Flow Diversion versus Standard Endovascular Techniques for the Treatment of Unruptured Carotid-Ophthalmic Aneurysms

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ABSTRACT

BACKGROUND AND PURPOSE: Over the past few years, flow diversion has been increasingly adopted for the treatment of intracranial aneurysms, especially in the paraclinoid and paraophthalmic carotid segment. We compared clinical and angiographic outcomes and complication rates in 2 groups of patients with unruptured carotid-ophthalmic aneurysms treated for 7 years by either standard coil-based techniques or flow diversion.

MATERIALS AND METHODS: From February 2006 to December 2013, 162 unruptured carotid-ophthalmic aneurysms were treated endovascularly in 138 patients. Sixty-seven aneurysms were treated by coil-based techniques in 61 patients. Flow diverters were deployed in 95 unruptured aneurysms (77 patients), with additional coiling in 27 patients. Complication rates, clinical outcome, and immediate and long-term angiographic results were retrospectively analyzed.

RESULTS: No procedure-related deaths occurred. Four procedure-related thromboembolic events (6.6%) leading to permanent morbidity in 1 case (1.6%) occurred in the coiling group. Neurologic complications were observed in 6 patients (7.8%) in the flow-diversion group, resulting in 3.9% permanent morbidity. No statistically significant difference was found between complication ($P = .9$) and morbidity rates ($P = .6$). In the coiling group (median follow-up, 31.5 ± 24.5 months), recanalization occurred at 1 year in 23/50 (54%) aneurysms and 27/55 aneurysms (50.9%) at the latest follow-up, leading to retreatment in 6 patients (9%). In the flow-diversion group (mean follow-up, 13.5 ± 10.8 months), 85.3% (35/41) of all aneurysms were occluded after 12 months, and 74.6% (50/67) on latest follow-up. The retreatment rate was 2.1%. Occlusion rates between the 2 groups differed significantly at 12 months ($P < .001$) and at the latest follow-up ($P < .005$).

CONCLUSIONS: Our retrospective analysis shows better long-term occlusion of carotid-ophthalmic aneurysms after use of flow diverters compared with standard coil-based techniques, without significant differences in permanent morbidity.

ABBREVIATION: PED = Pipeline Embolization Device

Carotid-ophthalmic aneurysms are defined as aneurysmal dilation of the supraclinoid internal carotid artery whose neck is attached to the origin of the ophthalmic artery. These intracranial aneurysms are challenging to treat because they are often prone to recanalization after endovascular treatment by conventional coil embolization.[1]

In recent years, flow-diverter stents have become an important tool in the management of intracranial aneurysms; they are now helpful in the endovascular treatment of intracranial aneurysms previously considered untreatable. These new devices are currently mainly indicated for the treatment of complex aneurysms such as large and giant ICA aneurysms and fusiform, dissecting, or blood blister-like aneurysms.[2-5]

Carotid-ophthalmic aneurysms represent an important subset of ICA aneurysms for which flow diversion may be a promising option in the quest for a safe and more effective treatment aiming for stable aneurysmal exclusion.

In this study, we sought to compare clinical and angiographic outcomes between the 2 groups of patients with carotid-ophthalmic aneurysms treated by either standard coil-based techniques (ie, regular coiling, balloon-assisted coiling, or stent-assisted coiling) or with flow diversion, during a 7-year period.

MATERIALS AND METHODS

Ethical Statement

Neither approval of the institutional review board nor patient informed consent is required by the ethics committee of our

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institutions for retrospective analyses of patient records and imaging data.

Patient Population and Treatment

From prospectively maintained data bases of 2 institutions (Pitié-Salpêtrière Hospital and Fondation Ophtalmologique Adolphe de Rothschild), we identified 138 consecutive patients with 161 unruptured, previously untreated, carotid-ophthalmic aneurysms treated by endovascular means between April 2006 and December 2013. Therapeutic alternatives were discussed between neurosurgical and neurointerventional teams in a multidisciplinary decision-making process; patient selection for treatment with standard techniques versus flow diversion was left to the operator's discretion. Eight operators with at least 5 years' experience were involved in the endovascular treatments.

Sixty-seven aneurysms were treated by coil-based techniques in 61 patients. Within this group, 7 patients presented with a history of subarachnoid hemorrhage due to rupture of another intracranial aneurysm. Another 5 patients were treated in the setting of a subarachnoid hemorrhage due to the rupture of a second aneurysm that was treated in the same session. A balloon-remodeling technique was adopted in 32 procedures, elective stent-assisted technique in 23, and both techniques in 12. The Neuroform EZ stent (Stryker Neurovascular, Fremont, California) and the Enterprise self-expanding stent (Codman & Shurtleff, Raynham, Massachusetts) were used in 16 and 7 patients, respectively. The Solitaire AB stent (Covidien, Irvine, California) and the LVIS stent (MicroVention, Tustin, California) were used in 3 and 2 aneurysms respectively. Stent-assisted coiling was performed by using the microcatheter jailing technique in 9 patients.

Ninety-five aneurysms were treated by flow diversion in 77 subjects. Patients undergoing either flow-diversion treatment or stent placement received 75 mg/day of clopidogrel and 160 mg/day of aspirin for 5 days before the intervention. In the first institution (Fondation Ophtalmologique Adolphe de Rothschild), platelet function tests were routinely performed by using the VerifyNow P2Y12 assay (Accumetrics, San Diego, California) with a target of platelet inhibition between 30% and 90%. Patients with inhibition of <30% were reloaded with a double dose of clopidogrel, and the assay was rechecked. In the second institution (Pitié Salpêtrière Hospital), platelet aggregation was tested by aspirin assay and the P2Y12 assay (Multiplate 5.0 analyzer; Roche, Basel, Switzerland). In case of a poor response, patients were switched to ticagrelor. An initial 50 IU/kg heparin bolus was administered, and activated clotting time was maintained between 2- and 3-fold of the baseline intraoperatively. Heparin was discontinued but not reversed at the end of the procedure. Patients were subsequently left on dual antiplatelet therapy for 3 months, then on aspirin-only for 9 months. Procedures were performed with the patient under general anesthesia.

The Pipeline Embolization Device (PED; Covidien) was deployed through a Marksman microcatheter (Covidien) by using a triaxial guide-catheter system. The Silk flow diverter (Balt Extrusion, Montmorency, France), the Surpass stent (Stryker), and the FRED flow diverter (MicroVention) were used in a minority of cases at the operator's discretion. The number of stents deployed was left to the operator's discretion, but in general, only a single device was used for most aneurysms. The correct apposition of the flow diverter was documented under fluoroscopy and with additional flat panel CT angiography at the operator's discretion. Any stent misopening was remedied with either the Gateway PTA balloon catheter (Stryker) or the HyperGlide balloon (Covidien) angioplasty when needed. When bilateral aneurysms were treated, the contralateral aneurysm was treated usually 3 months after the first one.

Table 1: Baseline characteristics for the 2 study groups

	Coil-Based Technique (n = 61)	FD (n = 77)	P Value
Mean age (yr)	49.2 ± 13.9	49.7 ± 11.8	.79
Male patients	10 (16.4%)	17 (22.1%)	.52
Female patients	51 (83.6%)	60 (77.9%)	
An. size (mm) (mean)	6.7 ± 3.6	8.7 ± 6.3	.03
D/N ratio	1.8 ± 0.63	1.9 ± 1.05	.46

Note:—An. indicates aneurysm; FD, flow diverter; D/N, dome/neck.

Medical charts were reviewed to determine patient demographics, aneurysm characteristics, procedural techniques, and complications. The outcomes of 77 patients treated by flow diversion and 61 patients treated by coiling techniques were compared. Clinical follow-up was performed by the referring interventionalist through physical examination in most cases. Patients unable or unwilling to reach the treatment center for logistic reasons were assessed by telephone interview by the referring interventionalist. An independent neurologist was consulted in case of clinical signs of procedural complications. Angiographic follow-up by either digital subtraction angiography or MR angiography was scheduled at 3–6 months. A further control DSA was performed at 6 months to 1 year. In case of complete aneurysm thrombosis, follow-up was then continued by MRA scans on a yearly basis. Deployment of additional flow diverters was considered at follow-up if the aneurysm remained unchanged or did not thrombose completely.

For statistical analysis, angiographic outcome was dichotomized into complete (100%) and incomplete obliteration (<100%). Regardless of the need for further intervention, any filling at the neck or the dome of the aneurysm was considered incomplete obliteration. Clinical outcomes at the last available follow-up were classified according to the modified Rankin Scale.

Statistical Analysis

The Student t test was used to compare continuous variables, whereas the χ^2 test or the Fisher exact test was used for categoric variables. Univariate conditional analysis was used to test covariates predictive of treatment complications, follow-up obliteration, and clinical outcome (mRS, 0–2 versus 3–6). Factors predictive in univariate analysis ($P < .20$) were entered into a multivariate conditional logistic regression. P values ≤ .05 were statistically significant. Calculations were made by using MedCalc for Windows software, Version .7.4 (MedCalc Software, Mariakerke, Belgium).

RESULTS

Demographics and Aneurysm Characteristics

Main baseline characteristics are summarized in Table 1.

The percentage of aneurysms of >6 mm was similar in patients with flow diverters (60%) and those with coils (46.2%, $P = .4$). Bilateral aneurysms were treated in 4 patients in the coiling group and in 12 patients in the flow-diversion group.

Postprocedure Angiographic Results

In the coiling group ($n = 67$), initial self-adjudicated Roy Raymond scores were 1 (complete occlusion) in 39 (58.2%) cases, 2 (residual neck) in 14 (20.9%), and 3 (residual sac) in 14 (20.9%).

In the flow-diversion group ($n = 95$), a single device was deployed in 82 (86.3%) aneurysms. The PED was used in most of the procedures ($n = 55$, 57.9%). Two or more devices were used in 13 (13.7%) patients. Adjunctive coils were deployed within the aneurysmal sac in 27 patients, in a loose fashion, notably in large and giant aneurysms. Device deployment was successful in 94/95 (99%) aneurysms. In 1 patient, the deployment of the stent was too proximal and the distal end fell into the aneurysmal sac. The delivery of a second stent was attempted unsuccessfully; therefore, a carotid occlusion test and parent vessel occlusion were performed. Balloon angioplasty was performed successfully for better flow-diverter expansion in 3 patients. In another 3 patients, a second laser-cut stent (Enterprise; Codman & Shurtleff) was deployed inside the flow diverter (Silk; Balt Extrusion) to ensure better wall apposition.

The initial occlusion rate after the procedure was 6.4% (6/94; 1 patient was excluded because he or she was treated by parent vessel occlusion).

Procedural Complications

Neither procedure-related deaths nor aneurysmal bleeding was reported during the procedure or follow-up in either group.

In the coiling group, 4 procedure-related thromboembolic events (6.6%) occurred, causing neurologic symptoms in 3 patients (NIHSS scores of 3, 5, and 4, respectively) and leading to permanent morbidity in 1 case of monocular blindness due to occlusion of the central artery of the retina (1.6%).

All procedures in the 28 patients treated by stent-assisted coiling were uneventful.

In the flow-diversion group, 2 delayed homolateral intraparenchymal hemorrhages (2.6%) were reported at days 10 and 15, respectively; 2 optic nerve compressions and 2 thromboembolic events, with NIHSS scores of 4 and 5 respectively, were observed (7.8% complication rate) and resulted in 3.9% permanent morbidity, consisting of 1 case of monocular blindness, 1 case of secondary epilepsy, and 1 visual field reduction due to hypoperfusion of the ophthalmic artery after parent vessel occlusion. In the latter case, the choice of parent vessel occlusion was motivated by a technical complication (ie, device foreshortening due to downsizing and/or stretching, which subsequently caused the distal end to fall into the aneurysmal sac, with failure to retrieve the device or to deploy a second one). No statistically significant difference was found between complication ($P = .9$) and morbidity ($P = .63$) rates.

The following factors were tested as predictors of complications: age, sex, aneurysm size, dome/neck ratio, and type of treatment. In univariate analysis, only aneurysm size (OR, 1.78; 95% CI, 0.14–3.23; $P < .01$) predicted procedural complications in the flow-diversion group. This finding was confirmed in multivariate analysis (OR, 1.43; 95% CI, 0.41–4.96; $P < .001$). The type of treatment was not a predictor of complications after adjusting for age.

Table 2: Comparison of rates of aneurysmal occlusion according to follow-up intervals for coil-based techniques and flow-diversion groups

	≤6 Months	7–12 Months	>12 Months	Latest Follow-Up
Coiling group	17/26 (65.4%)	16/28 (57.1%)	23/50 (46%)	27/55 (49,1%)
Flow diverter	21/39 (53.8%)	16/22 (72.2%)	35/41 (85.3%)	50/67 (74.6%)
P value	.44	.37	.00015[a]	.0047[a]

[a] Significant.

Table 3: Comparison of rates of aneurysmal occlusion according to follow-up intervals for the stent-assisted coiling subgroup and flow-diversion group

	≤6 Months	7–12 Months	>12 Months	Latest Follow-Up
Stent-coil	9/11 (81.8%)	11/17 (64.7%)	14/24 (58.3%)	16/24 (66.7%)
Flow diverter	21/39 (53.8%)	16/22 (72.2%)	35/41 (85.3%)	50/67 (74.6%)
P value	.16	.73	.019[a]	.59

[a] Significant.

Angiographic Outcome

Angiographic follow-up was available for 66/95 (69.4%) aneurysms treated by flow diverters and 55/67 (82.1%) patients treated with coil-based techniques. Median angiographic follow-up time was 13.5 months in the PED group and 31.5 months in the coiling group ($P < .001$). At the latest follow-up, a higher proportion of aneurysms treated by flow diverters (85.3%; $n = 35/41$) showed complete obliteration (100%) compared with 46% ($n = 23/50$) in the coiling group ($P = .0047$, Table 2). A comparison between patients with flow diverters and those with stent-coils showed a significant difference in favor of flow diversion after only 12 months from treatment (Table 3). In the flow-diversion group, no aneurysmal recanalization was observed after thrombosis had occurred. In the coiling group ($n = 67$), self-adjudicated Roy Raymond scores at the latest follow-up were 1 (complete occlusion) in 27 (49%) patients, 2 (residual neck) in 13 (23.6%) patients, and 3 (dome filling) in 15 (27.3%).

We tested the following factors as predictors of angiographic outcome: age, sex, aneurysm size, dome/neck ratio, and type of treatment. In univariable analysis, dome/neck ratio (OR, 1.54; 95% CI, 0.76–2.87; $P < .033$) and type of treatment (OR, 2.67; 95% CI, 0.56–1.83; $P < .02$) were predictive of angiographic exclusion. In multivariable analysis, flow-diversion treatment was found to be a predictor of complete angiographic exclusion (OR, 4.3; 95% CI, 1.98–9.35; $P < .005$).

Retreatment

Retreatment was necessary for 2/95 (2.1%) aneurysms that showed only partial thrombosis in the flow-diversion group, the procedure consisting of the positioning of a second device within the previous one. One patient was retreated a second time 1 year after retreatment due to a persisting residual sac. In the coiling group, retreatment was performed in 6/68 aneurysms (9%, $P =$

.068). Two patients were retreated once by laser-cut stents and coils. Two patients were retreated twice: the first time by simple coiling, then by stent-assisted coiling; the second time by stent-coils and then by flow diversion.

Clinical Outcome

Clinical follow-up was available for 75 (97.5%) patients in the PED group and 59 (96.7%) patients in the stent-coil group. The median follow-up time was 18.5 months in the PED group and 37.4 months in the stent-coil group ($P < .001$). The proportion of patients with mRS 0–2 was 97.3% (73/75) in the PED group and 96.6% in the coiling group (57/59, $P = 1$). The proportion of patients with mRS 0–1 was 96% (72/75) in the flow-diversion group and 95% in the stent-coil group (56/59, $P = 1$). The 5 patients who had presented with a contemporary history of subarachnoid hemorrhage in the coiling group all had a favorable outcome (mRS 1) at latest follow-up.

None of the following factors proved as predictors of clinical outcome after testing: age, sex, aneurysm size, type of treatment, and complications.

DISCUSSION

The adoption of flow diverters has begun a new concept in the endovascular treatment of intracranial aneurysms. Since their introduction into clinical practice, however, a debate has ensued concerning both the long-term stability of treatment and complication rates. Many interventionalists still prefer traditional endovascular approaches.

The complications of coiling and stent-assisted coiling are essentially limited to thromboembolic events and intraprocedural aneurysmal rupture.[3,6] Even in flow diversion, cases of thromboembolism due to in-stent thrombosis or delayed migration of the device, distal parenchymal hemorrhage, or aneurysm rupture due to degradation of the aneurysmal wall or endoleak have been reported.[4,7-12]A meta-analysis by Brinjikji et al,[13] including 1451 patients with 1654 aneurysms, found procedure-related morbidity and mortality rates for flow diversion of 5% and 4%, respectively. The authors concluded that the procedure-related risk with flow diverters is not negligible and should be taken into account when considering the best therapeutic option. Conversely, several studies have presented convincing evidence that the PED carries a high safety and efficacy profile. A first multicenter international trial reported a success rate of 99%, an occlusion rate of 74%, and a major ipsilateral stroke or neurologic death rate of only 5.6%.[2] A more recent retrospective international study on 906 aneurysms showed a morbimortality rate of 4.8% in the anterior circulation.[14] Burrows et al[15] reported a mortality and permanent morbidity rate of 1%, with an occlusion rate of 69% at 1 year. These studies, however, analyzed a heterogeneous population and did not compare directly the results of flow diversion with those of conventional endovascular techniques, especially stent-assisted coiling, for which excellent safety and efficacy in several studies have been proved.[3,6,16,17]

In our study, the technical success rate was high (99%) and consistent with that in the published literature. Most interesting, there was no significant difference in terms of complication rates between flow diversion and conventional endovascular techniques. We did not report any procedure-related deaths, and the permanent morbidity rate in the flow-diversion group was 3.9% (ie, nonsignificantly higher than that in the coiling group) despite an evident numeric trend toward a higher morbidity rate in the flow-diversion group. Thus, a possible lack of statistical power cannot be excluded. However, our results are still in line with the results from the other studies,[4,5,18] including smaller series on carotid-ophthalmic aneurysms that reported an occlusion rate at latest follow-up between 73% and 92.1%, an overall permanent morbidity between 0% and 2.3%, and a mortality between 0% and 4.4%.[19-21]

Moreover, our results are similar to those reported in a recent study comparing flow diversion and stent-coiling for aneurysms of <10 mm by Chalouhi et al,[22] who reported complication rates of 5% and 3%, respectively. Procedure-related mortality was 0% in both groups. Concerning aneurysm occlusion on long-term follow-up, the authors did not find any statistical difference between the 2 groups, though a trend in favor of flow diversion (80% versus 70%) was reported. The authors concluded that the study was likely underpowered to detect small differences between the 2 techniques, both leading to high occlusion rates. In a previous report, the authors had compared the procedural, angiographic, and clinical outcomes of flow diversion and coiling in unruptured, large (>10), and giant (>25 mm) aneurysms,[3] thereby finding a similar complication rate (7.5%) along with a higher aneurysm occlusion rate (86% versus 41%) and a lower retreatment rate with flow diversion (2.8% versus 37%). These results led to the conclusion that flow diverters were a preferred option for large and giant aneurysms because they resulted in similar clinical outcomes compared with stent-assisted coiling.

In the present study, we observed a stable progression with time toward complete aneurysm occlusion in the flow-diversion group, as opposed to a gradual increase in the number of recanalized aneurysms in the coiling group. The difference between the long-term aneurysm occlusion rates was strong and statistically significant. In a multivariate analysis, treatment by flow diversion was an independent predictor of long-term aneurysmal occlusion. Nonetheless, retreatment rates did not differ significantly between the 2 groups, despite a lower rate for patients with flow diverters.

Lanzino et al[23] compared 22 paraclinoid aneurysms treated by flow diversion with conventional coiling. The authors reported a significantly higher rate of complete occlusion in patients with flow diverters (76%) than in those with coils (21%), with a similar rate of morbidity, and concluded that long-term follow-up was important to validate flow diversion as a superior therapeutic strategy for proximal internal carotid artery aneurysms.

The present study is thus not the first to compare flow diverters with coiling, but to our knowledge, it is the first to specifically compare these 2 techniques in a homogeneous subset of carotid-ophthalmic aneurysms divided into 2 well-matched groups in terms of demographics and aneurysm features.

Randomized controlled trials comparing flow diversion and conventional endovascular techniques are currently underway[24-26] and may provide high-level evidence on the safety and efficacy of flow diversion.

Limitations

This study is retrospective and reflects the experience of only 2 centers. Patients were not randomized to either one technique or the other. In the flow-diversion group, imaging follow-up was available in <70% of patients only, because several patients were foreigners and returned to their home country after treatment. As in the study by Chalouhi et al,[22] we could not provide occlusion rates at standard time points, which would have allowed a better comprehension of the history of aneurysm thrombosis. Instead, we compared aneurysm occlusion rates at the latest follow-up. Moreover, we were bound to include different techniques (simple coiling, balloon remodeling, stent placement), all within the same coiling group, to reach an acceptable statistical power. For the same reason, we did not distinguish between those aneurysms treated by flow diverter only and those treated by flow diverter + coils. This omission, in our opinion, does not impair the significance of our findings in terms of treatment results at follow-up. All estimates of aneurysm occlusion and complications were adjudicated by the team of interventionalists, and these do often differ from estimates of blinded core laboratories.

A separate comparison between patients with flow diverters and the subset treated by stent-assisted coiling led to less conclusive results, showing a slightly statistically significant difference in favor of flow diversion-only after 12 months of follow-up. As in the study by Chalouhi et al,[22] this analysis may have a lack of statistical power, given the small sample of patients with stent-coils ($n = 28$).

Despite the good match between the 2 groups in terms of demographics, aneurysm location, and size, the clinical and angiographic follow-up time differed significantly. We hypothesize, therefore, that the occlusion rate with flow diverters may have been even higher if patients had been followed up for longer periods; this potential outcome adds further support to the efficacy of flow diverters.[5,27]

Even if one considers these limitations, this study provides a comparative analysis of clinical and angiographic outcomes in a homogeneous cohort of carotid-ophthalmic aneurysms treated with either flow diversion or coiling.

CONCLUSIONS

In our retrospective study, flow diversion for elective treatment of carotid-ophthalmic aneurysms was feasible and effective, with complication and morbidity rates comparable with those of standard endovascular approaches. At long-term follow-up, flow diversion achieved a more stable sac thrombosis compared with other techniques. Further larger prospective studies may help confirm these findings and better assess complication rates of aneurysms treatment with flow diverters.

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