

**Atherosclerotic plaque evolution predicts cerebral ischemic
events in patients with intracranial atherosclerosis: a
multicentre longitudinal study using high-resolution MRI**

ELECTRONIC SUPPLEMENTARY MATERIAL

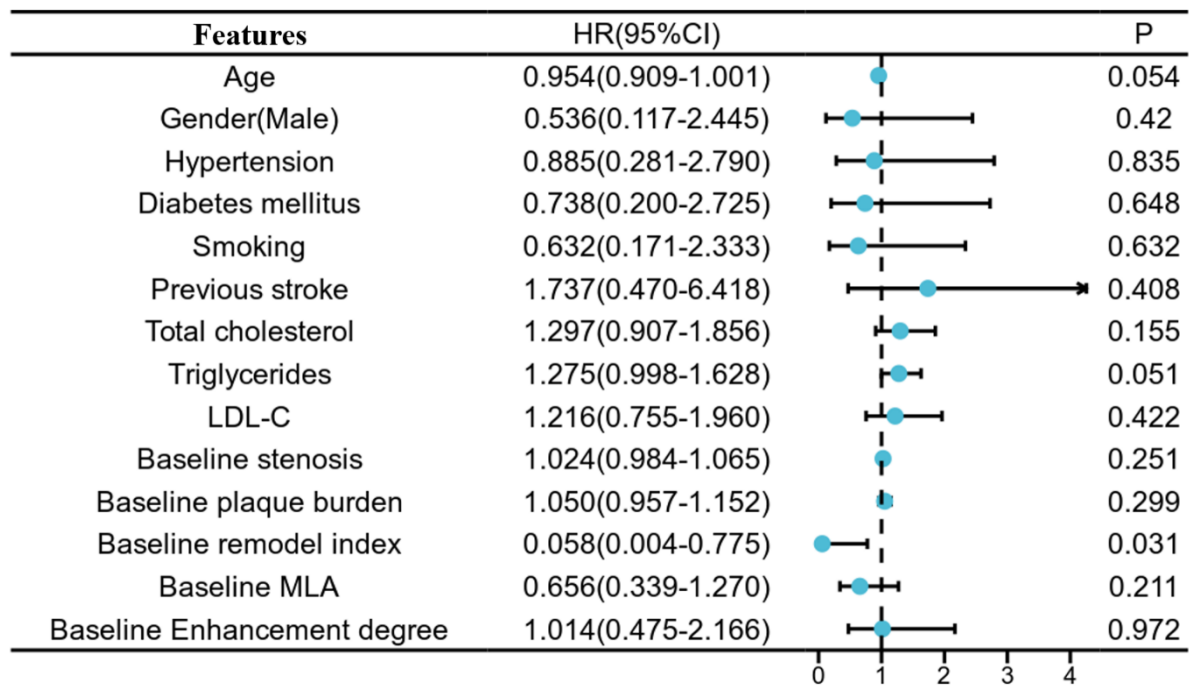
1. MR protocol

In Zhongshan hospital, high-resolution, multi-contrast vessel wall magnetic resonance imaging (hrMRI) was performed using a 3.0 Tesla (T) MR scanner (Verio, SIEMENS, Erlangen, Germany) with a dedicated 18-channel phased array head coil. The protocol included, three-dimensional time-of-flight angiography (3D TOF); black blood two-dimensional fast spin-echo (FSE) T₁-weighted imaging (T1WI), echo time (TE)=27 ms; repetition time (TR)=700 ms, number of excitations (NOX)=4, FOV=100×100 mm², spacing between slices: 2.4 mm; slice thickness: 2 mm; black blood two-dimensional FSE T₂-weighted imaging (T2WI), TR/TE=3070/56 ms, NOX=3. Field of view (FOV): 130×130 mm²; spacing between slices: 2.5 mm; slice thickness: 2 mm, matrix: 256×256.

In Jinling hospital, Medical school of Nanjing University, hrMRI was performed using a 3.0T MR scanner (Discovery MR750, GE Healthcare, Waukesha, WI, USA) with a dedicated 32-channel head coil. The protocol included, 3D TOF; T1WI, TR/TE=560/15.9 ms; T2WI, TR/TE=3400/58 ms. The following parameters were used for both T1WI and T2WI sequences, FOV=100×100 mm²; spacing between slices=2.2 mm; slice thickness=2 mm; matrix=320×256.

In Changhai hospital, high-resolution, multi-contrast vessel wall magnetic resonance imaging (hrMRI) was performed using a 3.0 Tesla (T) MR scanner (Signa HDxT, GE Medical Systems, Waukesha, WI, USA) with a dedicated 8-channel phased array head coil. The protocol included, three-dimensional time-of-flight angiography (3D TOF); black blood two-dimensional fast spin-echo (FSE) T₁-weighted imaging (T1WI), echo time (TE)=16 ms; repetition time (TR)=567 ms; number of excitations (NOX)=2; black blood two-dimensional FSE T₂-weighted imaging (T2WI), TR/TE=2883/50 ms, NOX=3. The following parameters were used for both T1WI and T2WI sequences, field of view (FOV): 100×100 mm²; spacing between slices: 2.5 mm; slice thickness: 2 mm, matrix: 320×256.

Sup. Fig 1 Forest figure of baseline features in predicting ischemic events



Sup. Tab 1 Intra and interobserver agreement for hrMRI measurement

Measurement	Intra-observer agreement	Inter-observer agreement
VA _{MLA}	0.881 (0.825-0.919)	0.923 (0.738-0.980)
LA _{MLA}	0.804 (0.713-0.866)	0.821 (0.722-0.953)
VA _{RA}	0.859 (0.801-0.902)	0.926 (0.741-0.981)
LA _{RA}	0.772 (0.677-0.841)	0.880 (0.592-0.969)
WT _{max}	0.730 (0.653-0.831)	0.846 (0.518-0.959)
WT _{min}	0.785 (0.694-0.849)	0.890 (0.638-0.971)
T1-CE signal	0.791 (0.705-0.853)	0.966 (0.876-0.991)
T1-CE signal of reference	0.731 (0.569-0.828)	0.893 (0.632-0.972)
T1 signal	0.830 (0.749-0.885)	0.852 (0.517-0.961)
T1signal of reference	0.871 (0.806-0.914)	0.929 (0.752-0.982)

VA_{MLA}, vessel area at the most stenotic site; VA_{RA}, vessel area at the healthy reference section nearby; LA_{MLA}, minimum luminal area; LA_{RA}, lumen area at the reference site; WT_{max}, maximum wall thickness.

Sup. Tab 2 Paired T-test in patients without ischemic events

	Baseline (n=74)	Follow-up (n=74)	p value
V _{AMLA} (mm ²)	13.53 (10.63-16.18)	14.78(11.54-15.99)	0.076
V _{ARA} (mm ²)	14.47 (11.99-16.23)	14.93(12.31-19.34)	0.002
L _{AMLA} (mm ²)	1.47 (0.77-2.37)	2.00(1.03-2.77)	<0.001
L _{ARA} (mm ²)	5.86 (5.10-7.24)	6.78(5.42-8.21)	0.023
WT _{max} (mm)	2.10 (1.85-2.59)	2.21(1.74-2.60)	0.936
Enhancement degree (%)			
0	12 (16.22%)	25(33.78%)	<0.001
1	20 (27.03%)	27(36.49%)	
2	42 (56.76%)	22(29.73%)	
Enhancement ratio	2.06(1.33-2.91)	1.73(1.50-2.48)	<0.001
Plaque burden	0.89 (0.83-0.94)	0.92(0.87-0.94)	0.001
Remodeling index	0.98 (0.84-1.09)	1.00(0.80-1.12)	0.542
Eccentric index	0.67 (0.56-0.74)	0.78(0.75-0.82)	<0.001

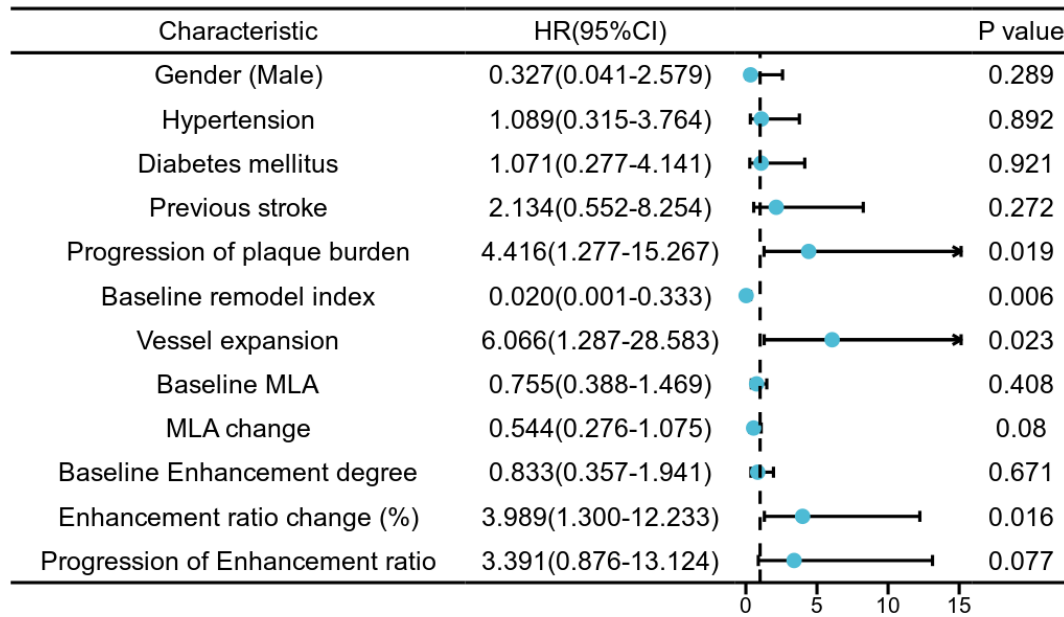
V_{AMLA}, vessel area at the most stenotic site; V_{ARA}, vessel area at the healthy reference section nearby; L_{AMLA}, minimum luminal area; L_{ARA}, lumen area at the reference site; WT_{max}, maximum wall thickness.

Sup. Tab 3 Paired T-test in patients with ischemic events

	Baseline (n=12)	Follow-up (n=12)	p value
V _{AMLA} (mm ²)	11.64 (9.33-15.55)	14.83(12.61-20.57)	0.003
V _{ARA} (mm ²)	15.61 (12.65-18.02)	14.22(11.41-19.86)	0.960
L _{AMLA} (mm ²)	1.10 (0.68-1.68)	1.16(0.58-1.55)	0.428
L _{ARA} (mm ²)	5.72 (4.52-7.26)	7.34(4.06-8.25)	0.308
WT _{max} (mm)	2.30 (1.80-2.54)	2.64(2.29-3.20)	0.032
Enhancement degree (%)			
0	1 (8.33%)	3(25.00%)	1.000
1	5 (41.67%)	1(8.33%)	
2	6 (50.00%)	8(66.67%)	
Enhancement ratio	2.22(1.56-3.07)	2.47(1.45-2.74)	0.823
Plaque burden	0.90 (0.87-0.92)	0.94(0.88-0.97)	0.127
Remodeling index	0.76 (0.64-0.97)	1.05(0.88-1.36)	0.022
Eccentric index	0.68 (0.61-0.71)	0.85(0.82-0.88)	0.047

V_{AMLA}, vessel area at the most stenotic site; V_{ARA}, vessel area at the healthy reference section nearby; L_{AMLA}, minimum luminal area; L_{ARA}, lumen area at the reference site; WT_{max}, maximum wall thickness.

Sup Fig 2 Forest figure of features in predicting ischemic events in symptomatic patients



Sup Fig 3 Image analysis procedure

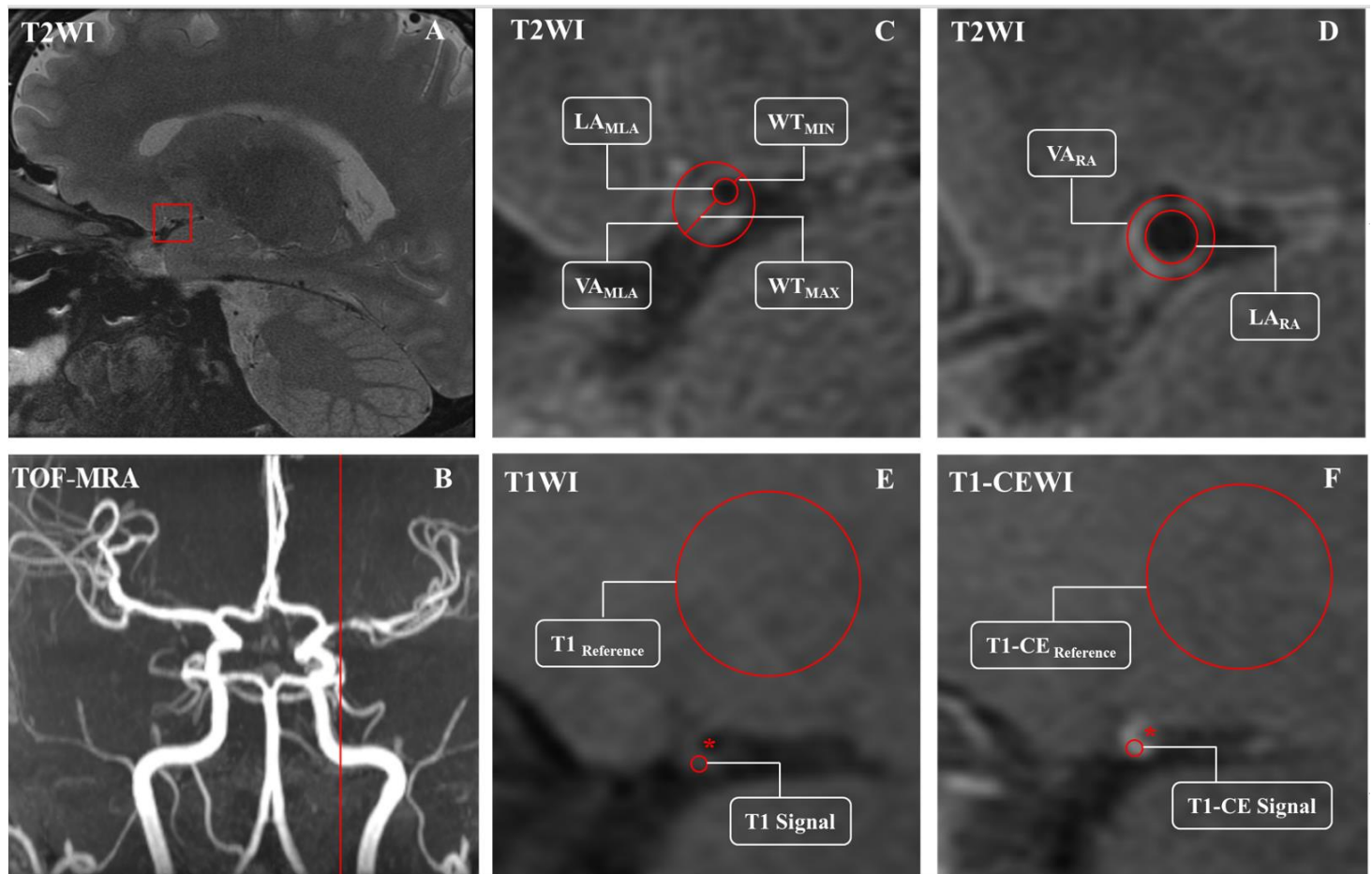


Image analysis procedure of vessel wall image. Firstly, in the black blood 2D-T2 sequence (A), the most stenotic and reference planes were clarified concerning the TOF-MRA sequence (B). We draw the lumen and vessel outer wall with a closed polygon tool in the most stenotic (C) and reference (D) planes and get their areas accordingly. The maximum and minimum plaque thickness passing through the center of the lumen is measured using a linear measurement tool (C). Finally, the signal intensity of the vessel wall and adjacent reference sites is measured in T1 (E) and T1-CE (F) sequences. Based on the above measurement parameters, the plaque features, such as plaque burden, eccentricity index, remodeling index, enhancement index, etc., are then calculated according to the formula. *Lumen