## The renal artery is involved in Chinese Takayasu's arteritis patients

Zhe Chen<sup>1</sup>, Jing Li<sup>1</sup>, Yunjiao Yang<sup>1</sup>, Hongchao Li<sup>2</sup>, Jiuliang Zhao<sup>1</sup>, Fei Sun<sup>1</sup>, Mengtao Li<sup>1</sup>, Xinping Tian<sup>1</sup> and Xiaofeng Zeng<sup>1</sup>

<sup>1</sup>Department of Rheumatology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, Beijing, China; and <sup>2</sup>Department of Rheumatology, Beijing Jishuitan Hospital, Beijing, China

Takayasu's arteritis is a rare systemic vasculitis mainly affecting the aorta and its major branches. Previous studies have suggested that almost half of the Asian Takayasu's patients have renal artery involvement. However, due to the rarity of the disease, little is known about renal artery involvement in Chinese Takayasu's arteritis patients. Here, we retrospectively reviewed and analyzed 411 patients diagnosed with Takayasu's arteritis in our center to explore the clinical features of renal artery involvement in this group of patients. Of these, 201 patients were diagnosed to have renal artery involvement, with stenosis (78.1%) the most common renal artery pattern. Compared to those without, patients with renal artery involvement were significantly younger at disease onset (23.5 vs 25.6 years) and more frequently had hypertension (74.6% vs 28.1%). Congestive heart failure (22.4% vs 7.6%) and pulmonary hypertension (19.9% vs 9.5%) were both significantly more prevalent among patients with than those without renal artery involvement. The estimated glomerular filtration rate (eGFR) significantly decreased as the severity of renal artery stenosis increased. Age at disease onset older than 24 years (odds ratio 6.06 [95% Confidence Interval 2.76-13.3]), disease duration longer than 19 months (3.35 [1.52-7.4]) and renal artery involvement (8.7 [3.8-20.1]) were independent risk factors for renal dysfunction (eGFR under 90 mL/min/1.73m<sup>2</sup>) among patients with Takayasu's arteritis. Thus, patients with renal artery involvement have more severe cardiac and renal dysfunction compared to those without. The eGFR is correlated negatively with the severity of renal artery stenosis.

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akayasu's arteritis (TA) is a rare chronic systemic vasculitis that mainly affects the aorta and its major branches.<sup>1</sup> The clinical manifestations of TA can be divided into the prodrome or prevasculitic phase, which is characterized by nonspecific systemic symptoms, and the stenosis phase, in which patients may present with protean symptoms of ischemia of the organs supplied by the involved arteries.<sup>2</sup> Renal complication of TA is characterized by renal ischemia resulting from renal artery involvement (RAI).<sup>3</sup> However, due to the rarity of the disease, very few studies have focused on RAI in TA patients. Thus, except for hypertension, little is known about the clinical characteristics of RAI in TA patients. In this study, we analyzed the demographic data, clinical manifestations, laboratory tests, and image findings of patients with RAI to explore the characteristics of RAI in Chinese TA patients and to facilitate physician understanding of this complication of TA.

## RESULTS

Among 411 TA patients, 201 were identified with RAI. The mean disease onset age for patients with and without RAI were 23.50  $\pm$  9.60 and 25.56  $\pm$  9.50 years, respectively (P = 0.029, Table 1). There were more symptoms or vascular findings suggesting aortic branch involvement among patients without RAI when compared with patients with RAI, such as ischemic stroke (2.98% vs. 7.62%, P = 0.037), upper limb claudication (10.45% vs. 18.57%, P = 0.020), and pulse deficit (31.84% vs. 44.76%, P = 0.008). Hypertension (74.63% vs. 28.10%, P < 0.001) was more common among patients with RAI than patients without RAI.

In addition, patients with RAI had higher levels of hemoglobin (Hb; 123.13  $\pm$  20.72 vs. 118.61  $\pm$  22.86 g/l, P = 0.040), a lower erythrocyte sedimentation rate (ESR; 36.55  $\pm$  32.58 vs. 44.52  $\pm$  39.86 mm/h, P = 0.034), lower levels of hypersensitive C-reactive protein (hsCRP; 14.93  $\pm$ 32.70 vs. 24.22  $\pm$  36.38 mg/l, P = 0.040) and a lower

**Correspondence:** Xinping Tian, Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, No. 41 Damucang Hutong, Xicheng District, Beijing, China 100032. E-mail: tianxp6@126.com; and Xiaofeng Zeng, Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Key Laboratory of Rheumatology and Clinical Immunology, Ministry of Education, No. 41 Damucang Hutong, Xicheng District, Beijing, China 100032. E-mail: xiaofeng\_zeng@cstar.org.com

Table 1 | Demographic, clinical characteristics and laboratory findings between patients with and without renal artery involvement

	With renal	Without renal	
Variable	(Mean $\pm$ SD/n)	artery involvement (Mean ± SD/n)	P value
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Female	159/201	168/210	0.822
Age at disease onset (yr)	23.50 ± 9.60/201	25.56 ± 9.50/210	0.029
Disease duration (mo)	51.10 ± 86.51/201	48.48 ± 76.44/210	0.745
Number of admissions	$1.38\pm0.810$	$\textbf{1.34} \pm \textbf{0.879}$	0.673
Constitutional symptoms			
Fever	54/201	74/210	0.067
Malaise	54/201	68/210	0.221
Weight loss	38/201	44/210	0.604
Arthralgia or arthritis	11/201	26/210	0.014
Neurological symptoms			
Headache	75/201	50/210	0.003
Ischemic stroke	6/201	16/210	0.037
Syncope	21/201	28/210	0.367
Vascular findings			
Upper limb claudication	21/201	39/210	0.020
Lower limb	43/201	14/210	<0.001
claudication			
Pulse deficit	64/201	94/210	0.008
Asymmetric blood	118/201	125/210	0.866
pressure			
SCA or aorta bruits	142/201	134/210	0.140
Hypertension	150/201	59/210	< 0.001
Funduscope findings			
Hypertensive	24/87	7/78	0.584
retinopathy			
Takayasu's	8/87	15/78	
retinopathy			
Laboratory data			
WBC (×10 <sup>9</sup> /l)	$9.03 \pm 3.87/201$	$9.22 \pm 3.67/210$	0.625
Hb (g/l)	$123.13\pm20.72/201$	$118.61\pm22.86/210$	0.040
ESR (mm/hr)	$36.55 \pm 32.58/201$	$44.52 \pm 39.86/210$	0.034
hsCRP (mg/l)	14.93 $\pm$ 32.70/135	$24.22 \pm 36.38/130$	0.040
eGFR (ml/min/1.73 m <sup>2</sup> )	$112.84\pm33.72/201$	$124.64 \pm 23.07/210$	< 0.001
TC (mmol/l)	$4.48\pm1.82/140$	4.34 $\pm$ 1.10/146	0.309
TG (mmol/l)	$1.21\pm0.68/140$	$1.18\pm0.80/146$	0.710
HDL (mmol/l)	1.35 $\pm$ 0.46/133	$1.27 \pm 0.41/140$	0.151
LDL (mmol/l)	$\textbf{2.68} \pm \textbf{0.99/133}$	$\textbf{2.68} \pm \textbf{0.90/140}$	0.973
Numano subtypes			
I	NA	91/210	NA
lla	NA	16/210	NA
llb	NA	16/210	NA
III	7/201	5/210	NA
IV	22/201	4/210	NA
V	172/201	78/210	NA

eGFR, estimated glomerular filtration rate; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; HDL, high-density lipoprotein; hsCRP, hypersensitive C-reactive protein; LDL, low-density lipoprotein; NA, not available; SCA, subclavical artery; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

estimated glomerular filtration rate (eGFR; 112.84  $\pm$  33.72 vs. 124.64  $\pm$  23.07 ml/min/1.73 m<sup>2</sup>, *P* < 0.001) compared with patients without RAI (Table 1). No differences in lipid levels between these 2 groups were observed.

Numano type V was the most common artery involvement pattern among the 201 patients with RAI (85.57%). While for those without RAI, type I (43.33%), followed by type V (37.14%) were the most prevalent subtypes (Table 1). Consistent with the symptoms and signs, patients without RAI showed a slightly higher incidence of aortic arch and involvement of its main branches. Detailed information is described in Figure 1. Stenosis and occlusion were observed in 182 and 43 patients with RAI, respectively. Eight aneurysms or dilations of renal arteries were identified, which were all secondary to pre- or post-stenosis.

There were 7, 46, 99, and 49 patients in the occlusion, severe stenosis, moderate stenosis, and mild stenosis groups, respectively. The eGFR decreased as the severity of renal artery stenosis increased (P < 0.001, Table 2). However, no statistically significant difference in 24-hour urine protein (24hUP) or ejection fraction (EF) was detected among the 4 groups (P = 0.564 and P = 0.128, respectively). The frequency of hypertension correlated positively with the degree of renal artery stenosis (r = 0.402, P < 0.001). Patients classified as Ishikawa's Group IIb/III were more common among those with RAI compared with those without (P < 0.001). However, the prevalence of Group IIb/III was not related to the severity of renal artery stenosis (r = 0.211, P = 0.059).

Spot urine protein (SUP) test results were available in 357 patients. Thirty-nine patients whose SUP test results  $\geq 0.3$  g/l were tested for 24hUP level. The 24hUP levels ranged from 0.13 to 14.91 g (median: 1.48 g) in these patients. Specifically, nephritic range was detected in 10 patients with RAI and 3 without RAI. Eighteen patients had medium 24hUP levels (0.5–3.5 g). The 24hUP levels were less than 0.5 g in the remaining 8 patients. Moreover, 24hUP levels were tested among 39 of the 57 patients with trace SUP levels and were all less than 0.5 g. Thus, the estimated prevalences of proteinuria and nephritic range in our study were 8.66% and 3.63%, respectively.

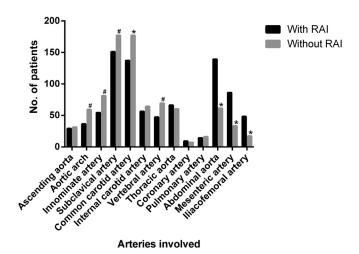


Figure 1 | Patients without renal artery involvement (RAI) showed a slightly higher incidence of aortic arch and involvement of its main branches, including the innominate artery, subclavical artery, common carotid artery, and vertebral artery. However, patients with RAI had more frequent involvement of arteries below the diaphragm, including the abdominal aorta, mesenteric artery, and iliacofemoral artery. #P < 0.05 compared with those with RAI. \*P < 0.01 compared with those with RAI.

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