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Endovascular Treatment for Lateral Wall Paraclinoid Aneurysms and the Influence of Internal Carotid Artery Angle

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Abstract

Lateral wall paraclinoid aneurysms (LPA) are a rare type of aneurysm located on the lesser curve side of the internal carotid artery (ICA) bend, at the level of the anterior clinoid process. The objective of this study was to assess the influence of flexion of the ICA on the morphology of aneurysms and outcome of endovascular treatment. Between 2003 and 2018, we treated 643 cases of unruptured paraclinoid aneurysms with endovascular therapy in our institution. Of those cases, aneurysms projecting laterally on preoperative angiography were defined as LPA. The degree of bending of the ICA (ICA angle) was measured and statistically analyzed in relation to the aneurysm characteristics and the occlusion status after treatment. In all, 43 aneurysms were identified. ICA angle was positively correlated with the maximum dome size of the aneurysm ($P < 0.01$) and the aspect ratio ($P < 0.01$), and negatively correlated with the volume coil embolization ratio ($P < 0.01$). Complete occlusion (CO) was achieved in 23 cases (53.5%) immediately after treatment, and in 35 cases (81.4%) at follow-up. The mean ICA angle in the incomplete occlusion group was significantly larger than in the CO group ($P = 0.01$). Larger ICA angle resulted in recurrence, whereas smaller ICA angle was more likely to obtain progressive thrombosis ($P = 0.02$). Endovascular treatment for LPA was safe and effective. The degree of flexion of the ICA may contribute to the level of hemodynamic stress on the aneurysm, its morphology, and the embolization effect.

Keywords: angle, endovascular, internal carotid artery, lateral wall, paraclinoid aneurysm

Introduction

To date, various classifications for the location of paraclinoid aneurysms, such as anterior wall aneurysms, ventral carotid aneurysms, true ophthalmic aneurysms, superior hypophyseal artery (SHA) aneurysms, carotid cave aneurysms, and transitional aneurysms, have been reported from the anatomical and therapeutic viewpoints.[1–4] Furthermore, good outcomes are being achieved with endovascular treatment because of recent developments in stent devices, such as neck-bridging stents and flow-diverters.[5–8] In particular, endovascular treatment for ophthalmic segment aneurysms, including true ophthalmic aneurysm and SHA aneurysm, is effective and safe.[9–11]

However, there are only a few reports of aneurysms with a dome projecting laterally and the neck originating from the lateral wall of the paraclinoid potion of the internal carotid artery (ICA).[4,12,13] These aneurysms are of the sidewall-type, occur at non-branching sites that do not have perforating vessels, and have an orifice located on the lesser curve side of the ICA bend at the level of the anterior clinoid process. The level of hemodynamic stress on the aneurysm can change depending on the degree of lateral flexion of the ICA as the parent artery, which may have a hemodynamic effect on aneurysm morphology and occlusion status after endovascular treatment.

In the present study, we retrospectively evaluated the relationship between the degree of flexion of the ICA and aneurysm morphology, as well as long-term outcomes following endovascular treatment.

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Materials and Methods

Case selection

Between January 2003 and September 2018, endovascular treatments were performed for 643 unruptured paraclinoid aneurysms in our institution. Of these aneurysms, ophthalmic segment aneurysms with a dome protruding outward in the anterior–posterior (A-P) view of angiography, and which formed a double contour with the ICA as the parent artery in the lateral view, or in which the neck arose from the outer surface of the ICA on three-dimensional digital subtraction angiography (3D-DSA), were defined as lateral wall paraclinoid aneurysms (LPA).

Measurement of the ICA angle

To evaluate the degree of lateral flexion of the supraclinoid region from just distal part of the anterior genu of siphon or the origin of the ophthalmic artery to the ICA terminal, two lines through the midpoints of the diameters[14,15] of the distal and proximal part of inflection point were traced in the A-P view of angiography (Figs. 1A and 1B). In the case where the ICA is either entirely curved or the inflection point is seen as a short axis in the A-P view, the lines were obtained by a linear approximation method based on the midpoints, which were placed to divide the distal and proximal to the inflection point into four equal parts, respectively, using the longest and most widely visible view of the bending area on 3D-DSA (Figs. 1C and 1D). The lesser angle obtained at the intersection was measured as the ICA angle. The software Image J Version 1.53a (National Institutes of Health, Bethesda, MD, USA) was used for all tracing and measurements.

Endovascular treatment

All patients were treated under general anesthesia. In patients with an unruptured aneurysm, we administered a single or dual anti-platelet drug (100 mg aspirin and/or 75 mg clopidogrel) at least 1 week before surgery. We selected the most suitable type of endovascular technique (simple, double catheter, balloon-remodeling, stent-assisted, flow-diverter placement) for each patient. All coils were bare platinum coils. In principle, we performed the jailing technique when using a stent together with the transcell technique, as appropriate. For patients with a high aspect ratio and a large aneurysm (>10 mm), into which there was a marked jet flow and inertia-driven flow on angiography, adjunctive coiling was applied as densely as possible to prevent delayed cerebral aneurysm rupture in cases using a flow-diveter.[16]

Post-treatment anti-platelet drug management continued for 1 month in patients not using a stent device. In many cases using stent-assisted or flow-diverter treatment, dual anti-platelet drug treatment was continued for 1 year, after which one antiplatelet agent was continued for a further year.

Volume embolization ratio

The coil volume (Vcoil) was calculated using the primary diameter (p) and length (L) of the coil (Vcoil $= \pi \times (p/2)^2 \times L$). The volume (Vaneurysm) was calculated using an equation that approximated an ellipsoid using the vertical diameter (a) and horizontal diameter (b) (Vaneurysm $= 4/3\pi \times a/2 \times b/2 \times (a + b)/4$). The volume embolization ratio (VER) was calculated as Vcoil/Vaneurysm × 100(%). VER of ≥25% is considered high.[17,18]

Assessment of the occlusion status after treatment and follow-up

The occlusion status of the aneurysms was evaluated by 3D-DSA and/or magnetic resonance imaging (MRI) or magnetic resonance angiography (MRA) at follow-up examinations performed every 6 months after treatment. The Raymond—Roy occlusion classification[19] was used to assess the occlusion status, as follows: complete occlusion (CO), neck remnant (NR), and body filling (BF). A change from CO to NR or BF, or a change from NR to BF, was defined as "recurrence." And a change from NR or BF to CO, or from BF to NR, was defined as "thrombosis." No change of occlusion status was defined as "no change." Patients treated with a flow-diverter stent were evaluated by silent MRA.[20]

Statistical analyses

All statistical analyses were performed using statistical software (EZR; Saitama Medical Centre, Jichi Medical University, Saitama, Japan), a graphical user interface for R (v2.13.0; The R Foundation for Statistical Computing, Vienna, Austria). Data are presented as mean ± standard deviation, and were analyzed with an unpaired t-test and the Pearson product–moment correlation coefficient. Jonckheere–Terpstra test was used to determine whether there were statistically significant trend between ICA angle and change of occlusion status. and we performed multivariate logistic regression analysis with the ICA angle and the other variables known to be risk factors for recurrence, such as dome size, wide neck (>4 mm), initial occlusion status, low VER (<25%), and non-stent devise,[5,19,21,22] to assess the association with recurrence and incomplete occlusion. Statistical significance was defined as P <0.05.

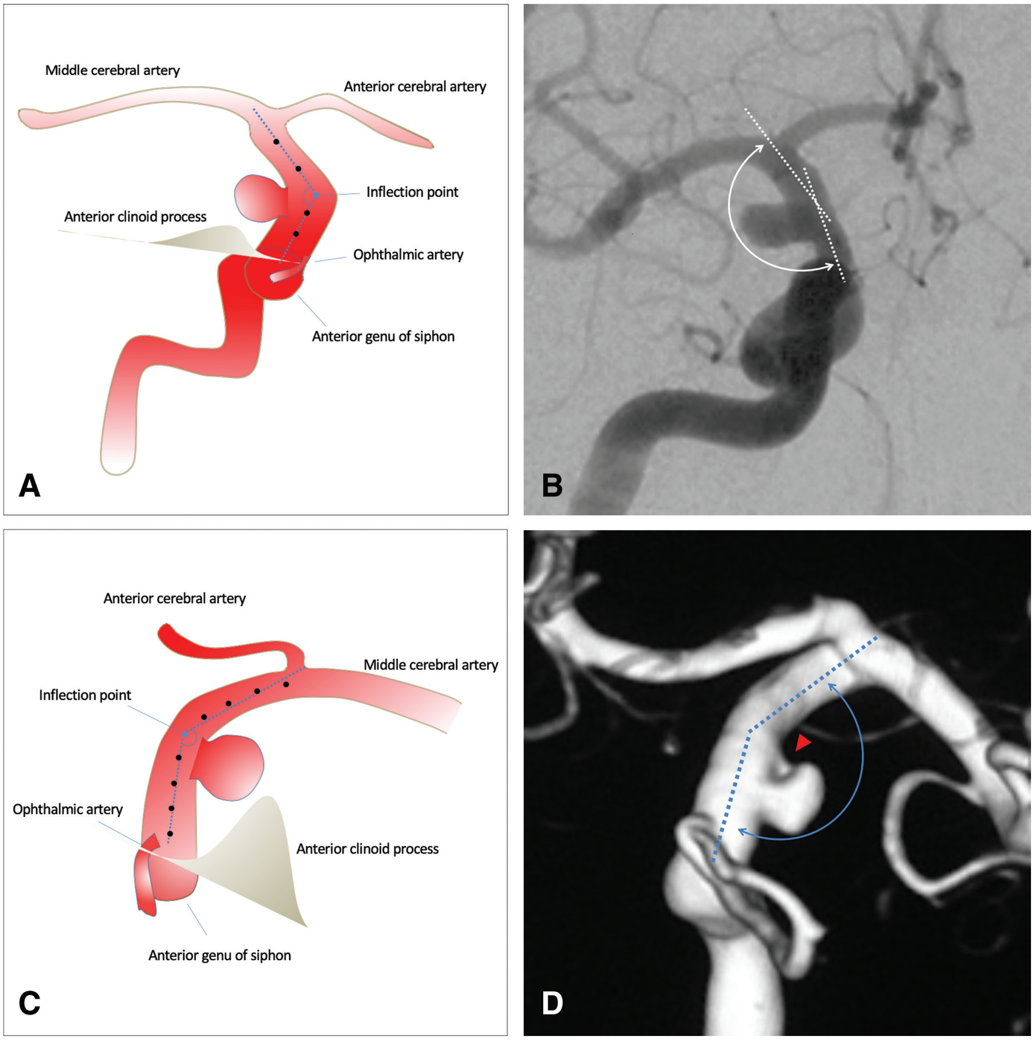


Fig. 1 Measurement method of the ICA angle on the lesser curve side. An illustration of the lateroflection angle of the ICA with lines traced through the midpoints of the diameters of the supraclinoid portion in the anterior–posterior view of angiography (A) and an actual measured example (B). An illustration of the measurement method on 3D-DSA (C). The intersection is consisted of two lines drawn by the linear approximation method based on the midpoints of the diameter of the curve vessel. An actual measured case (D). Local thrombosis was found as a contrast defect (arrowhead) in the inflow zone of the aneurysm in close proximity to the inflection point. ICA: internal carotid artery, 3D-DSA: three-dimensional digital subtraction angiography.

Results

In all, 43 cases of LPA in 43 consecutive patients (6.7%) were detected. The baseline characteristics and the outcomes of endovascular treatment are summarized in Table 1.

Patients' characteristics and aneurysm size

There were 13 cases of small aneurysms (<5 mm), 21 cases of aneurysms (≥5 mm and <10 mm), 9 cases of large aneurysms (≥10 mm), and a total of 19 cases of wide-necked aneurysms (>4 mm). Most of the cases were found incidentally during general MRI for brain health screening and headache examination, except for one case of a large aneurysm that developed during oculomotor nerve palsy. There was no correlation of aneurysm size with age, sex, presence of hypertension, smoking history, drinking history, family history, coexistence of other aneurysms, side of lesion, or shape.

The mean ICA angle was 116 ± 24°, with a range of 60–164°. There was a trend toward a greater mean ICA angle and a larger mean maximum aneurysm size in the female group and the >60 years old group (not significant). There was also no correlation of ICA angle with the presence of hypertension, smoking history, drinking history, family history, side of lesion, coexistence of other aneurysms, or shape.

Table 1 Clinical characteristics and treatment outcome of patients with lateral wall paraclinoid aneurysm (n = 43)

Parameters	Data
Age (year, mean ± SD)	60.4 ± 12.1
Sex (male : female)	4 : 39
Side (right : left)	28 : 15
Aneurysm dome size (mm, mean ± SD)	6.9 ± 3.1
Aneurysm neck size (mm, mean ± SD)	4.2 ± 1.6
Aspect ratio (mean ± SD)	1.5 ± 0.7
ICA angle (degree, mean ± SD)	116 ± 24
Shape (regular : irregular)	23 : 20
Coexistence of other aneurysms (n, %)	15 (34.9)
Past history of Hypertension (n, %)	13 (30.2)
Smoke (n, %)	9 (20.9)
Alcohol (n, %)	9 (20.9)
Family history (n, %)	7 (16.3)
Endovascular technique	
Simple technique (n, %)	2 (4.7)
Balloon remodeling technique (n, %)	12 (27.9)
Double catheter technique (n, %)	1 (2.3)
Stent assist technique (n, %)	19 (44.2)
Flow diverter placement (n, %)	9 (20.9)
VER (%, mean ± SD)	38.2 ± 19.5
Initial occlusion status	
CO (n, %)	23 (53.5)
NR (n, %)	4 (9.3)
BF (n, %)	16 (37.2)
Final occlusion status	
CO (n, %)	35 (81.4)
NR (n, %)	5 (11.6)
BF (n, %)	3 (7.0)
Recurrence status	
Thrombosis (n, %)	18 (41.9)
No change (n, %)	21 (48.8)
Recurrence (n, %)	4 (9.3)
Complication (n, %)	3 (7.0)
Follow-up duration (months, mean ± SD)	25.9 ± 24.6

BF: body filling, CO: complete occlusion, ICA: internal carotid artery, NR: neck remnant, VER: volume embolization ratio.

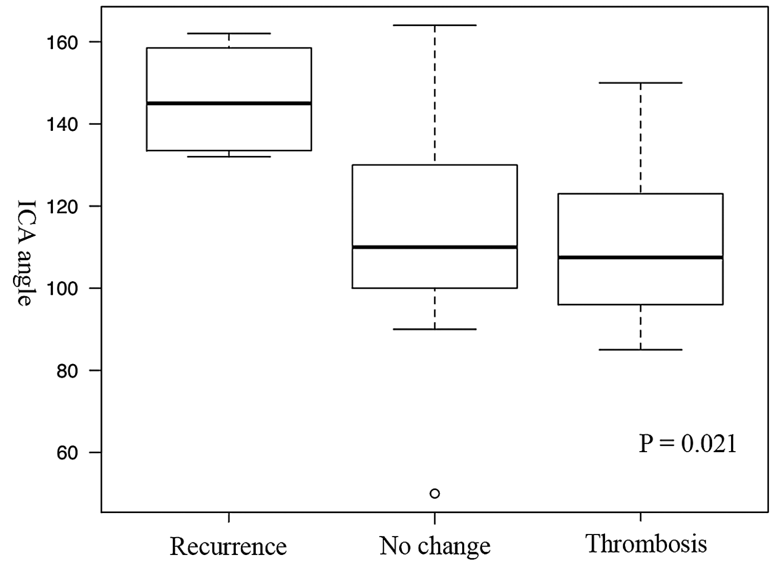
However, the ICA angle was significantly positively correlated with the maximum aneurysm diameter (r = 0.404, P = 0.007) and aspect ratio (r = 0.406, P = 0.006), except for neck size. Large aneurysms (>10 mm) had a significantly larger ICA angle than for smaller aneurysms (138 ± 20° vs. 112 ± 22°, respectively; P = 0.004). The ICA angle was also significantly larger in aneurysms with a higher aspect ratio (>2; 142 ± 15° vs. 112 ± 22°, respectively; P = 0.005). Three of five cases with a high aspect ratio (>2) were not large in size, but had a large ICA angle (132 ± 7°). By contrast, there was a significant negative correlation of ICA angle with VER (r = -0.439, P = 0.004), even when cases using the flow-diverter were excluded (r = -0.381, P = 0.02).

Outcomes of endovascular treatment

The occlusion status immediately after treatment was CO in 23 cases (5 cases with a flow-diverter placement, 10 cases with a neck-bridge stent, 8 cases with the other technique; P = 1). There was no significant difference in the ICA angle between the CO and non-CO cases immediately after treatment (117 ± 25° vs. 112 ± 20°, respectively; P = 0.45). COs were archived in 35 cases (9 cases with a flow-diverter placement, 15 cases with a neck-bridge stent, 11 cases with the other technique; P = 0.32) at follow-up, and 15 of 20 cases (75.0%) that were non-CO immediately after treatment became CO at follow-up. The mean ICA angle in non-COs at follow-up was significantly larger than in COs at follow-up (133 ± 23° vs 112 ± 22°; P = 0.01). The mean VER was 38.2 ± 19.5% and 6 (54.5%) out of 11 cases with a low VER (<25%) obtained progressive thrombosis with the mean ICA angle of 118 ± 23°.

The relationship between the change of occlusion status and ICA angle is shown in Fig. 2. The aneurysms in four recurrent cases (one case with balloon remodeling technique and three cases with a neck-bridge stent) were not large and obtained a high VER (45.0 ± 12.6%), but had a large ICA angle (146 ± 14°). Larger ICA angle resulted in recurrence, whereas smaller ICA angle was more likely to obtain progressive thrombosis (P = 0.02). All recurrent cases continue to be observed and no retreatment was performed because there was no residual enlargement. In multivariate analysis, ICA angle (odds ratio: 1.12; 95% confidence interval: 1.03–1.21; P = 0.005) and wide neck (odds ratio: 76.1; 95% confidence interval: 1.20–484; P = 0.04) were significant risk factors for the long-term incomplete occlusion and recurrence (Table 2).

A total of three cases showed complications. Of those, asymptomatic cerebral infarction indicated by a signal hyperintensity on diffusion-weighted imaging at post-procedural MRI was observed in three cases (two cases with a flow-diverter stent and one case with a neck-bridge stent). The overall permanent morbidity and mortality were 0% in our series.



The relationship between the recurrence status and ICA angle.

	Recurrence (n = 4)	No change (n = 21)	Thrombosis (n = 18)
ICA angle (°)	146.0 ± 14.1	114.5 ± 24.9	110.8 ± 19.0

ICA: internal carotid artery

Fig. 2 Correlation of ICA angle with recurrence status, which are recurrence, no change, and thrombosis. The correlation indicated that larger ICA angle results in recurrence, whereas smaller ICA angle was more likely to obtain progressive thrombosis (*P* = 0.02). ICA: internal carotid artery.

Discussion

Previous reports of LPAs only involved treatment studies of all paraclinoid aneurysms[4,13,23] or small surgical case series.[12] A key finding of the present study was that ICA angle is a hemodynamic factor that contributes to aneurysm morphology. In a study examining the relationship between ICA curvature and the presence of sidewall aneurysms, Lauric et al.[24] reported that curvature was highly correlated with aneurysm presence, but not with age, hypertension, or smoking status, as observed in the present study. Waihrich et al.[15] also measured the angle of the siphon part of the ICA using lateral view DSA images, and evaluated the location and size of the cerebral aneurysms. In that study, there was a significant independent direct relationship of greater angle with intracranial aneurysms located distal to the carotid siphon, larger aneurysms, and greater risk of rupture. The authors suggested that the linear velocity of the laminar flow in the parent artery, and the linear vector force in the form of a water hammer pulse into the aneurysm, varied depending on the degree of the angle. A similar hemodynamic situation is speculated for LPAs. As the ICA angle increases, the ICA tends to straighten, which reduces turbulence,

Table 2 Multivariate logistic regression analysis on factors associated with recurrence and incomplete occlusion in the final status

Factors	Odds ratio	95% confidence interval	*P* value
Dome size	0.51	0.22–1.14	0.098
ICA angle	1.12	1.03–1.21	0.005
Wide neck >4 mm	76.1	1.20–484	0.040
VER <25%	0.22	0.01–5.54	0.360
Non-stent devise	6.76	0.37–122	0.195
Initial occlusion status (BF, NR vs CO)	2.29	0.20–26.1	0.505

BF: body filling, CO: complete occlusion, ICA: internal carotid artery, NR: neck remnant, VER: volume embolization ratio.

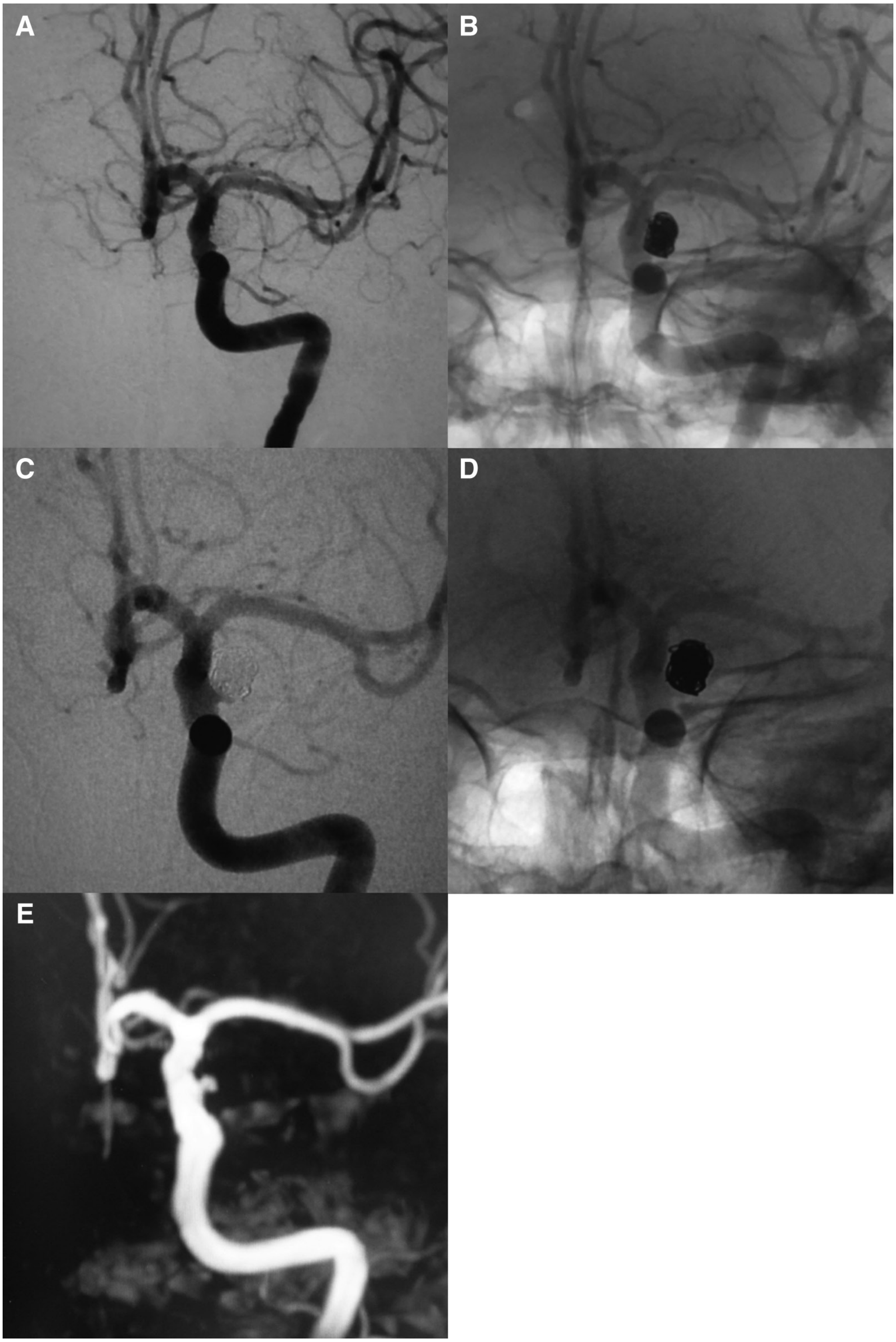


Fig. 3 A 62-year-old woman had left LPA and ICA angle of the patient showed 155° which was relatively large. Balloon remodeling coil embolization was performed (A: DSA, B: digital angiography) and occlusion status of the immediately after the procedure was CO. One year after the treatment showed NR of the aneurysm (C: DSA, D: digital angiography). (E) The head MRA 6 years after the treatment showed BF of the aneurysm. BF: body filling, CO: complete occlusion, DSA: digital subtraction angiography, ICA: internal carotid artery, LPA: lateral wall paraclinoid aneurysm, MRA: magnetic resonance angiography, NR: neck remnant.

while the linear vector force on the aneurysm increases the linear velocity laminar flow from the ICA. Based on a computational fluid dynamics study by Sforza et al.[25] describing hemodynamic conditions that may predispose aneurysms to growth, this situation may result in a higher concentration of wall shear stress, and thus larger aneurysms. In contrast to these LPAs, SHA aneurysms, which are also sidewall-type aneurysms, are located at the medial wall of the ICA on the side with the greater curve. In the present study, progressive occlusions showed an equivalent or greater outcome than that for SHAs. Of the 29 cases of SHA that were non-CO immediately after treatment, 17 cases (58.6%) were CO at follow-up.[10] By contrast, 15 of 20 non-CO cases (75.0%) transitioned to CO at follow-up in our series.

Using the natural world as an example, meandering rivers show less erosion on the side with the lesser curve compared with that on the side with the greater curve, and the river bed is formed on the lesser curve side. Natural science experiments also show that the lesser curve side has a lower flow velocity.[26,27] Because LPAs are located on the lesser curve side, there is less hemodynamic stress than that for SHAs located on the greater curve side, which show greater progression of post-treatment occlusion. Furthermore, those experiments show that erosion on the greater curve side increases, while that on the lesser curve side decreases, compared with the straight area of the river. As such, the larger the ICA angle, the more linear the ICA, which may increase blood flow stress on the lesser curve side, and thus increase the LPA size or recurrence after treatment. Conversely, flexion of the parent vessel may be a favorable condition for progressive occlusion of the LPA on the lesser curve side. In the present study, the four with recurrence did not have large aneurysms, but had a large ICA angle, suggesting that these hemodynamic conditions contributed to the aneurysm recurrence (Fig. 3).

The stability of the microcatheter during coil embolization is a factor related to the negative correlation of the ICA angle with VER. The microcatheter is usually curved in a C-shape against the parent artery, which is then shaped to fit the wall of the ICA opposite to the aneurysm orifice. When the microcatheter is placed in a straight vessel, the axis of the microcatheter is parallel to the parent artery, and the coil is inserted in a perpendicular direction. However, with tightening of the coil packing, the coil insertion vector tends to slip toward the distal direction of the ICA, rather than into the aneurysm, which reduces stability, and the finishing coil and microcatheter are kicked back and escape from the aneurysm. The use of a neck-bridging stent improves stability and provides higher coil packing (P <0.01).

In our multivariate analysis, a wide neck and a larger ICA angle were significantly associated with recurrence and long-term incomplete occlusion. With regard to aneurysm size, a wide neck is already well known as a risk factor for recurrence and incomplete occlusion,[21,22] whereas dome size was not significantly correlated in the present study. All cases of large aneurysms treated with flow-diverter placement achieved long-term CO without recurrence, and more than half of the cases with a low VER, non-stent devise or initial incomplete occlusion also had progressive thrombosis, which may be reflected in the results of the multivariate analysis that did not show significant differences in these variables. We consider that this is involved in localization characteristics that potentially lead to progressive occlusion and different hemodynamic stress depending on the degree of ICA angle. Flow-diverter placement is likely to be the most suitable treatment that takes advantage of their anatomical localization features to promote potential embolic effects.

The location selected for removal of the anterior clinoid process and the dural ring incision is an important consideration for direct surgery. These procedures have a risk for complications such as vision deficits and hemorrhage due to opening of the cavernous sinus and cerebrospinal fluid leakage. Nevertheless, in a report of more than 100 cases of paraclinoid aneurysms receiving endovascular treatment after 2010, the rate of complications was 2.5–4%, and mainly included thromboembolic events, while the rate of permanent morbidity was 0–1.4%.[5–7,28–30] In our series, there were no symptomatic complications due to the endovascular procedure, and no cases with permanent morbidity. Thus, because of modern developments in techniques and devices, endovascular treatment for paraclinoid aneurysms is safe and effective, especially for LPAs as they are at non-branching sites, and are sidewall-type aneurysms located on the lesser curve side of the ICA.

Limitations

There are limitations to this study. Due to a retrospective study of a rare type of aneurysm, the number of cases was limited and presumably affected the results of the multivariate analysis, which calculated a very large odds ratio and wide confidence intervals for one of the variables, wide neck. Besides, the hemodynamics within the aneurysm and the parent artery were not analyzed by computational fluid dynamics. In fact, the ICA entirely runs in a spiral upward from the cavernous portion to the supraclinoid portion including the top of the ICA, and the segment that appears to be a straight line in the A-P view, lateral view, or working view of the angiography may not actually be a straight line anatomically. Therefore, it is necessary to take measurements with the specified view according to the target lesion and pathology, as in endovascular treatment. In discussing the localization characteristic of the LPA with orifice in the lateral wall of the ophthalmic segment which bends from anterior medial to posterior lateral to run over the clinoid process,[31] we focused on the effect of lateral flexion rather than anterior–posterior flexion in this study, and basically measured the lateroflection angle on the standardized A-P view to most concisely capture the lateral bending of the ICA. There were three cases in which the supraclinoid portion of the ICA without straight parts, and the lines were traced by the linear approximation method. Even if these three cases were excluded, there was a statistically significant difference in the occlusion status ($P = 0.02$). It is necessary to accumulate further number of cases in the future and to investigate them in detail.

Conclusions

Endovascular treatment for LPAs was safe and effective. LPA may potentially acquire embolic characteristics because of their anatomical localization, in addition, the degree of flexion of the ICA may contribute to the level of hemodynamic stress on the aneurysm, its morphology, and the embolization effect.

Conflicts of Interest Disclosure

Oishi Hidenori received donations from Terumo Corporation, Stryker Japan K.K., Johnson & Johnson K.K., and Kaneka Medical Products. Oishi Hidenori received lecture fees from Stryker Japan K.K., Johnson & Johnson K.K., Medtronic Japan Co., Ltd., and Covidien plc. Oishi Hidenori received research funding from Otsuka Pharmaceutical, MSD K.K., Takeda Pharmaceutical, Daiichi Sankyo Co., Ltd., and Medikit Co., Ltd. The other authors declare no conflicts of interest. Every authors have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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