Coronary artery calcification in Takayasu's arteritis: clinical characteristics and risk factors

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Abstract

Objective

Coronary artery calcification (CAC) is frequently observed in Takayasu's arteritis (TAK). Our objective is to calculate the prevalence and severity of CAC in TAK, while evaluating the influence of traditional cardiovascular risk factors, glucocorticoid exposure, and disease activity on CAC.

Methods

This retrospective study involved 155 TAK patients. We measured the Agatston score by coronary computed tomography angiography (CCTA) and categorised all patients into groups with or without CAC (41 vs. 114) to compare clinical characteristics and ancillary findings between the two groups.

Results

Among the TAK patients, a total of 41 TAK patients (26.45%) exhibited CAC. Age of onset, disease duration, history of hypertension, history of hyperlipidaemia, Numano V and glucocorticoid use emerged as the independent risk factors for developing CAC in TAK (OR [95% CI] 1.084[1.028–1.142], p=0.003; 1.005 [1.001–1.010], p=0.020; 4.792 [1.713–13.411], p=0.003; 4.199 [1.087–16.219], p=0.037; 3.287 [1.070–10.100], p=0.038; 3.558[1.269–9.977], p=0.016). Nonetheless, CAC was not associated with disease activity. Moreover, the extent of calcification score in TAK showed a positive correlation with the number of traditional cardiovascular risk factors.

Conclusion

We recommend CCTA screening for Numano V classified TAK patients. Glucocorticoid usage significantly escalates the risk of CAC. Therefore, in cases of effectively controlled disease, the inclusion of immunosuppressants aimed at reducing glucocorticoid dosage is advisable.

Key words

Takayasu's arteritis, coronary artery calcification, risk factors, glucocorticoid

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Introduction

Takayasu's arteritis (TAK) is a chronic inflammatory disease primarily involving large vessels, notably the aorta and its main branches. It has a low incidence and has considerable heterogeneity across different geographic regions. High inflammatory load and hemodynamic disorders may lead to myocarditis and LV dysfunction. (1-3). Disease progression leads to the gradual development of stenosis, occlusion, dilation, and in some cases, aneurysm formation within the affected vessels, culminating in severe sequelae such as organ and limb ischaemia (4). The pathogenesis is currently unknown and is more common in young women. Fatty acid oxidation in fibrotic adventitia in TAK maybe play a fundamental role in LVV pathogenesis (5, 6).

While palpitations and chest tightness are not common complaints among most patients, 10–20% of individuals with TAK exhibit coronary lesions (7). Coronary artery involvement, encompassing stenosis, occlusion, and coronary artery calcification (CAC), significantly influences the long-term prognosis of TAK (8). Patients with high coronary calcification score have an extensive coronary plaque burden and contribute to a high risk of stress-induced ischaemic events (9).

In clinical work, we found an interesting phenomenon that CAC was more likely to appear in TAK patients than in age- and sex-matched controls. Current research predominantly focused on coronary lesions and prognosis analysis of TAK patients, with scant attention given to clinical characteristics and risk factors associated specifically with CAC in TAK. Our retrospective study collected comprehensive clinical data and explored whether traditional cardiovascular risk factors, inflammation and drugs contributed as risk factors for CAC in TAK. The insights gained from this investigation can serve as a foundation for early intervention targeting these identified risk factors and provide guidance for clinical practice.

Materials and methods

Participants

We consecutively enrolled 155 TAK patients from Beijing Anzhen Hospital between January 2015 and June 2022, all meeting the American College of Rheumatology classification criteria in 1990 and having undergone at least one CCTA examination (10). Patients must meet three or more criteria to be diagnosed: 1. The age of initial onset ≤40 years; 2. Intermittent claudication; 3. One or bilateral brachial artery beats weakened; 4. Systolic pressure of both upper limbs >10 mmHg; 5. Subclavian artery or aortic murmur; 6. Arteriogram abnormality.

Exclusion criteria encompassed the following three points: 1. Image quality affects the accuracy of calcification score assessment. 2. Previous coronary artery bypass surgery or coronary stenting. 3. Other autoimmune diseases. This study was permitted by the Ethics Committee of Beijing Anzhen Hospital (registered number of approvals: 2022237X) and abided by the ethical guidelines of the Helsinki Declaration and its amendments. Since the research thought is retrospective, informed consent forms are not required.

Clinical data collection

This study involved a retrospective collection of clinical data from patients' initial hospitalisation. All the data are obtained from the medical record system and clinical laboratory system of Beijing Anzhen Hospital. The angiographic genre of TAK was classified in line with the standard proposed by Numano and Hata (11). Disease activity was estimated using The National Institutes of Health (NIH) standard, ITAS with acute-phase reactants (ITAS-A), and the Indian Takayasu's Arteritis Activity Score (ITAS2010) (1, 12).

All the laboratory indicators are routinely tested at our hospital. XE2100 (SYMEX, Japan) was utilised to detect the 12-hour fasting venous blood collected at early morning. Serum samples was tested by Hitachi 7600-120 automatic biochemical analyser (Tokyo, Japan). Interleukin 6(IL-6), erythrocyte sedimentation rate (ESR), total cholesterol (TC), uric acid (UA), C-reactive protein (CRP), troponin I(TNI), homocysteine (HCY), creatinine (Cr), tumour necrosis factor-α (TNF-α), Brain

Table I. Baseline characteristics of TAK patients with or without coronary artery calcification.

Variables	Total (n=155)	With coronary calcification (n=41)	Without coronary calcification (n=114)	*p* value
Age (years)	40.00 (29.00, 49.25)	52.00 (41.50, 57.00)	37.00 (27.50, 46.00)	<0.001
Age of onset (years)	28.00 (22.00, 38.00)	33.00 (25.50, 43.00)	27.00 (21.75, 36.25)	0.014
Female (n%)	137.00 (88.40)	35.00 (85.40)	102.00 (89.50)	0.481
Disease duration (months)	72.00 (12.00, 180.00)	120.00 (24.00, 288.00)	50.00 (12.00, 156.00)	0.006
Body mass index (kg/m^2)	22.48 (20.29, 24.86)	23.31 (21.28, 25.78)	21.97 (19.42, 24.54)	0.047
Systolic BP (mmHg)	128.00 (112.75, 142.25)	133.00 (120.00, 152.00)	124.00 (110.00, 142.00)	0.039
Diastolic BP (mmHg)	70.00 (60.00, 80.00)	70.00 (60.00, 83.00)	70.00 (60.00, 80.00)	0.521
Menopause (n%)	35.00 (25.50)	17.00 (48.60)	18.00 (17.60)	<0.001
History (n%)				
Smoking	15.00 (9.70)	4.00 (9.80)	11.00 (9.60)	0.984
Drinking	8.00 (5.20)	1.00 (2.40)	7.00 (6.10)	0.358
Hypertension	55.00 (36.40)	26.00 (68.40)	29.00 (25.70)	<0.001
Diabetes	8.00 (5.20)	4.00 (9.80)	4.00 (3.50)	0.121
Hyperlipidaemia	21.00 (13.50)	14.00 (34.10)	7.00 (6.10)	<0.001
Coronary heart disease	13.00 (8.40)	7.00 (17.10)	6.00 (5.30)	0.019
Cerebral vascular disease	9.00 (5.80)	7.00 (17.10)	2.00 (1.80)	<0.001
Medication				
Glucocorticoid (n%)	52.00 (33.50)	19.00 (46.30)	33.00 (28.90)	0.043
Glucocorticoid -accumulation (g)	0 (0, 1.43)	0 (0, 4.28)	0 (0, 0.71)	0.029
Statin (n%)	55.00 (35.50)	22.00 (53.70)	33.00 (28.90)	0.005
Aspirin (n%)	58.00 (37.40)	16.00 (39.00)	42.00 (36.80)	0.804
Hydroxychloroquine (n%)	15.00 (9.70)	6.00 (14.60)	9.00 (7.90)	0.345
Methotrexate (n%)	66.00 (42.60)	15.00 (36.60)	51.00 (44.70)	0.365
Cyclophosphamide (n%)	37.00 (23.90)	10.00 (24.40)	27.00 (23.70)	0.928
Leflunomide (n%)	4.00 (2.60)	1.00 (2.40)	3.00 (2.60)	0.947
Mycophenolate mofetil (n%)	29.00 (18.70)	4.00 (9.80)	25.00 (21.90)	0.087
csDMARDs (n%)	109.00 (70.30)	28.00 (68.30)	81.00 (71.10)	0.740
Tocilizumab (n%)	45.00 (29.00)	8.00 (19.50)	37.00 (32.50)	0.117
bDMARDs (n%)	49.00 (31.60)	9.00 (22.00)	40.00 (35.10)	0.121
Clinical symptoms (n%)				
Dizziness	69.00 (44.50)	25.00 (61.00)	44.00 (38.60)	0.013
Headache	33.00 (21.30)	7.00 (17.10)	26.00 (22.80)	0.442
BP difference	57.00 (36.80)	20.00 (48.80)	37.00 (32.50)	0.063
Acrotism	25.00 (16.10)	5.00 (12.20)	20.00 (17.50)	0.425
Unconsciousness	5.00 (3.20)	3.00 (7.50)	2.00 (1.80)	0.078
Haemoptysis	5.00 (3.20)	2.00 (4.90)	3.00 (2.60)	0.485
palpitation	17.00 (11.00)	9.00 (22.00)	8.00 (7.00)	0.009
Chest pain	28.00 (18.20)	7.00 (17.10)	21.00 (18.60)	0.830
Cervicodynia	22.00 (14.20)	6.00 (14.60)	16.00 (14.00)	0.925
Arthralgia	15.00 (9.70)	7.00 (17.10)	8.00 (7.00)	0.062

TAK: Takayasu's arteritis; csDMARDs: conventional synthetic disease-modifying anti-rheumatic drugs; bDMARDs: biological disease-modifying anti-rheumatic drugs.

Natriuretic Peptide (BNP), alanine aminotransferase (ALT), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), calcium (Ca), phosphorus (PHOS) were tested, and counted the ratios of LDL-C/HDL-C, TC/HDL-C and TG/HDL-C.

Vascular involvement was defined as lumen stenosis, occlusion and aneurysm formation. We used ultrasound to assess the involvement of carotid artery, vertebral artery, subclavian artery, upper and lower extremity artery, common iliac artery, superior mesenteric artery and renal artery. Pulmonary artery and coronary artery involvement was assessed using computed tomography angiography. The involvement of thoracic, abdominal and intracranial arteries was assessed using magnetic resonance angiography.

CT imaging protocol

Aquilion ONE CT scanner completed coronary imaging in this study (Toshiba Medical Systems, Otawa, Japan). This 640 slice, 320-row CT scanner equip with 350 ms gantry rotation time, 0.5 mm detection components and up to 16 cm Z direction coverage. In the period of a breath hold, forty contiguous slices of 3-mm-thick was fetched from the start of carina's lower edge. For each slice, scanning will last 100 ms with 26 cm field of view and synchronous electrocardiographic (ECG) triggering at 35% of RR time intervals. Define a lesion demand at lowest two neighbouring pixels (*i.e.* area ≥0.93 mm^2), while density is more than 130 Hounsfield unit.

CAC is the calcification occurred in coronary artery and could be quantified using the Agatston method. We calculated CAC by multiplying the calcification density assignment by the calcification area. We defined the calcification integral level as follows: 0 as no calcification, 1–10 as microcalcification marked grade 1, 11–100 as mild

calcification marked grade 2, 101–400 as moderate calcification marked grade 3, and over 400 as severe calcification marked grade 4.

Statistical analysis

SPSS program (v. 26.0, SPSS Inc., Chicago, Illinois, USA) was utilised to perform statistical analyses during the research. Interquartile range (IQR) and median were calculated with regards to non-normal distributions and continuous variables. The form of numbers and percentages were used to show categorical variables. The Pearson method was applied to quantify the relevance among variables. ROC curve was adopted to compute cut-off values for the number of risk factors. In order to identify the correlative risk factors of CAC, the variables involved in the logistic regression model were as follows: disease duration, age of onset, hypertension and hyperlipidaemia history, Numano V and glucocorticoid. All the figures were created by RStudio with R version 4.2.1(PBC formerly RStudio, Posit Software, Boston, MA, USA). Statistical significance was defined as p-value <0.05.

Results

Clinical characteristics at baseline

The study encompassed a cohort of 155 individuals, featuring a female-to-male ratio of 7.61:1 (137 females and 18 males), among whom 41 cases (26.45%) exhibited CAC. Among these cases, 4 (9.76%) were within the 0–10 score range, 19 (46.34%) fell between 11-100 score, 12 (29.27%) ranged from 101–400 score, and 6 (14.63%) exceeded a score of 400. Our analysis revealed that patients with CAC were notably older (52 *vs*. 37years, p<0.001), had an older age of disease onset (33 *vs*. 27 years, p=0.014), longer disease duration (120 *vs*. 50 months, p=0.006), higher body mass index (23.31 *vs*. 21.97kg/m^2, p=0.047), higher systolic pressure (133 *vs*. 124 mmHg, p=0.039) and higher proportion of menopausal people (48.6% *vs*. 17.6%, p<0.001) compared to patients without CAC. Conversely, there was no notable difference in terms of gender and diastolic pressure between the two groups (Table I).

Table II. Laboratory indicators and disease activity evaluation of TAK patients with or without CAC.

Variables	Total (n=155)	With coronary calcification (n=41)	Without coronary calcification (n=114)	*p* value
Laboratory indicators:				
ESR (mm/h)	14.00 (8.00, 29.00)	10.00 (6.00, 24.00)	14.50 (8.00, 33.25)	0.068
CRP (mg/l)	3.18 (0.82, 9.85)	2.72 (0.84, 6.65)	3.67 (0.80, 11.72)	0.347
IL-6 (pg/ml)	6.00 (3.40, 13.65)	4.50 (3.27, 10.50)	7.74 (3.44, 14.29)	0.105
TNF-α (pg/ml)	8.37 (2.85, 26.60)	6.80 (1.95, 12.70)	10.00 (3.24, 41.05)	0.074
BNP (pg/ml)	51.00 (29.00, 152.00)	119.00 (26.25, 345.00)	48.00 (29.00, 114.00)	0.020
TNI (pg/ml)	0 (0, 0.01)	0.01 (0, 0.05)	0 (0, 0.01)	0.229
ALT (u/l)	12.00 (8.75, 17.00)	14.00 (11.00, 21.00)	11.00 (8.00, 17.00)	0.026
Cr (umol/l)	56.00 (48.10, 65.00)	56.30 (48.80, 67.80)	56.00 (48.05, 61.80)	0.314
UA (umol/l)	287.30 (243.40, 351.40)	308.10 (264.35, 388.75)	275.20 (238.20, 347.90)	0.034
TG (mmol/l)	1.04 (0.72, 1.42)	1.16 (0.76, 1.70)	1.02 (0.70, 1.38)	0.084
TC (mmol/l)	4.19 (3.55, 4.95)	4.21 (3.65, 5.38)	4.19 (3.44, 4.84)	0.291
HDL-C (mmol/l)	1.16 (0.98, 1.45)	1.13 (0.94, 1.39)	1.21 (1.00, 1.47)	0.409
LDL-C (mmol/l)	2.45 (1.85, 3.07)	2.55 (1.90, 3.41)	2.39 (1.83, 2.98)	0.316
LDL-C/HDL-C	2.18 (1.41, 2.74)	2.28 (1.65, 3.15)	2.17 (1.38, 2.68)	0.128
TG/HDL-C	0.89 (0.59, 1.28)	1.00 (0.70, 1.65)	0.80 (0.57, 1.16)	0.026
TC/HDL-C	3.66 (2.80, 4.30)	3.77 (3.18, 4.85)	3.61 (2.69, 4.23)	0.079
HCY (umol/l)	11.20 (9.00, 13.50)	12.40 (9.30, 15.60)	11.10 (8.93, 13.18)	0.085
CA (mmol/l)	2.29 (2.21, 2.35)	2.29 (2.21, 2.34)	2.29 (2.20, 2.37)	0.453
PHOS (mmol/l)	1.25 (1.13, 1.38)	1.18 (1.12, 1.28)	1.28 (1.15, 1.39)	0.039
Disease activity evaluation				
NIH	2.00 (2.00,3.00)	2.00 (2.00,3.00)	2.00 (2.00,3.00)	0.209
ITASA	7.00 (4.00,11.00)	7.00 (3.00,10.50)	7.00 (4.00,11.00)	0.576
ITAS.2010	6.00 (3.00,9.00)	7.00 (2.50,9.00)	6.00 (3.00,9.00)	0.872

TAK: Takayasu's arteritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; IL-6: interleukin 6; TNF-α: tumour necrosis factor-α; BNP: Brain Natriuretic Peptide; TNI: troponin I; ALT: alanine aminotransferase; Cr: creatinine; UA: uric acid; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; HCY: homocysteine; Ca calcium: PHOS phosphorus.

Table III. Vascular involvement and Numano type of TAK patients with or without coronary artery calcification.

Variables	Total (n=155)	With coronary calcification (n=41)	Without coronary calcification (n=114)	*p* value
Vascular involvement (n%)				
Carotid artery	112.00 (73.20)	35.00 (85.40)	77.00 (68.80)	0.040
Vertebral artery	33.00 (21.90)	13.00 (31.70)	20.00 (18.20)	0.074
Subclavian artery	109.00 (71.20)	35.00 (85.40)	74.00 (66.10)	0.020
Upper extremity artery	40.00 (28.20)	13.00 (34.20)	27.00 (26.00)	0.333
Lower extremity artery	30.00 (20.40)	13.00 (33.30)	17.00 (15.70)	0.019
Common iliac artery	12.00 (8.30)	8.00 (21.60)	4.00 (3.70)	0.002
Pulmonary artery	35.00 (33.70)	10.00 (34.50)	25.00 (33.30)	0.911
Superior mesenteric artery	42.00 (28.80)	13.00 (33.30)	29.00 (27.10)	0.462
Renal artery	57.00 (38.30)	21.00 (52.50)	36.00 (33.00)	0.030
Thoracic artery	72.00 (50.30)	29.00 (82.90)	43.00 (39.80)	<0.001
Abdominal artery	58.00 (38.90)	24.00 (61.50)	34.00 (30.90)	0.001
Intracranial artery	47.00 (34.10)	22.00 (57.90)	25.00 (25.00)	<0.001
Numano type (n%)				
Numano I	13.00 (8.40)	0 (0)	13.00 (11.40)	0.054
Numano IIa	9.00 (5.80)	3.00 (7.30)	6.00 (5.30)	0.926
Numano IIb	24.00 (15.50)	4.00 (9.80)	20.00 (17.50)	0.237
Numano III	7.00 (4.50)	0 (0)	7.00 (6.10)	0.236
Numano IV	3.00 (1.90)	0 (0)	3.00 (2.60)	0.566
Numano V	99.00 (63.90)	34.00 (82.90)	65.00 (57.00)	0.003

Numano type is defined according to the distribution of the involved artery. Type is divided according to Hata and Numano's criteria.

Furthermore, upon meticulous examination of medical records of TAK patients, we observed that patients with CAC exhibited a higher prevalence of hypertension (68.4% *vs*. 25.7%, $p<0.001$), hyperlipidaemia (34.1% *vs*. 6.1%, $p<0.001$), coronary heart disease (17.1% *vs*. 5.3%, $p=0.019$) and cerebral vascular disease (17.1% *vs*. 1.8%, $p<0.001$). However, no significant differences were noted in terms of smoking, drinking and diabetes. We evaluated the pre-admission medication status and found that patients with CAC had a greater proportion of glucocorticoid (46.3% *vs*. 28.9%, $p=0.043$), stain (53.7% *vs*. 28.9%, $p=0.005$) and had higher glucocorticoid accumulation ($p=0.029$) than patients without CAC. However, the discrepancy of using aspirin, disease-modifying anti-rheumatic drugs was not observed between the two groups (Table I).

Furthermore, there were remarkable differences in dizziness ($p=0.013$) and palpitation ($p=0.009$) between two groups, while other symptoms were not significantly different (Table I).

Laboratory indicators and disease activity evaluation of TAK

We analysed the laboratory data for both groups, and noted higher level of BNP (119 *vs*. 48pg/ml, $p=0.02$), ALT (14 *vs*. 11u/l, $p=0.026$), UA (308.1 *vs*. 275.2umol/l, $p=0.034$), TG/HDL-C (1 *vs*. 0.8, $p=0.026$) among patients with CAC compared to those without. Interestingly, phosphorus levels (1.18 *vs*. 275.2 umol/l, $p=0.034$) exhibited an opposite trend. However, the inflammatory markers such as ESR, CRP and cytokines including IL-6, TNF-α and disease activity score did not show statistical significance in two groups (Table II).

Vascular involvement and Numano type of TAK

We conducted an evaluation of vascular involvement among TAK patients. As described in Table III, patients with CAC exhibited a higher incidence of involvement in the carotid artery, subclavian artery, lower extremity artery, common iliac artery, renal artery, thoracic artery, abdominal artery and intracranial artery than patients without CAC. However, there were no statistically significant differences observed regarding the involvement of vertebral artery, double upper limb artery, pulmonary artery and superior mesenteric artery showed no significant statistical between the two groups. Numano type V was the most prevalent subtype among all patients, with its occurrence significantly higher in the CAC group compared to the non-CAC lesion group (82.9% *vs*. 57%, $p=0.003$). The frequencies of other Numano types were not distinctly disparate between the two groups. (Table III).

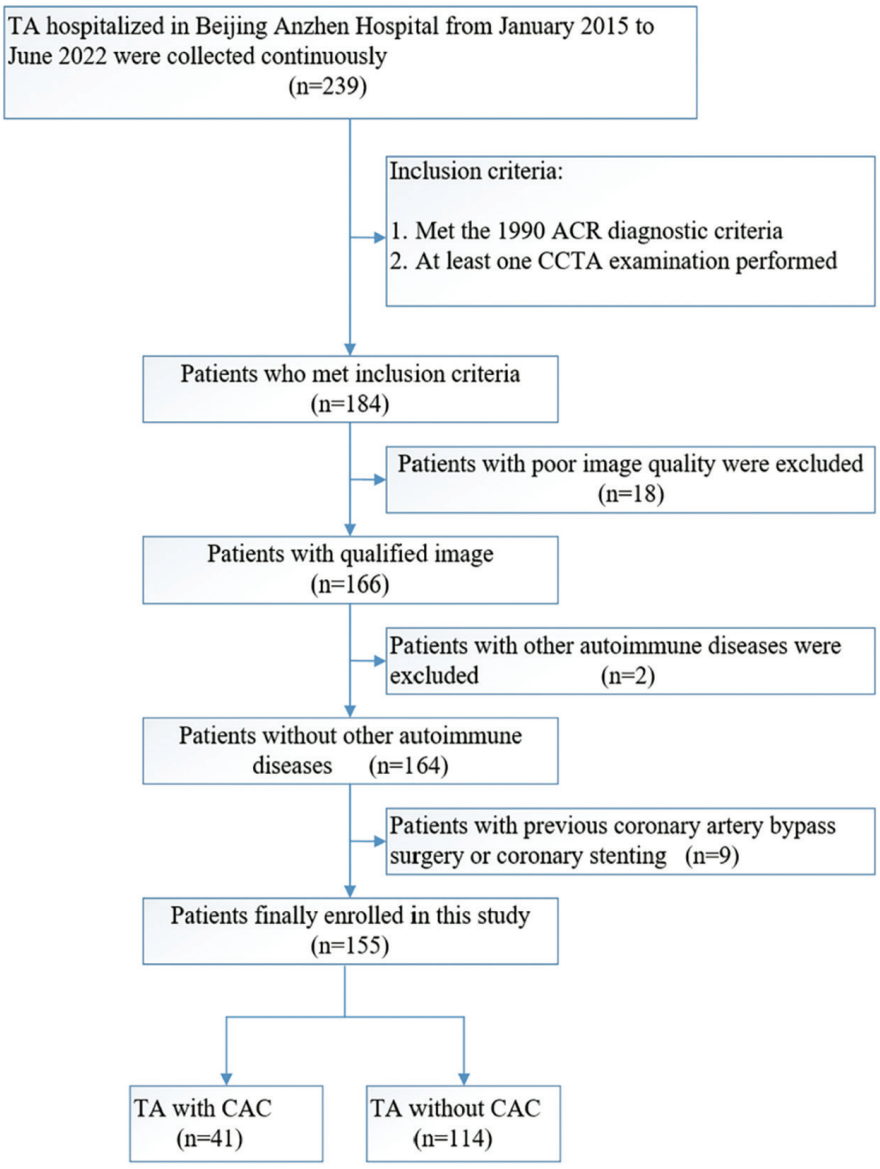

Fig. 1. Flow chart of the study.
TAK: Takayasu's arteritis; ACR: American College of Rheumatology; CCTA: coronary computed tomography angiography; CAC: coronary artery calcification.

Risk factors of CAC in TAK patients

For the logistic regression analysis of risk factors of CAC in TAK, we covered the age of onset, disease duration, body mass index, Numano type V and the history of hypertension, coronary heart disease, hyperlipidaemia, and glucocorticoid medication. Our findings revealed that age of onset, disease duration, hypertension, hyperlipidaemia, Numano V and glucocorticoid use were statistically related to CAC in TAK (OR [95% CI] 1.084[1.028–1.142], $p=0.003$; 1.005 [1.001–1.00, $p=0.020$; 4.792 [1.713–13.411], $p=0.003$; 4.199 [1.087–

16.219], p=0.037; 3.287 [1.070–10.100], p=0.038; 3.558[1.269–9.977], p=0.016) (Fig. 2).

Association between CAC integral level and the number of risk factors

As shown in Figure 3, the cumulative level of CAC exhibited a consistent increase corresponding to an escalating number of risk factors per participant (p<0.001). Because of only one person met all factors simultaneously, the level of calcification scores decreased when the number of risk factors was 6. We further correlated the number of risk factors with the level of calcification scores, yielding an R value of 0.532 and a significant correlation (p<0.001). Utilising the number of risk factors to predict CAC, we obtained an AUC area of 0.836 (p<0.001). Conspicuously, when the number of risk factors was 2.5, CAC was prone to appear with a sensitivity of 0.78 and specificity of 0.772 (Fig. 3).

Effect of other risk factors on the integral level of CAC

To further elucidate the impact of other risk factors other than traditional cardiovascular risk factors on CAC, we screened out the TAK patients with previous hypertension and hyperlipidaemia. The comparison results are presented in Figure 4 box plots. Our findings revealed that patients using glucocorticoids and type Numano V exhibited elevated level of coronary calcification scores (p=0.019, p=0.021), while no significant disparities were observed in terms of age of onset and disease course (Fig. 4).

Discussion

In this study, we conducted CCTA on 155 TAK patients and identified CAC in 26.45% of patients. The majority showcased calcification integral levels ranging between 11 and 100 points, predominantly presenting as Numano Type V. Our analysis revealed several risk factors associated with calcified atherosclerotic plaques in TA, including the age of onset, duration of the disease, history of hypertension and hyperlipidaemia, Numano Type V classification, and the use of glucocorticoids.

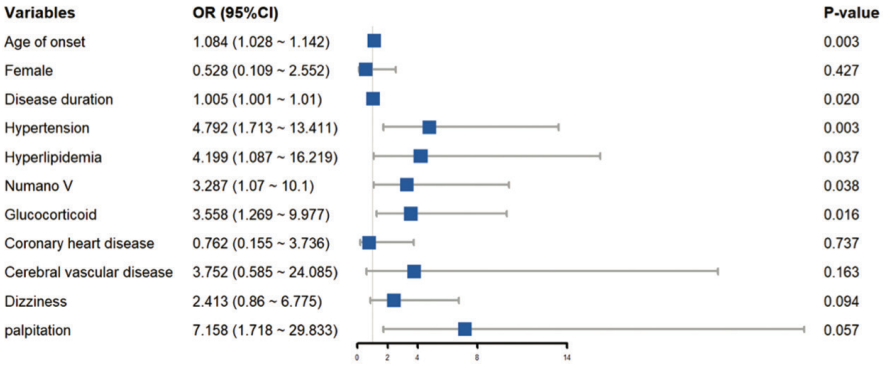

Fig. 2. Logistics regression analysis of risk factors in TAK patients with CAC. Age of onset, disease duration, hypertension, hyperlipidaemia, Numano V and glucocorticoid are significantly related to CAC in TAK patients.

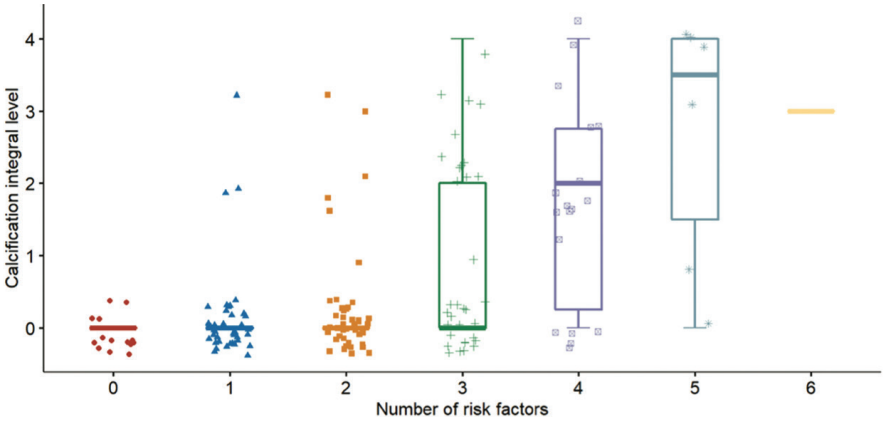

Fig. 3. Coronary artery calcification (CAC) level corresponding to the number of risk factors in each participant. CAC level on the y-axis corresponds to the number of risk factors on the x-axis. Included risk factors are the same as in Fig. 2.

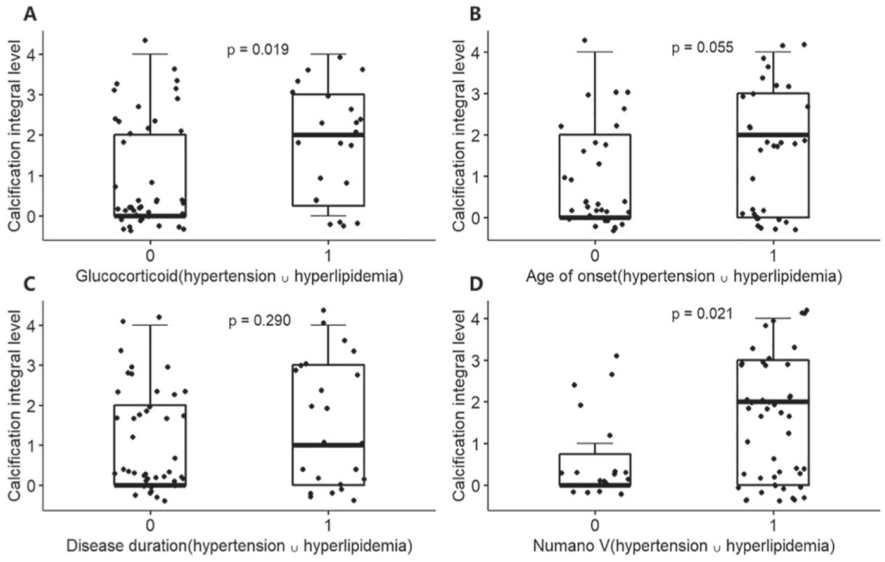

Fig. 4. CAC level for risk factors specific to TAK patients (including glucocorticoid, age of onset, disease duration, and Numano V).
Boxplots showing each special risk factor (x-axis, 0=absent and 1=present) and the CAC level (y-axis). The included population were TAK patients with a history of hypertension or hyperlipidaemia. (**A**) difference of glucocorticoid use between the two groups. (**B**) difference of age of onset between the two groups. (**C**) difference of disease duration between the two groups. (**D**) difference of Numano V between the two groups.

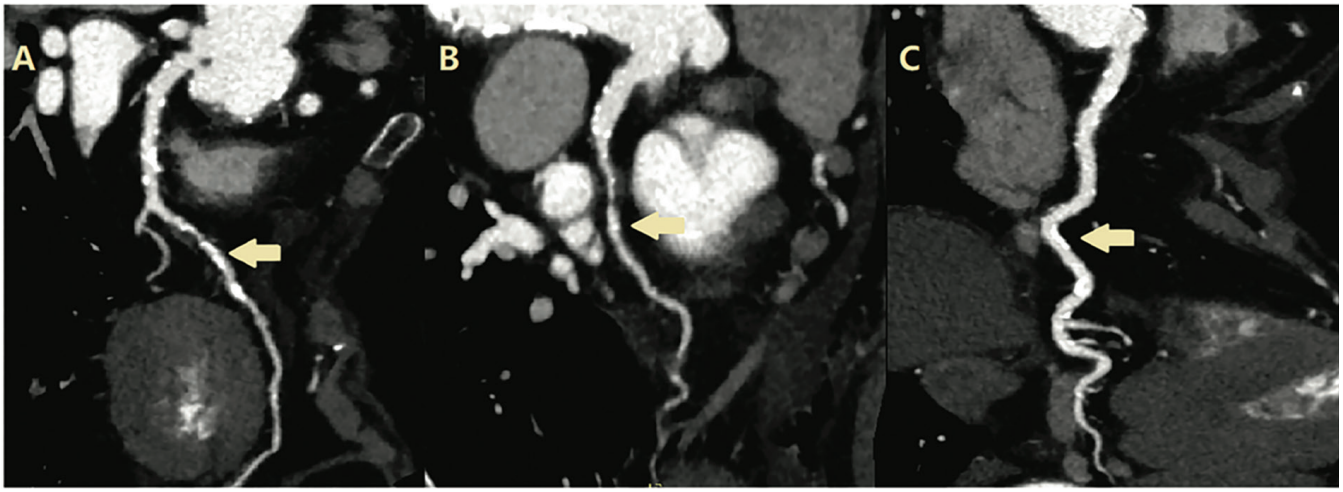

Fig. 5. Images of coronary artery calcification in a TAK patient: a 60-year-old woman with a total disease course of 25 years. She first developed clinical symptoms of dizziness and palpitations at 35 years. Her Numano classification was type V, which mainly involved the carotid artery, subclavian artery, axillary artery, abdominal aorta, superior mesenteric artery, pulmonary artery, and coronary artery. Currently, this patient had been taking glucocorticoids for 11 years. She had a previous history of hypertension for 10 years and hyperlipidaemia for 2 years. (**A**) left anterior descending branch with 818 score of calcification. (**B**) left circumflex with 104 score of calcification. (**C**)right coronary artery with 681 score of calcification.

Notably, in effectively managed cases, regular CCTA screening and timely withdrawal of glucocorticoids may significantly delay the onset of calcified atherosclerotic plaques. Previous studies predominantly focused on coronary lesions and prognostic factors in TA. Some studies have delved into patients with aortic calcification and CAC, comparing them with healthy people or patients with hyperlipidaemia (5, 10, 11). Consequently, our paper concentrates specifically on the examination of risk factors contributing to CAC in TAK.

McClelland *et al*. (13) reported that the calcium content and prevalence of CAC have steadily increased with age. Wang *et al*. (8) observed TAK patients with coronary involvement were older in age of onset and had longer disease course. This parallel aligns with our findings, suggesting that local vascular inflammation might exacerbate arterial calcification in TAK. Scientific evidence indicates that vascular smooth muscle cells could differentiate into osteogenic-like cells under specific stimuli (14). Shao *et al*. (15) proposed this process could significantly impact patients with cardiovascular disease arising from immune-mediated conditions characterised by chronic inflammation, thereby increasing the risk of vascular calcification diseases. Consequently, coronary arteries in TAK patients with older age and longer disease duration may be exposed to prolonged inflammation eventually leading to arterial calcification. Our research underscores the critical importance of coronary screening, particularly for patients displaying the aforementioned characteristics.

We also noticed a higher prevalence of menopause in patients with CAC, aligning with the findings of Fonseca *et al*. (16). Their research suggested an independent association between menopause and CAC, potentially attributed to decreased oestrogen levels that contribute to calcium deposition in coronary arteries (16). Our investigation revealed that hypertension, hyperlipidaemia, coronary heart disease and cerebrovascular disease are linked factors to CAC. Notably, even after performing a multivariate logistics regression, the history of hypertension and hyperlipidaemia persisted as significant risk factors associated with CAC. Khurrami *et al*. (17) stated that hypertension is associated with increased tensile load on the aortic tip and turbulence may cause endothelial damage, inflammation and calcification. Carracedo *et al*. (18) mentioned that hyperlipidaemia is associated with increased systemic chronic inflammation. Vascular calcification is closely associated with neointimal lipid deposition, and the oxidative stress induced by hyperlipidaemia facilitates the deposition of lipoprotein particles in vascular tissue (19). This elucidates the pivotal role of hyperlipidaemia in instigating vascular calcification.

In terms of medication usage, associations were found between CAC and the administration of glucocorticoids, statins, as well as the cumulative dosage of glucocorticoids. Banerjee *et al*. (20) mentioned that high doses of prednisone is correlated with an elevated burden of vascular calcification, likely attributable to multiple factors. Additional studies have reported that statin d is linked to an increased rate of conversion from coronary atherosclerosis to high-density calcium (21). In our analysis of clinical symptoms, a higher proportion of CAC patients reported experiencing dizziness and palpitations. Additionally, we observed a higher incidence of carotid artery and intracranial vessel involvement in patients with CAC. When these vessels are narrowed or even blocked, inadequate blood supply to the intracranial artery may result in dizziness. Similarly, CAC patients showed higher BNP values, which can reflect the healthy state of the heart. Seyahi *et al*. (22) reported that TAK with CAC are more prone to have coronary artery involvement, potentially leading to palpitations due to insufficient blood supply to the coronary artery.

Upon analysing the laboratory indicators, we noted inflammatory reactants, cytokines and disease activity did not exhibit significance. This observation may be related to disease characteristics of TAK. A majority of patients in our hospital tend to present a short disease course and have not undergone extensive glucocorticoid treatment. Consequently, short-term inflammatory infiltration might not suffice to induce severe vascular calcification. We noticed that the upper limit of uric acid levels among those with CAC has exceeded the reference range for women. Recent studies suggested uric acid can induce endothelial dysfunction and activate the inflammasome. These alterations may serve as bases for the pathophysiology between uric acid and atherosclerosis (23, 24). Additionally, Kiss *et al*. (25) highlighted that serum uric acid levels were positively correlated with total coronary artery calcification points. Furthermore, upon comparing lipid levels among patients, we found higher TG/HDL-C values in individuals with CAC. Our previous study identified a relationship between prolonged disease duration, elevated TG/HDL-C ratios, and the progression of atherosclerosis in TAK (26).

We routinely conduct a thorough vascular assessment in TAK cases to accurately determine the Numano classification. Previous research has indicated that patients with type V are easier to develop coronary involvement, which resonates with our results (27). In our subsequent risk factor analysis, the risk of CAC in type V increased 2.198-fold compared with non-V patients. Furthermore, we observed a correlation between the degree of coronary calcification integration and the number of identified risk factors. This association suggests that the cumulative number of risk factors may serve as a partial predictor for the occurrence of CAC. Hypertension and hyperlipidaemia are widely recognised as independent risk factors for CAC (28). To delve deeper into the impact of TAK-specific risk factors on CAC, we specifically examined TAK patients with concurrent hypertension and hyperlipidaemia. Our observations indicated a higher propensity for CAC in groups receiving glucocorticoids and those classified as type V. This suggests the need for regular monitoring of CAC in patients exhibiting these aforementioned characteristics. Such insights can guide proactive monitoring strategies for patients with these specific features.

This study was retrospective and therefore biased and limited in its impact. The incidence of TAK is low and some patients have failed to complete CCTA examination due to economic reasons.

Conclusions

In conclusion, this study identified several risk factors associated with CAC in TAK, including age of onset, duration of disease, history of hypertension and hyperlipidaemia, type Numano V and the use of glucocorticoids. We recommend incorporating routine CCTA examinations specifically targeting Numano Type V when evaluating the severity of coronary lesions and calcification. Moreover, upon achieving inflammation control, prompt reduction of glucocorticoid usage is highly advised.

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