SUPPLEMENTAL MATERIAL

Baseline Vessel Wall MRI characteristics Associated with In-stent Restenosis for Intracranial Atherosclerotic Stenosis

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Table S1. Clinical and Imaging Characteristics of the Patients at Baseline

	All patients(n=64)	Non-ISR(n=55)	ISR(n=9)	*P* value
Clinical				
Median age (IQR), yr	58(51-65)	58(55-61)	57(48-65)	0.84
Male, no. (%)	46(71.8)	41(74.5)	5(55.56)	0.24
Hypertension, no. (%)	40(62.5)	35(63.6）	5(55.56)	0.65
Hyperlipidemia, no. (%)	19(29.7)	17(30.9)	2(22.2)	0.60
Diabetes, no. (%)	21(32.8)	17(30.9)	4(44.4)	0.43
Smoking, no. (%)	16(25)	14(25.5)	2(22.2)	0.84
Pre-stenting symptoms				0.26
Stroke, no. (%)	60(93.8)	51(92.7)	9(100)	
TIA, no. (%)	4(6.2)	4(7.3)	0(0)	
Stenting				
Stenosis pre-stenting (%)	82±5	82±5	83±5	0.79
Stent location-anterior, no. (%)	53(82.8)	46(83.6)	7(77.8)	0.49
Stent type				0.80
Wingspan, no. (%)	19(29.7)	16(29.1)	3(33.3)	
Enterprise, no. (%)	45(70.3)	39(70.9)	6(66.7)	
Residual stenosis (%)	10±12	11±13	9±12	0.99
Imaging				
Acute infarct, no. (%)	32(50)	29(52.7)	3(33.3)	0.24
IPH, no. (%)	13(20.3)	10(18.2)	3(33.3)	0.26
Plaque burden	0.92(0.87-0.94)	0.92(0.87-0.95)	0.89(0.79-0.91)	0.04*
Minimum lumen area	0.006(0.003-0.012)	0.006(0.004-0.008)	0.009(0.005-0.028)	0.04*
Plaque eccentricity, no. (%)	54(84.4)	49(89.1)	5(55.6)	＜0.01*
Enhancement ratio	0.87(0.62-1.27)	0.84(0.61-1.18)	1.36(0.87-1.92)	＜0.01*
Enhancement involvement				0.03*
Type 1(＜50% area), no. (%)	20(31.3)	20(36.4)	0(0)	
Type 2(≥50% area), no. (%)	44(68.8)	35(63.6)	9(100)	

*P ＜ 0.05. ISR= in-stent restenosis, IPH= intraplaque hemorrhage. All continuous data was summarized as mean ± SD or median and inter-quartile range (IQR)

Table S2. Interreader agreement among the readers

	Intraclass correlation	**95% Confidence Interval**
ISR	0.9588	0.9385-0.9734
Acute infarct	0.9167	0.8773-0.9456
IPH	0.9085	0.8656-0.9401
Plaque eccentricity	0.9256	0.8900-0.9515
Enhancement type	0.9030	0.8578-0.9365
The minimum lumen area	0.9539	0.9312-0.9701
Plaque burden	0.9268	0.8919-0.9523
Enhancement ratio	0.9345	0.9029-0.9574

ISR= in-stent restenosis, IPH= intraplaque hemorrhage.

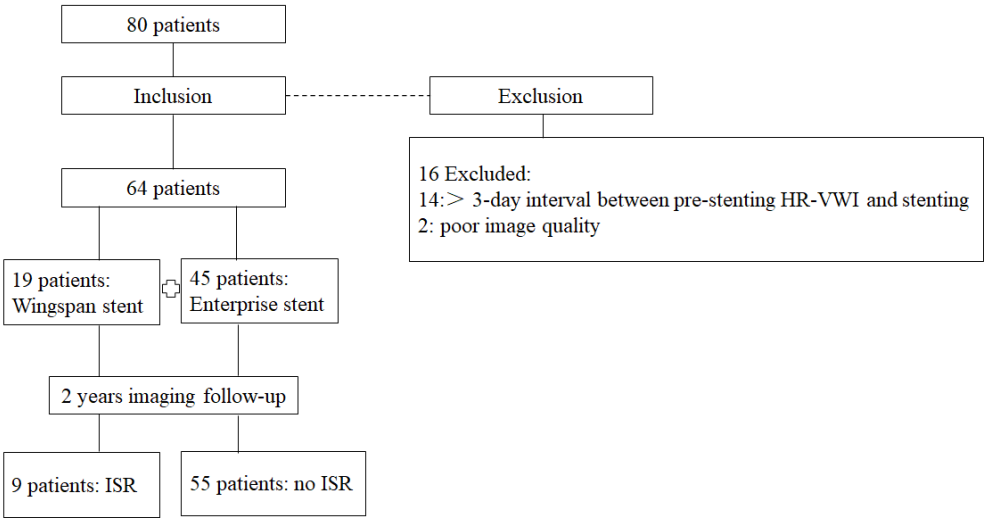

Figure SI. Patients flow diagram for analysis.

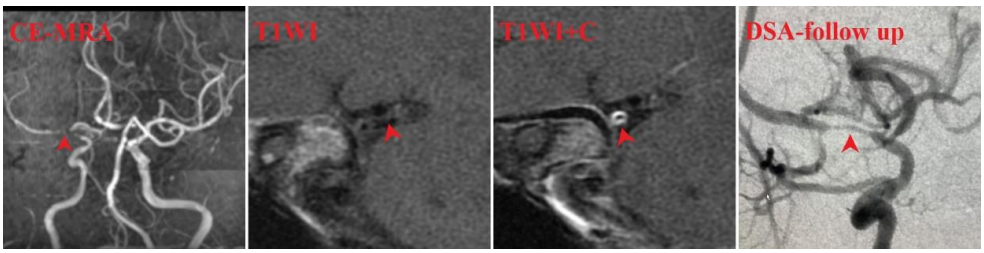

Figure S2. Patient in their 50s presented with more than 1 month history of left limb numbness, weakness, and speech disorder. CE-MRA showed severe stenosis of the right M1 segment of the middle cerebral artery (arrowhead), and HR-VWI (on 3.0T GE HDx system) showed corresponding circumferential plaque (T1WI, arrowhead) that enhanced (enhancement ratio: 1.16) (T1WI+C arrowhead). A Wingspan stent was placed in the diseased segment. The patient was readmitted 4 months after stenting due to acute left-sided limb weakness. Follow-up DSA showed in-stent restenosis of the right middle cerebral artery (arrowhead).

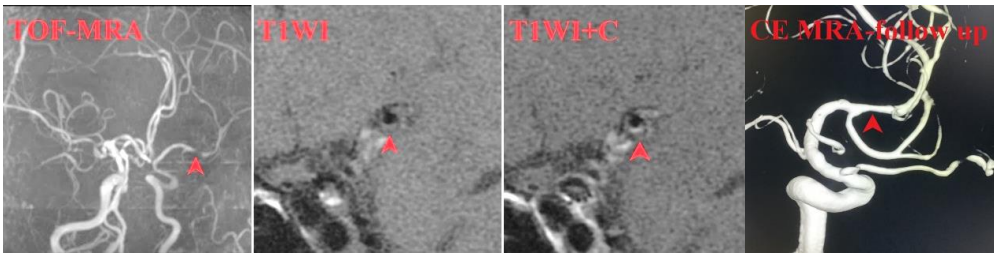

Figure S3. Patient in their 60s presented with 1 month history of right limb numbness and slurred speech. TOF-MRA showed severe stenosis of the left M1 segment of the middle cerebral artery (arrowhead). There was a corresponding eccentric plaque on HR-VWI, scanned on 3.0T GE HDx system (T1WI, arrowhead) and the plaque showed mild enhancement post-contrast (enhancement ratio: 0.87) (T1WI+C, arrowhead). An Enterprise stent was placed in the left middle cerebral artery. Follow up CE-MRA was performed 1 year after stenting, and showed no evidence of restenosis (arrowhead) and the patient had no new symptoms.

Lesion assessment

Lesion on HR-VWI was assessed for all patients included in our analysis, using a 4-point subjective scale (1 = poor, 2 = moderate, 3 = good, 4 = excellent) according to Okuchi S et al. The lesion assessment was defined as follows: 1(poor): slightly ill-defined margin and slightly obscure hyperintensity; 2(moderate): slightly ill-defined margin and recognizable hyperintensity; 3(good): relatively well-defined margin and recognizable hyperintensity; 4(excellent): well-defined margin and well recognizable hyperintensity. The interreader agreement of lesion was also assessed. For all 64 patients in our analysis, 43 patients were scanned on a 3.0T GE HDx scanner and 21 patients were scanned on a 3.0T Siemens Skyra system. As we mentioned in the inclusion/exclusion criteria, all 64 patients had sufficient image quality of HR-VWI for evaluation. Patients with insufficient image quality due to motion or other artifact degradation, or low signal-to-noise ratio were excluded. In the end, the average score for 2D (GE HDx scanner) and 3D (Siemens Skyra system) HR-VWI were 2.37±0.54 and 2.50±0.42 on pre-contrast sequence, and 3.75±0.32 and 3.81±0.25 on post-contrast sequence. There was no significant difference in ratings for image quality between 2D (GE HDx scanner) and 3D (Siemens Skyra system) HR-VWI both on pre- and post-contrast sequences (P=0.12). The ICC of image quality were 0.917 and 0.964 on pre- and post-contrast images for the three readers. As we mentioned in the Limitations section, one of the Limitations of our analysis was that 2D and 3D HR-VWI were both used in this study and have different resolution and imaging approaches. Spatial resolution may impact the ability to characterize plaque morphology and composition. However, these issues were mitigated by ensuring that 2D HR-VWI was only performed in a plane perpendicular to the involved arterial segment, thus reducing volume averaging and wall thickness overestimation.

Okuchi S, Fushimi Y, Okada T, et al. Visualization of carotid vessel wall and atherosclerotic plaque: T1-SPACE vs. compressed sensing T1-SPACE. Eur Radiol. 2019;29(8):4114-4122.

Procedure of stenting

The indications for stenting include: 1) Patients with symptomatic ICAS stenosis≥70%; 2) no response after 4-6 weeks of intensive medical therapy, and 3) tissue hypoperfusion downstream from the involved arterial segment. Before stenting, aspirin 100 mg/d and clopidogrel 75 mg/d were given to patients for five days. During this period, HR-VWI was performed. The endovascular treatment was performed under general anesthesia. A 6 F guiding catheter was introduced through a femoral sheath. During intervention, patients were heparinized to a doubled activated clotting time. A DSA run of the target vessel was performed using a biplane angiographic system (Artis zee Biplane; Siemens, Erlangen, Germany) or a single-arm angiosuite (Philips FD, Netherlands). Rotational angiography followed by 3D reconstruction was performed to understand the normal vessel diameter adjacent to the stenosis and the diameter and the length of the stenosis. The enhanced Dyna CT was also performed to assess the location of the plaque and the relationship between the stenosis and important vessel branches. A road-map was performed for guidance, and the vessel distal to the stenosis was catheterized using a Transcend Floppy microguidewire (Boston, Scientific), followed by balloon dilatation (Gateway, Stryker). After deflation and withdrawal of the balloon catheter, a flushed 0.021-inch microcatheter (Prowler Select Plus, Codman) was navigated over the exchange-wire. The stent was deployed to cover the targeted stenosis. A daily dose of aspirin (100 mg) and clopidogrel (75 mg) was recommended for 3 months after discharge followed by only aspirin. All patients received statin therapy after stenting, 40 (62.5 %) patients with hypertension were treated with antihypertensive drugs, and 21 (32.8 %) patients with diabetes mellitus received either metformin or insulin therapy.

Antiplatelet medication

Aggressive antiplatelet medical management was performed for all patients in our analysis. Aspirin 100 mg/d and clopidogrel 75 mg/d were given to patients before stenting for five days. After stenting, aspirin 100 mg/d and clopidogrel 75 mg/d were given for 90 days, then aspirin 100 mg/d for the entire follow-up.