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Flow Diversion Therapy of Remnant and Recurrent Intracranial Aneurysms Treated Surgically

Erol AKGUL[1], Hasan Bilen ONAN[2], Yusuf CAN[3], Gulhan ERTAN[3], Cengiz EROL[3], Ahmet CETINKAL[4], Celal CINAR[5], Bahattin HAKYEMEZ[6], Altan YILDIZ[7], Ismail ORAN[5], Zeki SEKERCI[8]

[1]Istanbul Medipol University, International School of Medicine, Radiology Department, Interventional Neuroradiology Section, Istanbul, Turkey
[2]Cukurova University, School of Medicine, Radiology Department, Interventional Neuroradiology Section, Adana, Turkey
[3]Istanbul Medipol University, School of Medicine, Radiology Department, Istanbul, Turkey
[4]Istanbul Medipol University, School of Medicine, Neurosurgery Department, Istanbul, Turkey
[5]Ege University, School of Medicine, Radiology Department, Interventional Neuroradiology Section, Izmir, Turkey
[6]Uludag University, School of Medicine, Radiology Department, Interventional Neuroradiology Section, Bursa, Turkey
[7]Mersin University, School of Medicine, Radiology Department, Interventional Neuroradiology Section, Mersin, Turkey
[8]Istanbul Medipol University, International School of Medicine, Neurosurgery Department, Istanbul, Turkey

Corresponding author: Erol AKGUL ✉ akgulerol@gmail.com

ABSTRACT

AIM: To evaluate the safety and efficacy of flow diverter stents (FDSs) for treating remnant or recurrent intracranial aneurysms that were treated surgically.

MATERIAL and METHODS: The patients who were treated with FDSs due to remnant or recurrent intracranial aneurysms after microsurgery were included in the study. The patients' demographics, treatment histories, aneurysm features, complications associated with flow diversion, and neurological and angiographic follow-up findings were evaluated.

RESULTS: Twenty patients (eight males) with 20 aneurysms were included in the study. Of 20 aneurysms, 18 (90%) were in the anterior, and two (10%) were in the posterior circulation. The initial treatment methods were clipping in 17 (85%) and wrapping in three (15%) aneurysms. The endovascular procedure was successful in all patients. In three patients (15%), periprocedural and postprocedural complications were encountered. No hemorrhagic complications were detected on cone-beam computed tomography. One patient with a basilary aneurysm died because of brain stem ischemia. The total morbimortality was 5%. The mean length of follow-up was 13.7 ± 7.3 months in 18 patients. The first angiographic follow-up (3–6 months) revealed the complete occlusion in 7 of 11 aneurysms (63.6%). By contrast, 16 aneurysms (94.1%) were occluded at the last angiographic follow-up, one aneurysm (5.9%) was still filling.

CONCLUSION: An FDS seems effective, safe, and extremely attractive in treating remnant and recurrent intracranial aneurysms treated surgically.

KEYWORDS: Flow diverter stent, Cerebral aneurysm, Recurrent aneurysm, Remnant aneurysm, Surgical treatment

ABBREVIATIONS: ACA: Anterior cerebral artery, **AChorA:** Anterior choroidal artery, **AComA:** Anterior communicating artery, **Aneu:** Aneurysm, **CT:** Computed Tomography, **D:** Derivo, **DSA:** Digital Subtraction Angiography, **F:** FRED, **FDS:** Flow diverter stent, **FRED:** Flow Re-direction Endoluminal, **ICA:** Internal carotid artery, **m:** Month, **MCA:** Middle cerebral artery, **Morb:** Morbidity, **Mort:** Mortality, **MRI:** Magnetic Resonance Imaging, **mRS:** Modified Rankin Scale, **N:** Number, **P:** Pipeline, **PComA:** Posterior communicating artery, **PED:** Pipeline Embolization Device, **PICA:** Posterior inferior cerebellar artery, **S:** Silk, **SD:** Standard deviation, **SP:** Surpass, **Tech:** Technical

Erol AKGUL : 0000-0003-0020-3759
Hasan Bilen ONAN : 0000-0002-1486-2782
Yusuf CAN : 0000-0002-5325-4704
Gulhan ERTAN : 0000-0002-0742-1305
Cengiz EROL : 0000-0003-3468-7712
Ahmet CETINKAL : 0000-0002-7597-1456
Celal CINAR : 0000-0002-3237-9268
Bahattin HAKYEMEZ : 0000-0002-3425-0740
Altan YILDIZ : 0000-0003-2379-3878
Ismail ORAN : 0000-0002-3546-7773
Zeki SEKERCI : 0000-0002-6983-8632

INTRODUCTION

In treating brain aneurysms, the main goal is to achieve complete occlusion of the sac with either of two methods, surgical or endovascular (36). In addition to ensuring total occlusion, it is essential to prevent the aneurysm from rebleeding and regrowing in the future and prevent it from creating a risk (19). Although surgical clipping is an effective treatment option for achieving this goal, complete aneurysm occlusion or regrowth cannot be achieved in all patients. The occurrence of remnant aneurysm after surgical clipping varies between 1.6% and 14.9% on follow-up angiography, whereas rebleeding occurs in 4%–14.7% of remnants (18). The recurrent aneurysm is seen in 1%–2% of the patients treated surgically (23). The rebleeding rate may be very high in these patients, up to 50% (47). Therefore, remnant or recurrent aneurysms should be treated when detected (18). Since previous surgery increased morbimortality in the reclipping of remnant or recurrent aneurysms, and remnant or recurrence was not few after retreating with standard endovascular techniques, treatment with flow diverter stents (FDSs) has found a field of application in such patients (1,19,24,39,41,53).

FDSs are the cornerstone in the endovascular treatment of intracranial aneurysms (2,39). The safety and efficacy of FDSs have been proven in the treatment of large, wide-necked carotid siphon and fusiform aneurysms (12,15,40). Additionally, recent publications have shown that they are feasible in the treatment of tiny ruptured (such as blister-like examples) and unruptured aneurysms (6,17). Indeed, they are even helpful for bifurcation aneurysms located distal to the Circle of Willis (55).

The safety and efficacy of FDSs in the treatment of almost any type and location of aneurysms make them a first-choice treatment method for aneurysms (20). However, data in the literature about the endovascular treatment of remnant or recurrent aneurysms seen after microsurgery are limited (1,24,28,39,53). In this retrospective, single-arm, multicenter study, we evaluated the safety and efficacy of the FDSs to treat remnant or recurrent intracranial aneurysms treated surgically. This study includes the largest cohort treated with FDSs in medical literature, based on PubMed and Google Scholar.

MATERIAL and METHODS

Patient Selection

Five center databases were retrospectively reviewed after obtaining institutional ethics committee approval to identify the consecutive patients treated with FDSs due to the remnant or recurrent intracranial aneurysms detected after microsurgery between 2011 and 2020 (Approval No: 10840098-604.01.01-E.9268; Date: 21.02.2020). The endovascular treatment decision with an FDS was made in cases of a continuous increase in the remnant or recurrent part of the aneurysms previously treated with surgery. Immediate treatment with an FDS was performed in remnant aneurysms that could not be treated with clipping or treated only with wrapping. The endovascular treatment method was the center's decision with a multidisciplinary approach. Remnant or recurrent aneurysms treated with any other endovascular technique beyond an FDS were excluded from the study. The patients' demographics, treatment histories, aneurysm features, complications associated with flow diversion, and neurological and angiographic follow-up findings were recorded (Table I). The aneurysm occlusion was evaluated as "complete" or "not." After preparing the tables, the results and discussion sections of the study were written. Subsequently, all the other necessary main sections and subsections were designed with the joint decision of all authors.

Endovascular Procedure

Under general anesthesia, the internal carotid artery was accessed by using long introducers and neurovascular distal access-guiding catheters. Passing the aneurysm neck by approximately 2–3 cm, a microcatheter suitable to deploy the chosen FDS was inserted in the parent artery. Then, the FDS was deployed to cover the neck of the aneurysm. Each patient received one of the following FDSs on the market: Silk, Balt, Montmorency, France or Derivo, Acandis, Pforzheim, Germany; or Surpass, Stryker Neuroendovascular, Kalamazoo, MI, USA; or Flow Redirection Endoluminal Device (FRED), Microvention Terumo, Tustin, CA, USA; or Pipeline Embolization Device (PED), Medtronic Covidien AG, Paris, France (Table I). The deployed stent's expansion and wall apposition were evaluated under fluoroscopy and cone-beam computed tomography (CT) if needed. In cases of incomplete stent expansion, we performed in-stent balloon angioplasty to achieve a complete wall apposition. A cone-beam CT was conducted just after the procedure before waking up the patient to identify any hemorrhagic complications.

Medication

Although there were some differences in the endovascular procedures and follow-up protocols, the primary approach used by the participating centers was similar. All procedures were performed as electives except two. The patients were premedicated before the interventions. Depending on the preference of each center, daily 100–300 mg of aspirin and either 75 mg of clopidogrel or 10 mg of prasugrel were started at least five days before the endovascular treatment. The response to the clopidogrel/prasugrel was verified before the procedure with a point-of-care assay. Patients with an inadequate response to clopidogrel were switched to prasugrel with a starting daily dose of 10 mg. In two patients with ruptured aneurysms, 300 mg of aspirin and 300 mg of clopidogrel were loaded 8 h before the procedure. Systemic anticoagulation was initiated after the insertion of a femoral introducer sheath with a bolus dose of 5000 IU of IV heparin or 70–100 IU/kg heparin based on operator preference. The bolus dose was followed by a 1000 IU IV bolus dose per hour to maintain an activated clotting time approximately twofold greater than the baseline value. Postprocedural dual antiplatelet therapy was continued for six months and was switched to daily aspirin after that.

Follow-up

The first follow-up digital subtraction angiography (DSA) was scheduled at 3–6 months. The second follow-up angiogram, either invasive or noninvasive, was performed at 9–12 months.

The neurological status of the patients was evaluated using the Modified Rankin Score (mRS) scale during discharge and at the angiographic follow-up.

Statistical Analysis

All data are presented as means and ranges for continuous variables and as frequencies for categorical variables.

RESULTS

Twenty patients (eight males) with 20 aneurysms were included. The mean age of the patients was 51.7 ± 15.8 years (range: 21–76 years). Of 20 aneurysms, 18 (90%) were in the anterior and two (10%) were in the posterior circulation. Table I shows the exact locations of the aneurysms and how they were previously treated in addition to demographic characteristics. The mean time between the initial surgical treatment and FDS insertion was 57.9 ± 96.7 months.

The initial treatment methods were clipping in 17 (85%) and wrapping in three (15%) aneurysms.

The endovascular procedure was successful in all patients. In three patients (15%), periprocedural and postprocedural complications were encountered. A technical complication developed in one patient: proximal migration of a Derivo FDS led to the stent deformation during resheathing; consequently, a new one was inserted. This complication did not cause any problem and the patient remained asymptomatic, and the mRS score of this patient was zero at discharge. We observed

Table I: Patient Data and Aneurysm Characteristics

	n (% or SD)
Number of patients	20
Age, years	21–76
Mean ± SD	51.7 ± 15.8
Sex	
Male	8 (40)
Female	12 (60)
Treated aneurysms, total	20
Time between ST and ET (mean), month	0.3–288 (57.9 ± 96.7)
Surgical treatment	
Aneurysm initial size (mean), mm	3–35 (9.5 ± 6.5)
Ruptured	13 (65)
Treatment	
Clipping	17 (85)
Wrapping	3 (15)
Endovascular treatment	
Aneurysm size (mean), mm	2–25 (8.5 ± 6.4)
Rupture	
Ruptured	2 (10)
Unruptured	18 (90)
Indication	
Remnant	13 (65)
Recurrence	7 (35)

	n (% or SD)
Aneurysm location	
Anterior circulation	18 (90)
ICA ophthalmic	3 (15)
PComA	3 (15)
AChorA	1 (5)
ICA terminal	1 (5)
MCA bifurcation	6 (30)
MCA M1	2 (10)
ACA	1 (5)
AComA	1 (5)
Posterior circulation	2 (10)
PICA	1 (5)
Basilar trunk	1 (5)
Aneurysm type	
Saccular	18 (90)
Fusiform	2 (10)
Aneurysm site	
Bifurcation	7 (35)
Sidewall	13 (65)
Pre-mRS	20 (100)
0	17 (85)
2	1 (5)
4	2 (10)

N: *Number,* ***SD:*** *Standard deviation,* ***ICA:*** *Internal carotid artery,* ***PComA:*** *Posterior communicating artery,* ***AChorA:*** *Anterior choroidal artery,* ***MCA:*** *Middle cerebral artery,* ***ACA:*** *Anterior cerebral artery,* ***AComA:*** *Anterior communicating artery,* ***PICA:*** *Posterior inferior cerebellar artery,* ***mRS:*** *Modified Rankin Scale.*

a periprocedural thrombotic complication in one patient. Intraprocedural control DSA images showed no thrombus, but diffusion magnetic resonance imaging performed 3 h later revealed acute brain stem ischemia. This patient died 2 weeks later. We observed a delayed complication in another patient. An inguinal hematoma developed a week later that was treated with intracavitary thrombin injection.

Hemorrhagic complications were not detected in any patients based on cone-beam CT performed immediately following the procedure. The total morbimortality was 5% (Table I).

The mean length of follow-up was 13.7 ± 7.3 months (range: 3–32 months) in 18 patients (of 20 patients, one died, and the other did not come for control). The first angiographic follow-up (3–6 months) revealed the complete occlusion in seven of 11 aneurysms (64%). Sixteen aneurysms (94%) were occluded at the last angiographic follow-up, whereas one aneurysm (6%) was still filling. No recanalization was seen during the follow-up period. The mRS at discharge in 19 patients and during follow-up in 18 patients was ≤2 (Table I and II).

Figure 1 shows a representative case.

DISCUSSION

Treatment of intracranial aneurysms with FDSs has been widely accepted as an endovascular method with a high aneurysm occlusion rate (39). Retreatment after FDS is very low, and recanalization after obtaining aneurysm occlusion is quite rare (7,37,39,40). Many studies have shown the safety and efficacy of FDSs in the treatment of remnant or recanalized aneurysms after any endovascular treatment (4,8,9,20,24,27,48). However, there are only a few studies with a small number of cases in which the authors evaluated FDSs in the treatment of remnants or recurrent aneurysms after surgery (1,19,24,39,53). As remnant and recurrence after any endovascular treatment beyond flow diversion in aneurysm treatment are issues, remnant or recurrent aneurysm cases after surgery cannot be neglected as well (1,39). Complete obliteration with surgical treatment is obtained in 92% of unruptured aneurysms, whereas total obliteration is 84% in ruptured ones (38,43). A meta-analysis by Kotowski et al. showed that the remnant of surgically treated aneurysms was 8.2% (38). Aneurysm remnants that may progress to recurrence were seen in 4%–8% of cases (1,25,56). Recurrence may also be an issue in a small number of totally clipped aneurysms. The annual recurrence rate of fully clipped aneurysms is 0.26%–0.52% (1,21,36,56). Owen et al. reported a 50% risk of recurrent aneurysm rupture, a phenomenon that requires retreatment (47). Retreatment of remnant or recurrent aneurysms can be performed either surgically or endovascularly. Surgical retreatment is usually associated with a higher rate of morbimortality (25,36). Difficulties of reoperation arise from adhesions, scar tissue formation, or anatomic distortion that have been caused by previous surgery and previous clips can obstruct the dissection making reclipping difficult (18,19,36). Thus, those aneurysms have been treated mainly by endovascular techniques such as simple coiling, balloon-assisted coiling, stent-assisted coiling, or, especially in recent years, flow diversion (1,18,19,53). Microsurgery may be reserved for complex recanalized aneurysms that need an external–internal carotid bypass, patients with uncorrectable coagulation disorders, or if antiplatelet agents are contraindicated.

Aneurysm therapy that involves parent artery reconstruction with an FDS results in a gradual but complete aneurysm obliteration, especially in large and giant aneurysms (52). In several studies (2,41,49), researchers have shown that the branches originating from the area covered by the FDS remain

Table II: Procedural and Follow-Up Data and Complications

	n (mean with SD or %)
FDSs, total used	20 (100)
Pipeline	10 (50)
Silk	6 (30)
Derivo	2 (10)
Surpass	1 (5)
FRED Jr	1 (5)
FDS with or without coil	20 (100)
With coil	3 (15)
Without coil	17 (85)
Follow-up duration, angiographic (month), n=18	3–32 (13.7 ± 7.3)
Closure rate, at 3-6th month	11 (100)
Complete	7 (64)
Incomplete	4 (36)
Closure rate, overall	17 (100)
Complete	16 (94)
Incomplete	1 (6)
Complications, total	3 (15)
Technical	1 (5)
Inguinal hematoma	1 (5)
Thromboembolic	1 (5)
Morbidity	0 (0)
Mortality	1 (5)
Post-mRS at follow-up	**18 (100)**
0	15 (83)
2	1 (6)
6	2 (11)

***N:** Number, **SD:** Standard deviation, **FDS:** Flow diverter stent, **mRS:** Modified Rankin Scale.*

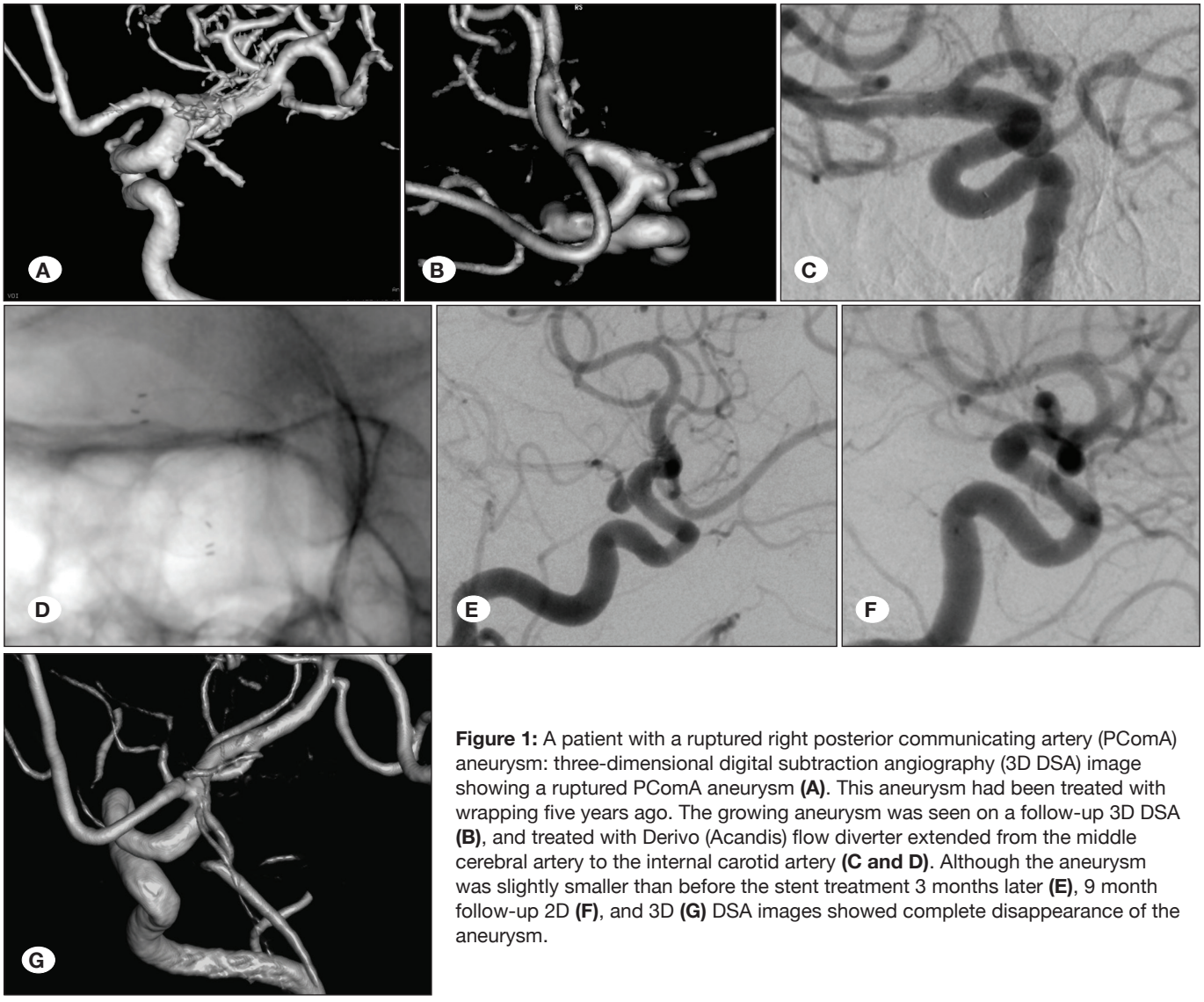

Figure 1: A patient with a ruptured right posterior communicating artery (PComA) aneurysm: three-dimensional digital subtraction angiography (3D DSA) image showing a ruptured PComA aneurysm **(A)**. This aneurysm had been treated with wrapping five years ago. The growing aneurysm was seen on a follow-up 3D DSA **(B)**, and treated with Derivo (Acandis) flow diverter extended from the middle cerebral artery to the internal carotid artery **(C and D)**. Although the aneurysm was slightly smaller than before the stent treatment 3 months later **(E)**, 9 month follow-up 2D **(F)**, and 3D **(G)** DSA images showed complete disappearance of the aneurysm.

open. Flow stasis after FDS insertion causes an inflammatory reaction inside the aneurysm, followed by thrombosis and healing of the aneurysm (59). Neointimal proliferation and remodeling of the parent vessel co-occur (48). Studies have shown the efficacy and safety of FDSs; hence, there has been increased utilization of FDSs in many unusual types of aneurysms (41,49). In addition to the intracranial complex, large, giant, wide-necked, fusiform, blister and bifurcation aneurysms, and recurrent or remnant aneurysms after any endovascular treatment (9,14,17,20,30,44,45,54,55), the flow diversion treatment of remnant or recurrent aneurysms after surgery can be performed with a high rate of occlusion and a low rate of complication as in shown in a few studies (1,19,24,39,53). Recanalization after obtaining complete aneurysm occlusion by using an FDS is very rare (7,11,22). This factor is the main reason why FDSs are preferred for remnant or recurrent aneurysms (48). It must be noted that the recurrence of coiled or stent-assisted-coiled aneurysms is not negligible. In fact, approximately 20% of coiled aneurysms and 12% of stent-assisted-coiled ones recur, and half of all recurrences require retreatment (16,26). Additionally, Kabbasch et al. reported 12.3% retreatment after recurrence in 122 patients with aneurysms treated with WEB device (31).

In our study, 20 remnant or recurrent aneurysms after clipping or wrapping were treated with FDSs. The closure rate was 64% (seven of 11 aneurysms) at an early period (3–6 months), whereas 16 aneurysms (94%) were occluded at the last angiographic follow-up (mean: 13.7 ± 7.3 months), and one aneurysm (6%) was still filling. In the literature, the cure rate of remnant or recurrent aneurysms after surgical treatment was between 66.7% and 100% (1,19,24,39,53). However, most of the published studies included a small number of patients (n: 4–7) (1,24,39,53), except one (19). In their study, da Silva Junior et al. showed a total occlusion with no complication in the cohort, including 18 patients at 12 month follow-up. Hence, a proper comparison of the study results is not satisfactory. Nevertheless, all authors have agreed on the

Table III: Studies Showing the Flow Diverter Treatment of Remnant or Recurrent Aneurysms Previously Treated with Microsurgery

Study	N of aneu.	FDS	Follow-up period (m)	Complete closure rate (%)	Complications (%)		
					Tech.	Morb.	Mort.
Adeeb et al. (1)	7	P	7.6 (3–12)	100	0	0	0
Kühn et al. (39)	6	P	6	66.7	4.2	0	0
Dornbos et al. (24)	4	P	26.1 (6–53)	100	0	0	0
Romagna et al. (53)	6	P	6	83.3	0	0	0
da Silva Junior et al. (19)	18	P, D, S, F	12	100	0	0	0
Current study	20	S, D, SP, F, P	13.7 (3–32)	94.1	5.0	0	5.0

N: *Number,* ***aneu:*** *Aneurysm,* ***FDS:*** *Flow Diverter Stent,* ***m:*** *Month,* ***Tech:*** *Technical,* ***Morb:*** *Morbidity,* ***Mort:*** *Mortality,* ***S:*** *Silk,* ***P:*** *Pipeline,* ***D:*** *Derivo,* ***SP:*** *Surpass,* ***F:*** *FRED.*

effectiveness and safety of FDSs in treating these aneurysms. The overall closure rate of our study was high (94.1%) as in that of da Silva Junior et al.'s study (19), and it was similar to in studies showing the effectiveness and safety of FDSs in the treatment of intracranial aneurysms with a high rate of occlusion. In these studies, the overall complete occlusion rate ranged from 53% to 96.3% depending on the size of the treated aneurysms (7,11,13,22,32,57). Many recent studies have shown that the FDS treatment of small- and medium-sized aneurysms has better results in terms of the closure rate and morbimortality frequency (3,29,42,51,58). In our study, the aneurysm size was smaller (mean: 8.5 ± 6.4 mm) than the original size (mean: 9.5 ± 6.5 mm) of the aneurysm because of the previous surgery. This feature might have contributed to the high closure rate and the lower morbimortality rate (29).

In our study, the morbidity and mortality rates were 0% and 5%, respectively, with a total complication rate of 15%. One patient died after coil embolization and insertion of the FDS because of acute brain stem ischemia. The other two complications, one technical and one inguinal hematoma, did not cause any neurological problems. In cerebral aneurysm treatment, flow diversion can cause morbidity and mortality in up to 22.4% and 8% patients, respectively (13,22,32,33). In a pooled analysis of 43 large studies that included 1092 patients with 1221 aneurysms treated with PED, Kallmes et al. reported that the major neurological morbidity was 5.7%, and the neurological mortality rate was 3.3% (32). In their study with 579 aneurysms in 531 patients treated with FRED FDS, Killer-Oberpfalzer et al. reported overall morbidity and mortality rates of 4.0% and 1.5%, respectively (34). Adeeb et al. (1), Kühn et al. (39), Dornbos et al. (24), and Romagna et al. (53) treated a small number of patients with remnant or recurrent aneurysms that had been previously clipped. The FDSs were used in these aneurysms and the morbimortality rate was zero. There were no complications except a technical one in the study of Kühn et al. (39). Using FDS, da Silva Junior et al. treated more remnant and recurrent aneurysms (n=18) after surgery (19). This study, including 70 patients, evaluated the endovascular therapy of remnant or recurrent aneurysms after surgical clipping. The stroke or mortality rate was seen in three patients treated with an endovascular technique other than FDS. The morbimortality was not faced in any patient after treatment with FDSs. In our study, the patient who died after FDS insertion had a recurrent basilar aneurysm. Although some recent studies have reported the safety and efficacy of treating posterior circulation aneurysms with FDSs, some neurointerventionalists have concerns about using FDSs in this area because of the richness of perforating arteries. As it may cause ischemia, most have used them as rescue therapy, as in our case (5,10,35). The other possible complications related to FDSs such as parenchymal hemorrhage, in-stent thrombus (acute or transient gradually developing) or stenosis, and nuisance bleeding were not seen in our cases during the follow-up period (12,46,50).

Owing to the risks mentioned above regarding the reoperation for recurrences of surgically treated aneurysms, endovascular treatment with FDSs appears to be a reasonable choice for these aneurysms. Nevertheless, we need additional studies and more aneurysms to reach a proper conclusion. The limitations of this study are its retrospective nature and the fact that there was no control group. Additionally, even though the complication and the mid- and long-term closure rates are similar in most of the different FDS studies, the aneurysm locations and FDSs used in the treatment were not homogeneous (2,7,11,22,32,33,37).

CONCLUSION

The FDS seems effective, safe, and attractive in treating remnant and recurrent intracranial aneurysms that had been treated surgically, as shown in a few similar studies. An FDS may be the first-line treatment with a low morbimortality and high closure rate in these patients.

AUTHORSHIP CONTRIBUTION

Study conception and design: EA, HBO, BH, AY, IO, ZS
Data collection: EA, HBO, YC, GE, CE, AC, CC, AY
Analysis and interpretation of results: EA, BH, AY, IO, ZS
Draft manuscript preparation: EA, BH, IO
Critical revision of the article: EA, BH, IO, ZS
Other (study supervision, fundings, materials, etc...): EA, IO, ZS
All authors (EA, HBO, YC, GE, CE, AC, CC, BH, AY, IO, ZS) reviewed the results and approved the final version of the manuscript.

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