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INTERVENTIONAL NEURORADIOLOGY

# Retreatment strategies for recurrent and residual aneurysms after treatment with flow-diverter devices

Lukas Goertz[1,2] · Nina Hesse[3] · Thomas Liebig[4] · Wael Ahmad[5] · Nuran Abdullayev[1] · Boris Krischek[2] · Christoph Kabbasch[1] · Franziska Dorn[4]

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## Abstract

**Purpose** The management of residual or persistent intracranial aneurysms after flow-diversion therapy is not well defined in the literature. In this multicentric study, we report clinical and angiographic outcomes of 11 patients that underwent retreatment for 12 aneurysms initially treated with flow-diverter stents.

**Methods** The median patient age was 53 years. Aneurysms (median size, 7.3 mm) were located at the internal carotid artery in 9 cases, and at the posterior circulation in 3. Treatment strategies, complications, and angiographic outcome were retrospectively assessed.

**Results** Retreatment was feasible in all cases and performed by overlapping flow-diverter implantation. Overall, 12 side vessels were covered during retreatment, whereof 10 (83.3%) remained patent until mid-term follow-up. There were no further technical or symptomatic complications and no treatment-related morbidity. Angiographic follow-up (median, 17 months) showed improved aneurysm occlusion in all patients. Complete or near-complete aneurysm occlusion was achieved in 11 aneurysms (91.7%).

**Conclusion** Required retreatment after failed flow-diversion therapy can be performed with adequate safety and efficacy by placement of additional flow-diverter stents.

**Keywords** Angiography · Endovascular treatment · Flow-diverter · Pipeline

## Introduction

Since the introduction of the Pipeline Embolization Device (PED, Covidien, Mansfield, MA, USA) in 2008, the concept of flow-diversion has evolved into an established technique for endovascular treatment of intracranial aneurysms [1]. In particular, flow-diverter devices (FDDs) have proven advantageous for the treatment of large, fusiform, and dissecting aneurysms that are otherwise difficult to treat [2–6].

Due to their flow-laminating capabilities, FDDs reduce the blood flow into the aneurysm and thereby lead to progressive aneurysm thrombosis over time [7]. Numerous comparative studies have shown that FDDs can provide more durable aneurysm occlusion when compared with other techniques such as conventional and balloon- or stent-assisted coiling, still offering acceptable morbidity and mortality rates [8–10].

However, there is a subset of—mainly large and complex—aneurysms in which complete occlusion does not occur after FDD treatment, even at long-term follow-up [11, 12]. The risk for rupture or re-rupture of those incompletely occluded aneurysms after flow-diversion is uncertain. The technical options for retreatment are limited—other than for aneurysm remnants and recurrences that were previously treated with other techniques: the dense mesh design and high metal coverage of FDDs make catheterization of the aneurysm sac with a microcatheter through the struts in general not

CK and FD contributed equally to this work.

✉ Lukas Goertz
lukas.goertz@uk-koeln.de

[1] Department of Neuroradiology, Medical Faculty and University Hospital, University of Cologne, Cologne, Germany

[2] Center for Neurosurgery, Medical Faculty and University Hospital, University of Cologne, Cologne, Germany

[3] Department of Radiology, LMU University Hospital of Munich, Munich, Germany

[4] Department of Neuroradiology, LMU University Hospital of Munich, Munich, Germany

[5] Department of Vascular and Endovascular Surgery, Medical Faculty and University Hospital, University of Cologne, Cologne, Germany

possible. Different from aneurysms after sole coiling, microsurgical clipping does not prove feasible either [13]. Therefore, retreatment strategies for this group of aneurysms are basically limited to overlapping implantation of more FDDs or definitive occlusion of the vessel. In an experimental study, Fahed et al. assessed occlusion rates of residual aneurysms after initial flow-diversion that were retreated by either FDD implantation alone or in combination with injection of liquid embolic agent between the layers of the FDDs. The authors reported improved aneurysm occlusion at follow-up; however, residual aneurysms were present in all cases. Moreover, parent artery occlusion occurred in 50% of aneurysms retreated with liquid embolic agent [14]. Although some studies investigated the risk factors for treatment failures related to flow-diversion [15–17], clinical reports on retreatment strategies and angiographic outcome are scarce in the available literature.

The objective of the current study was to present our dual-center experience in retreating aneurysms with residual filling after initial FDD implantation. We retrospectively evaluated retreatment strategies and report clinical and angiographic outcome.

## Methods

This is a retrospective review of consecutive patients treated with FDDs at two German neurovascular centers between January 2010 and December 2018. All patients that underwent retreatment of the index aneurysm were identified and enrolled in the present study. There were no specific exclusion criteria. In accordance with the institutional guidelines, an ethics committee approval could be waived for this retrospective study. The study was conducted in accordance with the 1964 Helsinki Declaration.

### Data collection

The following parameters were collected retrospectively from the medical records: patient age, sex, rupture status, initial FDD treatment (date, FDD type, use of adjunctive devices), and retreatment strategy (date, treatment technique). The neurological status was assessed at baseline, after treatment and at follow-up visits.

All neurological complications (e.g., aphasia, hemiparesis) and self-reported symptoms (e.g., impairment of vision, prolonged headache, dizziness) were recorded. We also report technical complications that did not result in neurological deficits including side vessel occlusion, in-stent stenosis, and procedural asymptomatic thromboembolic and hemorrhagic events. Functional outcome was evaluated by the modified Rankin scale (mRS) at discharge from hospital and at follow-up visits. Treatment-related morbidity was defined as any increase in the mRS score after the procedure. In patients with procedure-related cerebral infarction, the stroke severity was determined by using the National Institutes of Health Stroke Scale (NIHSS), whereby a score $\geq 4$ points was considered major stroke. We further report all technical adverse events such as thromboembolic and hemorrhagic events that were not associated with clinical symptoms.

Pre-interventional 4-vessel digital subtraction angiography (DSA) was reviewed to determine aneurysm location, morphology, size, and neck width. Aneurysm morphology was categorized as saccular, fusiform, dissecting, and blister-like. Based on aneurysm size and neck width, the dome-to-neck ratio was calculated for all aneurysms except for fusiform aneurysms.

Immediate and follow-up aneurysm occlusion was evaluated with the O'Kelly-Marotta (OKM) grading scale for flow-diversion: A = total filling (> 95%); B = subtotal filling (5–95%); C = entry remnant (< 5%); and D = complete occlusion [18]. A favorable aneurysm occlusion was defined as OKM C + D. Furthermore, the extent of intra-aneurysmal contrast stasis was categorized as: 1 = no stasis; 2 = moderate stasis; and 3 = significant stasis. Moreover, we evaluated if overstented side vessels remained patent at the end of the intervention or at follow-up.

### Procedure

The description of the procedure applies to both the initial and the retreatment. In the current study, the following FD types were used: Pipeline Embolization Device (PED; Medtronic, Dublin, Ireland), Flow Re-direction Endoluminal Device (FRED; MicroVention, Aliso Viejo, CA, USA), Silk (Balt Extrusion, Montmorency, France), and Derivo Embolization Device (DED; Acandis, Pforzheim, Germany). All interventions were performed via a transfemoral approach with the patient under general anesthesia in a biplane angiosuite (Philips, Best, the Netherlands, and Siemens, Erlangen, Germany). The patients received 5000 IE of heparin after groin puncture, followed by aliquots of 1000 IU/h until the end of the procedure.

The FDDs were deployed via a convenient 0.027″ microcatheter (Headway 27, MicroVention, Aliso Viejo, CA, USA, or Neuroslider 27, Acandis, Pforzheim, Germany). The appropriate size of the FDDs was determined based on the proximal parent artery diameter measured on 2D DSA. The implantation of multiple FDDs or adjunctive devices such as stents or the Woven EndoBridge (WEB, MicroVention, Aliso Viejo, CA, USA) was left to the neurointerventionalist's discretion and usually reserved for aneurysms with large size or complex anatomy. In case immediate aneurysm occlusion was requested (e.g., ruptured aneurysm), adjunctive coiling of the aneurysm sac was performed accordingly.

After initial FDD implantation, angiographic follow-up was scheduled at 6 and 24 months after the procedure using the DSA or magnetic resonance angiography according to our institutional guidelines. In case of incomplete aneurysm occlusion, the indication of retreatment was made individually after discussion within an interdisciplinary neurovascular team among neuroradiologists and vascular neurosurgeons. The decision of retreatment was made considering the potential risk of rupture or re-rupture and the patient characteristics (e.g., patient age, comorbidities, patient preference). In general, aneurysms with residual OKM A and B filling after 6 months were subjected to retreatment. Among neck remnants (OKM C), retreatment was only performed for complex aneurysms that carry per se an increased rupture risk and are prone for further aneurysm growth (e.g., giant and fusiform aneurysms). The endovascular retreatment method was left to the discretion of the operator and consisted mainly of implantation of additional FDDs.

### Antiplatelet regimen

Scheduled patients were treated with 100 mg acetylsalicylic acid (ASA) and clopidogrel 75 mg starting 5–7 days (d) prior to the procedure until 4 months postoperatively. ASA was continued life-long. In subarachnoid hemorrhage (SAH) patients, tirofiban (Aggrastat, Merck, West Point, PY, USA) was administered according to the manufacturer's guidelines starting just before stent placement and continued for 16–24 h after the procedure, followed by oral double antiplatelet therapy as stated above for scheduled cases. Platelet inhibition testing was performed using ASA, P2Y12 (Verify Now, Accumetrics, San Diego, CA, USA) and vasodilator-stimulated phosphoprotein-phosphorylation (VASP) assays [19]. Levels between 350 and 550 ARU (ASA Response Units) for ASA and 30–60% for clopidogrel were defined as sufficient platelet inhibition. Insufficient response to either drug was counteracted by dose escalation (e.g., clopidogrel 150 mg/d) or substitution with prasugrel (60-mg bolus, 10 mg/d).

## Results

### Patient and aneurysm characteristics

During the study period, a total of 284 patients underwent flow-diversion for 316 aneurysms. Thereof, angiographic follow-up was available for 235 aneurysms. After careful discussion of the cases within an interdisciplinary team, retreatment was performed for 11 patients with 12 aneurysms (5.1%). The median patient age at initial flow-diverter treatment was 53 years (range, 33–72 years) and 7 patients (63.6%) were female. Three patients were treated for a ruptured aneurysm in the acute phase of SAH (27.3%). There were no recurrent aneurysms that had been treated before. Nine aneurysms (75.0%) were located at the internal carotid artery and one at the vertebral artery (8.3%). One SAH patient had an aneurysm at the basilar tip (8.3%) and at the superior cerebellar artery (8.3%), which were initially treated by a single flow-diverter. Aneurysm morphology was saccular in 8 cases (66.7%), fusiform in 2 (16.6%), dissecting in 1 (8.3%), and blister-like in 1 (8.3%). The median aneurysm size was 7.3 mm (range, 1–26 mm) and the median neck width was 4.7 mm (range, 1–18 mm). Patient and aneurysm characteristics at baseline are presented in Table 1.

### Initial treatment

Procedural specifics of initial FDD treatment are outlined in Table 2. Three aneurysms were treated by a single FDD only (25.0%), while the remaining aneurysms were treated by multiple FDDs ($n = 7$, 58.3%) and/or in combination with other devices (coiling, $n = 2$; stent, $n = 1$; WEB, $n = 1$) due to complex aneurysm morphology. Side vessels were covered in 10 cases, in which 10 of 11 side vessels (90.9%) remained patent at the end of the procedure. Immediate complete aneurysm occlusion (OKM D) was achieved in two patients (16.7%), while a varying degree of aneurysm occlusion was obtained in the remaining cases.

There was one procedural complication. In this case, retraction of a FDD due to misplacement resulted in vessel wall injury of the ICA and consecutive carotid-cavernous fistula. The fistula could be occluded by implanting 3 PEDs. The patient did not have any symptoms after the intervention.

### Retreatment

Angiographic follow-up at a median of 59 days (range, 2–360) revealed entry remnants (OKM C) in 3 aneurysms (25.0%), subtotal filling (OKM B) in 7 (58.3%) and total filling (OKM A) in 2 (16.7%). The rationale for retreatment in each patient is listed in Table 2. The median interval between initial and retreatment was 118 days (range, 7–427 days). In three SAH patients, retreatment was performed between 7 and 22 days after initial treatment as we assumed an increased risk for re-rupture due to incomplete aneurysm occlusion (cases 1, 7, and 8). In all cases, retreatment consisted of additional FDD implantation (1 FDD in 9 cases, 2 FDDs in 2 cases). Adjunctive coiling was performed in one patient. In this case, the distal end of the initially implanted FRED dislocated partially into the aneurysm sac resulting in aneurysm regrowth. After embolization of the residual aneurysm with coils via the distal end of the FRED, a DED was implanted to ensure accurate vessel wall apposition.

Retreatment with additional FDDs was feasible in all cases, leading to immediately improved aneurysm occlusion in 4 cases (36.4%). During retreatment, 12 side vessels were covered in 9 cases, whereof two (16.6%) were occluded at the end

**Table 1** Baseline patient and aneurysm characteristics. *ICA*, internal carotid artery; *AChо*, anterior choroidal artery; *VA*, vertebral artery; *SUCA*, superior cerebellar artery

| Case | Initial rupture status | Aneurysm location | Aneurysm morphology | Aneurysm size (mm) | Neck width (mm) | Dome-to-neck ratio |
|---|---|---|---|---|---|---|
| 1 | Ruptured | ICA terminus | Blister | 1 | 1 | 1 |
| 2 | Unruptured | ICA paraophthalmic | Saccular | 25 | 8 | 3.1 |
| 3 | Unruptured | ICA paraophthalmic | Saccular | 10 | 5 | 2 |
| 4 | Unruptured | ICA/AChoA | Saccular | 7 | 4.5 | 1.6 |
| 5 | Unruptured | ICA paraophthalmic | Saccular | 3.9 | 3.7 | 1.1 |
| 6 | Unruptured | ICA paraophthalmic | Fusiform | | | |
| 7 | Ruptured | VA (V4) | Dissecting | 7.3 | 6.8 | 1.1 |
| 8 | Ruptured | Basilar tip | Saccular | 4.7 | 6 | 1.3 |
| | | SUCA | Saccular | 2.2 | 2.2 | 1.0 |
| 9 | Unruptured | ICA paraophthalmic | Saccular | 6.7 | 26 | 3.9 |
| 10 | Unruptured | ICA paraophthalmic | Fusiform | - | - | - |
| 11 | Unruptured | ICA paraophthalmic | Saccular | 26 | 18 | 2.2 |

of the procedure. In both cases, occluded side vessel occlusion was uneventful and did not have any neurological symptoms. During the procedures, there were no further thromboembolic or hemorrhagic events and there were no neurological complications. Hence, the technical complication rate was 16.6% and the symptomatic complication rate was 0%. All patients had an unchanged mRS score at discharge and at follow-up (Table 3).

At last available follow-up (median, 514 days; range, 186–1681 days), complete occlusion (OKM D) was obtained in 9 cases, entry remnants (OKM C) in 2 and subtotal filling (OKM B) in 1. Hence, favorable aneurysm occlusion was attained in 11 patients (91.7%). Progressive aneurysm thrombosis was observed in all cases. At follow-up, no further covered side vessels were occluded.

Illustrative cases of retreatment after FDD implantation are presented in Figs. 1, 2, and 3.

## Discussion

In the current study, we report our dual-center experience in treatment of residual aneurysms after previous FDD implantation. The predominant treatment strategy consisted of placement of additional FDDs, which was feasible and resulted in progressive aneurysm occlusion in all cases. There was no morbidity or mortality related to retreatment. To the best of our knowledge, the present series is the first to report clinical and anatomic results of retreatment after initial flow-diversion treatment with residual aneurysm perfusion.

### Efficacy

In general, FDDs provide progressive aneurysm thrombus resulting in comparably high aneurysm occlusion rates at long-term follow-up. To date, the best data on FDDs are available for the PED. In the cumulative population of the IntrePED (International Retrospective Study of the Pipeline Embolization Device), PUFS (Pipeline for Uncoilable or Failed Aneurysms Study), and ASPIRe (Aneurysm Study of Pipeline in an Observational Registry) trials, complete aneurysm occlusion was achieved in 75.0% at 6 months and 85.5% at 12 months after PED implantation [20]. The overall aneurysm retreatment rate in these three trials was 3.0%, which is considerably lower when compared with that in conventional coiling with reported retreatment rates up to 20% [21–23].

Daou et al. analyzed potential risk factors of failed aneurysm occlusion after PED implantation in a large single-center series. The authors reported residual aneurysms in 16.4%, and 6.8% underwent retreatment. Older patient age, prior stent implantation before flow-diversion, location in the distal anterior circulation, and longer follow-up duration were independently associated with treatment failure [16]. Shapiro et al. reported residual aneurysms in 19% and described fusiform shape, decreasing dome-to-neck ratio, and previous stent implantation as independent risk factors for treatment failure. The authors revealed FDD malapposition, inadequate coverage of the aneurysm neck by the FDD, and presence of a branching vessel from the aneurysm sac as potential mechanisms for delayed or insufficient aneurysm thrombosis [17]. Moreover, Kan et al. reported residual aneurysms in fetal posterior communicating artery aneurysms [15].

In our cohort, retreatment was performed in 5.1%, which is in the range of the abovementioned studies. Due to a paucity of studies and the overall small number of cases, the remaining rupture risk of aneurysms with residual or recurrent filling after FDD treatment and the indications for retreatment are not clear. Aneurysm recurrences after coiling are usually the sequel of compaction leading to exposure of some part of the

**Table 2** Procedural specifics of initial FDD treatment. *PED*, Pipeline Embolization Device; *FRED*, Flow Re-direction Endoluminal Device; *WEB*, Woven EndoBridge; *OA*, ophthalmic artery; *PICA*, posterior inferior cerebellar artery; *Pcom*, posterior communicating artery; *SUCA*, superior cerebellar artery; *P1*, P1-segment of the posterior cerebral artery; *N/A*, not applicable; *OKM*, O'Kelly-Marotta grading scale; *FDD*, flow-diverter device

| Case | Treatment modality | Complications | Vessel overstented | Vessel patency | Immediate angiogr. result (OKM) | Angiogr. FU, OKM (days) | Rationale for retreatment |
|---|---|---|---|---|---|---|---|
| 1 | PED 4.5 × 22 + Enterprise stent 22 mm | No | OA | Patent | A1 | A1 (12) | Growth of the blister aneurysm despite FDD implantation |
| 2 | PED 4 × 12 + PED 4 × 10 + 12 coils | No | OA | Patent | C2 | C2 (360) | No progressive aneurysm occlusion |
| 3 | PED 4 × 14 + PED 4 × 16 | No | OA | Patent | B3 | B3 (107) | No progressive aneurysm occlusion |
| 4 | FRED 4.5 × 20 + FRED 4.5 × 18 | No | OA | Patent | A3 | B2 (190) | Insufficient progressive aneurysm occlusion |
| 5 | PED + PED + PED | Carotid-cavernous fistula: implantation of 3 PEDs, no neurological symptoms | OA | Patent | A2 | B2 (342) | No progressive aneurysm occlusion |
| 6 | Silk 5 × 40 silk 5.5 × 40 | No | No | N.A. | B3 | C3 (59) | Persistent aneurysm remnant after FDD implantation |
| 7 | PED 3.25 × 16 + PED 3.25 × 18 | No | PICA | Patent | D | B2 (2) | Aneurysm recanalization after initial complete occlusion |
| 8 | PED 2.5 × 10 (+ 3 coils for BA aneurysm) | No | P1, SUCA | Occluded, patent | B2<br>A1 | B1 (9)<br>A1 (9) | Fixation of in-stent thrombus by additional FDD implantation |
| 9 | PED + 2 × WEB + 7coils | No | Pcom | Patent | D | B3 (105) | Aneurysm recanalization after initial complete occlusion |
| 10 | FRED 5 × 20 | No | OA | Patent | B | B(6) | No progressive aneurysm occlusion |
| 11 | FRED 4.5 × 18 | Dislocation of the distal end of the FDD into the aneurysm sac with consecutive aneurysm regrowth at 9-month follow-up | OA | Patent | B | C1 (5) | Insufficient progressive aneurysm occlusion |

**Table 3** Retreatment strategies with clinical and angiographic outcome. There were no procedural complications recorded. *PED*, Pipeline Embolization Device; *DED*, Derivo Embolization Device; *OA*, ophthalmic artery; *PICA*, posterior inferior cerebellar artery; *Pcom*, posterior communicating artery; *SUCA*, superior cerebellar artery; *P1*, P1-segment of the posterior cerebral artery; *N/A*, not applicable; *OKM*, O'Kelly-Marotta grading scale

| Case | Interval between initial and retreatment (days) | Retreatment strategy | Complications | Covered side vessel | Vessel patency | Immediate angiogr. result (OKM) | Angiogr. FU, OKM (days) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1st FU | Last FU |
| 1 | 16 | PED 3.5 × 10 + PED 3.5 × 12 | No | OA | Patent | D | D (145) | D (514) |
| 2 | 417 | PED 3.5 × 14 + PED 3.5 × 18 | Occluded side vessel (no deficit) | OA | Occluded | C2 | C3 (186) | |
| 3 | 118 | PED 3.75 × 14 | No | No | Patent | B3 | C3 (120) | C3 (1681) |
| 4 | 231 | PED 3.75 × 14 | No | OA | Patent | C2 | C2 (143) | D (752) |
| 5 | 427 | PED 4 × 14 | No | OA | Patent | B2 | D (229) | |
| 6 | 271 | Silk 4.5 × 30 | No | No | N.A. | C3 | D (182) | D (224) |
| 7 | 7 | PED 3.75 × 20 | No | PICA | Patent | C3 | D (225) | D (797) |
| 8 | 22 | PED 3.5 × 14 | Occluded side vessel (no deficit) | P1, SUCA | Occluded, patent | B1<br>A1 | D (92)<br>C3 (92) | D (1494)<br>D (1494) |
| 9 | 105 | PED 4.5 × 16 + PED 4.5 × 16 | No | Pcom | Patent | B3 | D (266) | |
| 10 | 53 | PED | No | OA | Patent | B2 | B3 (390) | |
| 11 | 215 | DED 4.5 × 30 + coils | No | Acom, OA, Pcom | Patent | D | D (180) | D (540) |

aneurysm wall to the pulsatile blood flow making it susceptible for rupture [24]. However, FDDs divert the blood flow away from the aneurysm itself resulting in reduced inflow and reduced wall shear stress and hemostasis within the aneurysm sac. Hence, one may assume that the risk of rupture of residual aneurysms after flow-diversion is low—even if

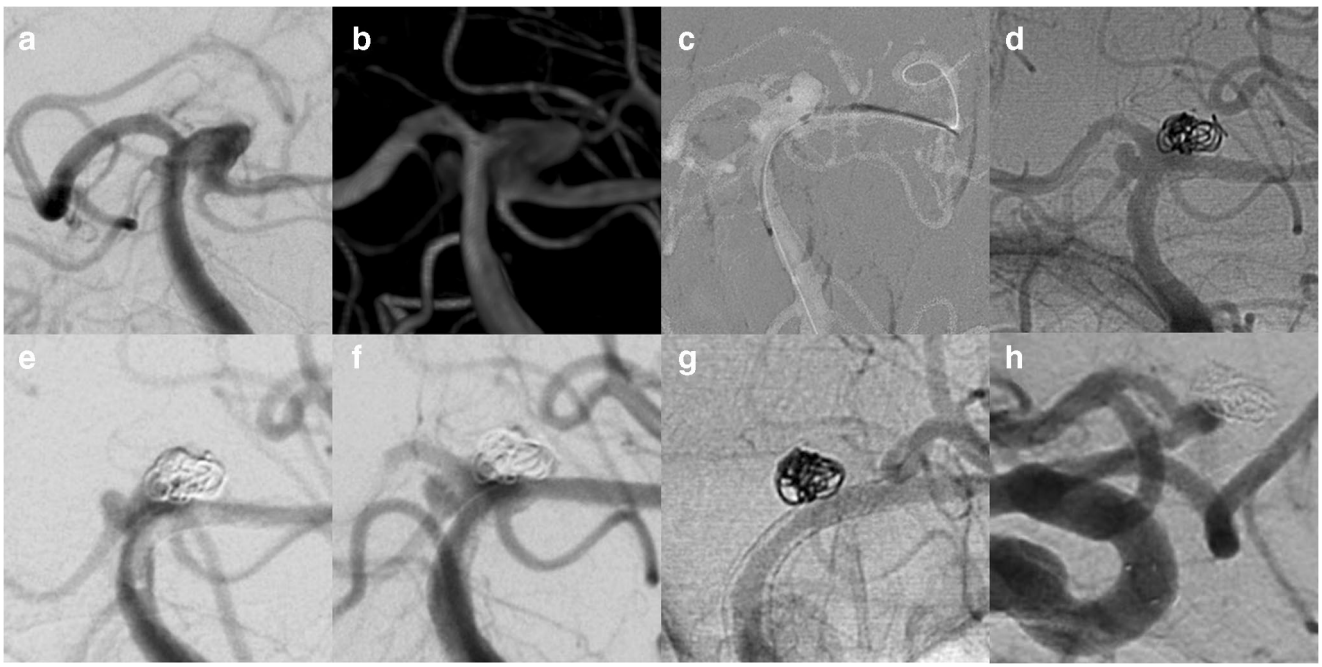


**Fig. 1** A patient presented with a ruptured aneurysm at the basilar artery/P1-junction (**a**, **b**). Due to the complex anatomy and the ruptured aneurysm status, the treatment strategy consisted of implantation of a PED 2.5 × 10 mm (**c**) and adjunctive coiling (3 coils), achieving immediate contrast stasis within the aneurysm sac (OKM B2; **d**). Short-term follow-up shows subtotal aneurysm filling (OKM B1; **e**). Due to initial aneurysm rupture, we expected a relevant re-rupture risk from the residual aneurysm and treated it by implantation of an additional PED (3.5 × 14 mm; **f**). Angiographic follow-ups at 6 months show complete aneurysm occlusion and subclinical intimal hyperplasia (**g**) that regressed almost completely at further follow-up (**h**). After PED implantation the right posterior cerebral artery and the superior cerebellar artery are retrogradely perfused via the right posterior communicating artery (**h**)

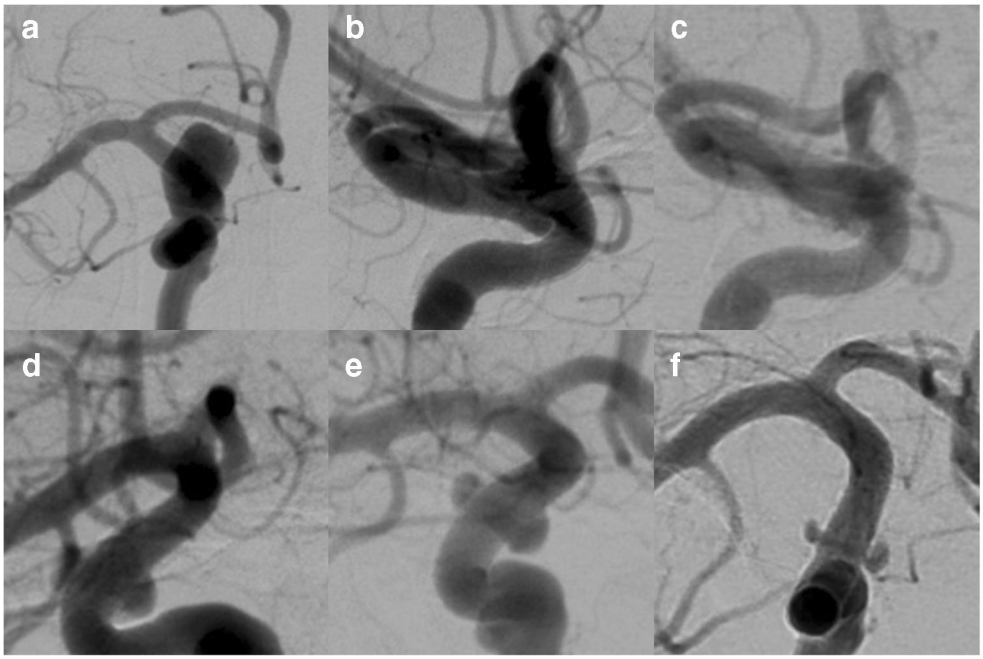


**Fig. 2** Digital subtraction angiography (DSA) shows an unruptured aneurysm (aneurysm size, 10 mm; neck width, 5 mm) at the paraophthalmic segment of the right ICA (**a**). After deployment of two PEDs (4 × 15 mm and 4 × 14 mm), a reduced inflow and significant contrast stasis (OKM B3) could be immediately achieved (**b**). Four-month angiographic follow-up shows a constant aneurysm remnant (OKM B3; **c**). After interdisciplinary discussion, the aneurysm was retreated by implantation of a PED 3.75 × 14 mm (**d**). Four-month angiographic follow-up after retreatment shows progressive aneurysm occlusion with a residual aneurysm neck (OKM C3; **e**). The neck remnant reduced slightly with persistent significant contrast filling (OKM C3) at long-term follow-up after 56 months (**f**)

complete occlusion of the aneurysm itself is not achieved. For these reasons, not all flow-diverter-treated aneurysms with residual filling are generally subjected to retreatment [16]. On the other hand, there are reports on postinterventional aneurysm rupture after flow-diverter treatment [25, 26] and an increase of pressure within the aneurysm due to alterations of the flow in the parent artery and subsequent cerebral autoregulation is discussed in these cases [24]. However, to the best of our knowledge, there is no longitudinal data available, which defines the rupture risk of incompletely occluded aneurysms after flow-diversion.

In the present series, we report 12 aneurysms that were subjected to retreatment due to residual aneurysm filling. The study cohort contains three aneurysms with neck remnants (OKM C) that were retreated. These aneurysms had a complex morphology (i.e., fusiform) or were large-sized and were thus expected to carry a relevant risk for aneurysm rupture or re-rupture.

Owing to the limited options of retreatment after FDD implantation, our treatment strategy consisted mainly of placement of additional FDDs. Complete occlusion of the parent artery, which can be performed in patients with sufficient collaterals, was not performed in any of our cases. This approach proved feasible and resulted in improved aneurysm occlusion in all cases. At mid-term follow-up, the rates of complete and favorable aneurysm occlusion were 75.0% and 91.7%, respectively, which correspond to the angiographic results reported by previous studies on FDDs [20].

## Safety

In general, flow-diversion is associated with higher morbidity and mortality rates when compared with conventional coiling, which is mainly related to ischemic complications [27, 28]. For instance, morbidity and mortality occurred in 5.4% in the IntrePED study [8] and 6.8% in the ASPIRe study [29]. These morbidity rates are not negligible and require careful pondering of treatment risks and benefits.

In this context, there is evidence that the complication rate correlates with the number of implanted FDDs [27]. Chalouhi et al. reported that complications occurred more often with implantation of multiple PEDs (15%) than with a single PED (5%), while there was no significant difference regarding the degree of aneurysm occlusion. For this reason, the authors recommend to keep the number of implanted FDDs to a minimum [30]. In the current series, most aneurysms were initially treated by multiple stents due to a complex morphology, large size, and/or insufficient immediate contrast stasis after placement of the first FDD. All patients received additional FDDs during retreatment; however, we did not observe any procedure-related morbidity. There were two occlusions of covered side vessels, which were regarded as technical complications. However, the patients remained asymptomatic in both cases and there were no further technical or symptomatic complications during a cumulative follow-up period of 19.4 patient years, hence indicating that retreatment with FDDs is reasonably safe, when required.

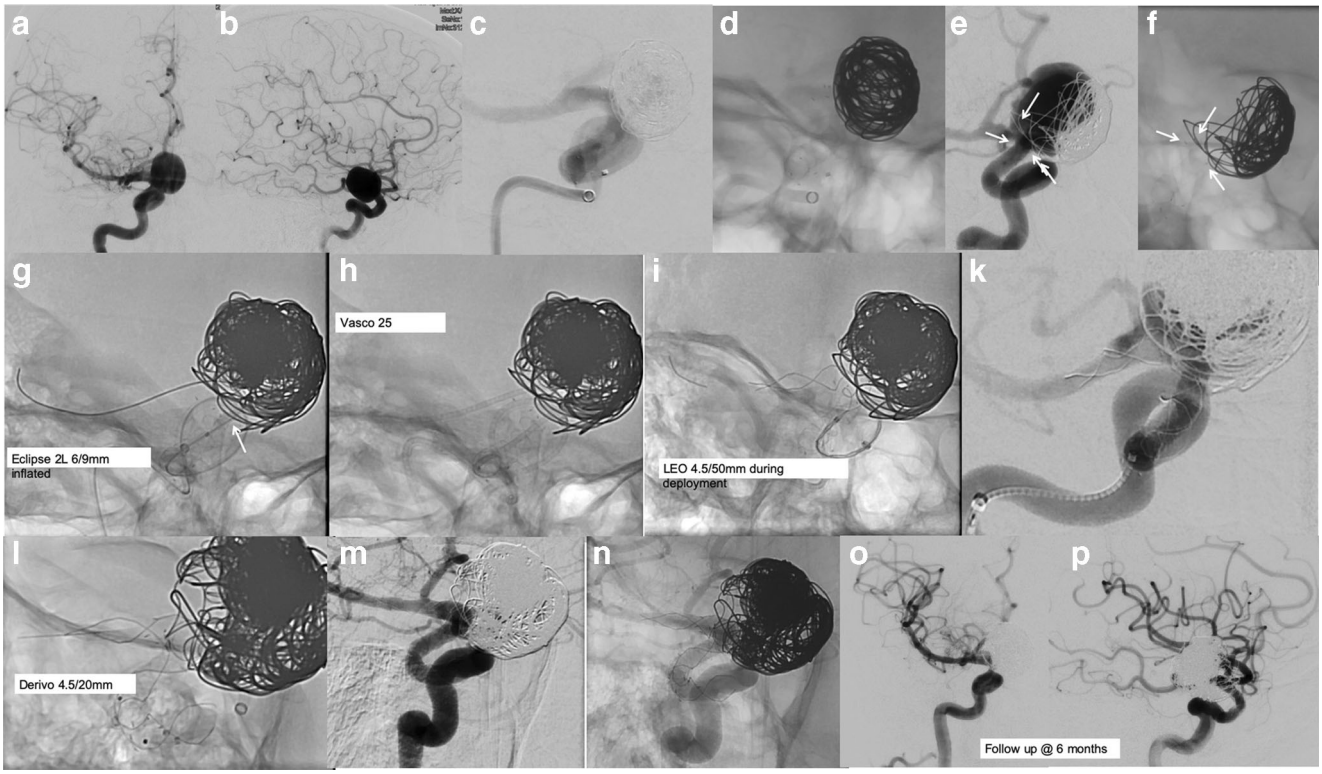


**Fig. 3** A large asymptomatic Pcom-aneurysm with tortuous anatomy of the ICA (**a**: pa, **p**: lateral view). First treatment was performed by implantation of a FRED flow-diverter and additional coiling in jailing technique (**c**, **d**). Twelve months after the treatment, massive enlargement of the previously occluded aneurysm sac was noted (**e**, **f**) and dislocation of the distal markers of the flow-diverter into the sac was identified (arrows). After recoiling, catheterization of the stent was possible with a microwire (**g**) and localization of the wire within the flared ends of the stent was verified by gentle balloon inflation (eclipse). Subsequently, a microcatheter was exchanged (**h**) and an overlapping Leo stent was implanted (**i**, **k**). Three months later, an overlapping Derivo flow-diverter was implanted (**l**, **m**, **n**). The angiogram after 6 months showed complete occlusion of the aneurysm (**o**: pa, **p**: lateral view)

The use of multiple FDDs correlates with an increased risk for side vessel occlusion, which can, depending on the location, result in severe neurological deficits such as visual impairment, or ischemic complications in general [31]. In our series, side vessels arising from the parent artery were covered by the FDD in all but one patient; however, 76.9% of these vessels remained patent until last follow-up. Similar to our results, side vessels were occluded in 20% in the study by Bhogal et al. [32], 21% in the study by Puffer et al. [33], and 27% in the study by Brinjikji et al. [34]. Evidence suggests that angiographic side vessel occlusion after flow-diverter treatment does not necessarily cause neurological deficits [32] which also applies to the patients in the current series.

## Limitations

The present series has several limitations. Although we performed a dual-center analysis of consecutive patients during a 9-year period, only a small number of patients could be identified. Moreover, the majority of patients had complex aneurysms; hence, the study sample is not representative. Although all patients were available for angiographic follow-up, the long-term clinical and angiographic results remain unclear. Furthermore, our series is retrospective; hence, minor neurological deficits might be underreported.

Acknowledging these limitations, our study provides novel insight into the treatment options for incomplete aneurysm occlusion after flow-diversion and might help other neurointerventionalists in their treatment decisions. Further studies will be necessary to confirm our results and to develop a treatment algorithm for aneurysm residuals after flow-diversion.

## Conclusions

In our dual-center series, retreatment of incompletely occluded aneurysms after initial flow-diverter treatment consisted of additional FDD implantation and resulted in progressive aneurysm occlusion in all cases. There were no complications and morbidity related to retreatment. Larger studies are required to validate our results.

**Author contributions** LG, NH, TL, WA, NA, and BK acquired the data. LG, CK, and FD developed the project, analyzed the data, and drafted the manuscript. All authors revised the paper critically for important intellectual content and provided final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Compliance with ethical standards

**Conflict of interest** FD and CK serve as consultants for Acandis GmbH (Pforzheim, Germany). CK and TL serve as proctors for MicroVention Inc./Sequent Medical (Aliso Viejo, CA, USA). The other authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in the 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** For this type of study, formal consent is not required.

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