Predictors of Peri-Ophthalmic Aneurysm Incomplete Occlusion and Visual Symptoms After Treatment with a Pipeline Embolization Device: A Multi-Center Cohort Study

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Research Article

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Abstract

Objective: Peri-ophthalmic aneurysm is a special type of aneurysm. We assessed the relationship between ophthalmic artery (OA) origin and aneurysm and examined the effect of a pipeline embolization device (PED, Covidien/Medtronic) with or without coils on aneurysm occlusion rate and visual outcomes.

Methods: We retrospectively analyzed 194 peri-ophthalmic aneurysms in 189 patients among 1,171 patients treated with a PED in a Chinese post-market multi-center registry study from November 2014 to October 2019. Peri-ophthalmic aneurysms were defined as carotid–ophthalmic segment aneurysms arising from the internal carotid artery dorsal wall at, or distal to, the OA origin, with a superior or superomedial projection. The relationship between OA origin and the aneurysm was classified as follows: Type A, OA originating separate from the aneurysm; Type B, OA originating from the aneurysm neck or dome. Patients with aneurysm were divided into the PED-only group and the PED + coils group according to treatment.

Results: The median follow-up time was 6.8 months (range, 5.3–20.2 months). There were 163 occluded aneurysms (84%) and 31 aneurysms with incomplete occlusion (16%). A multivariate analysis showed that Type B aneurysm was a risk factor for incomplete occlusion in the PED-only group (odds ratio [OR] 4.951, 95% confidence interval [CI] 1.904-12.875, $p = 0.001$). Visual symptoms at final follow up correlated with preoperative visual symptoms (OR 16.005, 95% CI 2.505-102.273, $p = 0.003$).

Conclusions: Type B aneurysm is associated with a lower occlusion rate after PED-only treatment. Patients with preoperative visual symptoms should be treated promptly to avoid permanent visual symptoms.

Introduction

Peri-ophthalmic aneurysms account for 5%–10% of intracranial aneurysms. Peri-ophthalmic aneurysms often involve ophthalmic arteries and may occur in combination with tandem aneurysms. The complication rate of peri-ophthalmic aneurysms remains high, regardless of clipping or stent-assisted embolization treatment[7, 9, 15, 21, 22]. However, a large number of researchers have reported the effectiveness and safety of pipeline embolization devices (PEDs) for the treatment of carotid–ophthalmic aneurysms[7, 9, 15, 21, 22]. Despite this, there are some issues that are rarely considered. On the one hand, little consideration has been given to the prognostic impact of the anatomical relationship between the ophthalmic artery and the aneurysm, on the other hand, different treatment methods, such as PED-only or PED + coils, have not been thoroughly investigated for their effect on aneurysm occlusion rate and visual symptoms. In this study, we retrospectively analyzed peri-ophthalmic aneurysms treated with a PED in the China post-market multi-center registry study (PLUS) to explore risk factors for aneurysm occlusion and visual symptoms.

Methods

Design and Process

We performed a retrospective review using a database of 14 participating Chinese institutions for aneurysms treated with PEDs between November 2014 and October 2019 in the PLUS. The study was a consecutive, real-world cohort registry study. Local institutional review boards or ethics committees approved the study and use of patients' data. All operations were performed with written informed consent from patients.

The inclusion criterion was peri-ophthalmic aneurysm identified as aneurysm of the carotid–ophthalmic segment arising from the dorsal wall of the internal carotid artery (ICA) at, or just distal to, the origin of the ophthalmic artery, with a superior or superomedial projection[15]. Aneurysms were not included if they arose from the ventral or lateral wall of the ICA, the carotid cave, or the cavernous segment. Recurrent, blister, pseudo, dissecting, and fusiform aneurysms were excluded. The relationship between ophthalmic artery origin and aneurysm was categorized according to the classification of Griessenauer et al[10]. Since Type 3 was only observed in two cases, we classified Type 1 as Type A and Type 2 and Type 3 as Type B. Because 36% of patients in this study used adjuvant coils, we divided patients into the PED-only group and the PED + coils group.

Data on patient demographics, clinical characteristics, aneurysm features (side, aneurysm classification, whether or not a combination of tandem aneurysms existed, parent artery diameter, maximum aneurysm diameter, aneurysm neck), treatment characteristics (PED size and PED number, intraoperative and postoperative complications), and follow-up characteristics (follow-up duration, aneurysm occlusion rate, ophthalmic artery fate, modified Rankin Scale [mRS] score, and visual symptoms) were collected.

Follow-up digital subtraction angiography (DSA) was performed 6 months after operation and repeated again between 12 and 36 months. Aneurysm occlusion was classified using the O'Kelly–Marotta (OKM) grading scale[16]. We described ophthalmic artery alterations covered by the PED as follows: 1) no change, 2) diminished flow, 3) occlusion.

Visual symptoms, such as loss of visual field, decreased visual acuity, blurred vision, and amaurosis fugax, were investigated. For patients with preoperative visual symptoms, visual acuity and visual field were examined by an ophthalmologist preoperatively and postoperatively. Visual acuity and visual field tests were also performed for patients who developed new visual symptoms postoperatively. Patients were grouped according to presence or absence of visual symptoms at final follow up.

Perioperative Management

All patients received an antiplatelet regimen that included aspirin (100 or 300 mg/day) and clopidogrel (75 mg/day for 5 days) prior to surgery. Patients who were identified as clopidogrel non-responders received aspirin (100 mg/day) and ticagrelor (90 mg twice/day). All patients demonstrated suppression of optimal platelet activity before PED placement. Board-certified neuro-endovascular surgeons performed all procedures. Intravenous heparin was administered intraoperatively to achieve an activated

clotting time of >250 seconds. Heparin was discontinued after completing the procedure. Patients were administered continuous dual antiplatelet therapy after PED placement, including aspirin (100 mg/day), clopidogrel (75 mg/day), or ticagrelor (90 mg/day) for 6 months. After 6 months, the decision to discontinue clopidogrel or ticagrelor was made according to the results of angiography. Aspirin (100 mg/day) was recommended for life.

Statistical Analysis

Categorical variables are reported as proportions, and continuous variables are reported as mean $\pm$ standard deviation or median and interquartile range, as appropriate. Between groups, variables were compared using the Chi-squared test, the Mann–Whitney U test, or the t-test. Factors related to incomplete aneurysm occlusion were analyzed in the PED-only group and the PED + coils group. A univariate analysis was used to test the following independent factors: age, sex, hypertension, diabetes, smoking, aneurysm features, treatment characteristics, and follow up duration. Factors that were predictive in the univariate analysis ($P < 0.20$) were entered into a multivariate regression analysis. P values of <0.05 were considered statistically significant. Univariate and multivariate analysis the relevant factors of visual symptoms of last follow-up. All statistical analyses were performed using SPSS 25 (IBM Corp., Armonk, NY, USA).

Results

Patient and Aneurysm Characteristics

Patient characteristics are summarized in Table 1. A total of 194 peri-ophthalmic aneurysms in 189 patients were retrospectively identified, 151 patients (79.9%) were female and 38 patients (20.1%) were male. The mean age of patients was 53 ± 9.4 years (range, 19–78 years). Five patients with 10 aneurysms were diagnosed with bilateral peri-ophthalmic aneurysm. Type A aneurysms were present in 130 patients (68.8%), while Type B aneurysms were present in 59 patients (31.2%). There were 55 patients with tandem aneurysms involving other locations. Of all 194 aneurysms, 79 (40.7%) exhibited headache as the clinical manifestation, 1 (0.5%) demonstrated subarachnoid hemorrhage for 40 days, 26 (13.4%) had a chief complaint of visual symptoms, and 88 (45.3%) were incidentally and asymptotically diagnosed. Smoking, hypertension, and diabetes mellitus were reported in 37 (19.6%), 48 (25.4%), and 11 (5.8%) patients, respectively. Parent artery diameter, maximum aneurysm diameter, and aneurysm neck width were 3.96 ± 0.63 mm, 7.49 ± 5.83 mm, and 5.27 ± 2.67 mm, respectively. Of 189 patients, 183 were treated with 1 PED, 5 were treated with 1 PED bilaterally, and 1 was treated with 2 PEDs. The mean PED size was 4.18 ± 0.46 mm. Among patients, 121 had 122 aneurysms treated with a PED-only, while 68 had 72 aneurysms treated with a PED + coils. In these two groups, hypertension was reported in 25 (20.7%) and 23 (17.3%) patients, respectively. Ten patients (8.2%) presented with visual symptoms in the PED-only group, while 16 patients (22.2%) presented with visual symptoms in the PED + coils group. The maximum aneurysm diameter was 5.90 ± 3.81 mm and 10.18 ± 7.46 mm, respectively, in

the PED-only and PED + coils groups. The aneurysm neck width was 4.58 ± 2.11 mm and 6.45 ± 3.07 mm, respectively, in the PED-only and PED + coils groups (Table 1).

Clinical and Imaging Findings

Preoperative mRS scores of 0-2 were available for 188 patients, 1 patient had an mRS score of 4, and a final postoperative follow-up mRS score of 0-2 was available for 189 patients. Complications occurred in 14 patients (7.2%), including intraoperative cerebral hemorrhage in 2 patients (1%), postoperative ischemia in 12 patients (6.2%), and ischemia at final follow up in 4 patients (2.1%). Postoperative ischemia occurred in 11 patients (15.3%) in the PED + coils group and in 1 patient (0.8%) in the PED-only group. A statistically significant difference was observed between the two groups. No significant difference in ischemia at final follow up was observed between the two groups, with 2 cases (1.6%) in the PED + coils group and 2 cases (2.8%) in the PED-only group.

Visual Outcomes

Of 194 aneurysms, 26 aneurysms (13.4%) were associated with visual symptoms as the chief complaint. At final follow up, visual symptoms occurred in 9 aneurysms (4.6%), 6 (66.7%) of which also had preoperative visual symptoms. Visual symptoms improved after operation in 20 aneurysms (76.9%), including 14 in the PED + coils group and 6 in the PED-only group. However, visual symptoms at final follow up were not significantly different between the two groups ($P=0.729$). Three cases of new visual symptoms after operation accounted for 1.7% of the non-visual symptoms group. Visual symptoms at final follow up was not significantly different between the Type A and Type B ($P=0.391$), either in the PED-only group ($P=0.187$) or the PED + coils group ($P=0.851$), (Table 2, Table 5).

Aneurysm Occlusion at Final Follow up

Angiography at final follow up (median, 6.8 months, range, 5.3–20.2) demonstrated OKM D type occlusion in 163 aneurysms (84%) (Table 2), including 96 aneurysms (78.7%) in the PED-only group (72 Type A [Fig. 1] and 24 Type B) and 67 aneurysms (93.1%) in the PED + coils group (49 Type A and 18 Type B) (Table 2, Table 5). Of the 61 Type B aneurysms, the aneurysm occlusion rate was 60% in the PED-only group (24/40) and 85.7% in the PED + coils group (18/21) (Table 5). OKM A-, B-, and C-type occlusion were observed in 31 aneurysms (16%), including 26 in the PED-only group (10 Type A and 16 Type B [Fig. 2]) and 5 in the PED + coils group (2 Type A and 3 Type B [Fig. 3]). The ophthalmic artery was occluded at final follow up in 1 case (0.5%), diminished flow was observed in 12 cases (6.2%), and no flow change was observed in 181 cases (93.3%) (Table 2).

Outcome of the Multivariate Analysis

Only Type B aneurysm was associated with incomplete aneurysm occlusion with a multivariate analysis in the PED-only group (odds ratio [OR] 4.951, 95% confidence interval [CI] 1.904-12.875, $p = 0.001$, Table 3). No factors associated with incomplete aneurysm occlusion were identified in the PED + coils group

(Table 3). Preoperative visual symptom complaints (OR 16.005, 95% CI 2.505-102.273, $p = 0.003$) in the multivariate analysis were predictors of visual symptoms at final follow up (Table 4).

Discussion

In the treatment of peri-ophthalmic aneurysms with PEDs, physicians are most concerned about factors related to aneurysm occlusion and changes in vision. However, the effect of the anatomical relationship between the ophthalmic artery and aneurysm on treatment is poorly studied. We reviewed peri-ophthalmic aneurysms treated in the PLUS study and explored factors that promote aneurysm occlusion and reduce visual symptoms.

Preoperative visual symptoms, preoperative mRS score, maximum aneurysm diameter, and aneurysm neck width in the PED + coils group in this study were more frequent/higher compared with the PED-only group, probably due to significant clinical symptoms produced by the large aneurysm diameter by compression of peripheral vessels, optic nerves, ophthalmic nerves, and trochlear nerves[22]. Previous studies suggest that PED + coils should be used for large wide-necked aneurysms, either to reduce jet flow, increase aneurysm wall protection and reduce the risk of aneurysm re-rupture, or act as a scaffold to fix the PED and prevent long-term PED migration and shortening[14]. Differences in morphology between the two groups may lead to greater selection bias in treatment. In this study, PED + coils treatment was used in 37.1% of patients. To avoid this effect, we analyzed the two treatment methods separately. Lin et al.[14] compared PED-only treatment with PED + coils treatment for intracranial aneurysms with a mean follow up of 7.8 months. They reported 74.7% occlusion in the PED-only group and 93.1% in the PED + coils group. Although only peri-ophthalmic aneurysms were included in our study, with a median follow-up time of 6.8 months, the occlusion rate was 78.7% in the PED-only group and 93.1% in the PED + coils group. A meta-analysis by Touzé et al.[25] examined 913 cases of ophthalmic segment aneurysm. In this meta-analysis, most studies used a PED only with an average follow-up duration of 16.4 months, and the aneurysm occlusion rate reached 85%. In our study, the median follow-up time was 6.8 months, and the total occlusion rate of peri-ophthalmic aneurysms reached 84%. This shows that PED + coils treatment significantly increases aneurysm occlusion rate.

In the present study, the relationship between ophthalmic artery origin and aneurysm was categorized according to the classification of Griessenauer et al.[10]. Since Type 3 only occurred in two cases, we classified Type 1 as Type A and Type 2 and Type 3 as Type B. In a retrospective study by Griessenauer et al.[9] 66 cases of para-ophthalmic aneurysm were followed up for 6 months and 18 months, and the aneurysm occlusion rates were 70.9% and 85.5%, respectively. Among 11 cases of incomplete aneurysm occlusion, ophthalmic arteries originated from the aneurysm body in two cases. It is believed that the ophthalmic artery originating from the aneurysm is an influencing factor for incomplete occlusion. In the PED-only group, the occlusion rate of Type A aneurysms was 87.8%, while the occlusion rate of Type B aneurysms was only 60%. Univariate and multivariate analyses in the PED-only group showed that Type B aneurysm with the ophthalmic artery originating from the neck of the aneurysm was an independent risk factor for incomplete aneurysm occlusion. This result is consistent with the conclusion of

Griessenauer et al.[10] on the importance of the anatomical relationship between the ophthalmic artery and the aneurysm. For aneurysms where the ophthalmic artery originates from the aneurysm body or aneurysm neck, after PED implantation, if the ophthalmic artery still has a sufficient pressure gradient to maintain forward blood flow, sufficient blood flow will be retained in the aneurysm to prevent thrombosis, resulting in an aneurysm that is difficult to occlude[12, 15]. This is similar to why aneurysms are difficult to occlude when a PED is used to treat fetal posterior communicating aneurysm[11, 26]. In our study, the occlusion rate of Type A aneurysm in the PED + coils group was 96.1%, and the occlusion rate of Type B aneurysm was 85.7%, compared with the 60% occlusion rate of Type B aneurysm in the PED-only group, indicating that application of coils increases the occlusion rate of Type B aneurysms. Univariate and multivariate analyses in the PED + coils group did not identify other factors that promote aneurysm occlusion. The long-term effects of coils on the ophthalmic artery and visual symptoms are worth exploring.

Previous reports have shown that with PED treatment of ophthalmic artery segment aneurysms, the preservation rate of the ophthalmic artery is between 68% and 97%[1, 3, 4, 7-9, 15, 17-19, 27]. Moreover, a recent meta-analysis by Touzé et al. suggested an ophthalmic artery preservation rate of 90%[25]. The overall ophthalmic artery preservation rate in this group was 93.3%, 94.3% in the PED-only group, and 91.7% in the PED + coils group. Although ophthalmic arteries with diminished flow and occlusion occurred more frequently in the PED + coils group compared with the PED-only group, there were no significant differences between the two groups.

Previous studies have shown that 16%–40% of patients with para-ophthalmic aneurysms have visual symptoms[5, 13, 20-22]. Among the 194 aneurysms in this group, 26 (13.4%) were associated with visual symptoms as the chief complaint, and 20 (76.9%) were associated with improved visual symptoms postoperatively. In a meta-analysis of ophthalmic segment aneurysms that presented with visual symptoms preoperatively, Sliva et al.[21] reported improvements of 58% and 49% after clipping and embolization, respectively, compared with an improvement of 71% after flow diverter device (FDD) placement. In Sliva's recent study, 15 patients with preoperative visual symptoms had an improvement of 93% after PED implantation[22]. The postoperative visual symptom improvement rate in this group was 76.9%, which is between the range presented Sliva et al.[21, 22] indicating that for patients with preoperative visual symptoms, FDD treatment has obvious advantages compared with other treatment methods. Because visual symptoms are most often caused by the aneurysmal mass effect, clipping may aggravate these symptoms due to optic nerve separation. Traditional embolization with dense coils cannot reduce the compression effect of aneurysms. After FDD implantation, as a thrombus forms within the aneurysm sac, the aneurysm gradually shrinks and compression on surrounding structures is relieved[21, 22, 28].

In our study, three cases of new visual symptoms after surgery accounted for 1.7% of the non-visual symptoms group. In the study of FDD treatment for para-ophthalmic aneurysms that focused on visual symptoms, the proportion of patients with new visual symptoms was less than 5%, but this proportion was higher in studies using specialized ophthalmic examinations[6, 7, 10, 17, 23, 24]. At present, no study

has illustrated that changes in the ophthalmic artery are associated with new visual symptoms in patients. Touzé et al.[24] believed that the ophthalmic artery has abundant external carotid anastomotic branch compensation, and when the origin of the ophthalmic artery is covered by FDD, the ophthalmic artery and the external carotid anastomotic branch need to achieve a new pressure balance. During establishment of this process, if retinal perfusion pressure is reduced, symptoms of amaurosis fugax may be apparent. For Type B aneurysms, dislodged microthrombi also cause emboli in retinal branch arteries after intra-aneurysmal thrombosis, resulting in visual field defects[19, 24].

In this study, although the visual symptom rate at final follow up was 5.6% in the PED + coils group and 4.1% in the PED-only group, there was no significant difference between the two groups. The multivariate analysis showed that the visual symptoms at final follow up had no correlation with changes in the ophthalmic artery, aneurysm type, or treatment method. This is consistent with the conclusion that visual symptoms at final follow up were not related to changes in the ophthalmic artery in a previous study[25]. In our study, 66.7% of patients with visual symptoms at final follow up had preoperative visual symptoms. First, it takes time to recover from the visual symptoms caused by the aneurysmal mass effect. Second, previous studies have suggested that 1 month of onset may be the optimal time for recovery of visual symptoms, since long-term compression may cause difficulty in recovery[2, 28], but the patients in our study all had visual symptoms for more than 2 months. In addition, we did not conduct objective and systematic eye examinations during follow up, thus, there may be certain deviations that affect the final multi-factor analysis results.

Limitations

There are some limitations to this study that should be noted. First, the study was a retrospective, multi-center study, and heterogeneity in operators' surgical preferences cannot be well quantified. Second, patients did not undergo an objective and systematic eye examination during follow up, which may have influenced the final results. We believe a prospective study with a systematic design is required to evaluate the current treatment of para-ophthalmic artery aneurysms with FDDs.

Conclusions

From our results, we conclude that PED-only treatment has a low occlusion rate for Type B aneurysm. Appropriate application of coils could increase the occlusion rate of aneurysms and the incidence of ophthalmic artery occlusion and visual symptoms is low. PED + coils treatment is safe for patients with Type B aneurysms. However, for patients with preoperative visual symptoms, some patients may not achieve relief of symptoms postoperatively. Such patients should be treated in a timely manner to avoid permanent visual symptoms.

Declarations

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Availability of data and material: All the data of this study can be obtained in the article and supplementary materials.

Code availability Not applicable.

Ethics approval: This trial was approved by the Institutional Review Board (IRB) of Beijing Tiantan Hospital Affiliated to Capital Medical University. Ethical review No: KY 2018-098-02.

Consent to participate: This trial was registered with ClinicalTrials.gov identifier: NCT03831672 and waiver of one or more elements of informed consent.

Consent for publication: The authors declare that there is no conflict of interest regarding the publication of this paper.

Author contributions: Conception and design: Xu, Wu. Acquisition of data: Xu, Wu, Luo. Analysis and interpretation of data: Xu, Sun, Luo. Drafting the article: Xu. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: HZ Shi. Statistical analysis: Xu, Shancai Xu. Study supervision: HZ Shi, XJ Yang.

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Characteristic	Total	PED-only	PED + coils	p Value
No. of patients	189	121 (64%)	68 (36%)	
No. of aneurysms	194	122 (62.8%)	72 (37.2%)	
Mean age in yrs (range)	53±9.4 (19-78)	52±9.1 (19-73)	53±9.9 (26-78)	0.462
Sex				0.165
Female	151 (79.9%)	93 (76.9%)	58 (85.3%)	
Male	38 (20.1%)	28 (23.1%)	10 (14.7%)	
Hypertension	48 (25.4%)	25 (20.7%)	23(17.3%)	0.046*
Diabetes	11 (5.8%)	5 (4.1%)	6 (8.8%)	0.207
Smoking	37 (19.6%)	26 (21.5%)	11(16.2%)	0.377
Presenting symptoms				
Headache	79 (40.7%)	51 (41.8%)	28 (38.9%)	0.690
SAH	1 (0.5%)	1 (0.8%)	0 (0%)	0.442
Visual symptoms	26 (13.4%)	10 (8.2%)	16 (22.2%)	0.006*
Asymptomatic	88 (45.3%)	60 (49.2%)	28 (38.9%)	0.164
Type of aneurysm				0.600
Type A	133 (68.6%)	82 (67.2%)	51 (70.8%)	
Type B	61 (31.4%)	40 (32.8%)	21 (29.2%)	
Bilateral	10 (5.2%)	3 (2.5%)	7 (9.7%)	0.027†
Tandem aneurysms	55 (28.4%)	34(27.9%)	21(29.2%)	0.846
Parent artery (SD) (mm)	3.96±0.63	3.94±0.62	3.99±0.65	0.639
Aneurysm				
Diameter (SD) (mm)	7.49±5.83	5.90±3.81	10.18±7.46	0.0001‡
Neck (SD) (mm)	5.27±2.67	4.58±2.11	6.45±3.07	0.0001‡
PED: pipeline embolization device. * Chi-square test. † Mann-Whitney U test. ‡ t-test.				

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TABLE 2. Outcome measures of 189 patients with 194 peri-ophthalmic aneurysms

Characteristic	Total	PED-only	PED + coils	p Value
Size of PED (SD)(mm)	4.18±0.46	4.17±0.46	4.19±0.46	0.806
Number of PEDs	195	123 (63%)	72 (37%)	0.442
Complications				
Hemorrhagic	2 (1%)	0 (0.0%)	2 (2.8%)	0.065
Ischemia	12 (6.2%)	1 (0.8%)	11 (15.3%)	0.0001†
Ischemia of LF	4 (2.1%)	2 (1.6%)	2 (2.8%)	0.591
Visual symptoms of LF	9 (4.6%)	5 (4.1%)	4 (5.6%)	0.729
IPV	20 (10.3%)	6 (3.1%)	14 (7.2%)	0.001†
New visual symptoms	3 (1.5%)	1 (0.5%)	2 (1%)	0.287
Pretreatment mRS				0.036†
0-2	188 (99.5%)	121 (100%)	67 (98.6%)	
3-5	1 (0.5%)	0 (0%)	1 (1.4%)	
mRS at LF				0.442
0-2	189 (100%)	121 (100%)	68 (100%)	
3-5	0(0%)	0(0%)	0(0%)	
Fate of ophthalmic artery				0.498
No flow change	181 (93.3%)	115(94.3%)	66 (91.7%)	
Diminished flow	12 (6.2%)	6 (4.9%)	6 (8.3%)	
Occlusion	1 (0.5%)	1 (0.8%)	0 (0.0%)	
Follow-up occlusion rate				0.008*
Occluded (OKM-D)	163 (84%)	96 (78.7%)	67 (93.1%)	
Incompletely occluded (OKM-A, B, C)	31 (16%)	26 (21.3%)	5 (6.9%)	
LAF months median (range)	6.8(5.3-20.2)	6.9 (5.3-20.2)	6.6 (5.4-16.8)	0.058
PED: pipeline embolization device; LF: last follow up; IPV: improved postoperative vision; LAF: last angiographic follow up. * Chi-square test. † Mann-Whitney U test.				

TABLE 3. Univariate and multivariate analyses of incomplete occlusion in the PED only group and the PED + coils group

Variable	Univariate Analysis*			Multivariate Analysis		
	OR	95%CI	p Value	OR	95%CI	p Value
PED-only group						
Type B aneurysm	4.800	1.922-11.987	0.001	4.951	1.904-12.875	0.001
Tandem aneurysms	1.875	0.751-4.683	0.178	1.650	0.608-4.478	0.326
MDA	1.070	0.969-1.181	0.183	1.096	0.981-1.224	0.104
LAF months (<6.8) †	0.765	0.319-1.834	0.548	1.073	0.408-2.823	0.887
PED + coils group						
Age	0.931	0.849-1.020	0.123	0.952	0.859-1.056	0.352
Type B aneurysm	4.083	0.630-26.466	0.140	4.040	0.566-28.821	0.164
Size of PED	0.217	0.027-1.777	0.155	0.290	0.022-3.866	0.349
LAF months (<6.8) †	0.541	0.085-3.448	0.515	0.952	0.118-7.654	0.963
<p>PED: pipeline embolization device; MDA: maximal diameter of aneurysm; LAF: last angiographic follow up.</p> <p>* Also entered in the univariate analysis but not significant: sex, diabetes, hypertension, smoking, presenting symptoms, maximum aneurysm diameter, aneurysm neck, number of PEDs, complications, fate of ophthalmic artery.</p> <p>† the median follow-up time was 6.8 months.</p>						

TABLE 4. Univariate and multivariate analyses of visual outcomes at final follow up

Variable	Univariate Analysis*			Multivariate Analysis		
	OR	95%CI	p Value	OR	95%CI	p Value
Hypertension	3.983	1.024-15.496	0.046	4.554	0.866-23.944	0.073
Visual symptoms	16.5	3.826-71.157	0.0001	16.005	2.505-102.273	0.003
Asymptomatic	0.141	0.017-1.148	0.067	0.491	0.041-5.825	0.573
LAF months (>6.8) †	3.694	0.748-18.257	0.109	6.386	0.912-44.704	0.062
PED + coils	1.376	0.357-5.301	0.642	1.069	0.214-5.343	0.935
Type B aneurysm	1.796	0.465-6.939	0.395	1.059	0.203-5.512	0.946
Occlusion of aneurysms	0.651	0.129-3.290	0.603	0.717	0.095-5.417	0.748
LAF: last angiographic follow up; PED: pipeline embolization device.						
* Also entered in the univariate analysis but not significant: age, sex, smoking, diabetes, maximum aneurysm diameter, aneurysm neck, size of PED, number of PEDs, complications.						
† the median follow-up time was 6.8 months.						

TABLE 5. Comparison of aneurysm occlusion rate and visual outcomes between Type A and Type B aneurysms

Variable	Type A, n=133	Type B, n=61	p Value
Total VSL	5 (3.8%)	4 (6.6%)	0.391
PED-only	82	40	
Occlusion of aneurysm	72 (87.8%)	24 (60%)	0.0001*
VSL	2 (2.4%)	3 (7.5%)	0.187
PED + coils	51	21	
Occlusion of aneurysm	49 (96.1%)	18 (85.7%)	0.118
VSL	3 (5.8%)	1 (4.7%)	0.851
VSL: visual symptoms at final follow up; PED: pipeline embolization device.			
* Chi-square test.			

Figures

Figure 1

A 58-year-old female presented with headache for 10 years. A: Left internal carotid artery angiogram shows a Type A peri-ophthalmic aneurysm (white arrow) and multiple tandem aneurysms with a cavernous sinus segment (arrowhead and double arrows). The parent artery diameter was 3.5 mm. B-C: The aneurysm was treated with one PED (3.75 × 35 mm) only, and postoperative angiography was performed. D: On 9-month follow-up angiography (three-dimensional reconstruction), the peri-ophthalmic aneurysm was occluded, but the aneurysm located at the cavernous sinus segment was not (arrowhead), and the ophthalmic artery remained patent. E-F: Three-dimensional views and anteroposterior angiogram showing persistent filling of the aneurysm located at the cavernous sinus segment (arrowhead).

Figure 2

A 45-year-old female was admitted to hospital with an intracranial aneurysm accidentally discovered 18 days prior. A: Right internal carotid artery angiogram shows a Type B peri-ophthalmic aneurysm measuring 4.5×3.1 mm with a 2.2-mm neck. The parent artery diameter was 4.0 mm. B: The aneurysm was treated with one PED (4.5×25 mm) only. C: On follow-up angiography (three-dimensional reconstruction) at 3 months, persistent filling of the aneurysm and ophthalmic artery are observed. D: On 15-month follow-up angiography (three-dimensional reconstruction), the aneurysm was not occluded (white arrow), and the ophthalmic artery remained patent. E: On 36-month follow-up angiography (three-dimensional reconstruction), persistent filling of the aneurysm (white arrow) and ophthalmic artery are observed. F: Neointima formed at the neck of the un-occluded aneurysm (white arrow). This shows that continuous blood flow in the ophthalmic artery is an important factor for incomplete aneurysm occlusion.

Figure 3

A 50-year-old female was admitted to hospital with an intracranial aneurysm accidentally discovered 1 week prior. A-B: Left internal carotid artery angiogram (three-dimensional reconstructed [A] and lateral [B] views) shows a peri-ophthalmic aneurysm. The ophthalmic artery originating from the neck of the aneurysm was defined as Type B. The aneurysm measured 18.3×17.4 mm with a 9.68-mm neck. The diameter of the parent artery was 3.4 mm. C: The aneurysm was treated with a PED (4.0×25 mm). D: Postoperative angiography after packing of four coils shows that blood flow in the ophthalmic artery was significantly slowed (white arrow). E: Follow-up cerebral angiography at 5 months shows the neck of the aneurysm still filling and more obvious blood flow in the ophthalmic artery (white arrow). F: On 17-month follow-up angiography, the aneurysm was not occluded (black arrow), and blood flow in the ophthalmic artery was obvious (white arrow).