



Original research

Vessel wall MRI characteristics associated with intraprocedural stent thrombosis during angioplasty for intracranial atherosclerotic stenosis

Xiaotong Ma,^{1,2} Peng Yan,¹ Jiachen Ju,¹ Zhengyu Yang,³ Wenjuan Wang,¹ Qiuting Wang,³ Xiaohui Liu,¹ Zhangyong Xia,^{2,4,5} Qinjian Sun^{1,3}

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jnis-2023-020941>).

For numbered affiliations see end of article.

Correspondence to

Dr Qinjian Sun, Key Laboratory of Endocrine Glucose & Lipids Metabolism and Brain Aging, Ministry of Education; Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, P.R. China; sqj1210@163.com and Dr Zhangyong Xia, Department of Neurology, Liaocheng People's Hospital, Shandong University, Liaocheng, Shandong, 252000, People's Republic of China; xiazhangyong2013@163.com

Received 21 August 2023
Accepted 30 October 2023

ABSTRACT

Background Few studies have so far explored plaque characteristics on high-resolution magnetic resonance vessel wall imaging (HR-VWI) associated with intraprocedural stent thrombosis (IPST) during angioplasty for intracranial atherosclerotic stenosis (ICAS). We aimed to investigate the plaque features on HR-VWI associated with IPST during stenting for ICAS. **Methods** This study recruited 77 patients with ICAS who underwent intracranial stenting using the Gateway-Wingspan system, and were performed with enhanced pre- and post-contrast T1-weighted HR-VWI on a 3.0T MRI scanner before angioplasty. During stenting for ICAS, eight patients (male: 100%, age mean \pm standard deviation (SD): 58.7 \pm 2.47) developed IPST within 30 minutes after stenting. To ensure comparability, 16 patients who had undergone intracranial stenting but did not develop IPST were matched as controls for this study. Univariable and binary logistic models were used to explore the plaque characteristics on HR-VWI associated with IPST.

Results Patients who developed IPST had less plaque diffusion (37.50% vs 81.25%, $p=0.036$), a more severe degree of area stenosis (median 96.30% vs 81.65%, $p<0.01$), and a higher plaque enhancement index (median 37.99 vs 13.12, $p<0.01$) compared with those who did not. After multivariate adjustment, IPST was independently associated with a more severe degree of area stenosis (adjusted odds ratio (OR) 1.20, 95% confidence interval (CI) 1.01–1.43, $p=0.044$) and a higher plaque enhancement index (adjusted OR 1.17, 95% CI 1.01 to 1.36, $p=0.036$).

Conclusion Intraprocedural stent thrombosis during intracranial angioplasty for patients with ICAS may be independently associated with a higher plaque enhancement index and a more severe degree of area stenosis on HR-VWI.

INTRODUCTION

Stroke is the second leading cause of death globally and the primary cause of death in China.^{1,2} Intracranial atherosclerotic stenosis (ICAS) is one of the leading causes of ischemic stroke in Asians, accounting for 46.6% of all ischemic stroke,³ while it only accounts for 10–15% of ischemic stroke in Western countries.⁴ Although most studies have showed that stenting and medical therapy have a similar effect and safety on patients with ICAS,⁵ individual studies have found that stenting

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Intraprocedural stent thrombosis (IPST) was an important complication during angioplasty for symptomatic intracranial atherosclerotic stenosis (ICAS). Previous studies have revealed several clinical risk factors associated with IPST, including antiplatelet resistance, long stenotic lesions, and use of multiple stents. High-resolution magnetic resonance vessel wall imaging (HR-VWI) can visualize the structure of the intracranial arterial wall and reveal the characteristics of high-risk plaques associated with ischemic stroke.

WHAT THIS STUDY ADDS

⇒ This study found that a higher plaque enhancement index and a more severe degree of area stenosis on HR-VWI might be associated with IPST in patients who underwent intracranial stenting.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study suggests the association between plaque characteristics on HR-VWI and IPST may be potentially helpful in angioplasty risk assessment and preoperative preparation for intracranial stenting.

compared with medical therapy resulted in an increased risk of stroke or transient ischemic attack (TIA).⁶ Among those studies, intraprocedural stent thrombosis (IPST) is a major risk factor for stroke recurrence and occurs in approximately 10.4% to 16.3% of patients who underwent stent placement.⁷

IPST, defined as a new, reappearing, or increasing thrombus, either occlusive or nonocclusive, within or adjacent to a stent implanted during the procedure, was first reported as a relatively rare but potentially serious event during percutaneous coronary intervention with drug-eluting stents.⁸ IPST was also an important complication during angioplasty for symptomatic ICAS. Previous studies found several clinical risk factors associated with IPST during carotid artery stenting, including antiplatelet resistance, long stenotic lesions, and use of more than one stent.⁹ Some studies on cardiovascular disease have shown that multiple plaque ruptures with large cavities more often evolve into IPST if



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Ma X, Yan P, Ju J, et al. *J NeuroIntervent Surg* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jnis-2023-020941

they used intravascular ultrasound (IVUS), which can visualize the structure of plaques.¹⁰ IVUS may not be suitable for curved intracranial arteries to evaluate the nature of plaques. High-resolution magnetic resonance vessel wall imaging (HR-VWI) can visualize the lumen and reveal high-risk plaque characteristics associated with ischemic stroke, such as plaque eccentricity, intra-plaque hemorrhage, and wall enhancement.^{11 12} Therefore, the plaque characteristics of symptomatic ICAS are usually evaluated via non-invasive HR-VWI. However, to the best of our knowledge, no previous study has characterized the plaque features on HR-VWI associated with IPST.

Therefore, the purpose of our study was to investigate the association between the plaque characteristics on HR-VWI and the occurrence of IPST in patients treated with intracranial stenting.

MATERIALS AND METHODS

Study population

This study used data from a prospectively maintained database of 145 patients who received intracranial angioplasty at Shandong Provincial Hospital Affiliated to Shandong First Medical University. Patients were recruited from December 2016 to June 2022. The selection criteria for intracranial angioplasty therapy were as follows. Inclusion criteria: (1) Digital subtraction angiography (DSA) showed severe ICAS ($\geq 70\%$); (2) Suffered from

recurrent ischemic events (TIA or ischemic stroke defined by WHO criteria) after intensive drug therapy; (3) Inadequate tissue perfusion downstream of the targeted arterial segment; (4) Having at least one risk factor for atherosclerosis; (5) At least 3 weeks after the latest ischemic event. Exclusion criteria: (1) Clinical evidence of the presence of inflammatory arteritis, Moyamoya disease, intracranial tumors, aneurysms, or arteriovenous malformations; (2) Patients who had suffered from a large cerebral infarction ($\geq 1/2$ territory of middle cerebral artery or vertebrobasilar artery); (3) Patients with lesion length greater than 14 mm.¹³

This study used HR-VWI to evaluate the plaque characteristics of ICAS, including pre-enhanced and post-enhanced T1WI sequences. Inclusion criteria included: (1) Undergoing HR-VWI within 7 days before stenting; (2) Using the Gateway-Wingspan system (Stryker, US). The exclusion criteria included: (1) Insufficient image quality; (2) More than one stent implanted. Finally, 77 patients were included in the analysis. Figure 1 shows a flowchart of this study.

Baseline clinical and imaging data from the database was analyzed for all eligible patients. Thromboelastogram testing was performed for all patients after they had undergone dual antiplatelet therapy for at least 5 days. Once antiplatelet resistance was detected, the patient was treated with cilostazol instead. Demographic and clinical data were collected

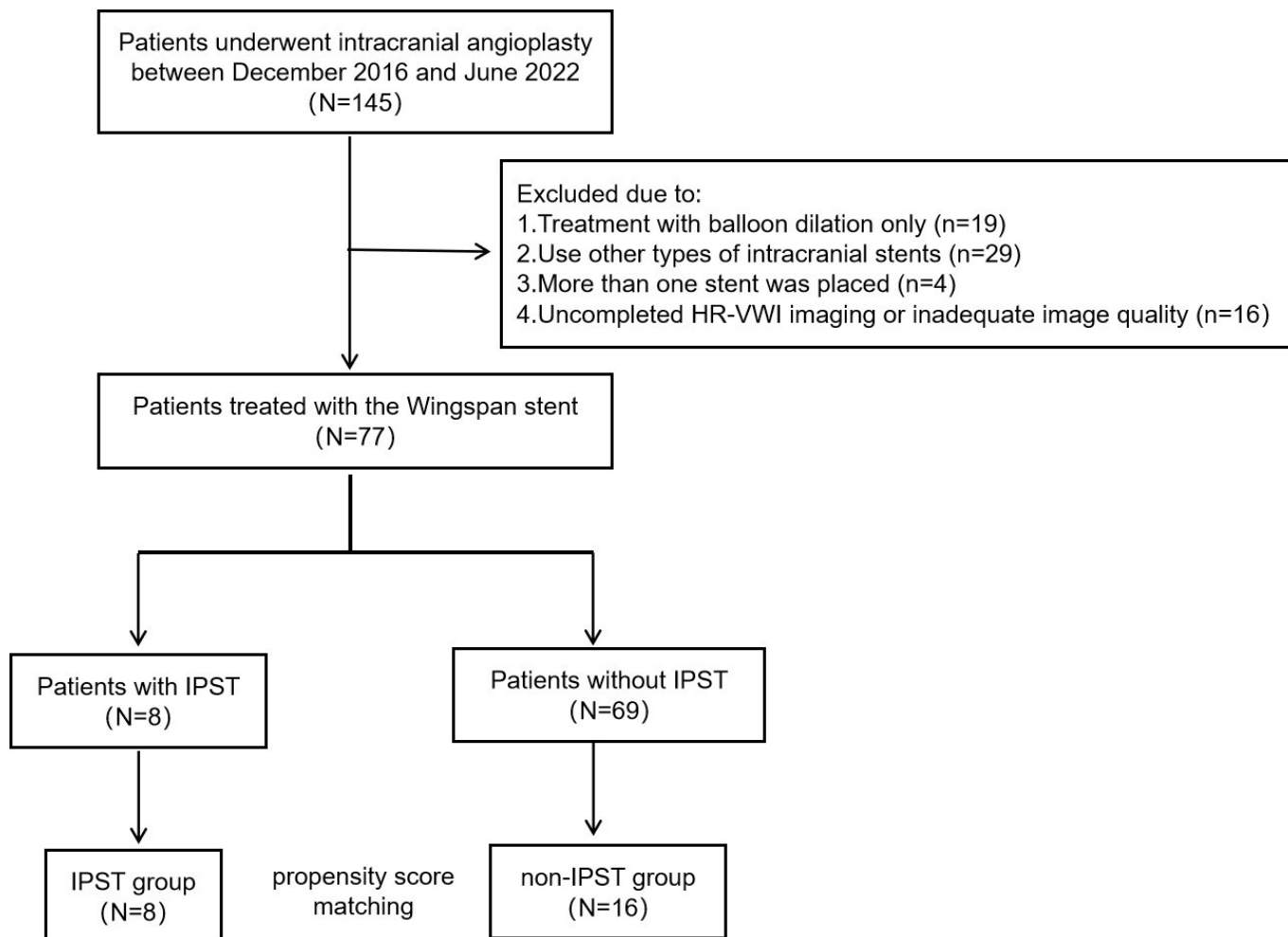


Figure 1 Flowchart of patients in this study.

Key: HR-MRI, high-resolution MRI; IPST, intraprocedural stent thrombosis.

including age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking, alcohol consumption, and location of stent placement.

This study protocol was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University (SWYX: NO.2021-012), and written informed consent was obtained from all participants.

High-resolution magnetic resonance vessel wall image acquisition

The detailed methods of acquiring vessel wall images are in the online supplemental materials.

Image processing and analysis

The part methods of image processing and analysis are in the online supplemental materials. The degree of area stenosis was calculated as (area of one lumen of the stenotic lesion/area of the reference lumen) \times 100%.¹⁴ Irregularity in the plaque surface was defined as discontinuity in the juxtaposed surfaces of the plaque, whereas regularity was defined as a smooth inner wall. Plaques spreading across four quadrants were defined as diffusion, and that involving ≤ 3 quadrants were defined as non-diffusion.¹⁵ Plaque eccentricity was defined as a localized plaque encircling less than 75% of the vessel wall or the thickest portion being greater than twice the thinnest portion.¹⁶ Intraplaque hemorrhage (IPH) was defined as signal intensity greater than 150% of the adjacent muscle T1 signal. The remodeling index (RI) was the ratio of the vessel area at the stenotic lesion to the area of the reference vessel. The vessel wall area index was the ratio of the vessel wall area at the stenotic lesion to the reference vessel wall area.¹⁴ The remodeling categories were based on reference intake (RI) values; $RI \geq 1.05$ was considered positive remodeling (PR), $RI \leq 0.95$ was considered negative remodeling (NR), and $0.95 < RI < 1.05$ was considered no remodeling.¹⁵ Plaque enhancement was quantified by manually tracing the lumen and outer edge vessel wall at the narrowest part of the responsible vessel and measuring the signal intensity of the plaque (SI plaque) on matched pre-contrast and matched post-contrast 3D T1 images. A 10–12 mm² circular area was plotted on the contralateral or proximal normal vessel wall on the matched pre-contrast and post-contrast T1-weighted images, respectively, and the signal intensity of the normal vessel wall was measured (SI normal vessel wall). The SI normal vessel wall located contralateral or proximal to the stenotic segment was evaluated as the reference. The enhancement grade was divided into three levels: no enhancement plaque group (grade 1, NO group, indicating enhancement was similar to or less than that of intracranial arterial walls without plaque in the same individual, mild enhancement group (grade 2, ME group, showing enhancement was greater than that of the NO group but less than that of the pituitary stalk), and significant enhancement group (grade 3, MA group, indicating similar or greater enhancement than the pituitary stalk).¹⁷ The enhancement index was calculated as follows: ((SI plaque/SI normal wall on post-contrast imaging) - (SI plaque/SI normal wall on matched pre-contrast imaging)) / (SI plaque/SI normal wall on matched pre-contrast imaging).¹⁸ All disagreements were resolved by consensus.

The intra-observer reliability of measuring and assessing the vessel wall was determined by the intra-group correlation coefficient (ICC) and Cohen's kappa value. A value of ICC and kappa > 0.75 indicates excellent agreement.

Perioperative management and stenting procedures

The detailed methods used in stenting are in the online supplemental materials.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The detailed methods are in the online supplemental materials.

RESULTS

Clinical characteristics of study participants

All patients in the IPST group were male. Consequently, 16 male patients without IPST were matched for analysis. All patients underwent HR-VWI 2.8 ± 1.5 days before intracranial stenting. There were no significant differences between the IPST group and the non-IPST group in age, sex, smoking, alcohol consumption, hyperlipidemia, hypertension, diabetes, diameter stenosis degree and time interval between HR-VWI and intracranial stenting (online supplemental table 1). Seven out of 8 patients in the IPST group were in good postoperative condition, with no complications such as infarction or bleeding. One patient suffered from postoperative symptoms of lung infection and dyspnea, but was soon discharged with symptomatic improvement.

Intraclass correlation coefficients to assess agreement of vessel wall measurements

The intraclass correlation coefficient (ICC) values were 0.95 (95% CI 0.86 to 0.98) for area stenosis degree, 0.96 (95% CI 0.90 to 0.98) for wall area index, 0.95 (95% CI 0.88 to 0.98) for enhancement index, and 0.93 (95% CI 0.87 to 0.97) for remodeling index. The Kappa values were 0.82 for plaque irregularity, 0.91 for plaque eccentricity, 0.91 for plaque diffusion, and 1.00 for intraplaque hemorrhage.

Quantitative analysis of plaques

As shown in table 1, patients with IPST showed less plaque diffusion (37.50% vs 81.25%, $p=0.036$), higher plaque enhancement index (median 37.99 vs 13.12, $p<0.01$), and more severe degree of area stenosis (median 96.30% vs 81.65%, $p<0.01$) compared with those without IPST. Figure 2 exhibited an example of one patient with IPST.

Association between IPST and plaque characteristics on HR-VWI

After adjusting for age, less plaque diffusion (Model 1: age-adjusted OR (OR) 0.09; 95% CI (CI), 0.01–0.87), higher plaque enhancement index (Model 1: age-adjusted OR, 1.10; 95% CI, 1.02 to 1.19), and more severe degree of area stenosis (Model 1: age-adjusted OR, 1.19; 95% CI, 1.02 to 1.39) remained significantly associated with IPST (table 2).

Model 2 was adjusted for variables with $p<0.1$ in the univariate analysis, which included age, hypertension, diabetes, smoking, alcohol consumption, and regularity in the plaque surface. After adjusting for multiple confounders, higher plaque enhancement index (Model 2: adjusted OR, 1.17, 95% CI 1.01 to 1.36, $p=0.036$) and more severe degree of area stenosis (Model 2: adjusted OR, 1.20, 95% CI 1.01 to 1.43, $p=0.044$) on HR-VWI was independently associated with IPST that occurred during intracranial stenting. However, the association between IPST and plaques diffusion was diluted and became statistically non-significant after adjusting for multiple confounders (Model 2: adjusted OR, 0.02; 95% CI, 0.00 to 1.36).

Table 1 Comparison of plaque characteristics between IPST and non-IPST groups

Characteristics of plaques	IPST group(n=8)	Non-IPST group(n=16)	P value
Plaque regularity, n (%)	7 (87.50)	8 (50.00)	0.080
Plaque eccentricity, n (%)	2 (25.00)	1 (6.25)	0.200
Plaque diffusion, n (%)	3 (37.50)	13 (81.25)	0.036
Area stenosis degree	96.30 (89.3, 99.0)	81.65 (75.0, 89.4)	0.009
Remodeling index	0.94 (0.31)	0.90 (0.34)	0.745
Remodeling categories, n (%)			0.519
Positive remodeling	2 (25.00)	5 (31.25)	
Negative remodeling	3 (37.50)	10 (62.50)	
No remodeling	3 (37.50)	1 (6.25)	
Wall area index	1.21 (0.46)	1.43 (0.80)	0.499
Enhancement grade, n (%)			0.545
Grade 1	0 (0.00)	2 (12.50)	
Grade 2	7 (87.50)	12 (75.00)	
Grade 3	1 (12.50)	2 (12.50)	
Enhancement index	37.99 (21.2, 46.9)	13.12 (12.1, 25.1)	0.008
IPH, n (%)	1 (12.50)	2 (12.50)	0.999

Continuous variables were represented as median (IQR) and mean (SD). Categorical variables were represented as frequency and percentage.
IPH, intraplaque hemorrhage; IPST, intraprocedural stent thrombosis.

Table 2 Association of plaque characteristics on HR-VWI with IPST

Characteristics of plaques	Model 1*	Model 2*		P value
	OR (95% confidence interval)	P value	OR (95% CI)	
Plaque diffusion	0.09 (0.01, 0.87)	0.038	0.02 (0.00, 1.36)	0.070
Area stenosis degree	1.19 (1.02, 1.39)	0.026	1.20 (1.01, 1.43)	0.044
Enhancement index	1.10 (1.02, 1.19)	0.018	1.17 (1.01, 1.36)	0.036

*OR and 95%CI were estimated from the multiple logistic regression models. Model 1 was adjusted for age. Model 2 was adjusted for age, hypertension, diabetes, smoking, alcohol consumption and regularities in the plaque surface.
CI, confidence interval; HR-VWI, high-resolution magnetic resonance vessel wall imaging; IPST, intraprocedural stent thrombosis; OR, odds ratio.

associated with IPST in patients who underwent intracranial stenting. Our finding may be helpful in angioplasty risk assessment and preoperative preparation for intracranial stenting. Previous studies found that antiplatelet resistance, long stenotic lesions, and use of more than one stent were associated with IPST. In this study, patients were treated with cilostazol when antiplatelet resistance was detected. Moreover, all patients were treated with only one Wingspan stent and followed a consistent procedure and standardized perioperative management, thus minimum potential interference to the largest extent. To our knowledge, this is the first study to investigate intracranial plaque characteristics associated with IPST during angioplasty for patients with ICAS.

Some studies on coronary and carotid artery atherosclerosis have shown that plaque enhancement is related to plaque vulnerability.^{19 20} Previous studies on HR-VWI about the pathological

DISCUSSION

In this study, we found that a higher plaque enhancement index and more severe degree of area stenosis may be independently

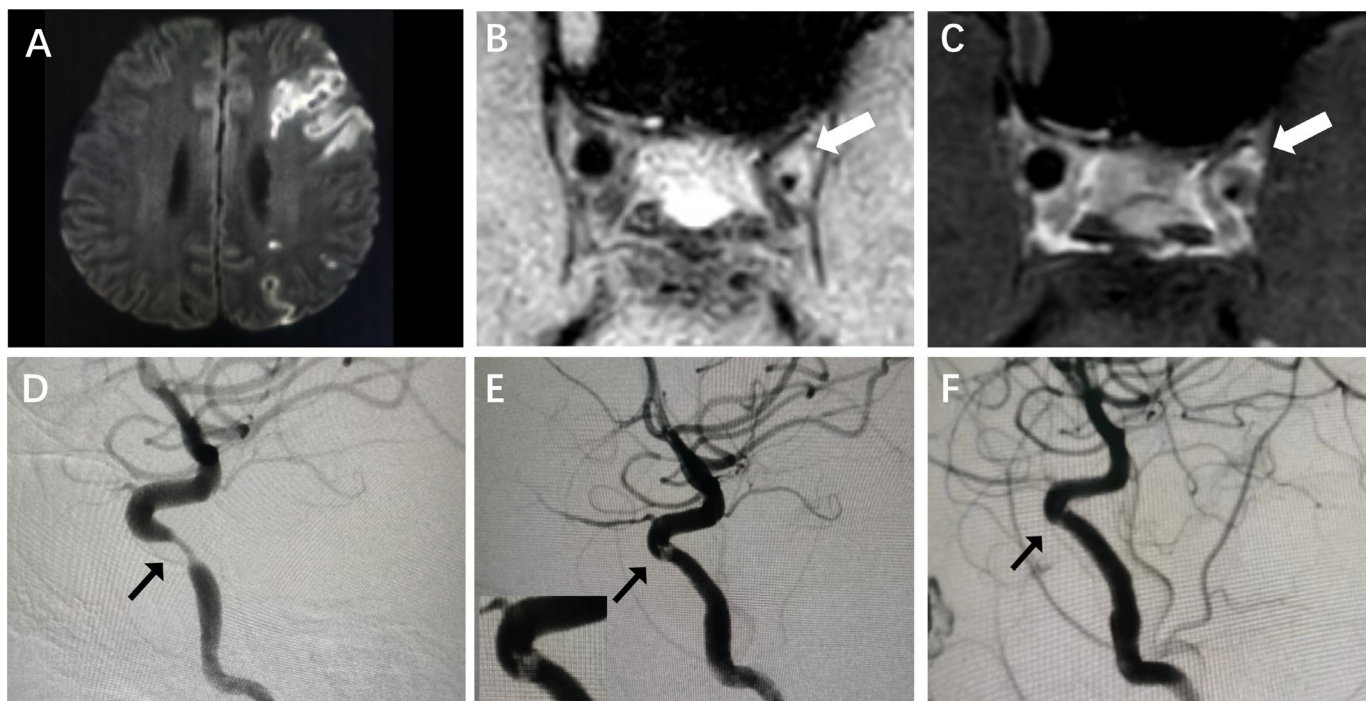


Figure 2 DSA of one patient with IPST. One adult patient presented with right limb weakness for 1 month. (A) Acute infarction in the center of the left semioval. (B) A diffuse distributive plaque in HR-VWI. (C) T1-weighted image after gadolinium injection. (D) Severe left internal carotid artery stenosis. (E) DSA showed stent thrombosis at 5 minutes after stent placement. (F) Complete recanalization after treatment with tirofiban.

Key: DSA: digital subtraction angiography; IPST, intraprocedural stent thrombosis; HR-VWI: high-resolution magnetic resonance vessel wall imaging.

specimen from carotid endarterectomy have shown that enhanced plaque was associated with abundant active inflammatory cells, neo-vessel formation, and fibrous cap thinning.²¹ The exact mechanism of intracranial plaque enhancement remains unclear because specimens are relatively inaccessible. However, we can understand the pathophysiology of plaque enhancement in the vessel wall of cerebral arteries through previous studies on extracranial carotid arteries. Previous studies also suggested that intracranial plaque enhancement on HR-VWI was associated with neovascularization, inflammation, and endothelial dysfunction leading to gadolinium leakage.²² Therefore, higher plaque enhancement, more active inflammation persisted in the plaque after stent placement promoted subsequent thrombosis. In the aforementioned studies, carotid plaque gadolinium enhancement has been associated with histological markers of vessel wall neovascularization and inflammation, both well-known markers of unstable atherosclerotic plaque.¹⁹ Enhancement detectable on MRI may be related to endothelial dysfunction present in the diseased intraplaque microvasculature of atherosclerotic vessels.²³ Such compromised microvascular endothelium may result in vascular leakage needed for gadolinium to accumulate in the perivascular spaces and become detectable on T1-weighted MRI sequences. An analogous process may occur in the intracranial vasculature. Thus, instability of atherosclerotic plaques secondary to neointima formation and inflammation can manifest itself as an acute thrombotic event. When the fibrous cap of vulnerable plaque ruptures under the influence of stenting, the plaque contents and the attached thrombus fall into the area covered by the stent and lead to thrombosis.

The degree of area stenosis is believed to be associated with ischemic stroke. Numerous studies have shown a significant association between vascular stenosis and the development and recurrence of symptomatic plaques or ischemic stroke.²⁴ In this study, we found a more severe degree of area stenosis in the IPST group compared with the non-IPST group. One possible mechanism is that severe ipsilateral stenosis is related to longer reperfusion times.²⁵ Another possible mechanism is that severe stenosis may place hemodynamic stress on brain circulation, which could lead to local endothelial injury, thrombus formation, plaque remodeling and rupture.

Vessels for intracranial stenting treatment including middle cerebral artery (MCA), basilar artery (BA), intracranial segment of internal carotid artery (ICA), and intracranial segment of vertebral artery (VA) were all involved in this study. There may be some differences in the structure of intracranial arteries in different segments especially for the intracranial segment of ICA considering the existence of vasa vasorum.²² Considering its potential effect, we analyzed the plaque characteristics of patients who underwent ICA stenting, although the sample was too small. We found that the enhancement index in the IPST group was higher than that in the non-IPST group, whether the patient underwent ICA stenting or other intracranial artery (MCA, BA and VA) stenting. Therefore, the effect of vasa vasorum in cavernous ICA on the results may be negligible in this study.

Our study had several limitations. First, the study included only eight patients with IPST, which may result in limited statistical power. In addition, all patients in the IPST group were male, potentially limiting the generalizability to female patients. Therefore, further studies are warranted in the future. Thirdly, all patients used the Gateway-Wingspan system, so the findings may be more applicable to patients proposed for self-expanding stents. Finally, this was a retrospective analysis, and only patients who underwent HR-VWI were included, which might introduce

a bias in patient selection. The findings of this study should be further validated in larger-scale prospective multicenter studies.

CONCLUSION

Intraprocedural stent thrombosis during angioplasty for patients with ICAS may be independently associated with a higher plaque enhancement index and a more severe degree of area stenosis on HR-VWI.

Author affiliations

¹Key Laboratory of Endocrine Glucose & Lipids Metabolism and Brain Aging, Ministry of Education; Department of Neurology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, P.R. China

²Department of Neurology, Liaocheng People's Hospital, Shandong University, Liaocheng, Shandong, P.R. China

³Department of Neurology, Shandong Provincial Hospital, Shandong University, Jinan, Shandong, P.R. China

⁴Department of Neurology, Liaocheng People's Hospital and Liaocheng Hospital Affiliated to Shandong First Medical University, Liaocheng, Shandong, P.R. China

⁵Department of Neurology, the second People's Hospital of Liaocheng, Liaocheng, Shandong, P.R. China

Contributors Conception/design: QS, ZX. Collection and/or assembly of data: PY, JJ, WW, QW, ZY, XL. Manuscript writing: XM, ZY, JJ, PY. Revised manuscript: XM, ZX, QS. Final approval of the manuscript and guarantor: QS.

Funding This study was supported by the Jinan Science and Technology Bureau (201704101), Department of Science and Technology of Shandong Province (ZR2020QH109, ZR2022LSW010), the National Natural Science Foundation (81971128, 82201477).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and the study protocol was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University (SWYX:NO.2021-012). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Qinjian Sun <http://orcid.org/0000-0002-9323-9154>

REFERENCES

- Feigin VL, Stark BA, Johnson CO, *et al*. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the global burden of disease study 2019. *Lancet Neurol* 2021;20:795-820.
- Zhou M, Wang H, Zeng X, *et al*. Mortality, morbidity, and risk factors in China and its provinces, 1990-2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2019;394:1145-58.
- Wang Y, Zhao X, Liu L, *et al*. Prevalence and outcomes of symptomatic intracranial large artery stenoses and occlusions in China: the Chinese Intracranial Atherosclerosis (CICAS) Study. *Stroke* 2014;45:663-9.
- White H, Boden-Albala B, Wang C, *et al*. Ischemic stroke subtype incidence among whites, blacks, and Hispanics: the Northern Manhattan Study. *Circulation* 2005;111:1327-31.
- Gao P, Wang T, Wang D, *et al*. Effect of Stenting plus medical therapy vs medical therapy alone on risk of stroke and death in patients with symptomatic intracranial stenosis: the CASSISS randomized clinical trial. *JAMA* 2022;328:534-42.

- 6 Zaidat OO, Fitzsimmons B-F, Woodward BK, *et al.* Effect of a balloon-expandable intracranial Stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis: the VISSIT randomized clinical trial. *JAMA* 2015;313:1240–8.
- 7 Sun L, Zhang J, Song Y, *et al.* n.d. Safety and efficacy of prophylactic Tirofiban infusion for acute intracranial Intraprocedural Stent thrombosis. *Sci Rep*;11:21326.
- 8 Chieffo A, Bonizzoni E, Orlic D, *et al.* Intraprocedural Stent thrombosis during implantation of sirolimus-Eluting Stents. *Circulation* 2004;109:2732–6.
- 9 Coelho AP, Lobo M, Nogueira C, *et al.* Overview of evidence on risk factors and early management of acute carotid Stent thrombosis during the last two decades. *J Vasc Surg* 2019;69:952–64.
- 10 Morofuji T, Inaba S, Hitsumoto T, *et al.* Usefulness of intravascular ultrasound for predicting risk of intraprocedural stent thrombosis. *Am J Cardiol* 2016;117:918–25.
- 11 Song JW, Pavlou A, Xiao J, *et al.* Vessel wall magnetic resonance imaging biomarkers of symptomatic intracranial Atherosclerosis: A meta-analysis. *Stroke* 2021;52:193–202.
- 12 Wang Y, Liu X, Wu X, *et al.* Culprit intracranial plaque without substantial stenosis in acute ischemic stroke on vessel wall MRI: a systematic review. *Atherosclerosis* 2019;287:112–21.
- 13 Gao P, Zhao Z, Wang D, *et al.* China Angioplasty and Stenting for Symptomatic Intracranial Severe Stenosis (CASSISS): a new, prospective, multicenter, randomized controlled trial in China. *Interv Neuroradiol* 2015;21:196–204.
- 14 Chung JW, Hwang J, Lee MJ, *et al.* Previous statin use and high-resolution magnetic resonance imaging characteristics of intracranial atherosclerotic plaque: the intensive statin treatment in acute ischemic stroke patients with intracranial atherosclerosis study. *Stroke* 2016;47:1789–96.
- 15 Xu Z, Li M, Hou Z, *et al.* Association between basilar artery configuration and vessel wall features: a prospective high-resolution magnetic resonance imaging study. *BMC Med Imaging* 2019;19:99.
- 16 Tian B, Zhu C, Tian X, *et al.* Baseline vessel wall magnetic resonance imaging characteristics associated with in-Stent Restenosis for intracranial Atherosclerotic stenosis. *J Neurointerv Surg* 2023;15:288–91.
- 17 Qiao Y, Zeiler SR, Mirbagheri S, *et al.* Intracranial plaque enhancement in patients with cerebrovascular events on high-spatial-resolution MR images. *Radiology* 2014;271:534–42.
- 18 Lou X, Ma N, Ma L, *et al.* Contrast-enhanced 3t high-resolution MR imaging in symptomatic atherosclerotic basilar artery stenosis. *AJNR Am J Neuroradiol* 2013;34:513–7.
- 19 Millon A, Bussel L, Brevet M, *et al.* Clinical and histological significance of gadolinium enhancement in carotid atherosclerotic plaque. *Stroke* 2012;43:3023–8.
- 20 Papini GDE, Di Leo G, Bandirali M, *et al.* Is carotid plaque contrast enhancement on MRI predictive for cerebral or cardiovascular events? A prospective cohort study. *J Comput Assist Tomogr* 2017;41:321–6.
- 21 Cai J, Hatsukami TS, Ferguson MS, *et al.* In vivo quantitative measurement of intact fibrous cap and lipid-rich necrotic core size in atherosclerotic carotid plaque: comparison of high-resolution, contrast-enhanced magnetic resonance imaging and histology. *Circulation* 2005;112:3437–44.
- 22 Portanova A, Hakakian N, Mikulis DJ, *et al.* Intracranial vasa vasorum: insights and implications for imaging. *Radiology* 2013;267:667–79.
- 23 Sluimer JC, Kolodgie FD, Bijnens APJJ, *et al.* Thin-walled microvessels in human coronary atherosclerotic plaques show incomplete endothelial junctions relevance of compromised structural integrity for intraplaque microvascular leakage. *J Am Coll Cardiol* 2009;53:1517–27.
- 24 Howard DPJ, Gaziano L, Rothwell PM, *et al.* Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol* 2021;20:193–202.
- 25 Gogela SL, Gozal YM, Zhang B, *et al.* Severe carotid stenosis and delay of reperfusion in endovascular stroke treatment: an interventional management of stroke-III study. *J Neurosurg* 2018;128:94–9.