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ORIGINAL ARTICLE

Endovascular Treatment of Fenestration-related Aneurysms

Morphological Features, Operative Techniques and Therapeutic Outcomes

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Abstract

Purpose Endovascular treatment of fenestration-related aneurysms (FAs) is prone to technical challenges, given the inherent complexities. Herein, we have analyzed FAs in terms of angioarchitectural characteristics and outcomes achieved through endovascular intervention.

Methods Data accrued prospectively between January 2002 and July 2020 were productive of 105 FAs in 103 patients, each classifiable by the nature of incorporated vasculature as proximal portion, fenestrated limb, or distal end. Our investigation focused on clinical and morphological outcomes, with emphasis on technical aspects of treatment.

Results The FAs selected for study originated primarily in anterior communicating artery (AcomA: 88/105, 83.8%), followed by basilar (7/105, 6.7%), anterior cerebral (4/105, 3.8%), and internal carotid (3/105, 2.8%) arteries. In nearly all locations, proximally situated aneurysms (43/105, 41%) were more frequent than aneurysms arising at distal ends (3/105, 2.8%), but the majority of AcomA lesions involved fenestrated segments (58/88, 65.9%); and most fenestrated channels (90/105, 85.7%) were asymmetric in size. Orifices of smaller fenestrated limbs were intentionally compromised during coil embolization in 23 aneurysms (21.9%), achieving complete ($n=19$) or incomplete ($n=4$) compromise, without resultant symptomatic ischemia. Saccular occlusion proved satisfactory in 77 lesions (73.3%). In follow-up monitoring of 100 patients for a mean period of 35.3 ± 26.5 months, 17 instances of recanalization (17.0%) occurred (minor, 9; major, 8). There was no recanalization of aneurysms with compromised limbs.

Conclusion Coil embolization of FAs is safe and effective, enabling tailored procedures that accommodate aberrant angioanatomic configurations. Compromise of a single limb during coiling also appears safe, conferring long-term protection from recanalization.

Keywords Fenestration · Aneurysm · Coil · Compromise · Recanalization

Introduction

Arterial fenestration is a well-known vascular variation in which redundant channels of an ordinarily single-bore vessel converge downstream. Each limb (or channel) has its own endothelial and muscular layers, although adventitial layers may or may not be shared [1, 2]. In previous studies, the reported prevalence of fenestration has varied by diagnostic modality: magnetic resonance angiography (MRA) (1.5–2.77%), computed tomography angiogra-

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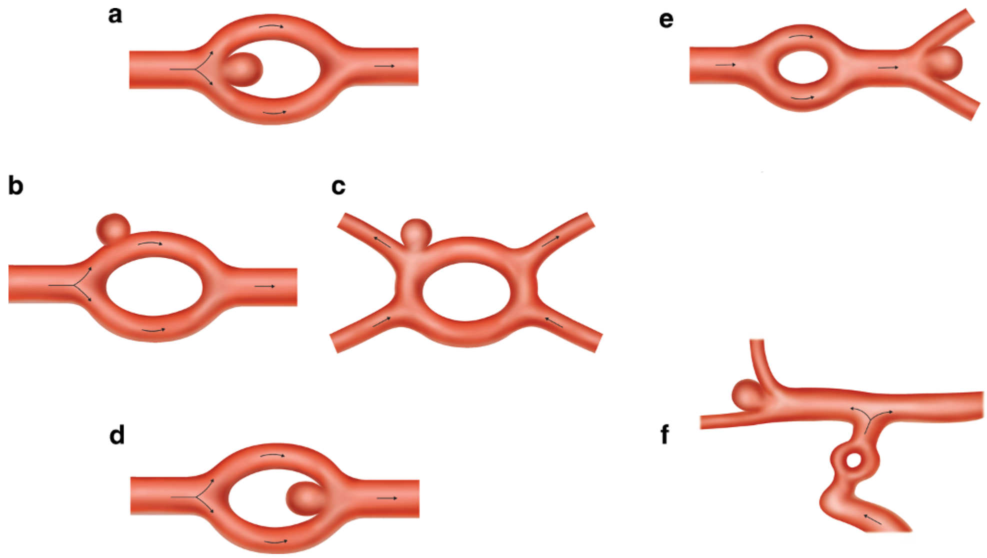

Fig. 1 Schematic of qualifying and ineligible patients with fenestration-related aneurysms (FAs): inclusion (**a**–**d**). Qualifying patients with true FAs, involving proximal end, fenestrated limb, or distal end; and exclusion (**e**, **f**). Ineligible subjects with FAs adjacent to/separate from fenestration or remotely located. **a** Proximal portion, **b**, **c** fenestration limb, **d** distal end, **e** aneurysm adjacent to separate from fenestration, **f** aneurysm located far from fenestration

phy (CTA) (2.3–12.9%), or digital subtraction angiography (DSA) (2.1–28%) [1, 3–15]. Fenestration is similar to arterial duplication (also dubbed extreme fenestration) in which redundant vessels originate separately and do not coalesce [3, 16, 17].

Aside from an aberrant nature, the clinical importance of fenestrations is their known association with other vascular conditions, such as cerebral aneurysms, ischemia, moyamoya disease (MMD), and arteriovenous malformations (AVMs) [1, 3, 8, 17, 18]. Aneurysms are the most frequently reported accompaniments in this setting for reasons that are not yet clear [4–6, 9, 18]. The complexities of fenestration-related aneurysms (FAs) pose technical difficulties to both surgical and endovascular modes of treatment [4, 5, 12, 17, 19, 20].

Available publications on endovascular treatment of FAs consist primarily of case reports or small case series. In the present study, we analyzed angioarchitectural characteristics of FAs and outcomes achieved through endovascular treatment, with emphasis on technical aspects of intervention.

Material and Methods

Study Population and Data Collection

Between February 2002 and July 2020, 5291 patients harboring 6170 intracranial aneurysms underwent endovascular treatments at our institute. Within this population, 103 patients (1.9%) with treated FAs ($n = 105$) were consecutively enrolled for the study. The FAs were qualified as any aneurysms involving fenestrations, classifiable by nature of incorporated vasculature (proximal portion, fenestrated limb, or distal end) (Fig. 1). Aneurysms adjacent to (but separate from) fenestrations or located remotely were ineligible (see Fig. 1). Conventional angiography and 3D rotational imaging provided confirmation of all lesions.

Medical variables reviewed in retrospect included sex, age, clinical presentation, i.e. subarachnoid hemorrhage (SAH) or unruptured intracranial aneurysm (UIA), and second embolization (retreatment) as patient-related factors. Angiographic features, specifically location and size of aneurysm, neck width, depth-to-neck (D/N) ratio, shape of aneurysm (without bleb vs. with bleb change), aneurysm/fenestration relation (proximal, distal, or fenestrated limb), symmetry of fenestrated limbs, embolization technique, and initial occlusive status, were also retrieved. Symmetric fenestrated limbs displayed diameter ratios >0.9. Configurations and arterial architectural views of all aneurysms relied on cerebral angiography and rotational angiography with 3D image reconstruction (Innova IGS 630, GE Healthcare, Chicago, IL, USA; Integris V or Allura Clarity, Philips Medical Systems, Best, The Netherlands). The 3D angiographic images supplied maximum dimensions and neck widths of aneurysms. We determined D/N ratios and fenestrated limb symmetry from working projections of cerebral angiography.

Each patient granted informed consent for treatment after careful consultation (evaluating risks, benefits, and alternatives, such as surgical clipping), as part of a multidisciplinary decision-making process backed by neurosurgical and neurointerventional teams. This study adhered to principles stipulated in the Declaration of Helsinki and received the approval of our Institutional Review Board. Required patient consent for this retrospective investigation for this study was waived.

Endovascular Procedure

Most endovascular procedures entailed general anesthesia. Patients with unruptured aneurysms routinely received pre-procedural antiplatelet agents (clopidogrel and aspirin), using the VerifyNow P2Y12 assay (Accumetrics, San Diego, CA, USA) to test for clopidogrel resistance. In November 2014, we introduced low-dose prasugrel as premedication, eliminating clopidogrel by June 2016.

A bolus of unfractionated heparin (3000 IU) given after femoral arterial sheath placement was then boosted at hourly intervals (1000 IU), with hourly monitoring of activated clotting times. Patients with acutely ruptured aneurysms were exempt from antiplatelet premedication, reserving systemic heparinization until adequate protection was in place. Coiling continued until lesions appeared satisfactorily obliterated. In patients with stents, we advised sustained dual antiplatelet therapy for at least 3 months postembolization, with single-agent maintenance thereafter for a minimum of 1 year. Maintenance antiplatelet regimens were otherwise prescribed in instances of prior antiplatelet agent use, coil protrusion, or procedural thromboembolic complications.

In some cases, we intentionally compromised one fenestrated limb during coil embolization by coiling the adjoining saccular neck. Entire limbs were not obliterated (Figs. 2 and 3). It was also essential to confirm that perforators were absent in targeted limb segments, using 3D rotational images and magnification views of working projections. Ultimately, limb compromise was deemed complete or incomplete, based on postprocedural angiographic flow determinations. In instances of complete compromise, completion angiography served to confirm retrograde filling of one limb through the other.

Angiographic Results and Clinical Outcomes

Two experienced neurointerventionists assessed initial angiographic occlusive states after coil embolization, using the Raymond classification (complete occlusion, residual neck, or residual sac), complete occlusion and residual neck signifying successful outcomes. Follow-up MRA was performed at 6, 18 (or 12, 24), and 36 months after coil embolization, invoking DSA to address retreatment of suspected recanalization. During follow-up visits, occlusive assessments relied on latest follow-up DSA and MRA studies. Recanalization was stratified by Raymond scale as complete, minor, or major. Major recanalization was a ground for repeat embolization.

Intraprocedural rupture (IPR) was identifiable via fluoroscopic angiography, shown by direct device visualization (extraneous to aneurysm) with extravasation of contrast agent. Thromboembolic (TE) events were marked by luminal filling defects, within-vessel contrast stagnation, or non-visualization of distal arterial segments. Postprocedural neurologic deterioration called for CT or MR scans to confirm any hemorrhage and ischemic lesions. Treatment-related infarctions in vascular territories likewise indicated TE events. The modified Rankin Scale (mRS) helped to score clinical outcomes 6 months after procedures. Poor functional outcomes corresponded with mRS scores >2.

Results

Patient Characteristics

Clinical data and demographics of the 103 patients (105 aneurysms) eligible for study (men 53; women 50; mean age 59.0 ± 10.3 years) are summarized in Table 1.

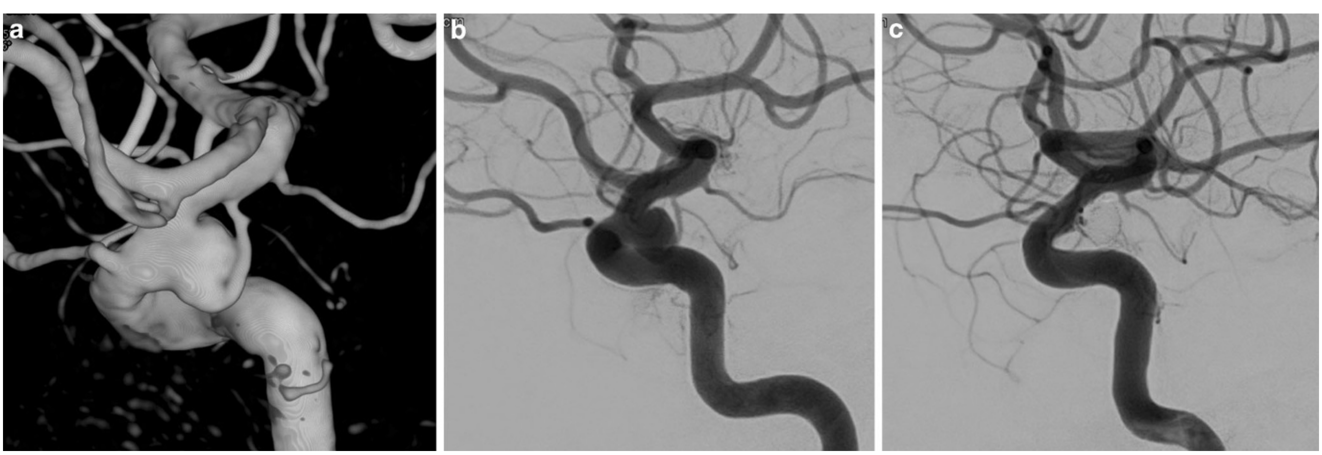

Fig. 2 Complete compromise of fenestrated limb: (**a**, **b**) three-dimensional and angiographic images of fenestration-related aneurysm (proximal end), involving paraclinoid internal carotid artery and (**c**) postembolization angiographic view showing complete compromise of smaller fenestrated limb orifice (flow to distal portion of compromised limb and posterior communicating artery due to retrograde fill)

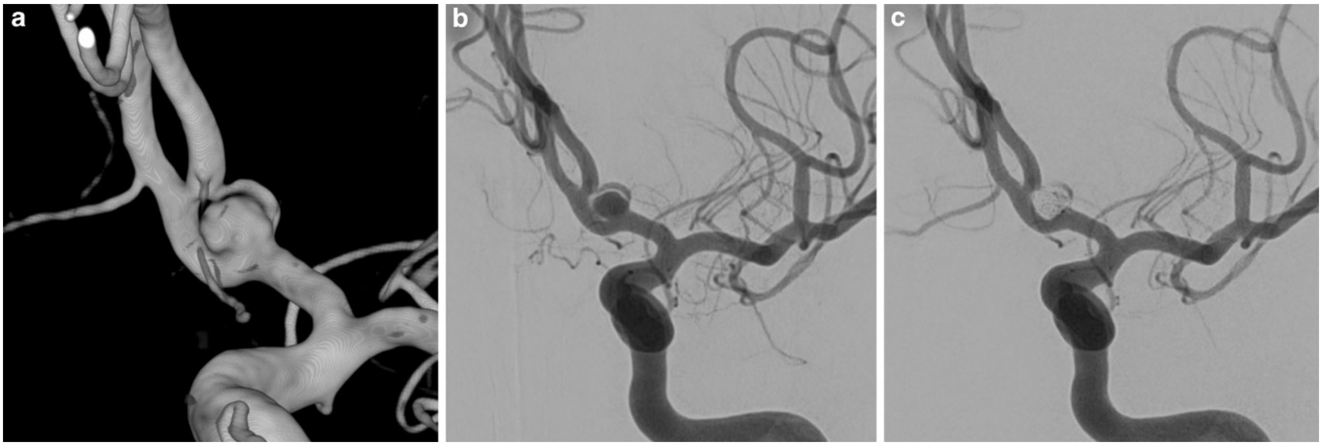

Fig. 3 Incomplete compromise of fenestrated limb: (**a**, **b**) three-dimensional and angiographic images of fenestration-related aneurysm (proximal end), involving anterior communicating artery and (**c**) postembolization angiographic view showing incomplete compromise of smaller fenestrated limb orifice, with sustained antegrade flow

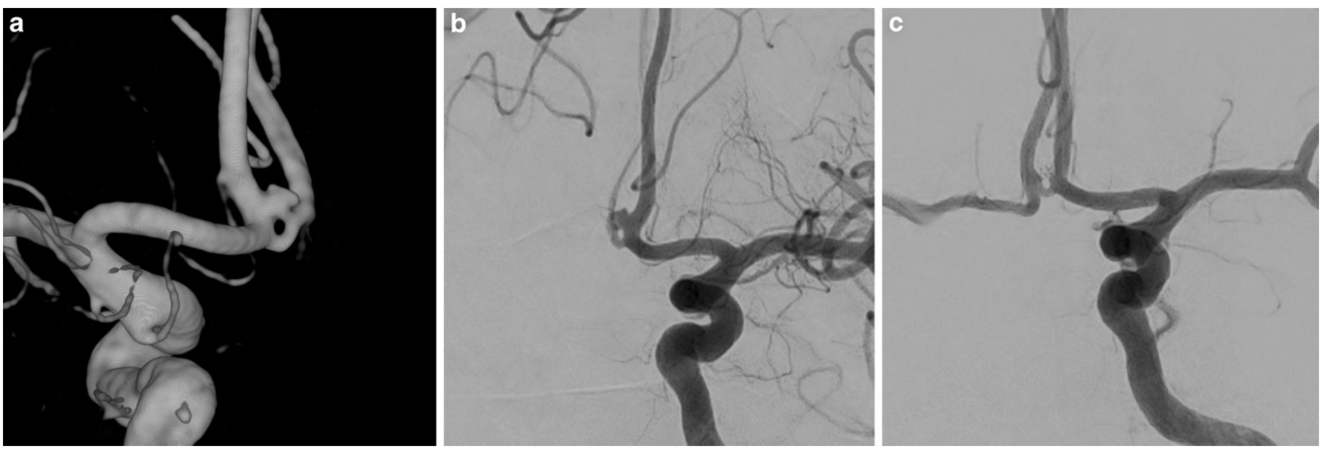

Fig. 4 Fenestrated limb type of FA: (**a**, **b**) three-dimensional and angiographic images of fenestration-related aneurysm (limb segment) and (**c**) postembolization angiographic view showing incomplete compromise of smaller fenestrated limb

Of the patients 2 had kissing FAs, 19 aneurysms showed rupture, and 3 recanalized aneurysms were included. Maximum diameters (excluding recanalized lesions) ranged from 1.8 mm to 15.3 mm (mean 5.1 ± 2.5 mm), and 62 (60.8%) were <5 mm across. The majority (56, 54.9%) were wide-necked, with dome-to-neck ratios <1.5. FAs were largely confined to anterior communicating artery (AcomA: 88/105, 83.8%), declining precipitously in basilar artery (BA: 7/105, 6.6%), anterior cerebral artery (ACA: 4/105, 3.8%), and internal carotid artery (ICA: 3/105, 2.8%) (Fig. 2). Middle cerebral artery (MCA), posterior cerebral artery (PCA), and vertebral artery (VA) contributed 1% (1/105) each. Fenestrated limbs were asymmetric for the most part (90/105, 85.7%), 29 patients had aneurysm(s) at other locations, and 17 had multiple fenestrations.

In this population, FAs were predisposed to limb segments (59/105, 56.2%), rather than proximal (43/105, 41.0%) (Figs. 2 and 3) or distal (3/105, 2.8%) ends. Majority of FAs at AcomA ($n=88$) occurred in limb segments (58/88, 65.9%) (Fig. 4), followed by proximal (27/88, 30.7%) and distal (3/88, 3.4%) ends, whereas those at other locations favored proximal ends (16/17, 94.1%) (Supplemental Tables 1, 2).

Procedural Details and Follow-up Outcomes

Of the 105 aneurysms subjected to coil embolization, occlusion proved successful in 77 (73.3%). In terms of technique, use of single microcatheters ($n=56$) predominated, followed by multiple microcatheters ($n=30$), stent assistance ($n=22$), microcatheter protection ($n=4$), and balloon remodeling ($n=1$). Eight aneurysms required combined protection. Procedure-related adverse events were limited, manifested as asymptomatic thrombi (two patients) and cerebral infarction (one patient) with non-permanent sequelae. All thrombi resolved subsequent to intra-arterial

Table 1 Baseline characteristics of patients ($n = 103$) with 105 fenestration-related aneurysms

Age, mean ± SD, [range], years	59.0 ± 10.3 [31–79]
Female/male	50/53
Ruptured/unruptured aneurysm	19/86
Hunt Hess grade 2/3/4/5	12/2/4/1
Initial/retreatment	102/3
Maximum diameter of aneurysm (n = 102; mean ± SD, [range], mm)	5.1 ± 2.5 [1.8–15.3]
Small (< 5 mm)	62
(≥ 5 mm, < 10 mm)	37
Large (≥ 10 mm)	3
Dome to neck ratio, mean ± SD, [range]	1.6 ± 0.5 [0.9–3.6]
< 1.5	56
≥ 1.5	46
Location of aneurysm with fenestration	
ICA	3 (2.8%)
ACA	4 (3.8%)
AcomA	88 (83.8%)
MCA	1 (1%)
Basilar artery	7 (6.7%)
VA	1 (1%)
PCA	1 (1%)
Type of aneurysm	
Proximal end	43 (41.0%)
Fenestration limb	59 (56.2%)
Distal end	3 (2.8%)
Symmetricity of fenestration channel	
Symmetric	15 (14.3%)
Asymmetric	90 (85.7%)
Multiple aneurysms	29 (27.6%)
Multiple fenestrations	17 (16.2%)
Multiple aneurysms with multiple fenestrations	3 (2.8%)

AcomA anterior communicating artery, *ACA* anterior cerebral artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *PCA* posterior cerebral artery, *VA* vertebral artery

Table 2 Endovascular treatment of fenestration-related aneurysms ($n = 105$)

Endovascular techniques	
Single microcatheter	56
Multiple microcatheter technique	30
Stent assisted	22
Microcatheter protection	4
Balloon remodeling	1
Combined	7
Bifemoral puncture	2
Initial occlusion status	
Complete occlusion	41 (39.0%)
Residual neck	36 (34.3%)
Residual sac	28 (26.7%)
Compromise of fenestration limb	23
Complete compromise	19
Incomplete compromise	4
Intraprocedural thrombosis/rupture	2/1
Postprocedural follow-up	
Follow-up loss	4
Mean follow-up period	35.3 ± 26.5 months [6–138]
Complete occlusion	83
Minor recanalization	9
Major recanalization	8
Additional coil embolization	7
Death	1

tirofiban infusion. One patient displayed procedural leakage. Although no treatment-related morbidity or mortality resulted, one death was attributable to poor-prognosis SAH (Table 2).

Imaging studies of 100 aneurysms were obtained in follow-up >6 months after coil embolization (mean interval, 35.3 ± 26.5 months; median, 36 months), for a rate of 96.1% (100/104). This excludes the single mortality. There was complete occlusion in 83 aneurysms (83.0%), minor recanalization in 9 (9.0%), and major recanalization in 8 (8.0%) (Table 2). Additional embolization was necessary in seven lesions with major recanalization.

Limb Compromise During Coil Embolization

As a technical issue, endovascular treatment of 23 aneurysms (21.9%) involved intentional compromise of one fenestrated limb, expecting flow restoration via retrograde filling. Such decisions stemmed from existing impediments to successful standard coiling approach. Compromise was complete (Fig. 2) in 19 aneurysms (82.6%) and incomplete in 4 (17.4%) (Figs. 3 and 4). Retrograde filling was observable through non-compromised channels in the former. All fenestrated channels compromised during coil embolization were smaller limbs (Table 3), producing no symptomatic cerebral ischemia thereafter. In follow-up imaging, no recanalization was evident.

Discussion

Fenestrations may seem innocuous, representing mere anatomic variants; however, their known association with other vascular disorders, such as cerebral aneurysms, AVM, MMD, and dissections, has proven clinically important [1, 10, 21]. In fact, some studies suggest that fenestrations alone are pathologic, linked to non-aneurysm-related SAH and cerebral ischemia [10, 13]. Past reports of FAs have

Table 3 Baseline features of treated aneurysms with compromised fenestrated limbs ($n=23$)

Location of aneurysm	
ICA	3
ACA	2
AcomA	17
VA	1
Ruptured aneurysm	4
Maximum diameter of aneurysm	5.3 ± 3.2 [1.8–15.3]
Dome to neck ratio	1.6 ± 0.5 [0.9–1.6]
Size of fenestration limbs	
Symmetric	0
Asymmetric	23
Compromised limb	
Smaller/larger	23/0
Compromise of limb	
Complete	19
Incomplete	4
Initial aneurysmal occlusion status	
Complete occlusion	10
Residual neck	6
Residual sac	7
Intraprocedural thrombus/rupture	0/0
Postprocedural follow-up	
Follow-up loss	4
Mean follow-up period	32.3 ± 20.3 [6–96]
Complete occlusion	18
Minor recanalization	0
Major recanalization	0
Additional coil embolization	0
Death	1

AcomA anterior communicating artery, *ACA* anterior cerebral artery, *ICA* internal carotid artery, *VA* vertebral artery

been few, with the prevalence ranging from 2.5% to 19.6% [1, 5, 6, 10, 15]. In our series of patients treated endovascularly, constituting the largest to date, the rate of FA was 1.9%. They also preferentially involved the AcomA and BA, reflecting the prevalence of fenestrations [1, 4, 5, 8, 22].

Aneurysms associated with fenestrations are classifiable by proximity to one another as follows: (1) those arising from fenestrations (true FAs), (2) those adjacent to but separate from fenestrations and (3) those remote from fenestrations. The second and third scenarios lack direct connections to fenestrations (Fig. 1) and were inadmissible in this study. True FAs are further characterized by sites of origin, affecting proximal portions, fenestrated limbs, or distal ends. The proximal and distal ends (divergent and convergent points, respectively) are structurally weak and plagued by media defects. Hemodynamic stress due to turbulent internal flow may encourage aneurysms to form, as in branching-site aneurysms [1–4, 7]. Proximal ends are especially susceptible to such stress and consequently are more likely to spawn aneurysms than distal ends [7, 19, 23, 24]. Our data are corroborative of other results in nearly all locations.

In the majority of AcomA fenestrations, limb segments (rather than proximal ends) seemed to incorporate the necks of FAs, differing from other vascular sites. There are two potential rationales for this perceived disparity. First, the inherent hemodynamic stress spurring aneurysms within limb segments reflects parent artery/fenestration (or fenestration/distal branch) relations and fenestration morphology [1, 2, 8]. The AcomA is subject to greater hemodynamic stress (relative to other locations) due to ACA size variations, increasing the likelihood of limb segment aneurysms [16, 24]. Perforating arteries may originate from AcomA fenestrations as well. A second explanation is that aneurysms of fenestrated limb segments are incidental phenomena. Several studies have found the same prevalence of aneurysms in patients with and without fenestrations [3–5, 7–9, 18]. Both aneurysms and fenestrations develop most frequently in AcomA, thus accounting for the relatively high number of limb aneurysms.

The complexities of FAs carry a host of technical difficulties, whether surgical and endovascular treatment is contemplated [4, 5, 12, 17, 19, 20]. Drawbacks of surgical treatment include difficulties in appreciating the structural intricacies of FAs and in fully isolating them from nearby structures. Clipping of FAs, without compromising limbs or perforators, is therefore technically problematic [3, 11, 17]. Coil embolization may be equally daunting from a technical perspective. The angioarchitectural details of FAs tend to evade full detection in single working projections due to anatomic overlap. Multidirectional views and 3D rotational imaging are usually required for accurate depiction [6–9, 17, 20, 23, 25]. Similarly, small fenestrations and perforators of fenestrated limbs may not be visible by angiography, impeding or undermining coil embolization. Nevertheless, we have shown that coil embolization is a safe and effective means of treating FAs, enabling tailoring of procedures to address the various angioanatomic aberrancies.

Occasionally, FAs of AcomA and BA are amenable to a bilateral access, provided both ACA and VA are of adequate caliber. This study included two aneurysms of AcomA and BA (one each) treated via bilateral approach. We used dual microcatheters, one to select each aneurysm and the other for stent delivery by opposite route. Kan et al. [26] reported a double-barrel stent technique for bilateral access to proximal end FAs of BA. During coil embolization, they deployed one stent from each VA in treating a unilateral fenestrated limb.

In our patients, limb compromise was selective (23/105, 21.9%), reserved for the following conditions: (1) compromised limb ≤ opposite limb regarding size, (2) compromised segment devoid of perforators and (3) coil embolization otherwise not feasible. We coiled adjoining saccular necks only and did not obliterate entire limbs, achieving complete ($n=19$) or incomplete ($n=4$) compromise. There was no symptomatic ischemia thereafter. Choi et al. reported that during coiling embolization of AcomA aneurysms, compromise of AcomA is relatively safe if both ACAs are symmetric and AcomA lacks visible perforators. In their hands as well, compromise of AcomA at adjoining saccular necks helped minimize perforator infarction [27]. Although some case reports have questioned the safety of limb compromise in patients with FAs [6, 11, 12, 14, 17, 19, 20, 28–30], we ensured that all compromised limbs filled retrograde with contrast agent and witnessed no recanalization during follow-up. Choi et al. [27] have further maintained that AcomA compromise as above confers some long-term protection from recanalization, possibly by compressing coil packed within the base to reduce intrasaccular flow.

The present study has certain limitations, chiefly its retrospective nature and single-center design, despite offering the largest series to date. There have also been many technical and instrumental advances in endovascular treatment during this protracted investigation that potentially influenced results. What is more, our institutional protocol does not routinely call for immediate postoperative MRI scans, thereby discounting any asymptomatic infarction. Finally, the follow-up period was short in recently treated patients, perhaps skewing the recanalization rate in coiled aneurysms.

Conclusion

Coil embolization of FAs is safe and effective, enabling tailored procedures that accommodate aberrant angioanatomic configurations. The necessary compromise of a single fenestrated channel during coiling of FAs also appears safe, conferring long-term protection from recanalization.

Supplementary Information The online version of this article (https://doi.org/10.1007/s00062-021-01043-z) contains supplementary material, which is available to authorized users.

Conflict of interest D. Jang, Y.D. Cho, D.H. Yoo, S.H. Kim, W.-S. Cho, H.-S. Kang, S.H. Lee, J.E. Kim, H.S. Lee and M.H. Han declare that they have no competing interests.

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