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ABSTRACT

BACKGROUND AND PURPOSE: Flow-diverter technology has proved to be a safe and effective treatment for intracranial aneurysm based on the concept of flow diversion allowing parent artery and collateral preservation and aneurysm healing. We investigated the patency of covered side branches and flow modification within the parent artery following placement of the Pipeline Embolization Device in the treatment of intracranial aneurysms.

MATERIALS AND METHODS: Sixty-six aneurysms in 59 patients were treated with 96 Pipeline Embolization Devices. We retrospectively reviewed imaging and clinical results during the postoperative period at 6 and 12 months to assess flow modification through the parent artery and side branches. Reperfusion syndrome was assessed by MR imaging and clinical evaluation.

RESULTS: Slow flow was observed in 13 of 68 (19.1%) side branches covered by the Pipeline Embolization Device. It was reported in all cases of anterior cerebral artery coverage, in 3/5 cases of M2-MCA coverage, and in 5/34 (14.7%) cases of ophthalmic artery coverage. One territorial infarction was observed in a case of M2-MCA coverage, without arterial occlusion. One case of deep Sylvian infarct was reported in a case of coverage of MCA perforators. Two ophthalmic arteries (5.9%) were occluded, and 11 side branches (16.2%) were narrowed at 12 months' follow-up; patients remained asymptomatic. Parent vessel flow modification was responsible for 2 cases (3.4%) of reperfusion syndrome. Overall permanent morbidity and mortality rates were 5.2% and 6.9%, respectively. We did not report any permanent deficit or death in case of slow flow observed within side branches.

CONCLUSIONS: After Pipeline Embolization Device placement, reperfusion syndrome was observed in 3.4%, and territorial infarction, in 3.4%. Delayed occlusion of ophthalmic arteries and delayed narrowing of arteries covered by the Pipeline Embolization Device were observed in 5.9% and 16.2%, respectively. No permanent morbidity or death was related to side branch coverage at midterm follow-up.

ABBREVIATIONS: ACA = anterior cerebral artery; PED = Pipeline Embolization Device

Flow-diversion systems appear to be promising tools for the treatment of giant, wide-neck, or fusiform intracranial aneurysms.[1-8] It allows not only the exclusion of the aneurysm sac but the treatment of the diseased arterial segment located on either side of the device by changing the hemodynamic conditions.[9,10] Blood flow is supposed to be disrupted in the aneurysm sac, while parent artery and collateral branches remain permeable. Modification of intra-aneurysmal flow after the implantation of flow diverters has been described as well in experimental and computational models,[11-13] but extra-aneurysmal flow modifications have rarely been explored. Clinical complications such as delayed aneurysm rupture,[14-16] delayed intraparenchymal hematoma,[17] and slow flow or occlusion of collateral branches covered by the device[18] have been reported, with sparse knowledge, considering the frequency.

The purpose of this study was to focus on hemodynamic changes induced by the Pipeline Embolization Device (PED; Covidien, Irvine, California) in collateral branches, perforators, and the parent artery.

MATERIALS AND METHODS

Patient Selection

We retrospectively analyzed the clinical and radiologic data of all consecutive patients treated with the PED from July 2009 to June 2012 in 2 large French neuroscience centers.

Therapeutic options were discussed by a multidisciplinary team. Patients were treated with endovascular reconstruction if they had wide-neck aneurysms (neck size, ≥4 mm, or dome-to-

neck ratio, <2) and/or if therapy was not feasible by conventional techniques (coils with or without remodeling or surgical clipping). The aneurysms treated were blister-like, fusiform, large, and giant aneurysms. The study was conducted following approval by an ethics committee, and written informed consent was obtained from every patient.

Endovascular Procedure

Medication. All patients were treated under general anesthesia and premedicated with clopidogrel (300 mg the day before). Platelet function was evaluated by using a VerifyNow P2Y12 assay (Accumetrics, San Diego, California) in the angiography suite just before the procedure.[19] Procedures were performed with the patient under systemic heparinization with an activated clotting time between 250 and 300 seconds. At the end of the procedure, each patient was given an intravenous bolus of 250–500 mg of aspirin, and heparin anticoagulation was maintained for 24 hours. Dual antiplatelet medication was then introduced (clopidogrel, 75 mg, and aspirin, 75 or 160 mg) and was maintained for at least 6 months following the procedure. At 6 months, clopidogrel was stopped and aspirin was maintained life-long.

Technique. All procedures were performed by a senior interventional neuroradiologist with experience in stent-placement techniques. The PED was implanted via a femoral artery approach across the aneurysmal segment; then, the delivery was via a 0.027-inch internal diameter microcatheter (Marksman; Covidien) that requires a 6F guide catheter support.

Morphologic characteristics of the aneurysm (morphology, volume, and neck size) and parent artery (diameter of the proximal and distal segment and collateral branches) were analyzed by using 2D and 3D reconstructed images to select the optimal device size and length.

Postoperative Management and Follow-Up. A neurologic examination was performed after the procedure. In the absence of a significant abnormality, patients were discharged after 72 hours. In cases with complications, a brain CT or MR imaging was performed. In the absence of clinical adverse events, patients were clinically followed by a stroke practitioner postdischarge at 6 and at 12 months after the procedure. All clinical adverse events (stroke, SAH, headache, nerve palsy, mass effect, or visual deficit) were documented in our prospectively populated data base before the procedure and then were re-evaluated during follow-up.

Follow-up included an MR imaging or conventional angiography at 6 and 12 months. We retrospectively analyzed flow modifications within side branches covered by the device. This assessment was made on the angiogram obtained immediately after the stent deployment, by using the same acquisition parameters (volume injected, speed, x-ray delay) as those obtained immediately before the implantation of the device. Flow modification was subjectively assessed by using a 3-point scale: 1) no modification (if the flow was the same as that before device deployment), 2) slow flow (if the contrast material became slower within the covered vessel), and 3) occlusion (if no contrast material entered the vessel). During the follow-up imaging, patency of side branches covered by the device was determined and the vessel size was reported as unchanged, narrowed, or occluded.

Table 1: Baseline characteristics

Characteristics	Value	%
Patients	59	
Age (mean, yr)	53.7	
Female sex	46	78
Aneurysms	66	
Morphology		
Saccular	44	66.7
Dissecting	16	24.2
Blister	2	3
Fusiform	4	6.1
Size (mean, mm)	10.7	
Size (maximum diameter)		
<10 mm (small)	38	57.6
>10–25 mm (large)	23	34.8
>25 mm (giant)	5	7.6
Neck ≥4 mm	50	75.8
Dome-to-neck ratio <2	36	54.5
Location		
Anterior circulation	54	81.8
CCA	25	37.9
COA	16	24.2
MCA	7	10.6
ACA	2	3
PcomA	4	6.1
Posterior circulation	12	18.2
BA	2	3
VA	7	10.7
PCA	2	3
PICA	1	1.5

Note:—CCA indicates cavernous carotid artery; COA, carotico-ophthalmic artery; BA, basilar artery; VA, vertebral artery; PcomA, posterior communicating artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery.

All conventional angiograms and MRIs were reviewed by 2 neuroradiologists and adjudicated in cases of disagreement.

In addition to patency of collateral branches, baseline characteristics including patient age, aneurysms morphology, size, and location were also reported.

RESULTS

Patient Population and Aneurysm Characteristics
Between July 2009 and June 2012, 66 aneurysms in 59 patients were treated with the PED in 2 French neuroscience centers (Table 1). Fifty patients were treated by 3 operators in Montpellier, and 9 patients were treated by 1 operator in Marseille without any significant imbalance between these 2 centers.

PED Procedures
A total of 96 devices were used to treat 66 intracranial aneurysms (1.5 device per aneurysm). PED deployment was achieved in 92 cases (95.8%). Four devices (4.2%) could not be deployed. No parent artery occlusion was reported during the perioperative period.

Coils were deployed in 7 aneurysms (10.6%), including 2 ruptured aneurysms. Coils were not used in cases of potential risk of side branch occlusion. PED implantation alone was performed in 59 aneurysms (89.4%). Patients were treated with 1–5 PEDs (the number of PEDs implanted was 1 in 48 cases, 2 in 10 cases, 3 in 2 cases, 4 in 3 cases, and 5 in 2 cases). Multiple PEDs were used with telescopic reconstruction in cases of large-neck aneurysms or to treat different aneurysms in the same arterial segment.

Table 2: Hemodynamic modifications within visible side branches covered by the PED and consequences

Side Branches	No. of PEDs Implanted	No. of Side Branches	Slow Flow within Side Branches	Transient or Permanent Neurologic Deficits[a]	Territorial Ischemic Lesions on MRI	Stenosis at 12-Mo Follow-Up	Occlusion at 12-Mo Follow-Up
Ophthalmic artery	1	25	3	0	NA	2	1
	2	5	1	0	NA	1	0
	3	1	0	0	NA	0	1
	4	3	1	0	NA	0	0
Anterior choroidal artery	1	11	0	3	0	0	0
	2	1	0	0	0	0	0
ACA	1	5	5	3	0	5	0
Callosomarginal artery	1	1	0	0	0	0	0
MCA	1	5	3	2	1	1	0
PcomA	1	2	0	0	0	0	0
PICA	1	5	0	0	0	2	0
	2	1	0	0	0	0	0
SCA	3	1	0	0	0	0	0
PCA	3	1	0	0	0	0	0
Anterior spinal artery	1	1	0	0	0	0	0
Total		68	13 (19.1%)	8	1	11	2
Perforators							
Sylvian perforators	1	4	NA	3	1	NA	NA
	2	1	NA	0	0	NA	NA
BA perforators	3	1	NA	0	0	NA	NA
	5	1	NA	0	0	NA	NA
Total		7	NA	3	1	NA	NA

Note:—SCA indicates superior cerebellar artery; NA, not available; BA, basilar artery; PcomA, posterior communicating artery; PCA, posterior cerebral artery; PICA, posterior inferior cerebellar artery.

[a] Related to the side branch covered.
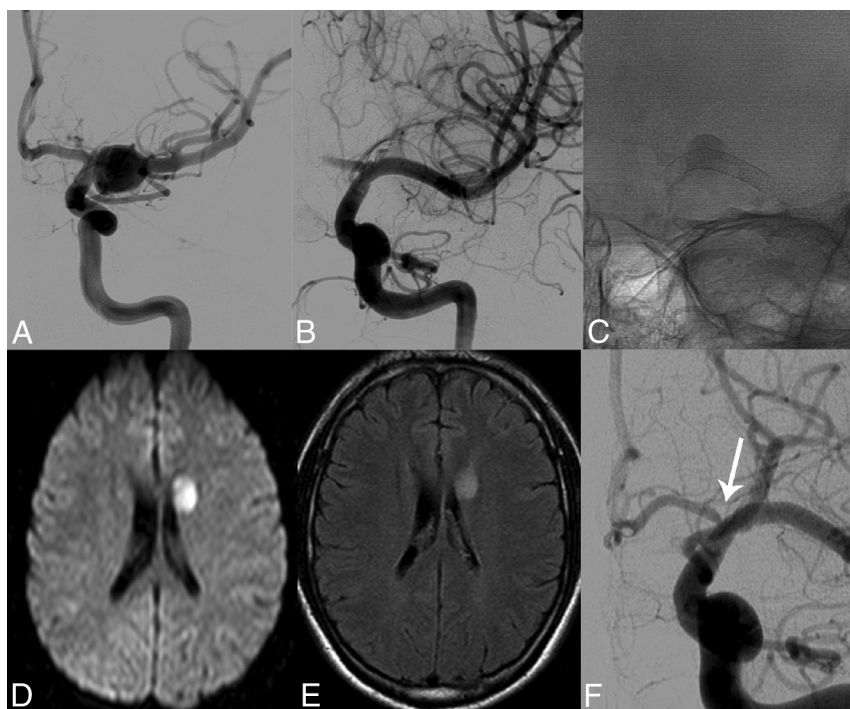
FIG 1. Perforator infarction following PED placement and arterial narrowing of the covered artery on a 12-month follow-up angiogram. *A*, Anteroposterior view shows the dissecting aneurysm of the left proximal M1 segment. *B*, Anteroposterior view after PED placement shows absence of filling of the aneurysm and slow flow within the A1 segment. The acquisition was performed with the same parameters but in a later phase to see the A1 segment. *C*, Single PED placement within the left M1 segment results in contrast stagnation within the aneurysm sac. *D* and *E*, DWI and FLAIR sequences performed 2 days later because of transient right brachiofacial hemiparesis demonstrate basal ganglial infarction. *F*, Twelve-month follow-up angiogram shows the ostial narrowing of the covered collateral branches (*arrow*).

Side Branches and Perforators Covered by the PED

Sixty-eight visible side branches were covered by the device. Immediately after PED placement, slow flow was angiographically identified within 13 branches (19.1%), including 5 of 34 (14.7%) ophthalmic arteries (Table 2), 5 of 5 (100%) anterior cerebral arteries (ACAs), and 3 of 5 (60%) M2-MCAs. In all cases of ACA coverage, the anterior communicating artery was functional. No side branch occlusion was demonstrated on the immediate angiography. Five patients presented with transient neurologic deficits. Four had multiple side branch coverage. Territorial ischemic lesions on MR imaging were reported in 2 cases: The first case was a 30-year-old man (patient 3) treated for a left dissecting ruptured MCA aneurysm. The covered branches were the ACA and MCA perforators, and an MR imaging performed the following day demonstrated a deep MCA infarct (Fig 1). The second case was a 60-year-old woman (patient 22) treated for an incidental MCA bifurcation aneurysm with a branch originating from the sac. On the final angiographic runs, slow flow was observed within the anterior MCA bifurcation branch (Fig 2). After extubation, the patient presented with mild aphasia, and MR imaging identified an MCA infarct. The patient was discharged without a significant deficit. Two patients with basilar artery PED placement died, one patient, in unclear circumstances, probably secondary to a delayed rup-

FIG 2. Slow flow within MCA side branch. *A*, Left MCA aneurysm treated with a PED covering the prefrontal branch. *B* and *C*, Slow flow within the covered side branch (*arrows*). *D* and *E*, MR imaging performed on day 1 after the procedure shows acute left anterior MCA infarct.

ture (patient 11), and the second following in-stent thrombosis (patient 24) related to premature discontinuation of antiplatelet therapy.

During follow-up angiography, 66 of 68 (97%) visible side branches covered by the PED remained patent with normal blood flow. We reported 2 cases (5.9%) of ophthalmic artery occlusion on the 12-month follow-up angiogram. Eleven cases (16.2%) of collateral branches remained patent but had an arterial narrowing, which was observed in all cases of ACA coverage. In all these cases of occlusion or narrowing, patients did not have transient or permanent deficits. The 2 patients with delayed ophthalmic artery occlusion had no flow modification on the angiogram immediately after PED placement. The 13 side branches with slow flow noted just after the procedure remained patent at 1-year follow-up.

The mean number of PEDs implanted in cases of occluded side branches was 2 (range, 1–3) versus 1.35 (range, 1–4) in cases of normal blood flow within side branches.

Clinical Follow-Up
Among 59 patients initially included in the study, 1 patient was lost to follow-up. Fifty-eight patients with 65 intracranial aneurysms underwent PED placement and discharge evaluation. During the hospitalization, we reported 19 (32.3%) minor reversible clinical adverse events: Six (10.3%) patients had headache, 5 (8.6%) had femoral puncture hematomas, and 8 (13.8%) had transient neurologic deficits. Two patients (1 man and 1 woman;

respectively, 82 and 78 years of age) treated for a large carotid cavernous aneurysm presented with transient hemiplegia within 5 hour after the procedure. In both patients, flow decrease was not observed during the procedure, and blood pressure was stable around 90 mm Hg without evidence of tensional disturbance during the procedure. On the MR imaging performed (Fig 3), there was no evidence of new ischemic or hemorrhagic lesions and the intracranial arteries remained patent. FLAIR images showed leptomeningeal hyperintensity without enhancement on the postgadolinium images. On the PWI sequence, there was no hyperperfusion seen. The neurologic deficit improved during several days, and the follow-up MR imaging performed 5–7 days after the procedure showed complete resolution of the leptomeningeal signal change.

At 12 months' follow-up, the overall morbidity rate was 5.2%, and the mortality rate was 6.9 (overall morbimortality rate of 12.1%). The rate of mortality was 27.3% in the posterior circulation and 2.1% in the anterior circulation. Three patients died during follow-up, at days 10, 15, and 25. Deaths were related to in-stent thrombosis in 1 case and delayed aneurysm rupture in 2 cases. Delayed aneurysm rupture occurred in an 86-year-old woman treated for a large basilar artery aneurysm in 1 case and a 56-year-old woman treated for a large carotico-ophthalmic aneurysm in the other case. One other patient died during further treatment performed 13 months after the initial therapeutic phase because of persistent aneurysm filling. No permanent morbidity or death was related to side branch coverage.

DISCUSSION
Side Branches and Perforators Covered by the PED
In our overall cohort, delayed occlusion of the ophthalmic artery, covered by the PED, occurred in 2 cases (5.9%) but was clinically silent. In the literature, patency of collateral branches is rarely reported. Concerning the ophthalmic artery, Szikora et al[6] reported immediate occlusion in 1 case, resulting in a retinal branch occlusion and a small visual field deficit, and delayed occlusion at 6 months in 2 other cases, which were clinically silent. This finding is consistent with a rate of delayed ophthalmic artery occlusion of 11.7%. More recently, Puffer et al[18] observed that 21% of the ophthalmic artery covered by a PED appeared occluded in subsequent angiographic follow-up. All reported cases of ophthalmic artery occlusion were clinically silent, perhaps due to the good collateral circulation.[18] In another study, Yu et al[20] did not report any occlusions among 107 ophthalmic arteries covered by the PED. Overall, the placement of 1 or multiple PEDs across the ophthalmic artery appears safe.
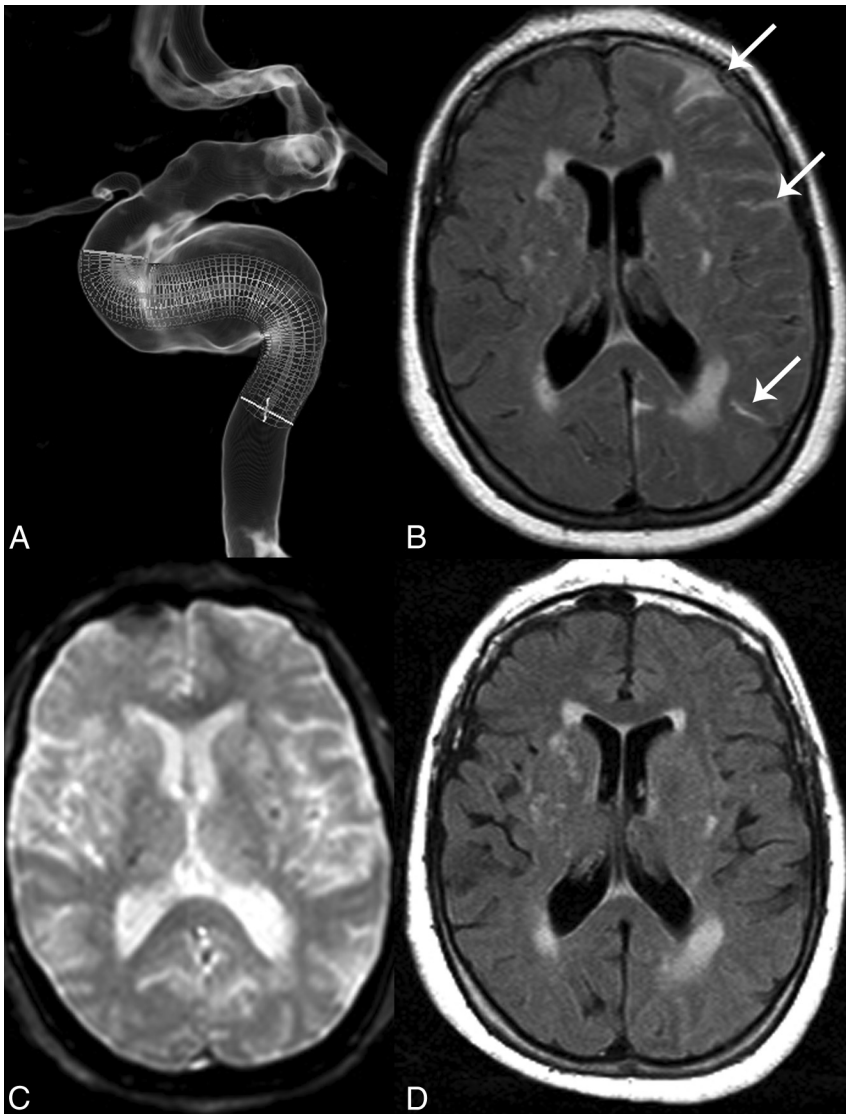
FIG 3. Imaging findings in a patient presenting with cerebral reperfusion syndrome. The patient was treated for a large left carotid cavernous aneurysm with the implantation of 2 overlapped PEDs (*A*). Seven hours after the procedure, the patient had severe headache and mild aphasia. *B* and *C*, FLAIR images show leptomeningeal hyperintensities in the left hemisphere (*arrows*) without evidence of hemorrhage on T2 gradient-echo (*C*). *D*, FLAIR performed 24 hours after the procedure shows complete reversibility of leptomeningeal hyperintensities.

on the initial imaging. Late narrowing or occlusion was observed in 38% (5/13) after initial slow flow and was observed in only 14.5% (8/55) when slow flow was not reported just after stent placement (*P* < .05), suggesting that peroperative slow flow is a strong predictor of late branch occlusion. In the literature, narrowing of collateral branches is rarely reported. Preclinical studies[9,22-26] reported that flow within collateral arteries was maintained after the placement of a flow diverter. However, these arteries were considered end vessels without distal collaterals. In a clinical study, Brinjikji et al[21] observed a decreased flow in 18% of posterior communicating arteries covered by a flow diverter with a patent P1. These findings suggest that the placement of a flow diverter is probably responsible for a vascular and hemodynamic remodeling of regional branches covered by the device, which can lead to arterial narrowing at midterm follow-up. This vascular remodeling is probably favored by flow competition from communicating arteries. The narrowing or occlusion of such arteries remains clinically silent due to good collaterality. In our practice, we now check the patency of the anterior communicating artery before placing a flow diverter in this segment.

Among the 5 cases of lenticulostriate coverage, we reported 1 case of infarction. This patient was treated for a dissecting MCA aneurysm with the placement of 1 PED, and it is not possible to conclude whether the infarct was due to extension of the dissection to the lenticulostriate arteries or due to the device. Overall, PED placement across perforating lenticulostriate arteries remains safe, probably due to the discrepancy between the wire size of the PED (30 μm) and the diameter of lenticulostriate arteries (mean, 480 μm; range, 100-1280 μm).[27] Furthermore, in a computational model, Appanaboyina et al[25] observed that the coverage of 90% of the perforating vessel ostium reduced <10% of the flow through the inlet. These data suggest that even if 3 wires cross a perforator ostium with a diameter of 100 μm, the coverage of the orifice area will never be >90%. However, tiny thrombi can develop on the surface of the PED and then migrate distally. A recent in vitro study observed that flow reduction within side branches was higher in cases of tight mesh or overlapping stents[24]; however, previous preclinical studies[9,22,28] did not observe side branch occlusion in rabbit models even when small branches, similar in diameter to human perforating arteries, were covered by 1 or multiple overlapped

In our study, as well as in the article by Szikora et al,[6] we did not report other side branch occlusions (anterior choroidal artery, posterior inferior cerebellar artery, superior cerebellar artery, posterior communicating artery, anterior spinal artery, ACA, or MCA). Brinjikji et al[21] reported an occlusion rate of 27% in cases of posterior communicating artery coverage without neurologic deficit. In all these cases, the P1 segment was patent on the initial angiogram.

In our series, slow flow was observed immediately after PED implantation in all cases of ACA coverage and in 3 of 5 cases of M2-MCA coverage. Most interesting, territorial infarction resulting in a transient aphasia was observed in only 1 case of M2-MCA slow flow.

In our series, 16.2% of collateral branches covered by the PED had arterial narrowing on the 12-month follow-up angiogram. In no case was it associated with a neurologic deficit. All cases of ACA coverage presented with delayed arterial narrowing. All patients had a patent anterior communicating artery and contralateral A1

PEDs. In our study, the number of overlapped PEDs implanted covering the lenticulostriate arteries was not a predictor of perforator infarction. Patency of perforating arteries in human clinical studies is rarely reported in the literature. van Rooij and Sluzewski[29] observed a case of perforator infarction in the territory of the lenticulostriate arteries covered by the flow diverter. Phillips et al[30] reported 3 cases of perforator infarction in the vertebrobasilar territory. Overall, the risk of occlusion of perforating arteries appears low, assuming an effective antiplatelet therapy.

Parent Artery Flow Modification
We did not observe any cases of delayed intraparenchymal hemorrhage,[17] but we reported 2 cases of reperfusion cerebral syndrome. In both cases, the patients were older than 75 years (78 and 82 years of age) and the aneurysms treated were large (13 and 15 mm) and involved a tortuous carotid artery. This syndrome has been described as a minor manifestation of the classic cerebral hyperperfusion syndrome.[31] This syndrome is a rare but well-described phenomenon occurring after a carotid endarterectomy, angioplasty, stent placement,[32] or aneurysm clipping.[33-35] It is related to a sudden increase in regional cerebral blood flow secondary to loss of cerebrovascular autoregulation.[31,32,36] The symptoms can range from headache and neurologic deficit (without any ischemic lesion on MR imaging) to intracerebral hemorrhage.[37] Several risk factors have been reported, including hypertension, diabetes, age older than 75 years, recent carotid surgery/intervention within 3 months, high-grade ipsilateral or contralateral stenosis, female sex, vascular malformation, and cerebrovascular reactivity.[32]

Recently, Chiu and Wenderoth[38] reported a case of hyperperfusion syndrome following flow-diverter treatment of a large paraclinoid aneurysm for which the clinical presentation and MR imaging findings were similar to those of our patients except that in this case, there was hyperperfusion on CT perfusion. In our study, there was no evidence of hyperperfusion on PWI-MR imaging; hence, we have to use the term "reperfusion syndrome".[31,39] Murakami et al[40] hypothesized that before treatment, giant aneurysms are responsible for the reduction in blood flow through the distal parent artery and might cause relative hypoperfusion in the ipsilateral cerebral cortex. Following aneurysm clipping, blood flow through the parent vessel suddenly increases, exceeding cerebral autoregulatory abilities, leading to cerebral hyperperfusion. One may hypothesize a similar phenomenon in aneurysms treated by surgical clipping or flow diverters, in which the stent redirects most of the blood flow into the parent artery. These data were reported in a computational fluid dynamics model,[41] in which an increase in blood flow was observed in the parent artery after PED placement. As in previous studies,[17,42] we hypothesized that these hemodynamic modifications after flow diversion could lead to delayed intraparenchymal hemorrhage.

Two patients died in unclear circumstances, and we strongly suspect delayed aneurysm rupture. These fatal events occurred a few days or weeks following flow diversion. Similar events have already been reported for the PED and Silk flow diverter (Balt Extrusion, Montmorency, France).[14-16,43,44] The reason for delayed aneurysm rupture is still uncertain. In computational models, Cebral et al[14] observed, after the placement of a flow diverter,

an increase of intra-aneurysmal pressure, which could lead to rupture, especially in cases of giant aneurysms, tortuous vessels, or pre-existing proximal parent artery stenosis. Most of these ruptures have been described in cases of large or giant aneurysms treated by flow diverters alone. Hence, some authors recommend the combined use of coils[15,43] for large and giant aneurysms and suggest a modest reduction of systemic blood pressure in the postoperative period.

Limitations
A limitation of this study is the relatively small number of aneurysms treated and side branches covered by the device, which can diminish the differences between groups. Thus, we did not perform any statistical analyses. Another limitation is the follow-up period, which may be too short to assess the long-term patency of side branches, especially those with narrowing on the midterm follow-up.

CONCLUSIONS
After PED placement, reperfusion syndrome was observed in 3.4%; slow flow within side branches, in 19.1%; and territorial infarction, in 3.4%. Delayed occlusion of the ophthalmic arteries and delayed narrowing of arteries covered by the PED were observed in 5.9% and 16.2%, respectively. No permanent morbidity or death was related to side branch coverage at midterm follow-up.

REFERENCES
1. Deutschmann HA, Wehrschuetz M, Augustin M, et al. **Long-term follow-up after treatment of intracranial aneurysms with the Pipeline embolization device: results from a single center.** *AJNR Am J Neuroradiol* 2012;33:481–86
2. Fischer S, Vajda Z, Aguilar Perez M, et al. **Pipeline embolization device (PED) for neurovascular reconstruction: initial experience in the treatment of 101 intracranial aneurysms and dissections.** *Neuroradiology* 2012;54:369–82
3. Lubicz B, Collignon L, Raphaeli G, et al. **Pipeline flow-diverter stent for endovascular treatment of intracranial aneurysms: preliminary experience in 20 patients with 27 aneurysms.** *World Neurosurg* 2011; 76:114–19
4. McAuliffe W, Wenderoth JD. **Immediate and midterm results following treatment of recently ruptured intracranial aneurysms with the Pipeline embolization device.** *AJNR Am J Neuroradiol* 2012;33: 487–93
5. Nelson PK, Lylyk P, Szikora I, et al. **The Pipeline embolization device for the intracranial treatment of aneurysms trial.** *AJNR Am J Neuroradiol* 2011;32:34–40
6. Szikora I, Berentei Z, Kulcsar Z, et al. **Treatment of intracranial aneurysms by functional reconstruction of the parent artery: the Budapest experience with the Pipeline embolization device.** *AJNR Am J Neuroradiol* 2010;31:1139–47
7. Chalouhi N, Tjoumakaris S, Starke RM, et al. **Comparison of flow diversion and coiling in large unruptured intracranial saccular aneurysms.** *Stroke* 2013;44:2150–54
8. Becske T, Kallmes DF, Saatci I, et al. **Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial.** *Radiology* 2013; 267:858–68

9. Kallmes DF, Ding YH, Dai D, et al. **A second-generation, endoluminal, flow-disrupting device for treatment of saccular aneurysms.** *AJNR Am J Neuroradiol* 2009;30:1153–58

10. D'Urso PI, Lanzino G, Cloft HJ, et al. **Flow diversion for intracranial aneurysms: a review.** *Stroke* 2011;42:2363–68

11. Kojima M, Irie K, Fukuda T, et al. **The study of flow diversion effects on aneurysm using multiple Enterprise stents and two flow diverters.** *Asian J Neurosurg* 2012;7:159–65

12. Roszelle BN, Gonzalez LF, Babiker MH, et al. **Flow diverter effect on cerebral aneurysm hemodynamics: an in vitro comparison of telescoping stents and the Pipeline.** *Neuroradiology* 2013;55:751–58

13. Shobayashi Y, Tateshima S, Kakizaki R, et al. **Intra-aneurysmal hemodynamic alterations by a self-expandable intracranial stent and flow diversion stent: high intra-aneurysmal pressure remains regardless of flow velocity reduction.** *J Neurointerv Surg* 2013;5(suppl 3):iii38–42

14. Cebral JR, Mut F, Raschi M, et al. **Aneurysm rupture following treatment with flow-diverting stents: computational hemodynamics analysis of treatment.** *AJNR Am J Neuroradiol* 2011;32:27–33

15. Hampton T, Walsh D, Tolias C, et al. **Mural destabilization after aneurysm treatment with a flow-diverting device: a report of two cases.** *J Neurointerv Surg* 2011;3:167–71

16. Siddiqui AH, Kan P, Abla AA, et al. **Complications after treatment with Pipeline embolization for giant distal intracranial aneurysms with or without coil embolization.** *Neurosurgery* 2012;71:E509–13

17. Velat GJ, Fargen KM, Lawson MF, et al. **Delayed intraparenchymal hemorrhage following Pipeline embolization device treatment for a giant recanalized ophthalmic aneurysm.** *J Neurointerv Surg* 2012;4:e24

18. Puffer RC, Kallmes DF, Cloft HJ, et al. **Patency of the ophthalmic artery after flow diversion treatment of paraclinoid aneurysms.** *J Neurosurg* 2012;116:892–96

19. Lee DH, Arat A, Morsi H, et al. **Dual antiplatelet therapy monitoring for neurointerventional procedures using a point-of-care platelet function test: a single-center experience.** *AJNR Am J Neuroradiol* 2008;29:1389–94

20. Yu SC, Kwok CK, Cheng PW, et al. **Intracranial aneurysms: midterm outcome of Pipeline embolization device–a prospective study in 143 patients with 178 aneurysms.** *Radiology* 2012;265:893–901

21. Brinjikji W, Lanzino G, Cloft HJ, et al. **Patency of the posterior communicating artery after flow diversion treatment of internal carotid artery aneurysms.** *Clin Neurol Neurosurg* 2014;120:84–88

22. Dai D, Ding YH, Kadirvel R, et al. **Patency of branches after coverage with multiple telescoping flow-diverter devices: an in vivo study in rabbits.** *AJNR Am J Neuroradiol* 2012;33:171–74

23. Lopes DK, Johnson AK. **Evaluation of cerebral artery perforators and the Pipeline embolization device using optical coherence tomography.** *J Neurointerv Surg* 2012;4:291–94

24. Roszelle BN, Babiker MH, Hafner W, et al. **In vitro and in silico study of intracranial stent treatments for cerebral aneurysms: effects on perforating vessel flows.** *J Neurointerv Surg* 2013;5:354–60

25. Appanaboyina S, Mut F, Löhner R, et al. **Computational modelling of blood flow in side arterial branches after stenting of cerebral aneurysms.** *Int J Comut Fluid Dyn* 2008;22:669–76

26. Sadasivan C, Cesar L, Seong J, et al. **Treatment of rabbit elastase-induced aneurysm models by flow diverters: development of quantifiable indexes of device performance using digital subtraction angiography.** *IEEE Trans Med Imaging* 2009;28:1117–25

27. Djulejić V, Marinkovic S, Malikovic A, et al. **Morphometric analysis, region of supply and microanatomy of the lenticulostriate arteries and their clinical significance.** *J Clin Neurosci* 2012;19:1416–21

28. Kallmes DF, Ding YH, Dai D, et al. **A new endoluminal, flow-disrupting device for treatment of saccular aneurysms.** *Stroke* 2007;38:2346–52

29. van Rooij WJ, Sluzewski M. **Perforator infarction after placement of a Pipeline flow-diverting stent for an unruptured A1 aneurysm.** *AJNR Am J Neuroradiol* 2010;31:E43–44

30. Phillips TJ, Wenderoth JD, Phatouros CC, et al. **Safety of the Pipeline embolization device in treatment of posterior circulation aneurysms.** *AJNR Am J Neuroradiol* 2012;33:1225–31

31. Cho AH, Suh DC, Kim GE, et al. **MRI evidence of reperfusion injury associated with neurological deficits after carotid revascularization procedures.** *Eur J Neurol* 2009;16:1066–69

32. Lieb M, Shah U, Hines GL. **Cerebral hyperperfusion syndrome after carotid intervention: a review.** *Cardiol Rev* 2012;20:84–89

33. Kuroki K, Taguchi H, Yukawa O. **Hyperperfusion syndrome after clipping of an unruptured aneurysm: case report.** *Neurol Med Chir (Tokyo)* 2006;46:248–50

34. Maruya J, Nishimaki K, Minakawa T. **Hyperperfusion syndrome after neck clipping of a ruptured aneurysm on a dolichoectatic middle cerebral artery.** *J Stroke Cerebrovasc Dis* 2011;20:260–63

35. Sugino T, Ohtaki M, Wanibuchi M, et al. **Hyperperfusion syndrome after clipping an unruptured cerebral aneurysm: two case reports.** *Neurol Med Chir (Tokyo)* 2010;50:306–09

36. Aubert S, Sellal F, Rouyer O, et al. **Reperfusion syndrome with cerebral vasogenic edema after carotid artery endarterectomy** [in French]. *Rev Neurol (Paris)* 2007;163:840–44

37. Narita S, Aikawa H, Nagata S, et al. **Intraprocedural prediction of hemorrhagic cerebral hyperperfusion syndrome after carotid artery stenting.** *J Stroke Cerebrovasc Dis* 2013;22:615–19

38. Chiu AH, Wenderoth J. **Cerebral hyperperfusion after flow diversion of large intracranial aneurysms.** *J Neurointerv Surg* 2013;5:e48

39. Karapanayiotides T, Meuli R, Devuyst G, et al. **Postcarotid endarterectomy hyperperfusion or reperfusion syndrome.** *Stroke* 2005;36:21–26

40. Murakami H, Inaba M, Nakamura A, et al. **Ipsilateral hyperperfusion after neck clipping of a giant internal carotid artery aneurysm: case report.** *J Neurosurg* 2002;97:1233–36

41. Levitt MR, McGah PM, Aliseda A, et al. **Cerebral aneurysms treated with flow-diverting stents: computational models with intravascular blood flow measurements.** *AJNR Am J Neuroradiol* 2014;35:143–48

42. Cruz JP, Chow M, O'Kelly C, et al. **Delayed ipsilateral parenchymal hemorrhage following flow diversion for the treatment of anterior circulation aneurysms.** *AJNR Am J Neuroradiol* 2012;33:603–08

43. Kulcsár Z, Houdart E, Bonafe A, et al. **Intra-aneurysmal thrombosis as a possible cause of delayed aneurysm rupture after flow-diversion treatment.** *AJNR Am J Neuroradiol* 2011;32:20–25

44. Velat GJ, Fargen KM, Lawson MF, et al. **Delayed intraparenchymal hemorrhage following Pipeline embolization device treatment for a giant recanalized ophthalmic aneurysm.** *J Neurointerv Surg* 2012;4:e24