Original article

Branch vessel occlusion in aneurysm treatment with flow diverter stent

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Summary. Flow diverter placement for treatment of intracranial aneurysms gained growing consensus in the past years. A major concern among professionals is the side branch coverage which leads in some cases to vessel occlusion. However, the lost vessel patency only infrequently is accompanied by a new onset of neurological deficits secondary to ischaemic lesions. A retrospective analysis of all patients treated with flow diversion at our hospital was aimed to better understand this phenomenon in order to formulate a hypothesis about the causes. We concluded that vessel occlusion occurs due to a reduced blood pressure gradient in those vessels with a strong collateral or anastomotic vascularization that refurnishes the same distal vascular territories. Indeed, we detected no new brain infarction since blood flow was always guaranteed.

Keywords: aneurysm, branch vessel, patency, side branches occlusion, flow diversion, flow diverter stent

Introduction

In recent years Flow Diverter Stents (FDS) gained growing consensus as an alternative treatment option for intracranial aneurysms (1-13) in response to extensive in vitro and in vivo studies (14-16) and encouraging clinical experiences. The placement of this device across the aneurysm neck alters intra-aneurysmal flow patterns redirecting flow away from the aneurysm and back into the parent vessel (17-20). This results in aneurysm thrombosis because of stagnating blood, followed ideally by shrinkage of the aneurysm as the clot organizes and retracts. One of the major concerns related to the use of flow diverters is the potential occlusion of side branches, with secondary ischemic complications.

Although the fate of the different major side branches of the distal internal carotid artery (ICA) has been examined in different small studies the overall literature regarding this topic is still scarce (21). Most studies focus only on one branch at a time whereas the minority (22,23) takes into consideration more side branches, simultaneously also including the posterior circulation aneurysms (24-26). Since the concerns about safety of FDS, especially regarding the patency of the covered side branches, are still ongoing, we aimed to contribute with an insight of the data collected on a large group of patients in our institution.

Material and Methods

The protocol for this single-centre retrospective study was approved by the Ethics Committee review board of the Policlinico Maggiore Hospital.

Medical records from consecutive patients with intracranial aneurysms treated with at least one flow diverter between 2009 and 2018 were reviewed retrospectively from a prospectively maintained database to obtain demographic data (including age and sex) as well as data regarding clinical presentation, complications, and outcome. We included all patients treated with at least one of the five following different types of flow diverters: the Pipeline Embolization Device (PED) (Medtronic, Irvine, California, USA), the Silk Flow Diverter (SFD) (Balt Extrusion, Montmorency, France), the Flow-Redirection Endoluminal Device (FRED) and FRED Jr systems (MicroVention, Tustin, California, USA), and the DERIVO embolization device (DED) (Acandis GmbH, Pforzheim, Germany). Both, anterior and posterior circulation aneurysms were taken into account. From this database we selected those patients with at least one covered side branch in addition to the parent vessel.

Our protocol for FDS deployment requires the procedures to be done under general anaesthesia. Distal access on the right femoral artery was obtained using a tri-axial access system consisting in a Neuron 6 French 105 cm long sheath (Penumbra, Alameda, California, USA); Vista Brite Tip 8 French Guiding Catheter (Cordis Corporation, Bridgewater, NJ, USA); and a microcatheter with sizes varying from 0,021 – 0,027 Inches to obtain distal access. The appropriate size of FDS was selected after measuring the parent artery and was deployed to cover the aneurysm neck.

All patients received dual antiplatelet therapy (Aspirin 300 mg and Clopidogrel 75 mg, both once daily) for 5 days prior to the procedure. When the procedure was done in an emergency setting (due to aneurysm rupture) the patient received Aggrastat (Tirofiban) (dose adjusted to body weight) intravenously in 30 min and a maintenance dosage for the following 24 hours, followed by oral antiplatelets drugs. In all scenarios the postprocedural antiplatelet therapy consisted in dual antiplatelet regimen of Aspirin 300 mg daily and Clopidogrel 75 mg daily for the first three months following the procedure. Afterwards single antiplatelet therapy with ASA 300 mg daily was continued until the 12 months follow-up.

Control digital subtraction angiography (DSA) was performed immediately following FDS placement and follow-up DSA was performed between 3 and 6 and at 12 months. At the one year follow-up, the patient performance status was scored with the Modified Rankin Scale (MRS). Furthermore, all patients that showed a reduced or absent blood flow in the covered side branches were subsequently evaluated by a neurologist.

All pre-procedure and post-procedure angiographic data, including aneurysm location (carotid-ophthalmic segment, MCA, ACA, posterior circulation, distal sites), type (saccular or dissecting) and size (small, large and giant); number and type of FDSs deployed (in combination with coiling or not), and patency of anterior and posterior circulation branch vessels (OphA, PComA, AChoA, ACA (A1), ACoA, M2, PICA, AICA, SCA, callosomarginal artery, pericallosal artery and PCA (P2-P3)) were reviewed by two different investigators independently. When, in the same patient with multiple aneurysms, more than one was treated with flow diversion, they were considered as different cases. At the first angiographic follow-up at 3 – 6 months we evaluated the change in flow (reduction or absence) and the calibre (due to intimal hyperplasia) of the covered side branches; at 12 months, again, we looked for side branch patency and exclusion of the aneurysm.

Results

We identified 137 patients with 147 aneurysm who were treated with flow diversion for aneurysms in the anterior and posterior circulation between 2009 and 2018 at our institution. Twenty-five patients were excluded from the analysis for reasons of no branch vessel coverage seen on angiography (n = 19) and lack of follow-up due to various reasons as acute parent vessel occlusion or death during acute treatment (n = 6). Therefore, we included 112 patients with 119 aneurysms in our subsequent analyses. Out of these 112 patients, 87 were females (78 %) and 25 were males (22%). The mean age was 54.8 ± 12.25 years. In terms of aneurysm dimensions the average aneurysm fundus size measured 11.2 ± 12.25 mm, including 8 giant aneurysms (diameter > 25 mm). In regard of the aneurysm type 92 were saccular berry aneurysms, 25 were dissecting aneurysms and 2 were blister aneurysms. The carotid-ophthalmic segment was the most frequent location for aneurysms in our series (81.51%). Baseline characteristics for these patients including demographics and aneurysm characteristics are presented in Table 1.

A total of 214 instances of branch vessel coverage were identified in the 112 patients with 119 aneurysms. These included 87 OphAs, 57 AChoAs, 32 PComAs, 19 ACAs, 6 ACoAs, 3 PICAs, 2 SCAs, 2 AICAs, 3 callosomarginal arteries, 2 pericallosal arteries, and 1 PCA (Table 2). Out of the 139 FDS used in total, the most utilized were the PED (n=113), followed by FRED (n=9), FRED Jr (n=9), SFD (n=5), and DED (n=3) (Table 3). Fifteen patients were treated with more than one FDS, however no patient had different types of FDS implanted simultaneously. Forty-three patients experienced a subarachnoid haemorrhage (SAH) due to aneurysm rupture and thus received adjunctive coils treatment.

There was evidence of branch vessel occlusion immediately after flow diverter deployment in 5 cases (2 OphAs, 2 PComAs, 1 A1). On follow-up angiography (at 3/6 and 12 months), we identified 22 and 23 branch vessel occlusions, respectively. At 3/6 months the occluded vessels were 4 OphAs, 10 PComAs, 5 A1, and 3 ACoAs. At the 12 months follow-up the occluded vessels were 5 OphAs, 10 PComAs, 4 A1, and 4 ACoAs.

Three ophthalmic arteries that were completely occluded at the three months follow-up were again patent at one year.

The OphA was occluded in 7 of 87 instances (8.04 %), the PComA was occluded in 11 of 32 instances (34.38 %), the ACA (A1 segment) in 5 of 19 instances (26.32 %), the ACoA in 5 of 6 instances (83,33 %). No instance of other vessel occlusion was observed on follow-up angiography. Subgroup analysis of PCoA vessel patency showed no occlusion when the PCoA was fetal-type. Branch vessel patency and occlusion are displayed in Table 4.

Thirty-three patients developed endothelial hyperplasia (30 mild, 3 severe) at the three months follow-up. At one year, five patients with mild hyperplasia showed complete vessel occlusion and two reduced flow. All three patients with severe hyperplasia had complete artery occlusion.

Table 1. Demographics and clinical characteristics

Characteristics	Results
No. of Patients	112
Mean age ± standard deviation (years)	54.8 ± 12.25
Sex	
Female	87 (78%)
Male	25 (22%)
SAH at presentation	43 (36.13%)
Aneurysms	119
Morphology	
Saccular	92 (77.31%)
Dissecting	25 (21%)
Blister	2 (1.68%)
Size (mean, mm)	11.2 ± 12.25
Size Maximum diameter	
<10 mm (small)	67 (56.3%)
>10-25 mm (large)	44 (36.97%)
>25 mm (giant)	8 (6.72%)
Location	
carotid-ophthalmic segment	97 (81.51%)
MCA	3 (2.52%)
ACA	3 (2.52%)
Posterior circulation	11 (9.24%)
Distal sites	5 (4.2%)
Aneurysm occlusion at 12 months (success rate)	93 (78.15 %)
Complete exclusion	83 (69.75%)
Reduction 70-80%	10 (8.4%)

Table 2. Covered branch vessels

Characteristics	Results
No. of branches covered	214
Anterior circulation	
OphA	87 (40.65%)
AChoA	57 (26.64%)
PComA	32 (14.95%)
ACA	19 (8.88%)
ACoA	6 (2.8%)
Posterior circulation	
PICA	3 (1.4%)
SCA	2 (0.93%)
AICA	2 (0.93%)
PCA	1 (0.47%)
Distal sites	
Callosomarginal artery	3 (1.4%)
Pericallosal artery	2 (0.93%)

Table 3. Flow Diverter Stents

Characteristics	No. of FDS	No. adjunctive coils
Tot. FDS	145	40 (33.61%)
PED	117 (78.4%)	34
SFD	6 (4.8%)	1
FRED	10 (8%)	4
FRED Jr	9 (6.4%)	1
DED	3 (2.4%)	0

Taking in consideration the patients that showed branch vessel occlusion due to the implantation of the FDSs and excluding those patients with acute procedure-related complications, only one presented with clinical symptoms. It is the case of a patient who experienced three episodes of amaurosis following the occlusion of the ophthalmic artery. However, the symptoms ceased one year after the procedure and did not represent. We observed no adverse clinical sequelae in the remaining patients who experienced branch vessel occlusion.

The number of aneurysms occluded at follow-up were 93 out of 119 (83 complete exclusion, 10 reduction 70-80%) (success rate 78.15 %).

Discussion

As the name suggests, the primary mode of action of FDS is diversion of blood flow from the aneurysm which is obtained by change in intra-aneurysmal flow and tissue growth across the aneurysm neck (2). Even though endothelization seems to be the dominant predictor of long-term occlusion, it is observed with a certain delay when compared to the intra-saccular thrombosis.

While FDS induce disruption of blood flow near the aneurysm neck, inducing thrombosis into the aneurysmal sac, they should preserve physiological blood flow in the parent vessel and adjacent branches. However, it has been increasingly reported that coverage of some side branches by the device might cause flow reduction and moreover their occlusion (2). The concerns regarding potentially secondary ischaemic lesions seem not to be supported by the investigations conducted so far.

A series of in vitro studies on models reproducing conditions in which a flow diverter is placed across aneurysmal neck and collateral branches has demonstrated that flow through the collaterals is usually preserved. Coverage of the collateral vessel inlet area greater than >90% resulted in a flow reduction of less than <10% (30,31). These results are not unexpected because flow through the collateral is driven by a pressure gradient even if the porous flow diverter is interposed. In vivo, this mechanism is encountered when taking in examination the patency of smaller vessels such as the **anterior choroidal** and **lenticulostriate arteries** and **perforating vessels** with no distal collaterals. These vessels may maintain flow due to a pressure gradient across the ostium and are more likely to remain patent (32-35). This is according to our findings as we experienced no occlusion of vital vessels due to the FDS implantation.

On the other hand, larger vessels such as the posterior communicating artery **PComA, A1, ACoA** and the **ophthalmic artery** usually have well-developed distal collaterals and anastomoses which makes them more prone to occlusion following placement of the flow diverter. This may be due to the insufficient pressure gradient across the device to maintain flow within

Table 4. Branch vessel coverage and occlusion rates

Side Branches	No. of Side Branches	Occlusion at 3/6-Mo Follow-Up	Occlusion at 12-Mo Follow-Up	Overall occlusion rate
Tot of branches covered	214	22	23	28
OphA	87 (40.65%)	4	5	7 (8.04%)
AChoA	57 (26.64%)	0	0	0
PComA	32 (14.95%)	10	10	11 (34.38%)
ACA (A1)	19 (8.88%)	5	4	5 (26.32%)
ACoA	6 (2.8%)	3	4	5 (83.33%)
PICA	3 (1.4%)	0	0	0
SCA	2 (0.93%)	0	0	0
AICA	2 (0.93%)	0	0	0
PCA	1 (0.47%)	0	0	0
Callosomarginal artery	3 (1.4%)	0	0	0
Pericallosal artery	2 (0.93%)	0	0	0

the artery caused by the opposing effect of the distal collateral flow (36,37).

- A1: The A1 also called the "pre-communicating" segment of the ACA originates from the terminal bifurcation of the ICA and terminates at the anterior communicating artery (ACoA), where the A2 (or "post-communicating") segment originates. The A2 segment receives blood from the ipsilateral A1 segment and from the contralateral A1 segment via the ACoA that connects the two ACAs. Therefore, the blood supply to the vascular territory of the ACA is preserved even if the A1 segment is occluded on one side and morphological variants of their absence exist in the general population.
- ACoA: The ACoA arises between the A1 and A2 segments of the anterior cerebral artery and acts as an anastomosis between the left and right anterior cerebral circulation but does not directly play a role in delivering blood to the brain parenchyma. Again, its occlusion is not vital, as it does not interfere with blood flow in the ACA, and in 5% of the population the ACoA is even absent (38).
- PComA: Also the PComA has as major role in the connection of two circulation districts, namely the anterior and the posterior circulation. It runs between the PCA and the C7 (communicating) segment of the ICA forming part of the Circle of Willis. PComA hypoplasia is a relatively common finding with an incidence of approximate 35%
- Ophthalmic artery: The preprocedural angiography of the patient shown in Fig. 1.A shows the ophthalmic artery (arrow) originating from the aneurysm site. At the 3 months follow-up, the same artery is not more visible at angiography (Fig. 1.B). The angiographic study of the external circulation clearly shows a retinal blush with the retinal artery being refurnished by the anastomoses with the branches of the internal maxillary artery (Fig.2). This communication is one of the best known anastomotic connections between the circulation of the internal and external carotid artery. The retina receives blood primarily via the intracranial circulation (ICA

and ophthalmic artery) but it is also refurnished by the external circulation by the meningolacrimal artery via foramen of Hyrtl and the infraorbital artery via the foramen Rotundum. As expected, the patient did not report any symptoms following the procedure and the aneurysm showed a complete exclusion at the 12-month follow-up. The reported case is in our eyes explicative in regard of the phenomena of blood flow inversion due to pressure gradient alterations observed after flow diverter placement.

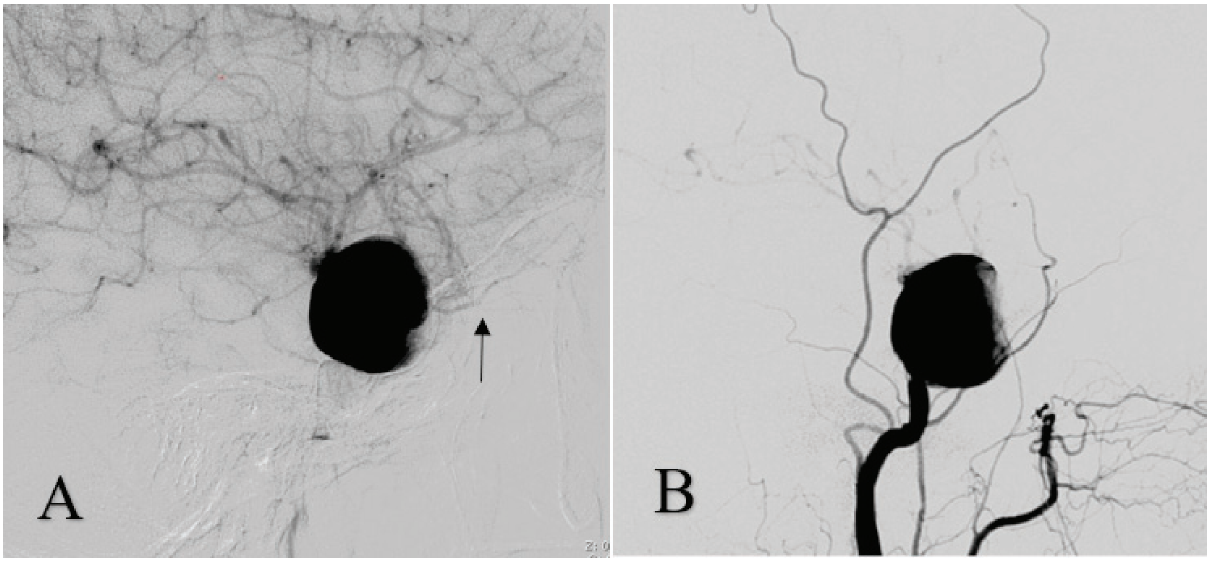

Figure 1. A. Preprocedural angiography shows the ophthalmic artery (arrow) originating from the aneurysm site. B. At the 3 months follow-up, the same artery is not more visible.

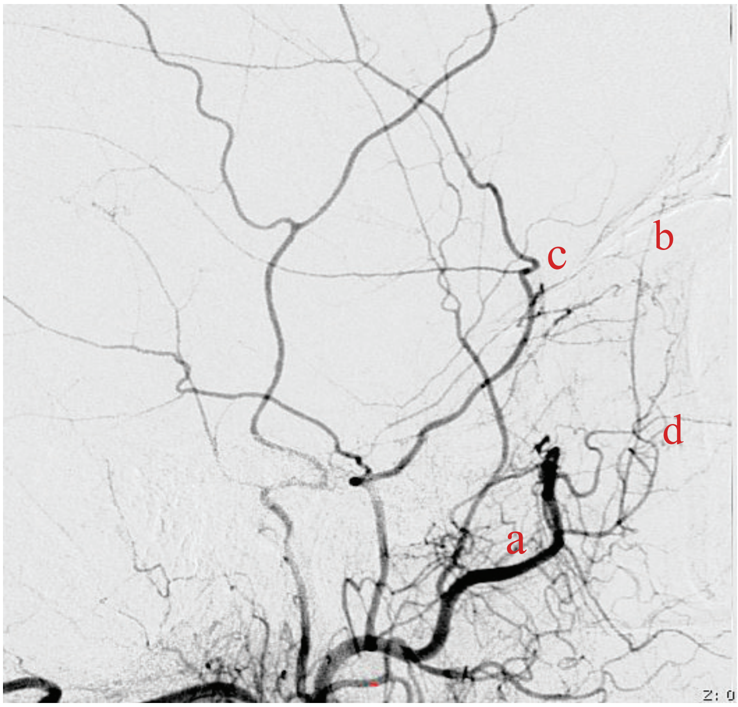

Figure 2. Angiographic study of the external circulation depicting the maxillary artery (a) that refurnishes the retinal artery (b) via the lacrimal artery (c) and the infraorbital artery (d).

ACoA and PComA showed the highest occlusion rates among all the collateral branches. The higher rate of ophthalmic artery patency after flow diversion (8.04%) when compared to PComA (34.38%) can probably be attributed to a higher continued physiological demand. Furthermore, because both systems have an adequate collateral circulation, clinical symptoms do not usually develop in these occluded arteries or in arteries with diminished flow.

Conclusion

Even though occlusion and diminished flow are common following FDS treatment, they are not clinically significant in most cases. Vessel occlusion in our series was not accompanied by any kind of deficit in the long term. The branches most commonly occluded were those arteries that are not indispensable due to their strong collateral blood supply that efficiently shunts the occluded portion and are namely PcomA, A1, AcoA and OphA. This is accompanied by a high success rate in treating the aneurysms with flow diversion and a low complication rate. Therefore, we conclude that FDS placement with coverage of side branches is safe as flow is only interrupted in the covered segment if the blood supply is maintained by collateral circulation.

Abbreviations

OphA: Ophtalmic Artery
PComA: Posterior Communicating Artery
AChoA: Anterior Choroidal Artery
ACA: Anterior Cerebral Artery
A1: First segment of Anterior Cerebral Artery
ACoA: Anterior Communicating Artery
M2: Second segment of Middle Cerebral Artery /division
PCA: Posterior Cerebral Artery
P2-P3: Second and Third segment of the Posterior Cerebral Artery
PICA: Posterior Inferior Cerebellar Artery
AICA: Anterior Inferior Cerebellar Artery
SCA: Superior Cerebellar Artery
ICA: Internal Carotid Artery
FDS: Flow Diverter Stent
DSA: Digital Subtraction Angiography
MRS: Modified Rankin Scale
SAH: Subarachnoid Haemorrhage

Ethical Approval: 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.

Informed Consent: Written informed consent to the interventions, CT and the MR exams was obtained from all subjects in this study.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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