Evaluation of the safety and efficacy of a Pipeline Flex embolization device for treatment of large, wide-necked intracranial aneurysms

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Abstract

Objective: To investigate the safety and effectiveness of the Pipeline Flex embolization device (PFED) in the treatment of large and wide-necked aneurysms in the internal carotid artery (ICA).

Methods: The clinical data of 78 cases of large and wide-necked aneurysms in the ICA treated with this Pipeline Flex embolization device in Shanghai Hospital of the Second Military Medical University and Southern Hospital of Southern Medical University from February 2017 to June 2018 were retrospectively analyzed.

Results: A total of 66 cases were treated with a Pipeline Flex embolization device, 10 with a pipeline flex embolization device, and 2 with a double tubride stent (10 patients were treated with a pipeline stent-assisted coil embolization in; and 2 patients were treated with two pipeline stents). The patients were followed up for 3 to 18 months (average, 9.25 months). Among them, 63 cases had complete occlusion of the neck of the aneurysm (Raymondl Class I; MRS score 0; 80.8%). Aneurysms recurred in 12 cases (Raymondl Class II; MRS score 1; 15.4%). Delayed ischemic complications were observed in 1 case (MRS score >2; 0.13%). There was 1 case of poor release of stent and 1 case of stent stenosis (0.13%).

Conclusion: The treatment of large, wide-necked aneurysms in the ICA with PFED has a high total occlusion rate and good prognosis was better than coil embolization, but the placement of PFED still has some neurological complications.

Keywords: Pipeline Flex embolization device; vascular reconstruction device; large, wide-necked aneurysms; neurological complications; curative effect.

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Availability of data and material: The folder or data is the property of the hospital and readily available with proper concern but for confidentiality of the patient the folder cannot to release to third party.

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INTRODUCTION

Large, wide-necked intracranial aneurysms are aneurysms with diameters larger than 10 mm and a neck wider than 4 mm. The incidence rate of large, wide-necked aneurysms is about 6%–10% of all intracranial aneurysms. Commonly, large, wide-necked aneurysms are seen in the cavernous and clinoid segments of the internal carotid artery (ICA), the bifurcation of the basilar artery, and the posterior cerebral artery. Clipping of craniotomy is difficult to cure. In recent years, vascular revascularization devices such as pipeline, silk, and surpass mesh stents have been successfully implanted in the treatment of medium and large aneurysms. We here retrospectively analyzed the clinical data of the treatment of giant (large), wide-necked aneurysms of the ICA with a new type of Pipeline Flex embolization device (PFED) from 2017 to 2018, to explore the safety and effectiveness of the PFED.

MATERIALS AND METHODS

Inclusion criteria

Inclusion criteria: 1) Patients with unruptured saccular aneurysm of the ICA (Hunt-Hess score < III grade, Fisher score < 2); 2) Aneurysm neck ≥ 10 mm and maximum diameter of aneurysm ≥ 5 mm; 3) Diameter of the tumor (aneurysm) bearing vessel is 2.0 mm–6.5 mm; 4) Exclusion of patients with definite cobalt chromium alloy and anticoagulant contraindications; and 5) Exclusion of unattached stents in target vessels of recurrent aneurysms.

Patients and general information

A total of 78 patients (22 males and 56 females) aged 20–78 years (mean, 52.3 years) were included in the study. There were 21 cases of hypertension, 6 cases of type II diabetes, 18 cases of oculomotor nerve compression, 19 cases of dyslipidemia, 2 cases of atrial premature beat, and 1 case after tubride (Enterprise) stent treatment. According to the location of the ICA segment aneurysms (28 cases of cavernous sinus segment, 21 cases of clinoid process segment, 18 cases of ophthalmic artery segment, 9 cases of posterior communicating segment, 2 cases of bilateral cavernous sinus segment), the average height of the aneurysm was 12.6 ± 1.92 mm, the average width of the aneurysm neck was 5.8 ± 1.97 mm, and the average ratio of body to neck was 0.46 ± 0.21. In the balloon occlusion test, the range of cerebral blood flow measured by the balloon occlusion experiment combined with single photon emission tomography was 75%–90% in 16 cases, 90%–95% in 37 cases, and 95% in 25 cases.

Embolization technique and treatment process

The clopidogrel (75 mg/d) and enteric-coated aspirin (100 mg/d) were given to patients orally for 3 days. Patients underwent bilateral femoral artery angiography under local anesthesia, and the next BOT test used to assess the affected side of the ICA occlusion after blood flow compensation. After hyperperform balloon occlusion, the compensation of cerebral blood flow measured by SPECT was good, and the BOT test was negative. After general anesthesia, the 6F Chaperon guiding catheter was placed near the petrosal segment of the right ICA. The proper working angle was selected after the 5S DSA 3D rotational angiography of the affected side of the ICA was performed. A 0.029-in endopipe microcatheter was used under the guidance of the microguide wire to superselect the affected middle cerebral artery segment in the road map. (The tip of the microcatheter can be molded for 20 s if necessary.) Then the Pipeline Flex embolization device was imported. We brought the Pipeline stent distal to the tip of the microcatheter, coincidence of the proximal portion of the development guide wire and the distal development label of the microcatheter. We fixed the guide wire and slowly retracted it until the microcatheter overlapped with the distal end of the stent. After fixing the microcatheter, we pushed the delivery guide wire for about 10 mm. We fixed the delivery guide wire and continued to slowly withdraw the microcatheter and completely release the distal end of the stent and increase the metal density at the neck of the aneurysm. We alternately pushed the wire and withdrew the microcatheter. We made the distal marking of the microcatheter coincide with the mark point of the delivery guide wire. Cerebral angiography was performed immediately after complete stent release to observe the change of the pattern of blood flow into the aneurysm. DynaCT reconstruction was performed to assess whether the stent was well-adhered to the artery wall. Three-dimensional reconstruction of the
stent using DynaCT to see if the stent was completely released and no stent stenosis Tirofiban hydrochloride was continuously pumped into the micropump within 24 h of the operation (5–6 mL/h).

Curative effect and prognosis

All patients were followed up for 3–18 months, average of about 9.25 months. Efficacy evaluation: 1) Total occlusion of the neck of the aneurysm; 2) Incomplete occlusion of aneurysm, residual neck of aneurysm; 3) Failure of sent to adhere to the vascular wall when it was opened; and 4) Lack of significant blood flow guidance. Prognosis evaluation: 1) Ischemic complication; 2) Delayed rupture of aneurysm; 3) Transient ischemic attack (TIA); 4) Hemorrhage intracranial; 5) Thrombotic stroke 6. Embolism and thrombosis; 7) Retroperitoneal hemorrhage; and 8) Visual field defect.

Statistical analysis

A 46-year-old female patient was admitted to hospital for 3 days with a headache and binocular vision (A 46-year-old female patient with three days history of headache and visual impairment before hospitalization). She had a history of hypertension and lumbar compression fractures. A physical examination reported the following: lucid, fluent speech, drooping of the right eyelid, normal limb muscle strength, and muscle tension. A magnetic resonance plain scan and contrast-enhanced examination indicated something occupying the right parasellar region; magnetic resonance angiography was performed to facilitate the diagnosis of aneurysm of the right ICA. Digital subtraction angiography (DSA) resulted in the diagnosis of a giant, wide-necked aneurysm in the cavernous segment of the right ICA (Figure 1A and 1B). The size of the aneurysm was determined using three-dimensional reconstruction (Figure 1C) and found to be 14.8 × 11.9 mm. The width of the aneurysm neck was 6.2 mm. After general anesthesia and general heparinization, synchro guide wire and a stent catheter were selected to M3 segment of right middle cerebral artery (to the third segment of the right middle cerebral artery). The Pipeline Flex embolization device was slowly released and allowed to unfold. Postoperative follow-up DSA and 3D reconstruction showed that the Pipeline Flex embolization device adhered to the artery wall well, which delayed imaging of the aneurysm (the way of blood flow in the aneurysm changes, and contrast

Figure 1. (A–G) Images of the treatment process of carotid cavernous segment aneurysms. (A) The anteroposterior position of digital subtraction angiography of the right ICA. (B) Lateral view of digital subtraction angiography of the right ICA. (C) Three-dimensional reconstruction of the aneurysm. (D) Positioning of the Pipeline Flex embolization device. (E) Three-dimensional reconstruction of the Pipeline Flex embolization device. (F) DSA examination after operation, showing that blood is directed to the distal end of the artery and does not pass through the aneurysm. (G) T1-weighted MRI shows a mixed and high signal. (H) Contrast-enhanced MRI in the aneurysm shows thrombosis.
blood flow in the aneurysm changes, and contrast agent is partially retained in the aneurysm) (Figure 1D). One year after the operation, these aneurysms were re-examined using DSA. Blood was directed to the distal end of the artery and did not pass through the aneurysm (Figure 1F). MRI imaging prompted intra-aneurysm thrombosis (Figure 1G and 1H).

RESULTS

Patient follow-up

Follow-up was performed through clinical check-up and radiological imaging with MRI and DSA. A total of 78 patients were examined. Among them, initial follow-up imaging and clinical evaluation was carried out in all patients at 3 to 18 months (mean, 9.25 ± 1.2 months) after the procedure. Here, 66 cases were treated with the Pipeline Flex embolization device alone; 10 patients were treated with a pipeline stent-assisted coil embolization in; and 2 patients were treated with two pipeline stents. Angiography was performed immediately after complete stent release. Changes in the pattern of blood flow injection into the aneurysm were observed. Intra-aneurysm contrast agent retention and Dyna CT reconstruction showed that the pipeline stent was well adhered to the artery wall. Total occlusion of the neck of the aneurysm was observed in 67 patients, (Raymond grade I; mRS score 0; 85.9%). Recurrence of the aneurysm due to the residual neck of the aneurysm took place in 8 patients (Raymond grade II; mRS score 1; 10.3%). Delayed ischemia was observed in 1 patient (mRS score >2; 0.13%). The stent failed to adhere to the vascular wall in 1 patient. Mild stent stenosis was observed in 1 patient.

Side effects and complications

Table 1 compares the serious neurological adverse events in the Pipeline Flex embolization device group, giving the cumulative incidence at 180 days, 1 year, and 540 days. Results of the analysis of the data from our two centers indicate that Pipeline Flex embolization device can cause such neurological complications as hemorrhagic complications and ischemic complication. We compared these three time nodes, showing the increased probability of ischemic events than hemorrhagic events (7.7% vs. 6.4%), especially for the rate of ischemic stroke (2.6% increase to 6.4%), showing a correlation between patients who failed to take aspirin on time.

Table 1 Neurological complication of the Pipeline Flex embolization device at 180 to 540 days.

| Complications                      | 180 days | 1 year | 540 days |
|-----------------------------------|----------|--------|----------|
| Number of patients                | 9 (11.5%)| 13 (16.7%)| 15 (19.2%)|
| Headache with dizziness           | 4 (5.1%)| 5 (6.4%)| 5 (6.4%)|
| Intracranial hemorrhage           | 3 (3.8%)| 3 (3.8%)| 4 (5.1%)|
| Ischemic stroke                   | 2 (2.6%)| 4 (5.1%)| 5 (6.4%)|
| Cerebral hematoma                 | 0 (0.0%)| 0 (0.0%)| 1 (0.13%)|
| Thrombotic stroke                 | 0 (0.0%)| 1 (0.13%)| 1 (0.13%)|

DISCUSSION

The Pipeline Flex embolization device (PFED) was a major breakthrough in endovascular treatment of large, wide-necked aneurysms. It reflects the philosophy of treatment from aneurysm embolism to vascular reconstruction. It differs from the traditional endovascular therapy. PFED can provide a physiologically appropriate treatment for aneurysms. It is the only clinical treatment for giant aneurysms of the internal carotid artery approved by the Food and Drug Administration (FDA) (in the United States). Changes in hemodynamics of aneurysms through the dense meshwork structure of stents (1,2), reduction of blood flow into the aneurysm sac, and stillness of local blood flow, all promote the formation of stable aneurysm thrombosis and endothelialization in the neck of the aneurysm. Due to the existence of a difference in pressure between artery-bearing aneurysms and the branch vessels, the branch vessels can be kept unobstructed after operation, which prevents local cerebral infarction caused by occlusion of perforating vessels. This can help achieve the optimal treatment of large intracranial aneurysms.

The close mesh structure of pipeline can reduce the oscillatory wall shear stress and improve vascular endothelial remodeling. It also has good adherence to the wall and high occlusive rate of aneurysms in the early stage of treatment. In one study based on the rat aneurysm model by Aquarius et al. (3), the average number of malapposed struts was lower for the occluded aneurysm group (4.4000±0.0021.9) than in the nonoccluded aneurysm group (7.7000±0.0022.6, P<0.01). The average distance between malapposed struts and the parent artery wall was lower for the occluded aneurysm group than for the nonoccluded aneurysm group, showing that wall apposition is more important than pore density for aneurysm occlusion. The study published by King et
al. (4) also showed the prolonged (long time) healing of aneurysms to be related to the parent artery and the blood shunt in the body of the aneurysm. Studies of the use of a Pipeline in an observational registry showed that 85.5% of the aneurysm patients received PFED therapy for 1092 patients (1221 intracranial aneurysms) with 3% patients treated with PFED therapy. The PFED adhered tightly to the vascular wall and hemodynamic changes stabilized.

There is still no clear method of predicting the efficacy of the PFED. There were significant individual differences between occlusion time and occlusion extent of aneurysms. Unlike with the tamponade spring coil placed inside the aneurysm, anticoagulation therapy is usually necessary after PFED placement, and excessive anticoagulant therapy often leads to complications (5,6). Brinjikji et al. (7) Meta-analysis of vascular remodeling devices showed that postoperative subarachnoid hemorrhage and cerebral parenchymal hemorrhage were estimated at 2%–4%. Griessenauer et al. (8) found there to be no significant association between aneurysm occlusion, retreatment, and packing density when cases were divided into high (>22%), moderate (12%–22%), and low (<12%) packing density categories. Aneurysm size remains the most important predictor of aneurysm recanalization and retreatment after stent-assisted coiling. The indications for the use of the PFED are giant, wide-necked aneurysms (9,10). The aneurysm recurrence rate was not closely associated with aneurysm size, so the PFED is safe for this type of aneurysm. This result also shows that the PFED has better therapeutic effects than normal coil embolism. Due to preliminary application of the PFED in clinical treatment, further prospective research on the PFED is essential.

REFERENCES
1. Meng H, Xiang J, Liaw N. The role of hemodynamics in intracranial aneurysm initiation. Int Rev Thromb 2012; 7:40–57.
2. Signorelli F, Sela S, Gesualdo L, et al. Hemodynamic stress, inflammation, and intracranial aneurysm development and rupture: A systematic review. World Neurosurg 2018; 115:234–244.
3. Aquarius R, de Korte A, Smits D, et al. The importance of wall apposition in flow diverters. Neurosurgery 2018: doi:10.1093/neuros/nyy092.
4. King RM, Brooks OW, Langan ET, et al. Communicating malapposition of flow diverters assessed with optical coherence tomography correlates with delayed aneurysm occlusion. J Neurointerv Surg 2017; 10:693–697.
5. Chalouhi N, Zanaty M, Whiting A, et al. Treatment of ruptured intracranial aneurysms with the pipeline embolization device. Neurosurgery 2015; 76:165–172.
6. Song J, Oh S, Kim MJ, et al. Endovascular treatment of ruptured blood blister-like aneurysms with multiple (>3) overlapping Enterprise stents and coiling. Acta Neurochir (Wien) 2016; 158:803–809.
7. Brinjikji W, Murad MH, Lanzino G, et al. Endovascular treatment of intracranial aneurysms with flow diverters. Stroke 2013; 44:442–447.
8. Griessenauer CJ, Adeeb N, Foreman PM, et al. Impact of coil packing density and coiling technique on occlusion rates for aneurysms treated with stent-assisted coil embolization. World Neurosurg 2016; 94:157–166.
9. Huang H, Liu J. Treatment of intracranial aneurysms by blood flow guidance device: Review and prospect of Pipeline decade. Chin J Cerebrovasc Dis 2018; 15:1–3.
10. Chen R, Guo R, Wen D, et al. Entire orifice blocking-assisted microsurgical treatment; Clipping of intracranial giant wide-neck paraclinoid aneurysms. World Neurosurg 2018; 114:e861–e868.