Flow-diverter stent to manage intracranial aneurysms: A single center experience

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Abstract

Background: Endovascular coil embolization is an important method for managing intracranial aneurysms. However, aneurysm coiling may fail or be insufficient in geographically difficult aneurysms. A flow-diverter stent (FDS) is an alternative in these difficult coiling aneurysms. Thus, this study reports the experience and outcome of FDS management of intracranial aneurysms.

Methods: Over 29 months, FDS treated 125 patients with 163 intracranial unruptured aneurysms. This study enrolled 31 men and 94 women, ranging from 17 to 81 years (mean, 58 years). Clinical data, aneurysm characteristics, and angiographic and clinical outcomes of patients treated by FDS were retrospectively assessed.

Results: The current study found 151 (93%) aneurysms in the internal carotid artery. Most aneurysms (n = 118; 72%) were small (<7 mm). The mean aneurysm size was 6.2 mm (range, 2–38 mm). Follow-up angiography was available in 53 patients with 74 aneurysms (mean, 13 months). Successful FDS deployment in an ideal position was found in 125 of 130 patients (96%). Complete obliteration (CO) was achieved in 58 aneurysms (78%) in the mean 13-month angiographic follow-up. Smaller aneurysms (<7 mm) had a CO tendency than larger aneurysms ($p < 0.01$) in midterm follow-up. Seven patients (5.6%) had intraprocedural complications (in-stent thrombosis, three patients; distal embolic, two patients; iatrogenic carotid-cavernous fistula, and subarachnoid hemorrhage, one patient). Two patients (1.6%) suffered from permanent procedure-related morbidity (n = 1) or mortality (n = 1). No late hemorrhagic events or stent displacement occurred during the follow-up period.

Conclusion: Despite few procedural complications and some pieces of evidence of insufficient aneurismal treatment in a midterm angiographic follow-up, FDS was effective and safe in managing intracranial unruptured aneurysms, particularly in smaller aneurysms, which had better CO than larger ones.

Keywords: Endovascular embolization; Flow diverter; Intracranial aneurysm; Stent

1. INTRODUCTION

Endovascular detachable coil embolization of intracranial aneurysms is an important, minimally invasive procedure for managing intracranial aneurysms with promising results.[1–3] Despite the increase in clinical experience, improvements in technology, and device innovations, endovascular treatment still has inherent limitations in managing geographically difficult intracranial aneurysms (e.g., small aneurysms with catheterization difficulty or large/giant aneurysm wide-neck aneurysms with easy recurrence after coiling). The flow-diverter stent (FDS) has better metallic surface coverage (MSC) than traditional stents. It was designed to manage intracranial aneurysms by endoluminal reconstruction rather than endovascular coiling.[4] Successful stent deployment at the target parent artery satisfying apposition of FDS to the vessel wall is more difficult than the traditional stent because of its complex designation.[4,5]

This study aims to report the experiences of using FDS to manage 125 patients with 163 intracranial unruptured aneurysms and reports the immediate and midterm angiographic and clinical outcomes.

2. METHODS

A series of 130 consecutive patients harboring 168 intracranial unruptured aneurysms underwent endovascular FDS to manage aneurysms in the study institute from October 2018 to March 2020. FDS was successfully deployed in the target parent arteries in 125 (96%) patients. Three giant and two small aneurysms were not treated with FDS due to the difficult aneurysm anatomy or tortuous parent artery in successfully deploying FDS in the ideal position. Of these 125 patients with 163 aneurysms, 31 (25%) and 94 (75%) were men and women, respectively, with ages between 17 and 81 years old (mean, 58 years). Table 1 summarizes information including gender, age distribution, clinical manifestations, and characteristics of aneurysms. Of these 125 patients, 16 were symptomatic because of giant (n = 11) or large (n = 5) aneurysm compression of the nearby cranial nerve

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Table 1

Demography and characteristics of 125 patients with 163 intracranial aneurysms managed by FDS

	Value (percentage)
No. patients successfully treat by FDS	125
No. aneurysms enrolled	163
No. patients with multiple aneurysms treated by FDS	33 (26%)
Aneurysms per patient	1.3
Mean age (yr)	58 (range 17–81)
Gender	
Female	94 (75%)
Male	31 (25%)
Number of symptomatic patients	16 (13%)
Location and number of aneurysms	
ICA	151 (93%)
MCA	2 (1%)
BA	4 (2%)
VA	6 (4%)
Size and number of aneurysms	
>25 mm	11 (7%)
13–24 mm	12 (7%)
7–12 mm	22 (13%)
<7 mm	118 (72%)
`Mean size of aneurysms	6.2 mm (range 2–38)
Adjunctive aneurysm coiling	26 (16%)

BA = basilar artery; CCA = common carotid artery; FDS = flow-diverter stent; ICA = internal carotid artery; MCA = middle cerebral artery; VA = vertebral artery.

or brain stem, leading to decreased visual acuity or limb weakness. The sizes of the aneurysms varied from 2 to 38 mm in their maximal dimension (mean, 6.2 mm), and most aneurysms were <7 mm (n = 118; 72%). The locations of the aneurysms were the internal carotid artery (ICA; n = 151; 93%), middle cerebral artery (n = 2; 1%), basilar artery (n = 4; 2%), and vertebral artery (n = 6; 4%). Regarding pharmacological therapy, clopidogrel (75 mg) and aspirin (200 mg) were given daily for 6 days before embolization.

2.1. Angiography protocol and endovascular management principle

The femoral arteries were catheterized using a percutaneous technique with patients under general anesthesia. Digital subtraction angiography (DSA) of the parent artery and rotational and three-dimensional reconstruction DSAs were routinely obtained to evaluate the angioarchitecture of the aneurysm and parent artery. A bolus of intravenous heparin (3000 units) was routinely administered after placing the guiding catheter into the parent artery. An activated clotting time to twice the baseline was maintained throughout the whole procedure. The 8-French (Fr) femoral sheath and guiding catheter were introduced and navigated into the parent artery, and a 6-Fr intermediate catheter was then coaxially placed to the parent artery as close as possible to the aneurysm. A 2.7-Fr microcatheter was then navigated to the distal parent artery or its branch, and a self-expandable Pipeline Flex (n = 38; Medtronic, Irvine, CA) or FRED (n = 89, MicroVention, Inc., Tustin, CA) with proper size and length was negotiated and deployed into the parent artery to bridge the aneurysm neck. The stent length was chosen to provide at least a 3-mm to 4-mm landing zone beyond the aneurysm neck on the proximal and distal parent arteries. The stent was ≥0.2 mm than the caliber of the parent vessel at the targeted landing zone. Regarding the 23 and three large/giant wide-neck and medium/small aneurysms, respectively, adjunctive aneurysm coiling was performed to enhance the aneurysm's complete obliteration (CO) of the aneurysm. The parent artery and aneurysm were accessed by contralateral femoral artery puncture, followed by navigation of a 6-Fr guiding catheter to the parent artery and the navigation of the microcatheter into the aneurysm sac before stent deployment (stent-jail catheter technique). After the FDS was deployed successfully into the target site, with the tip of the microcatheter stabilized in the aneurismal sac, the aneurysms were partially coiled using the proper size and length of detachable coils.

Dyna-computed tomography of the brain and stent-apposition images were routinely obtained to assess hemodynamic alteration of the aneurysm sac, parent artery patency and its intracranial branches, and FDS apposition on postembolization DSA. Moreover, clopidogrel (75 mg) and aspirin (200 mg) were given daily for 6 months, followed by clopidogrel (75 mg) and aspirin (100 mg) daily for the next 6 months. A period exceeding four months of DSA was obtained in 53 patients with 74 aneurysms. In addition, clinical follow-up exceeding three months was obtained in 124 patients (mean, 15 months).

2.2. Angiographic outcome evaluation

Two interventional radiologists with 28 and 23 (CBL and FCC) years of experience with the workstation evaluated these DSA findings and treatment outcomes. They reviewed the angioarchitectures and treatment outcomes, emphasizing location, the number of aneurysms, complications, and CO of the aneurysm sac. They resolved any discrepancy through reassessment and discussion to reach an agreement.

2.3. Statistical analysis

The SPSS statistical software package (version 20; SPSS, Armonk, NY) was used for all statistical analyses. Correlations between the age, gender, DSA findings, aneurysm size, adjunctive aneurysm coiling, and CO of the aneurysm were analyzed using the chi-square test for categorical variables. Continuous variables (e.g., age and aneurysm size) were analyzed using a one-way analysis of variance with post hoc Bonferroni correction. A p value <0.05 was considered statistically significant.

3. RESULTS

Tables 2 and 3 summarize the data on immediate, procedure-related complications, follow-up DSA, and clinical outcomes. Successful FDS deployment to an ideal location by covering the aneurysm neck was observed in 125 of the 130 patients, resulting in a deployment success rate of 96%. Two patients with giant aneurysms were successfully managed by two FDS using the telescoped technique. In three patients with giant or large ICA aneurysms, navigating the microcatheter to the distal ICA parent artery to allow FDS deployment failed because of the difficult anatomy of the aneurysm to the parent artery. Thus, ICAs and aneurysms were eventually occluded by coiling after the balloon occlusion test. Further stenting was not attempted in two patients with small aneurysms (3 and 4 mm) with FDS partial coverage of the aneurysm neck because of the small aneurysm size. Regarding the immediate hemodynamic alteration of the aneurysm sac, 124 (76%) aneurysms had immediately changed aneurysm hemodynamics by delayed washout of contrast material in the aneurysm sac. Moreover, CO was promptly found in two aneurysms, and the other 37 aneurysms showed no obvious hemodynamic change. The peri-procedural complication was found in seven (5.6%) patients and included in-stent thrombosis (n = 3) or distal embolism (n = 2), which were solved by percutaneous balloon angioplasty (n = 3) to improve the FDS apposition, followed by glycoprotein IIb/III administration. One patient had an iatrogenic direct carotid-cavernous fistula

Table 2

Outcomes of 125 patients with 163 aneurysms managed by FDS

	Number (percentage)
Immediately DSA outcomes (n = 125, 163 aneurysms)	
CO of aneurysm	2 (1%)
Delayed washout of contrast in aneurysm	124 (76%)
Unchanged of hemodynamic of aneurysm	37 (23%)
Follow-up DSA outcomes of 53 patients of 74 aneurysms (mean time of follow up)	13 mo
Obliteration of aneurysm	
Raymond class I	58 (78%)
Raymond class II	10 (14%)
Raymond class III	4 (5%)
Unchanged	2 (3%)
Parent artery stenosis/occlusion	
Occlusion of parent artery	1 (2%)
Mild in-stent stenosis (>20%)	2 (4%)
Procedural-related complication (n = 7, 5.6%)	
In-stent thrombosis	3 (2.4%)
Distal thromboembolic event	2 (1.6%)
Iatrogenic carotid-cavernous fistula	1 (1%)
Procedure-related subarachnoid hemorrhage	1 (1%)
Neurologic outcomes of 124 patients (mean follow-up time)	14 mos.
mRS 0	122(98%)
mRS 2	1 (1%)
mRS 6	1 (1%)

DSA = digital subtraction angiography; FDS = flow-diverter stent; mRS = modified Rankin scale (>3 months after discharge).

because of the perforation of cavernous ICA by the guidewire. Consequently, the patient underwent transvenous coiling with a fistula cure. Procedure-related fatal subarachnoid hemorrhage was observed in 1 (0.8%) patient resulting from the perforation of the M2 branch of the middle cerebral artery by the tip of the FDS push wire. Clinical follow-up extending longer than three months was available in 124 patients (range, 5–23 months; mean, 14 months). During follow-up, there was no hemorrhage event. Furthermore, 53 patients with 74 aneurysms had follow-up DSA. Moreover, CO of an aneurysm (Raymond class I), subtotal occlusion with small neck remnant (Raymond class II), partial obliteration of aneurysms (class III) with residual sac, and unchanged aneurysm morphology occurred in 58 (78%; Fig. 1), 11 (15%; Fig. 2), 4 (5%), and 2 (3%) aneurysms, respectively. There was no significant difference in the two FDS in periprocedural complication (5.2% of pipeline vs 5.6% of FRED) and CO of aneurysms (78% of pipeline vs 79% of FRED). Three patients had asymptomatic ICA occlusion (n = 1) or in-stent ICA stenosis (<30%; n = 2). Neurologic outcomes more than three months after discharge showed periprocedural stability in 123 patients. One patient was in the modified Rankin Scale (mRS) 2 because of late ICA occlusion due to discontinuation of antiplatelet therapy at one month of FDS. One patient suffered from fatal subarachnoid hemorrhage (mRS 6).

4. DISCUSSION

Endovascular embolization by coiling has become a standard technique to manage intracranial aneurysms. The microcatheter should be successfully navigated into the aneurysm sac, followed by aneurysm coiling, to achieve aneurysm coiling and maintain the flow of the parent artery. The advent of the self-expandable intracranial stent for assisting aneurysm coiling has increased the treatment options of geometrically difficult aneurysms, particularly in those aneurysms with a wide neck or unfavorable neck-to-dome ratios or even fusiform aneurysms.[2,6] The major drawback of simple- or stent/balloon-assisted aneurysm coiling is the potential risk of intraprocedural aneurysm perforation leading to catastrophic complications.[7] In addition, this technique may not provide durable angiographic outcomes because of coil compaction with aneurysm recurrence, particularly in large, giant wide-neck aneurysms with low packing density <20%.[8]

The FDS was designed as a single-stent treatment solution for intracranial aneurysms by endoluminal reconstruction instead of endovascular coiling. Most FDSs have denser MSCs with smaller porosity than the traditional stent, and the MSC coverage of FDS varied from 30% to 35%.[4] FDS take advantage of changing the parent artery/aneurysm sac interface altering the in-flow and out-flow hemodynamic to promote aneurysm thrombosis. Subsequent neointimal overgrowth covers the stent reconstructing the parent artery and eliminating the aneurysm/parent vessel interface while maintaining the patency of the side branch of the parent artery.[4,5] As opposed to aneurysm coiling, FDS gradually causes the aneurysm to thrombosis rather than immediately at the end of the procedure.

Theoretically, applying an FDS within the parent vessel for intracranial aneurysm treatment has four main advantages. The first advantage is that FDS could save procedure time and reduce intraprocedural aneurysm rupture by microcatheter or coil. The second advantage is that the FDS can simultaneously treat two or more aneurysms in one parent artery segment by FDS deployment. The current series had treated 26% of patients with multiple aneurysms in one segmental parent artery by single FDS. The third advantage is that it may

Table 3

Summarize of demography and angiographic outcomes of 53 patients with 74 aneurysms treated by FDS

	CO of aneurysm	Non-CO or unchanged aneurysm	Total	*p* value of total obliteration
No. patients	37	16	53	
No. aneurysms	58 (78%)	16 (22%)	74 (100%)	
Age (yr) (mean)	59	52	57	1.00
Gender				
Men	10 (27%)	5 (45%)	15	0.75
Women	27 (73%)	11 (54%)	38	0.75
Mean size of aneurysm (mm)	5.2	9.5	75	<0.01
Mean follow-up time (mo)	14	13	13	1.00
Adjunctive aneurysm coiling	9 (16%)	4 (25%)	13 (18%)	0.46
Alter aneurysm hemodynamic after FDS	41 (77%)	12 (75%)	56 (76%)	1.00

CO = complete obliteration; FDS = flow-diverter stent.

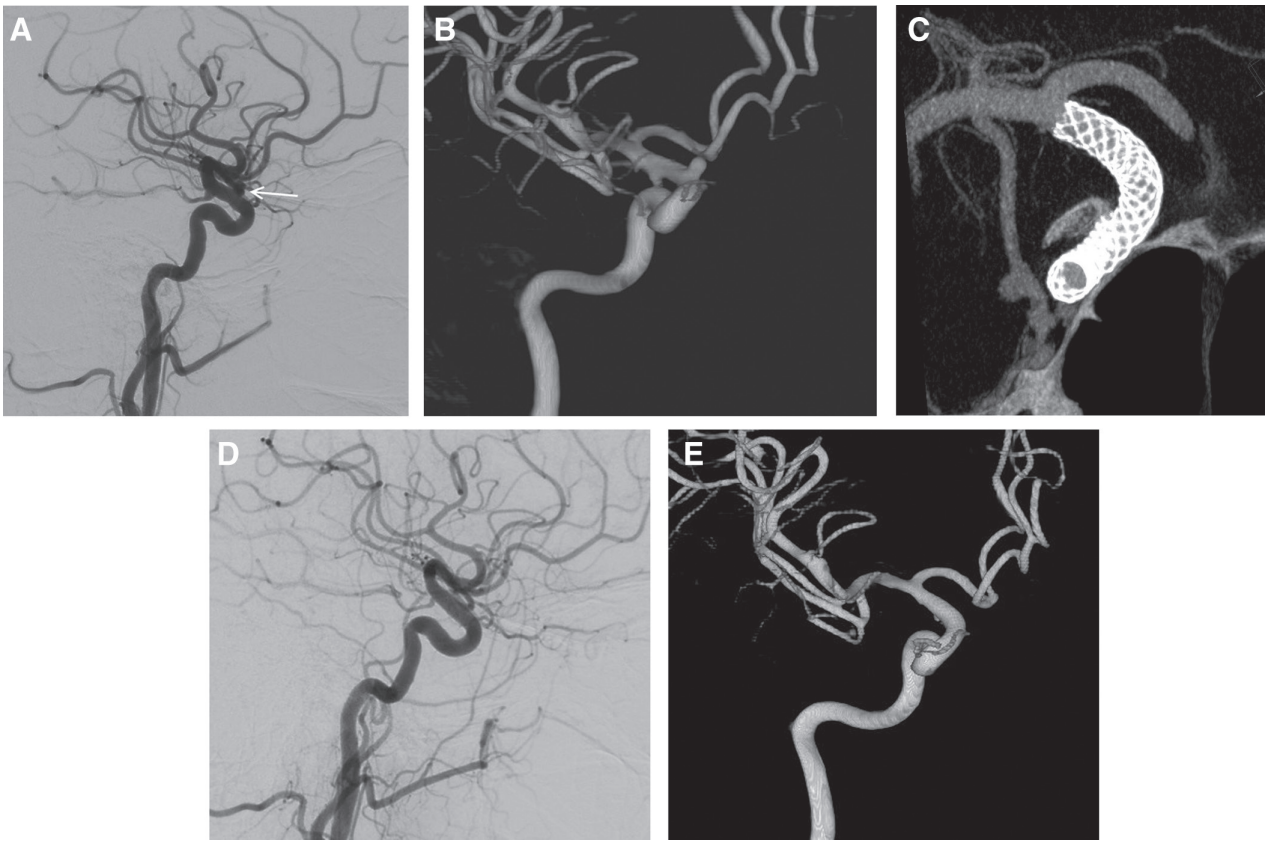

Fig. 1 The patient is a 57-year-old woman. **A**, **B,** The patient had a small asymptomatic aneurysm at the right supraclinoid ICA (*arrow*) demonstrated by DSA. **C,** The patient underwent FDS to manage this small aneurysm. **D**, **E,** Complete obliteration (Raymond I) of aneurysms was observed in the 12-month DSA follow-up. FDS = flow-diverter stent; ICA = internal carotid artery.

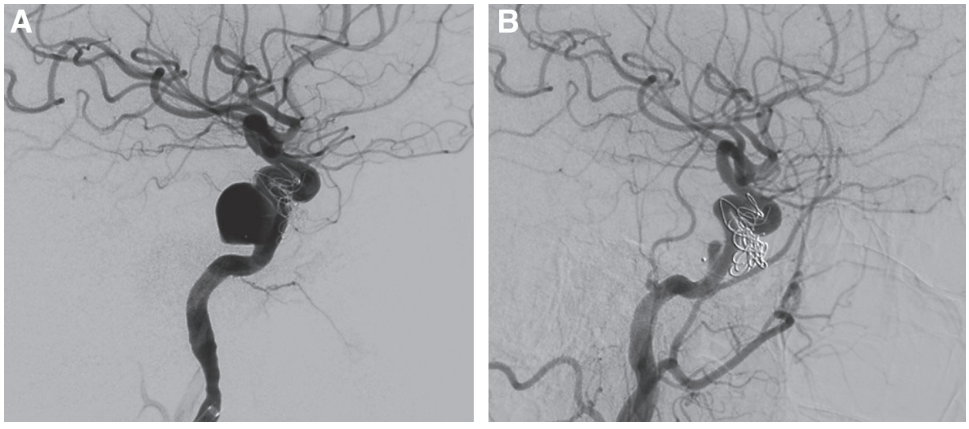

Fig. 2 The patient is a 40-year-old woman who had a history of right traumatic direct carotid-cavernous fistula and underwent embolization by coils eight years ago. The patient suffered from ptosis of the right eye. **A,** The right carotid angiography demonstrated a big saccular aneurysm at the right cavernous ICA. **B,** The patient underwent FDS to manage this large aneurysm. Carotid DSA on 9-month post-FDS showed subtotal obliteration of the aneurysm with the residual neck (Raymond II). Moreover, gradual resolution of ptosis was found. FDS = flow-diverter stent; ICA = internal carotid artery.

provide durable angiographic outcomes in most aneurysms, particularly in large and giant. The fourth advantage is that the CO of aneurysms is usually associated with aneurysm collapse and shrinkage, with a mass resolution effect to the surrounding brain parenchyma or nearby cranial nerve, which may not be solved by endovascular coiling. However, FDS has two drawbacks: (1) the stent is expensive; a currently available single FDS costs about $10 000–12 000 USD in Taiwan, and (2) the stent itself is made by more dense metallic materials than traditional stents for the parent artery, so it may have the potential risk of inducing in-stent thrombosis or arterial stenosis. Therefore, a larger dosage of the dual antiplatelet regime

before and after FDS is necessary to prevent thromboembolic events. In addition to these disadvantages, the navigation and deployment of the FDS to the ideal position to satisfy the FDS apposition in tortuous parent artery may be difficult and fail due to its complex design. Therefore, the operator usually needs more intensive training and skills than the traditional stent.

In 2011 and 2018, the US Food and Drug Administration approved FDS as a treatment for wide-neck large or giant ICA aneurysms. Many publications exist regarding off-label FDS application to aneurysms beyond the ICA termination or in the posterior circulation. Moreover, FDS is usually associated with higher complications in those aneurysms with off-label use largely because of smaller, distal, tortuous parent arteries, and the presence of critical side branches or perforators.[9–11] The reimbursement indication for FDS application in Taiwan was limited to ICA aneurysms. Therefore, about 93% of aneurysms were in the ICA in the presented series. The FDS in aneurysms of other locations (e.g., basilar or vertebral arteries) was applied. However, these aneurysms were symptomatic, large, or giant with the mass effect to the surrounding brain stem or cranial nerve, which may not have durable angiographic outcomes due to lower packing density. The current study successfully navigated and deployed 127 FDS in 125 (96%) patients into the targeted location of the parent arteries. The success rate of FDS deployment in the current series was comparable with previously published series, which ranged from 95% to 99%.[5,12]

Several systematic reviews and meta-analyses have demonstrated that the rate of CO in aneurysms varied from 76% to 81.5%, depending on the aneurysm size, location, and follow-up time frame.[13–15] One report demonstrated 96% of CO in a 5-year follow-up.[15] In the current series, CO of aneurysms was achieved in 78% of aneurysms in a mean 13-month DSA follow-up. This midterm angiographic outcome was comparable with those previously published FDS data in small and medium aneurysms.[14] The rate of CO in the current series was related to aneurysm size with a mean size of 5.2 mm compared with 9.5 mm of non-CO showing statistical significance ($p < 0.05$). Moreover, 124 (76%) aneurysms had immediately altered the hemodynamic of the aneurysm sac by CO (n = 2; 1%) or delayed washout of contrast media in the aneurysm sac (n = 124; 76%). Although FDS immediately altered the hemodynamic effect of aneurysms, the midterm of CO of the aneurysm was not statistically related to immediate hemodynamic effect, gender, and adjunctive aneurysm coiling series.

The complication rates for aneurysms treated with FDS are comparable to traditional coil embolization. The overall FDS complication rate to treat intracranial aneurysms was 17%.[16] The morbidity and mortality of FDS varied from 3.5% to 9.4% and 3.4% to 4.1%, respectively.[4] These complications were significantly higher in those aneurysms of ruptured, large/giant or fusiform, wide-neck, and distal or posterior circulation aneurysms, particularly in the posterior circulation, which may be up to 44.7% of patients.[4] The major FDS complication was ipsilateral ischemic stroke of in-stent thrombosis or branch vessels occlusion. This complication was due to poor apposition of FDS or insufficient dual antiplatelet treatment (DAPT) because of clopidogrel resistance.[17] In the current series, ischemic complications occurred in five (4%) patients because of poor FDS apposition (n = 3) or insufficient DAPT (n = 2). Most immediate FDS-related ischemic strokes can be solved by balloon angioplasty or catheter/guide massage to improve FDS apposition, plus glycoprotein IIb/IIIa intravascular infusion to lysis the early clots in the stent or distal arterial branch. Early or late intracranial hemorrhage may occasionally be found in giant aneurysms,[18] which will be aggravated by DAPT. Three patients had asymptomatic ICA occlusion (n = 1) or mild stenosis (n = 2). One patient suffered from fatal subarachnoid hemorrhage, presumed as a result of the tip of the stent push perforating the M2 branches of the MCA. The morbidity and mortality in the current series were 1% and 1%, respectively. These significant complications were lower than previously published data, largely due to high-selective patients for FDS with 93% aneurysms in the ICA with small to medium aneurysms in 85%. Also, the test for clopidogrel resistance was verified in 78% of patients in the current series to avoid thromboembolic events.

In conclusion, despite a low rate of procedural complications, with 78% CO of an aneurysm in the midterm DSA follow-up, FDS was proven effective and safe in most intracranial smaller aneurysms. The current study results also demonstrated the midterm durability and stability of intracranial aneurysms treated by FDS.

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