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Carotid Intima-media Thickness/Diameter Ratio and Peak Systolic Velocity as Risk Factors for Neurological Severe Ischemic Events in Takayasu Arteritis

Li Wang[1], Ying Sun[1], Xiaojuan Dai[1], Xiufang Kong[1], Lingying Ma[1], Xiaomin Dai[1], Lili Ma[1], and Lindi Jiang[2]

ABSTRACT. ***Objective.*** To characterize Takayasu arteritis (TA) with supra-aortic involvement and determine the associations between clinical features, carotid ultrasonographic (US) variables, and neurological severe ischemic events (SIEs).

Methods. Patients with supra-aortic involvement including brachiocephalic trunk, bilateral common carotid artery and internal carotid artery, and bilateral subclavian and vertebral artery and baseline carotid US examination were enrolled from the East China TA cohort. Bilateral carotid diameter, intima-media thickness (IMT), and peak systolic velocity (PSV) were measured by US. Then, the IMT/diameter ratio (IDR) was calculated. Risk factors associated with neurological SIEs were analyzed by multivariate logistic regression.

Results. In total, 295 patients were included, of whom 260 (88.14%) were female, and 93 (31.53%) experienced neurological SIEs. Involved supra-aortic artery distribution ($P = 0.04$) and number ($P < 0.01$) differed between subjects with neurologic and nonneurologic SIEs, showing higher prevalence of common carotid and vertebral artery involvement after Bonferroni correction and 56.99% patients having ≥ 4 involved arteries in the neurological SIE group. The bilateral IDR ($P < 0.01$) differed between patients with and without neurological SIEs. The carotid IDR (left: cut-off value ≥ 0.55, OR 2.75, 95% CI 1.24–6.07, $P = 0.01$; right: ≥ 0.58, OR 2.70, 95% CI 1.21–6.02, $P = 0.01$) and left carotid PSV (≤ 76.00 cm/s, OR 3.09, 95% CI 1.53–6.27, $P < 0.01$), as well as involved supra-aortic artery number (≥ 4, OR 2.33, 95% CI 1.15–4.72, $P = 0.02$) were independently associated with neurological SIEs.

Conclusion. The carotid IDR and PSV might be performed as valuable markers for recognizing neurological SIEs in patients with TA with supra-aortic lesions.

Key Indexing Terms: intima-media thickness/diameter ratio, neurological severe ischemic events, supra-aortic involvement, Takayasu arteritis

Takayasu arteritis (TA) is an idiopathic systemic vasculitis characterized by the involvement of the aorta and its major branches. It is more common in females, with a disease onset age < 40 years.[1] Transmural inflammation of the vessel wall might gradually lead to vascular stenosis or occlusion, resulting in end-organ ischemia.[2] The supra-aortic arteries are often involved in TA, with the reported prevalence ranging from 40% to 84%.[3,4] Importantly, patients with supra-aortic involvement carry a higher risk of neurological severe ischemic events (SIEs), including syncope, visual disturbance, and major central nervous system (CNS) events (stroke or transient ischemic attack [TIA]) that might result in considerably worse prognosis.[5,6,7,8] It has been reported that 11.7% of the patients with TA suffered a stroke during the course of the disease, and 5.5% experienced ischemic ocular events.[9] Therefore, finding potential risk factors associated with neurological SIEs is essential for clinical practice.

The common carotid artery (CCA) is the most affected artery and is more closely associated with neurologic symptoms than other supra-aortic arteries.[5] Previous studies have shown that the incidence of CCA involvement was 21–65% in patients with TA,[10,11] and approximately 50% of the neurological symptoms and signs were related to lesions in the CCA and/or vertebral artery.[12] Ultrasonography (US) has been regarded as the most popular, user-friendly, and repeatable tool for the diagnosis and follow-up of CCA injuries.[13,14] Our previous studies have indicated that US could be used to assess vascular inflammation and predict disease progression in patients with TA with carotid artery lesions.[15,16] Further, the CCA intima-media thickness

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[1]L. Wang, PhD, Y. Sun, PhD, X. Dai, PhD, X. Kong, PhD, L. Ma, PhD, X. Dai, PhD, L. Ma, PhD, Department of Rheumatology; [2]L. Jiang, PhD, MD, Evidence-based Medicine Center, Zhongshan Hospital, Fudan University, Shanghai, China.

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Address correspondence to Dr. L. Jiang, 180 Fenglin Road, Department of Rheumatology, Zhongshan Hospital, Fudan University, Shanghai 200032, China. Email: zsh-rheum@hotmail.com.

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(IMT) and diameter, assessed by US, have been reported to be predictive indicators for disease progression and subsequent clinical complications in atherosclerosis.[17] However, vascular diameter changes may not always be consistent with IMT, even though arteries might compensate for IMT by increasing vascular diameter in the early disease course.[18,19] Further, Denarié et al underlined that age, sex, and the side being measured should be considered in the reference values of the IMT and diameter of the vessels.[20] Previously, the IMT/diameter ratio (IDR) was used by Semmler in a healthy population of children to assess the carotid artery dimensions.[19] However, it is not clear whether US variables of CCA, including IMT and IDR, could be used to monitor disease features and what the links are between these variables and neurological SIEs in patients with TA.

Therefore, we conducted the current study to characterize patients with TA with supra-aortic involvement and highlight whether various US variables, especially the IDR of the CCA, as well as clinical features, were associated with neurological SIEs in this patient population.

METHODS

Study population. This research was based on the ongoing East China Takayasu Arteritis (ECTA) cohort (ClinicalTrials.gov: NCT03893136), initiated in Zhongshan Hospital, Fudan University, Shanghai, China, in 2009. All patients in the cohort were diagnosed with TA based on the 1990 American College of Rheumatology classification criteria.[21] The inclusion criteria for the present study were as follows: (1) first visit between July 2009 and March 2021; (2) supra-aortic involvement confirmed by magnetic resonance angiography (MRA) or computed tomography angiography (CTA); (3) US assessment of the carotid artery at baseline; and (4) no other autoimmune diseases or active infection (Figure 1).

The program followed the tenets of the Declaration of Helsinki and its amendments. Ethics approval was given by the Zhongshan Hospital Ethics Committees, Fudan University (B2016-168[2]R). Written consent for participation in the research program was obtained from all participants.

Clinical assessment. The baseline demographic characteristics, clinical manifestations, and major complications were recorded. Acute-phase reactants and cytokine measurements were conducted at the clinical laboratory of Zhongshan Hospital following standard operating procedures. Cytokines, such as interleukin (IL)-2 receptor (IL-2R) and IL-6, were detected by chemiluminescence assays. Disease activity was evaluated following the Kerr scoring system, with a Kerr score ≥ 2 defined as active disease.[1]

Imaging assessment. At least 1 imaging examination, including MRA or CTA, was performed at baseline to identify vessel involvement including luminal stenosis, vascular walls thickness, or inflammation. Supra-aortic involvement (range 1–9) was assumed when the brachiocephalic trunk, bilateral CCA or internal carotid artery, or bilateral subclavian or vertebral arteries were affected.[22] The imaging type was classified following the 1996 Numano classification.[23]

US assessment. All enrolled patients underwent carotid US assessment. All examinations were performed using a Philips Elite US instrument with an L9-3 linear array probe (Philips Medical Systems). A physician with 5 years' experience examined the bilateral CCA of all enrolled participants. The mechanical index was 0.07, and the gain was 70%. The instrument variables were kept constant for all patients.

The CCA diameter, IMT, and peak systolic velocity (PSV) were measured. IDR was calculated by IMT/diameter as previously described.[19] The diameter of occluded CCA was defined as 0 mm and for these cases, we defined the IDR value as 1 in the statistical analysis.

Definitions of neurological SIEs. Neurological SIEs related to supra-aortic involvement was defined as any occurrence of stroke, syncope, and visual disturbance within 3 months before the first visit.[8] Stroke was defined as an acute ischemic cerebrovascular event with neurological deficit confirmed by imaging, referring to CNS infarction accompanied by overt symptoms.[24] Syncope was defined as transient loss of consciousness and postural tone resulting from an abrupt, temporary decrease in cerebral blood flow.[25] Visual disturbance included amaurosis fugax or blurred vision/vision loss without a known ophthalmologic disorder to account for the symptoms.[26,27,28] These events were judged by a multidisciplinary team of rheumatologists, neurologists, ophthalmologists, and radiologists.

Statistical analysis. Categorical variables were summarized as counts and percentages and were compared using chi-square or Kruskal-Wallis test. If the chi-square test found significant differences, posthoc Bonferroni tests

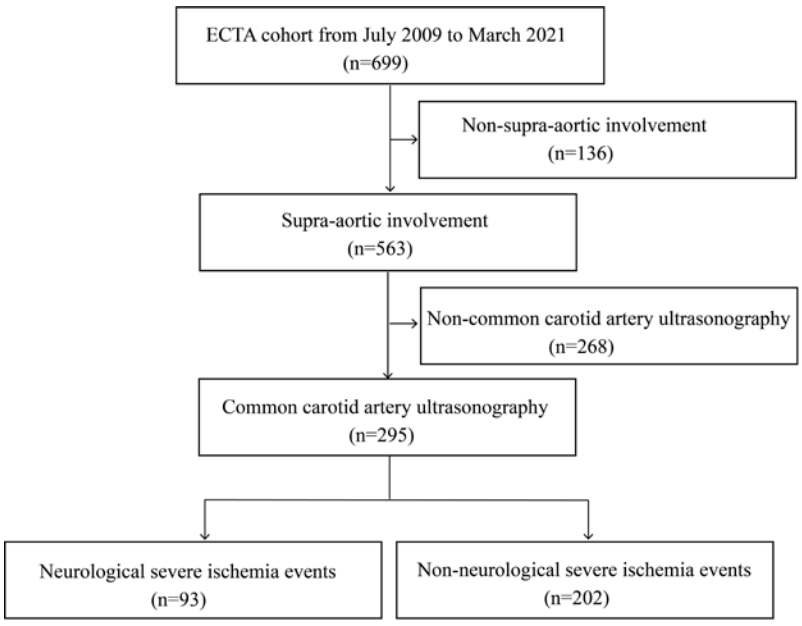

Figure 1. A flow diagram for the study design. ECTA: East China Takayasu Arteritis.

were performed to assess the intergroup differences. Continuous variables are presented as mean ± SD or as median with IQR, depending on the normality of distribution, and were compared using *t* tests or Wilcoxon tests. Receiver-operating characteristic curve analysis was performed to determine the cut-off values for all continuous variables to identify neurological SIEs. Clinically significant variables with an apparent difference between the neurological SIE and nonneurological SIE subgroups ($P < 0.10$) were performed in a univariate logistic regression analysis with the likelihood ratio forward step method. Candidate variables were further entered into multivariate logistic regression model adjusting clinical complications and disease activity to identify the independent factors associated with neurological SIEs, and the ORs and 95% CIs were calculated. Two-sided statistical significance was set at $P < 0.05$. Analysis was performed using SPSS Statistics for Windows, Version 24.0 (IBM Corp.).

RESULTS

General characteristics. In total, 295 subjects with supra-aortic involvement and US examination at baseline were included, among whom, 260 (88.14%) were female. The median age of enrolled cases was 33 (25–45) years, with disease duration of 13.50 (4.00–60.00) months. The most common neurologic symptoms were headache/dizziness (118/295, 40.00%), visual disturbance (68/295, 23.05%), and carotidynia (39/295, 13.22%). Stroke was observed in 21 (7.12%) cases. The most common Numano classification types were Type V (134/295, 45.42%) and Type I (111/295, 37.63%). Involvement of the CCA (216/295, 73.22%) and subclavian artery (247/295, 83.73%) was the most prevalent, whereas bilateral CCA was observed in 41.02% (121/295) of the cases (Supplementary Table 1, available from the authors upon request).

Among all the enrolled patients, 92/295 (31.19%) cases were treated before the first visit to our center. The median glucocorticoid (GC) dose was 28 (20–40) mg/day at baseline and 18 cases only used GCs without immunosuppressive therapy. For the remaining cases, ≥ 1 immunosuppressants were administered, including methotrexate (10–15 mg/week, orally) in 16 cases, cyclophosphamide (0.5–0.75 g/m^2 intravenously [IV] every 4 weeks) in 26 cases, mycophenolate mofetil (30 mg/kg/day, orally) in 10 cases, leflunomide (20 mg/day, orally) in 4 cases, and new targeted agents including tocilizumab (8 mg/kg/m^2 IV every 4 weeks) and tofacitinib (10 mg/day, orally) were given in 4 cases, respectively (Table 1).

In addition, the other 268 subjects with supra-aortic involvement in the cohort without baseline US examination were excluded from the current research. No differences were observed between cases included and excluded (Figure 1; Supplementary Table 1, available from the authors upon request).

Clinical characteristics in patients with neurological SIEs. Ninety-three (31.53%) patients experienced neurological SIEs in the current investigation. Among them, 76 (81.72%) had a single event, including visual disturbance (n = 51), syncope (n = 7), and stroke (n = 18). Sixteen (17.20%) cases had 2 events, with syncope accompanied by visual disturbance (n = 14) being the most commonly observed. Only 1 case had 3 events. In total, 6 cases suffered from neurological SIEs after treatment, including 2 cases which experienced syncope as a result of taking medication irregularly, whereas other neurologic SIEs all occurred before treatment.

Patients with neurological SIEs were more likely to complain of headache/dizziness (55.91% vs 32.67%, $P < 0.01$) than those without neurological SIEs, but showed lower incidence of heart dysfunction (3.22% vs 9.90%, $P = 0.04$), type 2 diabetes mellitus (0% vs 4.95%, $P = 0.03$), and had lower levels of IL-6 (4.30 [2.35–9.80] vs 6.50 [2.90–13.40] pg/mL, $P = 0.02$). Patients with and without neurological SIEs also differed in the involved supra-aortic artery distribution ($P = 0.04$) and the number of involved supra-aortic arteries ($P < 0.01$). There was higher prevalence of CCA ($P = 0.02$) and vertebral artery involvement ($P < 0.01$) after Bonferroni correction and 56.99% of patients had ≥ 4 involved arteries in the neurological SIEs group. There was no significant difference in disease activity defined by Kerr score between the 2 groups. Fewer patients had treatment history in the neurologic SIEs group compared with those without neurologic SIEs ($P < 0.01$). In addition, the initial GC (prednisone) dose in the neurological SIEs group was significantly higher than that in nonneurological SIE group (40 [20–50] vs 25 [11–40] mg/day, $P = 0.03$; Table 1).

US variables in patients with neurological SIEs. The median IMT, IDR, and PSV in patients with neurological SIEs was 1.40 (0.80–2.00) mm, 0.47 (0.17–1.00) and 102.50 (65.00–168.50) cm/s, respectively, in the left CCA; and 1.40 (0.70–2.20) mm, 0.35 (0.12–1.00), and 93.00 (72.00–158.50) cm/s, respectively, in the right CCA (Table 1).

In comparison with patients without neurological SIEs, patients with neurological SIEs had a significantly higher IMT for the left CCA ($P = 0.03$) and IDR for bilateral CCAs ($P < 0.01$) and lower diameters for bilateral CCAs ($P < 0.01$). Although the PSV value was not significantly different in the 2 groups, it was relatively lower in the left CCA of patients with neurological SIEs (Table 1 and Figure 2).

Potential associations between clinical and US variables in neurological SIEs. Univariate logistic regression found associations between neurological SIEs and lower IL-6 (cut-off value ≤ 4.65 pg/mL, OR 2.07, 95% CI 1.21–3.52; $P = 0.01$), IL-2R (≤ 422.00 U/mL, OR 2.42, 95% CI 1.14–5.56; $P = 0.02$), left CCA PSV (≤ 76.00 cm/s, OR 2.90, 95% CI 1.73–4.85; $P < 0.01$), left CCA IMT (≥ 0.95 mm, OR 1.91, 95% CI 1.10–3.32; $P = 0.02$), left CCA IDR (≥ 0.55, OR 4.51, 95% CI 2.62–7.77; $P < 0.01$), right CCA IDR (≥ 0.58, OR 3.42, 95% CI 1.96–5.94; $P < 0.01$), as well as the number of involved arteries (≥ 4, OR 2.92, 95% CI 1.76–4.85; $P < 0.01$; Table 2; Supplementary Figure 1, available from the authors upon request).

Further multivariate logistic regression analysis, adjusted for various factors, including disease activity and concomitant complications, found positive and independent associations between neurological SIEs and PSV (OR 3.09, 95% CI 1.53–6.27; $P < 0.01$), left CCA IDR (OR 2.75, 95% CI 1.24–6.07; $P = 0.01$), right CCA IDR (OR 2.70, 95% CI 1.21–6.02; $P = 0.01$), and the number of involved arteries (OR 2.33, 95% CI 1.15–4.72; $P = 0.02$; Table 2). After 6 months of immunosuppressive therapy, the PSV value was slightly improved in cases with neurological SIEs, though not significantly different (Supplementary Table 2, available from the

Table 1. Comparison of clinical characteristics and US parameters in patients with and without neurological SIEs.

	Neurological SIEs, n = 93	Nonneurological SIEs, n = 202	*P*
Demographics			
Female	82 (88.17)	178 (88.11)	0.99
Age, yrs	32 (23–45)	32 (25–46)	0.65
Disease duration, months	12.00 (2.00–84.00)	17.00 (6.00–60.00)	0.79
Symptoms			
Headache/dizziness	52 (55.91)	66 (32.67)	< 0.01*
Carotidynia	5 (5.37)	34 (16.83)	0.01*
Claudication	5 (5.37)	5 (2.48)	0.20
Chest tightness/pain	15 (16.13)	40 (19.80)	0.45
Systemic symptoms	39 (41.94)	65 (32.18)	0.10
Complications			
Hypertension	23 (24.73)	58 (28.71)	0.48
Heart dysfunction	3 (3.22)	20 (9.90)	0.04*
Hyperlipidemia	0 (0.00)	3 (1.49)	0.24
T2DM	0 (0.00)	10 (4.95)	0.03*
Laboratory values, median (IQR)			
IL-6, pg/mL	4.30 (2.35–9.80)	6.50 (2.90–13.40)	0.02*
IL-2R, U/mL	289.00 (186.00–389.00)	321.00 (223.00–429.00)	0.07
Kerr scores			0.48
≥ 2	63 (67.74)	145 (71.78)	
Involved supra-aortic artery[a]			0.04*
Common carotid arteries	76 (81.72)	140 (69.31)	0.02[b]
Internal carotid artery	22 (23.66)	25 (12.38)	—
Subclavian arteries	85 (91.40)	162 (80.20)	—
Vertebral artery	41 (44.09)	39 (19.31)	< 0.01[b]
Brachiocephalic trunk	30 (32.26)	41 (20.30)	—
No. of involved supra-aortic arteries[a]			< 0.01*
1 vessel	11 (11.83)	45 (22.27)	—
2 vessels	13 (13.98)	53 (26.24)	—
3 vessels	16 (17.20)	41 (20.30)	—
≥ 4 vessels	53 (56.99)	63 (31.19)	< 0.01[b]
US variables, median (IQR)			
Left CCA			
Diameter, mm	4.00 (2.00–6.00)	5.40 (3.90–6.20)	< 0.01*
IMT, mm	1.40 (0.80–2.00)	1.10 (0.70–1.80)	0.03*
IDR	0.47 (0.17–1.00)	0.23 (0.12–0.44)	< 0.01*
PSV, cm/s	102.50 (65.00–168.50)	122.00 (82.00–163.50)	0.09*
Right CCA			
Diameter, mm	5.00 (2.00–6.35)	5.65 (4.40–6.60)	< 0.01*
IMT, mm	1.40 (0.70–2.20)	1.10 (0.70–1.80)	0.10
IDR	0.35 (0.12–1.00)	0.20 (0.11–0.44)	< 0.01*
PSV, cm/s	93.00 (72.00–158.50)	114.50 (76.50–161.00)	0.41
Treatment before first presentation	15 (16.13)	77 (38.12)	< 0.01*
Initial GC dose, mg/d, median (IQR)	40 (20–50)	25 (11–40)	0.03*
DMARDs			0.17
CYC	3 (20.00)	23 (29.87)	
LEF	2 (13.33)	2 (2.60)	
MTX	1 (6.67)	15 (19.48)	
MMF	3 (20.00)	7 (9.09)	
Others	3 (20.00)	11 (14.29)	
New targeted agents			> 0.99
Tocilizumab	1 (6.67)	3 (3.90)	
Tofacitinib	0 (0.00)	4 (5.19)	

Values are n (%) unless otherwise indicated. [a] $P < 0.05$ after post hoc test (Bonferroni correction). [b] Brachiocephalic trunk, bilateral CCA and internal carotid artery, bilateral subclavian and vertebral artery; * P value < 0.05. CCA: common carotid artery; CYC: cyclophosphamide; DMARD: disease-modifying antirheumatic drug; GC: glucocorticoid; IDR: intima-media thickness/diameter ratio; IL-2R: interleukin-2 receptor; IL-6: interleukin-6; IMT: intima-media thickness; LEF: leflunomide; MMF: mycophenolate mofetil; MTX: methotrexate; PSV: peak systolic velocity; SIE: severe ischemic event; T2DM: type 2 diabetes mellitus; US: ultrasonography.

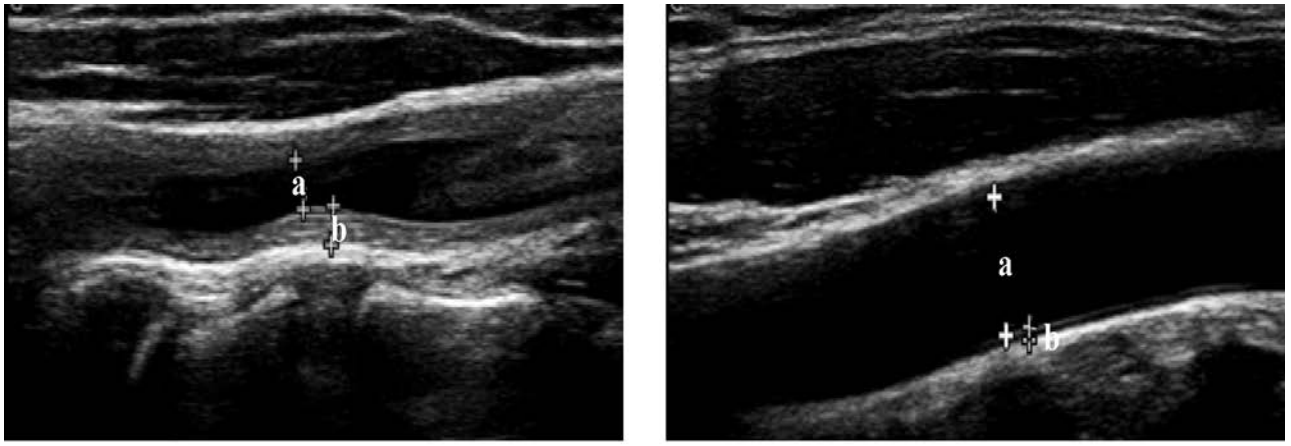

Figure 2. US variables of CCA in enrolled patients with TA. (A) A 48-year-old woman admitted to the hospital for > 1 month because of carotidynia, accompanied by sudden syncope. US measurement (left CCA): (a) diameter 2.30 mm, (b) IMT 1.80 mm, IDR 0.78, PSV 49.10 cm/s. (B) A 27-year-old woman admitted to the hospital for 3 years because of undetectable blood pressure of the right upper extremity, who had no neurological SIEs. US measurement (right CCA): (a) diameter 5.60 mm, (b) IMT 0.54 mm, IDR 0.09, PSV 79.70 cm/s. CCA: common carotid artery; IDR: intima-media thickness/diameter ratio; IMT: intima-media thickness; PSV: peak systolic velocity; SIE: severe ischemic event; TA: Takayasu arteritis; US: ultrasonography.

Table 2. Associations of different factors with neurological SIEs in univariate and multivariate logistic regression analyses.

	Univariate			Multivariate		
	OR	95% CI	*P*	OR	95% CI	*P*
IL-6 (≤ 4.65 pg/mL)	2.07	1.21–3.52	0.01	—	—	—
IL-2R (≤ 422.00 U/mL)	2.42	1.14–5.56	0.02	—	—	—
CCA	1.98	1.08–3.62	0.03	—	—	—
Brachiocephalic trunk	1.99	1.13–3.47	0.02	—	—	—
Left CCA-IMT (≥ 0.95 mm)	1.91	1.10–3.32	0.02	—	—	—
No. of involved arteries (≥ 4)	2.92	1.76–4.85	< 0.01	2.33	1.15–4.72	0.02
Left CCA-PSV (≤ 76.00 cm/s)	2.90	1.73–4.85	< 0.01	3.09	1.53–6.27	< 0.01
Left CCA-IDR (≥ 0.55)	4.51	2.62–7.77	< 0.01	2.75	1.24–6.07	0.01
Right CCA-IDR (≥ 0.58)	3.42	1.96–5.94	< 0.01	2.70	1.21–6.02	0.01

Artery involvement: brachiocephalic trunk, bilateral CCA and internal carotid artery, and bilateral subclavian and vertebral. Adjustments: clinical manifestations, disease activity, and concomitant complications. CCA: common carotid artery; IDR: intima-media thickness/diameter ratio; IL-2R: interleukin-2 receptor; IL-6: interleukin-6; IMT: intima-media thickness; PSV: peak systolic velocity; SIE: severe ischemic event.

authors upon request). PSV values, particularly, improved in 50.00% (5/10) of patients with neurological SIEs with IDR (≥ 0.55) and PSV(≤ 76.00 cm/s) of the left CCA.

DISCUSSION

We comprehensively reviewed the characteristics of TA with supra-aortic artery involvement in a prospective longitudinal cohort. We found that 80.54% of the patients with TA had supra-aortic lesions, and one-third of them experienced neurological SIEs during the disease course. IDR (≥ 0.55) and PSV (≤ 76.00 cm/s) of the left CCA, IDR (≥ 0.58) of right CCA, and the number of involved supra-aortic arteries (≥ 4) were associated with the occurrence of neurological SIEs.

Supra-aortic artery involvement was reported in 40–80% of the patients with TA.[3,4] These patients presented nonspecific symptoms, resulting in delayed diagnosis, a higher risk of severe vascular damage, and poor prognosis.[29] Therefore, early detection and a comprehensive understanding of disease features in patients with TA and supra-aortic arterial lesions are highly critical. Supra-aortic lesions were observed in 80.54% of our cohort, with headache/dizziness (40.00%) as the most common symptom, similar to previous reports.[4,30,31] Previous studies have shown that the prevalence of stroke/TIA was 10–20% in TA.[3,32,33,34] The prevalence of stroke in our current study was 7.12%, which was similar to several reports.[35,36,37] The differences in prevalence among studies may be explained by the different inclusion criteria as well as different definitions of stroke. In some studies, cases with lacunar infarction and TIA were included[33,34]; however, in our study, both these conditions were excluded. Further, only strokes that occurred within 3 months of carotid US were included. Herein, supra-aortic vessel lesions, particularly severe cases, often affected cerebral perfusion and might have contributed to cerebral ischemic signs such as visual disturbance, stroke, syncope, and transient hemiparesis.[5,38]

The occurrence of ischemic events, especially neurological SIEs, might greatly affect the quality of life and disease prognosis in patients with TA; therefore, increased attention and early recognition of neurological SIEs are called for in this population.[4,22] It has been reported that 33% of the patients with TA might experience SIEs during a follow-up of over 12 months,[39] presenting as neurological SIEs, including syncope, cerebrovascular events, and visual disturbance, was observed in 10.9–21.9% of the patients with TA.[8] We found that 31.53% of the patients with supra-aortic involvement had neurological SIEs, with visual disturbance, stroke, and syncope as the 3 most common events. Interestingly, we observed that patients with neurological SIEs had lower incidence rates of heart failure, hypertension, and diabetes than those without neurological SIEs. This might indicate that the CNS symptoms and events were likely related to supra-aortic artery involvement rather than other risk factors such as hypertension or diabetes.[6] In addition, the disease activity did not differ between cases with and without neurological SIEs. We also found that the prevalence of carotidynia and IL-6 levels, which were positively associated with disease activity,[6,15,16] were lower in patients with neurological SIEs. This phenomenon might be consistent with the research by Michailidou et al that CNS events including stroke and syncope were related to vascular damage in the corresponding vessel instead of vascular inflammation in TA.[6]

We also found that CCA was the artery most involved in TA with supra-aortic lesions, though multivessel lesions that included the subclavian artery and/or vertebral artery were frequently observed. The IMT of the CCA was reported to be increased in 59% of the patients with TA, regardless of the disease activity, whereas the diameter might remain unchanged when the IMT increases.[40] Therefore, we used IDR as a comprehensive indicator of lumen changes to avoid possible bias because of inconsistency between the diameter and IMT. We found that the IDR of bilateral CCA was significantly higher in patients with neurological SIEs, and positively related to an increased risk of neurological SIE, possibly implying that higher IDR of the CCA could effectively predict the occurrence of neurological SIEs.

Chuang et al found that PSV in CCA was negatively associated with the risk of stroke and ischemic heart disease, showing that subjects with PSV < 65 cm/s had a 3.23-fold higher risk of developing the disease than those with PSV ≥ 80 cm/s.[41] In the current research, we found that PSV ≤ 76.00 cm/s in the left CCA was associated with neurological SIE occurrence. Severe stenosis or near occlusion of the CCA initial segments in patients with neurological SIEs might decrease PSV. After 6 months of immunosuppressive therapy, PSV value improved in 50.00% (5/10) of patients with neurological SIEs with IDR (≥ 0.55) and PSV(≤ 76.00 cm/s) of the left CCA, which indicated that medical therapy might be effective. Moreover, Porter et al has reported that early use of therapy in those with supra-aortic TA presenting with cerebral ischemia might improve outcomes and reduce the numbers of patients requiring surgical intervention.[5] However, the precise value of PSV in identifying neurological SIEs for TA should be further investigated, taking cranial vessel data into consideration.[42,43]

Our study had 3 major limitations. First, 268 patients with supra-aortic involvement in the ECTA cohort were excluded in the analysis due to absence of US examinations (Figure 1). In order to avoid selection bias, we analyzed the difference between the enrolled and excluded patients and found no significant differences in terms of sex, age, and the prevalence of neurological SIEs (Supplementary Table 1, available from the authors upon request). Second, we could not obtain PSV values in the occluded CCA, possibly causing some bias in the analysis. Third, cranial vessels may be also related to the prevalence of neurological SIEs in this study and requires further investigation. Future studies with more variables, a larger sample size, and follow-up would be needed to confirm the risk factors for identifying neurological SIEs.

In summary, we found that 31.53% of the patients with supra-aortic involvement in TA experienced neurological SIEs. The carotid IDR, PSV, and number of involved supra-aortic arteries would be valuable markers for recognizing neurological SIEs in patients with TA with supra-aortic lesions.

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