Characteristics and clinical significance of aortic ulcer signs on computed tomography angiography in patients with Takayasu's arteritis

J. Wang[1], L. Shen[2], H. Liu[1], W. Wang[1], J. Ding[1], Z. Zheng[1]

[1]Department of Clinical Immunology, Xijing Hospital, Fourth Military Medical University, Xi'an, Shaanxi; [2]Department of Disease Prevention and Control, Xijing Hospital, Fourth Military Medical University Xi'an, Shaanxi, China.

Abstract

Objective

To explore the clinical and disease characteristics associated with aortic ulcers signs on computed tomography angiography (CTA) in patients with Takayasu's arteritis (TAK).

Methods

We retrospectively analysed CTA scans from consecutive TAK patients at Xijing Hospital between 2021 and 2025. We identified aortic ulcers and recorded their location, transverse diameter, and depth. Clinical, laboratory, and imaging data were compared between ulcer and non-ulcer groups. Multivariate regression analysed independent risk factors for ulcers.

Results

The prevalence of aortic ulcers was 7.6% (27/355) among overall screened TAK patients. Of 200 hospitalised patients in this study, 26 (13.0%) exhibited signs of aortic ulcers. Ulcers were predominantly located in the thoracic aorta, aortic arch, and left common carotid artery, with a median transverse diameter of 3.4 mm and a depth of 2.4 mm. The ulcer group demonstrated significantly higher rates of Numano V (69.2% vs. 40.8%, p=0.007), aortic regurgitation (52.4% vs. 21.8%, p=0.003), and T-SPOT TB positivity (43.5% vs. 19.2%, p=0.01). No significant differences in disease activity scores or most inflammatory markers were observed. Numano V was identified as an independent risk factor for the presence of aortic ulcers (OR 3.45, 95% CI 1.38-8.61, p=0.008). Follow-up CTAs in 5 patients indicated stable ulcer size despite vascular progression.

Conclusion

In TAK patients, aortic ulcers were independently associated with Numano V, but not with current systemic activity, suggesting they may represent chronic structural sequelae. Long-term monitoring is essential to reduce the risks of complications.

Key words

Takayasu's arteritis, ulcer, CT angiography, disease activity

*Jinghua Wang, MM**
*Li Shen, PhD**
Hao Liu, MM
Wenjuan Wang, MM
Jin Ding, PhD
Zhaohui Zheng, PhD

**Contributed equally.*

Please address correspondence to:
Zhaohui Zheng
Department of Clinical Immunology,
Xijing Hospital,
Fourth Military Medical University,
no. 127 Changle West Road,
Xi'an 710032, Shaanxi, China.
E-mail: zhengzh@fmmu.edu.cn

and to:
Jin Ding
(same postal address)
E-mail: dingjin@fmmu.edu.cn

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Introduction

Takayasu's arteritis (TAK) is a chronic, granulomatous large-vessel vasculitis primarily affecting the aorta and its major branches (1). Although relatively rare, it predominates in young women (2), and is a significant cause of severe vascular complications (such as stenosis, occlusion, and aneurysm formation) and end-organ damage (including stroke, myocardial infarction, renal hypertension, and limb ischaemia) in young populations. Consequently, it profoundly impacts quality of life and life expectancy (3, 4).

Accurate assessment of TAK disease activity is crucial for guiding treatment and preventing irreversible vascular damage (5). However, clinical evaluation remains challenging due to the non-specific clinical manifestations and insufficient sensitivity and specificity of serological markers (6). Imaging thus plays an indispensable role in TAK diagnosis, activity assessment, and monitoring (7). Computed tomography angiography (CTA) is widely available, and provides high spatial resolution and clear delineation of vessel walls and lumen; consequently, it has emerged as a primary non-invasive modality for evaluating TAK (8). CTA assessment of TAK disease activity is currently based on the following established imaging signs: all of which are widely incorporated into clinical evaluation criteria (9): vascular wall thickening, enhancement, and luminal changes (*e.g.* new or progressive stenosis, occlusion, dilation, or aneurysm formation).

Aortic ulcer is a morphological imaging term defined on CTA as a pit observed within the vascular wall contour, caused by local damage to the arterial intima, with the same degree of contrast enhancement as the aortic lumen (10). In the context of the differential diagnosis of aortic disease (11), this finding may represent various entities with distinct prognoses and aetiologies, including infectious, inflammatory, traumatic, and iatrogenic processes, as well as complications of atherosclerosis or intramural haematoma (12). Although aortic ulcers are widely recognised as markers of serious complications (13), they are also sequelae of inflammatory conditions, including TAK (14); furthermore, penetrating aortic ulcers can lead to serious adverse events, including aortic rupture (15). Therefore, investigating imaging signs of aortic ulcers is of substantial importance in the context of TAK. To date, only isolated case reports have documented this imaging feature (16, 17), leaving its incidence and clinical implications in TAK, including potential associations with disease activity or conventional atherosclerotic risk factors, unclear. Elucidating the clinical significance of the aortic ulcer sign will facilitate the identification of high-risk imaging features and the implementation of therapeutic strategies to prevent catastrophic vascular complications.

Thus, in this study, we aimed to determine the prevalence of the aortic ulcer sign on CTA in TAK patients and to investigate its associated clinical characteristics, risk factors and the correlation with disease activity.

Methods

Study design and participants

This retrospective analysis of a prospectively established TAK database enrolled consecutive TAK patients aged ≥18 years diagnosed who visited our department in Xijing Hospital (Xi'an, China) between January 1, 2021, and October 1st, 2025. Inclusion required fulfilment of the American College of Rheumatology classification criteria for TAK and the availability of at least one CTA examination (18). Exclusion criteria included incomplete clinical data, CTA image quality that was insufficient for analysis, and concurrent severe infections such as pulmonary infection or active tuberculosis (TB). Case eligibility was assessed independently by two senior physicians, with any discrepancies resolved through adjudication.

This study was approved by the Ethics Committee of Xijing Hospital (no. KY20242199-C-1) and was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments. The data analysed in this study were extracted from the Chinese Rheumatology Cohort Database of our department, with informed consent obtained

from all participants prior to their inclusion in the database.

Clinical data collection

Comprehensive clinical information was documented in a standardised manner. Angiographic TAK subtype was classified based on the criteria proposed by Numano (19). Disease activity was evaluated using the National Institutes of Health criteria (Kerr score) (20), Indian Takayasu Arteritis Activity Score (ITAS2010), and its version incorporating acute phase reactants (ITAS.A) (21). Disease activity was determined based on Physician's Global Assessment (PGA).

In this study, active disease was defined as PGA ≥6. Laboratory test results were extracted from the patients' electronic medical records and included leukocyte and platelet counts, haemoglobin concentration, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum amyloid A, complement C3 and C4, total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, creatinine, uric acid, T-SPOT.TB test results, interleukin-6, interleukin-8, TNF-α, and antiphospholipid antibody panel. For patients who had undergone transthoracic echocardiography, relevant parameters were documented, including those reflecting the presence of pulmonary hypertension, aortic regurgitation, mitral regurgitation and aortic sclerosis, along with the estimated pulmonary artery systolic pressure.

CT imaging acquisition and analysis

Aortic CTA was performed using a second-generation dual-source CT scanner (SOMATOM Definition Flash; Siemens Healthineers, Forchheim, Germany). The examination comprised a combined CTA of the neck and aorta, scanned in a craniocaudal direction with all patients in a supine position with both arms elevated. Scan parameters were as follows: tube voltage 100 kV, pitch 3.0, collimation of 2 x 128 x 0.6 mm achieved via z-flying focal spot technology, and a reference tube current-time product, 300 mAs. A bolus of 70 mL of the contrast agent iopromide (Ultravist 370, 370 mg I/mL, Bayer Schering Pharma, Berlin, Germany) was administered intravenously at a flow rate of 5 mL/s, followed by a 40 mL saline flush. Bolus tracking was performed the descending aorta at the level of the renal arteries as the region of interest, using a trigger threshold of 100 Hounsfield Units. The raw image data were transferred to an onsite workstation (syngo.via, VB10; Siemens Healthineers, Forchheim, Germany) for post-processing. Vascular involvement included conditions such as lumen stenosis, occlusion, dilation, and aneurysm formation, with all lesions documented for each patient. Two radiologists with ten and twenty years of experience, respectively, confirmed the presence of aortic ulcers and performed all measurements. The evaluation of aortic ulcers primarily focused on their transverse diameter and depth. For patients with aortic ulcers and more than one CTA, we documented any changes in imaging signs over time.

Statistical analysis

SPSS (v. 27; SPSS Inc., Chicago, Illinois, USA) was utilised to perform all statistical analyses, and statistical significance was defined as $p<0.05$. Numerical variables are displayed as mean (standard deviation, SD) or median (interquartile range, IQR) based on their distribution; categorical variables are presented as numbers (%). Continuous and ordered variables were analysed using the independent sample t-test or Mann-Whitney U-test, whereas the χ^2 test was used for categorical data.

We performed logistic regression to identify factors independently associated with aortic ulcers. Variable selection for multivariate modelling followed a purposeful selection approach, incorporating both clinically relevant factors and variables with $p<0.05$ in univariate logistic regression. The final model included traditional cardiovascular risk factors and TAK-specific variables. Multicollinearity among independent variables was assessed using the variance inflation factor (VIF); all VIF values were <2.0, indicating no significant collinearity. For continuous variables (age and disease duration), the linearity assumption in the logit was examined using the Box-Tidwell test; confirmed approximate linearity, supporting their inclusion as continuous predictors. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs) and *p*-values.

Results

Characteristics of TAK patients

A total of 355 patients were screened, and the overall prevalence of aortic ulcer signs was 7.6% (27/355). Given that most of these cases (26 cases) were identified among hospitalised inpatients and the high rate of incomplete data among outpatients, the final analysis cohort comprised 200 hospitalised patients, among whom the prevalence was 13.0% (26/200). The cohort comprised 178 females and 22 males, with a median age of 40 years (range: 18–72). The median age of onset was 31.5 years, and the median disease duration was 60 months. There were 81 (40.5%) treatment-naive patients, and 92 (46.0%) with prior glucocorticoid therapy; 89 (44.5%) patients were classified as Numano V (Table I).

Characteristics and distribution of aortic ulcers

Among the 200 hospitalised patients included in this study, 26 (13.0%) exhibited signs of aortic ulcer, and these were located primarily in the thoracic aorta (7/26), aortic arch (5/26) and left common carotid artery (5/26). Penetrating aortic ulcers were observed in 4 patients. The median transverse diameter was 3.4mm (range 1.0–12.5 mm), and the median depth was 2.4 mm (range 1.0–17.0 mm). The overall locations, depths, and transverse diameters of the aortic ulcers are detailed in Supplementary Table S1 and illustrated in Figure 1.

Clinical characteristics of TAK patients with or without aortic ulcers

The median age in the aortic ulcer and non-aortic ulcer groups was 45 and 40 years respectively ($p=0.18$). The disease course in the aortic ulcer group had a median duration of 144 months, compared with a median of 60 months in the non-aortic ulcer group; however, this difference did not reach statistical significance ($p=0.12$).

The prevalence of hypertension, diabe-

Table I. Baseline characteristics of TAK patients with or without aortic ulcers signs on CTA.

Variables	Total (n=200) (n=26)	With aortic ulcers (n=174)	Without aortic ulcers	*p*-value
Age, median (IQR), years	40.0 (31.0, 50.0)	45.0 (33.8, 50.3)	40.0 (30.8, 50.0)	*0.18*
Age of onset median (IQR), years	31.5 (24.8, 40.0)	32.0 (22.5, 41.0)	31.0 (24.0, 40.0)	*0.95*
Female, n (%)	178 (89.0)	22 (84.6)	155 (89.7)	*0.67*
Disease duration, median (IQR), months	60.0 (11.0, 144.0)	144.0 (26.5, 204.0)	60.0 (10.5, 126.5)	*0.12*
Complications, n (%)				
Diabetes	11 (5.5)	2 (7.7)	9 (5.2)	*0.95*
Hypertension	65 (32.5)	12 (46.2)	53 (30.5)	*0.11*
Hyperlipidaemia	27 (14.7)	2 (8.7)	25 (15.5)	*0.58*
Coronary heart disease	10 (5.0)	3 (11.5)	7 (4.0)	*0.25*
Cardiac insufficiency	22 (11.5)	5 (21.7)	17 (10.1)	*0.20*
History of tuberculosis infection	5 (2.5)	2 (7.7)	3 (1.7)	*0.13*
Transient ischaemic attack	3 (1.5)	0 (0.0)	3 (1.7)	*1.00*
Cerebral infarction	16 (8.0)	0 (0.0)	16 (9.2)	*0.22*
Clinical symptoms, n (%)				
Fatigue	91 (45.5)	12 (46.2)	79 (45.5)	*0.94*
Headache	72 (36.0)	10 (38.5)	62 (35.6)	*0.78*
Dizziness	112 (56.0)	13 (50.0)	99 (56.9)	*0.51*
Syncope	16 (8.4)	1 (4.4)	15 (8.9)	*0.73*
Black mumble	36 (18.0)	5 (19.2)	31 (17.8)	*0.92*
Loss of consciousness	13 (6.5)	1 (3.9)	12 (6.9)	*0.87*
Vision decline	32 (16.0)	6 (23.1)	26 (14.9)	*0.44*
Tinnitus	11 (5.5)	3 (11.5)	8 (4.6)	*0.32*
Chest distress	43 (21.5)	8 (30.8)	35 (20.1)	*0.22*
Chest and back pain	37 (18.5)	5 (19.2)	32 (18.4)	*0.39*
Neck pain	56 (28.0)	6 (23.1)	50 (28.7)	*0.55*
Chills in the limbs	5 (2.5)	2 (7.7)	3 (1.7)	*0.13*
Limb numbness	25 (12.5)	5 (19.2)	20 (11.5)	*0.43*
Limb lameness	23 (11.5)	4 (15.4)	19 (10.9)	*0.74*
Joint pain	39 (19.5)	7 (26.9)	32 (18.4)	*0.32*
Muscle pain	9 (4.5)	6 (3.5)	3 (11.5)	*0.18*
Treatment, n (%)				
Treatment-naive patients	81 (40.5)	6 (23.1)	75 (43.1)	*0.05*
Surgical treatment	41 (20.5)	6 (23.1)	35 (20.1)	*0.73*
Recent use of glucocorticoids	92 (46.0)	15 (57.7)	77 (44.3)	*0.20*
Recent use of tocilizumab	8 (4.0)	2 (7.7)	6 (3.5)	*0.62*
Antiplatelet drugs	47 (23.5)	8 (30.8)	39 (22.4)	*0.35*
Anticoagulant drugs	12 (6.0)	1 (3.9)	11 (6.3)	*0.99*
Lipid-lowering drugs	43 (21.5)	6 (23.1)	37 (21.3)	*0.83*

TAK: Takayasu's arteritis; CTA: computed tomography angiography; IQR: interquartile range.
* $p<0.05$, ** $p<0.01$.

tes, coronary heart disease, and heart failure was relatively high among patients with aortic ulcers; however, the prevalence of these comorbidities, as well as that of hyperlipidaemia, cerebral infarction, transient ischaemic attack, and previous TB infection history, was not significantly different ($p>0.05$). Similarly, clinical symptoms (all $p>0.05$), as well as the proportion of treatment-naive patients (aortic ulcer group *vs*. non-aortic ulcer group, 23.1%*vs*. 43.1%, $p=0.05$), did not differ between the groups. Additionally, the two groups did not differ in terms of recent treatment, including the use of glucocorticoids, tocilizumab, antiplatelet drugs, anticoagulants and lipid-lowering drugs, or previous vascular surgery (all $p>0.05$) (Table I).

Laboratory parameters and disease activity of TAK patients with or without aortic ulcers

Laboratory analysis revealed that the aortic ulcer group exhibited a significantly lower rate of elevated CRP levels than the non-aortic ulcer group (23.1% *vs*. 46.0%, $p=0.03$). When stratifying the analysis based treatment status, the proportion of those with elevated CRP levels did not differ among treatment-naive patients (aortic ulcer *vs*. non-aortic ulcer, 50.0% *vs*. 53.3%, $p=0.79$); however, among non-naive patients, a significant difference was observed between the two groups (aortic ulcer *vs*. non-aortic ulcer, 15.0% *vs*. 40.0%, $p=0.03$). This suggests that medication has a substantial impact on CRP levels in these patients. Additionally, T-SPOT.TB positivity was higher in the aortic ulcer group (43.5% *vs*. 19.2%, $p=0.01$). No significant differences were found in all other detection indicators, including routine blood parameters, lipids, renal function, inflammatory markers, complements, and antiphospholipid antibodies (all $p>0.05$).

No significant differences between the aortic ulcer and non-aortic ulcer groups were found in the assessment of disease activity including ITAS2010, ITAS.A, PGA, and Kerr scores (all $p>0.05$) (Table II). The proportion of patients with active disease was 65.4% in the aortic ulcer group, and 59.8% in the non-aortic ulcer group ($p>0.05$). The stratified analysis based on treatment status

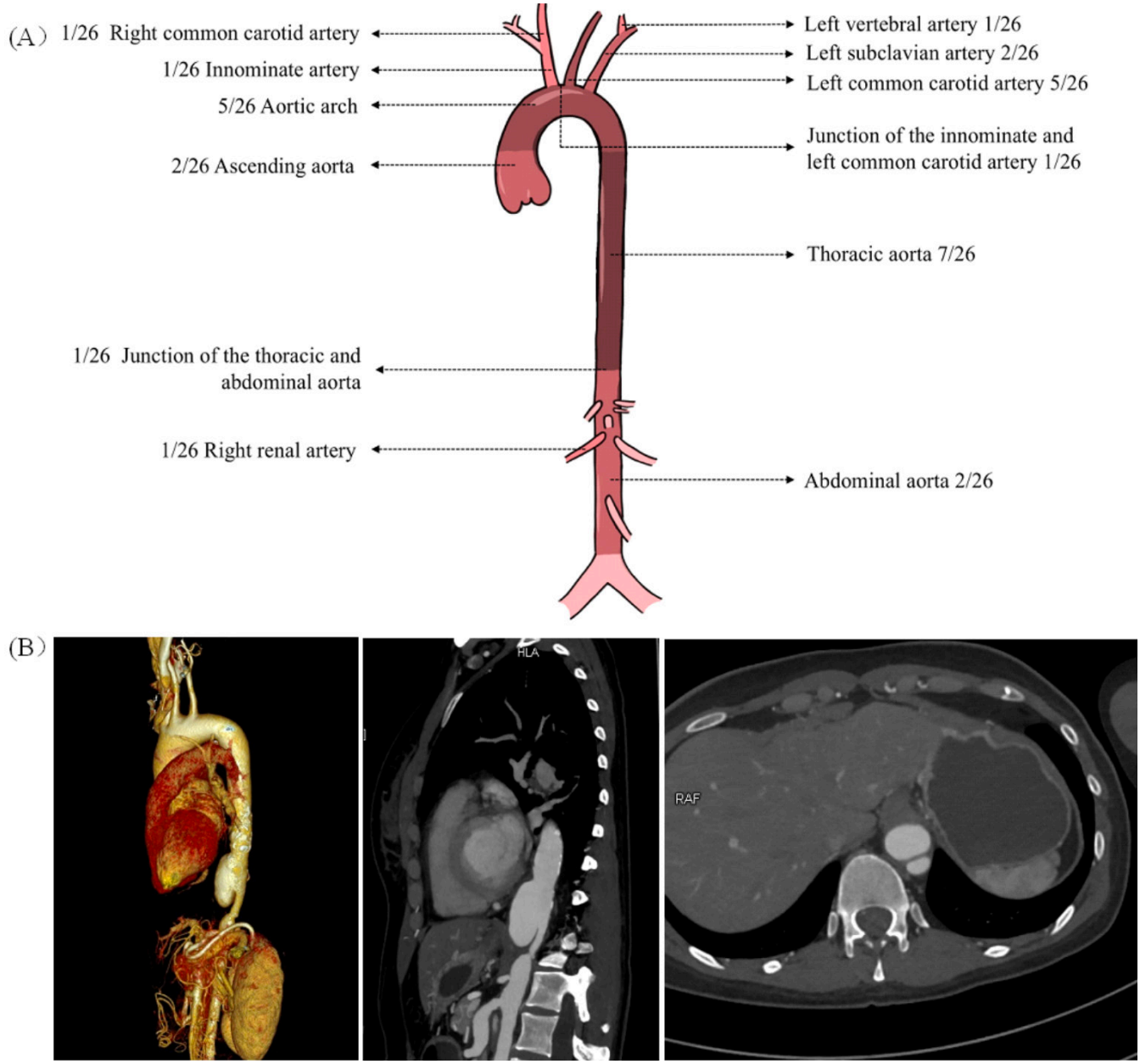

Fig. 1.
A: Location of aortic ulcers in 26 TAK patients.
B: Patient 26 (33-year-old female): Penetrating aortic ulcer in the thoracic aorta measuring 9.5 mm in transverse diameter and 17.0 mm in depth.

revealed no significant differences between treatment-naive and non-naive patients in terms of ITAS2010 (p=0.63), ITAS.A (p=0.29), PGA (p=0.88), or Kerr (p=0.81), nor in the proportion of patients with active disease determined by the rheumatologist (p=0.52).

Vascular involvement and Numano type of TAK patients with or without aortic ulcer

An analysis of aortic involvement demonstrated significant differences between the aortic ulcer and non-aortic ulcer groups in the following distributions: the left subclavian artery (p=0.01), right subclavian artery (p=0.003), overall involvement of subclavian arteries (p=0.03), thoracic aorta (p=0.02), and superior mesenteric artery (p=0.01). In contrast, no significant differences were observed in the prevalence of involvement in the other aortic segments (all p>0.05) or in the presence of atherosclerosis or calcification (both p>0.05).

The Numano type differed significantly between the two groups (p=0.02). Post hoc pairwise comparisons revealed that the primary source of this difference was between Numano I and Numano V (p=0.01). Numano V was the most prevalent pattern of vascular involvement, observed in 44.5% of participants, with a significantly higher prevalence in the aortic ulcer group than in non-aortic ulcer the group (69.2% *vs.* 40.8%, p=0.01) (Table III).

Echocardiography of TAK patients with or without aortic ulcers

A total of 168 TAK patients had avail-

Table II. Laboratory indicators and disease activity evaluation of TAK patients with or without arterial ulcers signs on CTA.

Variables	Total (n=200)	With arterial ulcers (n=26)	Without arterial ulcers (n=174)	*p*-value
Laboratory indicators				
Elevated ESR, n (%)	67 (33.7)	5 (19.2)	62 (35.8)	*0.10*
Elevated CRP, n (%)	86 (43.0)	6 (23.1)	80 (46.0)	*0.03**
Elevated SAA, n (%)	102 (62.6)	12 (52.2)	90 (64.3)	*0.27*
Complement 3, mg/dL, median (IQR)	93.5 (81.2, 113.0)	92.9 (77.3, 109.5)	94.2 (81.5, 114.0)	*0.38*
Complement 4, mg/dL, median (IQR)	22.7 (17.6, 26.9)	21.5 (14.6, 24.9)	22.9 (17.9, 27.3)	*0.14*
Positive T-SPOT.TB test results, n (%)	37 (22.6)	10 (43.5)	27 (19.2)	*0.01**
White blood cell, $\times10^9$/L median (IQR)	7.1 (5.4, 8.9)	7.5 (6.1, 9.1)	7.0 (5.3, 8.9)	*0.46*
Haemoglobin, g/L, median (IQR)	118.0 (107.0, 128.3)	119.5 (107.8, 135.3)	118.0 (106.8, 128.0)	*0.45*
Platelet, $\times10^9$/L median (IQR)	241.5 (193.8, 312.5)	219.5 (189.3, 268.3)	247.0 (196.5, 319.5)	*0.06*
Neutrophil, $\times10^9$/L median (IQR)	44.7 (3.3, 6.3)	5.1 (3.7, 6.3)	4.7 (3.3, 6.4)	*0.39*
Lymphocyte, $\times10^9$/L median (IQR)	1.7 (1.2, 2.2)	1.7 (1.1, 2.5)	1.7 (1.2, 2.2)	*0.57*
Albumin, g/L, median (IQR)	38.7 (36.2, 41.2)	38.7 (36.6, 41.5)	38.6 (36.1, 41.3)	*0.76*
Elevated triglyceride, n (%)	16 (8.7)	0 (0.0)	16 (9.9)	*0.24*
Elevated cholesterol, n (%)	9 (4.9)	2 (8.7)	7 (4.4)	*0.70*
Abnormal HDL, n (%)	134 (72.8)	16 (69.6)	118 (73.2)	*0.71*
Elevated LDL, n (%)	7 (4.1)	0 (0.0)	7 (4.6)	*1.00*
Serum uric acid, μmol/L, median (IQR)	258.0 (222.0, 331.5)	277.0 (248.0, 320.0)	253.0 (221.8, 335.0)	*0.41*
Serum creatinine, μmol/L, median (IQR)	52.0 (46.0, 61.8)	55.0 (46.0, 63.5)	51.0 (46.5, 61.0)	*0.34*
Elevated IL-6, n (%)	124 (63.9)	15 (60.0)	109 (64.5)	*0.66*
Elevated TNF-α, n (%)	68 (35.1)	6 (24.0)	62 (36.7)	*0.22*
Elevated IL-8, n (%)	67 (34.5)	9 (36.0)	58 (34.3)	*0.87*
Abnormal antiphospholipid antibody, n (%)	11 (7.9)	2 (13.3)	9 (7.2)	*0.74*
Disease activity evaluation				
ITAS2010, median (IQR)	8.0 (6.0, 10.0)	8.0 (7.0, 13.0)	8.0 (5.0, 10.0)	*0.06*
ITAS.A, median (IQR)	9.0 (7.0, 12.3)	9.0 (8.0, 14.0)	9.0 (6.0, 12.0)	*0.25*
PGA, median (IQR)	6.0 (5.0, 7.0)	6.0 (4.0, 7.0)	6.0 (5.0, 7.0)	*0.70*
Kerr, median (IQR)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	*0.78*
Active disease, n (%)	121 (60.5)	17 (65.4)	104 (59.8)	0.59

TAK: Takayasu's arteritis; CTA: computed tomography angiography; IQR: interquartile range; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; SAA: serum amyloid A; HDL: high-density lipoprotein; LDL: low-density lipoprotein; IL-6: interleukin-6; TNF-α: tumour necrosis factor-alpha; ITAS2010: Indian Takayasu Activity Score 2010; PGA: physician's global assessment.
*p<0.05, ** p<0.01.

able echocardiographic data, revealing a significantly higher prevalence of aortic regurgitation in the aortic ulcer group compared with the non-aortic ulcer group (52.4% *vs*. 21.8%, p=0.003). In contrast, no significant differences were observed for other parameters, including cardiac enlargement, regurgitation of other valves (tricuspid and pulmonary), ventricular dysfunction, and pulmonary artery systolic pressure (all p>0.05) (Table IV). Among the 11 patients with aortic valve regurgitation in the aortic ulcer group, 7 had mild regurgitation, and 4 exhibited moderate-to-severe regurgitation. Within this subgroup of 4 patients with more severe regurgitation, 3 had comorbid hypertension and 1 had cardiac insufficiency.

Logistic regression analysis of group differences

Univariate analysis identified Numano V as a significant risk factor, associated with a more than threefold increase in the likelihood of aortic ulcer signs (OR=3.26, 95%CI 1.38–8.61, p=0.01). In contrast, no statistically significant associations were found for age (OR=1.02, p=0.19), hypertension (OR=1.96, p=0.12), hyperlipidaemia (OR=0.45, p=0.30), T-SPOT positivity (OR=1.06, p=0.92), active disease (OR=1.27, p=0.59), or disease duration (OR=1.00, p=0.06).

Multivariate logistic regression analysis confirmed that Numano V (OR = 3.45, 95% CI 1.38–8.61, p=0.008) was the only significant independent factor associated with aortic ulcers signs in this cohort (Table V).

Follow-up of some patients with aortic ulcers

Of the 26 patients with aortic ulcers, 5 underwent 2 serial CTA scans during treatment; these scans demonstrated overall stability of the ulcers regardless of radiographic or clinical progression of the underlying vasculopathy. Specifically, in Patient 17 (17-month follow-up), generalised wall thickening and increased luminal stenosis were observed, accompanied by a rise in the ITAS2010 score (from 5 to 6) and elevated inflammatory markers (ESR and CRP); however, no significant change in ulcer size was noted. Similarly, Patient 26 (22-month follow-up) exhibited no significant alterations in their aortic ulcer despite extension of the lesion range in the right common carotid artery and new stenosis at the internal carotid artery bifurcation. Three additional patients (Patients 9, 14, and 21; follow-up at 7, 19, and 14 months, respectively) also showed stable vascular lesions on CTA, with no significant documented changes in their respective aortic ulcers.

Discussion

In this study, we found an overall prevalence of 7.6% for aortic ulcer signs on CTA, suggesting that this imaging

Table III. Vascular involvement and Numano type of TAK patients with or without aortic ulcers signs on CTA.

Variables, n (%)	Total (n=200)	With aortic ulcers (n=26)	Without aortic ulcers (n=174)	*p*-value
Intracranial arteries	24 (12.0)	5 (19.2)	19 (10.9)	*0.72*
Innominate artery	136 (68.0)	20 (76.9)	116 (66.7)	*0.30*
Common carotid artery	172 (86.0)	24 (92.3)	148 (85.1)	*0.49*
Left common carotid arteries	160 (80.4)	24 (92.3)	136 (78.6)	*0.10*
Right common carotid artery	139 (69.9)	22 (84.6)	117 (67.6)	*0.08*
Internal carotid artery	64 (32.2)	12 (46.2)	52 (30.1)	*0.10*
Left internal carotid artery	46 (23.0)	7 (26.9)	39 (22.4)	*0.61*
Right internal carotid artery	45 (22.5)	9 (34.6)	36 (20.7)	*0.13*
Vertebral artery	58 (29.2)	9 (34.6)	49 (28.3)	*0.51*
Left vertebral artery	38 (19.0)	6 (23.1)	32 (18.4)	*0.76*
Right vertebral artery	38 (19.0)	6 (23.1)	32 (18.4)	*0.76*
Subclavian artery	149 (75.3)	24 (92.3)	125 (72.7)	*0.03**
Left subclavian artery	135 (67.5)	23 (88.5)	112 (64.4)	*0.01**
Right subclavian artery	106 (53.3)	21 (80.8)	85 (49.1)	*0.003***
Axillary artery	43 (21.6)	6 (23.1)	37 (21.4)	*0.85*
Left axillary artery	30 (15.0)	4 (15.4)	26 (14.9)	*0.81*
Right axillary artery	20 (10.0)	3 (11.5)	17 (9.8)	*0.94*
Aortic arch	127 (63.8)	17 (65.4)	110 (63.6)	*0.86*
Ascending aorta	101 (50.5)	15 (57.7)	86 (49.4)	*0.43*
Thoracic aorta	119 (59.5)	21 (80.8)	98 (56.3)	*0.02**
Abdominal aorta	73 (36.5)	12 (46.2)	61 (35.1)	*0.27*
Coeliac trunk	32 (16.0)	8 (30.8)	24 (13.8)	*0.06*
Superior mesenteric artery	40 (20.0)	10 (38.5)	30 (17.2)	*0.01**
Inferior mesenteric artery	4 (2.0)	1 (3.9)	3 (1.7)	*0.43*
Renal arteries	33 (16.5)	7 (26.9)	26 (14.9)	*0.18*
Left renal artery	31 (16.2)	6 (26.1)	25 (14.9)	*0.22*
Right renal artery	35 (17.5)	6 (23.1)	29 (16.7)	*0.60*
Pulmonary artery	63 (31.8)	7 (26.9)	56 (32.6)	*0.56*
Atherosclerotic plaque	59 (29.7)	6 (23.1)	53 (30.5)	*0.44*
Calcified plaque	39 (19.6)	3 (11.5)	36 (20.8)	*0.27*
Numano type				*0.02**
I	25 (12.5)	0 (0.0)	25 (14.4)	*0.08*
IIa	29 (14.5)	3 (11.5)	26 (14.9)	*0.87*
IIb	46 (23.0)	5 (19.2)	41 (23.6)	*0.62*
III	4 (2.0)	0 (0.0)	4 (2.3)	*1.00*
IV	5 (2.5)	0 (0.0)	5 (2.9)	*1.00*
V	89 (44.5)	18 (69.2)	71 (40.8)	*0.007**

TAK: Takayasu's arteritis; CTA: computed tomography angiography.
*$p<0.05$, **$p<0.01$.

feature is not rare in TAK. Analysis of clinical data from patients with and without aortic ulcers demonstrated that those with aortic ulcers had a higher prevalence of Numano V, aortic regurgitation, and T-SPOT positivity; however, no significant differences were observed in disease activity, traditional cardiovascular risk factors or most inflammatory markers. Additionally, Numano V was identified as an independent risk factor for the occurrence of aortic ulcers in TAK patients.

Two possible interrelated mechanisms may explain the association between Numano V and aortic ulcers. First, the systemic inflammatory response associated with Numano V is typically more pronounced, characterised by infiltration of activated immune cells, including lymphocytes and macrophages, into the vessel walls. These cells release pro-inflammatory cytokines and proteolytic enzymes, such as matrix metalloproteinases, which can degrade elastic fibres and collagen, thereby weakening the vascular wall and increasing its intrinsic fragility (22). Second, secondary hypertension is prevalent in patients with Numano V, particularly due to lesions affecting the renal artery. This may result in prolonged high pressure and elevated haemodynamic stress on the vascular wall, further exacerbating intimal damage and promoting ulcer formation. Together, the inflammation-induced vascular fragility and hypertension-driven haemodynamic stress associated with Numano V may facilitate aortic ulcer development.

The prevalence of aortic regurgitation in our study was 26%, aligning with previous findings (23). While aortic regurgitation is typically valvular, the lack of significant valvular differences in our cohort suggests a distinct mechanism based in aortic root or ascending aortic pathology. In TAK, inflammatory dilation or wall dissection can mechanically separate the valve leaflets, causing maladaptation and regurgitation (24). Aortic diastolic regurgitation initiates a haemodynamic cascade: reduced diastolic pressure triggers compensatory rises in systolic pressure and pulse pressure, thereby creating a high-velocity state with shear stress fluctuations that impair organ perfusion and endothelial function (25). Over time, exposure to these abnormal forces may

Table IV. Echocardiography of TAK patients with or without aortic ulcers signs on CTA.

Variables	Total (n=168)	With aortic ulcers (n=21)	Without aortic ulcers (n=147)	*p*-value
Enlarged left heart, n (%)	31 (18.5)	5 (23.8)	26 (17.7)	*0.71*
Enlarged right heart, n (%)	8 (5.2)	0 (0.0)	8 (5.4)	*0.58*
Left ventricular diastolic dysfunction, n (%)	79 (47.5)	12 (50.0)	72 (47.1)	*0.79*
Left ventricular systolic dysfunction, n (%)	10 (6.0)	1 (4.8)	9 (6.1)	*0.81*
Aortic insufficiency, n (%)	21 (12.5)	5 (23.8)	16 (10.9)	*0.19*
Aortic sclerosis, n (%)	17 (10.1)	3 (14.3)	14 (9.5)	*0.77*
Pericardial effusion, n (%)	16 (9.5)	2 (9.5)	14 (9.5)	*1.00*
Aortic regurgitation, n (%)	43 (25.6)	11 (52.4)	32 (21.8)	*0.003***
Bicuspid valve regurgitation, n (%)	30 (17.9)	7 (33.3)	23 (15.7)	*0.09*
Tricuspid regurgitation, n (%)	75 (44.6)	12 (57.1)	63 (42.9)	*0.22*
Pulmonary valve regurgitation, n (%)	10 (6.0)	2 (9.5)	8 (5.4)	*0.81*
Pulmonary aortic hypertension, n (%)	14 (8.3)	4 (19.1)	10 (6.8)	*0.14*
Pulmonary artery systolic pressure, mmHg, median (IQR)	25.5 (20.0, 32.0)	27.0 (21.5, 33.0)	25.0 (22.0, 32.0)	*0.63*

TAK: Takayasu's arteritis; CTA: computed tomography angiography.
*p<0.05, **p<0.01.

Table V. Multivariate logistics regression analysis of risk factors for aortic ulcers in patients with TAK.

Exposure	OR	95% LCI	95% UCI	*p*-value
Age	1.02	0.98	1.05	*0.34*
Disease duration	1.00	1.00	1.00	*0.87*
Numano V	3.45	1.38	8.61	*0.008***
Hypertension	0.99	0.40	2.46	*0.98*
Hyperlipidaemia	2.42	0.81	7.20	*0.11*
Active disease	1.23	0.50	3.00	*0.65*
Positive T-SPOT.TB test results	0.75	0.23	2.44	*0.63*

TAK: Takayasu's arteritis; OR: odds ratio; LCI: lower confidence interval; UCI: upper confidence interval.
*p<0.05, **p<0.01.

promote maladaptive vascular remodelling, potentially contributing to the aortic ulcers observed in our study.

A history of TB infection is reported in approximately 10% of TAK patients in China (26). Consequently, *M. tuberculosis* is hypothesised to be a potential trigger for TAK in genetically susceptible individuals, potentially influencing its pathophysiology (27). In our study, although there was no significant difference in the clinical history of TB infection between groups, the aortic ulcer group exhibited a higher rate of positive T-SPOT.TB test results in univariate analysis (43.5% *vs*. 19.2%, p=0.01). However, this association was not retained after multivariate adjustment for potential confounders (OR 0.75, 95% CI 0.23–2.44, p=0.63). Importantly, this finding should be considered exploratory and hypothesis-generating rather than indicative of a causal relationship. Traditionally, aortic ulcers have been linked to atherosclerotic plaque rupture; however, our study found no significant differences in the presence of atherosclerotic plaques and its risk factors between the two groups. Conversely, tuberculous aortitis has been reported to cause complications such as aortic pseudoaneurysm, aortic ulcers, wall thickening, and stenosis (28). Therefore, the higher prevalence of a positive TB result observed in the aortic ulcer group implies the importance of investigating the multifactorial nature of inflammatory states that predisposes individuals to significant aortic wall injury.

We found no definitive association between aortic ulcers and heightened disease activity or elevated inflammatory markers. This lack of correlation may stem from the challenges in accurately assessing disease activity, particularly regarding ulcer development, due to limitations in current evaluation methods. The ITAS2010 primarily captures overt clinical manifestations based on symptoms and signs from the previous three months (21), whereas PGA incorporates clinical evaluations, serological markers and imaging assessment (29). Additionally, non-specific inflammatory marker such as CRP or ESR are not reliable indicators of disease activity (30), especially regarding local aortic inflammation (31). Furthermore, the aortic ulcers we observed likely arose in a subclinical state without specific clinical manifestations, making their detection reliant on imaging techniques. A temporal delay may exist between episodes of high disease activity and ulcer development, implying that some vascular abnormalities can arise or persist in the absence of active inflammation (32). Longitudinal CTA follow-up revealed that aortic ulcer size remained stable over time, irrespective of disease duration, overall vascular progression, or the emergence of active disease. This dimensional stability offers key pathophysiological insight: once formed, aortic ulcers likely represent a stationary sequela or quiescent fibrotic scar resulting from prior focal inflammation, rather than a dynamic lesion indicative of ongoing disease activity.

Nevertheless, the detection of aortic ulcers warrants heightened clinical vigilance. Among the 26 patients with aortic ulcers, 4 had penetrating lesions. Although currently asymptomatic and stable in follow-up cases, these penetrating ulcers carry a known risk of progression to rupture or dissection,

necessitating close surveillance to prevent life-threatening complications, with surgical evaluation when indicated. Additionally, although traditional cardiovascular risk factors did not differ significantly between groups, they showed a tendency to cluster in the aortic ulcer group. This underscores the need for further study and highlights the importance of monitoring long-term cardiovascular complications in these patients.

This study has some limitations. First, the retrospective, cross-sectional design limited the accurate determination of patients' disease status and pathophysiological context at the time of aortic ulcer formation, thereby hindering causal inference. Second, the single-centre design and modest sample size limit the generalisability of our findings. Additionally, due to incomplete clinical data in outpatients, we restricted our analysis to hospitalised patients, which may introduce selection bias. Hospitalised individuals often represent a more severe or active disease spectrum; therefore, the observed prevalence of 13.0% in this cohort may overestimate the true prevalence in the general TAK population. This limits the applicability of our results to outpatient or milder cases. Third, the inherently limited duration of this study and small number of patients with follow-up results may have hindered the comprehensive capture of the natural history of ulcer evolution, resulting in inadequately characterised long-term outcomes. Fourth, due to the practical and ethical challenges associated with obtaining tissue specimens, this study lacked pathological examination and primarily relied on clinical and imaging observation. Because of the ambiguity in the definition of aortic ulcers and limitations of current imaging techniques (33), differentiating aortic ulcers in TAK from other lesions, such as ulcerated plaques, remains a challenge. These limitations highlight the need for future prospective, multicentre studies with larger sample sizes and longer follow-up periods, incorporating pathological and molecular assessments to better elucidate the mechanisms and natural history of aortic ulcers.

Conclusion

The prevalence of aortic ulcer signs occurs with an incidence rate of approximately 7.6% in overall TAK patients. These signs were independently associated with Numano V but did not correlate with disease activity. Instead, our findings suggest that aortic ulcers may represent chronic structural sequelae rather than markers of current systemic activity. Given the potential risks associated with penetrating ulcers and their complications, long-term monitoring of these aortic ulcer signs is essential.

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