Predicting asymptomatic coronary artery stenosis by aortic arch plaque in acute ischemic cerebrovascular disease: beyond the cervicocephalic atherosclerosis?

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Abstract

Background: Asymptomatic coronary artery stenosis (ACAS) ≥50% is common in patients with acute ischemic cerebrovascular disease (AICVD), which portends a poor cardiovascular and cerebrovascular prognosis. Identifying ACAS ≥50% early may optimize the clinical management and improve the outcomes of these high-risk AICVD patients. This study aimed to investigate whether aortic arch plaque (AAP), an early atherosclerotic manifestation of brain blood-supplying arteries, could be a predictor for ACAS ≥50% in AICVD.

Methods: In this cross-sectional study, atherosclerosis of the coronary and brain blood-supplying arteries was simultaneously evaluated using one-step computed tomography angiography (CTA) in AICVD patients without coronary artery disease history. The patients were divided into ACAS ≥50% and non-ACAS ≥50% groups according to whether CTA showed stenosis ≥50% in at least one coronary arterial segment. The AAP characteristics of CTA were depicted from aspects of thickness, extent, and complexity.

Results: Among 118 analyzed patients with AICVD, 29/118 (24.6%) patients had ACAS ≥50%, while AAPs were observed in 86/118 (72.9%) patients. Increased AAP thickness per millimeter (adjusted odds ratio [OR]: 1.56, 95% confidence interval [CI]: 1.18–2.05), severe-extent AAP (adjusted OR: 13.66, 95% CI: 2.33–80.15), and presence of complex AAP (adjusted OR: 7.27, 95% CI: 2.30–23.03) were associated with ACAS ≥50% among patients with AICVD, independently of clinical demographics and cervicocephalic atherosclerotic stenosis. The combination of AAP thickness, extent, and complexity predicted ACAS ≥50% with an area under the receiver-operating characteristic curve of 0.78 (95% CI: 0.70–0.85, $P < 0.001$). All three AAP characteristics provided additional predictive power beyond cervical and intracranial atherosclerotic stenosis for ACAS ≥50% in AICVD (all $P < 0.05$).

Conclusions: Thicker, severe-extent, and complex AAP were significant markers of the concomitant ACAS ≥50% in AICVD, possibly superior to the indicative value of cervical and intracranial atherosclerotic stenosis. As an integral part of atherosclerosis of brain blood-supplying arteries, AAP should not be overlooked in predicting ACAS ≥50% for patients with AICVD.

Keywords: Asymptomatic coronary artery stenosis; Aortic arch plaque; Acute ischemic cerebrovascular disease; Atherosclerosis; Prediction

Introduction

Approximately 18% to 33% of patients with acute ischemic cerebrovascular disease (AICVD) had asymptomatic coronary artery stenosis (ACAS) ≥50%.[1-3] Although vascular risk factor reduction and antithrombotic therapy were generally initiated after AICVD, the incidence of myocardial infarction within a year in AICVD patients with no coronary artery disease history remained as high as 3%.[4] What is more, ACAS ≥50% in AICVD foreshadowed recurrent stroke and less survival in addition to the cardiac events.[5-7] Given the substantial vascular risk and preliminary evidence that ACAS-targeted treatment might favorably alter the prognosis,[8,9] early identification of the concomitant ACAS ≥50% was of great clinical relevance for patients with AICVD.

But not all AICVD patients warrant direct examination of coronary arteries. Those with high vascular risk factor profiles and carotid atherosclerotic stenosis were thought to be more likely to have ACAS ≥50%, and the American

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Heart Association/American Stroke Association recommended considering non-invasive coronary artery disease testing for them.[10] Recently, atherosclerotic stenosis of intracranial arteries was also suggested to be associated with ACAS ≥50% in patients with AICVD.[1,11] However, there are also data failing to confirm the predictive value of carotid or intracranial atherosclerotic stenosis for the coexistence of ACAS ≥50%.[12-14] In our previous research, cervicocephalic atherosclerotic stenosis was demonstrated to be associated with symptomatic coronary artery stenosis of ≥50% or ACAS ≥50%, but the relationship varied with different location of the cervicocephalic arterial stenosis.[15] It remained unknown whether atherosclerosis evaluation of the aortic arch, an integral segment of brain blood-supplying arteries located in the proximal of cervicocephalic arteries, would be helpful to predict ACAS ≥50% in AICVD.

Aortic arch plaque (AAP) is one of the earliest manifestations of systemic atherosclerosis,[16] making it an attractive candidate to suggest the coexistence of ACAS ≥50% in AICVD patients early on for further targeted and integrated management. AAP has been shown to indicate the presence of coronary artery disease in several patient populations whose aortic arch needed routine examination in clinical practice.[17,18] But for the general patients with AICVD, the aortic arch is not regularly assessed. Thus, the predictive value of AAP for ACAS ≥50% in AICVD would be often neglected, especially when ultrasound and magnetic resonance angiography are used to examine the cervicocephalic arteries. Only a few studies preliminarily investigated the relationship between AAP and ACAS ≥50% in patients with AICVD, and they concluded oppositely.[3,19] With the popularization of computed tomography angiography (CTA) of brain blood-supplying arteries, the aortic arch can be conveniently evaluated along with the cervicocephalic arteries of patients with AICVD. It is high time that we should clarify the association between AAP characteristics and ACAS ≥50% in a more detailed manner to improve the prediction of ACAS ≥50% in AICVD.

CTA has been proved to be a reliable method to evaluate AAP,[20,21] and the 192-slice computed tomography is capable of performing one-step CTA of the coronary and brain blood-supplying arteries with lower radiation dose than the traditional CTA of brain blood-supplying arteries [Figure 1].[22] With this technology, this study aimed to delineate the AAP characteristics in patients with both AICVD and ACAS ≥50%, and examine the predictive value of AAP for ACAS ≥50% in AICVD.

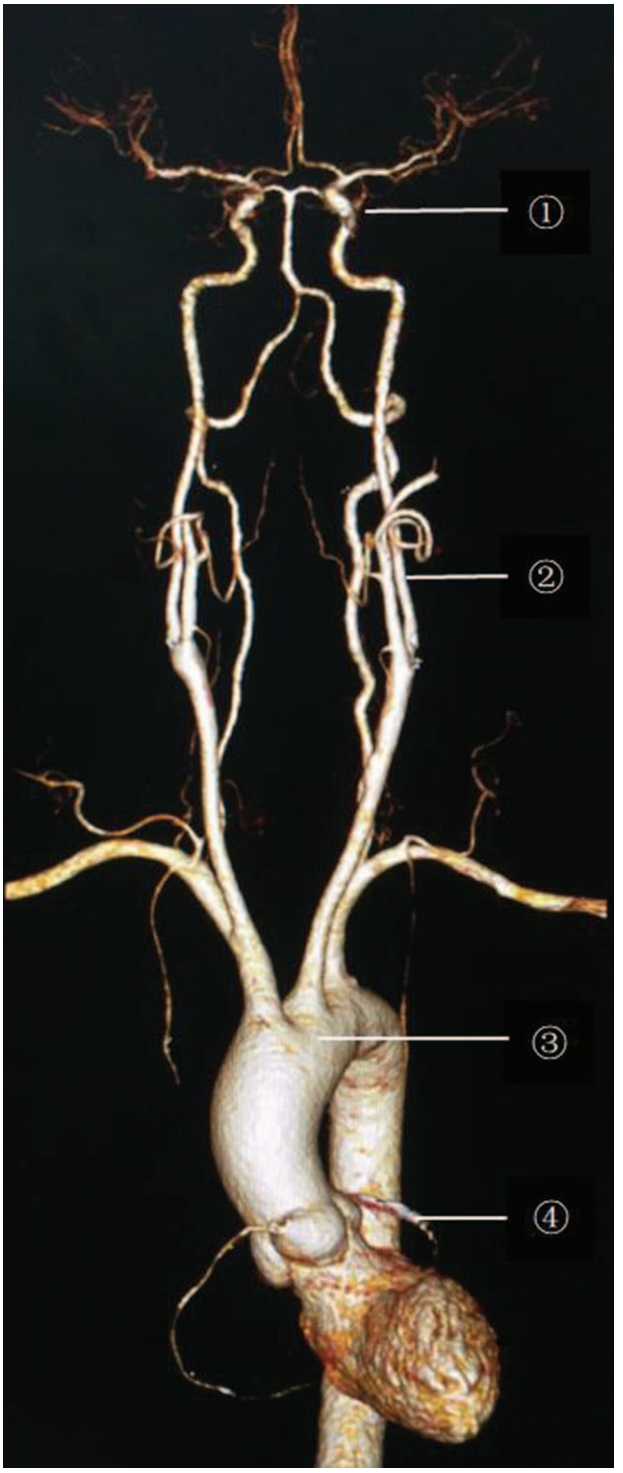

Figure 1: Simultaneous computed tomography angiography of coronary and brain blood-supplying arteries: ① intracranial arteries; ② cervical arteries; ③ aortic arch; ④ coronary arteries.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University. Informed written consent was obtained from all participants prior to their enrollment in this study.

General characteristics

This cross-sectional study was a single-center study. Participants enrolled in this study were based on a population reported by us before,[15] with further exclusion of patients with coronary artery disease history (typical symptoms confirmed using exercise electrocardiogram or coronary angiography, coronary artery stent or

angioplasty, or coronary artery bypass graft). In brief, patients with 18 to 85 years of age, and acute cerebral infarction or transient ischemic attack (TIA) within 14 days after onset were eligible. Those with suspected non-atherosclerotic arterial stenosis, AICVD related to cardioembolism or revascularization procedures, poor organ functions, hematologic diseases, or contraindications to CTA were excluded. Patients without interpretable CTA images were not included in the final analysis.

Demographic information, vascular risk factors, the National Institute of Health Stroke Scale score and the blood pressure at admission were recorded as previously described.[15] All patients underwent standard lab tests, brain magnetic resonance imaging or computed tomography scan, cervical and transcranial color Doppler ultrasound, 12-lead electrocardiogram and transthoracic echocardiography within 7 days after admission.

Coronary and brain blood-supplying arterial atherosclerosis measurements

The simultaneous coronary and brain blood-supplying arterial CTA was performed using a 192-slice computed tomography scanner (Somatom Force, Siemens Healthcare, Forchheim, Germany) as previously reported.[15] The existence of ACAS ≥50% was confirmed when there was a stenosis of ≥50% in at least one coronary arterial segment, given that all selected patients with AICVD had no coronary artery disease history. Only coronary arterial segments that were visually estimated to be ≥1.5 mm in diameter were analyzed.[1]

The images of the brain blood-supplying arteries were reviewed by another experienced radiologist. The aortic arch was assessed from the aortic root to the distal end of the left subclavian artery.[23] AAPs were measured across multiple contiguous, evenly spaced cross-sections with regular 5 mm intervals between perpendicular (axial) slices, and the vessel wall was divided into four quadrants on each perpendicular slice.[24] AAP was defined as the presence of calcium deposit, clearly visualized hypodensity, or focal aortic wall ≥2 mm in thickness.[25,26] AAPs were evaluated from the aspects of thickness, extent, and complexity. The AAP thickness was defined as the distance from the highest point of the maximal plaque perpendicular to the wall of the outer membrane of the aorta.[24] The AAP extent was assessed as absent, mild (occupying single perpendicular slice or single quadrant on the perpendicular slice), and severe (occupying multiple perpendicular slices and multiple quadrants on at least one perpendicular slice). An AAP thickness of ≥4 mm or associated ulcerations or mural thrombus was defined as complex AAP.[21] A defect ≥2 mm in depth and width on the AAP surface was considered ulceration.[27]

The percentage of arterial stenosis was quantified on orthogonal views using an automatic vessel analysis tool according to the North American Symptomatic Carotid Endarterectomy Trial method for the cervical arteries[28] and the Warfarin-Aspirin Symptomatic Intracranial Disease Study Trial method for the intracranial arteries.[29] The presence of cervical atherosclerotic stenosis (CAS) of ≥50% and intracranial atherosclerotic stenosis (IAS) of ≥50% was recorded.

Grouping of study subjects

The analyzed patients with AICVD were divided into the ACAS ≥50% and non-ACAS ≥50% groups according to whether there was ACAS ≥50% in simultaneous coronary and brain blood-supplying arterial CTA.

Statistical analysis

Statistical tests were performed using SPSS version 17.0 (IBM, Armonk, New York, USA) and MedCalc version 15.0 (MedCalc Software, Acacialaan, Ostend, Belgium). Data were presented as means ± standard deviation (SD) for continuous variables, counts (with percentages) for dichotomous variables, and medians (Q1, Q3) for ordinal variables. Odds ratios (ORs) for the presence of ACAS and areas under receiver-operating characteristic (ROC) curves were calculated with 95% confidence intervals (CIs). A $P < 0.05$ was considered statistically significant.

The general characteristics and AAP features were compared between the AICVD patients with and without ACAS ≥50%. The Student's *t*-test was used for continuous variable that was normally distributed, Chi-square test for unordered categorical variable, Mann-Whitney *U* test for continuous variable that was not normally distributed and ordinal variable. Logistic regression analysis adjusting for age, gender, and significant general characteristics (those with $P < 0.05$ in the univariate analysis) was used to determine the independent associations between AAP characteristics and the coexistence of ACAS ≥50%. The predictive power of AAP for ACAS ≥50% in the patients with AICVD was tested using a ROC curve analysis of different logistic regression models' predicted probabilities.

Results

A total of 176 patients with ischemic cerebrovascular disease were admitted to the stroke unit. Eight patients whose symptoms had lasted for more than 14 days before admission and 22 patients who had known coronary artery disease were excluded. Among the 146 eligible patients, 20 refused to participate. Of the 126 included patients, five patients could not undergo the simultaneous coronary and brain blood-supplying arterial CTA because of subsequent neurological deterioration, and three patients had non-interpretable CTA images. The 118 remaining patients were finally included in the analysis [Figure 2]. The mean dose-length-product for simultaneous coronary and brain blood-supplying arterial CTA was 125.9 ± 30.7 mGy × cm, and the image quality was diagnostic in 97.5% (118/121).

The analyzed patients (112 with acute cerebral infarction and six with TIA) had an average age of 58.7 years; they were predominantly males (83.1%). The simultaneous coronary and cerebral arterial CTA showed ACAS in 29 of the 118 (24.6%) patients. AAPs were observed in 86/118 (72.9%) patients and complex AAPs in 21/118 (17.8%)

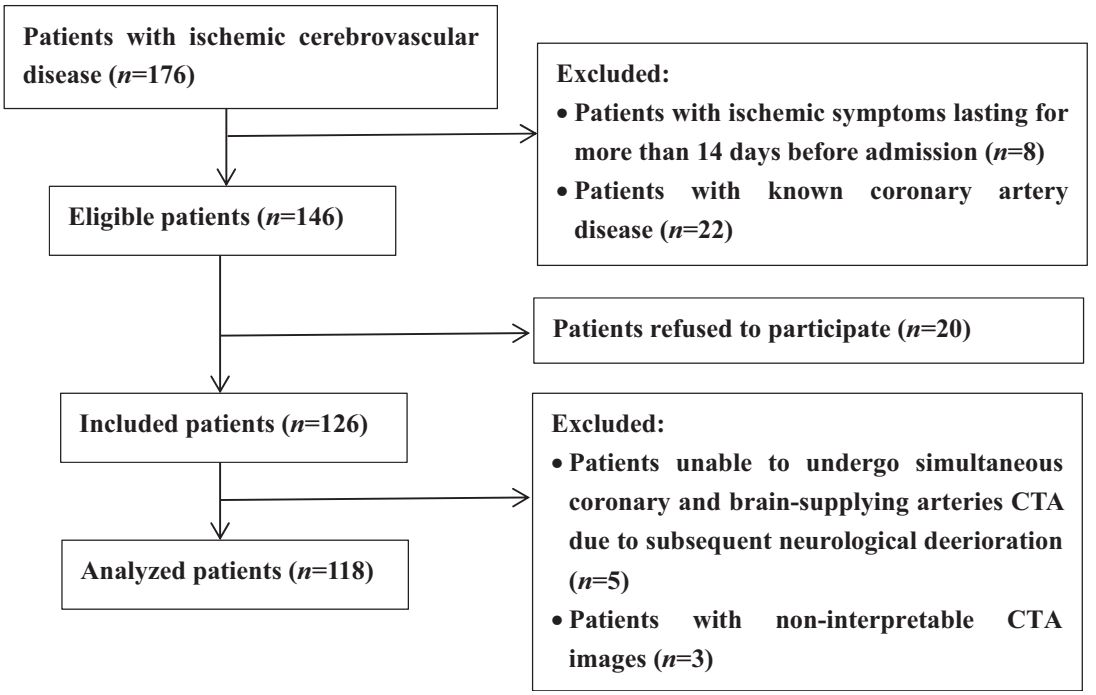

Figure 2: Flow chart of patients' enrollment. CTA: Computed tomography angiography.

patients. CAS ≥50% and IAS ≥50% were present in 46/118 (39.0%) and 87/118 (73.7%) patients, respectively.

Comparisons of the general characteristics

The patients with AICVD and ACAS ≥50% more likely had a history of diabetes mellitus (55.2% *vs.* 32.6%, $P=0.030$) and CAS ≥50% (58.6% *vs.* 32.6%, $P=0.013$), compared with those without ACAS. However, the presence of IAS ≥50% and transthoracic echocardiography characteristics were not significantly different between the two groups [Table 1].

AAP characteristics in the patients with AICVD and ACAS ≥50%

The median AAPs in the ACAS ≥50% group tended to be thicker (3.1 mm *vs.* 1.3 mm, $P=0.003$) and severe-extent (44.8% *vs.* 6.7%, $P<0.001$), with more frequent complex AAP (44.8% *vs.* 9.0%, $P<0.001$) than those in the non-ACAS ≥50% group [Table 2, Figure 3].

In the multivariate logistic regression analysis after adjusting for age, gender, and history of diabetes mellitus and presence of CAS ≥50%, increased AAP thickness per millimeter (adjusted OR: 1.56, 95% CI: 1.18–2.05), severe-extent of AAP (adjusted OR: 13.66, 95% CI: 2.33–80.15), and presence of complex AAP (adjusted OR: 7.27, 95% CI: 2.30–23.03) remained associated with concomitant ACAS ≥50% [Table 3].

Predictive power of AAP for ACAS ≥50% in AICVD

To examine the combined predictive power of the AAP thickness, extent, and complexity, a multivariate logistic regression model for ACAS ≥50% was built using the three AAP characteristics and their interactions as covariates. The logistic regression model's probabilities for predicting ACAS ≥50% showed an area under the ROC curve of 0.78 (95% CI: 0.70–0.85, $P<0.001$), with a sensitivity of 69.0% and a specificity of 78.7% [Figure 4].

Based on the ROC curve, the optimal cut-off value of the AAP thickness as a predictor for ACAS ≥50% was projected to be 2.95 mm, with the area under the curve at 0.75 (95% CI: 0.65–0.86; $P<0.001$). In 15 patients with AICVD whose AAP thickness was ≥2.95 mm and AAP extent was severe, with accompanying complex AAP, the percentage of the likelihood of developing ACAS ≥50% was 73.3% (11/15). In 32 AICVD patients without AAP, the percentage of the possibility of developing ACAS ≥50% was only 12.5% (4/32).

To determine whether AAP could offer further information beyond CAS and IAS in predicting ACAS, we established a basic logistic regression model including CAS ≥50% and IAS ≥50% as covariates to predict the coexistence of ACAS ≥50% (predicted probabilities' area under the ROC curve: 0.66, 95% CI: 0.57–0.75, $P=0.008$). Additionally, entering the AAP characteristics to the basic logistic regression model significantly increased these models' predictive power (changes in the predicted probabilities' area under the ROC curve: 0.11 for AAP thickness, $P=0.017$; 0.11 for AAP extent, $P=0.012$; 0.10 for presence of complex AAP, $P=0.040$) [Figure 5, Table 4]. In multivariable logistic regression analysis, AAP characteristics were predictors for ACAS ≥50% regardless of whether CAS ≥50% or IAS ≥50% existed, whereas presence of CAS ≥50% and IAS ≥50% had no predictive value independent of AAP characteristics [Table 5].

Table 1: General characteristics of AICVD patients with and without ACAS ≥50%.

Characteristics	ACAS ≥50% group (*n*=29)	Non-ACAS ≥50% group (*n*=89)	Statistical values	*P*
Age (years)	60.9±9.4	58.00±10.6	1.330*	0.625
Male, *n* (%)	27 (93.1)	71 (79.8)	2.760†	0.097
Vascular risk factors, *n* (%)				
History of hypertension	22 (75.9)	52 (58.4)	2.843†	0.092
History of diabetes mellitus	16 (55.2)	29 (32.6)	4.730†	0.030
History of hyperlipidemia	3 (10.3)	21 (23.6)	2.370†	0.124
History of AICVD	9 (31.0)	21 (23.6)	0.638†	0.424
Smoking	18 (62.1)	42 (47.2)	1.937†	0.164
Obesity	1 (3.4)	6 (6.7)	0.425†	0.514
Family history of cardiovascular disease	14 (48.3)	33 (37.1)	1.144†	0.285
Clinical findings				
NIHSS on admission	3 (1, 5)	3 (1, 6)	0.431‡	0.666
Systolic blood pressure on admission (mmHg)	162.2±24.9	148.7±19.5	3.028*	0.066
diastolic blood pressure on admission (mmHg)	89.7±15.2	85.9±10.7	1.517*	0.185
Laboratory findings				
glycosylated hemoglobin level (mmol/L)	6.5 (5.4, 7.6)	5.7 (5.3, 6.7)	1.921‡	0.055
Fasting blood glucose (mmol/L)	6.0 (5.1, 7.3)	5.5 (5.0, 6.7)	0.613‡	0.540
Triglycerides (mmol/L)	1.5 (1.0, 2.3)	1.3 (1.0, 1.8)	0.806‡	0.420
Total cholesterol (mmol/L)	4.3±1.1	3.9±1.0	1.666*	0.119
Low density lipoprotein (mmol/L)	2.8±1.0	2.4±0.8	1.738*	0.134
High density lipoprotein (mmol/L)	1.1±0.2	1.1±0.3	–0.560*	0.346
Homocysteine (mmol/L)	14.0 (12.4, 17.1)	13.5 (11.5, 18.7)	0.489‡	0.625
Fibrinogen (g/L)	3.3±0.9	3.3±0.9	–0.451*	0.969
D-dimer (mg/L)	0.3 (0.2, 0.6)	0.3 (0.2, 0.5)	0.140‡	0.889
Hypersensitive C reactive protein (mg/L)	2.9 (0.7, 5.8)	3.7 (1.3, 5.5)	0.329‡	0.742
Transthoracic echocardiography				
Segmental ventricular wall motion abnormality, *n* (%)	3 (10.3)	11 (12.4)	0.047†	0.828
Ejection fraction (%)	63.1±9.3	64.5±6.9	–0.732*	0.384
CAS ≥50%, *n* (%)	17 (58.6)	29 (32.6)	6.234†	0.013
IAS ≥50%, *n* (%)	25 (86.2)	62 (69.7)	3.091†	0.079

The data were shown as mean±SD, median (Q1, Q3), or *n* (%). *t values. †Chi-square value. ‡U values. AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; CAS: Cervical atherosclerotic stenosis; IAS: Intracranial atherosclerotic stenosis; NIHSS: National Institutes of Health Stroke Scale; SD: Standard deviation.

Table 2: AAP characteristics of AICVD patients with and without ACAS ≥50%.

Characteristics	ACAS ≥50% group (*n*=29)	non-ACAS ≥50% group (*n*=89)	*P*	OR (95% CI)	*P*
AAP thickness (mm)	3.1 (1.7, 4.9)	1.3 (0, 2.2)	0.003	1.60 (1.26–2.04)	<0.001
AAP extent, *n* (%)			<0.001		
Absent	4 (13.8)	28 (31.5)		1.00	
Mild	12 (41.4)	55 (61.8)		1.53 (0.45–5.17)	0.496
Severe	13 (44.8)	6 (6.7)		15.17 (3.64–63.12)	<0.001
Complex AAP, *n* (%)	13 (44.8)	8 (9.0)	<0.001	8.23 (2.93–23.07)	<0.001

The data were shown as median (Q1, Q3), or *n* (%). AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; AAP: Aortic arch plaque; OR: Odds ratio; CI: Confidence interval.

Discussion

In this study, atherosclerosis of the coronary and brain blood-supplying arteries in patients with AICVD but no coronary artery disease history were simultaneously evaluated using one-step CTA. Thicker AAP, severe-extent AAP, and presence of complex AAP were independently related to the coexistence of ACAS ≥50%. These AAP characteristics were suggested to be good indicators for the concomitant ACAS ≥50% in patients with AICVD and might provide more predictive information over CAS ≥50% and IAS ≥50%.

The prevalence of ACAS ≥50% (24.6%) in our study was comparable to existing data (18%–33%).[1-3] However, the importance of AAP for ACAS ≥50% in patients with AICVD had been rarely explored. In contrast with previous studies,[3,19] we profiled the AAP characteristics

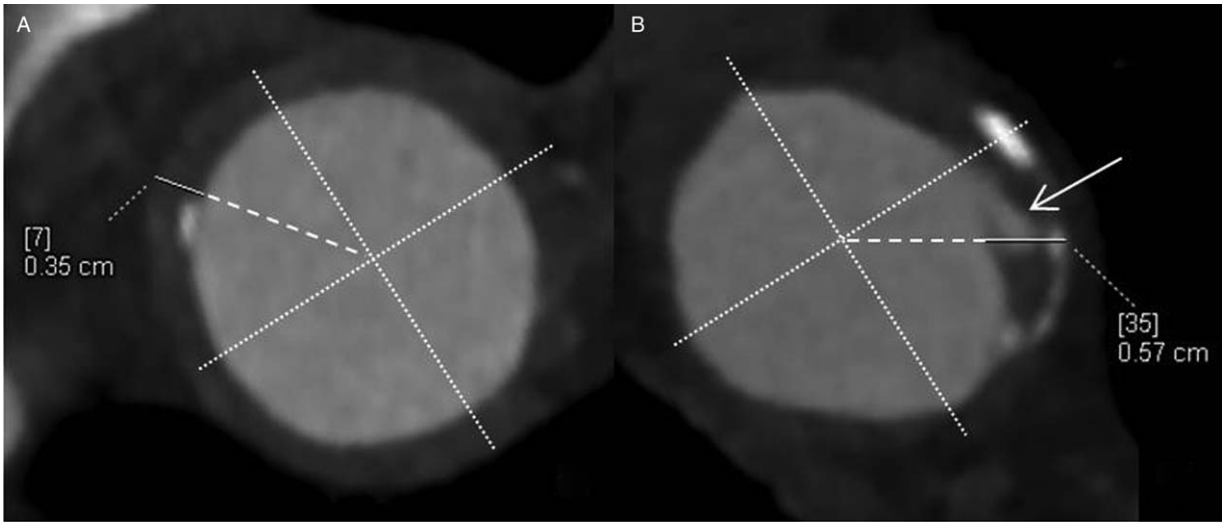

Figure 3: Computed tomography angiography of aorta arch on orthogonal views in two AICVD patients with different ACAS ≥50% conditions. (A) AAP of No. 7 patient (without ACAS) was 3.5 mm in maximum thickness, mild in amount (occupying single perpendicular slice and single quadrant) and no complex AAP was detected. (B) AAP of No. 35 patient (with ACAS) was 5.7 mm in maximum thickness, severe in amount (occupying multiple perpendicular slices and multiple quadrants) and a complex AAP was found (white arrow indicated the ulceration). AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; AAP: Aortic arch plaque.

Table 3: Multivariate logistic regression analysis of AAP characteristics for ACAS ≥50% in patients with AICVD.

	Model 1*		Model 2*		Model 3*	
Characteristics	**OR (95%CI)**	***P***	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Age (years)	0.99 (0.93–1.04)	0.633	1.00 (0.94–1.06)	0.908	1.01 (0.96–1.07)	0.681
Male	0.41 (0.08–2.02)	0.273	0.34 (0.07–1.75)	0.197	0.34 (0.07–1.73)	0.194
History of diabetes mellitus	2.64 (1.01–6.90)	0.048	2.80 (1.03–7.58)	0.043	3.03 (1.13–8.11)	0.027
CAS ≥50%	1.90 (0.71–5.07)	0.201	1.63 (0.59–4.53)	0.350	1.86 (0.69–5.01)	0.223
AAP thickness (mm)	1.56 (1.18–2.05)	0.002				
AAP extent						
Absent			1.00			
Mild			1.46 (0.36–5.91)	0.594		
Severe			13.66 (2.33–80.15)	0.004		
Complex AAP					7.27 (2.30–23.03)	0.001

*The Nagelkerke R^2 was 0.293, 0.322, and 0.300 respectively for models 1, 2, and 3. AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; CAS: Cervical atherosclerotic stenosis; AAP: Aortic arch plaque; OR: Odds ratio; CI: Confidence interval.

in a more comprehensive manner, and examined the predictive value of AAP for ACAS ≥50% in the patients with AICVD from various aspects.

Cho *et al*[19] found that the presence of complex AAP (thickness ≥4 mm or protruded or ulcerated) on CTA was an independent indicator of a coronary stenosis of ≥50% in patients with acute ischemic stroke without coronary artery disease history (adjusted OR: 5.71, 95% CI: 1.94–16.87), which were consistent with our findings. They focused on the complex AAP, which could serve as an independent cause of AICVD, but it was just a partial reflection of the AAP characteristics. More AAP markers were needed to more fully reveal the relationship of AAP with ACAS. Similarly, Amarenco *et al*[3] classified AAP into three categories based on its risk to incur a cerebral ischemic event (absence, <4 mm, and ≥4 mm). They found that AAP thickness <4 mm on transesophageal echocardiography was not related to "coronary plaques" or "coronary stenoses of ≥50%" on conventional coronary angiography in patients with cerebral infarction, while AAP thickness of ≥4 mm was associated with the presence of "coronary plaques" rather than "coronary stenoses of ≥50%." Of note, this study also included patients with coronary heart disease history, who were grouped in both "patients with coronary plaques" and "patients with coronary stenoses of ≥50%" in the analysis without undergoing coronary angiography. The authors declared that these results were similar when their analysis was restricted to patients with no coronary heart disease history; however, detailed data were not shown.

In our study, the presence of complex AAP and maximal thickness of AAPs were proven to be independently associated with ACAS ≥50% in the patients with AICVD; further, the AAP extent was also indicated as a parameter for predicting ACAS ≥50%. It echoed our previous findings that AICVD patients with symptomatic coronary artery stenosis of ≥50% or ACAS ≥50% had more diffused cervicocephalic atherosclerosis[15] and lent more

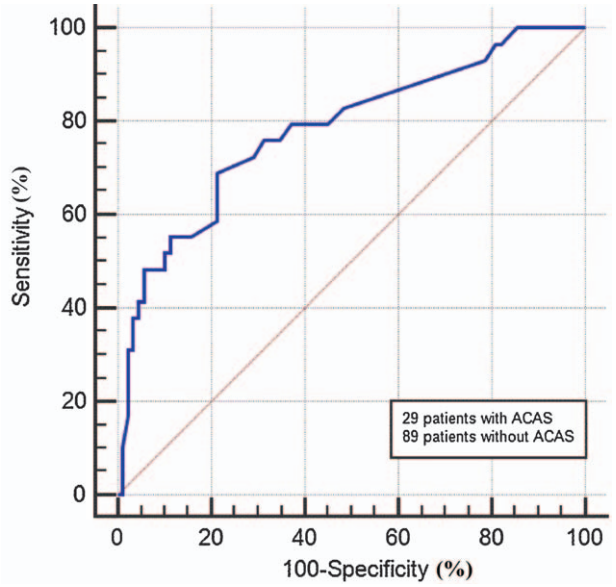

Figure 4: Receiver operating characteristic curve of predicted probabilities of logistic regression model using AAP thickness, AAP extent, complex AAP and their interactions as covariates for ACAS ≥50% in patients with AICVD. Area under the curve was 0.78 (95% CI: 0.70–0.85, $P < 0.001$), with a sensitivity of 69.0% and a specificity of 78.7%. AICVD: acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; AAP: Aortic arch plaque; CI: Confidence interval.

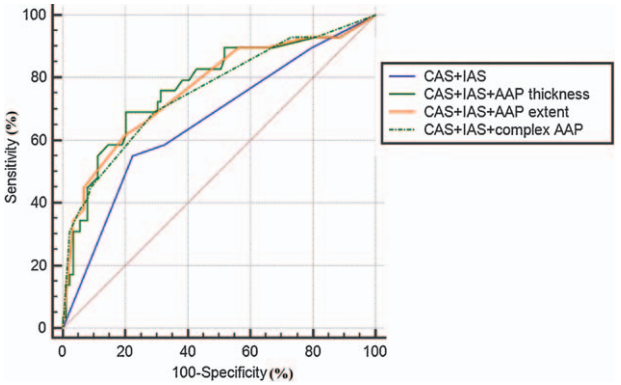

Figure 5: Areas under receiver operating characteristic curves increased after entering AAP characteristics into the basic logistic regression model using CAS ≥50% and IAS ≥50% as covariates to predict the coexistence of ACAS ≥50%. ROC curves of predicted probabilities of various logistic regression models for ACAS ≥50% in patients with AICVD were analyzed and compared. AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; CAS: Cervical atherosclerotic stenosis; IAS: Intracranial atherosclerotic stenosis; AAP: Aortic arch plaque.

weight to the notion that atherosclerosis was a generalized disease. This has been rarely examined before perhaps because previous studies on AAP mainly used transesophageal echocardiography, which failed to visualize the entire aortic arch and reliably determine the AAP extent. Although CTA could image the full length of the aortic arch and detect smaller plaques,[20,26] the relationship between the AAP extent on CTA and ACAS has not been explored in patients with AICVD yet. A CTA study on 48 patients with ischemic stroke of undetermined etiology, without excluding those with coronary artery disease history, did not show significant associations between the thoracic aortic plaque extent and coronary stenosis of ≥50%.[18] Aside from different study populations, distinct observing scope of thoracic aorta and relatively small sample size, they got negative results perhaps also because that they measured the aortic plaque extent with a semi-quantitative scale, where "rare, small plaques" and "frequent, large plaques" might be difficult to be clearly distinguished. Conversely, we applied a more quantitative approach that the mild- and severe-extent AAP were separated by counting the number of the perpendicular slices and quadrants on each perpendicular slice occupied by AAPs. In our study, severe-extent AAP exhibited independent relationship with ACAS ≥50%.

Moreover, our results suggested that the AAP characteristics might provide more information than the presence of CAS ≥50% and IAS ≥50% to indicate ACAS ≥50% in patients with AICVD. On one hand, neither CAS ≥50% nor IAS ≥50% showed a predictive value independent of the AAP characteristics in this study. On the other hand, we found that the AAP characteristics could add further power to CAS ≥50% and IAS ≥50% for ACAS prediction, with a significant increment in the area under ROC. Larger-scale studies are needed to verify these findings and the underlying mechanisms should be explored. A possible explanation may be the anatomical and physiological differences in various arterial beds, to some extent reflected by the developing order of atherosclerosis. Aortic and coronary arteries were usually affected earlier than the cervical and intracranial arteries;[16] thus, AAP may serve as a better marker for ACAS ≥50% in AICVD than CAS ≥50% and IAS ≥50%.

Although without known history of coronary artery disease, AICVD patients with ACAS ≥50% had significantly worse outcomes, suffering not only more cardiac events but also more recurrent stroke.[7] Early detection of ACAS ≥50% in patients with AICVD is of priority to make more targeted and integrated monitoring and intervening plans for these high-risk patients. However, routine screening of ACAS ≥50% in patients with AICVD might not be warranted. Our data supported a comprehensive evaluation of AAP characteristics to aid in selecting the very high risk AICVD patients who should proceed with further examination of coronary arteries, in addition to the established ACAS prediction paradigms based on traditional vascular risk factors, CAS and IAS. These AAP characteristics could be feasibly assessed with traditional CTA of brain blood-supplying arteries, thus it is highly applicable in current clinical settings of AICVD and should not be overlooked. Such a "one shot" prediction of ACAS ≥50% in the acute setting of AICVD without requiring additional screening imaging may be more clinically and economically efficient. In the future, larger-scale and prospective studies are needed to reevaluate the utility of AAP in the risk stratification and clinical management of AICVD patients, in light of the close association between AAP and ACAS ≥50%.

There were several limitations to this study. First, the sample size was not large, and all patients were Chinese. Given the ethnic differences in the atherosclerotic severity and distribution, correlations of various arterial beds may

Table 4: Predictive power added by AAP characteristics to CAS ≥50% and IAS ≥50% for ACAS ≥50% in AICVD.

Characteristics	Areas under ROC curves after entering AAP characteristics into the basic logistic regression* (95% CI)	*P*	Changes of areas under ROC curve	*P*
AAP thickness	0.77 (0.69–0.85)	<0.001	0.11	0.017
AAP extent	0.77 (0.68–0.84)	<0.001	0.11	0.012
Complex AAP	0.76 (0.67–0.83)	<0.001	0.10	0.043

* The basic logistic regression model to predict ACAS ≥50% included CAS ≥50% and IAS ≥50% as covariates (area under ROC curve = 0.66, 95% CI: 0.57–0.75, *P* = 0.008). AICVD: Acute ischemic cerebrovascular disease; ACAS: Asymptomatic coronary artery stenosis; CAS: Cervical atherosclerotic stenosis; IAS: Intracranial atherosclerotic stenosis; AAP: Aortic arch plaque; ROC: Receiver operating characteristic; CI: Confidence interval.

Table 5: Predictive value of AAP independent of CAS ≥50% and IAS ≥50% for ACAS ≥50% in AICVD.

Characteristics	Model 1*		Model 2*		Model 3*	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
CAS ≥50%	1.895 (0.731–4.914)	0.189	1.701 (0.636-4.550)	0.290	1.958 (0.754–5.085)	0.168
IAS ≥50%	2.218 (0.634–7.758)	0.212	1.937 (0.562–6.673)	0.295	2.947 (0.832–10.438)	0.094
AAP thickness (mm)	1.514 (1.181–1.940)	0.001				
AAP extent						
Absent			1			
Mild			1.302 (0.376–4.514)	0.677		
Severe			10.326 (2.299–46.379)	0.002		
Complex AAP					7.296 (2.438–21.830)	<0.001

* The Nagelkerke R^2 was 0.248, 0.265, and 0.256 respectively for model 1, 2, and 3. AICVD: Acute ischemic cerebrovascular disease; AAP: Aortic arch plaque; ACAS: Asymptomatic coronary artery stenosis; CAS: Cervical atherosclerotic stenosis; IAS: Intracranial atherosclerotic stenosis; OR: Odds ratio; CI: Confidence interval.

also be different. Second, CTA has a limited resolution in imaging AAPs. Small isodense AAPs might be overlooked. However, CTA is non-invasive and capable of evaluating AAPs along with routine examination of cervical and intracranial arteries in patients with AICVD. It potentially reduced the selection bias of our study subjects, and our data might be more easily translated into clinical practice. In addition, focusing on the relationship between AAP and ACAS ≥50%, we only evaluated atherosclerosis in the brain blood-supplying arteries without information on other arterial beds, which could have stronger inter-arterial correlations and more clinical impacts.

In conclusion, patients with both AICVD and ACAS ≥50% were more likely to have thicker, severe-extent, and complex AAP than those with AICVD only. These AAP characteristics were independent markers of ACAS ≥50% in AICVD, and their predictive power might be stronger than CAS ≥50% and IAS ≥50%. For AICVD patients with no history of coronary artery disease, evaluating AAP was important to prompt early identification of ACAS ≥50% and timely initiation of more integrated clinical management considering both coronary and brain blood-supplying arteries.

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Conflicts of interest

None.

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