Development of Endovascular Therapy for Intracranial Aneurysms

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Subarachnoid hemorrhage due to the rupture of intracranial aneurysms is one of the causes of life-threatening strokes. The incidence is about 20 per 100,000 among the Japanese population. An intracranial aneurysm is a bulging, weakened area in the wall of an artery in the brain, resulting in abnormal widening or ballooning. Because the aneurysm has a weakened spot, there is a risk of rupture. Although surgical clipping has been the standard treatment for intracranial aneurysms, the procedure is extremely invasive. Coiling is another recent endovascular therapy that has become an important alternative to clipping because it is considerably less invasive. The procedure uses a catheter percutaneously inserted into an artery under fluoroscopic imaging. When the microcatheter has been inserted into the aneurysm, platinum coils are inserted to occupy the aneurysm cavity, which prevents blood flow into the aneurysm. The simple technique, requiring only one microcatheter, without other assisting devices, is standard. When this simple technique cannot achieve satisfactory occlusion, adjunctive techniques using a balloon or stent are used. Coiling is more advantageous than surgical clipping because it does not involve opening the skull, and hospitalization and recovery times are often shorter than with surgical clipping. In the near future, the introduction of flow diverters may dramatically change the treatment outcome of large, fusiform or complex aneurysms.

Key words: subarachnoid hemorrhage, intracranial aneurysm, endovascular therapy, coiling

Introduction

Subarachnoid hemorrhage (SAH) due to the rupture of intracranial aneurysms is one of the causes of life-threatening strokes. The annual incidence of aneurysmal SAH is about 20 per one hundred thousand in the Japanese population¹⁾. An intracranial aneurysm is a bulging, weakened area in the wall of an artery in the brain, resulting in an abnormal widening or ballooning. Because the aneurysm has a weakened spot, there is a risk of rupture. The overall prevalence of unruptured intracranial aneurysms in the Japanese population is reported to be about 3% and increasing with age²⁾. Patients with ruptured aneurysms have to be treated as soon as possible, preferably within 72 hours after the initial rupture to prevent possible rebleeding. Patients with unruptured aneurysms require accurate risk assessment of potential rup-

ture, death, or disability due to rupture and must be informed of the risks related to various treatment options.

Figure-1 Illustration of coiling of an intracranial aneurysm

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Surgical clipping has been the standard treatment for intracranial aneurysms. However, less invasive treatment is on demand because surgical clipping is so invasive. Endovascular therapy has significantly progressed from the first cerebral angiography developed by the Portuguese neurologist, Egas Moniz, in 1927³⁾. The earliest endovascular therapy of aneurysms is attributed to Serbinenko in 1969, which used detachable balloons to occlude the aneurysm⁴⁾. Since the introduction of detachable coils by Guglielmi, the GDC® (Stryker Neurovascular, Fremont, CA, USA), in 1991^{5) 6)}, coiling has become the first option and mainstay of endovascular therapy for intracranial aneurysms (Figure-1). Coiling was approved in Japan in 1997.

Indications

In the beginning, endovascular therapy was favorably indicated for intracranial aneurysms with surgical access difficulty (posterior circulation, the paraclinoid region of the internal carotid artery), patients with severe systemic comorbidities, and elderly or high-grade SAH patients. In 2002, the International Subarachnoid Aneurysm Trial (ISAT) study group reported that endovascular therapy showed more favorable results in survival free of disability, 1 year after an aneurysmal SAH, than did neurosurgical treatment for patients suitable for either of the treatments⁷⁾. After the ISAT report, endovascular therapy has become an important alternative therapy for which the indications have considerably widened. However, ruptured aneurysms with massive intraparenchymal hematoma, aneurysms with voluminous intra-aneurysmal thrombus, or

aneurysms significantly compressing the optic nerve/brain parenchyma should be excluded from the indications. Three-dimensional (3D) computed tomographic angiography or magnetic resonance angiography could help physicians determine appropriate indications for coiling, but catheter angiography is the best modality to evaluate angioarchitecture most accurately.

1. Development of angiographic suites

Endovascular procedures require clear digital subtraction angiography (DSA) produced with the fluoroscopy technique and contrast medium injection. Angiographic suites have developed from a single-arm with a cathode ray to coupled image intensifiers, to biplanes with flat-panel detectors with enhanced resolution, and magnification (Figure-2), and have the capability of producing 3D-

Figure-3 3D-digital subtraction angiography (DSA) of aneurysm and surrounding vessels

Figure-2 Photograph of an angiographic suite

Figure-4 Virtual stenting image

rotational angiograms (Figure-3), 3D-roadmap capability, aneurysm metric analyses, and virtual stenting ability (Figure-4).

Materials and methods

While local anesthesia is feasible, most patients receive general anesthesia because of improved image quality and safety for intraprocedural aneurysm rupture. Patients receive systemic heparinization with an activated clotting time of greater than 5 minutes throughout the procedure. An antiplatelet medication is given several days before the procedure and continued for at least 1 to 2 months after the procedure. The puncture site is the femoral artery in most patients. When the femoral artery is not available, the brachial or carotid artery is alternatively used. A catheter (a long, thin tube) is inserted into an artery from the puncture site, and then advanced into the artery in the brain under fluoroscopic images. When the microcatheter has been inserted into the aneurysm, coils are then inserted to occlude the aneurysm cavity, which prevents blood flow into the aneurysm. The coils are left in place permanently in the aneurysm.

1. Catheters and guidewires

A guidingcatheter is a catheter that is typically placed in the internal carotid artery or vertebral artery and accommodates a microcatheter and other devices. Preferably it is 6 French in caliber to allow for guidingcatheter angiograms with a microcatheter or other devices in place. A soft tip guidingcatheter is flexible, allowing for positioning in the distal internal carotid or vertebral artery but is less stable. A rigid tip guidingcatheter provides

an adequate platform but increases the risk of vessel damage.

Microcatheters provide access to an aneurysm and are available in various sizes and shapes. Preshaped microcatheters are preferred. When preshaped devices are unavailable, steam shaping of the catheter tip is an option. Two-tipped microcatheters are necessary. The two tips in microcatheters are always 3 cm apart and can be used for recognizing the coil detachment position. Commonly used microcatheters include the Excelsior SL-10[®] (Stryker Neurovascular, Fremont, CA, USA) and the Excelsior 1018[®] (Stryker Neurovascular). The Excelsior 1018 can accommodate 10- and 18-system coils.

Microguidewires are used to navigate the microcatheter to the target aneurysm under the road-mapping image and provide other assistance. Various microguidewires are available that differ in size, degree of stiffness, visibility on fluoroscopy, and have the ability to shape, steer, track, and torque. Intermediate catheters are sized between a guidingcatheter and a microcatheter and provide stable access by functioning as a bridge between the two catheters in a triaxial configuration of the microguidewire and microcatheter, the intermediate catheter, and the guidingcatheter.

2. Coils

Currently, various platinum coils, differing in size, shape, design, stiffness, and detachment system are available (Figure-5A~C). Coils consist of a fine platinum thread looped around a thicker platinum core that is connected to a pusher wire. The detachment mechanisms are electrical, mechanical, or hydraulic. Coil sizes have been traditionally categorized into 10- and 18-system coils, a nomen-

Figure-5 Framing coils: A. 360° shape, B. 3D shape, C. helical shape

clature that originated with the introduction of the first microcatheters used to deploy GDCs[®]. The actual diameters of the 10- and 18-system coils are 0.008 and 0.016 inches, respectively. Although the 10-system is adequate for most aneurysms, the 18-system coils are preferred to frame larger, wide-neck aneurysms. At present, there are several coils on the market that have a larger diameter while maintaining the comparable softness of the 10-system.

Augmentations of platinum coils coated with polyglycolic polylactic acid (PGLA), the Matrix[™] (Stryker Neurovascular), and with hydrogel, the HydroCoil[®]

(MicroVention, Aliso Viejo, CA, USA), were developed to decrease the rate of aneurysm recanalization (Figure-6A, B). They each have shown variable degrees of efficacy⁸⁾⁻¹⁰⁾.

Coiling techniques

1. The simple technique

The simple technique is the gold standard, for which the appropriate aneurysm configurations are a narrow neck and small in size. This technique requires only one microcatheter without any other assisting devices. After the guiding catheter is advanced into the cervical vessels, the microcatheter is inserted into the target aneurysm with the assistance of a microguidewire. The appropriate size and shape of coils are inserted into the aneurysm until the aneurysm is satisfactorily occluded (Figure-7A~C). Coil insertion is carried out by framing, filling, and finishing. Ideally, framing coils extend across the neck to reduce the defective neck area. Filling coils are helical or expanding 3D and are intended to completely fill the aneurysms without compartmentalization. Finishing coils are the softest and are designed to finally pack the aneurysm. Coil insertion is done as tightly as possible, which is the best way to prevent recanalization and regrowth of the aneurysm. The packing density should be more than 20%¹¹⁾.

2. The adjunctive technique

Despite advances in coil shape technology, aneurysms with unfavorable morphology (wide neck, low dome-to-neck ratio) present the risk of coil herniation

Figure-6 Augmentations of platinum coils: A. A PGLA-coated coil, B. A hydrogel-coated coil

Figure-7 Aneurysm occlusion: (A) pretreatment (B) post-treatment DSA image, (C) native image

into the parent artery. Therefore, physicians tend to be less aggressive about achieving high packing densities, leading to higher rates of incomplete occlusions, increased neck remnants, and more recurrence over time. To address these problems, the adjunctive techniques of balloon- and stent-assisted techniques have been developed.

1) The balloon-assisted technique (Figure-8)

A microcatheter capable of delivering coils is positioned inside the aneurysm, and a balloon is then inflated in the parent artery across the neck of the aneurysm, stabilizing the catheter and allowing coil delivery without herniation into the parent artery^{12) 13)}. HyperGlide™, HyperForm™ (Micro Therapeutics, Irvine, CA, USA), and TransForm™ (Stryker Neurovascular), these are all single-lumen balloons that can be used for this purpose^{14) 15)}. The balloon will inflate after an appropriately sized wire is advanced past the catheter tip, which seals the catheter. The Scepter® (Terumo Corporation, Tokyo) has a double-lumen balloon that allows exchanging microguidewires^{16) 17)}. A few risks of using a balloon include aneurysmal rupture during inflation and arterial injury due to over inflation.

Figure-8 Illustration of balloon-assisted coiling

2) The stent-assisted technique (Figure-9)

Commercially available stents in Japan are the open-cell Neuroform EZ® (Stryker Neurovascular) and the closed-cell design, Enterprise™ (Codman, Raynham, MA, USA)^{18) 19)}. In the closed-cell design, all of the stent struts are connected, and the stent moves as a single piece, with the pores fixed and closed (Figure-10A). In the open-cell design, about half of the struts are not connected, allowing some of the pores to be open (Figure-10B). These properties may affect the stent apposition to the wall of the artery. Generally, the open-cell stents are often used in more tortuous artery segments. The goal of stent delivery is to cover the aneurysm neck and to provide structural support to keep the coils inside the aneurysm. The stents may also provide a hemodynamic benefit and may also serve as a scaffold for endothelialization^{18) 19)}.

There are two techniques in stent-assisted coiling: trans-cell and jailing. In the trans-cell technique, the stent is delivered followed by passing the microcatheter for coiling through the stent. In the jailing technique, the stent is delivered after the placement of the microcatheter to aide in coiling into the aneurysm. In order to prevent thromboem-

Figure-9 Illustration of stent-assisted coiling

Figure-10 Commercially available stents in Japan: A. open-cell stent, B. closed-cell stent

bolic complications related to the stents, patients have to be given dual antiplatelet medication initiated at least 7 days prior to the procedure and continuing until at least 6 months after.

Treatment results and complications

Although the operation times from puncture to removal of guiding catheter are variable depending on the technique used and characteristics of the aneurysms, the average time is about 1-2 hours. Patients with unruptured aneurysms may be hospitalized up to 1 week but may return to work in about 2 weeks unless otherwise instructed by their physicians. Most patients treated with coils for an unruptured aneurysm can expect to live normal and productive lives. Patients treated with coils for a ruptured aneurysm face challenges ranging from minor to serious, depending on the severity of the rupture. Short-term memory loss and headaches are common after a ruptured aneurysm. Some of these deficits may disappear over time with healing and therapy.

Aneurysm recurrence after coiling occurs in about 30% of patients^{7) 20)}. Recurrence happens if coils do not completely block off the aneurysm or if the coils become compacted within the aneurysm. A recurrence may not be significant enough to require additional treatment. If a major portion of the aneurysm remains unfilled, additional coiling or surgical clipping can be placed to stop the growth. All patients with coiled aneurysms are advised to undergo magnetic resonance angiography (MRA) 6 months after and catheter angiography 1 year after the procedure to monitor for a residual or recurring aneurysm. Further follow-up MRAs are then performed yearly depending on the presence of an aneurysm remnant.

No procedure is without risk. General complications related to surgical clipping include infection, allergic reactions to anesthesia, stroke, seizure, and bleeding. Complications specifically related to coiling include thromboembolism and intraprocedural aneurysm rupture. Thromboembolisms occur in 8% of cases, but stroke only occurs in 3%. Intraprocedural aneurysm rupture may be caused by puncture of the aneurysm with the microcatheter, guidewire, or the coils. This occurs in about 2% of ruptured aneurysm cases that already have a weakened wall²¹⁾.

Discussion

1. Flow diverters

The endovascular treatment paradigms for intracranial aneurysms can be divided into reconstructive strategies (aneurysm occlusion with parent artery preservation), previously mentioned, and deconstructive strategies (parent artery occlusion), with or without revascularization. Because reconstructive strategies are frequently not feasible for large, fusiform or complex aneurysms, deconstructive strategies are required. The introduction of flow diverters may dramatically change the treatment outcome of those aneurysms in the near future (Figure-11). The flow diverter placement in front of the aneurysm neck causes flow stagnation within the aneurysm due to the flow diversion function, which leads to thrombosis of the aneurysm, with flow preservation through the parent vessels and their branches. There are, as yet, no commercially available flow diverters in Japan. Despite the recent experience with flow diverters reported in other countries, the surmounting current data suggest that this technology is an effective therapeutic option, even though the risks associated with these procedures using these novel devices are not negligible²²⁻²⁵⁾.

Endovascular therapy for intracranial aneurysms has become an important option to surgical clipping. With the ever-increasing experience and beneficial prognostic evidence, along with the technological development of the requisite devices, the indications have considerably widened, and the safety and

Figure-11 Illustration of a flow diverter for an intracranial aneurysm

efficacy of endovascular therapy for the treatment of intracranial aneurysms have improved significantly.

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