Clinical value of diagnosing ischaemic stroke in patients with Takayasu's arteritis combining multiple arterial occlusion and high-grade enhancement

L. Cui[1], R. Liu[1], Y. Zhao[2], B. Tian[1], Y. Xing[1,3,4]

[1]Department of Vascular Ultrasound, Xuanwu Hospital, Capital Medical University, Beijing; [2]Department of Rheumatology and Allergy, Xuanwu Hospital, Capital Medical University, Beijing; [3]Beijing Diagnostic Center of Vascular Ultrasound, Beijing; [4]Center of Vascular Ultrasound, Beijing Institute of Brain Disorders, Collaborative Innovation Center for Brain Disorders, Capital Medical University, Beijing, China.

Abstract

Objective

To determine the vascular ultrasound and contrast-enhanced ultrasound characteristics of ischaemic stroke in patients with Takayasu's arteritis (TAK) and explore the diagnostic value of ultrasound characteristics for diagnosing ischaemic stroke in such patients.

Methods

We retrospectively analysed 80 patients with TAK who underwent vascular ultrasound and contrast-enhanced ultrasound on admission. We analysed the ultrasound characteristics of ischaemic stroke in these patients and performed multiple logistic regression analyses to determine the independent risk factors for ischaemic stroke in the patient cohort. The value of ultrasound characteristics in patients with TAK and ischaemic stroke was evaluated using the net reclassification and integrated discrimination improvement indices.

Results

Among 80 patients, 22 (27.5%) had ischaemic stroke. Fourteen patients had anterior circulation infarction, two had posterior circulation infarction, and six had both. Multivariate analysis showed that the number of occluded arteries (odds ratio (OR), 2.01; p=0.005), high-grade enhancement (grade ≥2, OR, 6.52; p=0.016), and revascularisation (OR, 0.05; p=0.002) were independent influencing factors for ischaemic stroke in patients with TAK. The area under the curve indicated that the number of occluded arteries (≥3) and high-grade enhancement (grade ≥2) can be used to identify patients with TAK at high risk for ischaemic stroke.

Conclusion

A higher number of cervical artery occlusions and high-grade enhancement (grade ≥2) are independent risk factors for ischaemic stroke in patients with TAK. The combination of these factors can facilitate the diagnosis of ischaemic stroke in these patients.

Key words

Takayasu's arteritis, ischaemic stroke, contrast agent, ultrasonography, risk factors

Liuping Cui, MD
Ran Liu, MD
Yi Zhao, MD, PhD
Bing Tian, MM
Yingqi Xing, MD, PhD

Please address correspondence to:
Yingqi Xing
Department of Vascular Ultrasound,
Xuanwu Hospital,
Capital Medical University,
45 Changchun Road, Xicheng District,
Beijing 100053, China.
E-mail: xingyq2009@sina.com

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Introduction

Takayasu's arteritis (TAK) is a common disease worldwide; however, it is more prevalent in Asia and among young women (1). TAK is a chronic, granulomatous, systemic vasculitis that primarily affects the aorta and its branches, resulting in arterial wall thickening, fibrosis, stenosis, or occlusion (2). The clinical manifestations of TAK are diverse and insidious. Ischaemic damage caused by the involvement of the cervical and cerebral arteries may result from vascular inflammation and haemodynamic alterations, which may lead to vascular involvement and/or embolisation (3).

Patients with TAK have an elevated risk of developing cerebrovascular ischaemic events. A study conducted in the United Kingdom revealed that the risk of ischaemic stroke in patients with TAK was three times higher than that in a control group (4). Another study conducted in South Korea indicated that the standardised incidence rate of ischaemic stroke in patients with TAK was seven-fold higher than that in the general population (5). Therefore, it is essential to identify the potential risk factors for ischaemic stroke in patients with TAK to facilitate clinical practice. Vascular ultrasound is the most common, widely accepted, and reliable diagnostic tool for cervical artery disease (6, 7). The combination of carotid ultrasound and transcranial colour-coded Doppler can reveal changes in the structure of the lumen and haemodynamics of cerebral arteries (8). Furthermore, contrast-enhanced ultrasound (CEUS) can detect vascular wall inflammation (9, 10). TA is a major cause of cerebral infarction in young people, and ultrasound is the first-line diagnostic tool for cervical artery disease in China; however, data on the ultrasound parameters related to ischaemic stroke in patients with TAK are lacking.

The purpose of our study was to describe the vascular ultrasound characteristics of patients with TAK and ischaemic stroke and to identify possible risk factors for such stroke.

Materials and methods

Patients

We included 100 patients with TAK who were hospitalised at Xuanwu Hospital of Capital Medical University between January 2019 and September 2023. The inclusion criteria required that the patients met the 1990 American College of Rheumatology diagnostic criteria, had complete clinical data, and underwent carotid ultrasound, transcranial colour-coded Doppler, and CEUS within 1 week of admission. The exclusion criteria were as follows: 1) the cervical artery and or brain artery were not involved, 2) cerebral infarction with potential causes of cardiac embolism (such as atrial fibrillation and patent foramen ovale), and 3) poor or closed bilateral temporal windows.

Ischaemic stroke was diagnosed based on clinical symptoms, physical signs, and imaging findings (including brain computed tomography and or magnetic resonance imaging). Patients who were diagnosed with ischaemic stroke were assigned to the 'ischaemic stroke group' and the remaining patients to the 'non-ischaemic stroke group'.

Clinical data collection

The following patient data were collected: 1) demographic data, including age, sex, body mass index, and age at onset of TAK; 2) traditional vascular risk factors; 3) serological parameters, including cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, fasting blood glucose, haemoglobin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), immunoglobulin G, immunoglobulin A, immunoglobulin M, complement C3, and complement C4; 4) clinical manifestations of TAK; 5) treatment, including glucocorticoids, immunosuppressants, biologics, and revascularisation; 6) ITAS 2010 score and Numano vascular classification; and 7) vascular ultrasound parameters that were assessed, including the thickest intima-media thickness and the circulation of open collateral and 16 brain-supplying arteries (the anonymous, basilar, and paired arteries, including the subclavian, common carotid, internal carotid, vertebral, middle cerebral, anterior cerebral, and posterior cerebral arteries).

Arterial stenosis was recorded as follows: inflammation (wall thickening or stenosis of <50%), moderate stenosis

(50–69%), severe stenosis (70–99%), occlusion (complete or near occlusion), carotid artery dissection, and thrombosis.

Protocol and analysis of the carotid CEUS

Carotid CEUS was performed using a Philips ultrasound machine (Epiq 7; Philips, Amsterdam, the Netherlands) and a linear probe (5–8 MHz). To prevent the destruction of the contrast agent microbubbles, the mechanical index was set to 0.16. The gain was adjusted accordingly to visualise microbubbles in the best way. SonoVue (The Bracco Group, Milan, Italy), a contrast agent, and 5 mL of physiological saline were used to prepare the suspension. Raw data were stored on a hard drive for offline analysis.

Two experienced ultrasonographers (XYQ and LR) performed all the examinations and analyses. They inspected both the carotid arteries and recorded the intima–media thickness in the thickest area. CEUS was classified into four levels based on the degree of contrast-agent enhancement in the area of the lesion: Grade 0 indicated no visible microbubbles, grade 1 indicated limited microbubbles, grade 2 indicated moderate microbubbles, and grade 3 indicated extensive microbubbles (Fig. 1). The ultrasonographers discussed inconsistent gradings and jointly determined the final results.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics (v. 26.0; IBM Corp., Armonk, NY, USA) and R v. 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables that followed a normal distribution are presented as mean ± standard deviation and were analysed using the Student's t-test; otherwise, data are presented as the median and interquartile range and were analysed using the nonparametric rank-sum test. Categorical variables were represented as frequencies (%) and analysed using the chi-square test. Multivariate logistic regression analysis was used to identify the independent risk factors for ischaemic stroke in patients with TAK. The receiver operating characteristic (ROC) curve was used to calculate the area under the curve (AUC) and to determine the optimal cut-off value. The incremental value of the CEUS high-grade enhancement was demonstrated using the net reclassification index (NRI) and integrated discrimination improvement index (IDI). A two-tailed test was used ($p<0.05$).

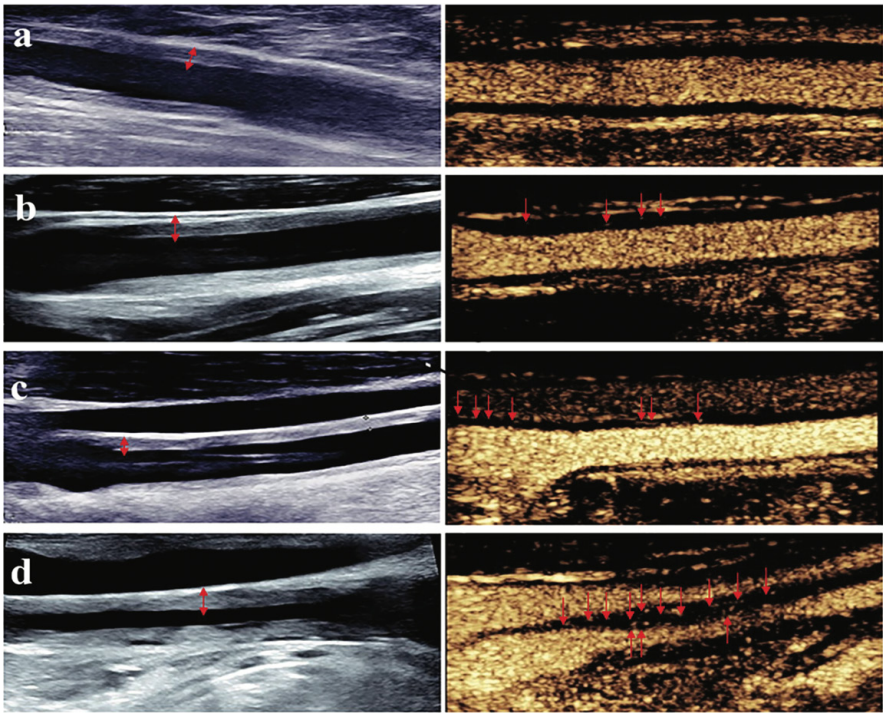
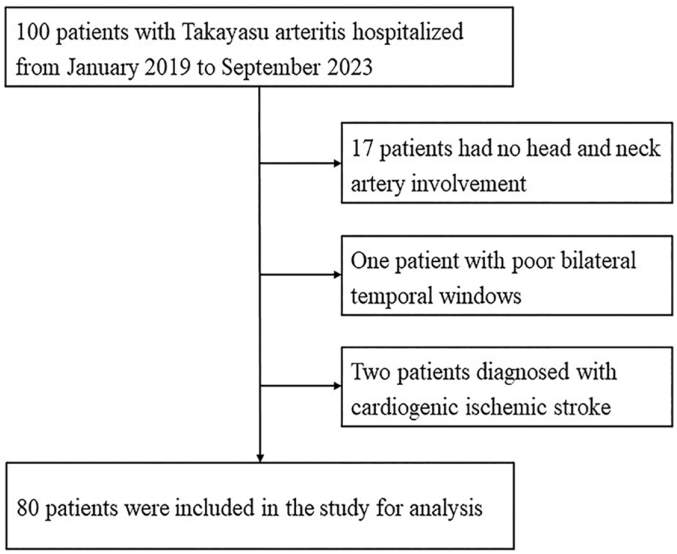


Fig. 1. Grading of intraplaque neovascularisation (Grades 0-3).
(**a**) Grade 0: no microbubbles, (**b**) Grade 1: limited microbubbles, (**c**) Grade 2: moderate microbubbles, (**d**) Grade 3: widespread microbubbles.

Fig. 2. Flow chart.



Results

Patient characteristics

Initially, 100 patients were included, of whom 20 were excluded from the study. Finally, we analysed 80 patients who met the inclusion criteria (Fig. 2). The average age of the patients was 39.5±13.1 years, 69 (86.3%) of whom were female. The average age at onset for TAK was 32.3±11.7 years. Among the 22 patients with TAK and ischaemic stroke, 14 experienced ischaemic stroke at the onset of TAK, whereas eight experienced ischaemic stroke after the diagnosis of TAK. Of these, 16

patients experienced a single ischaemic stroke, four experienced two ischaemic strokes, and two experienced multiple ischaemic strokes. In addition, among these 22 patients, there were 14 cases of anterior circulation infarction, two cases of posterior circulation infarction, and six cases involving both circulations. Nineteen patients (86.4%) had multiple infarctions. The most common sites of infarction were the basal ganglia (13 cases, 59.1%) and the frontal lobe (13 cases, 59.1%).

Clinical features of TAK

The time of diagnostic delay did not differ significantly between the 'non-ischaemic stroke group' and the 'ischaemic stroke group' (p=0.280). No significant differences in cardiovascular risk factors were observed between the two groups. However, complement C3 levels were higher in the 'ischaemic stroke group' compared to the 'non-ischaemic stroke group' (p=0.032). Other serologic parameters were similar between the groups (Table I).

The 'ischaemic stroke group' had a higher ITAS 2010 score than the 'non-ischaemic stroke group' (p=0.024), whereas the clinical symptoms were similar between the two groups. Dizziness (52.5%) was the most common clinical symptom, and vascular murmur (60%) was the most common physical sign (Fig. 3a).

Medication use between the two groups was similar. The number of patients in the 'ischaemic stroke group' who underwent revascularisation was much higher than that in the 'non-ischaemic stroke group' (p<0.05). No significant differences in the Numano classification between the two groups were observed (Table I).

Table I. Baseline characteristics of patients (n=80).

Characteristic	Non-ischaemic stroke group (n=58)	Ischaemic stroke group (n=22)	p-value
General information			
Age, years, mean ± SD	40.0 ± 13.1	38.2 ± 13.3	0.602
Sex, male, n (%)	7 (12.1%)	4 (18.2%)	0.483
BMI, kg/m^2, mean ± SD	23.2 ± 3.6	22.6 ± 3.1	0.533
Age at TA onset, years, mean ± SD	33.1 ± 12.5	29.7 ± 9.3	0.247
Diagnosis delay time (months), median (IQR)	6.0 (8.0)	4.0 (11.0)	0.280
Risk factors, n (%)			
Hypertension	15 (25.9%)	3 (13.6%)	0.370
Diabetes	2 (3.4%)	1 (4.5%)	1.000
Hyperlipidaemia	6 (10.3%)	3 (13.6%)	0.700
Smoking	4 (6.9%)	1 (4.5%)	1.000
Drinking	2 (3.4%)	1 (4.5%)	1.000
Coronary heart disease	1 (1.7%)	1 (4.5%)	0.477
Serological indicators			
Cholesterol, mean ± SD	4.3 ± 1.3	3.7 ± 0.9	0.063
Triglyceride, mean ± SD	1.0 ± 0.4	1.1 ± 0.4	0.750
HDL, mean ± SD	1.3 ± 0.3	1.3 ± 0.3	0.267
LDL, mean ± SD	2.4 ± 1.2	2.1 ± 0.5	0.268
FBG, mean ± SD	4.5 ± 1.0	4.3 ± 0.8	0.286
Glycosylated haemoglobin, mean ± SD	121.5 ± 18.2	117.3 ± 17.9	0.332
CRP, median (IQR)	3.5 (8.9)	6.3 (8.7)	0.113
ESR, median (IQR)	10.0 (20.0)	15.0 (24.0)	0.186
Immunoglobulin G, mean ± SD	11.5 ± 3.2	11.1 ± 3.2	0.657
Immunoglobulin A, mean ± SD	2.4 ± 1.3	2.8 ± 1.6	0.258
Immunoglobulin M, mean ± SD	1.4 ± 0.7	1.3 ± 0.5	0.713
Complement C3, mean ± SD	0.9 ± 0.2	1.0 ± 0.2	0.032
Complement C4, mean ± SD	0.2 ± 0.08	0.3 ± 0.09	0.089
ITAS 2010, scores	6.0 (8.0)	10.0 (5.0)	0.024
Numano classification, n (%)			0.678
Type I	23 (39.7%)	9 (40.9%)	
Type II	2 (3.4%)	0 (0%)	
Type V	33 (56.9%)	13 (59.1%)	
Treatment, n (%)			
Glucocorticoids	45 (77.6%)	20 (90.9%)	0.215
Immunodepressant	43 (74.1%)	15 (68.2%)	0.594
Biological agents	6 (10.3%)	3 (13.6%)	0.700
Revascularisation	3 (5.2%)	10 (45.5%)	<0.0001
Intima-media thickness, mean ± SD	2.5 ± 0.9	2.8 ± 0.7	0.160
Number of occluded arteries, median (IQR)	1.0 (0)	3.0 (7.0)	<0.0001
MCA involvement, n (%)	11 (19.0%)	9 (40.9%)	0.043
Circulation of open collateral, n (%)	27 (46.6%)	17 (77.3%)	0.014
Arterial dissection	2 (3.4%)	2 (9.1%)	0.303
Thrombosis	0 (0%)	1 (4.5%)	0.275
CEUS			0.008
Grades 0 and 1	40 (69.0%)	8 (36.4%)	
Grades 2 and 3	18 (31.0%)	14 (63.6%)	

BMI: body mass index; CEUS: contrast-enhanced ultrasound; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FBG: fasting blood glucose; HDL: high-density lipoprotein; IQR: interquartile range; LDL: low-density lipoprotein; MCA: middle cerebral artery; SD: standard deviation.

Vascular ultrasound parameters

Figure 3 b-f shows the degree of cervical artery involvement. In the 'non-ischaemic stroke group', the most frequently affected artery is the common carotid artery (56 cases, 96.6%). The middle cerebral artery (11 cases, 19.0%) is the most commonly affected intracranial artery. In the 'ischaemic stroke group', the common carotid artery is the most frequently affected artery (22 cases, 100%), followed by the subclavian artery (20 cases, 90.9%). The middle cerebral artery (nine cases, 40.9%) is the most commonly affected intracranial artery.

The number of arteries that were occluded in the 'ischaemic stroke group' was higher than that in the 'non-ischaemic stroke group' (p<0.0001). In addition, compared with the 'non-ischaemic stroke group', the 'ischaemic stroke group' had a higher proportion of involvement of the middle cerebral artery (p=0.043) and openings of collateral branches (p=0.014). In the 'ischaemic stroke group', 14 (63.6%) patients presented with CEUS high-grade enhancement (grade ≥2), whereas in the 'non-ischaemic stroke group', 18 (31.0%) patients exhibited a CEUS grade of ≥2, with a significant between-group difference (p=0.008) (Table I).

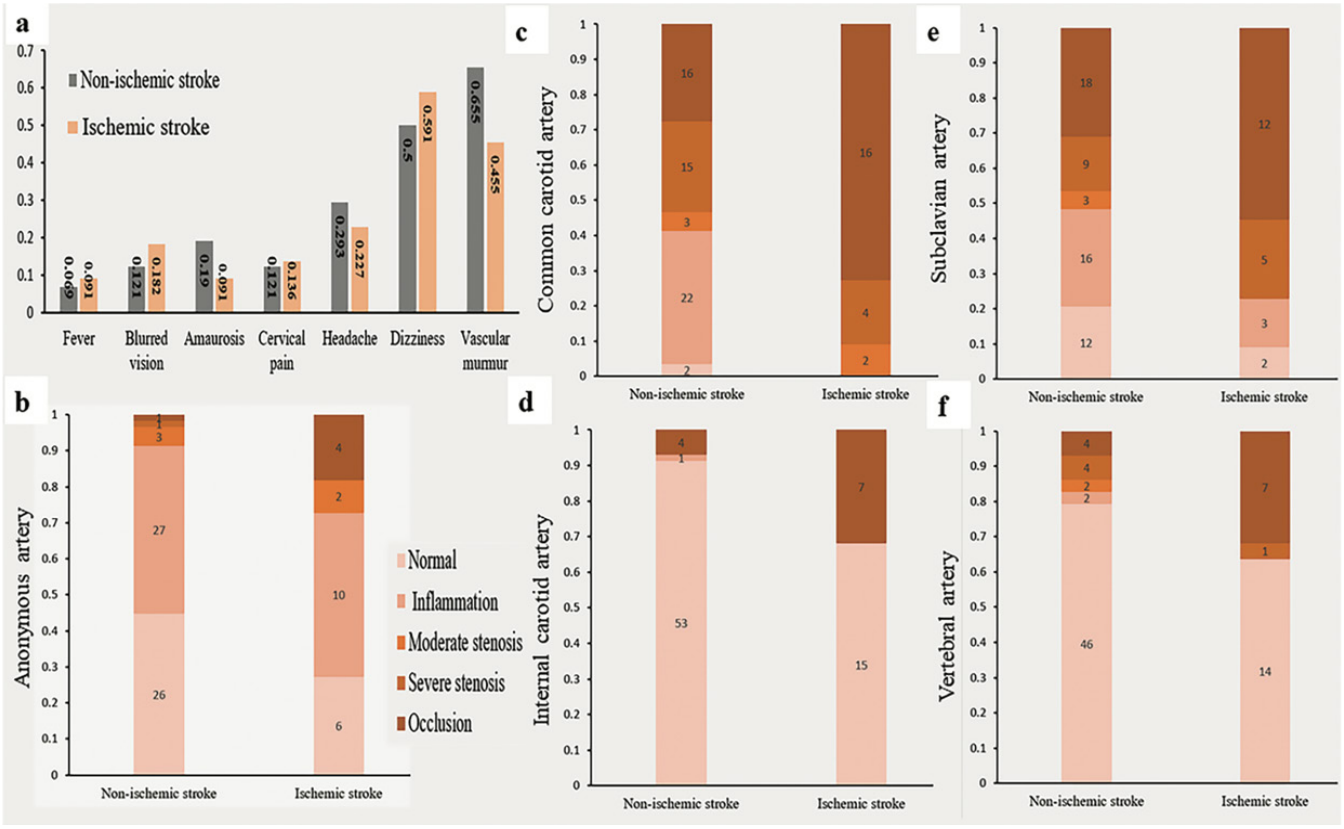


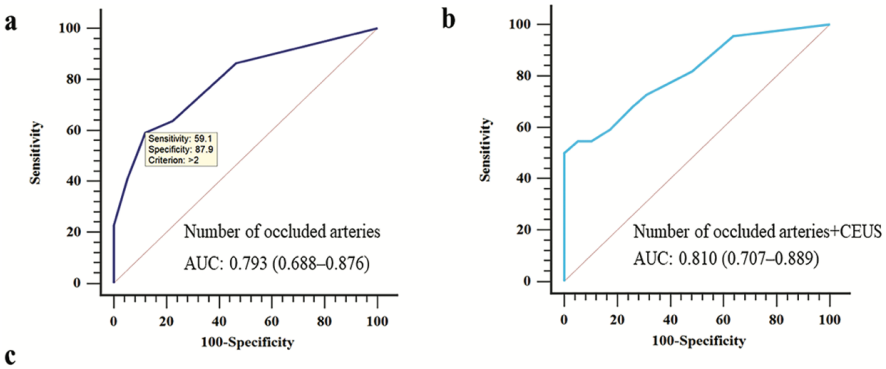
Fig. 3. Symptoms and distribution of cervical artery involvement.
(**a**) Common symptoms in patients with TAK. (**b-f**) Analysis of the degree of involvement of the cervical artery in patients with TAK.

Multivariate and ROC analyses

The multivariate analysis revealed that a CEUS grade of ≥2 (odds ratio (OR), 6.52; 95% confidence interval (CI), 1.41–30.14) and the number of occluded arteries (OR, 2.01; 95% CI, 1.24–3.27) were independent risk factors for ischaemic stroke in patients with TAK. Conversely, revascularisation (OR, 0.050; 95% CI, 0.007–0.34) was identified as a protective factor.

The ROC analysis indicated a cut-off value of ≥3 as the optimal threshold for the number of occluded arteries, with a sensitivity of 59.1% and a specificity of 87.9% (Fig. 4a). The AUC of CEUS grade ≥2 combined with occluded arteries was 0.81 (95% CI, 0.71–0.89) (Fig. 4b).

The results of the NRI and IDI indicated that, compared to the number of occluded arteries alone, the combination of CEUS grade ≥2 and number of occluded arteries more accurately identified patients with TAK combined with ischaemic stroke (NRI, 0.85; 95% CI, 0.40–1.30 and IDI index, 0.092; 95% CI, 0.03–0.16; $p<0.05$).



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	AUC	p-value	NRI	p-value	IDI	p-value
Number of occluded arteries	0.793 (0.688–0.876)		Ref		Ref	
Number of occluded arteries+CEUS	0.810 (0.707–0.889)	0.621	0.846 (0.397–1.296)	<0.05	0.092 (0.026–0.159)	<0.05

Fig. 4. Clinical value of ultrasound in identifying ischaemic stroke in patients with TAK.
(**a**) The optimal cut-off value of the number of occluded arteries. (**b**) The AUC when combining the number of occluded arteries and contrast-enhanced ultrasonography (CEUS). (**c**) Compared to the number of occluded arteries alone, the combination of CEUS ≥2 grade and occluded arteries could more accurately identify high-risk patients with TAK and ischaemic stroke.

Discussion

We report the vascular ultrasound characteristics of ischaemic stroke in patients with TAK. Our main finding was that patients with TAK and ischaemic stroke had a higher number of cervical artery occlusions than those without ischaemic stroke. Furthermore, compared to patients with low-grade enhancement on CEUS (grade <2),

patients with TAK with high-grade enhancement on CEUS (grade ≥2) have a five-fold increased risk of ischaemic stroke (Fig. 5).

We found that 27.5% (22/80) of patients with TAK had experienced ischaemic stroke, a higher percentage than that reported in previous studies; previous studies have shown an incidence of stroke with TAK ranging from 8.9% to 20% (11–15). However, because of our research centre's reputation in the field of neurology, the centre may attract patients with TAK and neurological symptoms. An earlier study conducted at our institution revealed that the prevalence of TAK in patients with ischaemic stroke was as high as 27.0%, which agrees with the results of the current study (16).

In the present study, among patients with TAK and ischaemic stroke, 14 had anterior circulation infarction, two had posterior circulation infarction, and six had both anterior and posterior circulation infarction. Consistent with this, the common carotid artery was the most affected, followed by the subclavian artery, which is consistent with previous studies (12, 17). Regarding intracranial arteries, the middle cerebral artery was the most commonly affected. A previous study on TAK reported that the middle cerebral artery was the most frequently affected intracranial artery in patients with ischaemic stroke, with a rate of intracranial vascular involvement of 38.5%, which is consistent with our findings (18). Intracranial arterial disease is common in patients with TAK, possibly because intracranial segment lesions of the internal carotid artery are a continuation of the extracranial segment (19). Among the 22 patients with ischaemic stroke, 19 had multiple infarctions, with the basal ganglia and frontal lobe being the most common sites of infarction, consistent with previous studies (18, 20). In addition, 14 patients (63.6%) experienced ischaemic stroke at the onset of TA, highlighting the critical role of TAK in diagnosing stroke aetiology in young individuals. This finding underscores the importance of considering TAK as a potential cause of stroke in this population (21). In this study, the multivariate logistic regression analyses revealed a significant association between occlusive lesions of the cervical artery and ischaemic stroke. Similarly, a significant correlation between stenosis and occlusion of the carotid and subclavian arteries and neurological manifestations in patients with TAK has been demonstrated (22).

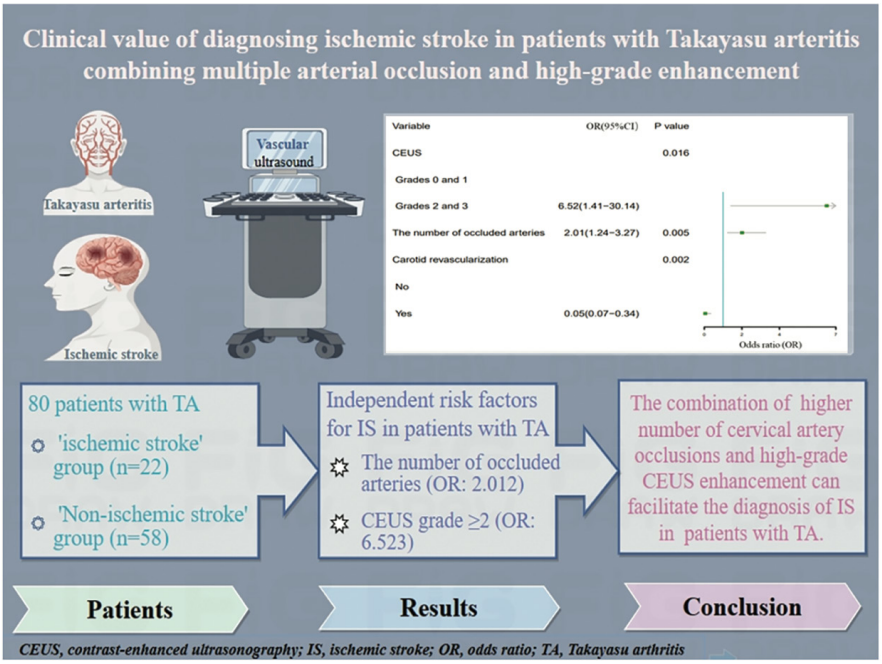

Fig. 5. patients with TAK with high-grade enhancement on CEUS (grade ≥2) have a five-fold increased risk of ischaemic stroke. The figure was drawn by Figraw.

The present study found that patients with TAK and ischaemic stroke were more likely to have high-grade CEUS. Compared to the gold standard of fluorodeoxyglucose F18-positron emission tomography, a sensitivity of 100% and a specificity of 80% has been reported for CEUS when a CEUS ≥2 was used to define vasculitis (23). A recent study suggested that CEUS may be useful for monitoring disease activity during the follow-up (24). Enhanced CEUS suggests inflammatory lesions in the vascular wall, a characteristic pathological change during TAK, and ischaemic stroke is a manifestation of TAK. Therefore, we consider that patients with TAK and ischaemic stroke are more likely to be in a state indicating the progression of vascular wall inflammation or an active inflammatory state, and CEUS may serve as a potential biomarker for such patients.

The association between ischaemic stroke and traditional vascular risk factors in patients with TAK remains controversial. Factors such as hyperlipidaemia, hypertension, and body mass index are associated with the occurrence of cardiovascular and cerebrovascular ischaemic events in patients with TAK (16, 25). However, in the current study, we did not observe any differences in cardiovascular risk factors between patients with TAK with and without ischaemic stroke. Data reported from a multicentre study in France and a national database in South Korea are consistent with our conclusions (5, 26). Nevertheless, a retrospective study reported that compared to patients with TAK without stroke or transient ischaemic attack (TIA), those with stroke/TIA were older and had a higher proportion of males. This discrepancy may be attributed to differences in sample size and study populations. Notably, our study excluded patients with TIA, as retrospective studies may introduce potential bias in TIA diagnosis (27). We observed that the ESR and CRP levels in the two patient groups were similar, as supported by the results of previous studies (16, 28). A possible explanation is that ESR and CRP are systemic inflammatory markers influenced by multiple factors, possibly leading to inconsistencies in ESR, CRP, and TAK activity (29).

Early diagnosis of TAK, progression of vascular disease, and lifelong monitoring of recurrence of disease activity are crucial for a good prognosis (30). Compared to computed tomography angiography and magnetic resonance angiography, vascular ultrasound has the advantages of easy accessibility, low cost, non-invasiveness, and a radiation-free nature, as well as being considered useful for diagnosis and monitoring. A meta-analysis revealed that in patients with TAK, ultrasound had a combined sensitivity of 81% using clinical or routine angiography as the gold standard; this was not inferior to positron emission tomography and magnetic resonance imaging (7). During the follow-up of patients with TAK, neovascularisation continued to be observed at the site of vascular lesions in patients with decreased ESR and CRP levels who achieved clinical remission, indicating that CEUS is more sensitive in evaluating vascular inflammation than acute-phase reactants (28). Therefore, the present study provides evidence for the early assessment and long-term monitoring of vascular disease progression in TAK using vascular ultrasound and CEUS.

This study had some limitations. First, this was a retrospective study; prospective studies are needed to validate the conclusions for clinical application. Second, ultrasound is operator-dependent: all diagnostic methods require training, standard operating procedures, and appropriate equipment. Third, this study included only hospitalised patients, possibly introducing a selection bias.

Our findings indicate that ischaemic stroke is relatively common in patients with TAK. A higher number of cervical artery occlusions, as assessed by vascular ultrasound, and high-grade enhancement on CEUS are independent risk factors for ischaemic stroke in patients with TAK. Furthermore, the combination of these factors may assist in the diagnosis of ischaemic stroke in patients with TAK.

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References

1. DANDA D, MANIKUPPAM P, TIAN X, HARIGAI M: Advances in Takayasu arteritis: an Asia Pacific perspective. *Front Med* (Lausanne) 2022; 9. https://doi.org/10.3389/fmed.2022.952972
2. HARKY A, FOK M, BALMFORTH D, BASHIR M: Pathogenesis of large vessel vasculitis: Implications for disease classification and future therapies. *Vasc Med* 2019; 24(1): 79-88. https://doi.org/10.1177/1358863x18802989
3. KIM HJ, SUH DC, KIM JK *et al*.: Correlation of neurological manifestations of Takayasu's arteritis with cerebral angiographic findings. *Clin Imaging* 2005; 29(2): 79-85. https://doi.org/10.1016/j.clinimag.2004.04.026
4. GOEL R, CHANDAN JS: Cardiovascular and renal morbidity in Takayasu arteritis: a population-based retrospective cohort Study from the United Kingdom. *Arthritis Rheumatol* 2021; 73(3): 504-11. https://doi.org/10.1002/art.41529
5. AHN SS, HAN M, PARK YB, JUNG I, LEE SW: Incidence, prevalence and risk of stroke in patients with Takayasu arteritis: a nationwide population-based study in South Korea. *Stroke Vasc Neurol* 2022; 7(2): 149-57. https://doi.org/10.1136/svn-2020-000809
6. BRKIC A, TERSLEV L, MØLLER DØHN U, TORP-PEDERSEN S, SCHMIDT WA, DIAMANTOPOULOS AP: Clinical applicability of ultrasound in systemic large vessel vasculitides. *Arthritis Rheumatol* 2019; 71(11): 1780-7. https://doi.org/10.1002/art.41039
7. SCHMIDT WA, SCHÄFER VS: Diagnosing vasculitis with ultrasound: findings and pitfalls. *Ther Adv Musculoskelet Dis* 2024; 16. https://doi.org/10.1177/1759720x241251742
8. LOPEZ D, GUEVARA M: Use of ultrasound in the diagnosis and management of the vasculitides. *Curr Rheumatol Rep* 2020; 22(7): 31. https://doi.org/10.1007/s11926-020-00902-x
9. SCHMIDT WA: Contrast-enhanced ultrasound for monitoring takayasu arteritis. *j rheumatol* 2022; 49(11): 1185-87. https://doi.org/10.3899/jrheum.220726
10. DONG Y, WANG Y, WANG Y *et al*.: Ultrasonography and contrast-enhanced ultrasound for activity assessment in 115 patients with carotid involvement of Takayasu arteritis. *Mod Rheumatol* 2023; 33(5): 1007-15. https://doi.org/10.1093/mr/roac107
11. COMARMOND C, BIARD L, LAMBERT M *et al*.: Long-term outcomes and prognostic factors of complications in Takayasu arteritis: a multicenter study of 318 patients. *Circulation* 2017; 136(12): 1114-22. https://doi.org/10.1161/circulationaha.116.027094
12. LI J, SUN F, CHEN Z *et al*.: The clinical characteristics of Chinese Takayasu's arteritis patients: a retrospective study of 411 patients over 24 years. *Arthritis Res Ther* 2017; 19(1): 107. https://doi.org/10.1186/s13075-017-1307-z
13. DUARTE MM, GERALDES R, SOUSA R, ALARCÃO J, COSTA J: Stroke and transient ischemic attack in Takayasu's arteritis: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis* 2016; 25(4): 781-91. https://doi.org/10.1016/j.jstrokecerebrovasdis.2015.12.005
14. KIM H, BARRA L: Ischemic complications in Takayasu's arteritis: A meta-analysis. *Semin Arthritis Rheum* 2018; 47(6): 900-6. https://doi.org/10.1016/j.semarthrit.2017.11.001
15. UNGPRASERT P, WIJARNPREECHA K, CHEUNGPASITPORN W, THONGPRAYOON C, KRONER PT: Inpatient prevalence, burden and comorbidity of Takayasu's arteritis: nationwide inpatient sample 2013-2014. *Semin Arthritis Rheum* 2019; 49(1): 136-39. https://doi.org/10.1016/j.semarthrit.2018.11.008
16. KONG F, HUANG X, SU L: Risk factors for cerebral infarction in Takayasu arteritis: a single-centre case-control study. *Rheumatology* 2021; 61(1): 281-90. https://doi.org/10.1093/rheumatology/keab308
17. MIROUSE A, DELTOUR S: Cerebrovascular ischemic events in patients with Takayasu arteritis. *Stroke* 2022; 53(5): 1550-7. https://doi.org/10.1161/strokeaha.121.034445
18. ZHANG G, NI J, YANG Y, LI J, TIAN X, ZENG X: Clinical and vascular features of stroke in Takayasu's arteritis: A 24-year retrospective study. *Rheumatol Immunol Res* 2023; 4(1): 22-29. https://doi.org/10.2478/rir-2023-0004
19. GUO Y, DU J, LI T, GAO N, PAN L: Clinical features and risk factors of intracranial artery disease in patients with Takayasu arteritis. *Clin Rheumatol* 2022; 41(8): 2475-81. https://doi.org/10.1007/s10067-022-06168-1
20. HWANG J, KIM SJ, BANG OY *et al*.: Ischemic stroke in Takayasu's arteritis: lesion patterns and possible mechanisms. *J Clin Neurol* 2012; 8(2): 109-15. https://doi.org/10.3988/jcn.2012.8.2.109
21. DE PAULA LE, ALVERNE AR, SHINJO SK: Clinical and vascular features of Takayasu arteritis at the time of ischemic stroke. *Acta Reumatol Port* 2013; 38(4): 248-51.
22. YANG L, ZHANG H, JIANG X *et al*.: Clinical features and outcomes of Takayasu arteritis with neurological symptoms in China: a retrospective study. *J Rheumatol* 2015; 42(10): 1846-52. https:// doi.org/10.3899/jrheum.150097
23. LI Z, ZHENG Z, DING J *et al*.: Contrast-enhanced ultrasonography for monitoring arterial inflammation in Takayasu arteritis. *J Rheumatol* 2019; 46(6): 616-22. https://doi.org/10.3899/jrheum.180701
24. DING J, WU D, HAN Q, ZHANG K, ZHENG Z, ZHU P: Follow-up contrast-enhanced ultrasonography of the carotid artery in patients with Takayasu arteritis: a retrospective study. *J Rheumatol* 2022; 49(11):1242-49. https://doi.org/10.3899/jrheum.220114
25. LIU Q, DANG A, LV N, WANG X, ZHENG D: Anaemia and low body mass index are associated with increased cardiovascular disease in patients with Takayasu arteritis. *Clin Exp Rheumatol* 2016; 34 (Suppl. 97): S16-20.
26. COUTURE P, CHAZAL T, ROSSO C *et al*.: Cerebrovascular events in Takayasu arteritis: a multicenter case-controlled study. 2018; 265(4): 757-63. https://doi.org/10.1007/s00415-018-8744-8
27. MISRA DP, RATHORE U, MISHRA P *et al*.: Comparison of presentation and prognosis of Takayasu arteritis with or without stroke or transient ischemic attack-a retrospective

cohort study. *Life* 2022; 12(11): 1904. https://doi.org/10.3390/life12111904
28. MA LY, LI CL, MA LL *et al*.: Value of contrast-enhanced ultrasonography of the carotid artery for evaluating disease activity in Takayasu arteritis. *Arthritis Res Ther* 2019; 21(1): 24. https://doi.org/10.1186/s13075-019-1813-2
29. MISRA DP, JAIN N, ORA M, SINGH K: Outcome measures and biomarkers for disease assessment in Takayasu Arteritis. *Diagnostics* (Basel) 2022; 12(10): 2565. https://doi.org/10.3390/diagnostics12102565
30. JOSEPH G, GOEL R, THOMSON VS, JOSEPH E, DANDA D: Takayasu Arteritis: JACC Focus Seminar 3/4. *J Am Coll Cardiol* 2022; 13: S0735-1097(22)07305-3. https://doi.org/10.1016/j.jacc.2022.09.051