Stroke

CLINICAL AND POPULATION SCIENCES

Internal Carotid Artery Tortuosity: Impact on Mechanical Thrombectomy

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BACKGROUND: Although tortuosity of the internal carotid artery (ICA) can pose a significant challenge when performing mechanical thrombectomy, few studies have examined the impact of ICA tortuosity on mechanical thrombectomy outcomes.

METHODS: In a registry-based hospital cohort, consecutive patients with anterior circulation stroke in whom mechanical thrombectomy was attempted were divided into 2 groups: those with tortuosity in the extracranial or cavernous ICA (tortuous group) and those without (nontortuous group). The extracranial ICA tortuosity was defined as the presence of coiling or kinking. The cavernous ICA tortuosity was defined by the posterior deflection of the posterior genu or the shape resembling Simmons-type catheter. Outcomes included first pass effect (FPE; extended Thrombolysis in Cerebral Infarction score 2c/3 after first pass), favorable outcome (3-month modified Rankin Scale score of 0–2), and intracranial hemorrhage.

RESULTS: Of 370 patients, 124 were in the tortuous group (extracranial ICA tortuosity, 35; cavernous ICA tortuosity, 70; tortuosity at both sites, 19). The tortuous group showed a higher proportion of women and atrial fibrillation than the nontortuous group. FPE was less frequently achieved in the tortuous group than the nontortuous group (21% versus 39%; adjusted odds ratio, 0.45 [95% CI, 0.26–0.77]). ICA tortuosity was independently associated with the longer time from puncture to extended Thrombolysis in Cerebral Infarction ≥2b reperfusion (β=23.19 [95% CI, 13.44–32.94]). Favorable outcome was similar between groups (46% versus 48%; *P*=0.87). Frequencies of any intracranial hemorrhage (54% versus 42%; adjusted odds ratio, 1.61 [95% CI, 1.02–2.53]) and parenchymal hematoma (11% versus 6%; adjusted odds ratio, 2.41 [95% CI, 1.04–5.58]) were higher in the tortuous group. In the tortuous group, the FPE rate was similar in patients who underwent combined stent retriever and contact aspiration thrombectomy and in those who underwent either procedure alone (22% versus 19%; *P*=0.80). However, in the nontortuous group, the FPE rate was significantly higher in patients who underwent combined stent retriever and contact aspiration (52% versus 35%; *P*=0.02).

CONCLUSIONS: ICA tortuosity was independently associated with reduced likelihood of FPE and increased risk of postmechanical thrombectomy intracranial hemorrhage.

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Key Words: catheters ■ intracranial hemorrhages ■ punctures ■ reperfusion ■ thrombectomy

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Nonstandard Abbreviations and Acronyms

aOR	adjusted odds ratio
CA	contact aspiration
CT	computed tomography
eTICI	extended Thrombolysis in Cerebral Infarction
FPE	first pass effect
ICA	internal carotid artery
ICH	intracranial hemorrhage
mRS	modified Rankin Scale
MT	mechanical thrombectomy
NIHSS	National Institutes of Health Stroke Scale
PH	parenchymal hematoma
SR	stent retriever
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology

Mechanical thrombectomy (MT) is the standard treatment for acute ischemic stroke resulting from anterior circulation large vessel occlusion.[1] Achieving an extended Thrombolysis in Cerebral Infarction (eTICI) score of ≥2c with few device passes as possible has been considered crucial to maximize the effectiveness of MT.[2–5] Therefore, achieving an eTICI 2c/3 reperfusion with first pass, that is, first pass effect (FPE), is the most important target that MT should achieve.[6]

Tortuous vascular anatomy is a common cause of the failed thrombectomy.[7] In curved vessels, stent retrievers (SRs) are stretched and may collapse during retrieval, which lead to loss of interaction with the clot.[8,9] Vessel tortuosity also reduces contact between the tip of the aspiration catheter and the clot and impairs clot aspiration.[10] Tortuosity reduces the performance of both SR thrombectomy and contact aspiration (CA) catheters, which increases the number of device passes needed and decreases the likelihood of achieving complete reperfusion.

Since the internal carotid artery (ICA) provides the only access to the anterior circulation, extra- and intracranial ICA tortuosity can pose a significant challenge when performing MT. Although the anatomic configurations of both the cervical and cavernous segments of the ICA have been classified previously,[11,12] there are few data on the impact of ICA tortuosity on MT outcomes.[13] We hypothesized that the ICA tortuosity adversely affects the likelihood of FPE because of reduced MT device performance. We aimed to investigate the association between the ICA tortuosity and outcomes of MT.

METHODS

The data that support the findings of this study are available from the corresponding author on reasonable request.

Study Subjects

All patients with acute ischemic stroke admitted to our institute within 7 days from last known well were prospectively registered in the National Cerebral and Cardiovascular Center Stroke Registry.[14–17] For the present study, we retrospectively reviewed consecutive patients enrolled in this registry from January 2014 to June 2021, who met the following criteria: (1) occlusion of the ICA or M1 or M2 segment of the middle cerebral artery and (2) those in whom MT was attempted for the occlusion of the ICA or M1 or proximal M2 segment of the middle cerebral artery. Patients with tandem occlusion (concomitant extracranial and distal intracranial artery occlusion) were also eligible. Patients who underwent intracranial angioplasty or stenting were excluded. We also excluded patients in whom ICA tortuosity could not be angiographically evaluated during the MT procedure. Written informed consent for study registration was waived because the study was retrospective in nature and utilized anonymized data. Ethics approval was obtained from the local institutional review board (M23-073-9). The National Cerebral and Cardiovascular Center Stroke Registry is registered with https://www.clinicaltrials.gov (NCT02251665). The present study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.[18] A completed STROBE Statement is included in the Supplemental Material.

Mechanical Thrombectomy

All endovascular procedures were performed by neurointerventionalists certified by the Japanese Society for Neuroendovascular Therapy, as recommended by the American Heart Association/American Stroke Association guidelines.[1] MT procedures included SR thrombectomy, CA, or combined SR and CA (retrieval of SR and aspiration catheter as a unit).[19] Groin puncture or navigation of a microcatheter for MT without use of thrombectomy devices was considered as an MT attempt. Procedural device selection was at the treating physician's discretion but limited to those available in Japan. The ones used are listed in Table S1. A balloon guide catheter was routinely used and navigated to the extracranial ICA as much as possible. All patients underwent MT under local anesthesia. Conscious sedation was added if necessary. Written informed consent for MT was obtained from each patient or a relative, if the patients had communication difficulties. Reperfusion status after MT was assessed according to the eTICI scale.[20] Follow-up brain computed tomography (CT) or magnetic resonance imaging was routinely performed after MT.

Clinical Data Collection

The following clinical data were collected: age, sex, premorbid modified Rankin Scale (mRS) score, baseline National Institutes of Health Stroke Scale (NIHSS) score, atrial fibrillation, cardiovascular risk factors (hypertension, diabetes, current smoking, dyslipidemia), ischemic heart disease (history of myocardial infarction, angina, or coronary revascularization treatment), previous stroke or transient ischemic attack, and systolic blood pressure on admission. The extent of ischemic change in the middle cerebral artery territory was graded using the Alberta Stroke Program Early CT Score on noncontrast CT or diffusion-weighted magnetic resonance imaging. Occlusion sites were determined using digital subtraction angiography on admission. All digital subtraction angiography studies were performed using biplane angiography units: Integris BV 3000 (Philips Medical Systems Nederland B.V., Best, the Netherlands), Allura Clarity FD 20/20 (Philips Medical System Nederland B.V.), and INX-8000 V/HT or V/JE (Canon Medical Systems, Tochigi, Japan). Intravenous thrombolysis was performed with alteplase at 0.6 mg/kg (the dose approved in Japan).[21]

Extracranial and Cavernous ICA Tortuosity

Tortuosity was independently classified by 3 specialists certified by the Japanese Society for Neuroendovascular Therapy (J.K., K.T., and T.Y.) who were blinded to clinical data. Tortuosity of the extracranial ICA was classified based on a previously reported grading system as follows: straight (angle between the centerlines of the common carotid artery and the ICA was <15°), tortuous (angle between the common carotid artery and the ICA centerlines was >15° or S- or C-shaped course of the ICA), coiled (an exaggerated S-shaped curve or circular configuration of the ICA), and kinked (acute [<90°] angulation associated with stenosis).[11] The extracranial ICA was considered tortuous if it was coiled or kinked (Figure 1).

Cavernous ICA tortuosity was also classified based on a previously reported grading system.[12] Briefly, type I has open configurations/angles of the anterior and posterior genus (the posterior genu angle ≥90°). Type II is characterized by a closed configuration of the anterior genu (more acute angle of the anterior genu than type I). Type III is defined by posterior deflection of the posterior genu, which gives it a buckled appearance. Type IV is the most tortuous and has a shape characteristic of the Simmons-style angiography catheter where the posterior genu is buckled superiorly compared with the anterior genu. Types III and IV were considered tortuous cavernous ICA (Figure 1).

Standard anteroposterior and lateral projection angiograms were analyzed for tortuosity classification. Baseline angiograms before MT were used for analysis when possible. For assessment of ICA tortuosity, the data set was divided into 3 subdatasets. In the first session, each of the 3 readers assessed tortuosity in 1 of the 3 subdatasets. In the second, each reader evaluated tortuosity in a sub-dataset different from the first session. The overall interobserver reliability for tortuosity (dichotomized as tortuous or nontortuous) in the extracranial and cavernous ICA was evaluated using the κ-coefficient between the interpretations of the first and second sessions. In cases with a discrepancy between the 2 sessions, disagreements were resolved by discussion among the 3 readers. For analyses, the data on the tortuosity after resolving the disagreements were used.

Patients were divided into 2 groups according to ICA tortuosity (tortuous or nontortuous). The tortuous group included patients with an extracranial or cavernous ICA classified as tortuous. Patients without tortuosity in either the cavernous or extracranial ICA were included in the nontortuous group.

Outcomes

Procedural outcomes were FPE (achievement of eTICI score 2c/3 after first pass), modified FPE (first pass eTICI score ≥2b), final eTICI 2c/3 reperfusion, final eTICI ≥2b reperfusion, time from puncture to eTICI ≥2b reperfusion, procedural time, procedural complications (arterial perforation, arterial dissection, and embolization in a new territory), and failure to reach the target occlusion (failure to navigate MT devices due to difficult access). FPE and modified FPE were assessed only among patients who underwent MT. Clinical outcomes were favorable outcome (mRS score of 0–2 at 3 months), excellent outcome (mRS score of 0–1 at 3 months), poor outcome (mRS score of 5–6 at 3 months), and neurological improvement (a ≥10-point decrease of the NIHSS score from baseline or the score of 0) at 7 days from onset. Safety outcomes were any intracranial hemorrhage (ICH) within 36 hours after the onset, the presence of subarachnoid hemorrhage, parenchymal hematoma (PH), and symptomatic ICH. ICH was assessed using CT or gradient echo magnetic resonance imaging. PH was defined as PH1 and PH2 as described in the hemorrhagic transformation classification system of the European Cooperative Acute Stroke Study.[22] Symptomatic ICH was defined as ICH associated with ≥4-point increase in NIHSS score.[22]

Statistical Analysis

Continuous data are summarized as means with SD or medians with interquartile range. Categorical data are shown as frequencies with percentage. Groups were compared using the Wilcoxon rank-sum test, Kruskal-Wallis test, or Fisher exact test as appropriate. Baseline characteristics and outcomes were compared between groups using univariate analysis. Logistic regression models were then constructed for each binary outcome, and odds ratios with 95% CIs were calculated for the tortuous group using the nontortuous group as reference. The interaction between groups according to ICA tortuosity and the occlusion site regarding FPE was evaluated in the logistic regression model with calculation of *P* for interaction. Multivariate linear regression models were used to evaluate the association of ICA tortuosity with time from puncture to eTICI ≥2b reperfusion and procedural time. For the procedural and clinical outcomes, the following prespecified variables were included: age, sex, body weight, premorbid mRS score, baseline NIHSS score, occlusion site, first-line MT strategy, and onset-to-puncture time. For the safety outcomes, adjustments for age, sex, body weight, baseline NIHSS score, occlusion site, intravenous thrombolysis, first-line MT strategy, and onset-to-puncture time were performed. Subgroup outcome analyses of patients grouped according to location of ICA tortuosity (extracranial or cavernous) were performed using logistic regression models with the nontortuous group as the reference. Missing data were handled using the pairwise deletion. $P<0.05$ was considered significant. Statistical analyses were performed using the R Software, version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria), with the following packages: tidyverse, dplyr, sjPlot, magrittr, lmtest, margin, ordinal, and ggplot2.

RESULTS

Patients' Characteristics

The study flowchart is shown in Figure 2. A total of 370 patients (167 women [45%]; median age, 78 [interquartile range, 71–83] years; median NIHSS score, 19 [interquartile range, 13–24]) were analyzed. Of the 370 patients, 128 patients (35%) had occlusion in the ICA,

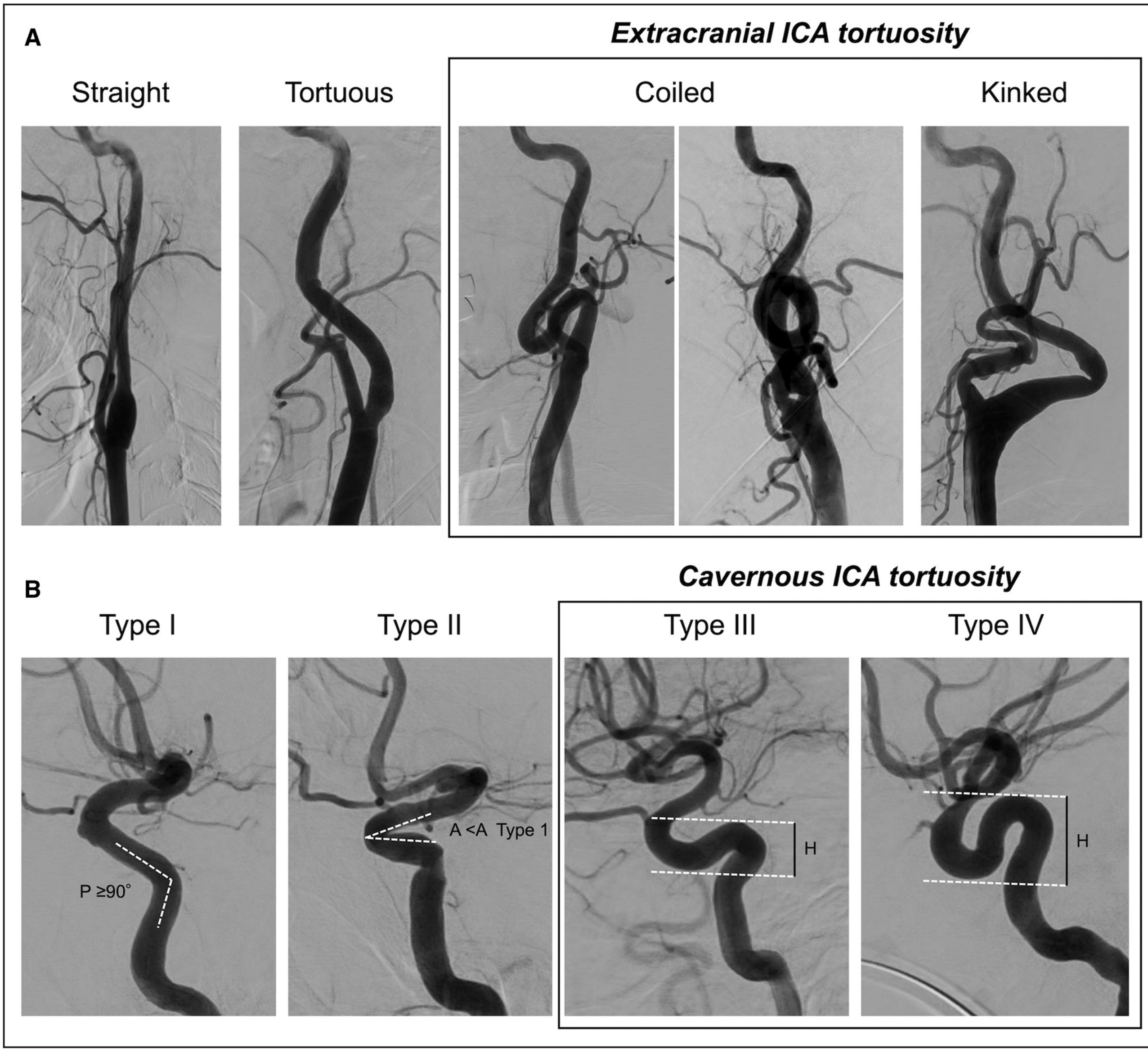

Figure 1. Classification of extracranial and cavernous internal carotid artery (ICA) tortuosity.
A, Tortuosity of the extracranial ICA was classified into 4 types as follows: straight (angle between the centerlines of the common carotid artery and the ICA was <15°), tortuous (angle between the common carotid artery and the ICA centerlines was >15; or S- or C-shaped course of the ICA), coiled (an exaggerated S-shaped curve or circular configuration of the ICA), and kinked (acute [<90°] angulation associated with stenosis).[11] The extracranial ICA was considered tortuous if it was coiled or kinked. **B**, Cavernous ICA tortuosity was classified into 4 types based on the geometry of the anterior and posterior genus. Type I has open configurations/angles of anterior and posterior genus (the posterior genu angle [P] ≥90°). Type II is characterized by a closed configuration of the anterior genu (more acute angle of the anterior genu [A] than type I). Type III is defined by posterior deflection of the posterior genu, which gives it a buckled appearance. Type IV is the most tortuous and has a shape characteristic of the Simmons-style angiography catheter where the posterior genu is buckled superiorly compared with the anterior genu.[12] H is the height difference of the anterior and posterior genus, measured from the peak of the posterior genu to the trough of the anterior genu. Types III and IV were considered tortuous cavernous ICA.

157 patients (42%) in the M1 segment, and remaining 85 patients (23%) in the M2 segment. One hundred and twenty patients (32%) were treated by SR thrombectomy, 132 patients (36%) by CA, and 96 patients (26%) by combined SR and CA as the first-line MT strategy. MT was only attempted in 18 patients (5%) due to difficult access in 4 patients, reperfusion before MT in 11 patients, and arterial perforation before MT in 3 patients. Successful reperfusion (final eTICI score ≥2b) was achieved in 315 patients (85%); median time from puncture to reperfusion was 45 minutes (interquartile range, 29–74).

Tortuosity in the extracranial ICA and cavernous ICA could be assessed by baseline angiography in 269 (73%) and 272 patients (74%), respectively. The overall κ-coefficient for interrater agreement of the dichotomized tortuosity status was 0.70 in the extracranial ICA and 0.79 in the cavernous ICA. For the extracranial ICA,

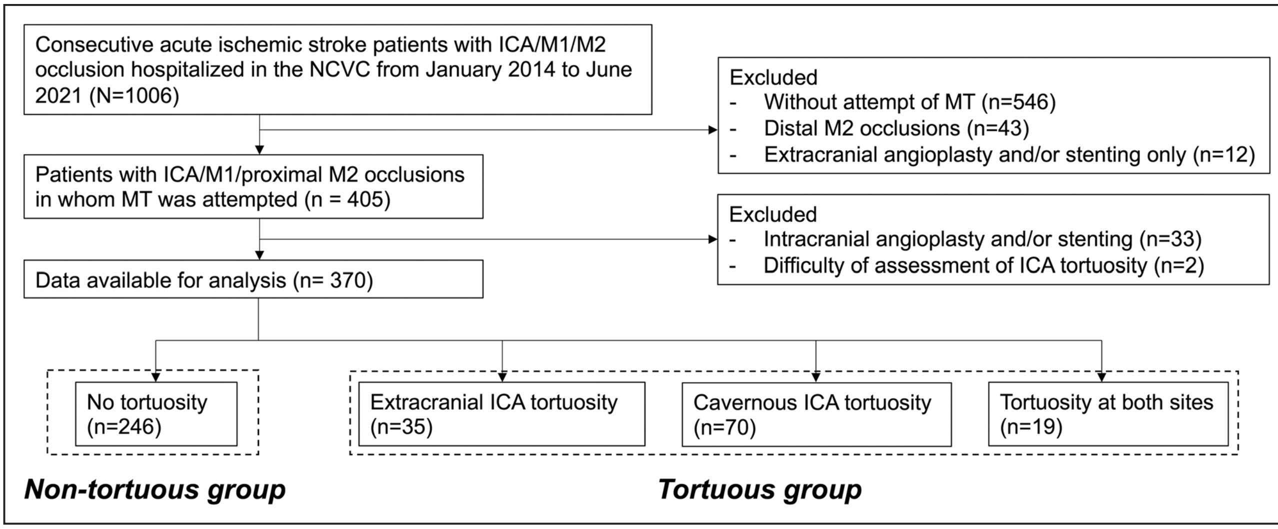

Figure 2. Study flowchart.

ICA indicates internal carotid artery; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; MT, mechanical thrombectomy; and NCVC, National Cerebral and Cardiovascular Center.

discussion was required to resolve discrepancies in 30 cases; among these, 14 were classified as tortuous and 16 as nontortuous. For the cavernous ICA, discussion was required for 33 cases; 11 were classified as tortuous and 22 as nontortuous.

The tortuous group comprised 124 patients (34%). Among these, location of tortuosity was extracranial ICA in 35 patients (9%), cavernous ICA in 70 patients (20%), and both sites in 19 patients (5%). The remaining 246 patients (66%) were assigned to the nontortuous group. Patient characteristics stratified according to the group are shown in Table 1. The tortuous group was older and more female and had shorter time from onset to hospital arrival than the nontortuous group. The tortuous group had the marginally higher baseline NIHSS score. Atrial fibrillation was more frequently observed in the tortuous group than in the nontortuous group. No significant difference was found in the first-line MT strategy (Table 1). Patient characteristics among the 4 subgroups of patients with no tortuosity, with extracranial ICA tortuosity, with cavernous ICA tortuosity, and those with tortuosity at both sites are shown in Table S2.

Procedural Outcomes

Procedural outcomes according to the group are summarized in Table 2. The rate of FPE was significantly lower in the tortuous group than in the nontortuous group (adjusted odds ratio [aOR], 0.45 [95% CI, 0.26–0.77]). The rate of achieving final eTICI 2c/3 reperfusion was also significantly lower in the tortuous group than in the nontortuous group (aOR, 0.60 [95% CI, 0.38–0.95]). There were no significant differences in the rates of final eTICI ≥2b and procedural complications. Failure to reach the target occlusion was observed in 3 patients (2.5%) of the tortuous group and 1 patient of the nontortuous group (0.4%; P=0.11). The tortuous group had higher number of passes (2 [1–3] versus 1 [1–3]; P=0.04), longer time from puncture to eTICI ≥2b reperfusion (59 [37–89] versus 40 [28–63] minutes; P<0.001), and longer procedural time (80 [56–117] versus 68 [42–112] minutes; P=0.009) than the nontortuous group. On multivariate linear regression analyses, ICA tortuosity was associated with time from puncture to eTICI ≥2b reperfusion (β=23.19 [95% CI, 13.44–32.94]) but not with procedural time (β=9.54 [95% CI, −11.27 to 30.35]). The median time from stroke onset to eTICI ≥2b reperfusion was similar between groups (239 [166–429] versus 232 [171–445] minutes; P=0.90). Procedural outcomes among the 4 subgroups according to location of ICA tortuosity are shown in Figure 3A and 3B.

In the tortuous group, the rate of FPE was similar in patients who underwent combined SR and CA and in those who underwent SR thrombectomy or CA alone (22% versus 19%; P=0.80). However, in the nontortuous group, the FPE rate was significantly higher in patients who underwent combined SR and CA (52% versus 35%; P=0.02; Figure 4).

The rate of FPE was lower in the tortuous group than the nontortuous group in patients with ICA occlusion (aOR, 0.25 [95% CI, 0.10–0.67]) and M1 occlusion (aOR, 0.38 [95% CI, 0.16–0.93]) but not in those with M2 occlusion (aOR, 1.63 [95% CI, 0.49–5.44]; P for interaction, 0.04; Figure S1).

Clinical and Safety Outcomes

The rates of favorable outcome did not differ between groups (Table 2). The excellent outcomes were numerically lower in the tortuous group than in the nontortuous group, though the difference did not reach statistical significance. Neurological improvement at 7 days was less frequent in the tortuous group than in the nontortuous

Table 1. Patient Characteristics According to the Presence of the ICA Tortuosity

	Tortuous ICA (n=124)	Nontortuous ICA (n=246)	*P* value
Age, y	80 (72–85)	77 (70–83)	0.04
Women	70 (57)	97 (39)	0.003
Body weight, kg*	54 (46–62)	57 (48–64)	0.18
Premorbid mRS score	0 (0–2)	0 (0–2)	0.11
Baseline NIHSS score*	20 (14–26)	18 (13–24)	0.07
Admission systolic BP, mm Hg	152 (135–170)	152 (134–172)	0.98
ASPECTS†	8 (6–9)	8 (6–10)	0.64
Medical history			
Atrial fibrillation‡	96 (77)	151 (62)	0.003
Hypertension*	90 (73)	178 (73)	1.00
Diabetes§	27 (22)	51 (21)	0.89
Dyslipidemia*	58 (47)	110 (45)	0.74
Ischemic heart disease*	16 (13)	38 (16)	0.54
Previous stroke/TIA*	24 (19)	54 (22)	0.59
Current smoking‖	13 (11)	36 (15)	0.35
Initial site of occlusion			0.50
Extracranial ICA	10 (8)	19 (8)	
Intracranial ICA	40 (32)	59 (24)	
Proximal M1	21 (17)	44 (18)	
Distal M1	26 (21)	66 (27)	
M2	27 (22)	58 (24)	
First-line MT strategy¶			0.68
SR	39 (32)	81 (33)	
CA	40 (32)	92 (37)	
Combined SR and CA	36 (29)	60 (24)	
Manual aspiration through the guide catheter	2 (2)	2 (1)	
Attempt only	7 (6)	11 (5)	
Onset-to-hospital arrival time, min	65 (42–258)	108 (49–326)	0.05
Onset-to-puncture time, min	160 (107–326)	190 (115–419)	0.15
Intravenous thrombolysis	62 (50)	107 (44)	0.27

Data are presented as medians (interquartile range) or number (%). ASPECTS indicates Alberta Stroke Program Early CT Score; BP, blood pressure; CA, contact aspiration; CT, computed tomography; ICA, internal carotid artery; M1, first segment of the middle cerebral artery; M2, second segment of the middle cerebral artery; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; SR, stent retriever; and TIA, transient ischemic attack.

*One missing value (1 in the nontortuous group).

†ASPECTS on noncontrast CT (n=112) and ASPECTS on diffusion-weighted MRI (n=257).

‡Two missing values (2 in the nontortuous group).

§Three missing values (2 in the nontortuous group).

‖Two missing values (1 in the nontortuous group).

¶Extracranial stenting was performed before MT in 4 patients of the nontortuous ICA group.

group (aOR, 0.56 [95% CI, 0.34–0.91]). The overall distribution of the mRS scores at 3 months in the tortuous and nontortuous groups is shown in Figure S2.

Regarding safety outcomes, the tortuous group had the higher frequency of any ICH than the nontortuous group (aOR, 1.61 [95% CI, 1.02–2.53]). PH was more frequent in the tortuous group (11%) than in the nontortuous group (6%; aOR, 2.41 [95% CI, 1.04–5.58]). However, frequency of symptomatic ICH did not significantly differ between groups. Frequency of ICH among the 4 subgroups is shown in Figure 3C.

Impact of Tortuosity Location on Outcome

Outcomes according to the location of ICA tortuosity are summarized in Table S3. The FPE rate was lower in patients with extracranial ICA tortuosity alone than in those without tortuosity (aOR, 0.37 [95% CI, 0.14–0.96]). The rate of achieving final eTICI 2c/3 reperfusion was lower in patients with cavernous ICA tortuosity alone than in those without tortuosity (aOR, 0.54 [95% CI, 0.31–0.94]). The frequency of subarachnoid hemorrhage (aOR, 1.96 [95% CI, 1.03–3.71]) was higher in patients with cavernous ICA tortuosity alone than in those without tortuosity. Patients with cavernous ICA tortuosity alone had numerically more PH than those without tortuosity (aOR, 2.65 [95% CI, 0.98–7.21]).

DISCUSSION

The major findings of the present study were that rates of FPE and final eTICI score ≥2c were significantly lower in patients with ICA tortuosity than those without. These patients also had an increased risk of post-MT ICH. The rate of favorable outcome was similar between patients with and without ICA tortuosity. Combined use of SR and CA was associated with a higher FPE rate than SR thrombectomy or CA alone in patients without ICA tortuosity but not in patients with ICA tortuosity.

ICA tortuosity was often present in elderly women with atrial fibrillation. Older age and higher frequency of atrial fibrillation in patients with ICA tortuosity has also been previously reported in other studies.[13,23] Moreover, stroke severity tended to be higher in patients with ICA tortuosity than in those without, which may be explained by their older age and multiple comorbidities. Such differences in clinical characteristics between patients with and without ICA tortuosity may influence the relationship between ICA tortuosity and MT outcome.

Prior studies have reported 1.7× higher odds of favorable outcome of FPE compared with non-FPE.[6,24] However, the lower FPE rate in patients with ICA tortuosity did not result in a lower favorable outcome rate compared with those without tortuosity in our cohort. Median onset-to-arrival time was 43 minutes shorter in patients with ICA tortuosity, which might compensate the time delay by the failure to achieve FPE; time from stroke onset to eTICI ≥2b reperfusion was similar between groups.

Table 2. Outcomes Between Tortuous and Nontortuous Groups

	Tortuous ICA (n=124)	Nontortuous ICA (n=246)	Unadjusted OR (95% CI)	aOR (95% CI)
Procedural outcomes*				
First pass effect†	24 (21)	91 (39)	0.41 (0.24–0.68)	0.45 (0.26–0.77)
Modified first pass effect†	50 (43)	128 (55)	0.62 (0.40–0.97)	0.69 (0.43–1.10)
Final eTICI score 2c/3	56 (45)	143 (58)	0.59 (0.38–0.92)	0.60 (0.38–0.95)
Final eTICI score 2b/3	107 (86)	208 (85)	1.15 (0.63–2.18)	1.26 (0.66–2.41)
Procedural complications	7 (6)	12 (5)	1.16 (0.42–2.96)	0.95 (0.35–2.61)
Clinical outcomes*				
Favorable outcome	57 (46)	118 (48)	0.92 (0.60–1.42)	1.05 (0.60–1.82)
Excellent outcome	33 (27)	82 (33)	0.73 (0.45–1.16)	0.75 (0.42–1.33)
Poor outcome	24 (19)	41 (17)	1.20 (0.68–2.08)	1.08 (0.56–2.10)
Neurological improvement at 7 d	65 (53)	155 (64)	0.63 (0.40–0.98)	0.56 (0.34–0.91)
Safety outcomes‡				
Any ICH	67 (54)	103 (42)	1.63 (1.06–2.53)	1.61 (1.02–2.53)
SAH	31 (25)	42 (17)	1.62 (0.95–2.73)	1.67 (0.96–2.90)
PH	14 (11)	15 (6)	1.96 (0.91–4.22)	2.41 (1.04–5.58)
Symptomatic ICH	6 (5)	8 (3)	1.51 (0.49–4.45)	1.82 (0.54–6.17)

Data are presented as n (%). aOR indicates adjusted odds ratio; eTICI, extended Thrombolysis in Cerebral Infarction; ICA, internal carotid artery; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; PH, parenchymal hematoma; and SAH, subarachnoid hemorrhage.

*Models for procedural and clinical outcomes were adjusted for age, sex, body weight, premorbid mRS score, baseline NIHSS score, occlusion site, first-line MT strategy, and onset-to-puncture time.

†First pass effect and modified first pass effect were assessed among 117 patients of the tortuous group and 235 patients of the nontortuous group.

‡Models for safety outcomes were adjusted for age, sex, body weight, baseline NIHSS score, occlusion site, intravenous thrombolysis, first-line MT strategy, and onset-to-puncture time.

Current devices and techniques would be sufficient to obtain substantial recanalization even for tortuous vessels. A recent study also reported no association between the presence of extracranial ICA tortuosity and TICI ≥2b reperfusion.[25] However, the rate of neurological improvement was lower in the tortuous group than in those of the nontortuous group, implicating that there is still room to improve stroke outcomes by improving the FPE rates in patients having tortuous ICA. Achieving the FPE remains challenging in patients with a tortuous ICA.

Our data also demonstrated an association between ICA tortuosity and post-MT ICH. Notably, the odds of a PH developing after MT were twice as high in the tortuous group than the nontortuous group after adjusting for potential confounders. The need to perform more maneuvers during MT because of tortuosity may explain the increased odds of post-MT ICH, as CA and SR both cause endothelial and vessel wall injury.[26] Other potential triggers for hemorrhagic transformations could be that the longer procedure time and lower rate of eTICI 2c/3 reperfusion in patients with tortuous ICA.[27,28]

How to improve procedural outcomes of MT in the tortuous vessel has been poorly documented. In curved vessels, the elongation and flattening of the SR during retrieval maneuvers, described as tapering,[9] and the misalignment of the axis between the aspiration catheter and clot can result in poor device-clot interaction.[10,29] Consequent fragmentation and distal embolization of the target thrombi in tortuous vessels may lead to the equally lower rate of FPE and final eTICI score 2c/3 in the SR thrombectomy and CA alone. Even use of combined currently available SRs and aspiration catheters could not compensate performance of each device in tortuous vessels. The bendable and segmented design of SR may avoid the tapering phenomenon and improve the rate of FPE in patients with tortuous vessels.[8] In addition, the technical tips such as steam shaping of the tip of the aspiration catheter may also be useful to overcome the tortuous vasculature.[30] Our study illustrates the unmet need for MT devices that does not lose contact with the clot in the tortuous vasculature.

Angiographic assessment of ICA tortuosity using standard anteroposterior and lateral projections may be useful to predict procedural outcomes in the clinical setting. Prior studies that have investigated the influence of extracranial ICA tortuosity on SR thrombectomy assessed degree of tortuosity using maximal intensity projection images or the tortuosity index in CT angiography.[13,23] Although those methods for assessment of the vessel tortuosity are highly accurate, they may be time-consuming for acute clinical setting. The present study also has the strength in the assessment of the cavernous ICA tortuosity and thrombectomy performance in various MT strategies.

The present study has several limitations. First, the inherent bias due to the single-center retrospective

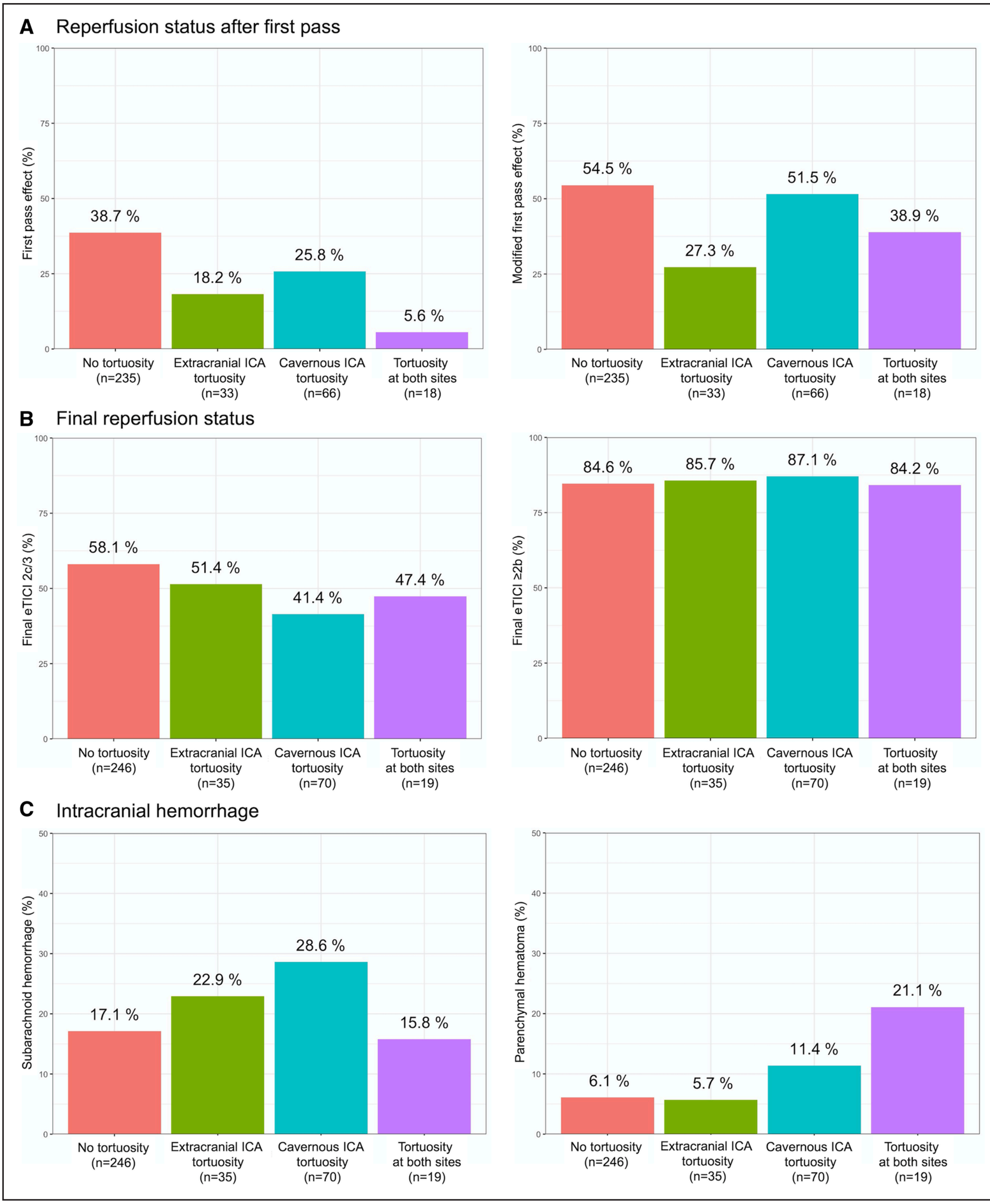

Figure 3. Procedural outcomes according to the location of internal carotid artery (ICA) tortuosity.
Outcomes according to location of ICA tortuosity are shown for (**A**) reperfusion status after first pass, (**B**) final reperfusion status, and (**C**) intracranial hemorrhage. eTICI indicates extended Thrombolysis in Cerebral Infarction.

nature of the study with relatively small numbers of patients in each group might affect the results. Second, we only assessed curvature in the ICA; curvature in other relevant vessels, including the middle cerebral artery, aorta, and cervical vessels was not assessed. Unmeasured confounding factors with respect to these vessels may have affected our results. Third, we assessed vessel anatomy based on anteroposterior

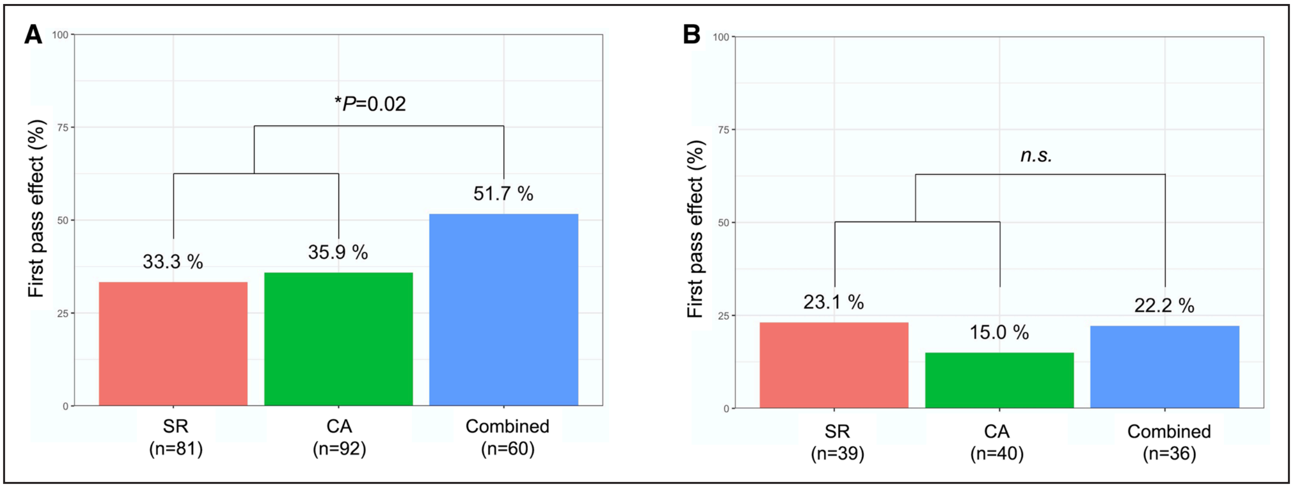

Figure 4. First pass effect according to the first-line mechanical thrombectomy strategy.
The rate of first pass effect according to the first-line mechanical thrombectomy strategy in the (**A**) nontortuous and (**B**) tortuous internal carotid artery groups. CA indicates contact aspiration; NS, nonsignificant; and SR, stent retriever. *Fisher exact test.

and lateral projections; however, 3-dimensional imaging provides the most precise angle measurements. Fourth, interrater agreement of ICA tortuosity assessed by the present methodology was moderate and may become even lower if assessed in an acute clinical setting, which might limit the clinical applicability of the present findings.

CONCLUSIONS

ICA tortuosity was independently associated with lower rates of FPE and higher frequency of post-MT ICH. ICA tortuosity had no significant effect on symptomatic ICH and favorable outcome. For the tortuous ICA, the synergistic effect of combined SR and CA was not observed, and the rate of FPE was equally low among all current MT strategies. To improve outcomes of MT, development of devices and techniques that show promise in the treatment of patients with tortuous vessels will be needed.

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Supplemental Material

Tables S1–S3
Figures S1–S2
STROBE Statement

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