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Ongoing Geometric Remodeling of the Parent Artery After Flow-Diverter Stent Reconstruction in Cerebral Aneurysms: The Device Design Matters

Yihui Ma[2], Miklos Krepuska[1], Jawid Madjidyar[1], Tilman Schubert[1], Patrick Thurner[1], Zsolt Kulcsar[1]

■ OBJECTIVE: **Configuration changes of the parent artery (PA) after flow-diverter (FD) stent reconstruction, caused by the bending force of the device, may have an additional role in aneurysm occlusion as a result of the secondary alteration of intra-aneurysmal hemodynamics related to the geometry alteration of the vessel. To determine the degree of PA deformation and aneurysm occlusion rates after deployment of 2 different types of FD.**

■ METHODS: **Patients treated with 2 different designs of cobalt-chromium braid (48 and 64 wire braid) structure FD were subject to analysis. Vascular angle changes at the level of the reconstructed segment immediately after FD deployment and at 1 year follow-up were measured and the potential relationship with aneurysmal occlusion rate was analyzed.**

■ RESULTS: **Forty-two patients harboring 48 aneurysms were included in the present study. The aneurysms were divided into side wall (85.4%) and bifurcation types (14.6%). Twenty-six aneurysms were treated using the Pipeline FD (48 wire braid; 54.2%) and 22 using the Evolve FD (64 wire braid; 45.8%). Of the 48 aneurysms, 42 (87.5%) met the primary end point of complete occlusion at 12 months. The median postdeployment angle change was 7.04° ± 4.59° for the Pipeline and 5.05° ± 2.49° for the Evolve, whereas the median 12 months follow-up angle change was 15.49° ± 10.99° and 10.01° ± 8.83°, respectively. PA angle changes were significantly higher in the bifurcation group compared with the side wall group both during procedure and at 12 months follow-up. Angle change had a statistically nonsignificant association with complete aneurysm occlusion.**

■ CONCLUSIONS: **PA deformation starts immediately after deployment and remodeling continues for 1 year after. Aneurysms located in the vessel bifurcation were more prone to PA straightening after FD deployment than were side wall aneurysms. Furthermore, Pipeline seemed to be more prone to inducing vascular deformation, compared with Evolve.**

INTRODUCTION

Flow-diverter (FD) stent reconstruction of the parent artery in aneurysm disease induces healing through modification of the hemodynamic conditions in the affected segment.[1-3] The device design, including braid geometry, pore size, pore density, and porosity, all have an effect on the flow pattern, flow velocity, and shear stresses inside the aneurysm, by facilitating progressive thrombosis and reverse remodeling of the aneurysm.[4-6] On the other hand, the different material and design properties of FD influence the longitudinal bending force of the device, which may have an effect on the original geometry of the treated vessel.

Morphologic changes caused by parent artery deformation (PAD) after FD stenting have been shown to be associated with low recurrence and higher aneurysm occlusion rates.[7-9] The Pipeline Embolization Device (PED) (Medtronic, Irvine, California, USA) is 1 type of FD, which consists of 48 cobalt-chromium wires.[10] The Surpass Evolve (Stryker Neurovascular, Fremont,

Key words
- Flow-diverter devices
- Intracranial aneurysms
- Parent artery deformation

Abbreviations and Acronyms
AcomA: Anterior communicating artery
DSA: Digital subtraction angiography
FD: Flow diverter
MCA: Middle cerebral artery
PAD: Parent artery deformation
PED: Pipeline Embolization Device
VA: Vertebral artery

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California, USA) has recently been introduced into the market and has a 64-wire cobalt-chromium design. Both FDs have been proved to be safe and effective in intracranial aneurysm treatment.[11,12] The objective of this study was to determine and compare the PAD induced by these 2 different FDs and compare their efficacy in aneurysm occlusion.

METHODS

Patient Population

All consecutive patients treated with FDs for intracranial aneurysms located in the carotid siphon, anterior communicating artery (AcomA), V4 segment of the vertebral artery (VA), bifurcation of the middle cerebral artery (MCA), basilar artery, and internal carotid artery between January 2018 and March 2021 were subject to analysis. Patients who did not consent to the study, those treated with multiple stents or previously treated by stent placement, patients without a 12 months digital subtraction angiography (DSA) follow-up, as well as patients for whom the DSA images did not allow for proper geometric angulation measurements were excluded. This study was approved by the cantonal ethics committee (BASEC number 2018−01212).

Treatment

The patients underwent an endovascular procedure for the aneurysm treatment under general anesthesia. In our study, we used 2 flow-diversion systems: the Pipeline Flex with Shield technology (48 wire braid) and Surpass Evolve (64 wire braid). The choice of FD was at the discretion of the performing physician.

Antiplatelet Therapy

All patients received a loading dose of 300 mg aspirin or 300−600 mg clopidogrel 1 day before intervention, followed by dual antiplatelet therapy with aspirin (100 mg/day) and clopidogrel (75 mg/day) for 3 months, and 100 mg/day of aspirin for a further 9 months. Antiplatelet efficacy and platelet function were measured before treatment with a Multiplate analyzer (Roche Diagnostics, Mannheim, Germany). In cases of inadequate response to clopidogrel, it was substituted by prasugrel (10 mg/day).

Imaging Follow-Up

The patients underwent 3T magnetic resonance imaging including time-of-flight angiography with and without contrast enhancement at 3 and 12 months to evaluate the status of the treated aneurysms. Follow-up DSA was performed 12 months after treatment. Angiographic results were classified as complete obliteration and remnant using the O'Kelly-Marotta grading scale based on the DSA images.[13]

Vascular Geometry Analysis

For assessment of the degree of aneurysmal occlusion, vascular angle, and stent position, 2 independent neurointerventionists (Y.H.M. and K.M.) performed these measurements on standard lateral or working DSA projections. The angular values of each image set from the 2 readers were averaged. The PAD analysis was performed on the PACS (picture archiving and communication system) (Dedalus Deep Unity Diagnostic, Bonn, Germany). For the vessel deformation analysis, the reconstructed segment of the parent artery with the FD was chosen. Angles were measured at the points of intersection between lines traced passing through the midpoints of the diameters of each straight section of the siphon or bifurcation. Two straight lines passing through the center of the artery, crossing each other at the angulation point, were used for angle measurement.[14] PAD was defined as the difference between the initial angle and the post deployment angle (Figures 1and2).

Statistical Analysis

Continuous variables are expressed as mean values ± standard deviation (SD). For complete aneurysm occlusion, univariate logistic regression models were used to test the association with PAD. Parent vessel angle changes were analyzed using the Fisher exact test. Statistical analysis was performed using SPSS version 16.0 (IBM Corp., Armonk, New York, USA). A P value ≤0.05 was considered statistically significant.

RESULTS

Characteristics of Aneurysms and Patients at Baseline

Forty-two patients harboring 48 aneurysms were included in the present study. The mean age was 50.31 ± 13.14 years, with 7 men (16.7%) and 35 women (83.3%). The maximum diameter of aneurysms >10 mm was observed in 16 patients (33.3%), and aneurysms ≤10 mm were observed in 32 patients (66.7%; Table 1). In 25 cases (52.1%), the maximum diameter of the aneurysm neck was >4 mm, and ≤4 mm in 23 cases (47.9%; Table 1). Based on the anatomic location, the aneurysms were divided into sidewall and bifurcation types. The side wall group included aneurysms located in the cavernous segment and V4 segment of the VA, with a total of 41 (85.4%) lesions (Figure 1). The bifurcation group comprised aneurysms located in the AcomA and bifurcation of the MCA, basilar artery, and internal carotid artery, with 7 lesions (14.6%) (Figure 2). Of the 42 cases, concomitant coiling was used in 4 (9.5%) and FD alone was used in 38 (90.5%). Twenty-six aneurysms were treated using a PED (54.2%) and 22 using an Evolve (45.8%). Of the 48 aneurysms, 42 (87.5%) met the primary end point of complete occlusion at 12 months. Complete occlusion rates at 12 months in the PED group were 23/26 (88.5%), and 19/22 (86.4%) in the Evolve group. Detailed characteristics are shown in Table 1.

Parent Artery Remodeling and Embolization Results

The mean preoperative parent artery angle at the affected segment was 40.45° ± 30.74°. The mean postdeployment angle immediately after the procedure was increased compared with the initial angle, but there was no significant difference (45.27°± 31.43°). The median postdeployment angle change immediately after the procedure was 7.04°± 4.59° for the Pipeline and for the Evolve stent 5.05°± 2.49° (Table 2). The mean 12-month follow-up angle was also increased compared with the initial angle (49.68° ± 33.56°). The median 12 months follow-up angle change was 15.49°± 10.99° for the PED and for the Evolve stent 10.01°± 8.83°. The angle change in the Pipeline group was higher compared with the Evolve group, but there was no significant difference between these groups (Table 2). In the sidewall aneurysm subgroup analysis, angle changes between these 2 FDs also showed no

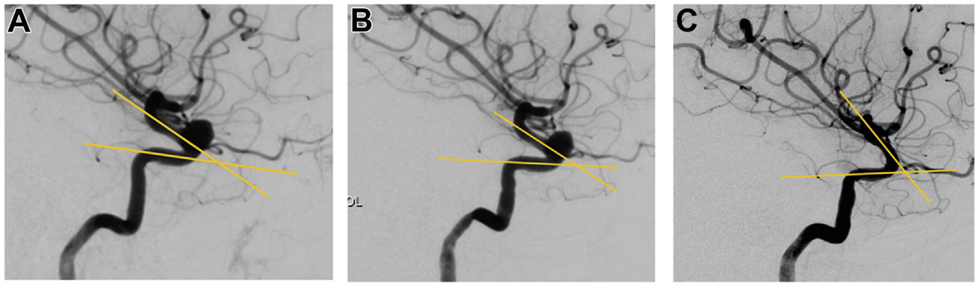

Figure 1. Angiography showing significant straightening of the parent vessels after flow-diverter implantation in internal carotid ophthalmic segment. (**A**) Before treatment; (**B**) immediately after treatment; (**C**) 12 months follow-up.

significant difference. However, parent artery angle changes were significantly higher in the bifurcation group compared with the sidewall group both immediately after the procedure and at 12 months follow-up (Table 3).

In univariate analysis, aneurysm size and aneurysm neck diameter were significantly associated with aneurysm occlusion (Table 1). There was no association with patient sex, age, aneurysm location, stent type, and associated coiling. Angle change showed an association with better radiologic results on 12 months follow-up. However, there was no significant association with complete aneurysm occlusion (Table 1).

DISCUSSION

In this study, we have shown that FDs induce a PAD deformation starting immediately after deployment and continuing over the 1 year follow-up period. FDs braid design had an influence on the degree of PAD, with the PED inducing a more pronounced deformation. The PAD was more pronounced in bifurcation aneurysms.

An FD changes the hemodynamic microenvironment inside the aneurysmal sac, resulting in progressive thrombosis and reverse remodeling of the aneurysm, achieving complete healing in 80%–90% of the patients already at 1 year and preventing the intracranial aneurysm from rupturing.[10,15] Several studies have shown that progressive thrombosis, and secondary hemodynamic changes are important characteristics of the treatment for aneurysms.[5,6,16] Furthermore, previous studies have evaluated the importance of wall apposition in achieving flow diversion, endothelialization of the FD surface, and aneurysm occlusion.[17,18] The observation of geometric deformity of the parent artery is not new and it is generally considered beneficial for the occlusion of intracranial aneurysms. Waihrich et al.[14] reported that FDs had a straightening effect on the parent artery after deployment, which may be associated with higher aneurysm occlusion rates. Ishii et al.[8] reported that a significant angular change of $\geq 20°$ most likely leads to decreased recanalization after stent-assisted embolization of large aneurysms. It has been shown that hemodynamic conditions at the level of the neck and in the aneurysm sac orchestrate the aneurysm life cycle, from the initiation through development until rupture.[19,20] These hemodynamic conditions, with specific focus on the inflow patterns, are highly dependent on the configuration of the parent artery.[21,22] Therefore, changing the parent artery geometry by an intravascular implant has important effects on the intra-aneurysmal conditions. In our study, embolization with FDs was proved to induce an angulation change of the parent artery caused by the straightening effect of the stent, which is likely related to aneurysm occlusion. The

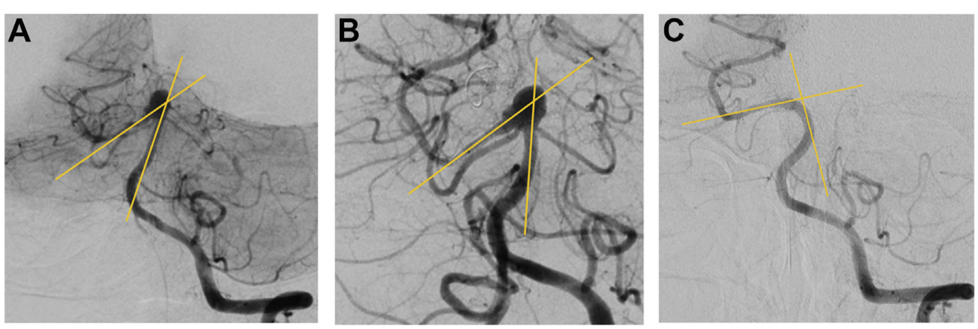

Figure 2. Angiography showing significant straightening of the parent vessels after flow-diverter implantation in bifurcation of basilar artery. (**A**) before treatment; (**B**) immediately after treatment; (**C**) 12 months follow-up.

Table 1. Demographic and Angiographic Data of Patients

Study	Complete Occlusion (n = 42)	Incomplete Occlusion (n = 6)	P Value
Gender			0.26
Male	5	2	
Female	31	4	
Age			0.16
<60 yearsa	25	2	
≥60 years	11	4	
Size			<0.05
≤10 mm	31	1	
>10 mm	11	5	
Neck			<0.05
≤4 mm	23	0	
>4 mm	19	6	
Location			1.00
Bifurcation	6	1	
Side wall	36	5	
Flow-diverter type			1.00
Pipeline	23	3	
Evolve	19	3	
Concomitant coiling			1.00
Yes	4	0	
No	32	6	
Parent artery deformation (°)			
Postangle change	6.39 ± 4.07	4.63 ± 2.59	0.49
12 months angle change	13.91 ± 10.74	7.63 ± 5.27	0.24

results were comparable to those in other recent studies.[14,23] Janot et al.[23] reported that the use of FD stents for distal aneurysms induces measurable parent artery straightening, which is associated with higher occlusion rates.

We have shown that aneurysms located in the bifurcation were more prone to parent artery straightening after FD deployment than aneurysms at the carotid siphon and V4 segment of the VA. Similar to our study results, a retrospective cohort study showed that aneurysms located in the AcomA and MCA were more prone to deformity after stent-assisted coiling than aneurysms at other locations in the anterior circulation.[9] This situation probably occurs because distal, smaller arteries on the brain surface are more likely to be deformed than those situated at the base of the skull.

Several studies have shown the parent artery straightening effect of different stents such as Enterprise and Neuroform.[7,24,25] Huang et al.[24]investigated 20 patients with wide-neck AcomA aneurysms treated with stent-assisted coiling and found that stent placement for AcomA aneurysms had a substantial effect on the vascular geometry, which may result in local hemodynamic changes. A retrospective study[23] suggested that parent artery straightening could be more important with cobalt-chromium FDs than with nitinol constructs. In our study, PED seemed to be more prone to inducing vascular deformation, compared with Surpass Evolve, which may be related to the larger diameter of the wires of the braid.[26,27] However, in our study, the PED was not shown to result in faster and better aneurysm occlusion rates compared with the Surpass Evolve. A previous study showed that Surpass Evolve has superior flow-diversion effects compared with the Pipeline Flex.[28] The superior flow diversion but lower PAD may explain the results of our study.

This study has several limitations. First, there may be biases because of its retrospective nature and the small number of patients included. Second, evaluation of arterial deformity was performed on two-dimensional angiographic images and most measurements in our study were in a lateral view, which may have been less accurate and underestimate the arterial deformity. Further studies with a large sample size may be required to assess the prognostic impact of the parent artery angle change after FD stenting.

Table 2. Parent Vessel Straightening Effect for Each Type of Stent

Variable	Evolve	Pipeline Embolization Device	P Value
Total (°)			
Postangle change	5.05 ± 2.49	7.04 ± 4.59	0.09
12 months angle change	10.01 ± 8.83	15.49 ± 10.99	0.08
Internal carotid artery/vertebral artery (°)			
Postangle change	4.86 ± 2.42	6.27 ± 3.21	0.14
12 months angle change	9.99 ± 9.09	13.34 ± 7.68	0.24

CONCLUSIONS

PAD starts immediately after deployment and remodeling continues for 1 year after. Aneurysms located in the vessel bifurcation were more prone to parent artery straightening after FD deployment than were side wall aneurysms. Furthermore, PED seemed to be more prone to inducing vascular deformation, compared with

Table 3. Parent Vessel Straightening Effect in Different Location

Variable	Side Wall (°)	Bifurcation (°)	P Value
Postangle change	5.57 ± 2.89	9.57 ± 6.95	<0.05
12 months angle change	11.67 ± 8.47	21.09 ± 16.79	<0.05

Evolve. The PAD had a positive influence on aneurysm occlusion rates.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Yihui Ma: Formal analysis, Investigation, Data curation, Writing — original draft. **Miklos Krepuska:** Formal analysis, Investigation, Data curation. **Jawid Madjidyar:** Investigation, Data curation. **Tilman Schubert:** Conceptualization, Methodology, Data curation. **Patrick Thurner:** Conceptualization, Methodology, Investigation, Data curation. **Zsolt Kulcsar:** Conceptualization, Methodology, Investigation, Writing — original draft, Writing — review & editing, Supervision.

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