Online Supplemental Data

Materials and Methods

Study Patients

The diagnosis criteria of each vascular risk factor were listed as follows.

(1) Hypertension was defined by a history of hypertension, treated with antihypertensive drugs before admission, or diagnosed at discharge.

(2) Diabetes mellitus was defined by a history of diabetes mellitus, or being treated with hypoglycemic agents before admission, or fasting blood glucose ≥ 7.0mmol/L, or diagnosed at discharge.

(3) Coronary heart disease was defined by a history of coronary heart diseases such as angina pectoris and myocardial infarction, or being treated for coronary heart disease before admission, or diagnosed at discharge.

(4) Hyperlipidemia was defined by a history of hyperlipidemia, treated with hypolipidemic agents before admission, or diagnosed at discharge.

(5) Smoking was defined as continuously smoking for at least six months with ≥ one cigarette a day.

Imaging Analysis

(3) *Plaque Feature Measurement*

The evaluation of plaque enhancement included enhancement ratio and enhancement grading. Both the pre-contrast and post-contrast HR-VWI images were used to assess plaque enhancement. Using the multiplanar reformation function of PACS, the

evaluation of enhancement ratio was measured at the most stenotic slice of the plaque, while the enhancement grading was evaluated by observation slice by slice on the reformatted cross-sectional images. Especially for the grading evaluation, the signal intensity (SI) of the brightest part in a plaque on post-contrast images was used. The SI of adjacent normal brain parenchyma was used for SI normalization. The following parameters were measured for further assessment.

①SI of post-contrast plaque (SI of post-P);

②SI of pre-contrast plaque (SI of pre-P);

③SI of post-contrast pituitary infundibulum (SI of post-Pi);

④SI of pre-contrast pituitary infundibulum (SI of pre-Pi);

⑤SI of post-contrast plaque-free reference arterial wall (SI of post-R);

⑥SI of pre-contrast plaque-free reference arterial wall (SI of pre-R);

⑦SI of post-contrast normal brain tissue (SI of post-B);

⑧SI of pre-contrast normal brain tissue (SI of pre-B);

⑨ΔSI of P = (SI of post-P / SI of post-B)-(SI of pre-P / SI of pre-B);

⑩ΔSI of R = (SI of post-R / SI of post-B)-(SI of pre-R / SI of pre-B);

⑪ΔSI of Pi = (SI of post-Pi / SI of post-B)-(SI of pre-Pi / SI of pre-B).

The enhancement ratio= (SI of post-P / SI of post-B) / (SI of pre-P / SI of pre-B).

The enhancement grading was as follows:

Grade 0: $\Delta SI \text{ of } P \leq \Delta SI \text{ of } R$;

Grade 1: $\Delta SI \text{ of } R < \Delta SI \text{ of } P \leq \Delta SI \text{ of } Pi$;

Grade 2: $\Delta SI \text{ of } Pi < \Delta SI \text{ of } P$.

(5) ***Reproducibility***

A subgroup of 60 cases was randomly selected from the studied population (30 cases in each group) for a reproducibility study. To ensure that the reviewers looked at the same lesions, the identification and 3D multiplanar reformation of plaques were performed by two reviewers together under the guidance of a senior neuroradiologist. Then on the reformatted cross-sectional HR-VWI images, two reviewers (X.X., X.X.) independently performed all measurements of 60 cases to evaluate the inter-reviewer agreement. One reader (X.X.) re-performed the measurement four weeks later for the intra-reviewer agreement assessment.

Online Supplemental Tables

Online Table 1. MR Imaging parameters

Sequences	FOV (mm)	Matrix Size	Slice Thickness (mm)	TR/TE (msec)	Flip Angle (degree)	Bandwidth (Hz/pixel)	Scan time
DWI	220×220	180×180	5.00	4000/93	90	1262	1min 2secs
FLAIR	220×220	256×192	4.00	9000/88	150	270	1min 50secs
STAGE-MRA	256×192	384×216	2.0	20/2.5,12.5	12	650	5mins 50secs
DSC-PWI	240×240	128×128	4.00	1710/30	90	1565	1min 40secs
HR-VWI	240×210	384×336	0.55	900/15	Variable [a]	521	7mins 57secs

STAGE = strategically acquired gradient echo; HR-VWI = high-resolution vessel wall imaging.

[a] flip angle sweep: start:90deg, min:31.6deg, end:133.8deg.

Online Table 2. Inter-reader and intra-reader reproducibility for quantitative measurements of plaque features

Indicators	Intraclass correlation coefficients (95%CI)	*P* value
Plaque area		
Inter-reader agreement	0.949(0.927-0.965) [a]	<0.001
Intra-reader agreement	0.956(0.936-0.970) [b]	<0.001
Plaque burden		
Inter-reader agreement	0.892(0.696-0.949) [a]	<0.001
Intra-reader agreement	0.940(0.913-0.958) [b]	<0.001
Arterial remodeling ratio		
Inter-reader agreement	0.917(0.851-0.950) [a]	<0.001
Intra-reader agreement	0.960(0.942-0.973) [b]	<0.001
Eccentric index		
Inter-reader agreement	0.924(0.854-0.956) [a]	<0.001
Intra-reader agreement	0.934(0.904-0.954) [b]	<0.001
Degree of stenosis		
Inter-reader agreement	0.917(0.731-0.963) [a]	<0.001
Intra-reader agreement	0.941(0.914-0.959) [b]	<0.001
Enhancement ratio		
Inter-reader agreement	0.900(0.905-0.968) [a]	<0.001
Intra-reader agreement	0.943(0.917-0.961) [b]	<0.001

Plaque volume		
Inter-reader agreement	0.943(0.892-0.969) [a]	<0.001
Intra-reader agreement	0.970(0.950-0.982) [b]	<0.001
Total plaque number		
Inter-reader agreement	0.890(0.843-0.924) [a]	<0.001
Intra-reader agreement	0.902(0.860-0.932) [b]	<0.001
Enhanced plaque number		
Inter-reader agreement	0.908(0.869-0.937) [a]	<0.001
Intra-reader agreement	0.931(0.901-0.952) [b]	<0.001

[a] intraclass correlation coefficient (two-way random effect with absolute agreement type)

[b] intraclass correlation coefficient (one-way random effect with absolute agreement type)

Online Table 3. The distribution and frequency of intracranial plaques

Location	Frequency	Median (range) [a]	Mean ± SD [b]
Total circulation	100%	4 (1-13)	4.5 ± 2.3
Anterior circulation	93.1%	3 (0-8)	2.8 ± 1.4
Anterior cerebral artery (left)	14.3%	0 (0-2)	1.1 ± 0.3
A1 segment	11.4%	0 (0-1)	1.0 ± 0.0
A2 segment	4.0%	0 (0-1)	1.0 ± 0.0
Anterior cerebral artery (right)	9.7%	0 (0-2)	1.1 ± 0.3
A1 segment	8.6%	0 (0-1)	1.0 ± 0.0
A2 segment	1.7%	0 (0-2)	1.3 ± 0.6
Middle cerebral artery (left)	64.0%	1 (0-3)	1.4 ± 0.6
M1 segment	45.1%	0 (0-3)	1.1 ± 0.4
M2 segment	39.4%	0 (0-2)	1.0 ± 0.1
Middle cerebral artery (right)	66.3%	1 (0-4)	1.5 ± 0.7
M1 segment	51.4%	1 (0-2)	1.1 ± 0.3
M2 segment	35.4%	0 (0-2)	1.1 ± 0.3
Internal carotid artery (left)	24.0%	0 (0-2)	1.0 ± 0.2
Internal carotid artery (right)	24.6%	0 (0-2)	1.0 ± 0.2
Posterior circulation	70.9%	2 (0-7)	2.6 ± 1.4
Posterior cerebral artery (left)	25.1%	0 (0-2)	1.4 ± 0.5
P1 segment	23.4%	0 (0-2)	1.1 ± 0.3

P2 segment	9.1%	0 (0-1)	1.0 ± 0.0
Posterior cerebral artery (right)	29.7%	0 (0-2)	1.3 ± 0.5
P1 segment	25.1%	0 (0-2)	1.0 ± 0.2
P2 segment	13.1%	0 (0-1)	1.0 ± 0.0
Basilar artery	38.9%	0 (0-2)	1.1 ± 0.3
Vertebral artery (left)	30.3%	0 (0-2)	1.1 ± 0.3
Vertebral artery (right)	32.6%	0 (0-3)	1.1 ± 0.4

SD = standard deviation.

[a] median and range values calculated in the complete study population

[b] mean and standard deviation calculated within subgroup with plaques at location

Online Table 4. Culprit plaque locations of the study population

	First-time stroke group (n=100)		Recurrent stroke group (n=75)		*P* value [b]
Location	Left [a]	Right [a]	Left [a]	Right [a]	0.36
Middle cerebral artery	32	34	16	28	
M1 segment	14	24	11	18	
M2 segment	18	10	5	10	
Internal carotid artery	2	3	6	3	
Posterior cerebral artery	4	4	2	1	
P1 segment	4	3	2	1	
P2 segment	0	1	0	0	
Vertebral artery	2	6	5	4	
Basilar artery	13		10		

[a] the number of plaques at each location

[b] comparison between recurrent stroke group and first-time stroke group

Online Table 5. Probably-culprit plaque features of the study population

Variables	All the patients (n=97) [a]	First-time stroke group (n=43) [a]	Recurrent stroke group (n=54) [a]	*P* value [b]
Plaque area, mm^2	5.6 (3.2-8.8)	6.0 (3.3-8.6)	5.5 (3.2-9.1)	0.95
Plaque burden, %	67.3 (48.6-82.7)	65.3 (49.7-79.9)	71.1 (44.6-83.8)	0.65
Plaque volume, mm^3	29.6 (20.9-46.5)	28.6 (19.2-39.8)	31.0 (22.3-50.9)	0.12
Arterial remodeling ratio	1.2 (1.0-1.7)	1.4 (1.0-1.8)	1.1(1.0-1.5)	0.43
Positive remodeling, n (%)	63 (64.9)	29 (67.4)	34 (63.0)	0.68
Eccentric index	0.6 (0.4-0.7)	0.6 (0.4-0.7)	0.6 (0.4-0.7)	0.88
Eccentricity, n (%)	59 (60.8)	24 (55.8)	35 (64.8)	0.35
Intraplaque hemorrhage, n (%)	20 (20.6)	6 (14.0)	14 (25.9)	0.18
Degree of stenosis, %	38.1 (18.9-55.7)	36.7 (18.1-55.4)	39.0 (18.9-58.6)	0.57
Enhancement ratio	1.5 (1.2-1.8)	1.4 (1.3-1.9)	1.5 (1.2-1.8)	0.74

[a] the number of probably-culprit plaques in different groups

[b] comparison between recurrent stroke group and first-time stroke group

Online Table 6. Multicollinearity diagnosis for variables associated with stroke recurrence

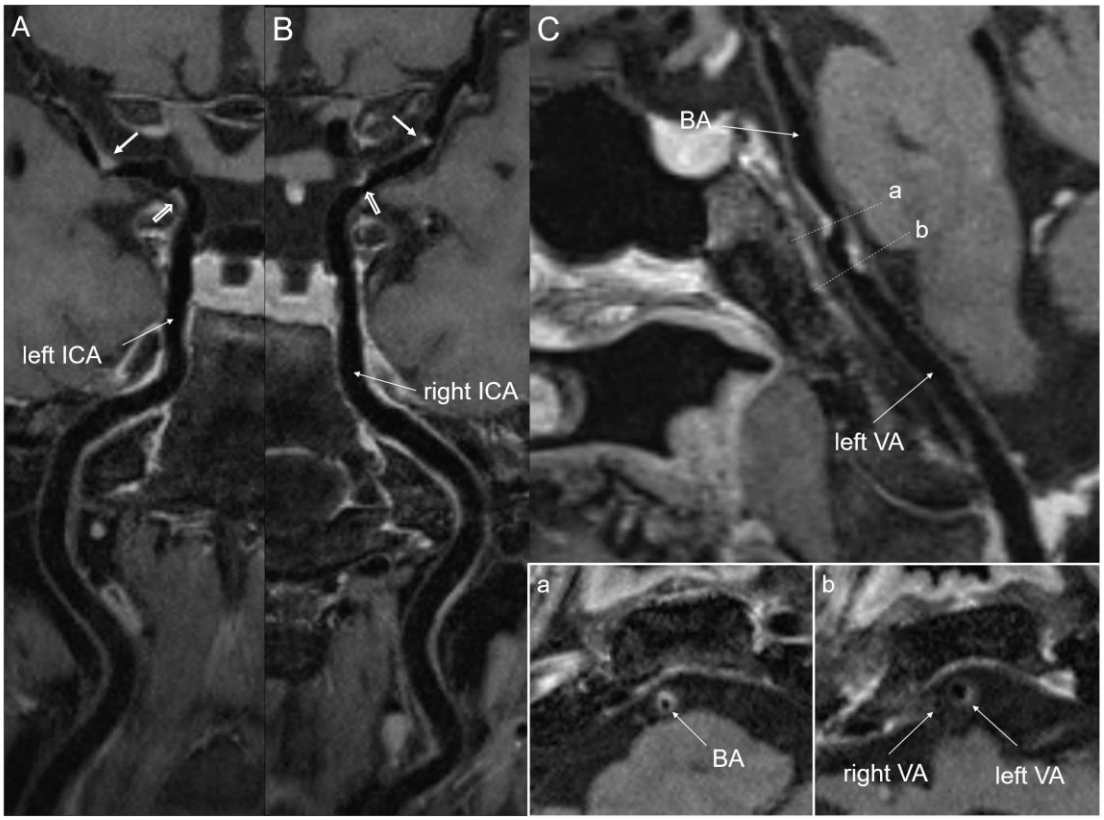
Imaging features	Tolerance	VIF
Culprit plaque volume *	0.989	1.011
Total plaque number	0.482	2.075
Enhanced plaque number	0.481	2.080

VIF = variance inflation factor

* values based on every 10 mm^3 increase

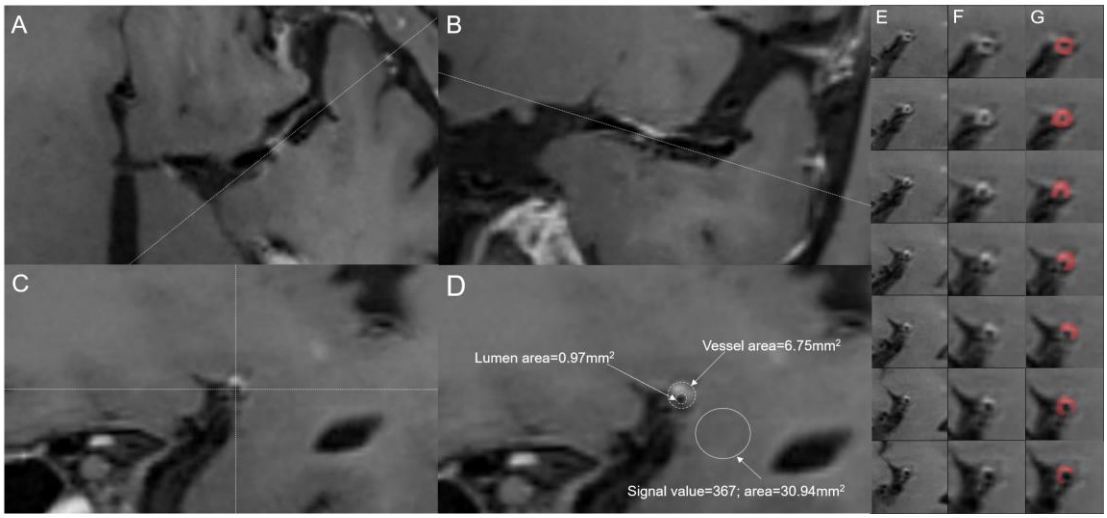
Online Supplemental Figures

Online Figure 1. The multiple plaque determination



The MPR views (A, B) of post-contrast HR-VWI images show four intracranial plaques, including two ICA plaques (hallow arrows) and two MCA plaques (arrows). These plaques are discontinuous and have the normal arterial wall between them. The MPR view (C) shows an enhanced plaque involving both the basilar artery (BA) and left vertebral artery (VA). Because it involves two segments, it is counted as two separate plaques. The local enlarged images (a, b) show the cross-sectional views of the plaques.

Online Figure 2. The detailed imaging measurement of intracranial plaque features (post-contrast HR-VWI images are shown)

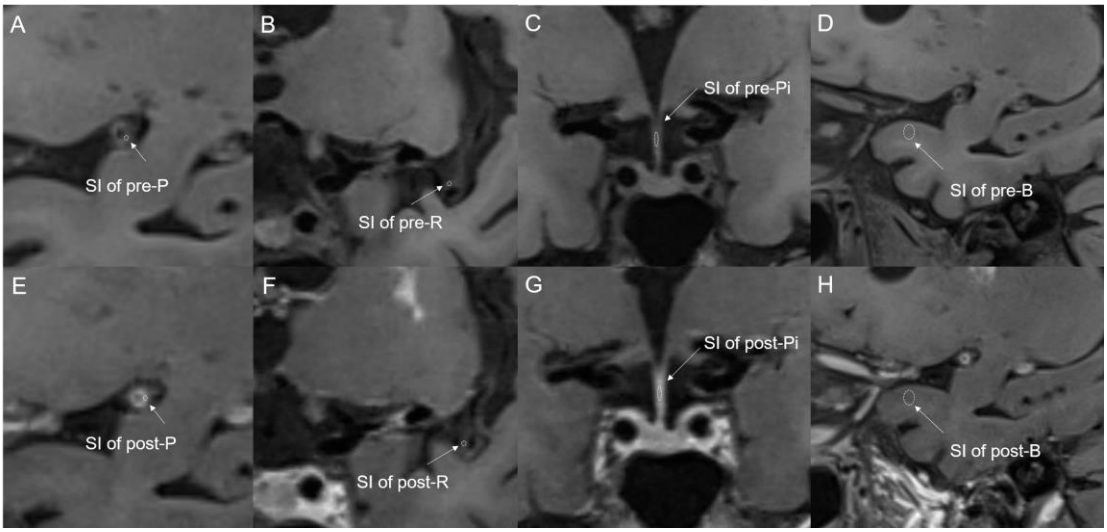


Plaque features are measured on HR-VWI images by PACS and commercial volumetric analysis software, ITK-SNAP 3.8.0.

Transverse view (A) and coronal view (B) of the plaque show that two position lines (dotted lines) are paralleled to the midline of the vessel lumen. The reconstructed cross-sectional view (C) and the enlarged view (D) show that the measurements are performed at the narrowest portion of the lumen. An M1 plaque is detected. Lumen and vessel boundaries are manually segmented. Vessel area=6.75mm^2, lumen area=0.97mm^2, diameter of vessel lumen=1.11mm, maximal/minimal thickness of plaque=1.39/0.63mm, post-enhanced signal value of adjacent normal brain parenchyma (standard area≈30mm^2)=367.

The continuous slices of the cross-section view of plaque (post-contrast images) are shown (E). The enlarged views (F, G) show the plaque is delineated manually (shaded in red) on the continuous slices. The plaque volume is subsequently automatically output.

Online Figure 3. The evaluation of plaque enhancement



Pre-contrast (A,B,C,D) and post-contrast (E,F,G,H) HR-VWI images are shown. The M1-located plaque is observed slice by slice on the reformatted cross-sectional images. The most stenotic slices are shown (A,E), and the most obviously enhanced part of plaque is also localized at the most stenotic slice after observation.

The pre-contrast and post-contrast signal intensity (SI) values are recorded, including SI values of the plaque (A: SI of pre-P; E: SI of post-P), the plaque-free reference arterial wall (B: SI of pre-R; F: SI of post-R), the pituitary infundibulum (C: SI of pre-Pi; G: SI of post-Pi), and the adjacent normal brain tissue (D: SI of pre-B; H: SI of post-B). The SI of brain tissue is used for SI normalization.