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New Diffusion Abnormalities Following Endovascular Treatment for Intracranial Atherosclerosis

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Conflicts of interest are listed at the end of this article.
See also the editorial by Russell in this issue.

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Background: There are limited data on new ischemic brain lesions after endovascular treatment for symptomatic intracranial atherosclerotic stenosis (ICAS).

Purpose: To investigate the *(a)* characteristics of new ischemic brain lesions at diffusion-weighted MRI (new diffusion abnormalities) after endovascular treatment, *(b)* characteristics between those treated with balloon angioplasty and stent placement procedures, and *(c)* predictors of new ischemic brain lesions.

Materials and Methods: Patients with symptomatic ICAS in whom maximum medical therapy failed were prospectively enrolled between April 2020 and July 2021 from a national stroke center and underwent endovascular treatment. All study participants underwent thin-section diffusion-weighted MRI (voxel size, 1.4 × 1.4 × 2 mm^3 with no section gap) before and after treatment. The characteristics of new ischemic brain lesions were recorded. Multivariable logistic regression analysis was performed to determine potential predictors of new ischemic brain lesions.

Results: A total of 119 study participants (mean age, 59 years ± 11 [SD]; 81 men; 70 treated with balloon angioplasty and 49 with stent placement) were enrolled. Of the 119 participants, 77 (65%) had new ischemic brain lesions. Five of the 119 participants (4%) had symptomatic ischemic stroke. New ischemic brain lesions were located in (61%, 72 of 119) and/or beyond (35%, 41 of 119) the territory of the treated artery. Of the 77 participants with new ischemic brain lesions, 58 (75%) had lesions located in peripheral brain areas. There was no evidence of a difference in the frequency of new ischemic brain lesions between the balloon angioplasty and stent groups (60% vs 71%, $P = .20$). In adjusted models, cigarette smoking (odds ratio [OR], 3.6; 95% CI: 1.3, 9.7) and more than one operative attempt (OR, 2.9; 95% CI: 1.2, 7.0) were independent predictors of new ischemic brain lesions.

Conclusion: New ischemic brain lesions on diffusion-weighted MRI scans were common after endovascular treatment for symptomatic intracranial atherosclerotic stenosis, and occurrence may be associated with cigarette smoking and the number of operative attempts.

Clinical trial registration no. ChiCTR2100052925

Supplemental material is available for this article.

Primary balloon angioplasty or stent placement may be selected to treat patients with symptomatic intracranial atherosclerotic stenosis (ICAS) in whom the maximum medical regimen failed (1–3). The main concern for wide clinical practice of endovascular treatment for patients with ICAS is the high risk of stroke and death within 30 days of the procedure. The Stenting and Aggressive Medical Management for the Prevention of stroke in Intracranial Stenosis (SAMMPRIS) trial demonstrated that the 30-day rate of stroke or death in the stent placement arm was 14.7%, including 10.3% ischemic stroke in the territory of qualifying artery and 4.5% symptomatic intracranial hemorrhage (4–6). Previous studies reported that the frequency of new ischemic brain lesions detectable at diffusion-weighted MRI (new diffusion abnormalities) after endovascular procedures, such as diagnostic angiography, carotid artery stent placement, intracranial aneurysm coiling, and cardiac valve replacement, was much higher than expected, but most of them were clinically silent (7–12). A systematic review reported that silent ischemic lesions are associated with subtle neurologic deficits such as cognitive decline, dementia, and depressive symptoms (13). The substudy of the International Carotid Stenting Study showed that silent ischemic lesions after carotid

Abbreviations

DWI = diffusion-weighted imaging, ICAS = intracranial atherosclerotic stenosis, OR = odds ratio

Summary

Although new ischemic brain lesions on diffusion-weighted MRI scans were common after endovascular treatment for intracranial atherosclerotic stenosis, symptomatic ischemic stroke was uncommon.

Key Results

- In a prospective study of 119 study participants with intracranial atherosclerotic stenosis undergoing endovascular treatment, the frequency of new ischemic brain lesions on posttreatment thin-section diffusion-weighted MRI scans was 65%, including 546 ischemic lesions; only 4% of participants were symptomatic.
- More than one operative attempt (odds ratio [OR], 2.9; $P = .02$) and cigarette smoking (OR, 3.6; $P = .01$) were independent predictors of new ischemic brain lesions after endovascular treatment.

artery stent placement may be harmful to cognition (14). Furthermore, silent ischemic lesions could be a surrogate marker of future stroke recurrence in patients with acute ischemic stroke (15) or carotid artery stent placement (16). However, the frequency and characteristics of new ischemic brain lesions after endovascular treatment for ICAS have rarely been reported in a systematic fashion in a prospective study.

The purposes of our study were to *(a)* determine the frequency, distributions, locations, and numbers of new ischemic brain lesions before and after endovascular treatment for patients with ICAS; *(b)* compare the characteristics of new lesions between the balloon angioplasty group and the stent placement group; and *(c)* identify the potential predictors of new ischemic brain lesions after endovascular treatment for patients with ICAS.

Materials and Methods

Study Design and Participants

This study was registered at *www.chictr.org.cn* (registration no. ChiCTR2100052925). The study protocol was approved by the ethics committee of our institution (no. KY2019-083-03). Written informed consent was obtained from all participants or their legal guardians. Patients presenting with symptomatic ICAS to an endovascular treatment team in a national stroke center were consecutively and prospectively enrolled between April 2020 and July 2021. All enrolled study participants underwent MRI 1–3 days before and after endovascular treatment. Inclusion criteria were as follows: *(a)* age at least 18 years; *(b)* ischemic stroke or transient ischemic attack attributed to at least 70% stenosis of a major intracranial artery, including the middle cerebral artery, intracranial internal carotid artery, basilar artery, and intracranial vertebral artery; *(c)* participants in whom the maximum medical therapy, including dual antiplatelet therapy and intensive management of risk factors, failed; *(d)* preprocedural modified Rankin score of 3 or less; and *(e)* two or more atherosclerotic risk factors, including hypertension, hyperlipidemia, diabetes mellitus, and cigarette smoking. The following participants were excluded from this study: *(a)* participants with nonatherosclerotic stenosis, such as moyamoya disease, intracranial arteritis, or intracranial dissection; *(b)* participants with tandem stenosis greater than 50%; *(c)* participants with intracranial aneurysms in the target artery; and *(d)* participants who were not cooperative or had contraindications to MRI.

Procedure Protocols

All study participants underwent endovascular treatment after at least 5 days of a dual antiplatelet regimen. All procedures were performed with the patient under general anesthesia and by a qualified neurointerventionalist (N.M., with 18 years of neurointervention experience). After femoral artery access was achieved, heparin was intravenously administered. The endovascular procedure methods and device selections were based on the anatomy of the culprit artery and the characteristics of the stenosis lesion. Participants' preferences were also considered. If the participants or their legal guardians refused stent insertion, balloon angioplasty was recommended. Balloon angioplasty was also recommended for participants with the following lesion characteristics: culprit artery diameter of less than 2 mm, tortuous access distal to the stenosis lesions, and angiographically visible branch artery originating from stenosis lesions. A Gateway PTA balloon (Stryker) was used to dilate the stenosis lesion of the culprit artery. Underdilation was performed to avoid arterial dissection, vessel rupture, and the "snow-plow" effect of compressed plaque into perforator arteries. The balloon size was 80% of the actual normal vessel luminal diameter or 60% in lesions directly adjacent to angiographically visible perforating arteries (17). The total stenosis length was covered by the chosen balloon. If the residual stenosis after balloon angioplasty was less than 50% on the angiogram and the antegrade blood flow was normal (defined as modified thrombolysis in cerebral infarction [TICI] grade 3), rescue stent placement was not performed. Rescue stent placement was performed in participants with iatrogenic arterial dissection with impaired antegrade blood flow (defined as modified TICI grade 0–2a) after balloon angioplasty. A balloon-mounted stent (Apollo Stent; MicroPort Medical) or self-expanding stent (Wingspan Stent [Stryker] or Enterprise Stent [Cordis Neurovascular]) was selected on the basis of lesion characteristics (18). An operative attempt was defined as device manipulation through the responsible lesion, including each balloon dilation, balloon-mounted stent implantation, or self-expanding stent release. The number of attempts was documented by the neurointerventionalists immediately after the intervention.

Noncontrast head CT (axial mode; 5-mm-thick sections; 5-mm section interval; 0.43-mm in-plane resolution; median volume CT dose index, 56 mGy [IQR, 52–57 mGy], median dose-length product, 902 mGy · cm [IQR, 833–904 mGy · cm]) was performed with a 256 detector-row CT scanner (Revolution CT; GE Medical Systems) after the procedure. The periprocedural medical treatment was the same as in the Wingspan Stent System Post Market Surveillance (WEAVE) study (17). If the blood pressure was more than 140/90 mm Hg, oral or intravenous antihypertensive treatment was required to lower the risk of hyperperfusion injury. Dual-antiplatelet therapy was maintained for at least 3 months after the procedure. Risk factor control targets were as follows: systolic blood pressure of less than 140

mm Hg (or 130 mm Hg in participants with diabetes mellitus); low-density lipoprotein level of less than 70 mg/dL, or a decrease by 50%; smoking cessation; and lifestyle modifications.

MRI Protocols

All participants underwent MRI 1–3 days before and after endovascular treatment. MRI scans were obtained with a 3-T MRI scanner (MAGNETOM Prisma; Siemens Healthineers) using a 64-channel head-neck coil. According to the product manual, the neurovascular stents used in this study can be safely scanned with a 3-T MRI scanner. The imaging protocols included diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery, susceptibility-weighted imaging, T2-weighted imaging, and noncontrast MR angiography. DWI parameters were as follows: repetition time msec/echo time msec of 4200/72, partial Fourier factor of 0.875, in-plane acceleration of 2, and section acceleration of 2. The field of view was 220 mm × 220 mm × 144 mm (anterior-posterior × right-left × foot-head), and the voxel size was 1.4 mm × 1.4 mm × 2 mm with no section gap. Three orthogonal diffusion-encoding directions were used to generate DWI scans. The DWI images were obtained with five averages for a *b* value of 1000 sec/mm^2 and four averages for a *b* value of 0 sec/mm^2. Total scanning time was 1 minute 42 seconds.

Evaluation of New Ischemic Brain Lesions

Two neurologists (Z.H. and J.J., with >5 years and >10 years of experience, respectively) who were blinded to clinical data and endovascular treatment independently reviewed all DWI scans and apparent diffusion coefficient maps before and after intervention. Any disagreements were resolved by a third reader (X.L., with >20 years of experience). Imaging analysis was based on acute periprocedural ischemic brain lesions, which were defined as diffusion restriction lesions (hyperintensity on DWI scans and hypointensity on apparent diffusion coefficient images) at posttreatment MRI that were not present at pretreatment MRI (9,19). New ischemic brain lesions were classified as symptomatic ischemic stroke and asymptomatic new lesions. Symptomatic ischemic stroke was defined as new lesions at DWI in participants presenting with new neurologic deficits after endovascular treatment. Asymptomatic new lesions were defined as new lesions in participants without any new neurologic deficits. The frequency of any new ischemic brain lesions after endovascular treatment was recorded. We further analyzed the distribution, location, and count of new lesions after endovascular treatment. The distribution of new lesions was divided into ischemic lesions in the territory of the treated artery and ones beyond the territory of the treated artery (including the territory of the noncatheterized artery and the territory of the catheterized artery). We classified the location of new lesions into peripheral brain areas (including the cortex and subjacent white matter) supplied by leptomeningeal branches of the anterior cerebral artery, middle cerebral artery, and posterior cerebral artery (also known as superficial or pial arteries) and deep brain areas supplied by perforating arteries (20). The total number of new lesions per patient (lesion count) was also recorded. Ischemic lesions were considered separate if there was no continuity between them on the same section as well as on adjacent sections (21).

Statistical Analysis

The sample size was calculated according to the formula suggested for the sample size estimation in prevalence studies (22). With a 95% confidence level, a 10% margin of error, and a maximal expected rate of new ischemic brain lesions of 59% (23), the minimum required sample size was estimated to be 93 participants. Continuous variables are presented as means ± SDs or medians with IQRs, and categorical variables are presented as percentages. The Cohen κ was used to test interrater reliability of occurrence, distributions, and locations of new ischemic brain lesions. κ values greater than 0.80, 0.60–0.80, 0.40–0.60, or less than 0.40 were considered as excellent, substantial, moderate, or poor agreement, respectively (24). Intraclass correlation coefficient and 95% CIs were calculated to evaluate the interrater reproducibility of new DWI lesion counts. Intraclass correlation coefficients less than 0.5, 0.5–0.75, 0.75–0.9, and greater than 0.90 were indicative of poor, moderate, good, and excellent reliability, respectively (25). We compared the frequency, distribution, location, and numbers of new ischemic brain lesions between participants treated with balloon angioplasty and those treated with stent placement using the Student *t* test or Mann-Whitney test for continuous variables and the χ^2 test or Fisher exact test for categorical variables. Generalized estimating equations were used to analyze the association between endovascular procedures (balloon angioplasty or stent placement) and the distribution or location of the new ischemic brain lesion, considering the repeated measure issue of distributions or locations of the new ischemic brain lesion per participant. The associations of the demographic information, vascular risk factors, qualifying events, and angiographic data with new ischemic brain lesions after endovascular treatment were assessed using the univariable logistic regression analysis and further using multivariable logistic regression analysis. The variables with unadjusted $P < .1$ in the univariable logistic regression model were considered potential confounders and subsequently included in the multivariable logistic regression model. Adjusted odds ratios (ORs) and their 95% CIs were calculated. Multicollinearity was tested using the variance inflation factor method, with a variance inflation factor of 5 or greater indicating the presence of multicollinearity (26). The goodness of fit of the model was evaluated with the Hosmer-Lemeshow test. Two-sided $P < .05$ was indicative of a statistically significant difference. All statistical analyses were performed using commercial SPSS software (version 26.0).

Results

Participant Baseline Characteristics

The flowchart of the study is shown in Figure 1. One hundred nineteen study participants (70 treated with balloon angioplasty and 49 with stent placement) were consecutively enrolled. The mean participant age was 59 years ± 11 (SD). Among the 119 participants, 81 (68%) were men. Sixty-two of the 119 participants (52%) underwent diagnostic angiography followed by endovascular treatment, and 57 of the 119 participants (48%) only received endovascular treatment because they had previously undergone diagnostic angiography. Pretreatment MRI was performed before endovascular treatment in these 57 participants.

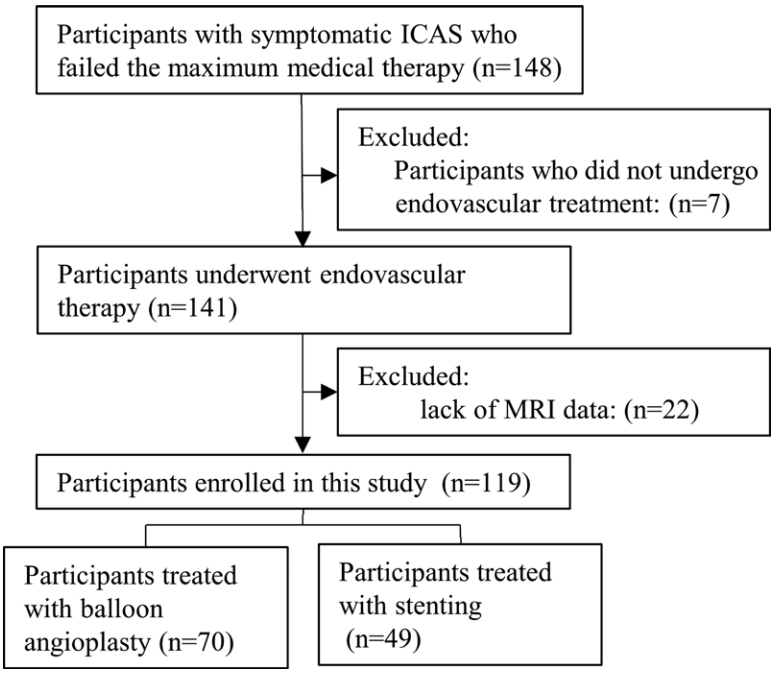

Figure 1: Flowchart shows participant enrollment in the study. ICAS = intracranial atherosclerotic stenosis.

The details of the vascular risk factors of the participants are summarized in Table 1. Seventy-seven of the 119 participants (65%) had ischemic stroke and 42 (35%) had a transient ischemic attack. The mean length of arterial stenosis lesions was 8.7 mm ± 4.6. The mean preprocedural and postprocedural stenosis degree were 86% ± 13 and 31% ± 18, respectively. In total, 70 of the 119 participants (59%) underwent balloon angioplasty only, 32 (27%) were treated with balloon angioplasty plus a self-expanding stent, and 17 (14%) were treated with a balloon-mounted stent.

There were more men in the balloon angioplasty group than in the stent placement group (54 of 70 [77%] vs 27 of 49 [55%], respectively; $P = .01$). There were more participants with hyperlipidemia in the balloon angioplasty group than in the stent placement group (45 of 70 [64%] vs 19 of 49 [39%], respectively; $P = .006$). The stenosis lesion was longer in the stent placement group than in the balloon angioplasty group (mean, 9.7 mm ± 5.1 vs 8.1 mm ± 3.9, respectively; $P = .01$). There was no evidence of a difference in the mean degree of preprocedure stenosis between the two groups (87% ± 11 in the balloon angioplasty group vs 84% ± 15 in the stent placement group; $P = .48$) However, the mean degree of postprocedural residual stenosis was higher in the balloon angioplasty group than in the stent placement group (40% ± 16 vs 20% ± 14, respectively; $P < .001$) (Table 1).

New Ischemic Brain Lesions Following Endovascular Treatment for ICAS

Overall, new lesions were identified in 77 of the 119 participants (65%), and a total of 546 ischemic lesions were recognized. The lesions were clinically silent in 72 of the 119 participants (61%) with new lesions after endovascular treatment, and only five of the 119 participants (4%) had a symptomatic ischemic stroke. In terms of distribution of new lesions, the new lesions were located in the territory of the treated artery in 72 of the 119 participants (61%) and beyond the territory of the treated artery in 41 (35%). Specifically, 15 of the 57 participants who received only endovascular treatment (26%) had new lesions in the territory of the noncatheterized artery, and 26 of the 62 participants who underwent diagnostic angiography before endovascular treatment (42%) had new lesions in the territory of the catheterized artery. With regard to the location of the new lesions, of the 77 participants with new lesions, 58 (75%) had lesions exclusively located in the peripheral brain areas, four (5%) had lesions exclusively in the deep areas, and 15 (20%) had lesions in both the peripheral and deep brain areas (Figs 2–4). A total of 424 new lesions were located in the territory of the treated artery. One hundred twenty-two new lesions were located beyond the territory of the treated artery, of which 50 were located in the territory of noncatheterized arteries and 72 were located in the territory of the catheterized artery. The average counts of new ischemic brain lesions per participant are summarized in Table 2. There was no evidence of a difference in the frequency of new ischemic brain lesions between the variable qualifying arteries (middle cerebral artery, 66% [31 of 47]; intracranial carotid artery, 67% [eight of 12]; basilar artery, 68% [26 of 38]; and intracranial vertebral artery, 55% [eight of 22]; $P = .74$).

Interrater Reliability of Characteristics of New Ischemic Brain Lesions

Interrater reliability analysis showed that the κ value was 0.93 (95% CI: 0.89, 0.96) for the occurrence of new ischemic brain lesions, 0.95 (95% CI: 0.92, 0.98) for new lesions in the territory of the treated artery, 0.96 (95% CI: 0.94, 0.99) for new lesions beyond the territory of the treated artery, and 0.82 (95% CI: 0.75, 0.88) for the location of new lesions (Tables S1–S4). Interrater reliability for new lesion counts was excellent (intraclass correlation coefficient, 0.99; 95% CI: 0.98, 0.99).

New Ischemic Brain Lesions after Balloon Angioplasty versus Stent Placement

The occurrence of new ischemic brain lesions after balloon angioplasty or stent placement had no evidence of a difference (42 of 70 [60%] vs 35 of 49 [71%], respectively; $P = .20$). There was also no evidence of a difference in the distributions (new lesions in the territory of the treated artery: 39 of 70 [56%] for the balloon angioplasty group vs 33 of 49 [67%] for the stent group, $P = .20$; new lesions beyond the territory of the treated artery: 20 of 70 [29%] for the balloon angioplasty group vs 21 of 49 [43%] for the stent group, $P = .11$]), locations (peripheral area only: 33 of 70 [47%] for the balloon angioplasty group and 25 of 49 [51%] for the stent group; deep area only: two of 70 [3%] for the balloon angioplasty group and two of 49 [4%] for the stent group; peripheral and deep area for the balloon angioplasty group: seven of 70 [10%] for the balloon

Table 1: Baseline Characteristics

Characteristic	All Participants (n = 119)	Balloon Angioplasty Group (n = 70)	Stent Placement Group (n = 49)	P Value
Age (y)*	59 ± 11 (25–81)	58 ± 12 (25–81)	59 ± 9 (34–80)	.98
Sex				.01
F	38 (32)	16 (23)	22 (45)	
M	81 (68)	54 (77)	27 (55)	
Risk factors				
Hypertension	90 (76)	52 (74)	38 (78)	.68
Diabetes mellitus	50 (42)	26 (37)	24 (49)	.20
Hyperlipidemia	64 (54)	45 (64)	19 (39)	.006
Coronary artery disease	15 (13)	9 (13)	6 (12)	.92
Current smoker	48 (40)	32 (46)	16 (33)	.15
Qualifying events				.37
Ischemic stroke	77 (65)	43 (61)	34 (69)	
Transient ischemic attack	42 (35)	27 (39)	15 (31)	
Time from qualifying event to endovascular treatment (d)†	45 (30–90)	60 (30–90)	45 (30–69)	.65
Time from endovascular treatment to posttreatment MRI (d)†	1 (1–2)	1 (1–2)	1 (1–2)	>.99
Qualifying artery				.34
Intracranial ICA	12 (10)	6 (9)	6 (12)	
MCA	47 (40)	28 (40)	19 (39)	
Intracranial VA	22 (18)	10 (14)	12 (25)	
BA	38 (32)	26 (37)	12 (25)	
Length of stenosis lesion (mm)‡	8.7 ± 4.6	8.1 ± 3.9	9.7 ± 5.1	.01
Degree of preprocedural stenosis (%)‡	86 ± 13	87 ± 11	84 ± 15	.48
Degree of postprocedural residual stenosis (%)‡	31 ± 18	40 ± 16	20 ± 14	<.001
No. of operative attempts				<.001
1	58 (49)	50 (71)	8 (16)	
>1	61 (51)	20 (29)	41 (84)	

Note.—Unless otherwise indicated, data are numbers of participants and data in parentheses are percentages. An operative attempt was defined as device manipulation through the responsible lesion, including each balloon dilation, balloon-mounted stent implantation, or self-expanding stent release. BA = basilar artery, ICA = internal carotid artery, MCA = middle cerebral artery, VA = vertebral artery.

* Data are means ± SDs, with ranges in parentheses.

† Data are medians, with IQRs in parentheses.

‡ Data are means ± SDs.

angioplasty group and eight of 49 [16%] for the stent group; P = .53), and counts (two [IQR: two to eight] for the balloon angioplasty group vs four [IQR: two to eight] for the stent group; P = .28) of new ischemic brain lesions between the two groups (Table 3). The generalized estimating equations model showed there is no evidence of a difference in the distributions (OR, 1.69; 95% CI: 0.93, 3.06) and locations (OR, 1.25; 95% CI: 0.90, 1.74) of new ischemic brain lesions between balloon angioplasty and stent groups.

Predictors of New Ischemic Brain Lesions

After adjusting the confounding factors, multivariable logistic regression analysis showed that cigarette smoking (adjusted OR, 3.6; 95% CI: 1.3, 9.7) and more than one operative attempt (adjusted OR, 2.9; 95% CI: 1.2, 7.0) were identified as independent predictors of new ischemic brain lesions after endovascular treatment for participants with ICAS (Table 4). The values of the variance inflation factor of variables in the multivariable regression model ranged from 1.00 to 1.38. The Hosmer-Lemeshow test indicated a goodness of fit of P = .93.

Discussion

New ischemic brain lesions after endovascular procedures such as carotid artery stent placement, intracranial aneurysm coiling or stent-assisted coiling, and cardiac valve implantation are relatively common complications (8–12). A prospective study (15) showed that the frequency of new ischemic lesions at 5 days and 30 days after index stroke was 24% and 7%, respectively, and a systematic review (27) reported that the frequency of new lesions after diagnostic angiography was 25%. However, the frequency and characteristics of new lesions seen at diffusion-weighted imaging after endovascular treatment for participants with intracranial atherosclerotic stenosis (ICAS) are rarely reported. In this prospective study, we sought to describe the frequency, distribution, location, numbers, and predictors of new ischemic brain lesions after endovascular treatment for participants with ICAS in whom maximum medical therapy failed. The frequency of new ischemic brain lesions after endovascular treatment for participants with ICAS was 65% (77 of 119), including 4% (five of 119) with symptomatic ischemic stroke. This finding showed

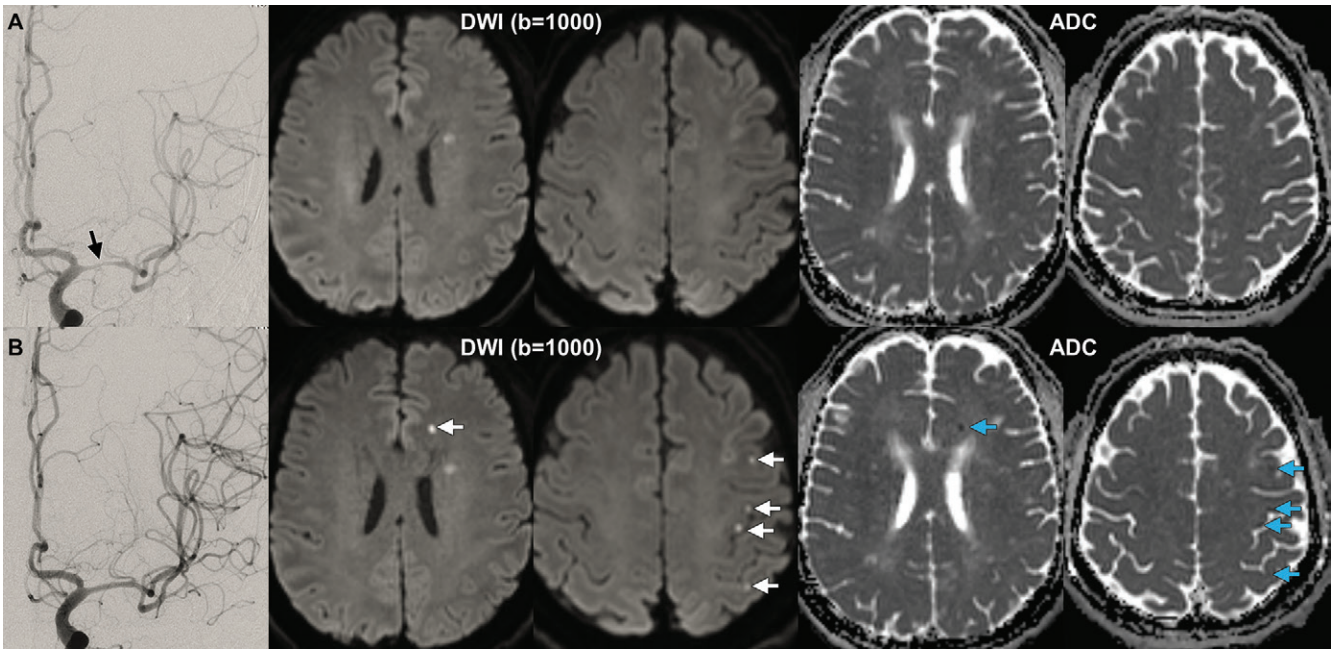

Figure 2: Images in a 59-year-old man who presented with right hemiplegia for 1 month and was diagnosed with severe stenosis in the M1 segment of the left middle cerebral artery. **(A)** Image from digital subtraction angiography (left) shows severe stenosis (arrow) located at the left middle cerebral artery. Pretreatment diffusion-weighted imaging (DWI) scans and apparent diffusion coefficient (ADC) maps show a small hyperintense lesion in the left periventricular area. The stenosis lesion was predilated with a 2.5 × 15-mm balloon and implanted with a 4.0 × 23-mm stent. Two operative attempts were recorded. **(B)** Image from digital subtraction angiography (left) shows that the stenosis degree of the left middle cerebral artery was significantly improved after stent implantation. Posttreatment DWI scans and apparent diffusion coefficient maps show multiple small (<5 mm) new ischemic brain lesions (arrows), which scatter over the peripheral brain areas, located in the territory of the treated artery.

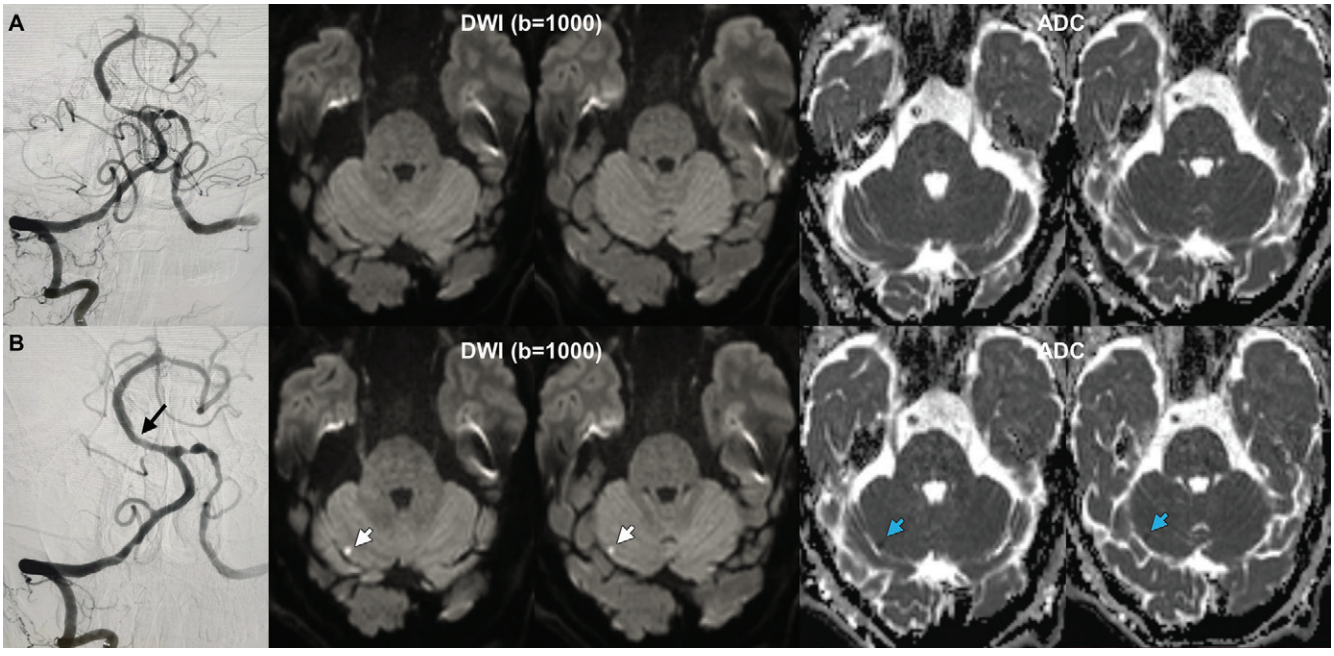

Figure 3: Images in a 68-year-old man with severe basilar artery stenosis who presented with recurrent dizziness for 3 months. **(A)** Image from digital subtraction angiography (left) shows severe stenosis at the proximal segment of the basilar artery. No new ischemic brain lesion is seen on the pretreatment diffusion-weighted imaging (DWI) scans and apparent diffusion coefficient (ADC) maps. The stenosis lesion was dilated with a 2.5 × 9-mm balloon. **(B)** Image from digital subtraction angiography (left) shows that the degree of stenosis of the proximal basilar artery was markedly improved after balloon angioplasty (arrow). Posttreatment DWI scans and apparent diffusion coefficient maps show small cerebellar cortical new ischemic lesions (arrows), which were located in the territory of the treated artery.

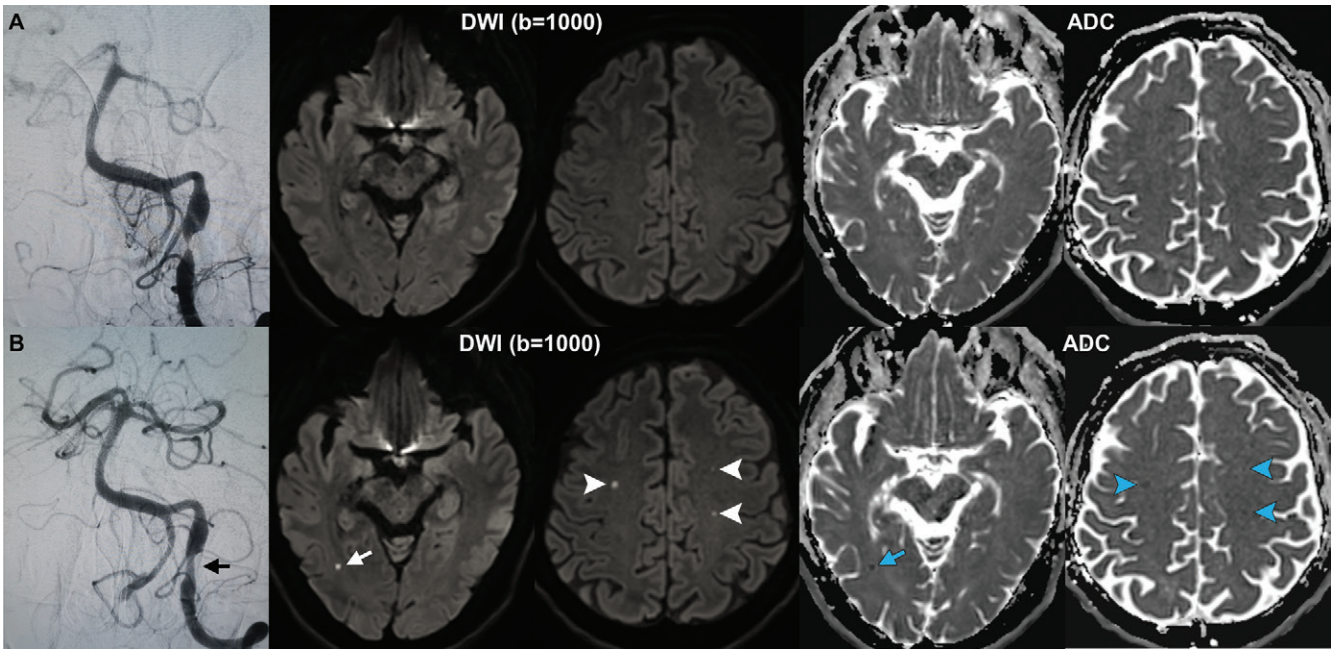

Figure 4: Images in a 51-year-old man with recurrent dizziness for 1 month who was diagnosed with severe stenosis in the V4 segment of the left vertebral artery. **(A)** Image from digital subtraction angiography (left) shows severe stenosis at the intracranial segment of the left vertebral artery. There is no new ischemic brain lesion on the pretreatment diffusion-weighted imaging (DWI) scans and apparent diffusion coefficient (ADC) maps. The stenosis lesion was dilated with a 3.0 × 15-mm balloon. **(B)** Image from digital subtraction angiography (left) obtained after balloon angioplasty shows that the degree of stenosis in the left vertebral artery was significantly improved (arrow). Posttreatment DWI scans and apparent diffusion coefficient maps show a small new ischemic lesion in the right temporal lobe (arrows) that was located in the territory of the treated artery and multiple small subcortical new ischemic lesions of the bilateral anterior circulation (arrowheads), which were located beyond the territory of the treated artery (in the territory of the catheterized artery).

that the majority of new lesions were asymptomatic. The new lesions were located in the territory of the treated artery in 72 of the 119 participants (61%) and beyond the territory of the treated artery in 41 (35%). Most of the new lesions were multiple small lesions involving peripheral brain areas (75%, 58 of 77 participants with new lesions). There was no evidence of a difference in the frequency of new lesions between the balloon angioplasty and stent groups (42 of 70 participants [60%] vs 35 of 49 participants [71%], P = .20). Our study showed that more than one operative attempt (odds ratio [OR], 2.9; 95% CI: 1.2, 7.0) and cigarette smoking (OR, 3.6; 95% CI: 1.3, 9.7) were independent predictors of new ischemic brain lesions after endovascular treatment.

In the stent group of the International Carotid Stenting Study, 50% of participants (62 of 124) had new ischemic brain lesions on posttreatment scans (9). A meta-analysis comprising 1363 patients (10) showed that the frequency of new ischemic brain lesions after carotid stent placement was 37%. Kim et al (23) reported that new ischemic brain lesions occurred in 59% of patients (41 of 69) with intra- or extracranial stenosis who underwent stent insertion. Park et al (28) reported that new ischemic brain lesions were observed in 35% of patients (43 of 123) with intracranial stent placement. The frequency of new ischemic brain lesions after endovascular treatment for participants with ICAS in our study was higher than that in these studies. We used a 3-T MRI scanner with thin-section DWI (2 mm, no gap) in our study, whereas most previous studies applied a 1.5-T scanner with thicker section DWI (3–5 mm) (7,9,23). Also, the improved image quality from novel MRI hardware (eg, high superficial brain sensitivity with a 64-channel coil) may contribute to the detection of cortical lesions.

The distribution of new ischemic brain lesions after endovascular treatment for participants with ICAS in our study was similar to that in a previous study. Kim et al (23) reported that 21 of 41 participants (51%) had new lesions located only in the territory of the stented vessel, eight (20%) had new lesions located only beyond the stented vessel territory, and 12 (29%) had new lesions located both in and beyond the territory of the stented vessel after endovascular treatment for patients with intra- or extracranial stenosis. The occurrence of new lesions was mainly caused by attempts at endovascular treatment. Therefore, most new ischemic brain lesions were distributed in the territory of the treated artery. The new ischemic brain lesions beyond the territory of the treated artery suggest that endovascular treatment can lead to ischemic lesions throughout the brain, even in territories without endovascular manipulation. The initial endovascular access in the procedure may be one source of emboli and lead to new ischemic brain lesions in the territory of noncatheterized arteries. Furthermore, possible emboli through the circle of Willis should also be suspected.

Most of the new ischemic brain lesions in our study were involved in cortical or subjacent white matter areas. This may suggest that embolism seems to be the main underlying mechanism of new lesions. Embolism may be caused by the dislodgement

Table 2: New Ischemic Brain lesions Detectable at Diffusion-weighted MRI after Endovascular Treatment for Symptomatic ICAS

Characteristic	No. of Participants
New ischemic brain lesions	77 (65)
Symptomatic ischemic stroke	5 (4)
Asymptomatic new lesions	72 (61)
Distribution of new lesions	
In the territory of the treated artery	72 (61)
Beyond the territory of the treated artery	41 (35)
Location of new lesions*	
Peripheral brain areas only	58 (75)
Deep brain areas only	4 (5)
Peripheral and deep brain areas	15 (20)
Total new lesion count†	546
In the territory of the treated artery	424 (78)
Beyond the territory of the treated artery	122 (22)
No. of new lesions per participant‡	4 (2–8)
No. of new lesions in the territory of the treated artery per participant§	3 (1–7)
No. of new lesions beyond the territory of the treated artery per participant‖	1 (1–2)

Note.—Unless otherwise indicated, data are numbers of participants, with percentages in parentheses. ICAS = intracranial atherosclerotic stenosis.

* For 77 participants with new ischemic brain lesions after endovascular treatment.

† For the number of new ischemic brain lesions after endovascular treatment. Data in parentheses are percentages.

‡ For 77 participants with new ischemic brain lesions after endovascular treatment. Data are medians, with IQRs in parentheses.

§ For 72 participants with new lesions in the territory of the treated artery. Data are medians, with IQRs in parentheses.

‖ For 41 participants with new lesions beyond the territory of the treated artery. Data are medians, with IQRs in parentheses.

of atheroma (23), in situ thrombosis, or microbubbles during the endovascular treatment (29). In the MRI substudy of the International Carotid Stenting Study (20), new lesions in the carotid stent placement group were more likely to occur in cortical areas and subjacent white matter supplied by leptomeningeal arteries. The mechanisms of new ischemic brain lesions may differ between patients with carotid stent placement and with intracranial stent placement and/or angioplasty. New lesions may also be involved in deep brain areas after endovascular treatment for participants with ICAS. In addition to the embolism mechanism, new lesions in the perforator territory may be caused by the forceful displacement of atheroma into the perforator ostia (ie, snow-plow effect) or in situ focal thrombosis secondary to intracranial balloon angioplasty and/or stent placement (30).

In this study, we found that cigarette smoking and more than one operative attempt were risk factors for new ischemic brain lesions after endovascular treatment, which seemed to be explained by the following reasons. Cigarette smoking increases the risk of plaque vulnerability (31), which may be the underlying reason for the higher frequency of new ischemic brain lesions in the participants with cigarette smoking after endovascular treatment. The culprit arterial lesions may be more susceptible to plaque rupture and in situ thrombus formation when there have

Table 3: Comparison of New Ischemic Brain Lesions at Diffusion-weighted MRI between Treatment with Balloon Angioplasty or Stent Placement for Symptomatic ICAS

Characteristic	Balloon Angioplasty Group (n = 70)	Stent Placement Group (n = 49)	P Value
New ischemic brain lesions	42 (60)	35 (71)	.20
Symptomatic ischemic stroke	3 (4)	2 (4)	>.99
Distribution of new lesions			
In the territory of the treated artery	39 (56)	33 (67)	.20
Beyond the territory of the treated artery	20 (29)	21 (43)	.11
Location of new lesions*			.53
Peripheral brain areas only	33 (47)	25 (51)	
Deep brain areas only	2 (3)	2 (4)	
Peripheral and deep brain areas	7 (10)	8 (16)	
No. of new lesions per participant†	2 (2–8)	4 (2–8)	.28
No. of new lesions in the territory of the treated artery per participant‡	2 (2–5)	3 (1–7)	.74
No. of new lesions beyond the territory of the treated artery per participant§	1 (1–2)	2 (1–3)	.36

Note.—Unless otherwise indicated, data are numbers of participants, with percentages in parentheses. ICAS = intracranial atherosclerotic stenosis.

* For 77 participants with new ischemic brain lesions after endovascular treatment.

† For 77 participants with new ischemic brain lesions after endovascular treatment. Data are medians, with the IQRs in parentheses.

‡ For 72 participants with new lesions in the territory of the treated artery. Data are medians, with IQRs in parentheses.

§ For 41 participants with new lesions beyond the territory of the treated artery. Data are medians, with IQRs in parentheses.

Table 4: Univariable and Multivariable Logistic Regression of Predictors of New Ischemic Brain Lesions after Endovascular Treatment for Patients with ICAS

Characteristic	OR	*P* Value	Adjusted OR*	*P* Value
Age (y)	1.04 (0.99, 1.07)	.06	1.04 (0.99, 1.08)	.09
Women	0.7 (0.3, 1.5)	.32	2.0 (0.7, 6.0)	.23
Hypertension	0.7 (0.3, 1.7)	.43	…	…
Diabetes mellitus	0.5 (0.2, 1.1)	.07	0.5 (0.2, 1.1)	.08
Hyperlipidemia	1.4 (0.7, 3.1)	.35	…	…
Coronary artery disease	0.9 (0.3, 2.9)	.87	…	—
Smoking	3.5 (1.6, 7.6)	.002	3.6 (1.3, 9.7)	.01
Time from qualifying event to endovascular treatment (d)	0.99 (0.98, 1.01)	.39	…	…
Time from endovascular treatment to posttreatment MRI (d)	0.7 (0.4, 1.1)	.11	…	…
Qualifying events	0.8 (0.4, 1.8)	.64	…	…
Length of stenosis lesion (mm)	1.04 (0.96, 1.14)	.34	…	…
Degree of preprocedural stenosis (%)	1.00 (0.97, 1.03)	.81	…	…
Degree of postprocedural residual stenosis (%)	1.00 (0.98, 1.02)	.86	…	…
>1 operative attempt	2.3 (1.1, 4.9)	.04	2.9 (1.2, 7.0)	.02

Note.—One-hundred nineteen study participants were enrolled in the study, and 77 participants had new ischemic brain lesions after endovascular treatment. Numbers in parentheses are 95% CIs. An operative attempt was defined as device manipulation through the responsible lesion, including each balloon dilation, balloon-mounted stent implantation, or self-expanding stent release. ICAS = intracranial atherosclerotic stenosis, OR = odds ratio.

* Variables with $P < .10$ in the univariable analysis were included in the multivariable model for independent predictors.

been multiple attempts at endovascular treatment. Furthermore, other potential injuries also increase, including plaque dislodgement in the arterial access and iatrogenic embolization (thrombus or microbubble formation). In addition, our study demonstrated that endovascular treatment methods (balloon angioplasty alone vs stent implantation) were not associated with the occurrence of new ischemic brain lesions. Our study did not show that age and diabetes mellitus are risk factors for new ischemic brain lesions after endovascular treatment. This finding was consistent with those in previous studies (23,28).

Factors such as plaque vulnerability and burden may also contribute to the new ischemic brain lesions. Imaging modalities such as head and neck vessel wall MRI or intravascular US may be used in future studies to help clarify whether these associations exist. Furthermore, the new ischemic brain lesions may be predictive of future stroke recurrence or cognitive impairment in participants with ICAS after endovascular treatment. Whether new ischemic brain lesions play a role in these aspects must be confirmed in future studies.

Our study had limitations. First, all procedures were performed by a qualified neurointerventionalist. The endovascular treatment approach and device selections were mainly based on the anatomy of the culprit artery and characteristics of the stenosis lesion. This limited the external validity of the study. Second, because of the small sample of the study, we did not compare the characteristics of participants with symptomatic and asymptomatic new ischemic brain lesions. Furthermore, the association between symptomatic ischemic stroke and the number of operative attempts was not analyzed. Third, the interrater reliability for the location of new lesions was not very strong. This may cause misclassification. Fourth, this was a single-center, small-sample-size study on a homogeneous ethnic population. A further justification must be done in a large-scale study to confirm these findings.

In conclusion, new ischemic brain lesions at diffusion-weighted MRI were common after endovascular treatment for intracranial atherosclerotic stenosis. However, the new ischemic brain lesions were clinically silent in most patients. The occurrence of new ischemic brain lesions at diffusion-weighted imaging may be associated with cigarette smoking and more than one operative attempt. Our findings must be confirmed in future studies with larger sample sizes, including a multiethnic sample.

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