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ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - ANEURYSM

Association between extracranial internal carotid artery tortuosity and thromboembolic complications during coil embolization of anterior circulation ruptured aneurysms

Atsushi Ogata[1] · Kenji Suzuyama[1,2] · Ryo Ebashi[1] · Yukinori Takase[1] · Kohei Inoue[1] · Jun Masuoka[1] · Fumitaka Yoshioka[1] · Yukiko Nakahara[1] · Tatsuya Abe[1]

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Abstract

Background The most frequent neurological complication during coil embolization of a ruptured cerebral aneurysm is a thromboembolic event. The association between the tortuosity of the internal carotid artery (ICA) and thromboembolic events (TEEs) during coil embolization of ruptured cerebral aneurysms remains unclear. The present study aimed to investigate the association between extracranial ICA tortuosity and thromboembolic complications during coil embolization of anterior circulation ruptured aneurysms.

Methods A cohort of 57 patients with 57 anterior circulation ruptured aneurysms who underwent endovascular embolization at a single institution was retrospectively investigated. Patients were divided into two groups, those who experienced TEEs and those who did not that were compared and analyzed based on patient baseline characteristics, procedural factors, and anatomical factors including those of aneurysms and extracranial ICA tortuosity. The anatomical factors of the aneurysms included maximum dome size, neck width, dome-to-neck ratio, and dome-to-neck aspect ratio. Extracranial ICA angles in the proximal and distal curvature were evaluated as ICA tortuosity.

Results Three of the 57 patients were excluded because of unavailability of data regarding ICA tortuosity; 54 patients were finally evaluated. TEEs occurred in six patients with five anterior cerebral and one internal carotid aneurysms. The extracranial distal ICA angle was significantly larger in patients with TEEs than in those without. Procedural factors and anatomical factors of the aneurysms were not associated with TEEs.

Conclusions Extracranial ICA tortuosity was significantly associated with an increased incidence of thromboembolic events during endovascular coiling of anterior circulation ruptured aneurysms.

Keywords Aneurysm · Coil embolization · Extracranial · Internal carotid artery

Introduction

Endovascular coil embolization has been widely performed as an acute-phase treatment for ruptured cerebral aneurysms. However, despite advances in device technology and techniques, endovascular coil embolization for cerebral aneurysms poses inherent risks [10]. The most frequently occurring neurological complication during coil embolization for treating a ruptured cerebral aneurysm is a thromboembolic event [13]. Procedure-related thromboembolic events (TEEs) are observed more frequently during the endovascular coil embolization of ruptured aneurysms than during the coiling of unruptured ones [6].

Anatomical risk factors investigated for the TEEs included a wide aneurysm neck, a small parent artery diameter, and an incorporated branch [1, 4]. A carotid stenosis trial reported that the tortuosity of internal carotid arteries was associated with thromboembolic complications during carotid artery stenting (CAS) but not in carotid endarterectomy (CEA) [7].

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✉ Atsushi Ogata
ogata.a24@gmail.com

[1] Department of Neurosurgery, Faculty of Medicine, Saga University, 5-1-1 Nabeshima, Saga-shi, Saga 849-8501, Japan

[2] Department of Neurosurgery, Karatsu Red Cross Hospital, Karatsu, Saga, Japan

The association between the tortuosity of the extracranial internal carotid artery (ICA) and TEEs during coil embolization of ruptured cerebral aneurysms is yet to be elucidated.

The present study aimed to investigate whether the tortuosity of the extracranial internal carotid artery was a risk factor for TEEs during coil embolization of ruptured cerebral aneurysms.

Methods and materials

Patient population and study design

Patients who underwent the endovascular coil embolization of ruptured cerebral aneurysms within 72 h of symptom onset at our institution between January 2008 and December 2017 were retrospectively investigated. Patients with posterior circulation aneurysms ($n = 25$), those who underwent endovascular parent artery occlusion ($n = 3$), and those who had aneurysms associated with arteriovenous malformations ($n = 1$) were excluded from this study. In patients with multiple aneurysms, only one aneurysm that was most likely to have ruptured was determined on the basis of clot distribution and aneurysmal morphology. Consequently, medical and surgical records of 57 consecutive patients with 57 treated anterior circulation aneurysms were reviewed. The study protocol was approved by the regional ethics committee, and all patients provided informed consent to participate, with no unique patient identifiers being obtained in the study.

All patients underwent a head CT scan including three-dimensional CT angiogram (3D-CTA) on admission. We determined the choice of surgical clipping or endovascular coil embolization through discussions involving surgical and endovascular teams. Endovascular coiling was typically selected for patients with older age, poor grade subarachnoid hemorrhage (SAH), small neck aneurysms, and no incorporated branch.

Endovascular procedure

Endovascular procedures were performed by experienced neurosurgeons (AO and YT) using an angiography imaging system that allowed three-dimensional image reconstruction (Axiom Artis Zeego, Siemens, Munich, Germany) under general anesthesia and systemic heparinization. An intravenous bolus dose of 3000 or 4000 units of heparin was administered immediately after the femoral sheath introducer insertion. Activated clotting time (ACT) was measured after 10 min, and an additional bolus dose of 1000 or 2000 units of heparin was administered for achieving an ACT of between 200 and 250 s. Neither preprocedural antiplatelet therapy nor postprocedural reversal of heparin was performed in any case. A 6-Fr or 7-Fr guiding catheter was navigated into the extracranial ICA. Subsequently, a microcatheter was navigated into the aneurysm and detachable platinum coils such as Target (Stryker Neurovascular, Kalamazoo, MI, USA), Axium (Medtronic, Minneapolis, MN, USA), Trufill DCS Orbit (Johnson & Johnson, New Brunswick, NJ, USA), or ED (Kaneka Medics, Osaka, Japan) were inserted into the aneurysm. A 4F intermediate catheter (4F Cerulean) was additionally used if required. An adjunctive technique, such as balloon-assisted coil embolization or a double catheter procedure, was primarily performed for broad-necked aneurysms for preventing the coil from protruding into the parent artery. Stent-assisted coil embolization was not performed. When the thrombus formed in the parent artery during the procedure, heparin was added for raising the ACT to approximately 300 s and sodium ozagrel (80 mg) was intravenously administered. Glycoprotein IIb/IIIa inhibitors were not used because they are not approved in Japan. The aneurysm occlusion grade was evaluated as per the modified Raymond scale [12] as follows: grade 1, complete occlusion (no contrast agents observed in the aneurysm); grade 2, neck remnant (contrast agents observed in the aneurysmal neck); and grade 3, partial occlusion (contrast agents observed in the aneurysmal cavity). General anesthesia was continued for 24 h following the procedure. All patients underwent a neurological examination at recovery from general anesthesia.

Radiological evaluation

Neck width, height (distance from the neck center to the top of the dome), and width (perpendicular to the aneurysm height) of the aneurysm were measured using a three-dimensional rotational angiography. Dome-to-neck ratio and dome-to-neck aspect ratio were calculated. The dome-to-neck ratio was defined as width to neck. The dome-to-neck aspect ratio was defined as height to neck. Aneurysms with a neck width of > 4 mm were classified as wide-necked. The tortuosity of extracranial ICA was evaluated using cervical carotid angiograms in a lateral projection. Angles were measured by positioning the angle apex at the turning point of the artery and the angle legs at the center of the proximal and distal segment. Angles of extracranial proximal and distal ICA were defined as ICA angle 1 and ICA angle 2, respectively (Fig. 1a). The position of the tip of the guiding catheter including that of the intermediate catheter was categorized as high or low for the analysis. A high-guiding catheter position was defined as C1 or higher in the ICA (Fig. 1b).

Variables and analysis

Thromboembolic events were defined as a new focal neurological deficit with corresponding areas of hypodensity on head CT or high intensity on diffusion-weighted MRI. Patients were divided into the following two groups: those who experienced TEEs and those who did not. The groups were compared and analyzed regarding the following factors. Patient baseline characteristics and initial neurological status represented by the world

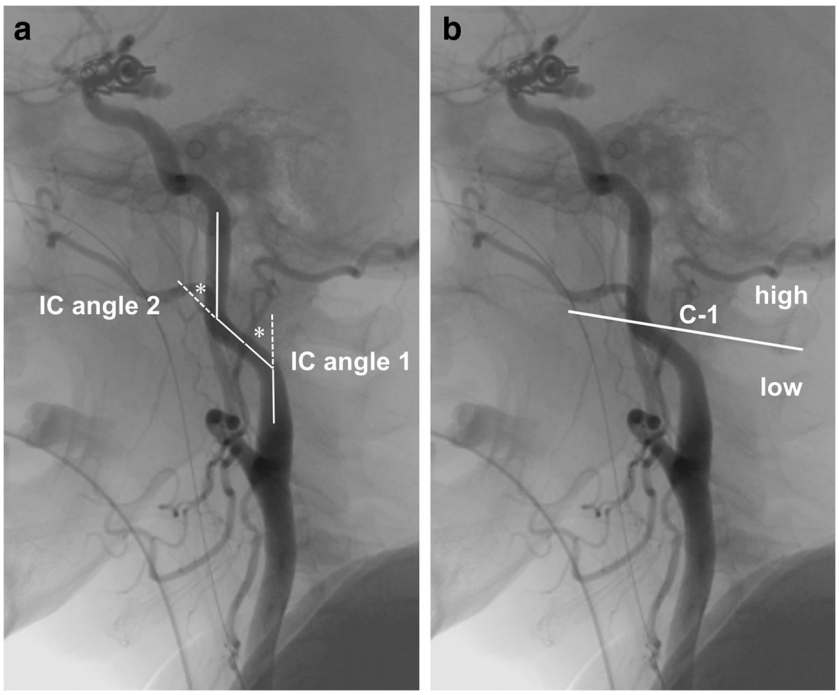

Fig. 1 **a** The evaluation of angles in the course of the internal carotid artery (ICA) using a cervical carotid angiogram in a lateral projection; the angle apex was positioned at the turning point of the vessel and the legs at the center of the ICA with respect to its distal and proximal course. Angles were measured as the change in direction from the caudal to the cranial segments by subtracting the angle between the two legs from 180° as shown by an asterisk (*). Angles of the extracranial proximal and distal ICA were defined as ICA angle 1 and ICA angle 2, respectively. **b** Lateral cervical carotid angiograms for locating the tip of the guiding catheter. The white line indicates a level below the C1 vertebral body, which categorizes the location of the tip of the guiding catheter as high or low

federation of neurological societies (WFNS) grade were analyzed. Next, procedural factors including the position of the guiding catheter (high-guiding catheter or low-guiding catheter), intermediate catheter use, diameter of guiding catheter, the adjunctive technique (double microcatheter or balloon-assisted), modified Raymond scale, intraprocedural thrombus formation, and length of procedure were analyzed. Further, we analyzed the anatomical factors as follows: maximum aneurysm size, neck width, dome-to-neck ratio, dome-to-neck aspect ratio, ICA angle 1, and ICA angle 2.

Statistical analysis

Nominal data were analyzed using Fisher's exact test. Parametric and nonparametric numerical data were analyzed using the *t* test and the Mann–Whitney *U* test, respectively. To find independent variables for TEEs, only variables with $P < 0.10$ on univariable analysis were entered into multivariable analysis with binary logistic regression. Correlations between patient age and ICA angles were examined using Spearman's rank correlation test. We used the software JMP Pro 11 (SAS Institute Inc., Cary, NC) for the statistical analyses. A p value < 0.05 was considered statistically significant.

Results

Three of the 57 patients were excluded because no data regarding the ICA angle was available in their cases. These patients did not experience TEEs. We finally evaluated 54 patients (15 males and 39 females) with a mean age of 69.5 ± 15.2 years (41–95) who underwent endovascular procedures within 72 h of symptom onset. Among them, 33 (61.1%) had a medical history of hypertension, four (7.4%) had type 2 diabetes, six (11.1%) had hyperlipidemia, and five (9.3%) had received oral antiplatelet or anticoagulation agents. The aneurysm was located at the anterior cerebral artery in 28 patients (51.9%), the ICA in 23 patients (42.6%), and the middle cerebral artery in three patients (5.6%). Wide-necked aneurysms were present in eight patients (14.8%). Patient characteristics are shown in Table 1. Thirteen patients with an initial WFNS grade V were included because they showed improvement because of medical treatment or external ventricular drainage before the endovascular procedures, and we could thus evaluate their focal neurological deficits.

TEEs occurred in six patients (11.1%), with five anterior cerebral and one internal carotid aneurysm, and these patients were categorized into the TE (thromboembolic) group. All patients with TEEs had multiple infarcts that suggested embolism in the vascular area of the guiding catheter insertion. Forty-eight patients without TEEs were categorized into the NTE (non-thromboembolic) group. Even though the difference was not significant, the age in the TE group was higher than that in the NTE group (81.3 ± 3.8 vs. 68.9 ± 15.6 years, respectively, $p = 0.058$). No differences were noted between the groups in terms of medical histories, oral antiplatelet agent use, oral anticoagulation agent use, initial WFNS grade, or the location of aneurysms. Comparison of the patient characteristics between the groups is shown in Table 2.

There was no significant difference between the groups in terms of the procedural factors including the position of the guiding catheter, intermediate catheter use, diameter of

Table 1 Patients characteristics

Variable ($n = 54$)	Value
Mean age (years)	69.5 ± 15.2
Female sex, *n* (%)	39 (72.2)
Hypertension, *n* (%)	33 (61.1)
Type 2 diabetes, *n* (%)	4 (7.4)
Hyperlipidemia, *n* (%)	6 (11.1)
Antiplatelet/anticoagulant use, *n* (%)	5 (9.3)
WFNS grade, *n* (%)	
I	16 (29.6)
II	11 (20.4)
III	2 (3.7)
IV	12 (22.2)
V	13 (24.1)
Aneurysm location	
ACA, *n* (%)	28 (51.9)
ICA, *n* (%)	23 (42.6)
MCA, *n* (%)	3 (5.6)
Aneurysms with wide neck (> 4 mm), *n* (%)	8 (14.8)

ACA, anterior cerebral artery; *ICA*, internal carotid artery; *MCA*, middle cerebral artery. Values are presented as mean ± SD when appropriate

guiding catheter, the adjunctive technique, successful embolization of aneurysms (modified Raymond scales 1 and 2), intraprocedural thrombus formation, or length of procedure. The position of the tip of the catheter was high in all the 8 cases using 4F intermediate catheter. No significant differences were noted between the groups in terms of anatomical factors including maximum aneurysm size, neck size, dome-to-neck ratio, dome-to-neck aspect ratio, and ICA angle 1. ICA angle 2 was significantly larger in patients with TE than in those without (74.0 ± 24.9° vs. 49.6 ± 22.5°, respectively, $p = 0.017$). Comparison of the procedural and anatomical factors between the groups is summarized in Table 3. In the multivariable analysis, both patients age (OR 1.04, 95% CI 0.95–1.14, $P = 0.39$) and ICA angle 2 (OR 1.03, 95% CI 0.99–1.08, $P = 0.17$) were not independent predictors of TEEs. Even though the age and ICA angle 1 were partially correlated ($r^2 = 0.08$, $p = 0.04$), the correlation between age and ICA angle 2 was noted to be significant ($r^2 = 0.38$, $p < 0.0001$). Although there was no significance, TEEs frequently occurred in patients with anterior cerebral aneurysms. Patients with anterior cerebral aneurysms were older than the other patients (74.1 ± 14.5 vs 66.1 ± 15.2, $P = 0.05$) with acute ICA angle 2 (57.4 ± 21.4° vs 46.9 ± 25.4°, $P = 0.11$). A representative case with a thromboembolic event is shown in Fig. 2.

Table 2 Comparison of patient characteristics between patients with and without thromboembolic events

	TE ($n = 6$)	NTE ($n = 48$)	*p* value
Mean age (years)	81.3 ± 3.8	68.9 ± 15.6	0.058
Hypertension, *n* (%)	5 (83.3)	28 (58.3)	0.39
Type 2 diabetes, *n* (%)	0	4 (8.3)	1.0
Hyperlipidemia, *n* (%)	1 (16.7)	5 (10.4)	0.53
Antiplatelet/anticoagulant use, *n* (%)	1 (16.7)	4 (8.3)	0.46
WFNS grade (median)	2	3	0.36
Aneurysm location			
ACA, *n* (%)	5 (83.3)	23 (47.9)	0.19
ICA, *n* (%)	1 (16.7)	22 (45.8)	0.22
MCA, *n* (%)	0	3 (6.3)	1.0

TE, thromboembolic; *NTE*, no thromboembolic; *ACA*, anterior cerebral artery; *ICA*, internal carotid artery; *MCA*, middle cerebral artery. Values are presented as mean ± SD when appropriate

Discussion

In the present study, we found an association between the tortuosity of the distal extracranial ICA and TEEs during the coil embolization of ruptured aneurysms. We also found a positive correlation between age and angle of the distal extracranial ICA.

In previous studies, a wide aneurysm neck (> 4 mm) was reported as an anatomical risk factor for TEEs during the coil embolization of ruptured aneurysms [1, 4]. In the present study, aneurysm neck diameter did not differ between patients with or without TEEs. We selected patients with small-necked aneurysms and without an incorporated branch for endovascular coiling, and the proportion of patients with wide-necked aneurysms was relatively small (14.8%). Therefore, the effect of aneurysm neck diameter on TEEs may have been weak. To our knowledge, the present study is the first to show an association between the tortuosity of the extracranial ICA and TEEs during coil embolization of ruptured aneurysms. In addition, we showed a significant correlation between age and angle of the distal extracranial ICA. Patients with TEEs were older than those without TEEs (81.3 ± 3.8 vs. 68.9 ± 15.6 years, respectively, $p = 0.058$). The tortuosity of the distal extracranial ICA may increase TEEs in elderly patients. Although there was no significance, TEEs frequently occurred in patients with anterior cerebral aneurysms. The patients with anterior cerebral aneurysms who were selected for endovascular coiling were elderly with acute ICA angle 2. These factors may cause frequent TEEs in patients with anterior cerebral aneurysms.

Reportedly, etiological factors involved in thromboembolism formation during coil embolization include blood-flow stagnation, intimal injury, various devices (catheters/coils/stents) in contact with blood, and intra-aneurysmal thrombus protrusion [2]. The proportion of patients in the present study with a high-guiding catheter position was similar to those with TEEs and those without. The wall of the ICA may be

Table 3 Comparison of the procedural and the anatomical factors between patients with and without thromboembolic events

	TE ($n = 6$)	NTE ($n = 48$)	p value
Procedural factors			
High-guiding catheter position, n (%)	5 (83.3)	40 (83.3)	1.0
Intermediate catheter use, n (%)	2 (33.3)	6 (12.5)	0.21
Diameter of guiding catheter (French)	5.5 ± 1.2	6.2 ± 0.9	0.10
Adjunctive technique, n (%)	2 (33.3)	17 (35.4)	1.0
Modified Raymond scale 1, 2	5 (83.3)	41 (85.4)	1.0
Intraprocedural thrombus formation	1 (16.7)	2 (4.2)	0.30
Length of procedure (min)	244 ± 67	201 ± 59	0.10
Anatomical factors			
Aneurysm size			
Dome maximum (mm)	6.1 ± 1.7	6.1 ± 2.4	1.0
Neck (mm)	3.3 ± 1.0	3.0 ± 1.1	0.50
Dome–neck ratio	1.4 ± 0.3	1.7 ± 0.5	0.18
Dome–neck aspect ratio	1.6 ± 0.5	1.9 ± 0.7	0.24
ICA tortuosity			
ICA angle 1 (degree)	56.5 ± 29.7	56.5 ± 30.0	1.0
ICA angle 2 (degree)	74.0 ± 24.9	49.6 ± 22.5	0.017

TE, thromboembolic events; *NTE*, no thromboembolic events; *ICA*, internal carotid artery. Values are presented as mean ± SD when appropriate

compressed during straightening with a guiding catheter in patients with a tortuous ICA, which may cause blood-flow stagnation and thrombus formation. Transcranial Doppler measurements during CEA and CAS studies have demonstrated that low-middle cerebral artery mean blood velocity was significantly associated with thromboembolic events in patients with microembolic signals [8, 9]. Blood-flow impairment owing to straightening of a tortuous ICA

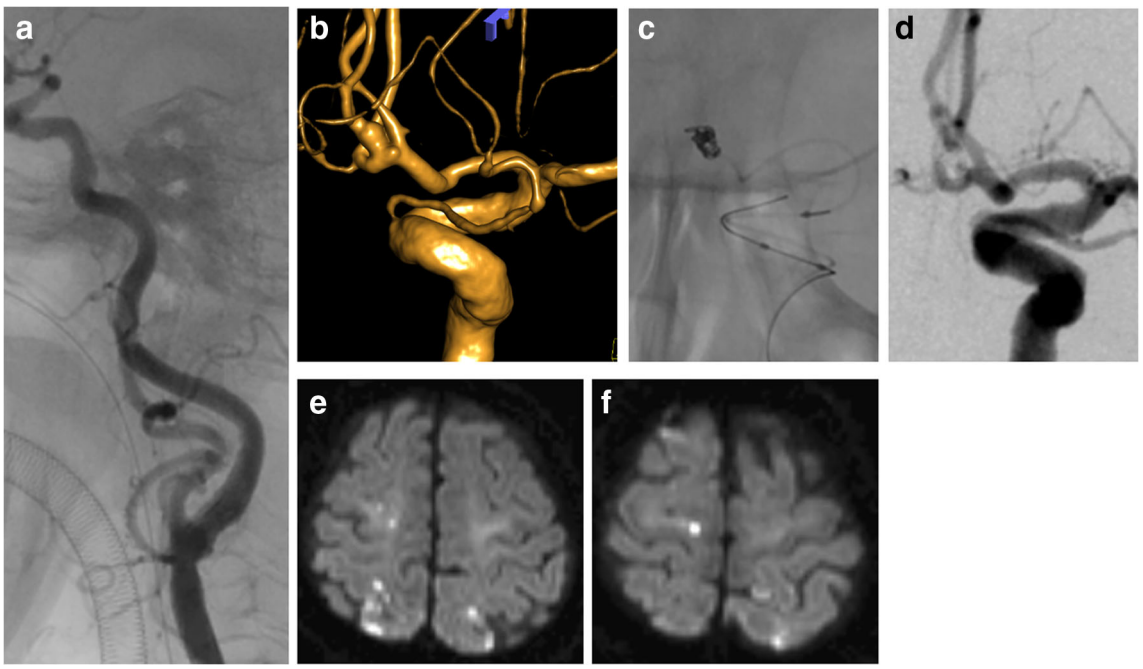

Fig. 2 An 82-year-old woman underwent coil embolization for a ruptured anterior communicating artery aneurysm. She experienced left hemiparesis after the procedure. **a** A lateral left cervical carotid angiogram shows a tortuous ICA with a 75° distal ICA angle. **b** Three-dimensional digital subtraction angiogram shows a small anterior communicating artery aneurysm. **c** Coil mass in the aneurysm immediately after coil embolization. **d** Digital subtraction angiogram immediately after coil embolization shows the anterior communicating artery aneurysm with a neck remnant. **e**, **f** Diffusion-weighted MRI on the day after the procedure shows multiple high-intensity signals in bilateral cerebral hemispheres

may have caused neurological deficits resulting from thromboembolism in this study. Further, intimal injury induced by the guiding catheter may cause TEEs in patients with a tortuous ICA. A sub-analysis study of the Internal Carotid Stenting Study showed that ICA tortuosity increased thromboembolism during CAS, but not during CEA, and proposed that the catheter and guidewire may cause not only atherosclerotic plaque dislodgement but also endothelial microtrauma and ultimately thromboembolism [7]. The present study indicates an association between extracranial ICA tortuosity and TEEs during the coil embolization of ruptured aneurysms as well as during CAS.

For preventing TEEs during the coil embolization of ruptured aneurysms in patients with a tortuous ICA, it may be preferable to avoid the straightening of the ICA. However, a low-positioned guiding catheter reportedly increased the risk of intraoperative aneurysm rupture [3]. Accordingly, the guiding catheter should be positioned sufficiently high for avoiding intraoperative aneurysm rupture even in patients with a tortuous ICA. In patients with tortuous ICA anatomy, the flexible intermediate catheter may preserve native ICA anatomy when compared with single guiding catheter, and TEEs may be eliminated. However, in the present study, the rate of TEEs was not be significantly different between with and without 4F intermediate catheter. This study is a small-sample size, and further study is necessary to investigate whether intermediate catheter reduces TEE in patients with tortuous ICA. A previous study indicated that administration of acetylsalicylic acid during coil embolization reduced TEEs in patients with acute SAH [11]. In the previous study, aneurysm perforation events during or immediately after the procedure were observed equally often in patients who were administered acetylsalicylic acid and those who were not [11]. In acute SAH patients with a tortuous ICA, the administration of antiplatelet agents prior to the manipulation of the guiding catheter may reduce TEEs.

The present study had few limitations, including its retrospective design and its location at a single institution. In the multivariable analysis, ICA angle 2 was not an independent predictor of TEEs and ICA angle 2 significantly correlated with age. Thromboembolic events may have occurred because of other factors, particularly in elderly patients, such as hypercoagulability [4] or atherosclerotic aortic arch plaques [5]. This study is a small-sample size study, and further study is necessary to investigate whether tortuous extracranial ICA is an independent predictor of TEEs. It remained unclear whether the straightening of a tortuous ICA was directly associated with thromboembolic events because we lacked data for analyzing the straightening of tortuous ICAs using guiding catheters. We referred previous studies about ICA stenosis and evaluated two angles as tortuosity of extracranial ICA using cervical carotid angiograms in a lateral projection [7]. However, three-dimensional imaging might be objective and precise to evaluate ICA tortuosity because of complex geometry of extracranial ICA. Three-dimensional imaging of extracranial ICA was not examined in this study. An IC angle that is predictive for TEEs during coil embolization of ruptured aneurysms would be useful. However, establishing its predictive value from this small-sample study may not be adequate, and further multicenter studies are required.

Conclusions

The tortuosity of the extracranial ICA was significantly associated with an increased incidence of thromboembolic events during endovascular coiling of anterior circulation ruptured aneurysms.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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