


# Intracranial Aneurysms Treated by Flow-Diverting Stents: Long-Term Follow-Up with Contrast-Enhanced Magnetic Resonance Angiography

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## Abstract

**Purpose** Long-term data on aneurysm treatment with flow-diverting stents are still sparse, and follow-up protocols differ widely between institutions. We present long-term results, with a focus on the usefulness of contrast-enhanced MR angiography (ceMRA).

**Materials and Methods** Interventions and follow-up imaging of patients with aneurysms treated by flow-diverting stents (“Pipeline,” “Silk” and “FRED” models) without additional coiling were analyzed. All MRI scans included dedicated two-phase ceMRA. Aneurysm occlusion rates, size of the aneurysmal sac and complications were evaluated on MRI and digital subtraction angiography (DSA), where available. The ability of ceMRA to depict aneurysm occlusion and stent patency was graded on a three-point scale.

**Results** Twenty-five patients with 102 MRI scans were included. The median duration of follow-up was 830 days. Aneurysm occlusion rates were 52% at 3 months (10 of 19 patients), 72% at 6 months (18/25) and 84% overall (21/25). Shrinkage of the aneurysmal sac was found in 19 patients (76%) and in 12 cases to <50% of the original size (48%). CeMRA assessability of aneurysmal occlusion was graded as good in all cases. When compared to DSA (18 cases), ceMRA had a sensitivity of 100% and specificity of 91% regarding aneurysm remnant detection. Assessability of the stent lumen varied and was limited in most cases.

**Conclusions** Flow-diverter treatment achieves high occlusion rates and can cause major aneurysm shrinkage.

CeMRA is highly valuable regarding imaging of the aneurysmal sac. There are limitations regarding the assessability of the stent lumen on ceMRA.

**Level of Evidence** Level 4, Case Series.

**Keywords** Brain · Aneurysm · Flow diverter · Stent · Follow-up · MRI

## Introduction

Having been introduced in 2006–2007 [1], flow diverters (FD) are still relatively new devices for the treatment of intracranial aneurysms. Their mode of action differs from the established technique of coiling aneurysmal sacs. FDs are stent-like devices designed to reconstruct the parent artery and change hemodynamics in order to trigger aneurysm thrombosis. This allows therapy of fusiform and wide-neck aneurysms, including cases which would previously have been deemed untreatable [2–5]. However, long-term data are still sparse [6, 7]. Early studies show that the development of aneurysm thrombosis over time differs widely and cannot be securely predicted [8, 9]. Moreover, delayed complications have been reported, such as in-stent stenosis [10, 11], perianeurysmal edema [12] and delayed hemorrhage [13–16]. For these reasons, high-quality follow-up imaging is crucial. So far, there are no generally established follow-up intervals and imaging protocols. Digital subtraction angiography is considered the gold standard for follow-up imaging of coiled aneurysms [17] and is the most reliable modality to image the parent vessel and prove aneurysm occlusion. However, DSA is associated with the drawbacks of invasiveness and radiation exposure. Moreover, it is important to depict the brain parenchyma, the surroundings of the aneurysm and a

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thrombosed aneurysmal sac, particularly in patients treated by flow diversion. For these purposes, cross-sectional imaging is required. At our institution, we have implemented a 3-Tesla MRI follow-up protocol for patients treated with FDs which includes dedicated two-phase contrast-enhanced magnetic resonance angiography (ceMRA). The aim of this study was to evaluate the long-term development of aneurysms after FD therapy and to assess the value of ceMRA as a follow-up imaging tool.

## Materials and Methods

We identified all patients treated with FDs for intracranial aneurysms at our institution in the years 2011–2013. Only patients with follow-up imaging including 3T ceMRA after at least 6 months were included. Patients with aneurysms treated with coils additionally to FD placement were excluded in order to create a homogeneous study group. Furthermore, we excluded fusiform vertebrobasilar artery giant aneurysms, as these represent a distinct entity and the data of our patients are already reported elsewhere [18].

The anti-platelet medication regime was identical for all stent types and included dual inhibition with clopidogrel and acetylsalicylic acid (ASA) for 6 months and continued ASA monotherapy lifelong.

At our institution, the standard follow-up protocol after FD treatment includes an MRI scan after 3 months, DSA and MRI after 6 months, MRI after 18 months and further follow-up depending on the findings. However, there were several deviations due to individual patient findings and compliance.

MRIs were performed on a 3T scanner (Signa HDx, GE Healthcare, Milwaukee, WI, USA) using an eight-channel head coil. CeMRA is a 3D spoiled gradient echo sequence performed after injection of contrast agent (0.1 mmol gadolinium/kg body weight). CeMRA was first executed as a first-pass arterial angiography using bolus tracking. Subsequently, a second ceMRA sequence with a longer scanning time and higher in-plane resolution was performed. In addition to depicting both arterial and venous vasculature, the purpose of the delayed ceMRA is to better delineate small aneurysms and thrombosed aneurysmal sacs due to its higher resolution. The technical parameters of the ceMRA sequences are shown in Table 1. In addition to ceMRA, the MRI protocol included diffusion-weighted imaging (DWI), axial fluid-attenuated inversion recovery (FLAIR) with 5 mm slice thickness and axial T2 with 2 or 3 mm slice thickness. The overall scanning time was 15 min.

The location and shape (saccular, fusiform or “blister”-type) of the aneurysms were assessed. The FD models applied were recorded. Either the Pipeline embolization device (ev3, Irvine, CA, USA), the Silk stent (Balt,

**Table 1** Technical parameters of contrast-enhanced MR angiography

	Arterial ceMRA	Delayed ceMRA
Echo time (TE)	1.644	2.968
Repetition time (TR)	5.308	8.300
Flip angle	20°	20°
Field of view	20 × 20 cm	22 × 22 cm
Matrix	300 × 300	450 × 450
Slice thickness	0.6 mm (Zip 2)	0.6 mm (Zip 2)
Scanning time	1:09 min	4:00 min

Montmorency, France) or the flow-redirection endoluminal device (FRED; MicroVention, Tustin, California) was used. All pre-treatment and follow-up MRI scans were assessed by two readers separately. The perfused parts of the aneurysms were measured in three orthogonal planes and categorized on follow-up scans according to the Kamran scale [19] as modified by Darsaut et al. [20], 1 = unchanged, 2 = reduced perfusion, over 50% of the original lumen, 3 = reduced perfusion, <50% of the original lumen, 4 = almost complete occlusion (remnant of <2 mm diameter) or 5 = complete occlusion. The overall size of the aneurysmal sac, including both perfused and thrombosed parts, was also measured in three orthogonal planes and categorized as 0 = increase in size, 1 = unchanged, 2 = shrinkage to over 50% of the original size or 3 = shrinkage to <50% of the original size. Additionally, the assessability of the ceMRA sequences regarding aneurysm perfusion and stent patency was graded as 1 = no assessability, 2 = limited assessability or 3 = good assessability. All follow-up DSA examinations were evaluated for aneurysm perfusion by the same two readers, and the same categorization as for MRI scans was applied. DSAs were compared to the MRI which was performed on the date closest to the DSA. All complications, both peri-interventional and on follow-up, were recorded.

The gradings of the two readers were compared, and interreader reliability was calculated using Cohen’s Kappa. The few discrepancies (see “Results” section) were solved in consensus. Diagnostic accuracy values with 95% confidence intervals (CI) were calculated regarding the ability of ceMRA to detect aneurysm remnants (grades 1–3) in cases where DSA was available as a reference standard.

## Results

### Baseline Data and Interventions

Twenty-five patients with 25 aneurysms were included in the study. Nineteen aneurysms originated from the internal

carotid artery (ICA), four were located in the intradural vertebral artery (VA), and two at the vertebrobasilar junction. Fifteen aneurysms were classified as saccular, nine as fusiform, and one as “blister” type. Nineteen of the aneurysms were incidental findings, while five were symptomatic with cranial nerve palsies. The blister-type aneurysm had caused a minor subarachnoid hemorrhage. The maximum diameter of the aneurysms ranged from 2 to 47 mm (Median 12 mm).

The stents applied were the Pipeline embolization device in 17 patients, the Silk stent in four patients, and the FRED stent in four patients. Four patients were treated with two, one patient with three and one patient with four Pipeline devices. Two Silk stents were applied in one patient. Eighteen patients were treated with only one FD stent. Baseline data for each patient are presented in Table 2.

Asymptomatic procedural complications included one incomplete stent deployment with stenosis which required post-dilatation, one stent dislocation into the aneurysmal sac and one stent dislocation with subsequent retrieval of the stent. One patient suffered from peri-interventional clinically apparent ischemia (moderate hemiparesis), which was attributed to another stent dislocation and retrieval maneuver.

### Follow-up Results

Overall, 102 MRI scans were evaluated. The minimum number of MRIs in one patient was one, and the maximum number was six. Follow-up covered a time span of over 24 months in 17 patients, 12–24 months in five patients and 6–12 months in three patients. The length of follow-up ranged from 182 to 2038 days (Median 830 days). An early MRI scan 3 months after treatment was available in 19 patients. Twenty-two follow-up DSA examinations were performed in 16 patients.

Complete or nearly complete occlusion of the aneurysm occurred in 21 of the 25 cases (84%). Occlusion rates were 52% after 3 months (10 of 19 aneurysms) and 72% after 6 months (18 of 25 aneurysms). Thus, late occlusion after more than 6 months was found in three patients (12%). In two patients with large aneurysms in whom no occlusion or relevant aneurysm thrombosis had occurred after six and 12 months, respectively, an ICA occlusion was performed for definite aneurysm treatment. In two patients, the aneurysms were only partially occluded at the time of the study. Only two MRI scans were graded discrepantly by the two readers regarding aneurysm occlusion; thus, interreader agreement was very good (Cohen’s Kappa 0.960, 95% confidence interval 0.905–1.000).

Some reduction of the size of the aneurysmal sac was found in 19 aneurysms (76%). Major shrinkage to <50% of

the original size occurred in 12 cases (48%). Size reduction was found only in occluded aneurysms. Figure 1 shows imaging examples of different developments of aneurysm size.

Regarding delayed complications, we found one small perianeurysmal hemorrhage on follow-up MRI and one in-stent stenosis on MRI and DSA (see Fig. 2). The hemorrhage was detected on a routine MRI scan in the fronto-basal parenchyma adjacent to a large ICA aneurysm (Case 7, see Table 2). Its maximum diameter was 8 mm. DSA was performed and demonstrated complete occlusion of the aneurysm. Further MRI follow-up showed no further hemorrhage and resolution of the hematoma. Both hemorrhage and in-stent stenosis were asymptomatic and did not require further treatment.

Three of the five patients with ICA aneurysms and cranial nerve compression syndromes improved clinically: Two had reduced double vision due to oculomotor nerve palsy, and one recovered fully from visual field defects due to optic nerve compression. In all three of them, a major size reduction (>50%) of the aneurysm had occurred. In two patients with ptosis and visual field defects, respectively, no aneurysm occlusion or mass effect resolution was achieved by FD placement and symptoms persisted. These patients were subsequently treated by ICA occlusion. The patient with minor subarachnoid hemorrhage did not suffer from re-bleeding.

Follow-up data of all patients are shown in Table 2.

### MRI Assessability

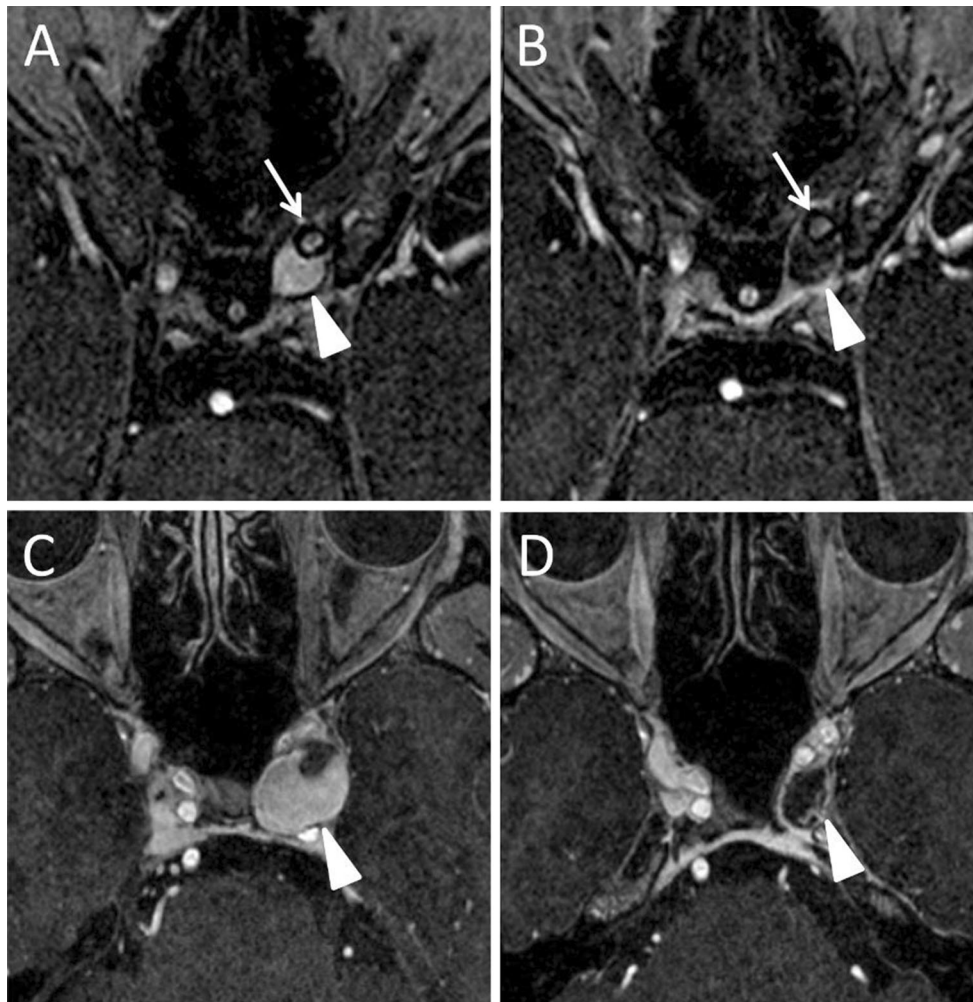
The assessability of aneurysm occlusion on MRI was graded as “good” in all cases by both readers. A direct comparison of a follow-up MRI with DSA was possible in 18 cases. Aneurysm occlusion grades on DSA were “5” in 12 cases and “4,” “3” and “1” in 2 cases each. There were no discrepant findings regarding aneurysm occlusion between DSA and MRI except for one case. In that case, DSA was graded “5” and MRI was graded “3”; thus, MRI was false positive for aneurysm remnant (Fig. 3). Accordingly, sensitivity of ceMRA for the detection of an aneurysm remnant was 100% (CI 59.0–100%), specificity was 90.9% (CI 58.7–99.8%), positive predictive value was 87.5% (CI 47.4–99.7%), and negative predictive value was 100% (CI 69.2–100%). Figure 4 shows concordant findings of DSA and ceMRA.

The gradings of stent lumen assessability were consistent in the different MRI scans of a single patient in 25 of the 27 cases. Assessability of the parent artery on ceMRA was graded as “not possible” in five cases, limited in 16 patients and good in four cases (Fig. 5). With only three differing gradings, over all MRI scans, interreader agreement regarding assessability of the stent lumen was very

**Table 2** Patient data

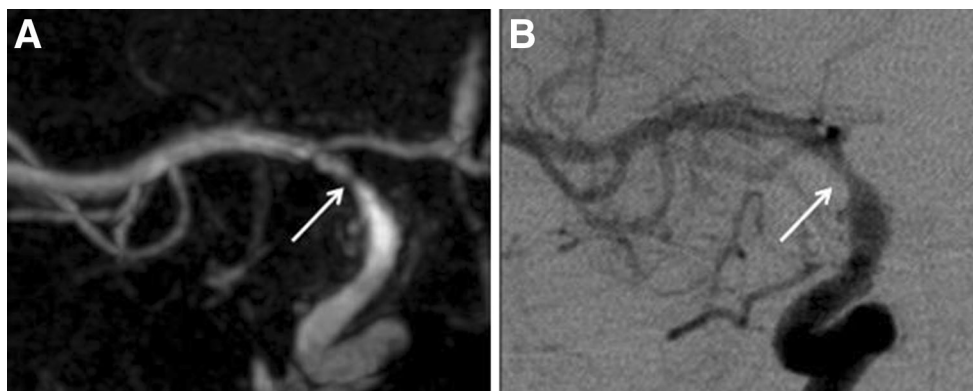
Patient number	Sex	Age	Symptoms	Aneurysm location	Maximum aneurysm diameter (mm)	FD type (number)	Length of follow-up (days)	Number of follow-up MRIs	Final aneurysm size	Final aneurysm occlusion	Time to documented occlusion
1	F	48	N. III palsy	Infraoph. ICA	20	Pipeline (1)	800	2	3	5	6 mo
2	M	41	None	Paraoph. ICA	7	Pipeline (1)	729	3	2	5	15 mo
3	M	53	None	Supraoph. ICA	6	Pipeline (1)	728	3	2	5	3 mo
4	M	41	N. VI palsy	Paraoph. ICA	19	Pipeline (1)	843	4	3	5	6 mo
5	F	74	Ptosis	Infraoph. ICA	22	Pipeline (1)	369	4	1	1	–
6	F	54	None	Supraoph. ICA	9	Pipeline (1)	1086	4	3	5	3 mo
7	F	59	None	Supraoph. ICA	19	Pipeline (1)	1412	6	3	5	3 mo
8	M	68	None	Intradural VA	12	Pipeline (3)	1482	6	1	2	–
9	F	63	N. III palsy	Infraoph. ICA	36	Pipeline (1)	830	4	3	5	3 mo
10	F	64	None	Supraoph. ICA	10	Pipeline (2)	2038	6	2	5	6 mo
11	F	71	Minor SAH	VA–BA junction	2	Silk (1)	854	4	3	5	3 mo
12	M	35	None	Supraoph. ICA	5	Pipeline (1)	874	4	3	5	3 mo
13	M	44	None	Extradural VA	10	Pipeline (2)	201	1	3	5	6 mo
14	M	50	None	Intradural VA	8	Pipeline (1)	269	4	2	5	3 mo
15	F	59	None	Supraoph. ICA	4	Pipeline (2)	1045	3	3	5	3 mo
16	F	60	None	Supraoph. ICA	14	Pipeline (1)	1094	5	3	5	6 mo
17	M	73	None	VA–BA junction	12	Pipeline (4)	176	2	1	4	3 mo
18	F	65	Visual field def. (N.II)	Supraoph. ICA	16	Silk (2)	1050	5	3	5	3 mo
19	F	62	None	Supraoph. ICA	19	Silk (1)	1392	6	3	5	6 mo
20	F	68	Visual field def. (N.II)	Paraoph. ICA	42	Silk (1)	169	4	1	3	–
21	M	70	None	Intradural VA	10	Pipeline (2)	1156	6	1	5	6 mo
22	F	46	None	Supraoph. ICA	11	FRED (1)	621	4	2	4	21 mo
23	F	59	None	Paraoph. ICA	14	FRED (1)	727	5	1	3	–
24	F	54	None	Paraoph. ICA	8	FRED (1)	596	3	2	4	18 mo
25	F	40	None	Supraoph. ICA	7	FRED (1)	483	4	2	5	6 mo

FD flow-diverter stent; N. VI abducens nerve; N. III oculomotor nerve; N. II optic nerve, SAH subarachnoid hemorrhage; Def. defect, ICA internal cerebral artery, Infraoph. infraophthalmic, Supraoph. supraophthalmic, Paraoph. paraophthalmic, VA vertebral artery, BA basilar artery

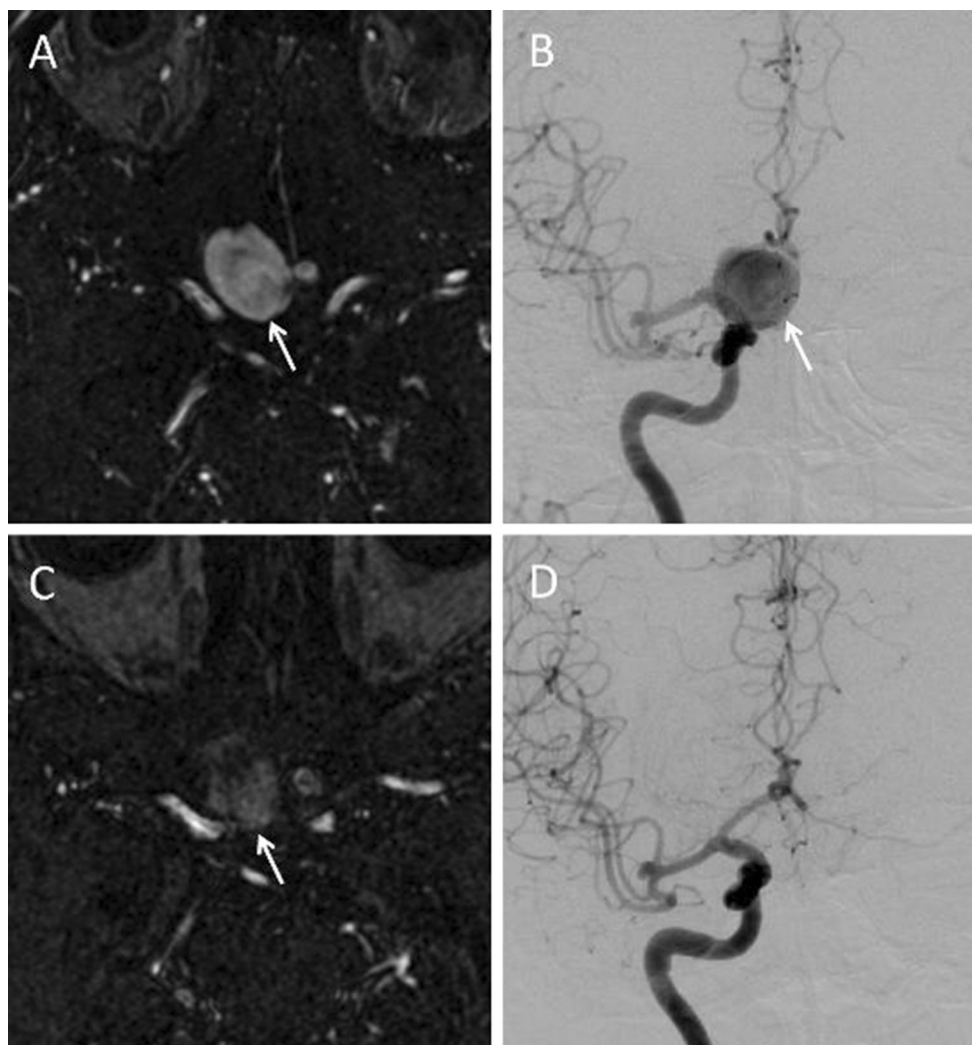


**Fig. 1** **A, B** CeMRA images of one patient show perfused left ICA aneurysm 3 months after flow diverter (Pipeline) treatment (**A**) and complete occlusion without shrinkage of the aneurysmal sac at 6 months (**B**). **C, D** CeMRA images of one patient show the initial

finding of a partially thrombosed left ICA aneurysm (**C**) and the completely occluded and shrunk aneurysm 6 months after flow diverter (Pipeline) treatment (**D**). *Arrows* indicate flow diverter stent; *Arrowheads* indicate the aneurysmal sac



**Fig. 2** **A** CeMRA maximum intensity projection (MIP) showing in-stent stenosis (*arrow*) of a Silk flow diverter in the intradural ICA (**A**), which is confirmed by a DSA run of the right ICA (**B**)



**Fig. 3** **A, B** Arterial ceMRA (**A**) and DSA of a patient with right ICA aneurysm before flow diverter treatment. On arterial ceMRA, the aneurysm has the same signal intensity as other depicted arteries. **C, D** Arterial ceMRA (**C**) and DSA (**D**) of the same patient 6 months after flow diverter (Pipeline) treatment. There is hyperintensity of the

aneurysmal sac, but the signal intensity is lower compared to other arteries. DSA proves complete aneurysm occlusion. DSA images (**B, D**) show an untreated right MCA aneurysm as an additional finding. *Arrows* indicate the aneurysmal sac

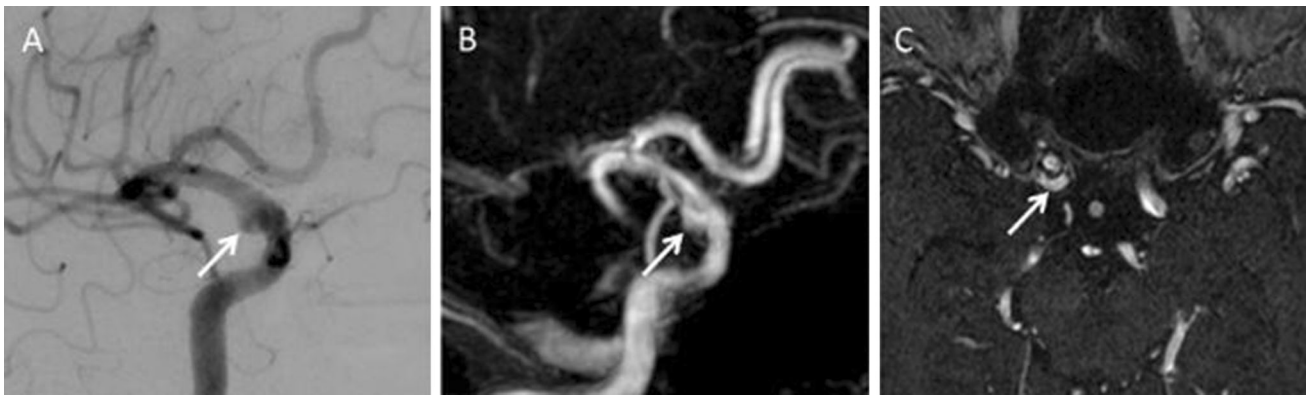
good (Cohen's Kappa 0.933, 95% confidence interval 0.858–1.000).

## Discussion

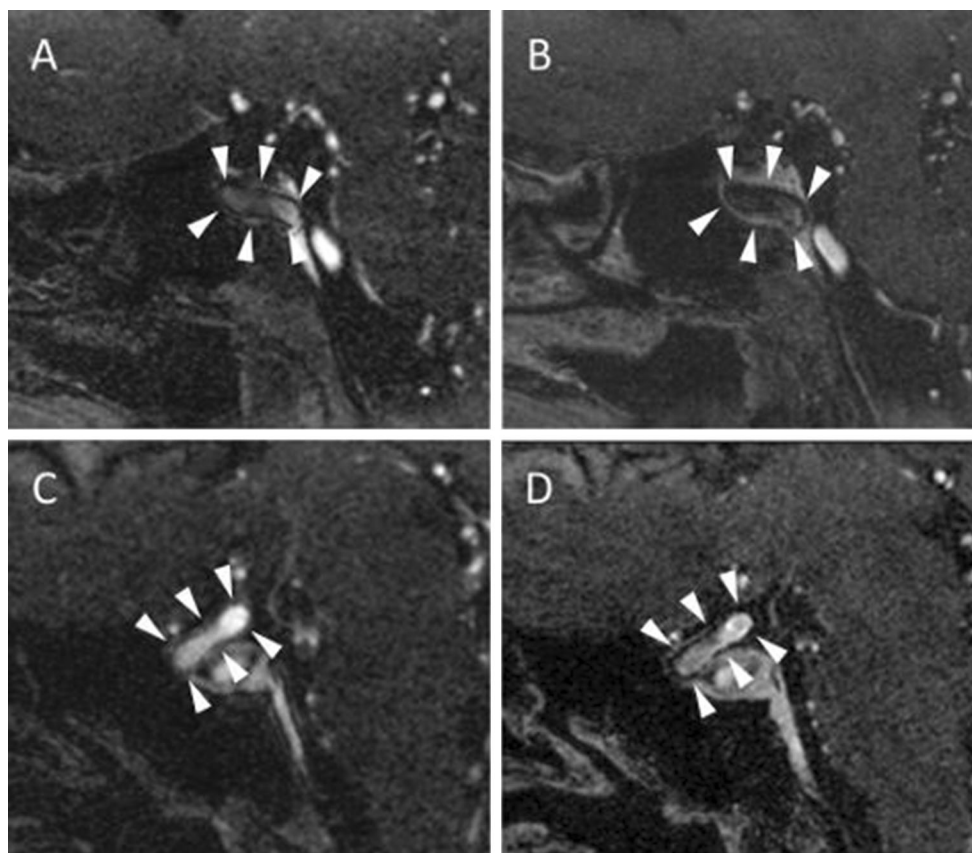
In recent years, a few studies reporting long-term data after FD treatment have been published [21, 22]. These studies focus on complications and angiographic outcome. Follow-up studies which specifically report the data of cross-sectional imaging are even more sparse. With a median follow-up period of 830 days, our study is one of only few detailed reports [8, 23] of long-term data covering more than 2 years after FD therapy. We found that many aneurysms occlude within 3 months (52% in our study) and

most within 6 months (72%), but late complete thrombosis can occur in a few cases. There were three cases of aneurysm occlusion between 12 and 24 months in our study. This time course is similar to the one found in the previous long-term studies, who also reported high occlusion rates at 6 months and late thrombosis at up to 29 months in a few cases (1 of 11 and 2 of 35 aneurysms, respectively [23] [8]). These findings indicate that endpoints of six or even 12 months, which have so far been used in most larger studies on FDs, are not sufficient to exactly determine occlusion rates and outcome.

Apart from eliminating the risk of rupture, resolution of mass effect can be another major goal of aneurysm treatment. We specifically included only aneurysms which were treated by flow diversion alone—without additional



**Fig. 4** **A** DSA of the right ICA shows small aneurysm remnant (*arrow*) after flow diverter (Silk) treatment. **B, C** Correlating ceMRA depicts the aneurysm remnant (*arrow*) in identical size on maximum intensity projection (**B**) and source image (**C**)



**Fig. 5** **A, B** Limited assessability of the ICA segment (*arrowheads*) treated with a flow diverter (*Pipeline*) on arterial (**A**) and delayed (**B**) ceMRA images. **C, D** Good assessability of the ICA segment

(*arrowheads*) treated with a flow diverter (*Silk*) on arterial (**C**) and delayed (**D**) ceMRA

coiling—in order to be able to determine the development of the size of the aneurysmal sac. Some aneurysm shrinkage was found in 72% of the cases, and major size reduction up to complete resolution of the aneurysm occurred in 48%. Although these rates are not as high as reported by Szikora et al. [24], our findings underline the potential of FDs to decrease the space occupation of

aneurysms. When packing an aneurysm with coils, the mass effect can be reduced only to a limited degree. Thus, flow diversion alone should be considered particularly in patients with aneurysms which cause cranial nerve compression syndromes.

Due to the delayed effect of flow diversion, follow-up of patients with aneurysms after FD treatment is even more

important than for endovascular coiling or surgical clipping. Many imaging examinations are required to monitor the development of aneurysmal thrombosis and discover potential delayed complications such as in-stent stenosis and perianeurysmal edema. Detecting such complications is important as they might warrant re-interventions or a change in medication regarding anti-platelet drugs or the use of steroids, although there is no reliable data concerning the latter [12]. The use of DSA should be limited because of irradiation exposure and the risk of complications such as cerebral ischemic events and groin hematoma. Although limitations by streak and blooming artefacts caused by stents have been partially overcome by modern dedicated CT angiography [25, 26], CT also carries the disadvantage of ionizing radiation. Moreover, MRI is clearly superior to CT in depicting ischemic, hemorrhagic and inflammatory complications. Thus, MRI should be the modality of choice for frequent follow-up imaging of treated aneurysms. While a good assessability of MR angiography for coiled aneurysms has been shown [27–30], however, data regarding intracranial stenting and particularly FD stenting are very sparse. Stent braids and radiopaque markers cause susceptibility artefacts and radiofrequency shielding [25], thus potentially limiting assessment of the stent lumen and the adjacent aneurysm. Time-of-flight (TOF) MRA is associated with the additional drawbacks of methemoglobin T1 shine-through effects [27] and signal loss due to spin saturation particularly in large aneurysms with turbulent flow [31]. We therefore prefer ceMRA for imaging of treated intracranial aneurysms which is supported by the findings of Attali et al. [32], who found ceMRA to be superior to TOF MRA when evaluating aneurysms treated by FDs. Additionally to first-pass ceMRA in arterial phase, our protocol includes a delayed steady-state ceMRA with a longer scanning time. The second ceMRA allows for a higher in-plane resolution and thus further facilitates image interpretation. The combined interpretation of the two ceMRA sequences was found to be very reliable in the assessment of aneurysm occlusion in our study. We did not find stent artefacts to limit evaluation of the adjacent aneurysmal sac, and there was only one discrepant grading between DSA and ceMRA. However, some experience is needed when interpreting the ceMRA sequences. In several cases, delayed ceMRA showed partial enhancement of the aneurysmal sac, while first-pass ceMRA did not reveal inflow. We believe such findings to be caused by thrombus enhancement rather than aneurysm perfusion. Both readers were aware of this phenomenon from clinical routine experience and diagnosed an aneurysm remnant only if inflow was visible on both ceMRA sequences. Hyperintensity of the aneurysmal sac on both sequences led to

misinterpretation as aneurysm remnant in one case by both readers. The signal intensity of the aneurysmal sac was lower than that of the parent artery, and DSA did not show any inflow even in venous phase (Fig. 3). Therefore, this finding is retrospectively thought to be due to methemoglobin T1 shine-through, which has not yet been described for ceMRA. Consequently, one should consider including a native T1 sequence when using ceMRA. Moreover, aneurysmal inflow should only be diagnosed if the signal intensity of the aneurysm matches the signal intensity of the parent vessel on arterial ceMRA.

The visibility of the stent lumen varied significantly (Fig. 5). There were cases with complete obscuration of the vessel by stent artefacts and others with very good assessability, even making the correct diagnosis and grading of an in-stent stenosis possible on ceMRA (Fig. 2). In most cases, however, the assessability was limited, with a reduced signal intensity of the stented segment. This variability could be explained by differences regarding the type of flow diverter, the number of flow diverters used and the vessel location and surroundings. Stent visibility on MRI might become a criterion for the selection of the FD model in the future. For now, in most cases DSA will be necessary to reliably depict the stent lumen. Therefore, we believe that at the first control visit (e.g., at 3 or 6 months), both DSA and MRI should be performed, but for further follow-up imaging MRI with ceMRA only will be sufficient in most cases.

Our study has several limitations. Due to the limited number of patients, no definite conclusions can be drawn about the frequency of delayed complications after FD treatment. The study group was inhomogeneous regarding the size and location of the aneurysms. MRI assessability was graded by subjective impressions, and DSA was available as a reference standard in a limited number of cases.

## Conclusions

Our study confirms that high occlusion rates as well as resolution of mass effect of intracranial aneurysms can be achieved by flow diversion without additional coiling. At a low percentage, late aneurysm occlusion after more than 6 months occurs. MRI with dedicated ceMRA proved highly valuable in the depiction of aneurysms treated by FDs. The assessability of the stent lumen on ceMRA is limited in most cases.

## Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflicts of interest regarding this study.



**Ethics and Consent** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This is a retrospective study. For this type of study, formal consent is not required.

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