The value of ultrasonography combined with clinical features for predicting carotid imaging progression of Takayasu's arteritis: a prospective cohort study

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ABSTRACT

Objective. *To identify valuable ultrasonography findings combined with clinical markers for predicting carotid progression of Takayasu's arteritis (TAK) on imaging during a 1-year follow-up period.*

Methods. *From May 2016 to June 2019, 77 Chinese TAK patients with carotid artery involvement were enrolled in the present study. The patients' clinical characteristics and serological test and carotid ultrasonography results were recorded at baseline and each visit. Carotid progression was evaluated by ultrasonography every 3 months during the 1-year follow-up. Baseline clinical characteristics and ultrasonography results for predicting progression on imaging were identified.*

Results. *Sixteen (20.8%) patients presented with carotid progression on imaging during the 1-year follow-up period. The patients in the progressive group were younger (23.4±3.7 vs. 32.3±9.8 years, p<0.01) than those in the non-progressive group. At baseline, the vessel wall was thicker in the progressive group than in the non-progressive group (2.4±0.8 vs. 1.9±0.5 mm, p=0.041). Furthermore, the proportion of patients with refractory disease (87.5% vs. 16.4%, p<0.01) was higher in the progressive group than in the non-progressive group. Patients with a thickened carotid wall (≥1.9 mm), refractory disease, and younger age (≤30 years) might be at a high risk of carotid progression on imaging (75%, AUC: 0.93, sensitivity: 75%, specificity: 93.4%).*

Conclusion. *Younger patients with early vascular structural changes at baseline as well as refractory disease seemed more likely to show carotid progression on imaging.*

Introduction

Takayasu's arteritis (TAK) is a progressive, inflammatory type of vasculitis mainly involving the aorta and its branches, which predominantly affects young women aged <40 years in eastern countries. The disease onset and progression are often insidious, with alternating disease course involving exacerbation, flare, and remission. Glucocorticoids (GCs) combined with immunosuppressors is the first-line therapy for TAK. However, approximately 20% of patients have been reported to have poor or no response to the current medications (1). Some patients have even showed progression on imaging in the chronic stable phase (2, 3). Persistent inflammation of the arteries involved aggravates stenosis, occlusion, and/or aneurysm, which would finally lead to organ ischaemia and disease prognosis. Thus, it is crucial to determine valuable markers to predict disease progression in order to prevent adverse vascular complications.

Imaging techniques are important for detecting and monitoring vascular inflammation and structural changes (4, 5). Inflammation of the arteries progresses from the adventitia to the intima and finally encompasses the full layer. Early detection of TAK-related changes on imaging is critical to disease outcomes. However, studies on continuous imaging follow-up are limited.

Compared to computed tomography angiography (CTA), magnetic resonance angiography (MRA), color Doppler ultrasonography (CDUS), and contrast-enhanced US (CEUS) are promising imaging techniques. These techniques could afford the visualisation of changes in vascular structure and neovascularisation of the vessel wall in a timely manner. We have previ-

ously reported that US could detect early carotid artery lesions in TA patients, and the changes could be observed on US within 3 months (6). The use of CEUS in the follow-up of large vascular disease can reflect inflammation of the vessel wall in a timely and sensitive manner (6). The thickness and neovascularisation of vessel walls on US are also markers of treatment response in TAK (7). However, the early imaging features as well as clinical measurements in the prediction of long-time disease progression for TAK are unclear and need to be studied further.

Carotid involvements are very common in TAK and account for more than 45% of the total patients with TAK (8). US has shown great advantages for evaluating carotid vascular involvements. However, until now, no effective index has been found for predicting progression of TAK on imaging. Hence, the aim of this study was to clarify early carotid progression and the predictive values of baseline clinical characteristics and US for carotid progression during a 1-year follow-up period in a large Chinese TAK cohort.

Patients and methods

Patient and population

This study was designed based on a prospective Chinese cohort, namely the East China Takayasu's Arteritis (ECTA) cohort, in Zhongshan Hospital, Fudan University. All patients registered in the cohort were diagnosed with TAK according to the 1990 American College of Rheumatology diagnostic criteria (9). Patients who were enrolled in the cohort from May 2016 to June 2019 and had carotid artery involvements were included in the present investigation. Meanwhile, those younger than 18 years old, for whom the use of contrast agents was contraindicated, and without complete records for a 1-year follow-up were excluded. Finally, 77 cases were enrolled in this study and followed-up according to the schedule designed.

Informed written consent was obtained from each participant. The study was approved by the ethics committee of Zhongshan Hospital, Fudan University (B2013-115(3)).

Disease assessment and follow-up

All patients were followed up every month, and follow-up data were collected and recorded in a database according to the study plan. CDUS and CEUS were performed every 3 months. Clinical characteristics and physical examination results at baseline and each visit during the 1-year follow-up were recorded. Serological tests, such as complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and serum amyloid A (SAA) level, were performed according to the standard protocols in the central laboratory of our hospital within 3 days of the CEUS examination. The Kerr index (10) was used as the gold standard for disease activity assessment. Indian Takayasu Activity Score (ITAS) 2010 scores (11) were also recorded.

Treatment response

Treatment response was evaluated every 3 months and classified as clinical remission (CR) and refractory disease (RD) (12). Patients were considered as showing CR if all the following criteria were satisfied: i) prednisone dose reduced to 0.1-0.2 mg/kg/day (≤15 mg/day) at 6 months and ≤10 mg/day at 12 months; ii) no new or aggravated symptoms; iii) normal ESR (<30 mm/H); and iv) Kerr score of less than 2 during the remaining follow-up period. Patients were considered as showing RD if active disease was still observed through 6 months of successive treatment with GCs combined with more than two immunosuppressors.

CDUS and CEUS examinations

All 77 patients underwent carotid CDUS connected with CEUS. The examinations were performed using a Philips Elite US instrument (Philips Medical Systems, Bothell USA) with an L9-3 linear array probe. In total, 154 common carotid arteries were examined by an experienced physician. The wall thickness of lesions was measured. The mechanical index was 0.07 and the gain was 70%. The instrument parameters were kept consistent for all patients. CEUS was performed at the thickest part of the common carotid artery wall after the CDUS examination. A US contrast agent (SonoVue, Bracco, Italy) was used in this study. A semi-quantitative visual score was used to determine the vessel wall vascularisation (13).

The parameters examined during the carotid US were artery wall thickness, artery diameter, proportion of vascular stenosis or occlusion, peak flow rate, and the resistance index. Carotid wall vascularisation was semi-quantitatively graded according to the neovascularisation at the thickening wall (6). Stenosis severity was assessed using the Society of Radiologists in Ultrasound criteria (14). Patients were considered as showing progression on imaging if there was a more than 20% increase in one of the US parameters (wall thickness and lesion range), or aggravations on lumen stenosis or CEUS semi-quantitative analysis during the 1-year follow-up compared with the corresponding baseline finding. CEUS outcomes were evaluated by 2 independent observers who were blinded to clinical and laboratory data. The interobserver agreement for the CEUS score was strong (κ=0.93).

Statistical analysis

Statistical analysis was performed used SPSS (version 22, IBM, USA). Continuous variables were described as mean ± SD values for normally distributed data or median (IQR) values for non-normally distributed data and compared using Student's *t*-test or Wilcoxon rank-sum test. Categorical variables were described in numbers (%) and compared using the Chi-square test. Kaplan-Meier survival curves, drawn using GraphPad Prism 7 (GraphPad), were used to depict the occurrence of progression on imaging during the 1-year follow-up. Correlations between clinical symptoms and stenosis severity were analysed by Spearman's rank correlation coefficient. Hazard ratios (HRs) and 95% confidence intervals (CI) were examined using Cox regression. Multivariate analyses involved adjustments for age, Kerr score, luminal stenosis, and CEUS grade 2, and included all markers whose *p*-value was <0.1 in the univariate analysis. Significance was defined at $p<0.05$ (two-sided). The ability

Table I. Baseline characteristics of TAK patients.

	Total (n=77)	Kerr <2 (n=28)	Kerr ≥2 (n=49)	*p*
Sex, female (%)	70 (90.9)	27 (96.4)	43 (87.8)	0.203
Age, years	30.4 ± 9.6	33.1 ± 9.9	28.9 ± 9.1	0.065
Disease duration, months, median (IQR)	25 (5-58)	36 (15-60)	24 (3-60)	0.221
Hypertension (%)	13 (16.9)	8 (28.6)	5 (10.2)	0.035
Pulselessness (%)	4 (5.2)	0	4 (8.2)	0.127
Dizziness (%)	7 (9.1)	2 (7.1)	5 (10.2)	0.687
Neck pain (%)	13 (16.9)	0	13 (26.5)	0.003
Fever (%)	5 (6.5)	0	5 (10.2)	0.086
ESR, mm/H, median (IQR)	30 (11-66)	11 (4-22)	48 (23-81)	<0.001
CRP, mg/L, median (IQR)	8.5 (1.5-33.0)	1.9 (0.5-4.9)	17.7 (7.2-63.2)	<0.001
SAA, mg/L, median (IQR)	20.7 (8.2-86.3)	9 (6-24.3)	38.9 (9.2-177)	0.001
Hb, g/L	119 ± 17.2	126 ± 12.3	115 ± 18.4	0.012
Platelet count, $\times 10^9$/L, median (IQR)	299 (218-370)	236 (204-296)	336 (255-395)	0.001
Average prednisone dose, mg/d, median (IQR)	30 (10-40)	10 (5-15)	30 (25-50)	<0.001
Methotrexate (%)	12 (15.6)	7 (25.0)	5 (10.2)	0.108
Cyclophosphamide (%)	4 (5.2)	0	4 (8.2)	0.290
Mycophenolate mofetil (%)	17 (22.1)	10 (35.7)	7 (14.3)	0.051
Leflunomide (%)	40 (51.9)	11(39.3)	29 (59.2)	0.104
Tocilizumab (%)	4 (5.2)	0	4 (8.2)	0.290
Ultrasound features of carotid arteries in 77 patients (n=154)				
Right carotid artery (%)	68 (88.3)	25 (89.3)	43 (87.8)	1.000
Left carotid artery (%)	70 (90.9)	26 (92.9)	44 (89.8)	0.986
Thickness, mm	2.1 ± 0.8	1.9 ± 0.8	2.3 ± 0.7	0.013
Lumen stenosis (%)				
<50%	44 (28.6)	23 (41.4)	21 (21.4)	0.009
50-69%	47 (30.5)	12 (21.4)	35 (35.7)	0.064
70-99%	30 (19.5)	9 (16.1)	21 (21.4)	0.419
Occlusion	17 (11.0)	7 (12.5)	10 (10.2)	0.664
Carotid wall vascularisation on CEUS (%)				
Grade 0	34 (22.1)	30 (53.6)	4 (4.1)	0.006
Grade 1	52 (33.7)	10 (17.9)	42 (42.9)	0.031
Grade 2	68 (44.2)	16 (28.5)	52 (53.0)	0.037

TAK: Takayasu's arteritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; SAA: serum amyloid A; Hb: haemoglobin; CEUS: contrast-enhanced ultrasound.

of the markers at baseline to diagnose imagine progression was assessed by receiver operating characteristic (ROC) curve analysis.

Results

Patient characteristics at baseline

There were 123 TAK patients (123/298, 41.3%) with carotid artery involvement in our cohort. Forty-six patients were excluded from the present study, among whom, 11 patients were younger than 18 years 2 were allergic to the agents, 10 had acute heart failure, 4 had unstable angina, and 19 did not reach the time to follow-up. In all, there were 77 patients with carotid artery involvement. There were no statistical differences in clinical characteristics and laboratory and US parameters between the enrolled and excluded patients (data not shown).

The mean age of the 77 TAK patients was 30.4 ± 9.6 years, with the female-to-male ratio being 10:1. The disease duration was 25 (5–58) months. At baseline, 49 patients (63.6%) showed active disease according to Kerr scores. The major clinical symptoms were neck pain (16.9%), hypertension (16.9%), dizziness (9.1%), fever (6.5%), and pulselessness (5.2%). The median ESR and CRP levels were 30 (11–66) mm/H and 8.5 (1.5–33.0) mg/dl respectively (Table I). Induction treatment was administered to patients with active disease. The baseline prednisone doses were 0.8–1 mg/kg/day and 0.1–0.2 mg/kg/day for patients with and without active disease, respectively. One or more immunosuppressors were administered simultaneously, including methotrexate (MTX, 10–15 mg/week, p.o.; n=12), cyclophosphamide (CYC, 0.5–0.75 g/m^2 i.v. every 4 weeks up to a cumulative dose of 6–7 g; n=4), mycophenolate mofetil (MMF, 30 mg/kg/day, p.o.; n=17), leflunomide (LEF, 20 mg/day, p.o.; n=40), and tocilizumab (8 mg/kg/m^2 i.v. every 4 weeks; n=4). The median prednisone dose in the active group was significantly higher than that in the inactive group (30 [25–50] *vs*. 10 [5–15] mg/day, $p<0.001$). There were no statistical differences in terms of immunosuppressors between these two groups. Further, 22 patients were newly diagnosed and had a disease duration of less than 6 months. Subgroup analysis between patients with disease duration of <6 months and ≥6 months indicated that the median prednisone dose at baseline was higher in those with disease duration of <6 months (40 [30–50] *vs*. 15 [7.5–30] mg/day, $p<0.001$).

Carotid imaging features and follow-up

Carotid US was performed in all the patients enrolled. Sixteen patients (20.8%) had unilateral carotid lesions and 61 patients (79.2%) had bilateral carotid artery lesions. Sixty-eight patients (88.3%) showed right carotid artery lesions, and 70 (90.9%) had left

carotid artery diseases. Among the 154 common carotid arteries examined, 44 (28.6%), 47 (30.5%), and 30 (19.5%) showed stenosis of <50%, 50–69%, and 70–99%, respectively. Carotid occlusion was observed in 17 (11.0%) arteries, while 68 (44.2%) vessels showed grade 2 wall vascularisation. The mean arterial wall thickness was 2.1±0.8 mm (Table I).

Sixteen (20.8%) patients presented with carotid progression on imaging examinations, while 43 (55.8%) cases showed improvement on imaging and 18 (23.4%) showed a stable imaging status during the 1-year follow-up. Of the total 154 vessels examined, 22 (14.3%) showed lesion progression while 59 (38.3%) showed improvement. Among the vessels showing progression, 5 showed increased wall thickness (increase: 0.7–1.2 mm), 7 showed enlargement (increase in lesion length: >10 mm), 3 showed narrower lumen (lumen stenosis from <50% to >70%), and 7 showed aggravation on CEUS semi-quantitative analysis (enhanced vascularisation of the artery wall) (Fig. 1).

Among the patients with progression on imaging, 3 (7.8%) showed progression at 3 months, 6 (9.1%) at 6 months, and 9 (18.2%) at 9 months (Fig. 2). Compared to those without progression, in the patients with carotid progression on imaging, a higher proportion of wall vascularisation of grade 2 (37.5% *vs*. 9.8%, p=0.014) and a thicker vascular wall (2.1±0.7 *vs*. 1.7±0.7 mm, p=0.048) was observed at the end of the 1-year follow-up (Table II). During the follow-up period, RD were observed in 24 (31.2%) patients, including 14 patients (87.5%) in the progressive group and 10 (16.4%) in the non-progressive group (p<0.001).

Comparisons of features between patients with and without progression on imaging

Baseline features were compared between the patients with and without carotid progression. Patients in the progressive group were younger at baseline (23.4±3.7 *vs*. 32.3±9.8 years, p<0.001) and had higher baseline CRP levels, platelet count, and Kerr scores as shown in Table II. With regard to pre-existing cardiovascular risk factors, there was no significant difference in hypertension, hyperlipidaemia, smoking, family history of cardiovascular events, and BMI between the two groups. Carotid US revealed that patients in the progressive group had a thicker vessel wall (2.4±0.8 *vs*. 1.9±0.5 mm, p=0.041) at baseline. The proportion of patients with artery wall enhancement was not different between the two groups (Table II).

Among cases with carotid progression, 8 cases were newly diagnosed and the other 8 cases had been previously treated. The newly diagnosed patients had a shorter disease duration than did the previously treated patients (6 [2–39] *vs*. 48 [36–60] months, p=0.041). All patients in the newly diagnosed group showed active disease with a Kerr score of 3 at baseline, while five patients in the previously treated group showed active disease with a Kerr score of 2. The ESR and CRP levels, median prednisone dose, as well as wall thickness on US were higher in the newly diagnosed patients than in the previously treated patients, although the differences were not statistically significant. There were no statistical differences in terms of clinical parameters, the use of immunosuppressive agents, and lumen stenosis between these two subgroups (data not shown).

Among patients with carotid progression on imaging, 4 complained of clinical symptoms (dizziness: 3 and neck pain: 1). These 4 patients showed a significantly thickened vessel wall (3.4 [2.3–3.8] *vs*. 1.9 [1.5–2.2] mm, p=0.005) and higher Kerr score (2 [2–3] *vs*. 1 [0–2], p=0.035) compared with those without clinical symptoms in the progressive group (data not shown).

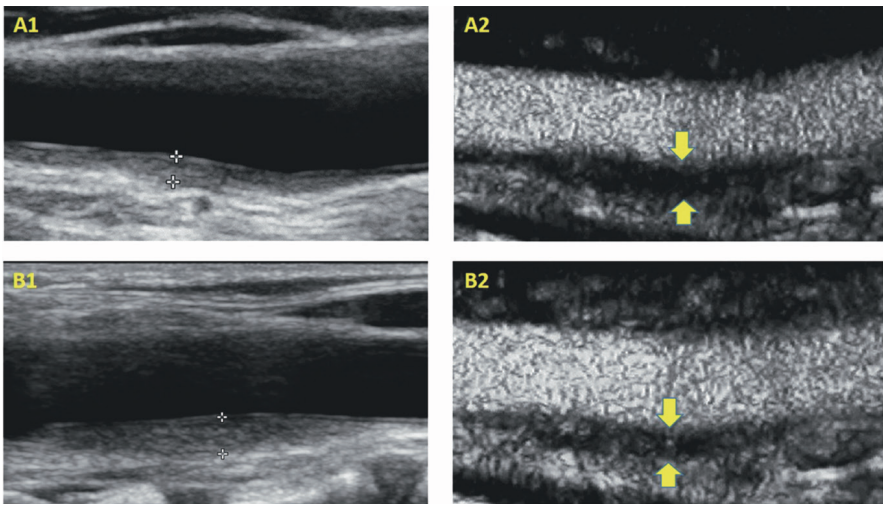

Fig. 1. Carotid progression on CEUS after 6-month treatment in one TAK patient.
A 25-year-old female patient complained of fatigue and low-grade fever for 2 years before being diagnosed with TAK in our hospital. Carotid artery CDUS at baseline showed a significantly thickened vessel wall (A1). Further, CEUS examination showed limited or moderate vascularisation in the thickened wall (A2). After treatment with a glucocorticoid and cyclophosphamide for 6 months, the lesion wall thickness increased from 1.6 to 2.8 mm (B1), with severe vascularisation observed on CEUS (B2).

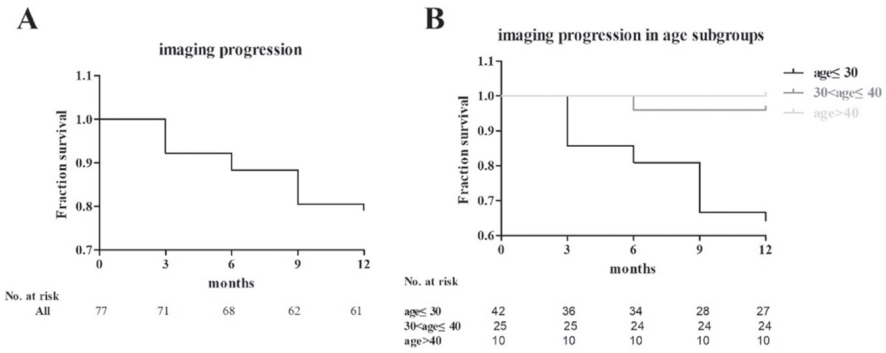

Fig. 2. Kaplan-Meier curve of progression on imaging. A, Kaplan-Meier curve of progression on imaging during the 1-year follow-up. B, Kaplan-Meier curve of progression on imaging in age subgroups.

Table II. Characteristics of TA patients at baseline and the end of the 1-year follow-up.

	Progression group (16)		Alleviation or stabilisation group (61)		*p* value	
	Baseline	1-year follow-up	Baseline	1-year follow-up	p1	p2
Sex, female (%)	15 (93.8)	/	55 (90.2)	/	0.657	/
Age, years	23.4 ± 3.7	/	32.3 ± 9.8	/	<0.001	/
Disease duration, months, median (IQR)	36 (2-52)	/	24 (6-69)	/	0.486	/
Induction treatment (%)	8 (50.0)	/	24 (39.3)	/	0.575	/
Hypertension (%)	1 (6.3)	/	12 (19.7)	/	0.187	/
Hyperlipidaemia (%)	0	/	2 (3.3)	/	0.625	
Smoking (%)	1 (6.3)	/	2 (3.3)	/	0.585	/
Family history of cardiovascular events (%)	1 (6.3)	/	1 (1.6)	/	0.375	/
BMI, kg/m^2	21.5 ± 3.3	/	22.4 ± 3.4	/	0.410	/
RD (%)	/	14 (87.5)	/	10 (16.4)	/	<0.001
ESR, mm/H, median (IQR)	46 (13-81)	15 (9-31)	26 (10-54)	14 (3-30)	0.127	0.606
CRP, mg/L, median (IQR)	23.1 (1.9-95.9)	2.6 (1.9-18.6)	7.4 (1.5-27.7)	3.1 (0.7-10.3)	0.019	0.430
SAA, mg/L, median (IQR)	40.1 (8.5-184.5)	18.5 (7.9-120.7)	18.3 (7.2-65.0)	10.9 (5.8-42.9)	0.635	0.393
Hb, g/L	121.4 ± 22.2	124.3 ± 17.2	118.8 ± 15.7	116.7 ± 19.3	0.589	0.168
Platelet count, ×10^9/L, median (IQR)	358 (255-463)	275 (198-301)	287 (213-355)	246 (208-300)	0.023	0.482
Kerr score ≥ 2 (%)	13 (81.3)	5 (31.3)	36 (59.0)	8 (13.1)	0.085	0.083
Kerr scores, median (IQR)	3 (2-3)	0 (0-2)	2 (1-3)	0 (0-1)	0.049	0.165
ITAS 2010 scores, median (IQR)	4 (1-5)	0 (0-2)	1 (0-4)	0 (0-1)	0.477	0.632
Carotid artery wall thickness, mm	2.4 ± 0.8	2.1 ± 0.7	1.9 ± 0.5	1.7 ± 0.7	0.041	0.048
Carotid wall vascularisation grade 2 on CEUS (%)	7 (43.8)	6 (37.5)	27 (44.3)	6 (9.8)	0.971	0.014

TA: Takayasu arteritis; RD: refractory disease, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, SAA: serum amyloid A, Hb: haemoglobin, CEUS: contrast-enhanced ultrasound
p1 was defined for groups at baseline, *p2* was defined for groups at the 1-year follow-up.

Valuable factors for predicting carotid progression

Cox regression was performed to identify risk factors associated with carotid progression on imaging. The results demonstrated that age (HR 0.82, 95% CI 0.72–0.94), wall thickness (HR 5.24, 95% CI 1.49–18.48), and RD (HR 60.85, 95% CI 8.92–415.06) were positively associated with carotid progression on imaging, after adjustments for ESR, Kerr scores, lumen stenosis, and CEUS grade. Further, ROC curve analysis indicated that carotid wall thickness of ≥1.9 mm, age ≤30 years, and RD could predict progression on imaging with AUCs of 0.68, 0.80, and 0.86, respectively. (Supplementary Table S1).

Based on these results, the patients could be divided into different risk groups considering progression on imaging. Patients with younger age and early vascular structural changes had a higher risk of progression on imaging. When wall thickness of ≥1.9 mm was combined with age ≤30 years and the presence of RD, the incidence of progression on imaging was up to 75%, with a specificity of 93.4% and AUC of 0.93 (Suppl. Table S1).

Discussion

Carotid involvements are common in TAK patients and can be easily monitored by US. Thus, we designed this study to identify possible predictors including the baseline clinical characteristics as well as US features of carotid progression over a 1-year follow-up period. We found that patients with the following features were more likely to show progression on imaging: i) younger age with active disease; ii) thickened carotid artery wall at baseline; and iii) RD during the follow-up.

Predicting progression on imaging is remains an important challenge in clinical practice. Studies based on successional imaging evaluation are still lacking, due to the safety and economic factors associated with traditionally used imaging examinations including CTA, MRA and positron emission tomography/computed tomography (PET/CT). US is an inexpensive, safe, and easily operable imaging technique without radiation. In recent years, it has become an important and promising imaging method for evaluating vascular involvements, especially those of the temporal and carotid arteries. For TAK patients with carotid artery involvement, US is far superior to other imaging methods (1). Carotid wall thickness detected by US is an important feature of early imaging changes in TAK (6). Furthermore, CEUS can help assess wall neovascularisation in the early disease phase (15) and reflect carotid wall inflammation simultaneously (16-18). Our previous study also yielded similar results (6). However, these former studies yielded no evidence indicating that CDUS or CEUS can predict the progression of TAK.

In the present study, the value of carotid features combined with CEUS for predicting progression of TAK on imaging were analysed. To our knowledge, this was the first study in which corresponding carotid progression on US has been explored. We found that patients with carotid progression on imaging had a thicker artery wall and higher proportion of wall vascularisation of grade 2 at baseline. Notably, patients with a thickened carotid wall at baseline had an independent 5.24-fold higher risk of disease progression after 1 year. We also noted that patients in the active-phase disease, early vascular structural changes, or vascular remodelling seemed more likely to show pro-

gression on imaging. Thus, US showed great value in predicting progression on imaging.

Comarmond *et al*. reported a relapse rate of 42.7% in a 15-year long-term TAK cohort, with 20% of the relapses occurring in the first year (19). In another Indian TAK cohort, 7.2% of the patients were reported to show RD over a median follow-up period of 42 months (20). Similar results were found in our study, and 31.2% of the patients in our cohort showed poor treatment response during the first year of follow-up. The rate increased up to 87.5% in the progressive group. In addition, we found that the CRP level was significantly higher in the progressive group than in the non-imaging progressive group. However, CRP could not be identified as an independent risk factor for progression on imaging in further analysis. Other disease activity scores, including Kerr index and ITAS scores, were not associated with progression on imaging. These results suggest that neither inflammatory nor active indicators alone were suitable for predicting progression on imaging. In addition, our study suggested no correlation between progression on imaging and clinical symptoms. This may explain why US was sensitive for the visualisation of the subtle structural changes of the carotid artery, which occurred earlier than clinical symptoms.

To better identify patients with high risk of progression on imaging, we classified patients into different risk groups. In patients showing carotid wall thickness ≥1.9 mm at baseline, with age ≤30 years, and with RD, the risk of progression on imaging was up to 75%, while wall thickness ≥1.9 mm at baseline and age ≤30 years at baseline increased the risk of disease progression from 31% to 52%. These data can help distinguish patients with high risk of progression on imaging, and a closer follow-up of these high-risk patients is required to improve prognosis.

Our study has several limitations, although the present results are convincing despite the focus on the progression of carotid lesions. First, we restricted enrolment to patients with carotid artery involvement, which limited the sample size. Subsequent studies with larger sample sizes need to be performed. Second, the follow-up period was relatively short in the present study, and a longer follow-up in future studies is needed to further confirm the conclusions and the relationship between clinical symptoms and imaging. Lastly, the value of US in monitoring the status of other arteries such as the thoracic aorta, abdominal aorta, and renal artery, should also be investigated in future studies.

In conclusion, during the 1-year follow-up, 20.8% of the TAK patients showed progression on imaging. Younger patients with early vascular structural changes and vascular remodelling at baseline seemed more likely to show progression on imaging.

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