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Treatment of Wide-Neck Intracranial Aneurysm: Current Concepts and Endovascular Approach

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ABSTRACT

A wide-neck aneurysm, described as an aneurysm with a neck of ≥4 mm or a dome-to-neck ratio of <2, requires more advanced endovascular treatment than a narrow-neck aneurysm. Stent-assisted coiling (SAC) was the sole endovascular approach for wide-neck cerebral aneurysms, which were difficult to treat surgically or by embolization. More advanced endovascular approaches have since been developed in recent years, namely the flow diverter (FD) as an endovascular treatment for wide-neck cerebral aneurysms with an endoluminal reconstruction approach. Both techniques have advantages and disadvantages that must be studied further to develop a wide-neck cerebral aneurysm therapy. Therefore, based on the current literature, this article intends to review the differences in the efficacy and complications of SAC and FD for wide-neck aneurysm therapy.

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INTRODUCTION

A cerebral aneurysm is a cerebral blood vessel wall protrusion caused by hemodynamic stress, endothelial dysfunction, or inflammatory processes. A wide-neck aneurysm with a neck size of ≥4 mm or a doom-to-neck ratio of >2 requires more sophisticated endovascular approaches than its narrow-neck counterpart. Special attention is needed for both wide-neck aneurysms and giant aneurysms. When left untreated, the risk of rupture for lesions found in the intradural anterior cerebral circulation with internal carotid artery distribution can increase by 14.5% to 40% within the next five years, depending on the site. Untreated aneurysms, therefore, pose considerable morbidity and mortality. [1,2,3]

Endovascular treatment for aneurysms has developed in recent years, ranging from coil embolization to flow diverter (FD). Endovascular treatment aims to form a complete or near-complete occlusion of the aneurysm. Studies have demonstrated that endovascular treatment shortens hospitalization time. Essential factors to consider when performing endovascular treatment include the aneurysm's size, location, clinical profile, and operator's skill.[4,5] Stent-assisted coiling (SAC) is an endovascular technique originally performed for wide-neck aneurysms that were difficult to treat with surgery or coil embolization.[6] Over time, FD was developed as an endovascular treatment with an endoluminal reconstruction approach to large unruptured aneurysms.[7] This literature research was carried out by searching medical journals and publications listed in PubMed and Google Scholar.

REVIEW

Definition

Wide-neck aneurysms are categorized into two groups: sidewall and bifurcation. Sidewall aneurysms can develop from a single parent vessel (e.g., cavernous carotid artery) or from the origin of a branch vessel with a smaller caliber than its parent vessel (e.g., posterior communicating artery, ophthalmic artery, superior pituitary artery). Meanwhile, bifurcation aneurysms arise from major vascular bifurcations whose branches are of equal size. Proximally, the bifurcation aneurysm comprises the basilar apex and the tip of the internal carotid artery. Distally, it includes the bifurcation of the middle cerebral artery and the anterior communicating artery.[8]

a) Stent-Assisted Coiling (SAC)

Principle

Previously, it was thought that coil embolization could not be used to treat giant, wide-neck, or fusiform aneurysms. Over time, stents have been designed specifically for intracranial circulation. Until now, these types of aneurysms could be safely managed endovascularly.

SAC is beneficial when dealing with wide-neck aneurysms and other cases with complex vascular anatomy. The main concept of coiling in the treatment of aneurysms is the creation of an intra-aneurysm thrombus. Theoretically, SAC aims to provide a barrier, thus remodeling blood flow to heal the vessel wall. In this healing process, neointima formation and thrombus organization occur, during which regulatory cells migrate from the main arterial wall. The migration of cells from the coiled aneurysm wall and the arterial stem cells allows for continuous endothelialization throughout the lumen of the parent artery. The occlusion in the aneurysm, especially complete occlusion, indicates successful SAC treatment.[9,10]

Indication

The indication for SAC treatment in cerebral aneurysms is generally related to vascular morphology. SAC is indicated in ruptured wide-neck aneurysms, especially if surgery is not an option. Stents can be placed in any aneurysms or dissections in the posterior circulation.[11,12] This is an illustration of the use of SAC in treating aneurysms (Figure 1).

Devices

1. Laser-cut nitinol design

Laser-cut Nitinol is a cylindrical stent made of nickel-titanium alloy (nitinol), with the first laser-cut design used intracranially. This type of stent also has the advantage of better navigating and spreading the arterial curve. These first-generation stents are designed with either an open-cell or a closed-cell configuration.[13]

1.1. Open-cell stents

The open-cell stent is made of several circular rows of nitinol that create a cylindrical network of cells. This stent design covers the aneurysm neck better and induces less vascular alignment than closed-cell stents, although the wall apposition is less optimal than closed-cell designs. Neuroform is an open-cell stent for intracranial use that received FDA approval in 2002.(13) Research conducted by Wang *et al*. demonstrated that neuroforms have a lower rate of intraprocedural complications, such as rupture (2/102) and stent-associated thrombotic events (4/102).[14]

1.2. Closed-cell stents

Closed-cell stents are made of fused nitinol cells that stick together. This kind of stent has low mobility among segments. The closed-cell design has a greater risk of unsatisfactory bending and opening than the open-cell design of a curved artery. But, unlike open-cell stents, closed-cell stents can be reassembled (resheathed) after insertion. Placing the stent in the vessel is important for keeping the microcatheter centered in the artery.[13,15,16] Several closed-cell stents include Solitaire, Enterprise, and Acclino. Stent thrombosis and bleeding are the most common complications in post-stent-assisted coiling of wide-neck aneurysms. Li *et al*. reported that about 6.7% (8/120) had severe complications post-stent-assisted coiling.[17]

2. Braided stents

The braided stent comprises thin, intertwined nitinol wires, forming a cylindrical mesh with closed loops on each end. It confers better visibility, manages over-wall apposition, and increases radial forces. This type of stent is useful in treating aneurysms with wide-neck bifurcations because the neck coverage of the aneurysm can be accelerated by the stent protruding within the curve.[13,16] Several braided nitinol stents used for stent-assisted coiling in wide-neck intracranial aneurysms include the Leo Stent and the LVIS. The LVIS has a similar principle to the flow diverter, which affords better flow diversion and causes delayed thrombosis of the aneurysm, inducing complete occlusion. Wang *et al*. suggested that although direct angiography showed a relatively lower initial RRGS I rate of 47.9% (35/73), progression to total occlusion was excellent, with a high RRGS I rate of 81.7% (49/60) on follow-up imaging. The rate of delayed thrombosis in aneurysm occlusion in the LVIS group was better than in the Neuroform and Enterprise groups. The LVIS group also had a lower recurrence rate than other stents.[13,14]

Technical aspect

SAC is performed under general anesthesia. The stent is inserted with a microcatheter through the femoral artery. After the placement of the stent, the delivery microcatheter is eliminated. A lower-profile microcatheter is inserted through the stent support into the aneurysm, and a coil is positioned until the aneurysm becomes occluded. The stent placement is simulated on a 3D software machine.[11]

There are various stent placement techniques. Generally, the placement of stents is adjusted to the morphology of the aneurysm. These techniques include coil-through, jailing, semi-jailing, stent-jack, coiling-stenting-coiling, waffle-cone configuration, balloon-stenting, horizontal stenting, Y-configuration, X-configuration, and linear configuration techniques. The jailing technique places the microcatheter into the aneurysm sac before stent placement and between the stent and the vessel wall. In the semi-jailing technique, a stent is partially or entirely placed, bridging the neck of the aneurysm, and then coiling is performed. Stents can be removed or permanently installed. In the coil-through technique, the microcatheter is advanced through the end of the stent after the placement. Coil embolization is carried out by placing a stent during vascular transformation or restricting the prolapsed coil loop. Other techniques, such as the coiling-stenting-coiling technique, waffle cone configuration, stent plus multi-catheter or balloon, horizontal stenting, Y-configuration, X-configuration, and linear configuration, are used in cases with unusual aneurysms, difficulties guiding the catheter across the aneurysm's neck, where one stent may not be adequate, or with other types of aneurysms such as ultra-wide neck circumferential or fusiform aneurysms.[14,18]

Throughout the coiling of an aneurysm rupture, heparin is loaded through a pressure bag (1000 U/500 mL saline). Intravenous anticoagulants such as aspirin (500 mg) are given immediately before the stent placement. Following that procedure, the patient is given an anticoagulant such as clopidogrel, with an initial loading dose of 300 mg administered right away, accompanied by a dual anti-platelet therapy (DAPT) consisting of 75 mg of clopidogrel daily for six months and 80 mg of aspirin daily for life. For 48 hours after the procedure, 7500 U of subcutaneous heparin is administered twice daily. Patients with ruptured aneurysms are preloaded for four days with clopidogrel and aspirin and heparinized throughout the procedure.[11]

Complications

The most common complications after SAC are thrombosis and bleeding.[10,17] Since antiplatelet drugs have to be used, special attention should be paid to the placement of intracranial stents in the acute phase of intracranial hemorrhage. Thus, the presence of vascular tortuosity, atherosclerotic disease, and coagulation problems are contraindications to SAC.[12] The study by Chalouhi *et al.* found that 6.8% of complications occurred following SAC, with thromboembolic complications of 4.65% and bleeding complications of 1.2%. The permanent morbidity rate was 2.6%, and the mortality rate was 2.6%.[10]

b) Flow Diverter

Principle

Flow Diverter is a stent-shaped device that has evolved to treat wide-neck aneurysms. Initially, FD was used to treat giant wide-neck internal carotid artery aneurysms that could only be performed surgically with or without bypass. Nowadays, FD can be used for other types of cerebral aneurysms.[19] The mechanism of aneurysm occlusion with an FD is obtained through three main processes: hemodynamic processes, intra-aneurysmal thrombosis, and endothelialization. Flow diverters, therefore, work by constructing the parent blood vessel with a stent and changing the flow leading back to the parent blood vessel. In addition, the vessel where the FD is placed will fuse through the endothelialization process at the aneurysm neck to achieve endoluminal reconstruction, resulting in aneurysm occlusion.[8,20,21]

Indication

Until now, there has been no definitive provision regarding the indications for FD. However, several clinical studies found that FDs were generally performed on giant intracranial aneurysms (fusiform), wide-neck aneurysms, multiple aneurysms with segmental artery disease, and recurrent aneurysms, with the type of unruptured aneurysm.[22,23] FD are mostly performed on unruptured aneurysms due to the possible complication of bleeding, i.e., subarachnoid hemorrhage (SAH), thus necessitating more intensive antiplatelet therapy than other endovascular approaches. Kulcsar et al. found that the use of FD to treat very small, non-coilable ruptured aneurysms conferred complete remodeling of the vessel in the short term, although concerns remain about the risk of recurrent SAH due to antiplatelet therapy while remodeling is ongoing. FD provides an alternative treatment option for this type of aneurysm.[22] This is an illustration of the use of FD in treating aneurysms (Figure 2).

Devices

1. Pipeline Embolization Device (PED)

The Pipeline Embolization Device is a flow diverter fabricated from 25% platinum and 75% nickel–cobalt chromium alloy with a 65–70% porosity. PEDs have different sizes, diameters, and several PED telescopes can be used to change the porosity.[12,24] The multi-center clinical study conducted by Becske *et al.* demonstrated a one-year aneurysm occlusion rate of 86.8% and an ischemic stroke risk of 3.7%.[2]

2. The Silk Flow Diverter

The Silk Flow Diverter is fabricated from 48 strands of nitinol with a porosity of 45–60%.[12,24] A study by Murthy *et al*. found that the one-year aneurysm occlusion rate was 81.8%, with ischemic complications occurring in 10% of patients and a cumulative mortality of 4.9%.[25] Meanwhile, Lubicsz *et al.* saw a complete occlusion in 73% of cases, neck remains in 16% of cases, and an incomplete occlusion in 11% of cases. The rate of medium-term intrastent stenosis was 57%, of which 60% improved or disappeared, 28% were stable, and 12% resulted in vascular occlusion.[26]

3. The Surpass Flow Diverter

The Surpass Flow Diverter is made of a cobalt-chromium alloy, and it has 12 platinum wires to assist radio-opacity with a porosity of nearly 70% over a wide range of diameters.[24] The study by Wakhloo *et al*. demonstrated complete occlusion in 75% of patients who underwent follow-up angiography. Notably, 3.7% of patients developed ischemic stroke within 30 days with intra-parenchymal hemorrhage, whereas 2.5% of patients developed subarachnoid hemorrhage within seven days.[27]

Technical aspect

Patients about to undergo FD receive a daily dose of a dual antiplatelet drug consisting of 75 mg of clopidogrel and 300 mg of aspirin for at least three days before the procedure. Single or multiple antiplatelet drugs are administered to prevent thromboembolic events.[23]

FD is performed under general anesthesia. The stent is inserted with a microcatheter through the unilateral femoral artery via a percutaneous technique. A guiding catheter is then inserted into the relevant carotid or vertebral artery. Next, a microcatheter is guided through the aneurysm using a standard microguide wire, which is converted into a guidewire to guide the stent.

In some cases, the stent is attached directly with the help of microguide wires of standard length. After a guiding catheter is placed into the main artery, intravenous heparin boluses (3000 units) are routinely administered, with the clotting time activated up to twice the initial doses maintained during the procedure. Digital subtraction angiography (DSA) of the main artery is reconstructed in a rotational and three-dimensional manner to assess the angioarchitecture of the aneurysm and stem arteries. A stent is placed into the main artery to bridge the neck of the aneurysm, with a selected stent length measuring 3 mm to 4 mm outside the aneurysm neck in the proximal and distal stem arteries.

The aneurysm is partially coiled using the correct size and length of the removable coil after the FD has been successfully placed, with the tip of the microcatheter stabilized in the aneurysm sac. Flat-panel computed tomography (Dyna-CT) of the brain and stent apposition images are then acquired to evaluate hemodynamic changes of the aneurysm sac, patency of the parent artery and its intracranial branches, as well as the apposition of FDS in postembolization DSA. After the procedure, the patient receives the anticoagulant drugs clopidogrel 75 mg and aspirin 100-325 mg given daily for six months, followed by clopidogrel 75 mg and aspirin 100 mg daily for the next six months.[24,28]

Complications

Given the potential for postoperative parenchymal bleeding and ischemic stroke, not to mention the risk of further morbidity, the safety of FD is a major concern. Some complications that can happen, whether periprocedural or delayed, include side branch occlusion, perforator occlusion, FD thrombosis, intraprocedural vascular perforation, perianeurysmal edema, distant infarction, and delayed bleeding.[24] However, the DIVERSION cohort study in patients with intracranial aneurysms undergoing FD in France demonstrated that endovascular treatment with FD is safe for patients with intracranial aneurysms. At 12 months, post-FD patients with free neurologic deficits had a survival rate of 86.9% and a permanent serious event rate of 5.9%, with a mortality rate of 1.2%. In unruptured aneurysms, the rate of permanent neurologic deficit was 2.3% at 12 months.[29]

Discussion

Endovascular treatment of cerebral aneurysms relies on aneurysm morphology (size, shape, aspect ratio, etc.).[30] SACs and FDs are the most widely used endovascular therapies for wide-neck intracranial aneurysms. While they are generally used for wide-neck aneurysms located in the carotid and MCA, the SAC has the advantage of being able to reach the posterior circulation.[11,12] SAC is also effective for sidewall aneurysms. However, performing SAC in bifurcation aneurysms poses a challenge, as the operator must choose which branch of the vessel to stent, thereby increasing the risk of coil herniation. This was prevented by developing of Y-stent and waffle-cone techniques to increase the effectiveness of SAC in bifurcation aneurysms.[8] SAC also offers another advantage in terms of cost-effectiveness, as it tends to be less expensive than FD. Nevertheless, the disadvantage of SAC in giant aneurysms is the high risk of recurrence, especially if the aneurysm neck is too large. In general, FD is safer for use in large aneurysms.[31] Parkinson *et al*. revealed that >50% of recanalized aneurysms were treated with endovascular coiling.[32] Another notable disadvantage of SAC is its procedure time, which tends to be longer than FD despite having the same difficulty.

Endovascular SAC therapy is typically more frequently used than FD in wide-neck ruptured cerebral aneurysms due to the increased risk of periprocedural bleeding and ischemic complications from using FD in ruptured aneurysms, especially in the acute phase.[33] However, Bechan *et al*. showed the rate of short-term complications from SAC in ruptured aneurysms was ten times higher than in unruptured aneurysms.[11] A higher complication rate was related to ruptured aneurysm treatment. Some operators do not use antiplatelet therapy in patients with SAH due to the possibility of future invasive interventions, ventriculostomies, and the potential for secondary infarction. Thus, stent placement in acutely ruptured aneurysms is generally avoided, and dual antiplatelet therapy is not mandatory.[10]

The effectiveness of SAC can be seen immediately after treatment. In contrast to FD, the complete occlusion of aneurysms occurs after a few months. This is due to the FD's mechanism, which requires time when the parent vessel, where it is placed, fuses through endothelialization to completely occlude the aneurysm.[8,20,21] Guo *et al*. reported satisfactory rates of aneurysm occlusion and reduced intracranial aneurysm recurrence rates in FD without significant differences in safety between FD and coiling.[34] Similarly, Zhang *et al*. revealed that FD provided a higher rate of complete occlusion at a 6-month follow-up, although the value of direct occlusion was like that of SAC. From a safety viewpoint, periprocedural complication rates and the proportion of patients who achieve a comparable outcome were similar.[35] Chalouhi *et al*. also found that FDs provided a significantly higher occlusion rate than coiling in large, unruptured saccular aneurysms, thereby reducing the need for aneurysm re-treatment. There were no significant differences in morbidity or short-term clinical outcomes.[31] These explain the advantages of FD over SAC in the endovascular treatment of giant and wide-neck unruptured aneurysms (Table 1).

CONCLUSION

SACs and FDs have become well-known as endovascular approaches to treating wide-neck cerebral aneurysms. Each approach has advantages and disadvantages, which the operator must consider to treat aneurysms successfully.

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Author contributions
RK, BP, and BR contributed to the conception, design, and acquisition of the study. BR, PW, and KG conducted the data analysis and wrote the manuscript. BP, RK, BR, and AA contributed to manuscript revision. The submitted version of the manuscript was read and approved by all authors

Conflict of Interest
There was no conflict of interest.

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TABLES AND FIGURES

Table 1. Comparison of Stent-Assisted Coil and Flow Diverter

Aspect	Stent-Assisted Coil	Flow Diverter
Indication		
- Location	Carotid, MCA, Posterior	Carotid, MCA
- Size	Small	Small, Large
- Form	Saccular	Saccular
Rupture aneurysm	Yes	No
Procedure Time	Takes more time	Fast
Cost	Less expensive	Expensive
Difficulty	Very difficult	Very difficult
Complication	Thrombosis, Rupture	Thrombosis, Rupture
Effectiveness	Immediately after treatment	After a few months
Durability	Moderate	Good

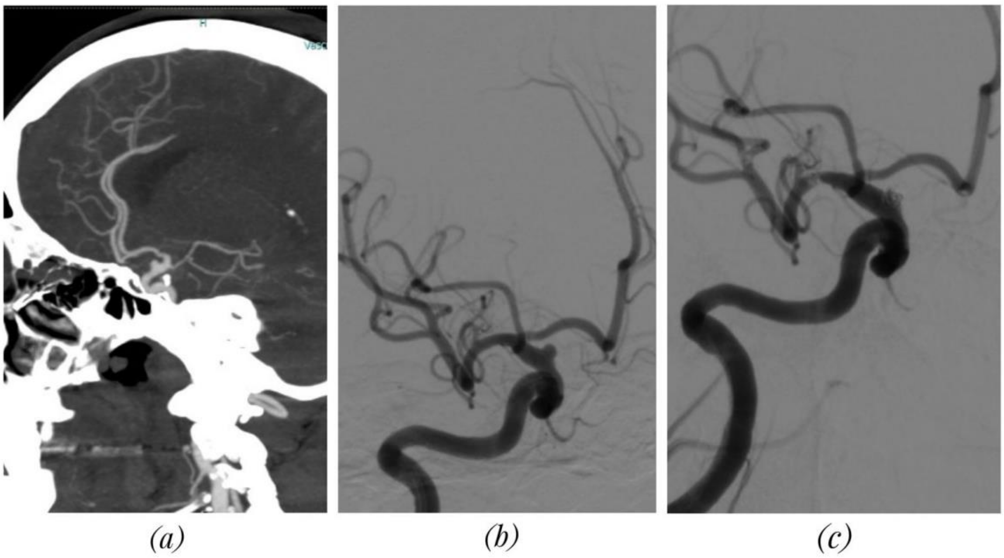
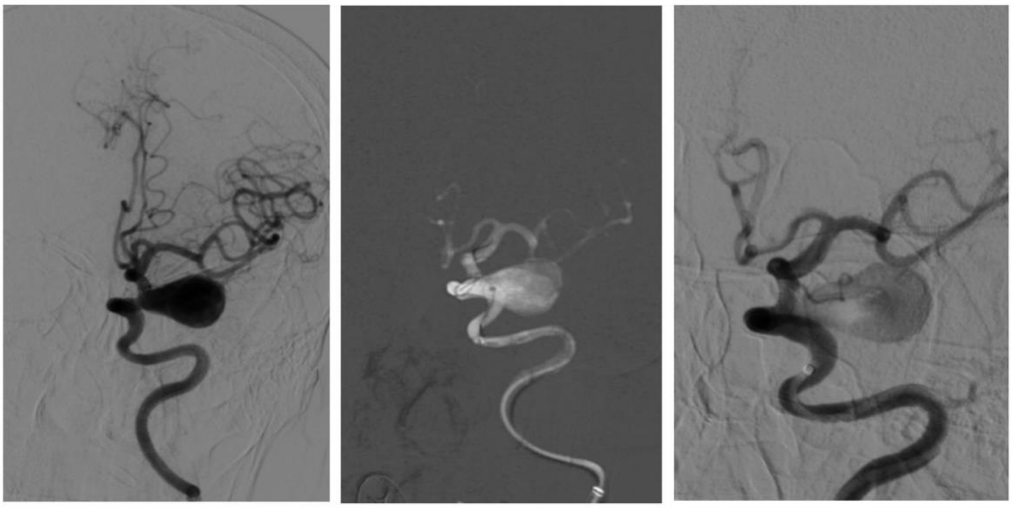


Figure 1: A 52-year-old woman was admitted to the National Brain Center Hospital with complaints of a sudden and severe headache that had been felt for 3 days before admission. After performing a Digital Subtraction Angiography (DSA) of the brain, a saccular aneurysm was found in the supraclinoid segment with a neck size of 3 mm and a dome size of 3.2 mm x 2.7 mm superiorly. (a) CTA images showed an aneurysm (b) DSA images obtained before SAC (c) DSA images obtained after SAC.



(a) (b) (c)

Figure 2: A 61-year-old woman was admitted to the National Brain Center Hospital with a complaint of headache that had been present for the past 10 years. After a Digital Subtraction Angiography (DSA) of the brain, a giant saccular aneurysm in the cavernous was found, with a size of 24.25mm (24.25/width x 16.76/height x 10.9/length mm, neck 6.41mm). (a) DSA images obtained before FD placement (b) CTA images obtained during FD placement (c) DSA images obtained after FD placement.