Pipeline—Indications, Patient Selection, and Avoidance of Complications

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The indication for a Pipeline Flex in Japan is internal carotid artery aneurysms proximal to the posterior communicating artery with maximum diameter of more than 10 mm and neck of more than 4 mm. Total coverage of neck and wall apposition to the parent artery are both necessary to obtain total occlusion using a Pipeline. Nevertheless, it is not necessarily technically feasible. It becomes more challenging to appropriately deploy a Pipeline particularly if there are multiple tortuous curvatures adjacent to the aneurysm, wide-neck of more than 8 mm, or discrepancy of more than 2 mm in the proximal and distal artery. There are several reports of delayed aneurysmal rupture following flow diverter treatment for intra-dural extra-large or giant aneurysms. Coil embolization immediately after Pipeline placement is the only way to possibly prevent this fatal complication. Physicians are recommended to begin with a straightforward case by skipping these challenging aneurysms.

Keywords ▶ flow diverter, aneurysm, pipeline

Introduction

In this article, appropriate patient selection and trouble-shooting for the avoidance of complications in using Pipeline Flex (PF) (Medtronic), which is the first flow diverter (FD) approved in Japan, are described.

Indications

In Japan, PF was approved to be used for “internal carotid aneurysms proximal to the posterior communicating artery 10 mm or greater in maximum diameter and 4 mm or greater in neck length.” Thus, it is indicated for internal carotid aneurysms of the parasellar region and those in the cavernous segment alone. It is not indicated for aneurysms at the internal carotid-posterior communicating artery junction or in the posterior circulation. It is also not indicated for aneurysms in the acute phase after rupture or dissecting brain aneurysms. In the training programs in Japan, proctorship under a proctor physician is necessary for treating the first five cases, and the presence of the maker is required for treating the sixth to the 10th cases after proctorship. The physician is certified as a PF operator by completing these 10 cases.

Appropriate Patient Selection

Internal carotid aneurysms that are indications for PF vary widely in the difficulty of placement. Treatment using PF itself is inappropriate for some patients. The difficulty of PF placement is markedly affected by factors including the diameter of the parent vessel, meandering of the parent vessel, aneurysm size, and neck length. Patients appropriate during an early period of PF treatment (about the first five cases), those appropriate for PF treatment after some experience (from about the sixth case), and those inappropriate for PF treatment are explained in connection with these factors.

Diameter of the parent vessel

The diameter of the parent vessel is the most important factor that affects the success in FD therapy. Accurate determination of the vascular diameter is important for the judgment of the appropriateness of FD therapy. The authors always judge the possibility of FD deployment after measuring the diameter of the parent vessel by cerebral angiography (DSA). At present, we use the diameter of the parent vessel...
Fig. 1    Cases in which Pipeline Flex deployment was relatively difficult. (A) In patients with a diameter of the parent vessel exceeding 5 mm, sufficient apposition of Pipeline Flex to the vessel cannot be obtained. (B) In patients with a 2 mm or greater difference in diameter of the parent vessel between the proximal (arrowhead) and distal (arrow) sides of the aneurysm, the telescoping technique to connect vessels different in size is necessary. (C) Patients in whom the neck length (dotted line) is greater than 8 mm. This patient, in whom the neck length was 19.6 mm, was excluded from proctor cases (provided by Dr. Fujinaka, T. of Osaka National Hospital). (D) Patients with multiple sites of marked meandering in the intended area of device deployment. This patient had 2 aneurysms in the cavernous segment, and the placement of Pipeline Flex at 2 markedly meandering areas was necessary for their treatment. Since this procedure was relatively difficult, the patient was excluded from proctor cases (provided by Fujinaka T. of Osaka National Hospital).

Fig. 2    Measurement of the diameter of the parent vessel flattened near the aneurysm. (A) Internal carotid aneurysm in the cavernous segment. In a 3D-DSA volume rendering image, the diameters of the distal (arrow) and proximal (arrowhead) parts of the parent vessel measured 3.50 mm and 4.40 mm, respectively. (B) On observation of a cross-section perpendicular to the vascular axis by 3D-DSA, since the distal side of the vessel (A, arrow) was flattened with long and short diameters of 5.01 mm and 3.30 mm, respectively, the mean value, i.e., 4.16 mm, was adopted as the diameter of the parent vessel. (C) Since the proximal side (A, arrowhead) was markedly flattened with long and short diameters of 4.37 mm and 2.18 mm, respectively, the mean value, i.e., 3.28 mm, was adopted. 3D-DSA:
Fig. 3  A case with a marked difference in the diameter of the parent vessel between the two sides of the aneurysm. (A) The diameter measured 3.4 mm on the distal side (arrow) and 4.7 mm on the proximal side (arrowhead). (B) The so-called telescoping technique was performed by placing Pipeline Flex 4.0 mm × 25 mm (solid line) on the distal side and Pipeline Flex 5.0 mm × 25 mm (dotted line) on the proximal side.

Fig. 4  A case with multiple segments of meandering in the intended area of deployment of Pipeline Flex. (A) A giant aneurysm in the cavernous segment of the right internal carotid artery. There are two sites of marked meandering (arrows) in the intended area of placement of Pipeline Flex (dotted line). (B–E) Pipeline Flex 4.50 mm × 35 mm was placed from the distal side. Navien (arrow) was brought as close to the site of deployment of Pipeline as possible and descended to the proximal side gradually with the progression of deployment. (F) Corb beam CT image after placement.
Ishii A and Oishi H measured by CT angiography (CTA) as a reference. Also, as measurement of the vascular diameter by 3D-DSA is not necessarily accurate, we also measure it by conventional 2D-DSA without exception.

If there is a part with a vascular diameter markedly exceeding 5 mm at the intended site of deployment, treatment using PF is impossible. While the largest PF 5 mm in diameter can be dilated to about 5.25 mm, we exclude aneurysms 5.3 mm or greater in diameter measured by 2D-DSA from indications (Fig. 1). However, the parent vessel is often flattened near the aneurysm, and, in such a case, the mean of the long and short diameters is adopted as the diameter (Fig. 2). If the mean diameter is 5 mm or less, treatment using PF is possible. If the diameter of the parent vessel differs markedly between the proximal and distal sides of the aneurysm, it is necessary to use PFs different in size for the proximal and distal sides, and they must be connected by the so-called telescoping technique (Fig. 3). Treatment of such cases should be avoided in an early period. The authors employ the telescoping technique if the difference in the vascular diameter is 2 mm or greater.

**Meandering of the parent vessel**

Along with PF, Navien (Medtronic), which is a distal access catheter, was approved to be used for PF deployment in tortuous vessels. Therefore, guiding PF via the meandering vessel on the proximal side per se is relatively easy. However, if there are multiple large curves at the intended site of deployment, appropriate placement of FD is difficult (Figs. 1 and 4). “Appropriate placement” means placement with complete apposition to the vascular wall, and it is relatively difficult to achieve apposition at multiple curves. It is necessary to guide Navien to a site immediately before the most distal
part of meandering, achieve apposition to the meandering vessel, descend Navien to a site immediately before the next part of meandering, and deploy it (Fig. 4). Since manipulation of Navien may cause marked shortening of PF, the procedure should be avoided in an early period if there are multiple curves at the intended site of deployment.

**Neck length**

A very long neck not only makes the neck bridging manipulation that guides the micro catheter Marksman (Medtronic) to distal parts of the parent vessel difficult but also makes deployment of PF itself extremely difficult. Particularly, if the neck diameter is greater than 8 mm, the stent length may change markedly depending on the porosity of PF at the neck portion. Usually, as the stent length is at the neck portion, the telescoping technique often becomes eventually necessary. Also, as PF is deployed basically by being pushed out, it may protrude markedly into the aneurysm if the neck length exceeds 8 mm, and experience is needed for its control (Fig. 5). Treatment of aneurysms with a neck length exceeding 8 mm should be avoided in an early period and be attempted after having gained some experience.

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**Fig. 6** A case with difficulty in placing Pipeline due to mis-selection of the size. (A) Since the vascular diameter at the intended area of placement measured 3.36 mm at the minimum and 4.49 mm at the maximum by 3D-DSA, Pipeline Classic 4.25 mm × 16 mm was selected. (B) Since maldeployment occurred at the siphon, Pipeline was recovered. (C) Measurement by 2D-DSA showed minimum and maximum diameters of 3.18 mm and 4.01 mm, respectively. Pipeline Classic 3.75 mm × 18 mm was newly selected. (D) Satisfactory apposition could be obtained without maldeployment at the siphon.
Giant intradural aneurysms

In intradural aneurysms exceeding 15 mm in maximum diameter, delayed rupture after PF deployment has been reported. Rupture of an aneurysm under dual antiplatelet therapy is fatal. The concomitant use of a coil after deployment of PF is recommended. If a coil is used concomitantly, placement of multiple guiding catheter systems (we use 7 Fr and 5 Fr) in the same vessel is necessary to avoid interference between the catheter for Pipeline deployment and the one for coil embolization. Since this slightly complicates the system, it is safe to avoid the procedure in a few initial cases performed under proctorship. Since coil embolization after PF deployment itself is very easy, the procedure can be performed readily after the operator has become accustomed to PF.

As observed above, in an early period of proctorship (the first few cases), the procedure is recommended to be performed when (1) the difference in the diameter of the parent vessel is 1 mm or less; (2) the diameter of the parent vessel is 5 mm or less; (3) there is 1 curve in the intended site of deployment; (4) the neck length is 8 mm or less, and (5) the lesion is 10 mm–15 mm in diameter and located in the parasellar or cavernous segment of the internal carotid artery. PF treatment is impossible in patients with a part 5.3 mm or greater in diameter in the intended site of deployment. Otherwise, PF treatment is possible but should be attempted after the operator has become accustomed to PF.

Avoidance of Complications

Maldeployment

Maldeployment of PF is the problem most often encountered in an early period of FD therapy. It is caused occasionally by problems with the vessel to be treated such as marked tortuosity and flattening of the parent vessel but more often by the inexperience of the operator. Many problems can be avoided once the operator becomes able to perform the basic
two-hand manipulation of "positioning the microcatheter in the center of the vessel with the left hand and deploying the stent by pushing it with the right hand." Particularly, as PF, even if maldeployed, can be withdrawn into the catheter and deployed again, maldeployment markedly decreased compared with Pipeline Classic. Another cause of maldeployment is mis-selection of the stent diameter. If a stent with a diameter markedly larger than the parent vessel is selected, its deployment is extremely difficult (Fig. 6). An excessive stent length also makes deployment difficult. If the parent vessel is very tortuous, many problems can be solved by properly adjusting the position of Navien during deployment.

**Malapposition**

If malapposition is confirmed after deployment, the stent can be dilated to an extent by first passing a guidewire through the microcatheter in the stent and then stimulating the stent from inside by shaking the microcatheter. This is called "massaging." If the stent still fails to dilate, the vessel is directly dilated by exchanging the microcatheter for a balloon catheter using a 300-cm guide wire. The authors use Hyperform 7 mm × 7 mm (Medtronic) or Sceptor XC 4 × 10 (Terumo) (diameter at maximum dilation: 5.9 mm).

**Stent shortening**

The proximal or distal end of the deployed PF may slip into the aneurysm due to shortening of the stent. This may occur due to the massaging manipulation described above or vasodilation. Since the proximal end of the stent may also be markedly shortened in re-guiding the microcatheter to a more distal position after PF deployment because of the ledge between the microcatheter and delivery wire, caution is necessary. If the end of PF falls into the aneurysm, the only solution is to catch the true lumen in the stent again and performing the telescoping technique, but this is very difficult (Fig. 7). It must be remembered that PF can shorten readily even after deployment.

**Thromboembolism**

If FD is deployed properly under dual antiplatelet therapy (aspirin 100 mg and clopidogrel 75 mg), thromboembolism occurs rarely. Even if the patient is suspected to be unresponsive to 1 drug, the procedure is performed as scheduled if the other drug is effective. However, if the patient is suspected to be unresponsive to both drugs, caution is necessary. In such patients, the authors administer aspirin or clopidogrel in twice the conventional dose. Even when the antiplatelet drugs are sufficiently effective, branch occlusion may occur if there is a branch in the area of malapposition of FD. Also, if FD covers the posterior communicating or anterior cerebral artery with a very rich collateral blood flow, the antegrade flow may immediately disappear and change to a retrograde flow. In such a situation, the authors perform general heparinization for about 1 week.

**Rupture of aneurysm after FD deployment**

A maximum diameter of 15 mm or greater, jet flow after FD deployment, and symptomatic aneurysm (neurological symptoms) have been proposed as risk factors of rupture after deployment.\(^1\) The cases that the authors experienced in the Pipeline Classic trial had all these risk factors.\(^1\)
Intraparenchymal hemorrhage

Hyperperfusion syndrome and overdosing of antiplatelet medication after FD deployment have been suggested as causes of intraparenchymal hemorrhage, but the true causes are unclear. The authors have experienced asymptomatic intraparenchymal hemorrhage considered to be due to overdosing of antiplatelet drugs for microembolism after FD deployment on the 5th day after PF deployment (Fig. 9). Appropriate judgment of the effectiveness of antiplatelet drugs is important also for preventing such overdosing.

Exacerbation of cranial nerve compression symptoms

In the process of thrombosation of aneurysm after FD deployment, new cranial nerve compression symptoms may
appear, or existing neurological symptoms may be temporarily exacerbated. Also, symptoms such as headache and ocular pain may appear. These are considered to be symptoms of inflammation around the aneurysm in the process of thrombus formation, and they respond markedly to steroid administration. The authors administer prednisolone at an initial dose of 60 mg (about 1 mg/kg of body weight) and taper it off over 2–3 months (Fig. 9).

## Conclusion

The greatest characteristic of FD therapy is its excellent radicalness, but the therapy has a strong all-or-none nature as inappropriate deployment immediately leads to complications such as occlusion of the parent vessel and thromboembolism. This is its notable difference compared with coil embolization, which does not cause complications even if it proves insufficient. We would like to emphasize the importance of appropriate patient selection again, particularly, in early cases of treatment using PF.

## Disclosure Statement

The first author, Akira Ishii has been provided with a research fund and devices for animal experiments concerning delayed rupture after deployment of Pipeline from Medtronic. The COI to be disclosed by the co-author concerning the present paper is that he has been paid 1 million yen or more annually from Medtronic Japan for the time and effort required for attending conferences (presentations) and 2 million yen or more annually from Medtronic Japan as a scholarship donation to an endowed chair.

## References