%)	26 (26.2%)	231 (36.8%)	0.02*
Dizziness	271 (37.1%)	27 (28.2%)	244 (38.9%)	0.01*
Syncope	91 (12.5%)	8 (7.8%)	83 (13.2%)	0.12
Stroke	62 (8.5%)	18 (17.5%)	44 (7.0%)	<0.001***
TIA	54 (7.4%)	9 (8.7%)	45 (7.2%)	0.58
Cranial nerve injury	3 (0.4%)	1 (1.0%)	2 (0.3%)	0.37[F]
Renal abnormalities				
Abnormalities in renal arteries	242 (33.2%)	35 (34.0%)	207 (33.0%)	0.85
Urine protein over 0.2g in 24 hours	13 (1.8%)	1 (1.0%)	12 (1.9%)	1.00[F]
Cutaneous and mucosal lesions	124 (17.0%)	16 (15.5%)	108 (17.2%)	0.67
Oral ulceration	73 (10.0%)	12 (11.6%)	61 (9.7%)	0.55
Erythema nodosum	38 (5.2%)	3 (2.9%)	35 (5.6%)	0.26
Cutaneous vasculitis	22 (3.0%)	1 (1.0%)	21 (3.2%)	0.35[F]
Skin ulceration	4 (0.5%)	1 (1.0%)	3 (0.5%)	0.46[F]
Skin Purpura	7 (1.0%)	1 (1.0%)	6 (1.0%)	1.00[F]
Ocular involvement	112 (15.3%)	7 (6.8%)	105 (16.7%)	<0.01**
Amaurosis	85 (11.6%)	6 (5.8%)	79 (12.6%)	0.047*
Retinal vasculitis/ischemic retinitis	36 (4.9%)	2 (1.9%)	34 (5.4%)	0.13
Diplopia	33 (4.5%)	1 (1.0%)	32 (5.1%)	0.07[F]
Optic atrophy	1 (0.1%)	0	1 (0.2%)	1.00[F]
Pulmonary abnormalities	72 (9.1%)	12 (11.7%)	60 (9.6%)	0.51
Pulmonary arterial hypertension	30 (4.1%)	3 (2.9%)	27 (4.3%)	0.79[F]
Pulmonary infarction	14 (1.9%)	2 (1.9%)	12 (1.9%)	1.00[F]
Gastrointestinal tract abnormalities	29 (4.0%)	4 (3.9%)	25 (4.0%)	1.00[F]
Mesenteric ischemia	14 (1.9%)	2 (1.9%)	12 (1.9%)	1.00[F]
Intestinal perforation/infarction	2 (0.3%)	0	2 (0.3%)	1.00[F]
Angioplasty	199 (27.3%)	34 (33.0%)	165 (26.3%)	0.16
Venous thrombosis in vessels	36 (4.9%)	10 (9.7%)	26 (4.1%)	0.02*
Collapse of vertebra/Osteoporosis	7 (1.0%)	0	7 (1.1%)	0.60[F]
Aseptic necrosis	4 (0.5%)	0	4 (0.6%)	1.00[F]

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. [F]Fisher's exact test.
Abbreviation: PUMCH, Peking Union Medical College Hospital. CRSV, Chinese Registry for Systemic Vasculitis. ESR, erythrocyte sediment rate. CRP, c-reactive protein. BVAS, Birmingham vasculitis activity score. VDI, vasculitis damage index. TIA, transient ischemic attack.
Legend: The clinical characteristics of patients with Takayasu's arteritis registered by Peking Union Medical College Hospital (PUMCH) in Chinese Registry for Systemic Vasculitis (CRSV) database were summarized. The comparisons between male and female patients were made. The data was up to February 28 of 2020.

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are conducted in accordance with disease categories and patients' disease status with at least 1 visit every 6 months to evaluate the disease activity if the patient is in a stable condition in the present follow-up visit. Emergency contact messages were provided to patients and could be transferred to the caring rheumatologist within 24 h.

Classification Criteria

All patients registered in the CRSV were diagnosed with primary systemic vasculitis; vasculitis secondary to infection or malignancy were excluded. Patients with TAK,[2] PAN,[3] granulomatosis with polyangiitis (formerly called Wegener granulomatosis),[4] and eosinophilic granulomatosis with polyangiitis (formerly called Churg-Strauss syndrome)[5] were diagnosed according to the1990 ACR classification criteria, respectively. Patients with microscopic polyangiitis were diagnosed according to the 2012 Chapel Hill consensus,[6] and patients with BD were diagnosed according to the 2013 international criteria for BD.[7] Other patients with systemic vasculitis who could not be classified into the above six types of disease and did not fulfill the classification criteria of giant cell arteritis[8] were registered as USV.

Data Quality Control

The CRSV is an electronic data registry system, and measures have been applied to control the quality of data input. Auto-checking mechanism and data auditing system are applied as the essential data quality control measure. The second-level quality control is logical checking to make sure that the data entered into the system are not logically contradictory. We also built-up a predefined treatment regimen menu to facilitate treatment data entry. Finally, quality inspection and feedback are conducted by a professional third-party quality control team.

Ethical and Legal Consideration

Informed consent was obtained for each individual patient who was registered in the CRSV registry in full compliance with Chinese laws and regulations. The patients' private information is stored in an encrypted manner, and only the physicians who are taking care of the patients and the patients themselves are eligible to access these data. This registry was approved by the Institutional Review Board of PUMCH (S-478).

Data Analysis

Since the detailed information of individual patients from other centers could not be identified due to the privacy management rule of CRDC, we included only the data from PUMCH single center for analysis. The demographic data and clinical features were summarized herein. Furthermore, comparisons between genders and age were made.

Statistical Analysis

Since all data were not distributed in a normal pattern, we described the numerical variables as medians (Q1, Q3), and the categorical variables as numbers (percentage). Comparisons between different populations were made using Chi-square tests for categorical data. Fisher's exact tests were conducted when the expected frequencies were <5. A two-sided *P*-value <0.05 was considered to be statistically significant. Analysis was performed with the SPSS software (version 19.0; IBM SPSS statistics, Armonk, New York, USA).

Results

Up to February 28, 2018, 2051 patients with systemic vasculitis were registered into the CRSV database, including 778 patients with BD, 737 patients with TAK, 339 patients with AAV, 167 patients with USV, and 30 patients with PAN. After 2 years (up to February 28, 2020), 3852 patients with systemic vasculitis were registered into the CRSV database in total, including 1390 patients with BD, 1318 patients with TAK, 773 patients with AAV, 317 patients with USV, and 54 patients with PAN (Figure 1). A total of 1348 patients were registered by PUMCH, including 730 patients with TAK, 343 patients with BD, 191 patients with AAV, 53 patients with USV, and 31 patients with PAN. We summarized the gender distribution of these 1348 patients from 5 types of systemic vasculitis diseases, respectively, in Figure 2. The proportions of male patients were higher than females in PAN (20/31, 64.5%), BD (205/343, 59.8%), and AAV (100/191, 52.4%). On the contrary, the proportion of female patients was higher in TAK (627/730, 85.9%) and USV (29/53, 54.7%) patients than in males (Figure 2).

There was an uptrend in the age at disease diagnosis and registration for patients with TAK (29.6/32.3), BD (33.2/35.7), PAN (38.6/41.0), USV (39.4/40.6), and AAV (48.1/49.4) (Tables 1–4). As patients with BD usually have a long-term history of oral ulceration without a specific time of disease onset, their age on diagnosis during registration was not accurately required. Comparison between ages at diagnosis and registration of patients with TAK and AAV were statistically significantly different ($P < 0.001$).

The major clinical characteristics of TAK, BD, AAV, USV, and PAN are summarized in Tables 1–5. Vascular abnormalities including physical findings of vessel bruits (73.2%), asymmetric blood pressure in bilateral limbs (61.9%), limbs claudication (46.0%), and carotidynia (26.7%) were the most common clinical findings in TAK patients, and the constitutional symptoms were also common, such as fever (25.3%) and weight loss (17.5%). Heart (53.6%) and kidney (33.2%, mainly as a consequence of involvement of renal artery) were the most commonly involved organs in TAK. Cutaneous and mucosal lesion (17.0%), ocular

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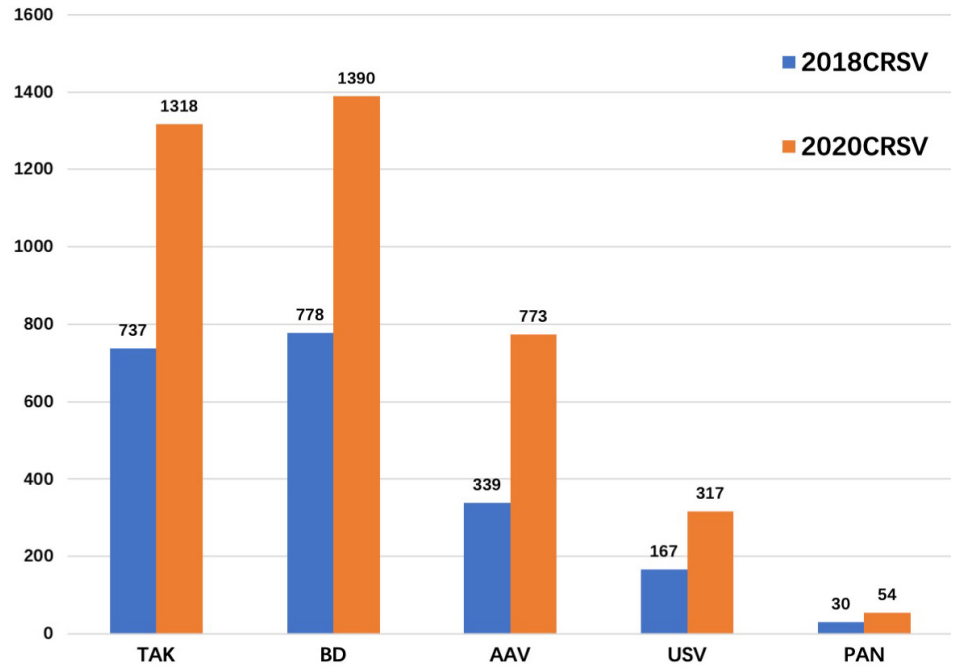

Figure 1: Patients with TAK, BD, AAV, USV, and PAN registered in the CRSV increased rapidly from 2018 to 2020. Up to February 28 of 2020, compared with 2 years ago (up to February 28 of 2018), the patients with TAK, BD, AAV, USV and PAN registered in the CRSV nationwide increased rapidly. AAV, ANCA-associated vasculitis; BD, Behcet's disease; CRSV, Chinese Registry for Systemic Vasculitis; PAN, polyarteritis nodosa; TAK, Takayasu's arteritis; USV, unclassified systemic vasculitis.

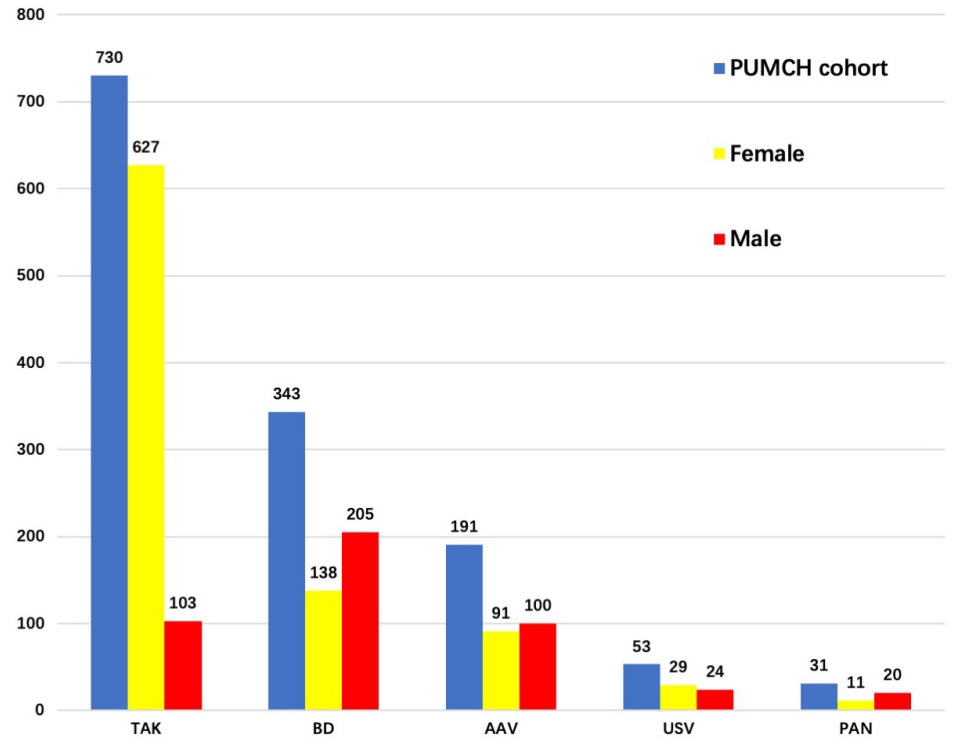

Figure 2: Patients TAK, BD, AAV, USV, and PAN registered in one center (PUMCH) with gender distributions. In a single center of the CRSV, PUMCH, the proportions of male patients were higher than female ones in BD, AAV, and PAN. On the contrary, the proportion of female patients was much higher in TAK patients than male ones. AAV, ANCA-associated vasculitis; BD, Behcet's disease; CRSV, Chinese Registry for Systemic Vasculitis; PUMCH, Peking Union Medical College Hospital; PAN, polyarteritis nodosa; TAK, Takayasu's arteritis; USV, unclassified systemic vasculitis.

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Table 2: The clinical characteristics of patients with Behcet's disease registered by PUMCH in CRSV

	Total	Male	Female	*P*-value
Number of Patients	**343**	**205 (59.8%)**	**138 (40.2%)**	
Age at diagnosis (years)	33.2±10.3 (11.6, 59.6)	33.1±10.0 (11.6, 58.6)	33.4±10.6 (11.8, 59.6)	0.80
Age at registration (years)	35.7±10.7 (14.2, 69.2)	35.4±10.5 (14.2, 69.2)	36.3±11.0 (15.7, 64.3)	0.47
Disease duration before registration (years)	2.5±4.2 (0, 26.7)	2.3±4.1 (0, 26.7)	2.9±4.5 (0, 20.3)	0.21
Laboratory results				
White blood cells ($\times10^9$/L)	8.0±2.9	8.5±2.8	7.3±2.8	<0.01**
Hemoglobin (g/L)	134.6±19.3	142.0±18.1	124.2±15.8	<0.001***
Platelet ($\times10^9$/L)	265.4±88.7	254.7±82.8	279.7±94.6	0.03
ESR (1st hour)	20.1±21.7	19.4±22.3	21.1±20.8	0.54
CRP (mg/L)	15.0±23.3	16.3±22.2	13.0±24.8	0.29
Clinical manifestations				
VDI	1.5±1.1 (0, 6)	1.6±1.1 (0, 6)	1.4±1.0 (0, 6)	0.30
Clinical manifestations				
Fatigue	178 (51.9%)	110 (53.7%)	68 (49.3%)	0.43
Fever (≥38°C)	100 (29.2%)	63 (30.7%)	37 (26.8%)	**0.43**
Arthralgia/arthritis	66 (19.2%)	38 (18.5%)	28 (20.3%)	0.69
Weight loss	57 (16.6%)	34 (16.6%)	23 (16.7%)	0.98
Cutaneous and mucosal lesions	276 (80.5%)	161 (78.5%)	115 (83.3%)	0.27
Oral ulcer	276 (80.5%)	162 (79.0%)	114 (82.6%)	0.41
Genital ulcer	201 (58.6%)	104 (50.7%)	97 (70.3%)	<0.001***
Erythema nodosum	121 (35.3%)	74 (36.1%)	47 (34.1%)	0.70
Pseudofolliculitis	56 (16.3%)	42 (20.5%)	14 (10.1%)	0.01*
Papular pustule	34 (9.9%)	24 (11.7%)	10 (7.2%)	0.18
Acne like rash	30 (8.7%)	24 (11.7%)	6 (4.3%)	0.02*
Skin ulcer	10 (2.9%)	8 (3.9%)	2 (1.4%)	0.33[F]
Ocular involvement	98 (28.6%)	63 (30.7%)	35 (25.4%)	0.28
Blurred vision	69 (20.1%)	50 (24.4%)	19 (13.8%)	0.02*
Uveitis	63 (18.4%)	47 (22.9%)	16 (11.6%)	<0.01**
Diplopia	61 (17.8%)	40 (19.5%)	21 (15.2%)	0.31
Retinal vasculitis	15 (4.4%)	11 (5.4%)	4 (2.9%)	0.27
Visual loss	14 (4.1%)	11 (5.4%)	3 (2.2%)	0.14
Cataract	14 (4.1%)	12 (5.9%)	2 (1.4%)	0.04*
Pulmonary abnormalities	25 (7.3%)	15 (7.3%)	10 (7.2%)	0.98
Abnormalities of heart	24 (7.0%)	17 (8.3%)	7 (5.1%)	0.25
Gastrointestinal tract involvement	74 (21.6%)	40 (19.5%)	34 (24.6%)	0.26
Esophageal ulcer	20 (5.8%)	12 (5.9%)	8 (5.8%)	0.98
Ulcers of colon	17 (5.0%)	9 (4.4%)	8 (5.8%)	0.56
Renal abnormalities	6 (1.7%)	3 (1.5%)	3 (2.2%)	0.69[F]
Epididymitis	21 (6.1%)	21 (10.2%)	NA	
Neurological involvement	58 (16.9%)	34 (16.6%)	24 (17.4%)	0.85
CNS involved	21 (6.1%)	11 (5.4%)	10 (7.2%)	0.48
PNS involved	9 (2.6%)	7 (3.4%)	2 (1.4%)	0.32[F]
Vascular involvement	71 (20.7%)	56 (27.3%)	15 (10.9%)	<0.001***
Venous embolism	54 (15.7%)	44 (21.5%)	10 (7.2%)	<0.001***
Arterial embolism	15 (4.4%)	9 (4.4%)	6 (4.3%)	0.99
Aneurysm	18 (5.2%)	15 (7.3%)	3 (2.2%)	0.04*

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, [F] Fisher's exact test.
Abbreviation: PUMCH, Peking Union Medical College Hospital. CRSV, Chinese Registry for Systemic Vasculitis. ESR, erythrocyte sediment rate. CRP, c-reactive protein. VDI, vasculitis damage index. CNS, central nervous system. PNS, peripheral nervous system.
Legend: The clinical characteristics of patients with Behcet's disease(BD) registered by Peking Union Medical College Hospital (PUMCH) in Chinese Registry for Systemic Vasculitis (CRSV) database were summarized. The comparisons between male and female patients were made. Those patients were registered by PUMCH up to February 28 of 2020.

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abnormalities (15.3%), and pulmonary involvement (9.1%) were not rare (Table 1).

Cutaneous and mucosal involvements (80.5%) were the most common lesions in BD patients, followed by ocular involvement (28.6%), gastrointestinal involvement (21.6%), vascular involvement (20.7%), and neurological involvement (16.9%). Abnormalities of lungs (7.3%) and heart (7.0%) were also common (Table 2).

The involvement of ear, nose, and throat (69.6%) was common in AAV patients, followed by involvement of lungs (46.6%), kidneys (46.1%), and eyes (32.9%). The constitutional symptoms were also common, such as fatigue (50.3%), fever (39.8%), and weight loss (34.0%). Cutaneous and mucosal lesions were found in 30.9% of patients. Arthralgia and/or arthritis was found in 27.2% patients, while myalgia in 22.0%. Involvement of the neurological system (20.9%) and heart (10.5%) was not uncommon (Table 3).

Comparisons between genders of these patients were made. A significant difference in hemoglobin was found between male and female patients with TAK, BD, and AAV, physiologically (Tables 1–3). In TAK patients, higher rates of hypertension (57.3% vs. 43.4%), stroke (17.5% vs. 7.0%), and venous thrombosis (9.7% vs. 4.1%) were found in male

Table 3: The clinical characteristics of patients with ANCA-associated vasculitis registered by PUMCH in CRSV

	Total	Male	Female	*P*-value
Patients numbers	**191**	**100 (52.4%)**	**91 (47.6%)**	
Age at diagnosis (years)	48.1±16.9 (14.7, 83.0)	52.0±15.6 (15.4, 83.0)	44.0±17.3 (14.7, 82.8)	0.001**
Age at registration (years)	49.4±16.4 (15.5, 83.3)	53.0±15.3 (16.5, 83.3)	45.4±16.7 (15.5, 82.8)	0.001**
Disease duration before registration (years)	1.5±2.4 (0, 15.0)	1.3±1.8 (0, 12.2)	1.7±2.9 (0, 15.0)	0.30
Laboratory findings				
White blood cells ($\times10^9$/L)	9.7±4.1	10.1±4.0	9.4±4.1	0.24
Hemoglobin (g/L)	129.2±20.9	137.7±20.0	119.2±17.3	<0.001***
Platelet ($\times10^9$/L)	263.5±104.4	255.5±102.9	273.0±105.9	0.27
ESR (1sthour)	27.8±30.3	25.4±27.8	30.4±32.8	0.30
CRP (mg/L)	24.3±44.9	28.5±51.1	18.9±35.2	0.23
ANCA positive	131 (68.6%)	71 (71.0%)	60 (65.9%)	0.45
c-ANCA positive	38 (19.9%)	22 (22.0%)	16 (17.6%)	0.45
p-ANCA positive	44 (23.0%)	18 (18.0%)	26 (28.6%)	0.08
anti-PR3-ANCA positive	61 (31.9%)	41 (41.0%)	20 (22.0%)	<0.01**
anti-MPO-ANCA positive	65 (34.0%)	27 (27.0%)	38 (41.8%)	0.03*
Clinical evaluations				
BVAS	9.2±6.8 (0, 36)	8.4±6.5 (0, 28)	10.1±7.1 (0, 36)	0.15
VDI	2.1±1.6 (0, 7)	2.2±1.6 (0, 7)	2.0±1.6 (0, 6)	0.41
AVID	2.4±1.8 (0, 7)	2.4±1.8 (0, 7)	2.4±1.7 (0, 6)	0.79
Clinical manifestations				
Fatigue	96 (50.3%)	54 (54.0%)	42 (46.2%)	0.28
Fever (over 38 centigrade)	76 (39.8%)	47 (47.0%)	29 (31.9%)	**0.03***
Weight loss	65 (34.0%)	35 (35.0%)	30 (33.0%)	0.77
Arthralgia/arthritis	52 (27.2%)	29 (29.0%)	23 (25.3%)	0.56
myalgia	42 (22.0%)	24 (24.0%)	18 (19.8%)	0.48
Involvement of ear, nose and throat	133 (69.6%)	71 (71.0%)	62 (68.1%)	0.67
Nasal blockage/chronic discharge/crusting	82 (42.9%)	44 (44.0%)	38 (41.8%)	0.76
Sinusitis	76 (39.8%)	41 (41.0%)	35 (38.5%)	0.72
Crusting/nasal ulcer	69 (36.1%)	37 (37.0%)	32 (35.2%)	0.79
Bloody nasal discharge	53 (27.7%)	29 (29.0%)	24 (26.4)	0.69
Hearing loss	49 (25.7%)	27 (27.0%)	22 (24.2%)	0.66
Hoarseness	36 (18.8%)	19 (19.0%)	17 (18.7%)	0.96
Nasal bridge collapse	26 (13.6%)	12 (12.0%)	14 (15.4%)	0.50

(*continued*)

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Table 3: Continued

	Total	Male	Female	*P*-value
Subglottic stenosis	16 (8.4%)	3 (3.0%)	13 (14.3%)	<0.01**
Septal perforation	11 (5.8%)	7 (7.0%)	4 (4.4%)	0.44
Nasal polyps	10 (5.2%)	5 (5.0%)	5 (5.5%)	1.00[F]
Pulmonary abnormalities	89 (46.6%)	49 (49.0%)	40 (44.0%)	0.49
Nodules/cavity	45 (23.6%)	23 (23.0%)	22 (24.2%)	0.85
Hemoptysis	24 (12.6%)	11 (11.0%)	13 (14.3%)	0.49
Pleurisy/pleural effusion	17 (8.9%)	11 (11.0%)	6 (6.6%)	0.29
Renal abnormalities	88 (46.1%)	45 (45.0%)	43 (47.3%)	0.76
Proteinuria (>0.2g/24 hours)	72 (37.7%)	38 (38.0%)	34 (37.4%)	0.93
Hematuria	42 (22.0%)	22 (22.0%)	20 (22.0%)	1.00
Increased serum level of creatinine	34 (17.8%)	20 (20.0%)	14 (15.4%)	0.41
Ocular involvement	63 (32.9%)	37 (37.0%)	26 (28.6%)	0.22
Blurred vision	37 (19.4%)	21 (21.0%)	16 (17.6%)	0.55
Conjunctivitis/episcleritis	24 (12.6%)	13 (13.0%)	11 (12.1%)	0.85
Diplopia	22 (11.5%)	15 (15.0%)	7 (7.7%)	0.11
Ophthalmodynia	18 (9.4%)	9 (9.0%)	9 (9.9%)	0.83
Exophthalmos	15 (7.9%)	8 (8.0%)	7 (7.7%)	0.94
Scleritis	13 (6.8%)	5 (8.0%)	8 (8.8%)	0.30
Cutaneous and mucosal lesions	59 (30.9%)	33 (33.0%)	26 (28.6%)	0.51
Oral ulcer	27 (14.1%)	16 (16.0%)	11 (12.1%)	0.44
Purpura	15 (7.9%)	6 (6.0%)	9 (9.9%)	0.32
Neurological involvement	40 (20.9%)	29 (29.0%)	11 (12.1%)	<0.01**
CNS involved	12 (6.3%)	9 (9.0%)	3 (3.3%)	0.11
PNS involved	29 (15.2%)	19 (19.0%)	10 (11.0%)	0.12
Motor polymononeuritis	23 (12.0%)	16 (16.0%)	7 (7.7%)	0.08
Sensory peripheral neuropathy	13 (6.8%)	7 (7.0%)	6 (6.6%)	0.91
Abnormalities of heart	20 (10.5%)	10 (10.0%)	10 (11.0%)	0.82
Collapse of vertebra	16 (8.4%)	9 (9.0%)	7 (7.7%)	0.75
Aseptic necrosis	9 (4.7%)	5 (5.0%)	4 (4.4%)	1.00[F]

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, [F] Fisher's exact test.
Abbreviation: AAV, ANCA-associated vasculitis. ANCA, anti-neutrophil cytoplasm antibody. c-ANCA, cytoplasmic ANCA. p-ANCA, perineuclear ANCA. anti-PR3, anti-proteinase 3. Anti-MPO, anti-myeloperoxidase. PUMCH, Peking Union Medical College Hospital. CRSV, Chinese Registry for Systemic Vasculitis. ESR, erythrocyte sediment rate. CRP, c-reactive protein. BVAS, Birmingham vasculitis activity score. VDI, vasculitis damage index. AVID, ANCA-associated vasculitis index of damage. CNS, central nervous system. PNS, peripheral nervous system.
Legend: The clinical characteristics of patients with ANCA-associated arteritis(AAV) from Peking Union Medical College Hospital (PUMCH) cohorts in Chinese Registry for Systemic Vasculitis (CRSV) database were summarized. The comparisons between male and female patients were made. Those patients were registered by PUMCH up to February 28 of 2020.

patients, and higher disease activity (Birmingham vasculitis activity score [BVAS] 9.8 vs. 8.4), higher rates of vessel bruits in neck (76.4% vs. 53.4%), asymmetric blood pressure in bilateral limbs (63.8% vs. 50.5%), intermittent limbs claudication (47.8% vs. 35.0%), carotidynia (28.2% vs. 17.5%), headache (36.8% vs. 26.2%), dizziness (38.9% vs. 28.2%), ocular involvement (16.7% vs. 6.8%), and amaurosis (12.6% vs. 5.8%) were found in female patients (Table 1). In BD patients, higher peripheral blood white blood cells count (8.5 vs. 7.3 $\times$ 10^9/L), higher rates of pseudofolliculitis (20.5% vs. 10.1%), acne-like rash (11.7% vs. 4.3%), blurred vision (24.4% vs. 13.8%), uveitis (22.9% vs. 11.6%), cataract (5.9% vs. 1.4%), vascular involvement (27.3% vs. 10.9%), including venous embolism (21.5% vs. 7.2%) and aneurysm (7.3% vs. 2.2%), were found in male patients, with higher rate of genital ulcer (70.3% vs. 50.7%) in females (Table 2). In AAV patients, higher rate of fever (47.0% vs. 31.9%) and neurological involvement (29.0% vs. 12.1%), as well as higher positive rates of PR3-ANCA (41.0% vs. 22.0%), were found in male patients, and younger age at diagnosis (44.0 years vs. 52.0 years) and higher positive rate of MPO-ANCA (41.8% vs. 27.0%) were found in females (Table 3).

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In 31 patients with the definite diagnosis of PAN in the CRSV-PUMCH cohort, only 1 patient had evidence of hepatitis B virus (HBV) infection, and 4 patients had evidence for history of HBV infection. The clinical features of these patients are summarized in Table 4. The clinical manifestations of 53 patients with USV are summarized in Table 5.

In addition to the major clinical characteristics, specific minor features were further investigated in our cohort and are summarized in Tables 1–5.

Table 4: The clinical characteristics of patients with PAN registered by PUMCH in CRSV

	PAN (N=31)
Male patients number, n (%)	20 (64.5%)
Age at diagnosis (years)	38.6±14.4 (14.8, 71.1)
Age at registration (years)	41.0±15.1 (15.7, 71.3)
Disease duration before registration (years)	0.9±1.3 (0, 5.6)
Laboratory findings	
White blood cells (×10^9/L)	9.5±3.9
Hemoglobin (g/L)	138.4±20.8
Platelet (×10^9/L)	293.9±97.6
ESR (1sthour)	22.3±29.0
CRP (mg/L)	13.0±18.3
Clinical evaluations	
BVAS	4.9±6.8 (0, 27)
VDI	1.8±1.8 (0, 8)
Clinical manifestations	
Fatigue	12 (38.7%)
Fever (over 38 centigrade)	10 (32.3%)
Weight loss	9 (29.0%)
Arthralgia/arthritis	11 (35.5%)
myalgia	16 (51.6%)
Pulmonary abnormalities	1 (3.2%)
Nodules/cavity	1 (3.2%)
Wheeze	1 (3.2%)
Renal abnormalities	3 (9.7%)
Proteinuria (>0.2g/24 hours)	1 (3.2%)
Hematuria	2 (6.5%)
Increased serum level of creatinine	1 (3.2%)
Ocular involvement	5 (16.1%)
Blurred vision	2 (6.5%)
Conjunctivitis/episcleritis	2 (6.5%)
Exophthalmos	2 (6.5%)
Cutaneous and mucosal lesions	19 (61.3%)
Oral ulcer	3 (9.7%)
Livedo reticularis	7 (22.6%)
Skin ulcer	7 (22.6%)
Gangrene	5 (16.1%)
Purpura	3 (9.7%)
Raynaud's phenomenon	2 (6.5%)
Neurological involvement	10 (32.3%)
CNS involved	2 (6.5%)
Stroke	3 (9.7%)
PNS involved	8 (25.8%)
Motor polymononeuritis	2 (6.5%)
Sensory peripheral neuropathy	1 (3.2%)
Disappeared peripheral arterial pulsation	2 (6.5%)
Intermittent claudication of limbs	7 (22.6%)
Myocardial infarction	1 (3.2%)
Angioplasty	2 (6.5%)
fragile fracture	1 (3.2%)
Aseptic necrosis	2 (6.5%)

PAN, polyarteritis nodosa. PUMCH: Peking Union Medical College Hospital. CRSV: Chinese Registry for Systemic Vasculitis.
Legend: The clinical characteristics of patients with polyarteritis nodosa (PAN) were summarized. Due to the limited number of patients, comparison between genders was not performed. Those patients were registered by PUMCH up to February 28 of 2020.

Table 5: The clinical characteristics of patients with USV registered by PUMCH in CRSV

	USV (N=53)
Male, n (%)	24 (45.3%)
Age at diagnosis (years)	39.4±15.9 (14.7, 86.9)
Age at registration (years)	40.6±14.9 (15.5, 87.0)
Disease duration before registration (years)	1.2±2.1 (0, 9.3)
Laboratory findings	
White blood cells (×10^9/L)	8.2±2.8
Hemoglobin (g/L)	132.8±23.8
Platelet (×10^9/L)	274.2±104.8
ESR (1sthour)	27.4±31.8
CRP (mg/L)	19.7±30.3
Clinical evaluations	
BVAS	2.8±2.9 (0, 10)
VDI	1.6±1.1 (0, 5)
Clinical manifestations	
Fatigue	24 (45.3%)
Fever (over 38 centigrade)	11 (20.8%)
Weight loss	14 (26.4%)
Arthralgia/arthritis	15 (28.3%)
myalgia	12 (22.6%)
Involvement of ear, nose and throat	15 (28.3%)
Nasal blockage/chronic discharge/crusting	3 (5.7%)
Sinusitis	2 (3.8%)
Crusting/nasal ulcer	37 (37.0%)

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Table 5: Continued

	USV (N=53)
Bloody nasal discharge	2 (3.8%)
Hearing loss	2 (3.8%)
Hoarseness	6(11.3%)
Nasal bridge collapse	2 (3.8%)
Subglottic stenosis	4 (7.5%)
Auricular cartilage involvement	3 (5.7%)
Pulmonary abnormalities	8 (15.1%)
Nodules/cavity	3 (5.7%)
Hemoptysis	1 (1.9%)
Pleurisy/pleural effusion	4 (7.5%)
Renal abnormalities	2 (3.8%)
Proteinuria (>0.2g/24 hours)	2 (3.8%)
Hematuria	1 (1.9%)
Increased serum level of creatinine	1 (1.9%)
Ocular involvement	9 (17.0%)
Blurred vision	6 (11.3%)
Amaurosis	2 (3.8%)
Conjunctivitis/episcleritis	2 (3.8%)
Diplopia	1 (1.9%)
Ophthalmodynia	2 (3.8%)
Scleritis	1 (1.9%)
Uveitis	3 (5.7%)
Cutaneous and mucosal lesions	14 (26.4%)
Oral ulcer	9 (17.0%)
Livedo reticularis	1 (1.9%)
Skin ulcer	5 (9.4%)
Gangrene	2 (3.8%)
Purpura	3 (5.7%)
Raynaud's phenomenon	1 (1.9%)
Gingivitis	7 (13.2%)
Neurological involvement	14 (26.4%)
CNS involved	7 (13.2%)
Stroke	6 (11.3%)
PNS involved	9 (17.0%)
Motor polymononeuritis	2 (3.8%)
Sensory peripheral neuropathy	1 (1.9%)
Intermittent claudication of limbs	3 (5.7%)
Abnormalities of heart	5 (9.4%)
Myocardial infarction	1 (1.9%)
Valvar abnormalities	3 (5.7%)
Gastrointestinal abnormalities	2 (3.8%)
Mesangial ischemia	1 (1.9%)
Intestinal perforation	1 (1.9%)
Angioplasty	4 (7.5%)
Aseptic necrosis	2 (3.8%)

USV, unclassified systemic vasculitis. PUMCH: Peking Union Medical College Hospital. CRSV: Chinese Registry for Systemic Vasculitis.
Legend: The clinical characteristics of patients with unclassified systemic vasculitis (USV) were summarized. Due to the limited number of patients, comparison between genders was not performed. Those patients were registered by PUMCH up to February 28 of 2020.

Discussion

Several registries for patients with vasculitis have been developed by different countries. The best known registry database and patient cohort for systemic vasculitis are the Vasculitis Clinical Research Consortium (VCRC) in the United States,[9] and the French vasculitis study group (FVSG) developed by French rheumatologists, which mainly included patients with PAN and AAV.[10,11] There are also several databases for systemic vasculitis in Europe, Canada, and Asia. All these registries for systemic vasculitis have made important contributions to further the understanding of the nature and characteristics of systemic vasculitis. Based on these patient cohorts and registry databases, we achieved several milestones in the history of vasculitis study such as the Chapel Hill consensus on vasculitis classification and nomenclature,[6] five-factor score (FFS) for outcome evaluation, BVAS for disease activity assessment,[12,13] particularly for AAV, and the Diagnosis and Classification of Vasculitis Study (DCVAS) study.[14] From these databases, we know that there are ethnical differences in the clinical spectrum of systemic vasculitis.

The CRSV is the only nationwide registry for systemic vasculitis in China and is also the biggest one in the world, according to our knowledge. From 2018 to 2020, the numbers of registered patients had doubled, which demonstrated that the application of the CRSV had accelerated in these recent 2 years. As the leading unit, PUMCH had registered about one-third patients of the CRSV. This registry not only provides valuable information about the clinical features and prognosis of Chinese patients with vasculitis but also provides the infrastructure for conducting clinical research. We carried out several studies with the support of the CRSV, including observational studies and drug studies. In this study, we analyzed the major clinical manifestations of several types of vasculitis, and compared the clinical profiles of these vasculitis based on age and gender.

In our TAK cohort, vascular abnormalities—including physical findings of vessel bruits, asymmetric blood pressure in bilateral limbs, limbs claudication, and carotidynia—were the most common clinical findings, and the constitutional symptoms were also common, such as fever and weight loss. Among the internal organs involved, heart and kidney were the most common. Symptoms related with nervous system involvement, including headache, dizziness, and syncope were more frequently found in female patients, while stroke was more common in males. Cutaneous and mucosal lesions, as well as ocular abnormalities, were not rare in TAK patients. In addition, pulmonary involvement was found in 9.1% patients with TAK, including pulmonary infiltration and abnormalities of pulmonary artery (wall thickness, stenosis, dilation, occlusion/infarction, and hypertension). More than one-fourth of patients (27%) were treated with angioplasty

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or stent implantation or open surgery, which was close to other cohorts (one-third).[15]

BD patients are the second largest patient population in our cohort (Figure 2). Cutaneous and mucosal involvements were the most common lesions, followed by ocular, gastrointestinal, vascular, and neurological involvements. Ocular involvement (including blurred vision, uveitis, and cataract) and vascular involvement (especially venous embolism and aneurysm) were more commonly found in male patients than in female BD patients, which was similar to other cohorts reported in the literature.[16]

The possible reason for the relatively small proportion of AAV registered might be that some AAV patients visited nephrologists or pulmonary physicians because of the most prominently involved organ being kidney and lung in China. A similar situation was found while comparing the study populations of AAV patients between different databases, such as VCRC and the European Vasculitis Society (EUVAS).[9] The most commonly involved organs in our cohort were ear, nose, and throat, followed by the lungs and kidneys. Comparisons of clinical manifestations between genders revealed that the frequency of fever and neurological involvement in male patients with AAV was higher than in females. Both the peripheral and central nerve systems were involved in AAV patients. This was quite different from patients with TAK, in which only central nerve system involvement was observed, while no evidence of peripheral nerve system involvement was found.

We only had 31 patients with a definite diagnosis of PAN. The major reason is the wide use of HBV vaccination in China; consequentially, HBV-infection-related PAN has become very rare in clinical practice. The majority of our PAN patients are non-HBV-related.

The analysis of the demographic characteristics of patients with these 5 systemic vasculitis have shown that BD, AAV, and PAN are more prevalent in male patients than in females, while the situation of TAK patients is on the contrary. This is similar to the descriptions in the review by Gonzalez-Gay *et al*.,[17] although the number of patients with PAN is very limited in the CRSV. The age at disease diagnosis is also different among these 5 vasculitis diseases. The average age at diagnosis is 29.6 years in TAK patients, while it is 48.1 years in AAV patients. In patients with AAV, age at diagnosis and registration of female patients are younger than in males in our cohort, but we failed to find similar results in other cohort reported in the literature.[18–21] However, this needs to be confirmed by large sample studies, as opposed to the limited sample size of our cohort.

The strength of this study is that all the information is derived from the largest database of systemic vasculitis in the country. There are some limitations in this study. PUMCH is a national referral center of China; thus, disease severity of patients of PUMCH may be more severe than patients from other hospitals in the country. Another limitation is that some AAV patients with predominant renal or pulmonary involvement may not come to the rheumatology department, and so the clinical presentation of AAV patients of the registry may be biased.

Conclusion

The clinical features of Chinese patients with systemic vasculitis are different from other reported cohort studies, based on the data from the CRSV, which is the first registry database for systemic vasculitis by rheumatologists in China.

Ethics Approval and Consent to Participate

This study was approved by Institutional Review Board of Peking Union Medical College Hospital, Beijing, China (S-478). Written informed consent was obtained from all participants and the study was performed in accordance with the Declaration of Helsinki. Personal information was protected and kept anonymous in the Chinese Registry of Systemic Vasculitis (CRSV) database.

Availability of Data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

Xiaofeng Zeng is the Editor-in-Chief of the journal, Xinping Tian is the executive Editor-in-Chief, and Mengtao Li is an Associate Editor-in-Chief. The article was subject to the journal's standard procedures, with peer review handled independently of these members and their research groups.

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Authors' Contributions

XT and XZ conceived and designed the study. ML advised on the design of the study. JL, WZ, and YY collected the data. JL, JZ, and YW analyzed and interpreted the patient data. JL and XT were major contributors in writing the manuscript. JL, XT, and XZ edited and revised the paper. All authors read and approved the final manuscript.

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