Original Article

Patterns and implications of artery remodeling based on high-resolution vessel wall imaging in symptomatic severe basilar artery stenosis

Jichang Luo[1,2#], Xuesong Bai[1,2#], Qiuyue Tian[3], Long Li[1,2], Tao Wang[1,2], Ran Xu[1,2], Haozhi Gong[1,2], Yabing Wang[1,2], Yanfei Chen[1,2], Peng Gao[1,2,4], Jian Chen[1,2], Bin Yang[1,2], Yan Ma[1,2], Adam A. Dmytriw[5,6], Liqun Jiao[1,2,4]

[1]China International Neuroscience Institute (China-INI), Beijing, China; [2]Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing, China; [3]Beijing Key Laboratory of Clinical Epidemiology, School of Public Health, Capital Medical University, Beijing, China; [4]Department of Interventional Radiology, Xuanwu Hospital, Capital Medical University, Beijing, China; [5]Neurointerventional Program, Departments of Medical Imaging & Clinical Neurological Sciences, London Health Sciences Centre, Western University, London Ontario, Canada; [6]Neuroendovascular Program, Massachusetts General Hospital & Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Contributions: (I) Conception and design: L Jiao; (II) Administrative support: L Jiao, Y Ma; (III) Provision of study materials or patients: Y Wang, Y Chen, P Gao, J Chen, B Yang, Y Ma, L Jiao; (IV) Collection and assembly of data: J Luo, X Bai, L Li, R Xu, H Gong; (V) Data analysis and interpretation: Q Tian, J Luo, T Wang, AA Dmytriw; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Liqun Jiao. Department of Neurosurgery & Department of Interventional Radiology, Xuanwu Hospital, Capital Medical University, No. 45 Changchun Street, Xicheng District, Beijing 100053, China. Email: liqunjiao@sina.cn.

Background: Knowledge regarding the influence of arterial remodeling patterns on plaque characteristics and postoperative outcomes in patients with severe basilar artery (BA) stenosis after endovascular treatment is lacking. The purpose of this study was to investigate plaque characteristics, remodeling patterns, and perioperative outcomes in patients with severe BA stenosis.

Methods: A prospective cohort study was conducted on symptomatic patients with severe BA stenosis who underwent high-resolution MRI before endovascular treatment. The remodeling index, plaque burden, and area of stenosis were evaluated for each plaque. Based on the remodeling index calculated by high-resolution MRI, remodeling patterns were classified as negative remodeling (NR) or non-negative remodeling (non-NR). Baseline demographics, plaque features, and treatment characteristics were compared between the NR and non-NR groups. Correlations between the remodeling index, plaque burden, and stenosis severity were also examined.

Results: In total, 140 eligible patients were included and analyzed, including 91 non-NR cases and 49 NR cases. A strong correlation existed between the remodeling index and plaque burden ($r=0.973$, $P<0.001$), and a marginal correlation was observed between the remodeling index and degree of stenosis by area ($r=-0.261$, $P=0.0019$). There was no significant difference between the two groups in terms of perioperative complications related to ischemic events and new ischemic cerebral lesions (NICLs).

Conclusions: Under the current submaximal angioplasty and/or stenting treatment paradigms, remodeling patterns may not influence the outcome of ischemic events and NICLs. However, the remodeling index is strongly associated with plaque burden, which may provide insight for the evaluation of severe BA stenosis. Further research is warranted.

Keywords: Basilar stenosis; atherosclerosis; magnetic resonance imaging; vascular remodeling; stroke

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Introduction

Symptomatic severe basilar artery (BA) stenosis is a major cause of ischemic stroke, accounting for 15% of all strokes and 10.7% of ischemic strokes annually, despite the existence of aggressive medical therapies (1). Endovascular treatment, such as angioplasty and stenting, are available for stroke prevention in symptomatic patients with severe (≥70%) BA stenosis. Periprocedural stroke or death is significantly higher in the posterior circulation than the anterior circulation, with a reported risk of 21.6% in the BA (2). Perforator infarction is the main cause of periprocedural stroke or death in patients with severe BA stenosis after endovascular treatment (2,3).

Arterial remodeling, comprising positive, intermediate, and negative remodeling (NR), reflects incremental changes of an arterial wall in response to stress-related atherosclerotic processes and may affect the outcomes of endovascular treatment for ischemic lesions (4). Positive remodeling (PR) is regarded as the compensatory outward expansion of the arterial wall to maintain lumen patency despite plaque development. Luminal compromise occurs principally due to plaque expansion exceeding the limit of compensatory remodeling (5,6). In contrast, NR is defined as the adaptive constriction of the vessel, which may exacerbate luminal stenosis. Intermediate remodeling is a state between PR and NR, in which marginal changes of the outer wall are exhibited despite luminal stenosis (7,8). A previous study reported that NR was associated with an increased risk of perforator stroke in patients with basilar stenosis; however, this study was limited by its small sample size (9). Several studies have shown that PR may increase the risk of major adverse cardiac events in patients undergoing coronary intervention, whereas NR may increase the risk of perioperative complications, such as vascular injury, during treatment (6,8). It is still unclear whether remodeling patterns are related to the occurrence of perioperative complications after endovascular treatment in symptomatic patients with severe BA stenosis.

High-resolution MRI (HR-MRI) is a reliable imaging modality for the qualitative and quantitative assessment of arterial remodeling. Several studies to evaluate HR-MRI have suggested a relationship between remodeling patterns and plaque characteristics in extracranial and intracranial arteries (10-12). Nevertheless, studies focusing on the plaque characteristics and different remodeling patterns in patients with BA stenosis are scarce. In the current study, we sought to determine the relationship between plaque characteristics and perioperative complications in patients with severe BA stenosis, with a focus on remodeling patterns. We present the following article in accordance with the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-771/rc) (13).

Methods

Study design

The study cohort was derived from the Clinical Registration Trial of Intracranial Stenting for Patients with Symptomatic Intracranial Artery Stenosis (CRTICAS) database (ClinicalTrials.gov Identifier: NCT01994161) (14). The protocol, which adhered to the ethical principles of the Declaration of Helsinki (as revised in 2013) (15) and the Guideline for Good Clinical Practice, was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University (No. [2013] 004). Informed consent was obtained from all patients.

From December 2013 to December 2015, patients with BA stenosis at several high-volume tertiary centers in China were enrolled for analysis according to the following criteria: (I) had BA stenosis of more than 70% confirmed by digital subtraction angiography (DSA); (II) had ischemic symptoms caused by BA stenosis including dizziness, vertigo, headache, double vision, double vision, slurred speech, numbness, or weakness of limbs; (III) treated with endovascular therapy; (IV) underwent HR-MRI before intervention; and (V) underwent MRI within the 72 hours before and the 72 hours after intervention. The following patients were excluded: (I) patients with a history of acute stroke caused by BA occlusion; (II) patients who had received simultaneous endovascular therapy of another intracranial or extracranial vessel; (III) patients with BA stenosis in combination with moderate-to-severe vertebral artery stenosis; and (IV) patients whose BA stenosis had a non-atherosclerotic cause (e.g., Moyamoya disease,

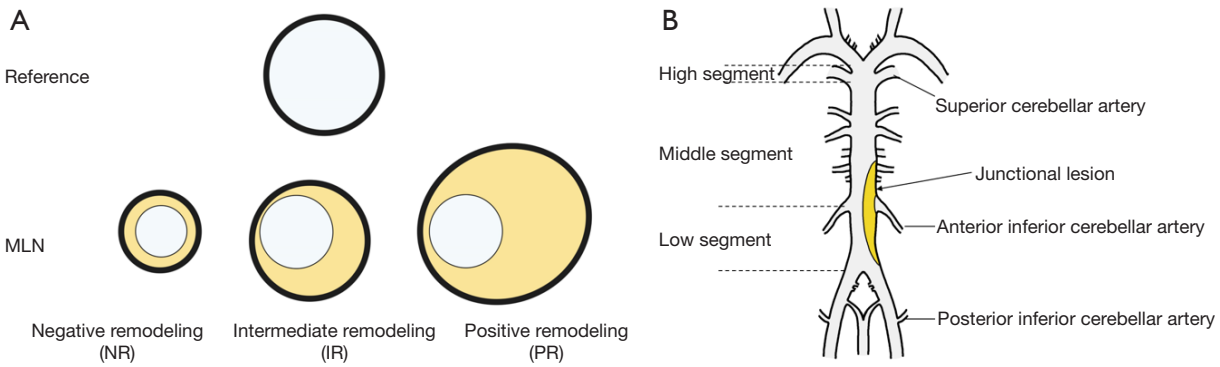

Figure 1 The schematic of plaque remodeling and plaque distribution. (A) Arterial remodeling patterns include negative remodeling (NR), intermediate remodeling (IR), and positive remodeling (PR) at the site of maximal luminal narrowing (MLN) compared with the reference site. (B) The anatomy of the basilar artery shows the segmentation referred to as the superior cerebellar artery and anterior inferior cerebellar artery. A junctional lesion was considered when the lesion crossed the anterior inferior cerebellar artery.

vasculitis, or dissection).

The baseline clinical information of all eligible patients was collected for analysis.

Imaging protocols

A 3.0-T MRI scanner (Magnetom Spectra; Siemens Healthineers, Erlangen, Germany) with a standard 8-channel head coil was used to image all eligible patients with BA stenosis. The multi-sequence protocol is described in Table S1. Imaging acquisition was performed in the sagittal plane covering the BA vessel, and multiplanar reconstructions were obtained for image analysis.

Imaging measurement and analysis

All images were independently reviewed by radiologists at the IsCore Image Corelab (http://imagecorelabcn.com/en/). The radiologists did not participate in the statistical analyses and were blinded to the clinical data of the patients. Five percent of the data in the cohort were used to train raters before a formal assessment of the imaging data was performed. The formal assessment was conducted when the agreement achieved between the two raters (reliability >0.75) was graded 'excellent'.

The characteristics of BA lesions, such as diameter, area, and signal intensity, were measured. The lumen diameter, vessel area (VA), and lumen area (LA) at the site of maximal luminal narrowing (MLN) and the reference site were manually traced for measurement. According to the Warfarin versus Aspirin for Symptomatic Intracranial Disease (WASID) criteria, the reference site was defined as the normal segment proximal to the stenosis and the distal vessel was used when the proximal segment was diseased (16).

The parameters based on HR-MRI and DSA were defined as follows: wall area (WA), VA – LA; plaque burden, $[(WA_{MLN} - WA_{reference})/VA_{MLN}] \times 100\%$; and remodeling index, $[VA_{MLN}/VA_{reference}]$. The classification of vessel remodeling was divided according to the remodeling index into the following three types: PR (≥1.05), NR (≤0.95), and intermediate remodeling (0.95–1.05; *Figure 1A*). For simplicity, PR and intermediate remodeling were classified as non-NR.

The cross-sectional culprit lesion was divided by two perpendicular lines into the following quadrants, as described in a previous study: ventral, dorsal, left, and right (17). For simplicity, the left and right sites were classified as lateral sites. If a plaque was large and the thickest part spanned two quadrants, it was defined as being distributed across more than two quadrants.

In DSA imaging, the BA was divided by branches of the anterior inferior cerebellar artery and superior cerebellar artery into three segments: low, middle, and high (18). Due to its rarity (1.2% of the incidence reported), the single high segment identified was sorted into the middle segment (18). Classification as a junctional segment lesion was considered when lesions crossed the anterior inferior cerebellar artery (*Figure 1B*).

The stenotic diameter based on DSA was calculated as [1 – (luminal diameter at MLN)/(luminal diameter at reference site)] ×100%. The degree of stenosis by area

based on HR-MRI was calculated as [1 – LA at MLN/LA at reference site] ×100%.

Interventional procedure and outcomes assessment

All patients were treated by neurointerventionalists with at least 15 years of experience in endovascular treatment. Therapeutic strategies, including primary angioplasty, balloon-mounted stent, and self-expanding stent, were determined by experienced operators and informed by lesion characteristics (19). In the days leading up to the procedure, each patient was prescribed aspirin (100 mg daily) and clopidogrel (75 mg daily). A 2/3 mg/kg dose of systemic heparin was injected intravenously during the procedure. An additional half dose of heparin was injected after 1 hour (20). After intervention, dual antiplatelet therapy was maintained for 3 months with aspirin (100 mg daily) and clopidogrel (75 mg daily).

Perioperative cerebrovascular events, including stroke, transient ischemic attack (TIA), and new ischemic cerebral lesions (NICLs), were assessed by neurosurgeons and neuroradiologists based on patients' clinical information and imaging. Stroke, including ischemic and hemorrhage stroke, was defined as a neurological deficit lasting for more than 24 hours. A TIA was defined as a neurological deficit lasting for less than 24 hours (21). An NICL of the BA territory was identified as a new high signal on diffusion-weighted imaging and a new low signal on apparent diffusion coefficient imaging within 72 hours after the operation (22). The mechanism of stroke or NICLs in the distribution of the BA was divided into artery-to-artery (A-A) embolism, local perforator infarction, and mixed mechanism (19). For simplicity, mixed mechanisms involving local perforator infarction were also classified as perforator infarction in this study.

Statistical analysis

Analyses were conducted with Statistical Analysis System (SAS) software, v. 9.4 (SAS Institute Inc., Cary, NC, USA). Quantitative variables were presented as mean ± standard deviation or median with interquartile range, and qualitative variables were presented as number and percentage. We performed descriptive analyses of all study participants, dividing them into NR and non-NR groups. Comparisons of categorical variables were performed using the χ^2 test or Fisher's exact test, as appropriate. The Student's *t*-test or Wilcoxon tests were used to compare quantitative variables. Scatter diagrams and fitted curves of the remodeling index, plaque burden, and degree of stenosis by area were produced using the ggplot2 package in R v. 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria; http://www.R-project.org/) software. The evaluation of correlations between these variables was performed by a Spearman rank correlation analysis with two-tailed significance. The value of $P<0.05$ was considered statistically significant.

Logistic regression was performed to assess whether remodeling patterns were associated with the perioperative composite outcome of TIA, stroke, or both. Age and sex were treated as prognostic factors when adjusting the model. In cases where the comparison of the two groups revealed an imbalance between them ($P=0.2$), the imbalance factors were also introduced as adjustment variables. The same strategy was used for analysis of NICLs on diffusion-weighted imaging.

Results

Baseline characteristics

There were 281 consecutive patients with symptomatic severe BA stenosis treated with endovascular therapy. Following screening, 140 patients were eligible for inclusion in the study (Figure S1). The average age of these patients was 61.9±7.7 years. According to the remodeling pattern, 91 (65.0%) patients were classified as NR and 49 (35.0%) patients as non-NR. There was no significant difference between the two groups in terms of baseline characteristics, such as age, sex, and preoperative modified Rankin Scale score (*Table 1*).

Characteristics based on HR-MRI, DSA, and treatment

The NR group had a higher degree of stenosis by area than did the non-NR group (81.8%±9.1% *vs.* 78.1%±8.3%, respectively; $P=0.019$) but lower proportions of low and junctional segment stenosis (28.6% *vs.* 46.9%, 2.2% *vs.* 8.2%, respectively; $P=0.010$). The plaque burden (–8.6%±40.4 % *vs.* 33.6%±12.2%, respectively; $P<0.001$) and the remodeling index (0.7±0.2 *vs.* 1.2±0.2, respectively; $P<0.001$) were lower in the NR group than in the non-NR group (*Tables 2,3*). There was no difference in the treatment type, diameter ratio of balloon/stent to stenosis, or reference site between the two groups (*Table 3*). Regarding the relationships between the remodeling index, plaque burden, and degree of stenosis by area, the remodeling index was

Table 1 Baseline characteristics of patients with severe basilar artery stenosis

Items	All patients (n=140)	NR (n=91)	Non-NR (n=49)	P value
Age, year, mean ± SD	61.9±7.7	61.5±7.9	62.6±7.5	0.442
Sex, n (%)				0.386
Male	106 (75.7)	71 (78.0)	35 (71.4)	
Female	34 (24.3)	20 (22.0)	14 (28.6)	
BMI, kg/m^2, mean ± SD	26.2±3.0	26.4±2.9	26.0±3.4	0.540
Hypertension, n (%)	117 (83.6)	77 (84.6)	40 (81.6)	0.650
DM, n (%)	58 (41.4)	36 (39.6)	22 (44.9)	0.541
Hyperlipidemia, n (%)	36 (25.7)	23 (25.3)	13 (26.5)	0.871
CAD, n (%)	14 (10.0)	10 (11.0)	4 (8.2)	0.813
Smoking, n (%)	58 (41.4)	36 (39.6)	22 (44.9)	0.541
Drinking, n (%)	38 (27.1)	23 (25.3)	15 (30.6)	0.498
OTA, day, median (IQR)	44.7 (40.9)	42.6 (40.0)	50.0 (40.5)	0.420
Qualifying event, n (%)				0.650
TIA	23 (16.4)	14 (15.4)	9 (18.4)	
Stroke	117 (83.6)	77 (84.6)	40 (81.6)	
Preoperative mRS, n (%)				0.115
<2	125 (89.3)	84 (92.3)	41 (83.7)	
≥2	15 (10.7)	7 (7.7)	8 (16.3)	

NR, negative remodeling; SD, standard deviation; BMI, body mass index; DM, diabetes mellitus; CAD, coronary artery disease; OTA, onset to admission; IQR, interquartile range; TIA, transient ischemic attack; mRS, modified Rankin Scale score.

Table 2 Lesion characteristics of patients with severe basilar artery stenosis based on high-resolution MRI

Items	All patients (n=140)	NR (n=91)	Non-NR (n=49)	P value
OTE, day, median (IQR)	37.5 (44.8)	32.0 (42.0)	43.0 (43.5)	0.512
Lesion location (axial view), n (%)				0.865
Ventral	18 (12.9)	13 (14.3)	5 (10.2)	
Lateral	31 (22.1)	21 (23.1)	10 (20.4)	
Dorsal	48 (34.3)	30 (32.9)	18 (36.7)	
≥2 quadrants	43 (30.7)	27 (29.7)	16 (32.7)	
Stenosis (area), %, mean ± SD	80.5±9.0	81.8±9.1	78.1±8.3	0.019*
Plaque burden, %, median (IQR)	9.3 (43.9)	–8.6 (40.4)	33.6 (12.2)	<0.001*
Remodeling index, median (IQR)	0.8 (0.4)	0.7 (0.2)	1.2 (0.2)	<0.001*

*, P<0.05. NR, negative remodeling; OTE, onset to examination of HR-MRI; IQR, interquartile range; SD, standard deviation; HR-MRI, high-resolution MRI.

Table 3 Lesion features of patients with severe basilar artery stenosis based on digital subtraction angiography and treatment type

Items	All patients (n=140)	NR (n=91)	Non-NR (n=49)	P value
Lesion location (coronal view), n (%)				0.010*
Low segment	49 (35.0)	26 (28.6)	23 (46.9)	
Middle segment	85 (60.7)	63 (69.2)	22 (44.9)	
Junctional segment	6 (4.3)	2 (2.2)	4 (8.2)	
Diameter at MLN, mm, mean ± SD	0.6±0.2	0.6±0.2	0.6±0.2	0.876
Diameter at reference, mm, mean ± SD	2.7±0.5	2.8±0.6	2.6±0.5	0.141
Plaque length, mm, median (IQR)	5.9 (3.8)	5.6 (3.6)	6.2 (3.3)	0.139
Stenosis (diameter), %, median (IQR)	77.7 (9.3)	77.8 (8.9)	77.2 (9.7)	0.287
Treatment type, n (%)				0.106
PA	26 (18.6)	14 (15.4)	12 (24.5)	
BMS	30 (21.4)	24 (26.4)	6 (12.2)	
SES	84 (60.0)	53 (58.2)	31 (63.3)	
Diameter ratio of stenosis#, median (IQR)	5.2 (3.0)	5.2 (3.1)	5.4 (2.8)	0.756
Diameter ratio of reference#, median (IQR)	1.2 (0.3)	1.1 (0.3)	1.2 (0.3)	0.428

*, P<0.05; #, the diameter ratio was defined as the maximal diameter of the implant divided by the vessel diameter at the MLN reference site. NR, negative remodeling; MLN, maximal luminal narrowing; SD, standard deviation; IQR, interquartile range; PA, primary angioplasty; BMS, balloon-mounted stent; SES, self-expansion stent.

strongly associated with plaque burden, fitting an inverse equation between them (r=0.973, P<0.001; *Figure 2A*) and marginally associated with the degree of stenosis by area (r=–0.261, P=0.0019; *Figure 2B*). The degree of stenosis by area was not related to plaque burden (r=0.068, P=0.520; *Figure 2C*).

Periprocedural outcomes

Regarding the composite outcome of TIA/stroke, there were 11 (12.1%) events in the NR group (3 TIAs, 5 A-A strokes, and 3 perforator strokes) and 5 (10.2%) events in the non-NR group (3 A-A strokes and 2 perforator strokes). Based on univariable analysis, none of the subcategories of TIA/stroke (TIA, A-A stroke, perforator stroke) showed significant differences (*Table 4*). After multivariable adjustment for age, sex, preoperative modified Rankin Scale score, stenosis site, plaque length, stenosis by area, plaque burden, and remodeling pattern, the NR group showed no significant difference in perioperative outcome compared to the non-NR group for these composite events.

In addition, postoperative NICLs on diffusion-weighted imaging were not rare in either group, with 47 (51.6%) cases in the NR group (38 A-A NICLs and 9 perforator NICLs) and 29 (59.2%) cases in the non-NR group (19 A-A NICLs and 10 perforator NICLs). Univariable analysis showed no significant difference between the NR and non-NR groups in total postoperative NICLs or all NICLs, and the difference remained insignificant after multivariable adjustment for confounders (*Table 4*).

Discussion

Arterial remodeling is an adaptive process vessels undergo in response to mechanical or chemical factors, which arise principally from blood flow and inflammation, respectively. Remodeling patterns may indicate differences in pathophysiology during the atherosclerotic process. It is likely that PR is a mechanism of compensation for plaque accumulation to prevent luminal stenosis. However, a larger burden ultimately increases the risk of plaque rupture; thus, there is an apparent limit to this compensatory process. In contrast, NR appears to accelerate luminal narrowing but the risk of plaque rupture is smaller when the plaque itself is diminutive (23). In the current study, we found that NR is dominant in symptomatic patients with severe BA stenosis

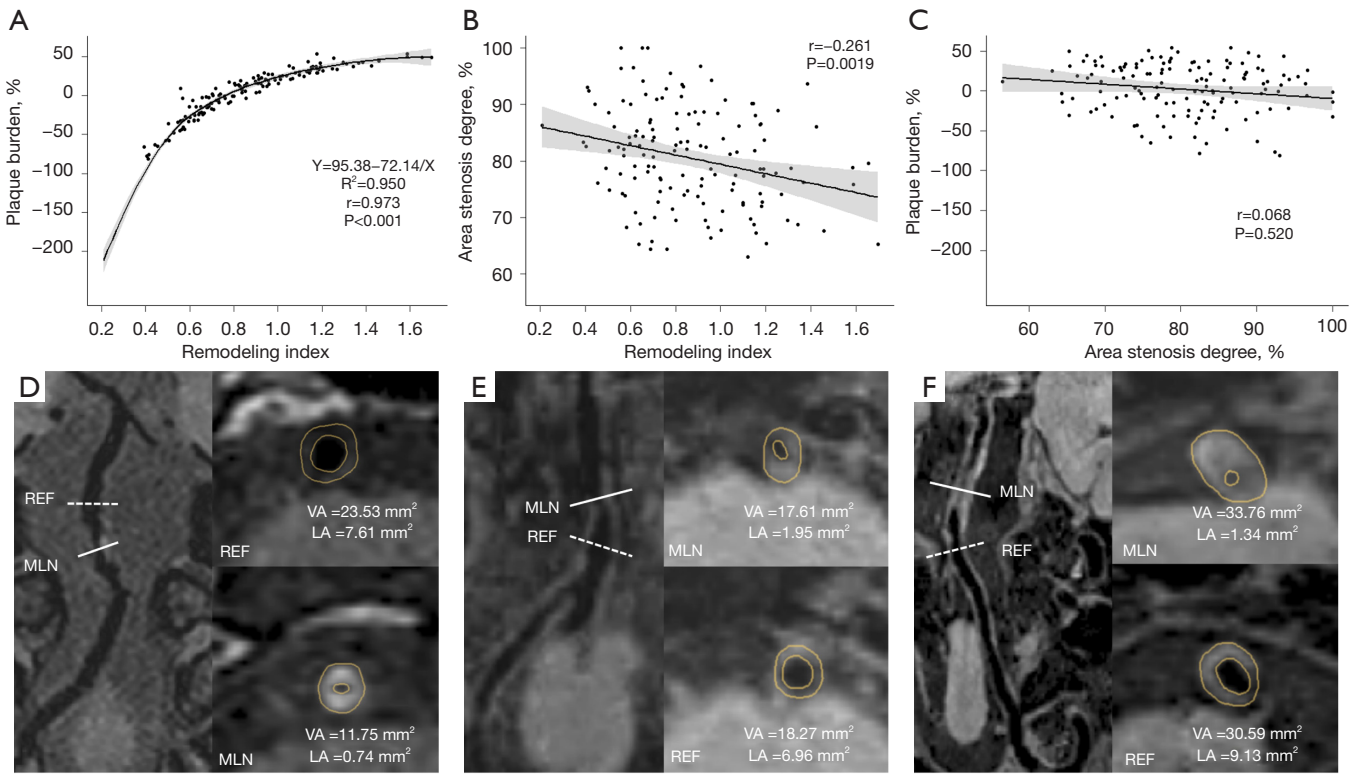

Figure 2 The graphs in the upper row show the relationships between the remodeling index, plaque burden, and area of the degree of stenosis. (A) The remodeling index was strongly associated with plaque burden, fitting an inverse equation between them (r=0.973, P<0.001). (B) The remodeling index was marginally associated with the area of the degree of stenosis (r=−0.261, P=0.0019). (C) The area of the degree of stenosis was not related to plaque burden (r=0.068, P=0.520). The images in the lower row demonstrate basilar artery remodeling patterns based on high-resolution magnetic resonance. Vessel area (VA) and lumen area (LA) at the site of maximal luminal narrowing (MLN) and reference (REF) site were manually traced for measuring. (D) An adult patient showed negative remodeling with a plaque burden of −41.9% and remodeling index of 0.50. (E) An adult patient showed intermediate remodeling with a plaque burden of 24.7% and remodeling index of 0.96. (F) An adult patient showed positive remodeling with a plaque burden of 32.5% and remodeling index of 1.10.

Table 4 Comparison of perioperative outcomes between the negative remodeling and non-negative remodeling groups

Outcomes	NR group (n=91)	Non-NR group (n=49)	Unadjusted P	Adjusted P*	Adjusted OR (95% CI)
TIA/stroke, n (%)	11 (12.1)	5 (10.2)	0.739	0.226	2.86 (0.52–14.29)
TIA	3 (3.3)	0 (0)	0.552	NA	NA
A-A stroke	5 (5.5)	3 (6.1)	1.000	0.345	2.86 (0.32–25.00)
Perforator stroke	3 (3.3)	2 (4.1)	1.000	0.601	0.44 (0.02–9.09)
NICLs on DWI, n (%)	47 (51.6)	29 (59.2)	0.394	0.663	0.82 (0.34–2.00)
A-A NICLs	38 (41.7)	19 (38.8)	0.732	0.945	0.97 (0.40–2.38)
Perforator NICLs	9 (9.9)	10 (20.4)	0.089	0.718	0.77 (0.19–3.13)

*, outcomes adjusted by age, sex, preoperative modified Rankin Scale score, lesion location (coronal view), plaque length (mm), degree of stenosis (area), and plaque burden. NR, negative remodeling; OR, odds ratio; CI, confidence interval; TIA, transient ischemic attack; A-A, artery-to-artery; NICLs, new ischemic cerebral lesions; DWI, diffusion-weighted imaging.

and is associated with a lower plaque burden. Moreover, the relationship between the mathematical formulas associated with the remodeling index and plaque burden has a high degree of fit to an inverse equation.

The prevalence of arterial remodeling patterns varies among arteries and clarification of this variation may provide deeper insight into atherosclerotic progress and the occurrence of clinical events (24). For example, PR is prevalent in the renal artery and common carotid artery, whereas NR is prevalent in the femoral artery (23). Compared to the anterior circulation, the posterior circulation appears to be more capable of PR as it has a lower blood flow and less sympathetic innervation (25-28). However, we observed NR to be more common in patients with severe BA stenosis. Studies on coronary atherosclerosis have shown NR to occur more frequently than PR in lesions imparting symptomatic severe stenosis, which is in keeping with our findings for the BA (29). We speculate that the reasons for the high prevalence of NR in this study may include the following. Firstly, plaques with NR are relatively stable, and symptomatic presentations are mainly caused by a luminal stenosis obstructing the blood flow. In contrast, symptoms are more likely to occur in patients with PR following plaque rupture due to a large plaque size. Therefore, symptomatic patients with PR may not have severe stenosis and, thus, were not enrolled for endovascular treatment, in keeping with global practice patterns for intracranial atherosclerosis (30). Secondly, histopathological studies suggest that PR may transform into NR due to intimal healing and proliferation in response to repetitive micro-ruptures of a high-risk plaque (31,32). Furthermore, the risk of endovascular treatment is higher for the posterior circulation than it is for the anterior circulation (2). Therefore, we focused our research on severe BA stenosis. The present study, to our knowledge, is the first to analyze distribution differences in remodeling patterns in patients with severe BA stenosis. NR is more common in the middle segment of the BA than in the low or junctional segment. This difference in remodeling patterns in the BA may be associated with anatomical and hemodynamic factors (33), and understanding it would in turn provide researchers with a unique basis for understanding BA atherosclerosis.

Importantly, we have provided a new perspective on the relationships between remodeling patterns and plaque characteristics. The remodeling index was strongly associated with plaque burden using an inverse equation, which may provide a simple and objective radiographic approach to quantify the plaque burden for BA stenosis by overcoming the complexity of plaque burden measurement (*Figure 2D-2F*). On the other hand, this study observed that the plaque burden did not infinitely increase but reached a plateau along with arterial PR. Additionally, the remodeling index was marginally associated with the degree of stenosis by area. Previous studies have suggested that NR accelerates luminal narrowing, leading to a higher degree of stenosis by area (34,35). The association between the remodeling index, plaque burden, and degree of stenosis by area may simplify the assessment of plaque characteristics in future clinical practice.

In terms of perioperative complications, no association was found between BA remodeling patterns and the risk of an adverse perioperative outcome, which differs from the findings of related studies in coronary artery research. A previous coronary investigation reported that selecting balloon or stent size based solely on the reference luminal diameter but ignoring constriction of the outer wall at the lesion site may increase the risk of vessel dissection and rupture (5). Several subsequent studies on intracranial atherosclerotic stenosis reported that submaximal balloon inflation may lower the risk of perioperative complications compared with maximal balloon inflation (36). Endovascular treatment for intracranial stenosis has been progressively more judicious in the post-Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial era (37). Strict selection of patients, submaximal balloon inflation and stenting, and operator experience may be factors that improve the outlook of endovascular therapy (19).

Study limitations

In this study, there were some limitations. Firstly, despite of the small sample size, it is the largest study to date to analyze HR-MRI-based plaque characteristics and clinical outcomes in patients with symptomatic BA stenosis. Secondly, only half of the patients with symptomatic BA stenosis in CRTICAS were enrolled into the study because HR-MRI was not available at several centers in the early stage of the study, which may have resulted in a slight selection bias. In addition, the measurement of several variables, including the remodeling index, plaque burden, and degree of stenosis, was dependent on the reference site adjacent to the lesion. There is evidence that the reference site may have also undergone remodeling, resulting in the underestimation or overestimation of these variables (5). Furthermore, the current study included only patients with

symptomatic severe BA stenosis. Consequently, the findings in the current study regarding remodeling patterns and implications may not be applicable to patients with mild to moderate symptomatic BA stenosis, or to patients with asymptomatic BA stenosis. Finally, arterial remodeling, as a dynamic process, along with plaque development, requires further research to examine the impact it has on patients' long-term outcomes.

Conclusions

Under the current treatment paradigms for BA stenosis, remodeling patterns may not be associated with perioperative outcomes of ischemic events or NICLs but with plaque characteristics, especially plaque burden. A fitted curve and equation between the remodeling index and plaque burden may provide a straightforward and objective method for quantifying the plaque burden in severe BA stenosis. However, further studies on the relationship among plaque characteristics in BA stenosis are warranted.

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Footnote

Reporting Checklist: The authors have completed the STROCSS reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-771/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-771/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The protocol adheres to the ethical principles of the Declaration of Helsinki (as revised in 2013) and Guideline for Good Clinical Practice, and was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University (No. [2013] 004). Informed consent was obtained from all patients.

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Supplementary

Table S1 Parameters of sequences on a 3.0-T Siemens MR scanner

Parameters	TOF	T1
TR (ms)	22	900
TE (ms)	3.74	20
FOV (mm^2)	200×175	200×158
Matrix	320×240	320×252
Slice thickness (mm)	0.6	0.7
Flip angle (°)	18	Variable
Turbo factor (ms)	–	52
Bandwidth (Hz/pixel)	186	326
Scan time	4 min 55 s	9 min 53 s

TOF, time of flight; T1, T1-weighted imaging; TR, repetition time; TE, echo time; FOV, field of view.

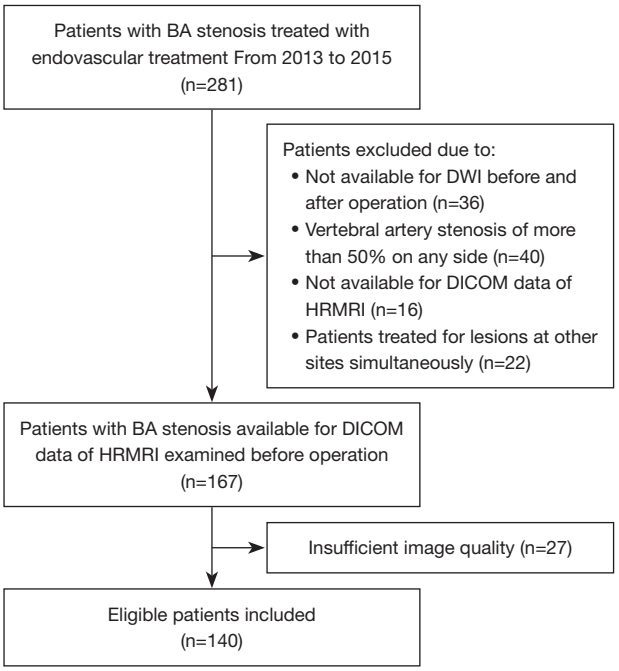

Figure S1 Flow chart of screening

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