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Treatment of Ruptured Blister-Like Aneurysms with the FRED Flow Diverter: A Multicenter Experience

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ABSTRACT

BACKGROUND AND PURPOSE: Treatment of ruptured blister-like aneurysms is technically challenging. This study aimed at analyzing the safety and efficacy of the Flow-Redirection Endoluminal Device (FRED) in the treatment of ruptured blister-like aneurysms.

MATERIALS AND METHODS: In a retrospective multicenter study, all patients treated with the FRED due to a ruptured intracranial blister-like aneurysm between January 2013 and May 2019 were analyzed. The primary end points for clinical safety were mRS 0–2 at 6 months after treatment and the absence of major ipsilateral stroke or death. The primary end points for efficacy were the absence of rebleeding after treatment and complete angiographic occlusion according to the O'Kelly-Marotta classification at 6 months after treatment.

RESULTS: In total, 30 patients with 30 ruptured blister-like aneurysms were treated. Immediate complete aneurysm obliteration (O'Kelly-Marotta classification D) with the FRED was achieved in 10 patients (33%). Of the 26 patients with follow-up, complete obliteration was achieved in 21 patients (80%) after 6 months and in 24 patients (92%) in the final follow-up (median, 22 months). Twenty-three patients (77%) achieved mRS 0–2 at 6 months. Major stroke or death occurred in 17%. Two patients died due to pneumonia, and 2 patients died due to infarction following cerebral vasospasm. There was no case of rebleeding after FRED implantation. There was 1 case of delayed asymptomatic stent occlusion.

CONCLUSIONS: Treatment of ruptured blister-like aneurysms with the FRED is safe and effective.

ABBREVIATIONS: OKM = O'Kelly-Marotta; FRED = Flow-Redirection Endoluminal Device; PED = Pipeline Embolization Device

Blister-like aneurysms are a subtype of intracranial aneurysm. It is assumed that blister-like aneurysms are a laceration of the arterial wall based on degeneration of the internal elastic lamina. This focal wall defect seems to be covered with normal adventitia and fibrinous tissue.[1] Blister-like aneurysms are characterized by a thin vessel wall and the absence of an aneurysm neck. There is no pseudolumen or organized thrombus. Blister-like aneurysms typically arise at nonbranching segments of the supraclinoid internal carotid artery, but they can also arise at other locations such as the basilar artery.[2-6]

Surgical treatment and endovascular coiling of blister-like aneurysms are technically challenging.[7] The introduction of flow diverters, however, has allowed a safe and effective treatment option for blister-like aneurysms.[8,9] Several studies on the treatment of blister-like aneurysms with the Pipeline Embolization Device (PED; Medtronic) have shown good clinical and angiographic results.[4,10-15]

The aim of this retrospective multicenter study was to analyze the safety and efficacy of the Flow-Redirection Endoluminal Device (FRED; MicroVention) in the treatment of ruptured blister-like aneurysms.

MATERIALS AND METHODS

Patient Population

This retrospective multicenter study at 3 centers was approved by the local institutional review board at each participating center (Heidelberg/Germany, Istanbul/Turkey, Salzburg/Austria). Between January 2013 and September 2019, all patients with ruptured blister-

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like aneurysms treated with the FRED as an off-label therapy were included. Blister-like aneurysms were defined according to Peschillo et al[6] as small, conical, wide-neck aneurysms located at a nonbranching site of the circle of Willis. Data collection included demographics, clinical data, imaging data, aneurysm features, details of the aneurysm treatment, and clinical outcome.

FRED

A detailed description of the FRED has been published previously. Briefly, the FRED is a braided self-expandable closed-cell flow diverter. The midsection, which encompasses 80% of its total length, has a dual-layer-design low-porosity inner mesh of higher pore attenuation (48 wires) and an outer stent with high porosity (16 wires). The inner mesh and the outer stent are attached by an interwoven double helix of tantalum strands. The FRED is currently available in 5 different diameters (3.5, 4.0, 4.5, 5.0, and 5.5 mm), recommended for vessel diameters from 3.0 to 5.5 mm, at working lengths from 7 to 56 mm.[16-18]

Aneurysm Treatment

Endovascular treatment was performed with the patient under general anesthesia. All patients were treated with the FRED. FRED size was chosen according to the maximal diameter of the parent artery. FRED length covered the parent artery at least 3 mm proximal and distal to the blister-like aneurysm. Decisions for additional coiling (eg, due to aneurysm size) were at the discretion of the treating physician. Antiplatelet medication was given according to in-house protocols at each site.

Imaging Data

Imaging was performed according to in-house protocols of each participating site. In general, patients were followed up at least once by DSA. Thereafter, aneurysms were followed up by DSA, flat panel CT angiography with intravenous contrast agent injection, or contrast-enhanced TOF-MRI. Local experienced neurointerventionalists not involved in the aneurysm treatment reviewed the imaging data.

Outcome Measures

End points for clinical safety were mRS 0–2 at 6 months after treatment and absence of major ipsilateral stroke or death. End points for efficacy were absence of rebleeding after treatment and complete angiographic occlusion according to the O'Kelly-Marotta classification (OKM) at 6 months after treatment.[19]

RESULTS

Study Subjects

In total, 30 patients with 30 ruptured blister-like aneurysms were included in this study. The mean age was 55.6 years, and 63.3% of the patients were female. Hunt and Hess grades and Fisher grades are shown in Table 1.

Procedure

The median duration from onset to aneurysm treatment was 2 days. Treatment was delayed due to either delayed detection of the blister-like aneurysm and/or delayed referral of patients from other hospitals.

Table 1: Baseline characteristics

Characteristic	Value
Age (mean) (SD) (yr)	55.6 (12.9)
Female (No.) (%)	19 (63.3)
Hunt and Hess grade (No.) (%)	
1	13 (43.3)
2	4 (13.3)
3	5 (16.7)
4	6 (20.0)
5	2 (6.7)
Fisher grade (No.) (%)	
1	3 (10.0)
2	14 (46.7)
3	7 (23.3)
4	6 (20.0)
Extraventricular drain (No.) (%)	
Before aneurysm treatment	14 (46.7)
After aneurysm treatment	0 (0)
None	16 (53.3)

Table 2: Aneurysm characteristics

Characteristics	Value
Aneurysm rupture to treatment (No.) (%)	
0–1 day	13 (43.3)
2–7 days	8 (26.7)
>7 days	9 (30.0)
Aneurysm location (No.) (%)	
Internal carotid artery	19 (63.3)
Basilar artery	7 (23.3)
Vertebral artery	2 (6.7)
Anterior communicating artery	1 (3.3)
Posterior cerebral artery	1 (3.3)
Median aneurysm height (No.) (mm)	1.7
Median aneurysm diameter (No.) (mm)	2
Median diameter of parent vessel proximally (No.) (mm)	3.5
Median diameter parent vessel distally (No.) (mm)	3
Median diameter of FRED (No.) (mm)	4
Median length of FRED (No.) (mm)	13
Median No. of FREDs used	1
Aneurysms that were additionally coiled (No.) (%)	2 (6.7)

A ventricular drainage was placed in 14 patients (46.7%) before aneurysm treatment. No ventricular drainage was placed after flow diversion.

Aneurysm location was mostly the supraclinoid ICA (63.3%) and basilar artery (23.3%), with a median aneurysm size of 2 mm (Table 2). All aneurysms were initially treated with a single FRED flow diverter each. In 29 of 30 cases, the FRED was completely adherent to the wall of the parent artery immediately after deployment. In 1 case, the FRED opened; however, additional angioplasty was necessary to adhere the FRED completely to the vessel wall.

In 2 cases, the treating physician decided to place coils inside the blister-like aneurysm in addition to flow-diverter implantation because of the aneurysm size. The maximum aneurysm diameters in these 2 cases were 4 and 2 mm, respectively.

Medication

Antiplatelet medication was given according to in-house protocols at each site. Preoperatively, dual-antiplatelet therapy with aspirin and clopidogrel was given in 8 patients (26.7%), and prasugrel was given in 4 patients (13.3%). Intraoperatively, 20

Table 3: Aneurysm occlusion

Occlusion Grading	End of the Procedure ($n = 30$)	At 6 Months ($n = 26$)	At 12 Months ($n = 26$)	Last Follow-Up[a] ($n = 26$)
OKM (No.) (%)				
D	10 (33.3)	21 (80.8)	22 (84.6)	24 (92.3)
C	4 (13.3)	3 (11.5)	3 (11.5)	2 (7.7)
B	16 (53.3)	2 (7.7)	1 (3.8)	0 (0)
A	0 (0)	0 (0)	0 (0)	0 (0)

[a] Median last follow-up was approximately 22 months (interquartile range, 12–37 months).

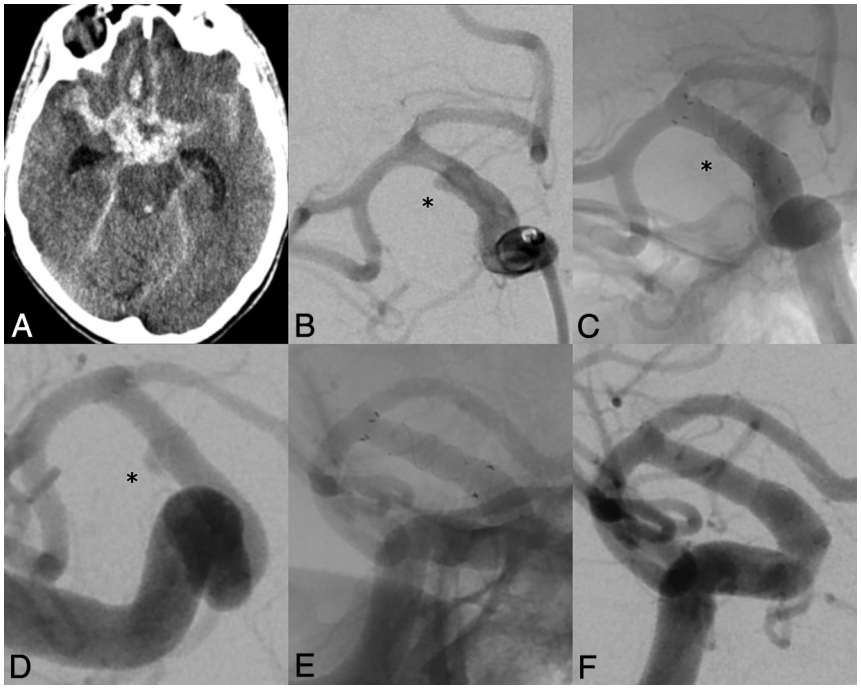

FIGURE. *A*, Nonenhanced head CT of a female patient in her 50s showing subarachnoid hemorrhage, Hunt and Hess grade 4, and Fisher grade 4. *B*, Angiography reveals a blister-like aneurysm of the right supraclinoid ICA with a maximum neck diameter of 3.3 mm. *C*, Angiographic result immediately after deployment of FRED 4.0 × 13 mm. *D*, Follow-up angiography at day 17 shows a residual aneurysm filling. *E* and *F*, Follow-up angiography at 3 months demonstrates complete aneurysm obliteration. mRS score at 3 months was 1.

patients (66.7%) received glycoprotein IIb/IIIa inhibitors, and 7 patients (23.3%) received heparin. Postoperatively, dual-antiplatelet therapy with aspirin and clopidogrel was given in 21 patients (70.0%); ticagrelor, in 5 patients (16.7%); and prasugrel, in 4 patients (13.3%). Patients continued antiplatelet therapy according to the standard of care in the respective hospital for at least 6 months.

Safety

Twenty-three patients (76.7%) achieved mRS 0–2 after 6 months (Online Table). Two patients died due to pneumonia, and 2 patients died due to SAH-related delayed cerebral ischemia.

Procedure-related complications occurred in 4 cases: One patient with a basilar blister-like aneurysm had a major stroke after flow diversion. MR imaging revealed a left paramedian pontine infarction indicating a perforator stroke despite premedication of the patient with tirofiban and heparin before deployment of the FRED. Another patient with a blister-like aneurysm of the ICA had a minor stroke due to distal cerebral emboli. Both patients received tirofiban during the procedure and were on dual-antiplatelet therapy after treatment. They were discharged with mRS 4, and both recovered to mRS 2 one year after treatment. In 1 case, there was partial thrombus formation within the FRED. However, this was not hemodynamically relevant, and the FRED was patent on follow-up images. The patient received tirofiban during the procedure and ticagrelor thereafter. There was 1 case of retroperitoneal hematoma requiring medical management.

In 1 patient, asymptomatic FRED occlusion occurred, which was diagnosed during a routine follow-up 19 months after aneurysm treatment. In this case, aspirin had been discontinued 12 months before.

There was no case of recurrent hemorrhage before or after flow diversion.

Efficacy

Complete aneurysm obliteration (OKM D) at the end of the procedure was achieved in 10 patients (33.3%).

Follow-up imaging was not possible in 4 patients due to death as described above. Except for 1 patient who was followed up only once by flat panel CT with intravenous contrast agent injection, all patients underwent DSA at least once.

Follow-up imaging was available in 26 patients. Six months after aneurysm treatment, 21 patients (80.8%) achieved complete obliteration (OKM D). A residual neck (OKM C) was visible in 3 patients (11.5%), and a residual aneurysm (OKM B) was visible in 2 patients (7.7%). In the final follow-up (median, 22 months), complete obliteration was observed in 24 patients (92.3%) (Table 3).

One patient required additional implantation of another FRED 10 days after the initial treatment due to aneurysm growth. Another patient required implantation of a second FRED 2 years after initial treatment because the blister-like aneurysm was not sufficiently obliterated. No complications occurred in either case, and the aneurysms were completely obliterated at follow-up imaging.

DISCUSSION

The present retrospective study adds evidence that treatment of ruptured blister-like aneurysms with the FRED is safe and effective. Complete aneurysm obliteration with the FRED was achieved in 80% at 6 months and in 92% in the final follow-up.

Most important, there was no case of rebleeding after FRED implantation. About 77% achieved mRS 0–2 at 6 months. Major stroke or death occurred in 17%.

The results of the present study with the FRED are similar to those of Mokin et al,[15] who analyzed treatment of ruptured blister-like aneurysms with the PED. Mokin et al reported complete aneurysm obliteration in 87.5% on follow-up angiograms in patients treated with the PED. Furthermore, they reported that 68% of their patients achieved good clinical outcome at 3 months. The results of the present study suggest that the FRED and PED show similar safety and efficacy in the treatment of blister-like aneurysms. While the PED is a 48-strand braided mesh, the FRED is a dual-layer stent with an inner stent consisting of 48 wires and an additional outer stent with 16 wires serving as a scaffold for the inner stent. This design might potentially increase aneurysm obliteration after flow diversion with the FRED.[18,20] However, there are currently no data supporting this hypothesis.

For many years, treatment of blister-like aneurysms has been technically challenging for both clipping and coiling. Today, flow-diverter implantation allows the endovascular treatment of blister-like aneurysms just as in wide-neck and fusiform aneurysms.[7,21] The mesh design of flow diverters alters blood flow into the aneurysm and induces a thrombosis within the aneurysm (Figure).[4]

There are often concerns regarding stent or flow-diverter deployment in patients with aneurysmal SAH because it requires antiplatelet and/or anticoagulation treatment to avoid thrombosis.[7] Antiplatelet therapy, however, increases the risk of intracranial rebleeding. There was no rebleeding in any cases in this study, though. Mokin et al[15] reported that 1 of 49 patients had delayed aneurysmal rerupture. Mazur et[22] and Nerva et al[23] each reported 1 case of delayed rebleeding after PED deployment in a patient with a ruptured blister-like aneurysm. There are, however, case studies by Ryan et al[14] ($n = 13$), Linfante et al[12] ($n = 10$), Capocci et al[24] ($n = 8$), Chalouhi et al,[10] ($n = 8$), Cerejo et al ($n = 8$),[25] Çinar et al ($n = 7$),[26] and Hu et al[11] ($n = 3$) reporting no rebleeding after flow-diverter implantation in patients with ruptured blister-like aneurysms. Ryan et al[14] ($n = 13$) reported 1 case of rebleeding, however, due to an unrecognized additional aneurysm. The data of the present study and previous studies show that the risk of rebleeding after flow-diverter implantation in blister-like aneurysms is low.

There was 1 case (3.3%) of delayed asymptomatic in-stent thrombosis in the present study. Thrombosis was diagnosed 19 months after aneurysm treatment during a routine follow-up. In this case, aspirin had been discontinued 12 months before. Thrombosis might have been prevented by a longer period of antiplatelet medication. Mokin et al[15] reported 2 cases of intraprocedural in-stent thrombosis, 2 cases of intraprocedural thrombosis in an M3 segment, 1 case of delayed asymptomatic in-stent stenosis, and 1 case of delayed asymptomatic in-stent thrombosis. These data suggest that the risk of thrombosis might be higher than that of rebleeding. Sufficient antiplatelet therapy is therefore mandatory.

This study has several limitations mostly due to its retrospective multicenter design with a potential selection and reporting bias. Aneurysm treatment and medication differed at each participating site. Also imaging data and clinical outcome were not reviewed by a central core laboratory.

CONCLUSIONS

This study adds evidence that treatment of blister-like aneurysms with the FRED is safe and effective. Outcome results are similar to those of the PED.

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