Unyielding Progress: Treatment Paradigms for Giant Aneurysms

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Despite advances in the management of both ruptured and unruptured aneurysms, the management of giant aneurysms remains extraordinarily challenging. In this article, we review the indications for their treatment and the microsurgical and endovascular options and propose a treatment algorithm.

WHAT ARE GIANT ANEURYSMS?

Aneurysms are classified depending on their size and shape. Aneurysms can be defined as small (≤ 6 mm), medium (7-12 mm), large (13-24 mm), or giant; giant aneurysms have arbitrarily been defined as those ≥ 25 mm by a number of studies, including the International Cooperative Study on Aneurysms published in 1966.[1,2] Giant aneurysms are further subdivided by shape into either saccular or fusiform conformations, with saccular being the most common.[3] Large and giant aneurysms share similar features, problems, and treatment strategies.

Despite the fact that enormous technical advancements have been made in the fields of neuroradiology, neuroanesthesia, neuroendovascular surgery, and microsurgery over the past 2 decades, the treatment of giant aneurysms remains a formidable challenge. In particular, giant aneurysms have a host of specific problems, their large size notwithstanding. Frequently, calcification, thrombosis, and wall thickening are observed in and around the neck or sac.[4-6] The presence of multiple perforators, especially in the case of fusiform giant aneurysms, and branch vessels arising directly from aneurysmal walls contributes substantial complexity to their management.[7] Even when these aneurysms are saccular in shape, they can grow to encompass a large portion of the parent vessel circumference. Through mass effect alone, giant aneurysms can present with compression of adjacent brain, brainstem, and cranial nerves, and such compression can worsen after treatments such as endovascular coiling.[8,9]

INCIDENCE AND PRESENTATION

Giant aneurysms represent only 3% to 5% of all intracranial aneurysms, with a predilection for female patients of 2:1 or 3:1.[10-12] In contrast, in the pediatric population, some studies have reported that they represent 20% to 40% of cerebral aneurysms.[13-15] Although they can be found in any age group, the majority come to clinical attention between the fifth and seventh decades of life.[10,11] Up to 70% of patients harboring these aneurysms manifest with symptoms of mass effect, including headaches and neurological deficits such as cranial neuropathies.[16-19] One-quarter present after subarachnoid or intracerebral hemorrhage.[1,12,17,20-23] Up to 5% of patients may present with seizures.[15]

NATURAL HISTORY OF GIANT ANEURYSMS

The International Study of Unruptured Intracranial Aneurysms provides the best available information to date regarding the natural history of unruptured intracranial aneurysms (Table 1).[24] It confirms that the tendency for rupture is substantially higher in giant aneurysms. In addition, the mortality observed once giant aneurysms have ruptured is greater than that for small or medium aneurysms.[18-20] Thus, when an unruptured giant aneurysm is discovered, the natural history generally favors treatment, provided that the patient's physiological age and medical condition are suitable. All viable microsurgical and endovascular treatment options should be taken into consideration, with careful evaluation of associated morbidities factored into the final treatment approach. Accordingly, treatment should be performed in centers with great experience (≥ 100 aneurysms cases per year) and expertise in both endovascular and microsurgical interventions, including high-flow bypasses.

TREATMENT OPTIONS

The treatment options for giant aneurysms are summarized in Table 2. More endovascular options are available when an unruptured giant aneurysm is discovered. Although there is increasing experience in the literature with stent-assisted coiling in the setting of aneurysmal subarachnoid hemorrhage, the dual antiplatelet therapy required for endovascular stents currently limits widespread use in acute subarachnoid hemorrhage patients. The presence of antiplatelet agents substantially complicates the management of cerebrospinal fluid diversion and hydrocephalus secondary to subarachnoid hemorrhage and intraventricular blood, specifically with maintaining external ventriculostomy drains or inserting shunts.

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TABLE 1. Natural History of Unruptured Aneurysms From the International Study of Unruptured Intracranial Aneurysms[a24]

	Annual Rate of Bleeding, %
Anterior circulation aneurysms except PCOM, mm	
7-12	0.5
13-24	2.9
≥ 25	8
Posterior circulation aneurysm+ ICA-PCOM aneurysm, mm	
7-12	2.9
13-24	3.7
≥ 25	10

[a]ICA, internal carotid artery; PCOM, posterior communicating artery.

TABLE 2. Treatment Options for Unruptured vs Ruptured Giant Aneurysms

	Unruptured Aneurysms	Ruptured Aneurysms
Microsurgical options	Clip reconstruction	Clip reconstruction
	Deep hypothermic circulatory arrest	Deep hypothermic circulatory arrest.
	Bypass with proximal occlusion/trapping /distal occlusion	Bypass with proximal occlusion/trapping/distal occlusion
Endovascular options	Proximal occlusion/ trapping after test occlusion	Proximal occlusion/ trapping after test occlusion
	Primary coiling with or without stent placement	Primary coiling, without stent placement
	Flow diversion device	

LEVEL OF EVIDENCE

There are no randomized trials available to compare various treatment methods. Both microsurgical treatments (high-flow bypasses) and endovascular treatments (flow-diversion stents) have evolved over the last decade, and the recommendations presented here are based on the experience at our center and on other case series of microsurgical[18,25-63] and endovascular[18,31,33,64-76] therapies. Because of the concentration of giant aneurysm cases in large centers and the treatment preferences of individual surgeons, multiple biases are inherent in published case series. Therefore, the level of evidence must be considered to be Class III.

We discuss microsurgical clipping, bypass with aneurysm occlusion, deep hypothermic circulatory arrest with aneurysm clipping, endovascular proximal occlusion, endovascular coiling without or with high-porosity stents, and flow-diversion devices (stents) in the role of management of giant aneurysms.

MICROSURGICAL CLIP RECONSTRUCTION

In general, an aneurysm must have a "neck," even if it is very broad, to be optimally treated with microsurgical clipping. However, with some carotid and vertebral aneurysms, encircling or fenestrated clips can be fashioned for clip reconstruction of the vessel wall. In such cases, a standard craniotomy is usually combined with a skull base approach such as an orbital osteotomy to enhance the exposure and to reduce brain retraction. Preparations for a bypass procedure must be done in select patients, in the event that the reconstruction technique cannot preserve the patency of ≥ 1 involved arteries. In situations potentially requiring bypass, patients are loaded with aspirin, with its clinical activity measured by a VerifyNow aspirin assay (Accumetrics, Inc, San Diego, California).

Total intravenous anesthesia is usually used to permit neurophysiologic monitoring of motor evoked and somatosensory evoked potentials, as well as brainstem auditory evoked potentials in those cases with the potential for brainstem involvement. Proximal and distal arterial control of the aneurysm is secured, and the patient is placed into burst suppression with propofol (Diprivan; AstraZeneca plc, London, United Kingdom). Temporary trapping is performed before aneurysm dissection, and systolic blood pressure is

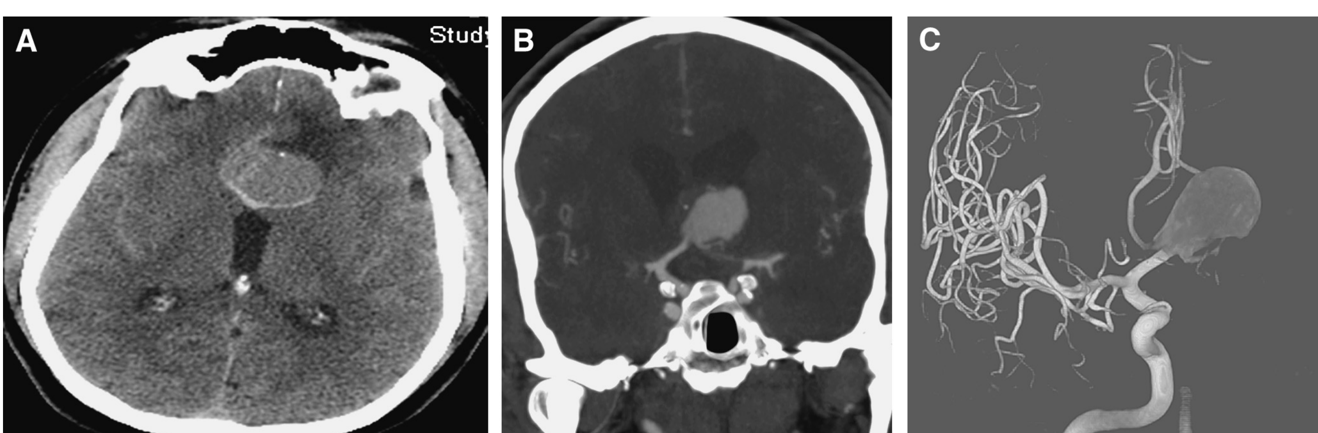

FIGURE 1. A and B, a 57-year-old man presented with subarachnoid hemorrhage, Hunt and Hess grade 4, Fisher grade 3/4. Computed tomographic angiography revealed a ruptured giant aneurysm measuring 2.8 cm in the greatest dimension with areas of partial thrombosis and calcification. C, angiogram revealed a dominant A1 and a small left A1.

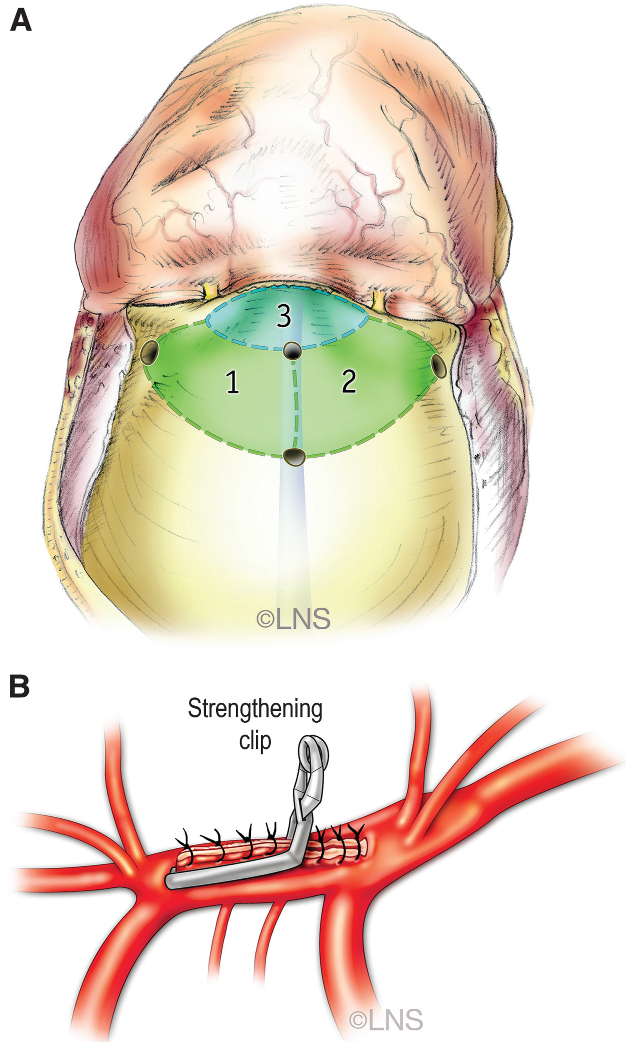

FIGURE 2. A, surgery drawing showing exposure (bifrontal and right temporal craniotomy and basal frontal osteotomy; (© Copyright L.N. Sekhar). B, the suture line along the neck of the aneurysm is reinforced with a right-angle FT820T clip.

then elevated approximately 20% above baseline to enhance collateral arterial flow while temporary clips are in place. Adenosine-induced flow arrest can also be used only if tolerated by the patient to enhance dissection of the aneurysm, to aid in the placement of permanent clips, or to ameliorate bleeding in the operative field.

The aneurysm can be directly punctured to empty blood if there is no thrombus inside, or suction decompression (Dallas Technique[77]) can be performed with proximal internal carotid artery (ICA) aneurysms. When thrombus, calcification, or extensive atheroma is present, the aneurysm sac must be opened distal to the neck to facilitate its removal; this is called an endoaneurysmectomy procedure. The orifices of the inflow and the outflow vessels must then be cleared of atheroma or thrombus. It is imperative that sufficient neck must be preserved to enable a repair, which can be accomplished with monofilament sutures and/or aneurysm clips.

Intraoperatively, direct micro-Doppler insonation, indocyanine green angiography fluorescence angiography, or C-arm angiography is then used to confirm vessel patency and aneurysm obliteration. Postoperative digital subtraction angiography is performed to obtain high-resolution images to exclude the possibility of neck remnants not discoverable by other methods. If a neck remnant is found on this study, an early follow-up angiogram (2-3 months postoperatively) is recommended.

CASE EXAMPLE 1

A 57-year-old man presented to the emergency department after a seizure and collapse and on arrival was found to be following commands with his left upper extremity, withdrawing on the right side, and opening eyes to voice (Glasgow Coma Scale score, 11). A noncontrast head computed tomography (CT) disclosed subarachnoid hemorrhage, Hunt and Hess grade 4, and Fisher grade 3 to 4 and revealed a giant anterior communicating artery aneurysm measuring 2.8 cm along its long axis with regions of partial thrombosis and a crescentic rim of calcification (Figure 1A and 1B). The CT angiogram showed a dominant right A1 and an atretic left A1 supplying the aneurysm (Figure 1C). Intraoperatively, a right occipital external ventriculostomy was placed using frameless neuronavigation to avoid the frontal horn of the lateral ventricle. Next, a saphenous craniotomy with a right temporal craniotomy and basal frontal osteotomy was performed to gain bilateral access to the aneurysm (Figure 2A). After temporary clip application on bilateral A1 and A2 vessels, an endoaneurysmectomy was performed, aided by a Sonopet ultrasonic aspirator (Stryker, Mahwah, New Jersey) and followed by resection of the dome and wall of the aneurysm. The neck of the aneurysm was closed with 6-0 and 7-0 Prolene (Johnson & Johnson, New Brunswick, New Jersey) monofilament, and the suture line was reinforced with a single right-angle FT820T clip (Aesculap, B. Braun Melsungen AG, Melsungen, Germany; Figure 2B). The frontal sinuses were exenterated and sealed with autologous abdominal fat graft and vascularized pericranium. Postoperative CT angiography (Figure 3A) and cerebral angiography (Figure 3B and 3C) demonstrated complete occlusion of the aneurysm with preservation of bilateral anterior cerebral artery circulation.

During the postoperative phase, symptomatic vasospasm was treated with hypervolemic, hemodilution, and hypertensive therapy. The right occipital ventriculostomy was later converted to a right occipital ventriculoperitoneal shunt. The patient was subsequently discharged home on postoperative day 53 after a 2½-week course of in-patient rehabilitation. At 3 months postoperatively, the patient had complete resolution of his hemiparesis and was independent in his activities of daily living (modified Rankin Scale [mRS] score, 2) with partial impairment of his short-term memory.

DEEP HYPOTHERMIC CIRCULATORY ARREST TECHNIQUE

The deep hypothermic circulatory arrest (DHCA) technique has been used to treat giant aneurysms at some centers[45,47,78-85]; the senior author (L.N.S.) has experience with a more limited number of patients.[86] Its popularity for the treatment of giant aneurysms of the anterior circulation has waned in recent years owing to the success of current neuroprotective agents and the refinement of bypass techniques

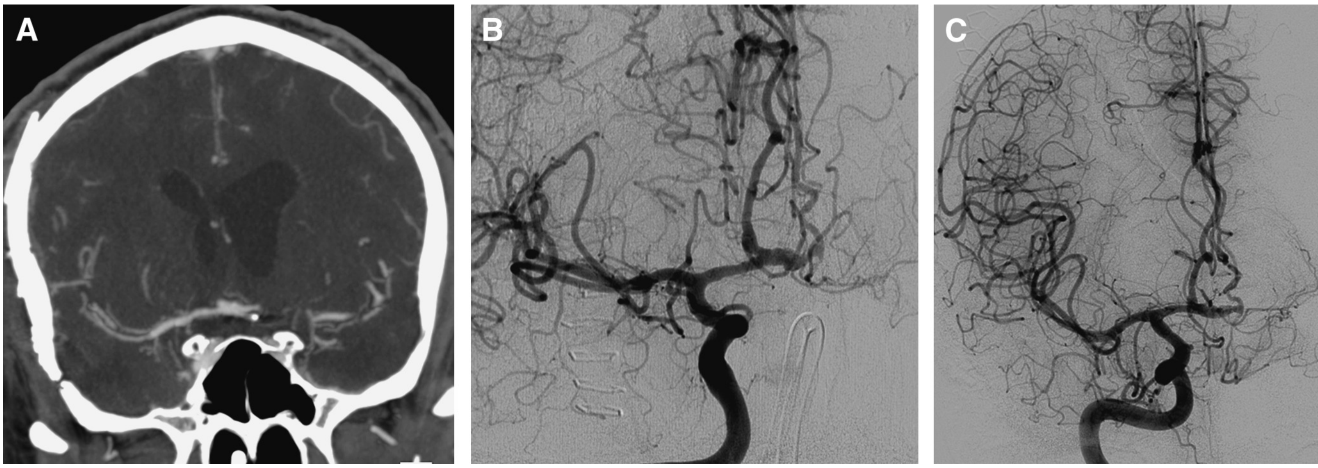

FIGURE 3. A (axial), postoperative computed tomographic angiography showing complete occlusion of the aneurysm. B and C, postoperative angiogram showing complete exclusion of the aneurysm with no residual, along with patent bilateral anterior cerebral artery circulation.

that minimize the need for prolonged temporary occlusion. The DHCA technique still has benefits for posterior circulation aneurysms, particularly those involving the basilar tip. The primary difficulty with DHCA is unpredictable recovery after circulatory arrest, with good results reported in about 63% to 75% of patients.[61,69] Other significant complications are related to postoperative brain hemorrhage. To be suitable for circulatory arrest, the aneurysm must have a neck or the surgeon must be able to recreate a neck through the removal of thrombus, atheroma, coils, etc, to enable clipping. A direct saphenous vein graft bypass into the basilar artery after DHCA with debulking of a giant basilar aneurysm has also been performed by the senior author.[81]

BYPASS FOR GIANT ANEURYSMS

Various bypass and reconstructive techniques for giant aneurysms have been iteratively refined over the preceding decade.[28,37-43,50,51,55,58,83,87] These techniques include local revascularization such as direct vessel reimplantation, side-to-side vessel anastomosis, low-flow extracranial-intracranial bypass (including superficial temporal artery or occipital artery vessels as sources), and high-flow extracranial-intracranial bypasses using the radial artery or the saphenous vein grafts. The purpose of revascularization can be to replace the parent vessel (in which case a high-flow bypass is used) or a branch vessel (in which case a local anastomosis or a low-flow extracranial-intracranial bypass is used).

Bypass techniques require the same preparation as extensive clip reconstruction. Cerebral angiography with external carotid runs is used to assess suitable superficial temporal artery or occipital sources and to the suitability of the external carotid artery for graft implantation. If a high-flow bypass is intended, bilateral upper-extremity radial and ulnar artery mapping with an ultrasonic Allen test is performed, along with bilateral saphenous vein mapping to ensure that vessels of suitable caliber are available for harvesting. Patients are placed on aspirin 325 mg at least the day before surgery, and during the operation, the brain is subjected to burst suppression before temporary clip application. Blood pressure is kept normotensive or slightly hypertensive (elevated by 20%) during temporary occlusion of unruptured aneurysms. Intravenous heparin, usually 2000 to 3000 U, is administered during the bypass, with activity monitored by activated clotting times.

The aneurysm is generally explored after all preparations are made for the bypass to see if it can be directly clipped. If not, the bypass proceeds under temporary clip occlusion and burst suppression. After completion of the bypass, luminal patency is confirmed by use of intraoperative micro-Doppler and either indocyanine green angiography or standard intraoperative angiography. The aneurysm is then treated during the same session; otherwise, the bypass may occlude or the aneurysm may rupture as a result of increased intra-aneurysmal pressure in the presence of altered flow dynamics. Aneurysmal treatment may consist of proximal occlusion only or trapping. Occasionally, distal occlusion of the aneurysm can be done in unruptured cases to preserve the patency of branch vessels or perforators arising from the aneurysm neck area.

CASE EXAMPLE 2

This 47-year-old man presented with a 1-month history of progressive right hemiparesis, intermittent right facial weakness, and dizziness. A preoperative magnetic resonance imaging scan showed a 35 × 25 × 23-mm basilar tip aneurysm, partially thrombosed, with severe midbrain compression (Figure 4A and 4B). Cerebral angiography showed a very complex aneurysm, encompassing 270° of the basilar apex, with the left posterior cerebral artery arising from the neck (Figure 4C and 4D), rendering the aneurysm unsuitable for endovascular treatment. The absence of a defined neck and an essentially fusiform conformation of the aneurysm further excluded the possibility of clip reconstruction under coverage of DHCA. Terminal basilar occlusion, Hunterian ligation, also was considered but was handicapped by the absence of sufficient collaterals from the posterior cerebral artery (Figure 4E and 4F). Previous

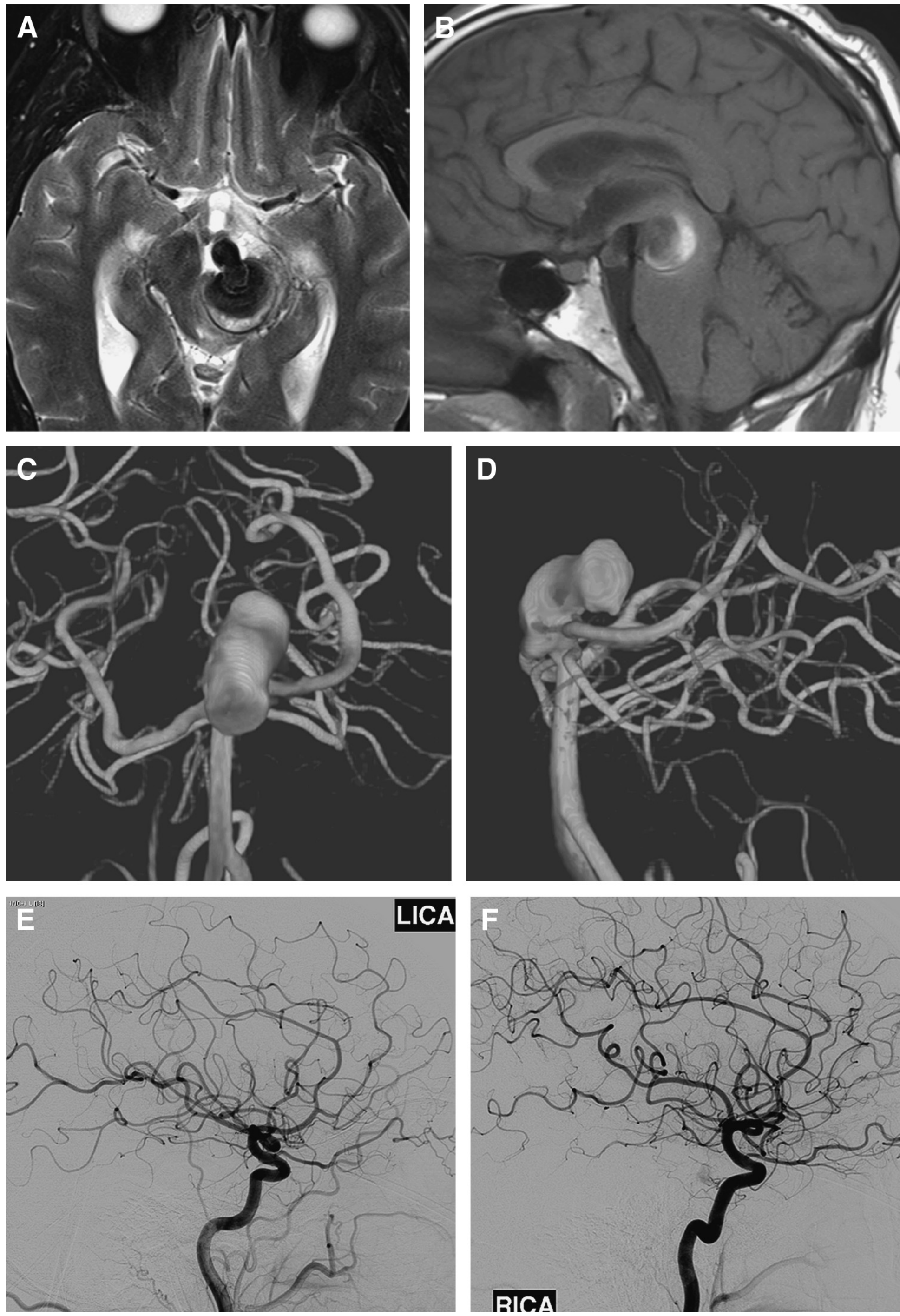

FIGURE 4. A (axial view) and B (sagittal view), preoperative magnetic resonance imaging scan showing 35 × 25 × 23-mm basilar tip aneurysm, partially thrombosed, with severe midbrain compression. C and D, angiography showing a complex aneurysm encompassing 270° of the basilar apex (C), with the left posterior cerebral artery arising from the neck (D). E and F, absent collaterals from the posterior communicating artery shown in an angiogram in the left internal carotid artery lateral view (E) and right internal carotid artery lateral view (F).

experience from the Steinberg et al[26] series showed that terminal basilar occlusion is successful in 96% of cases with 2 posterior communicating arteries (PCOMs) > 1 mm in diameter and 74% of cases with a single PCOM > 1 mm in diameter. This has been confirmed in a more recent series from the Columbia Presbyterian Hospital.[88]

We opted to construct an artificial PCOM artery by means of a radial artery graft bypass connecting the vertebral artery to the proximal posterior cerebral artery. A transpetrosal approach and far lateral approach were performed during the first stage (Figure 5A) for exposure, followed by the bypass (Figure 5B and 5D) and terminal basilar artery occlusion during the second stage (Figure 5C). The aneurysm ruptured between the 2 operations, but ultimately, the basilar artery occlusion was successfully performed. The patient underwent significant deterioration in the immediate postoperative phase but gradually improved after 10 days. After 2 months, he

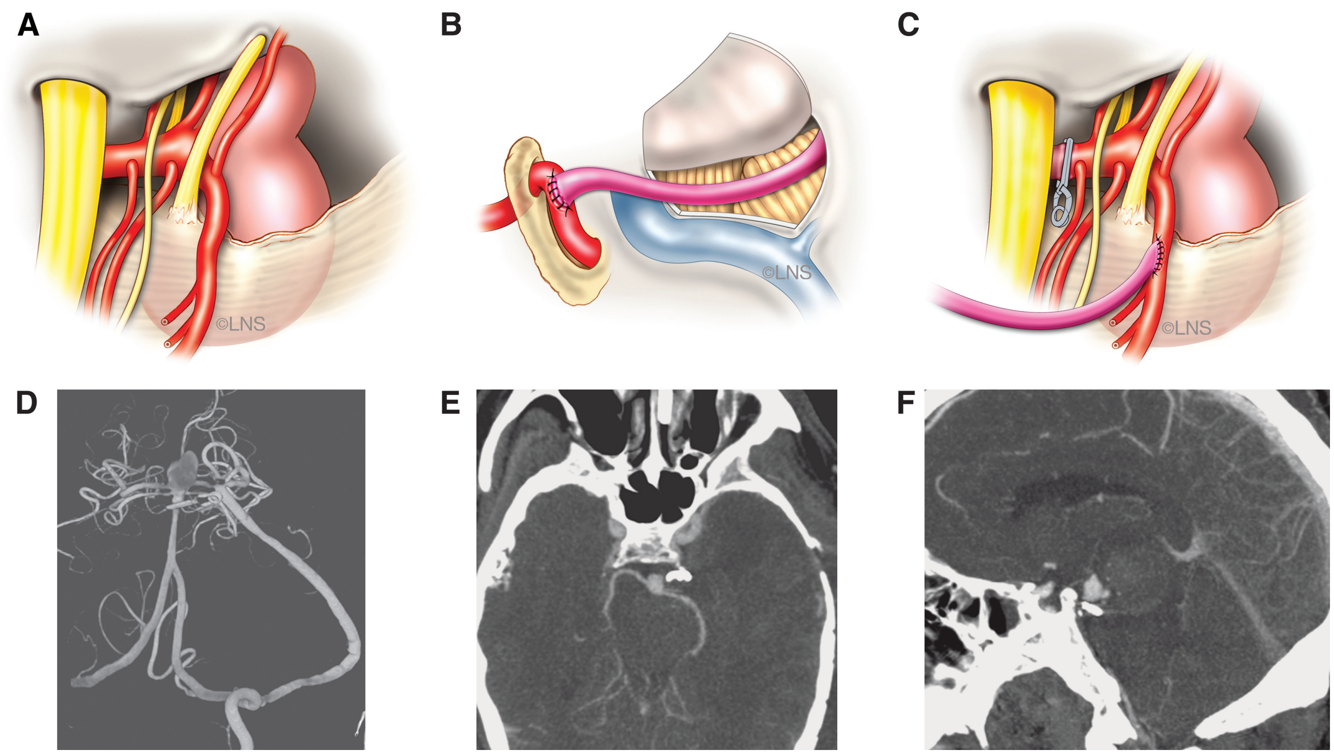

FIGURE 5. A, initial view of the aneurysm after transpetrosal approach and far lateral approach were performed in the first stage of the operation (© Copyright L.N. Sekhar). B, radial artery graft harvest and left V3 segment of the vertebral artery to the left posterior cerebral artery (PCA) bypass (© Copyright L.N. Sekhar). C, terminal basilar artery occlusion performed in the second stage of the operation (© Copyright L.N. Sekhar). D, angiogram performed on postoperative day 2 showing radial artery graft bypass left from V3 to left PCA. E (axial view) and F (sagittal view), postoperative computed tomographic angiography done at day 23 showing a small aneurysm remnant at the base.

demonstrated a mild hemiparesis and dysphasia yet was independent for activities of daily living (mRS score, 3) and continuing to improve. His CT angiography demonstrated a small aneurysm remnant near the base (Figure 5E, 5F), which is still being followed up.

CASE EXAMPLE 3

This 21-year-old man with a rare neurocutaneous vascular syndrome, cutis marmorata telangiectatica saphenous, involving the right side of his body underwent endovascular occlusion of a giant right ICA aneurysm at 9 years of age. He subsequently presented with asymptomatic and progressive growth of a giant right vertebral artery aneurysm spanning the distal V3 and V4 segments with a waisting between where the right posterior inferior cerebellar artery (PICA) originated (Figure 6A and 6B). Additionally, there was a small aneurysmal dilatation of the right PCOM, which went on to supply the entire right middle cerebral artery territory. A balloon test occlusion of right vertebral artery was performed, which the patient tolerated clinically, but the right PICA failed to fill from the contralateral vertebral artery injection.

We opted to perform a right occipital artery to PICA bypass with proximal occlusion of the right vertebral artery aneurysm (Figure 6C-6E). The patient made an excellent recovery from this procedure; however, to augment collateral circulation in the hopes of reducing the likelihood of developing further aneurysms, he underwent a subsequent radial artery bypass (extracted from the patient's unaffected arm) from the right external carotid artery to the right middle cerebral artery (Figure 6F). The patient recovered well and returned to his previous work.

CASE EXAMPLE 4

This 40-year-old doctor presented with severe visual loss and headache with a left homonymous hemianopsia on examination. Cerebral angiography disclosed a giant ICA aneurysm involving the terminal ICA segment. Collaterals from the contralateral ICA were poor because of a small caliber anterior cerebral artery on the ipsilateral side (Figure 7A and 7B). The patient underwent a radial artery graft from the external carotid artery to the MCA (Figure 7E), and then the aneurysm was clip occluded in such a way that flow was preserved to the anterior choroidal artery (Figure 7F). The patient suffered mild hemiparesis, which resolved completely after 3 days. He was able to return to work as a physician and continues to work full-time after 7 years. Late follow-up has demonstrated that his graft has remained patent by CT angiography without evidence of aneurysmal recurrence (Figure 7E and 7F).

RESULTS OF BYPASSES FOR ANEURYSMS

It is difficult to directly compare outcomes from an endovascular (stent-assisted) series with a microsurgical bypass series because they are often performed in discrete, nonoverlapping subsets of patients harboring giant aneurysms. However, some general information can be gleaned from a review of the senior author's series of bypasses for

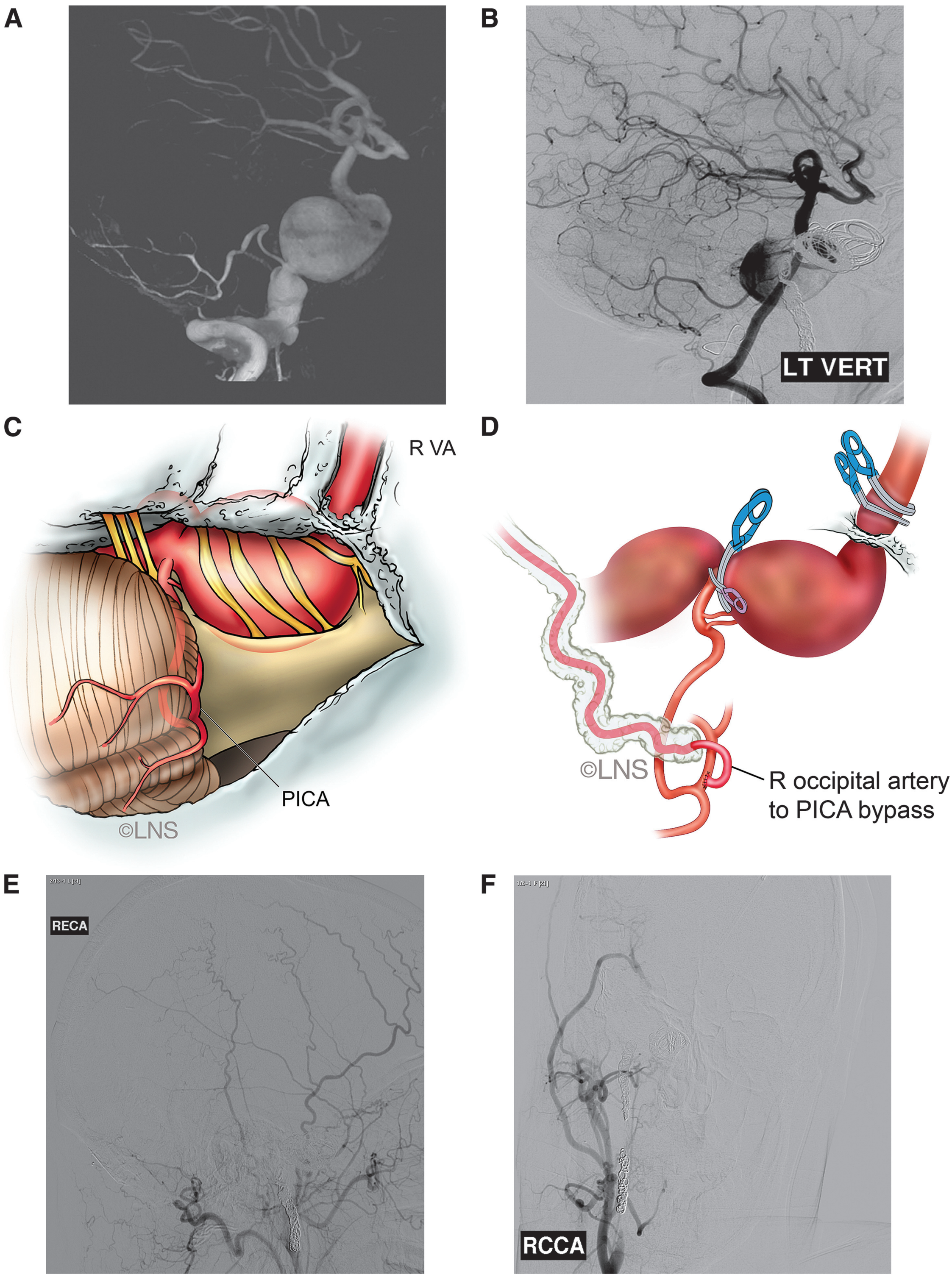

FIGURE 6. A and B, 3-dimensional angiography showing a giant right vertebral artery aneurysm, which involves the distal V3 and V4 segments, with a waisting between where the right posterior inferior cerebellar artery (PICA) originates (© Copyright L.N. Sekhar). C, initial view of the aneurysm after far lateral approach is performed (© Copyright L.N. Sekhar). D, surgery drawing showing the occipital-PICA anastomosis and proximal occlusion and clipping of aneurysm. E, postoperative angiogram showing occipital to PICA bypass and saphenous vein graft (SVG) bypass. F, postoperative angiogram after the second operation showing the external carotid artery (ECA) to right middle cerebral artery (MCA) radial artery graft (RAG).

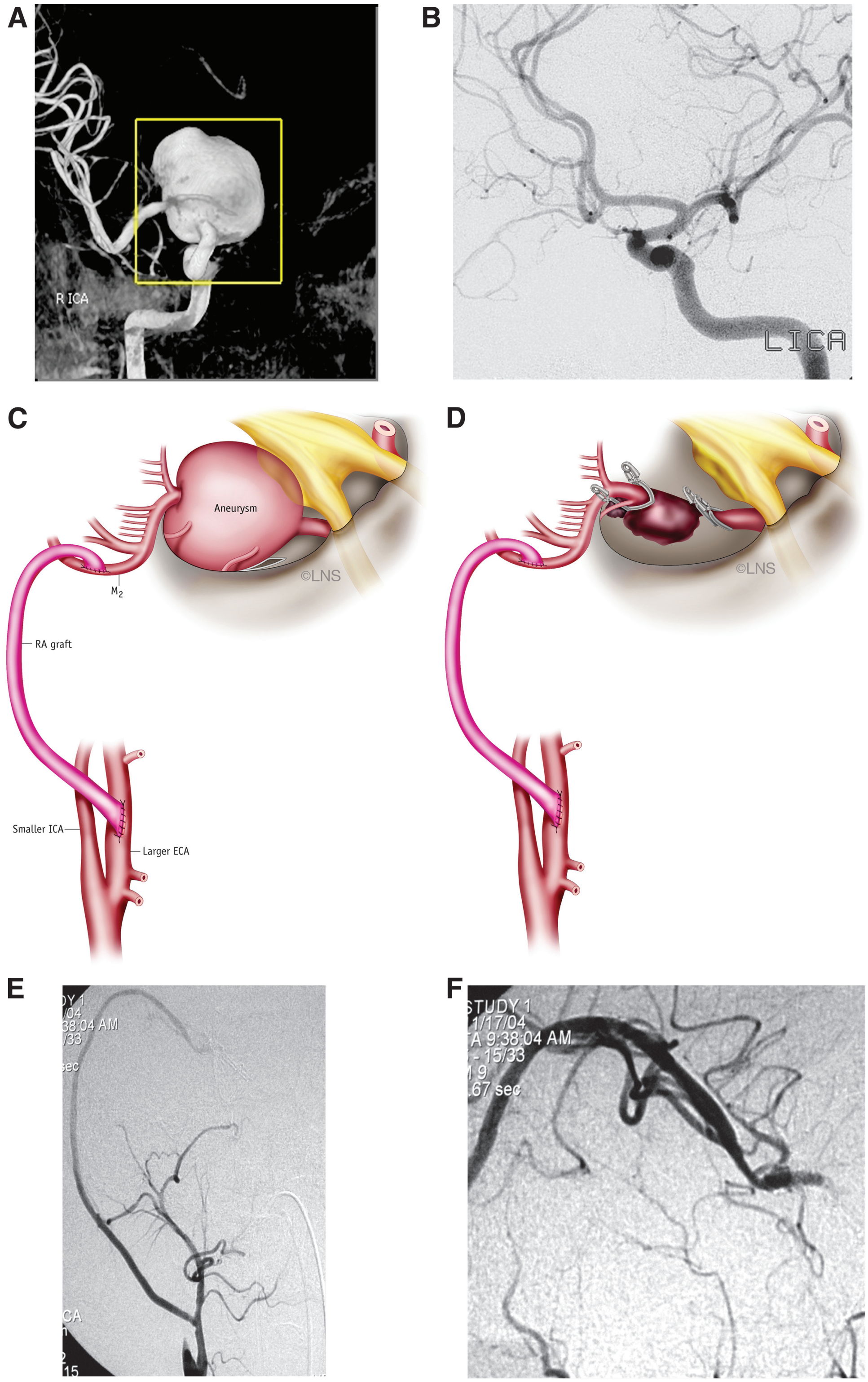

FIGURE 7. A, preoperative angiogram revealing aneurysm involving the terminal internal carotid artery (ICA). B, angiogram revealing poor collateral flow from the contralateral ICA. C, surgery drawings showing radial artery graft (RAG) from the external carotid artery (ECA) to the middle cerebral artery (MCA; © Copyright L.N. Sekhar). D, surgery drawing revealing preservation of the anterior choroidal artery through the clip reconstruction (© Copyright L.N. Sekhar). E, postoperative angiogram showing the patent RAG from the ECA to MCA. F, postoperative angiogram showing patent anterior choroidal artery flow.

aneurysms. From 1988 to 2011, 182 bypasses were performed in 172 patients. A careful analysis of results and complications (Table 3) was performed in the patients operated on during the last 6 years at Harborview Medical Center (Table 4). Giant aneurysms made up only 14% of the total group. In addition, ruptured aneurysms formed 32% of the group, with some patients presenting with poor Hunt and Hess grades preoperatively. The outcomes after surgery were

TABLE 3. Complications of Aneurysm Operations With Bypasses Done at Harborview Medical Center During the Past 6 Years

Stroke, n/N (%)	6/104 (5.7)
Complete recovery, n/N (%)	3/6 (50)
Hematoma (epidural, subdural, Intraparenchymal), %	4
Infection (local/systemic), n (%)	6 (5)
Deaths, n (%)	5 (4.8)
Bypass related, n (%)	1 (0.9)
Disease related (subarachnoid hemorrhage), n (%)	3 (2.8)
Other causes, n (%)	1 (0.9)
Correction needed (surgical or endovascular), n (%)	10
Graft patency after correction, n (%)	98

strongly correlated to the preoperative Hunt and Hess grade for ruptured giant aneurysms or the mRS scores for unruptured giant aneurysms (Table 5). Cavernous and ophthalmic aneurysms, a group that may be eligible for treatment with the Pipeline Embolization Device, formed a small cohort of 23 patients with excellent outcomes (Table 6).

COMPLICATIONS AND OUTCOMES OF MICROSURGERY FOR GIANT ANEURYSMS

Potential complications during the microsurgical treatment of giant aneurysms include intraoperative rupture (before or during craniotomy and during dissection), ischemic stroke (major or minor), thrombosis of a branch or parent artery postoperatively, and incomplete clipping with recurrence. A review of multiple series of cases published in the literature shows that an excellent to good outcome (mRS score, 0-3) was obtained in 58% to 84% of the patients, and a mortality rate of 14% to 22% was observed.[25-43,48,52-61] Rebleeding was observed in 0% to 3%, and retreatment was required in up to 1% of cases.[50]

TABLE 4. Results of Operations for Aneurysm Patients Treated With a Bypass at Harborview Medical Center From 2005 to 2011[a]

Total patients (aneurysms), n	90 (94 aneurysms)
Total bypasses, n	104
Ruptured,[32] n (%)	32 (34.7)
Hunt and Hess grade 1-3, n	22
Hunt and Hess grade 4-5, n	10
Unruptured, n (%)	60 (65.2)
Previously treated, n (%)	18 (19.5)
Surgery, n	9
Endovascular, n	9
Location, n (%)	
ICA	32 (34.7)
Cavernous	12
Ophthalmic/paraclinoid	11
Others	9
MCA, n (%)	28 (30.4)
Anterior cerebral artery, n (%)	17 (18.4)
Posterior circulation, n (%)	15 (16.3)
Size of aneurysms, n (%)	
0-13 mm	50 (54.3)
12-24 mm	28 (30.4)
≥ 25 mm	13 (14.1)
Bypass types, n (%)	
Extracranial-intracranial bypasses	69 (66.3)
Intracranial graft	12 (11.5)
Intracranial-reimplantation	23 (22.1)

[a]ICA, internal carotid artery; MCA, middle cerebral artery.

TABLE 5. Outcomes of 90 Patients Operated on With 104 Bypasses at Harborview Medical Center Over the Past 6 Years (2005-2011)[a]

Ruptured aneurysms, n (%)	
Preoperative Hunt and Hess	
1-3	22 (69)
4-5	10 (31.2)
Follow-up mRS	
0-3	23 (72)
4-6	9 (28)
Unruptured aneurysms, n (%)	
Preoperative mRS	
0-3	55 (95)
4-5	3 (5)
Follow-up mRS	
0-3	55 (95)
4-6	3 (5)

[a]ACA, anterior cerebral artery; mRS, modified Rankin Scale.

ENDOVASCULAR TREATMENTS: PROXIMAL OCCLUSION

Proximal occlusion of the aneurysm via endovascular embolization is a viable option for those giant aneurysms that have sufficient collateral circulation. Specifically, this option is very useful for intracavernous ICAs and selects large and giant vertebral artery aneurysms with few perforators and no major branches. Preoperatively, aspirin 325 mg is given by mouth; heparin is given intravenously to achieve the activated

TABLE 6. Outcomes of Cavernous and Paraophthalmic Aneurysms Treated With Bypasses at Harborview Medical Center From 2005 to 2011[a]

Total, 23 (of 90 total)
Unruptured, 18 (78.2%)
Ruptured, 5 (21.7%)
Hunt and Hess grade 1-3, 3
Hunt and Hess grade 4-5, 2
Complete occlusion of the aneurysm, 100%
Patency of bypass, 100%
Follow-up outcomes
mRS 0-3 = 22 (95.6%)
mRS 4-6 = 1 (4.4%)

[a]mRS, modified Rankin Scale.

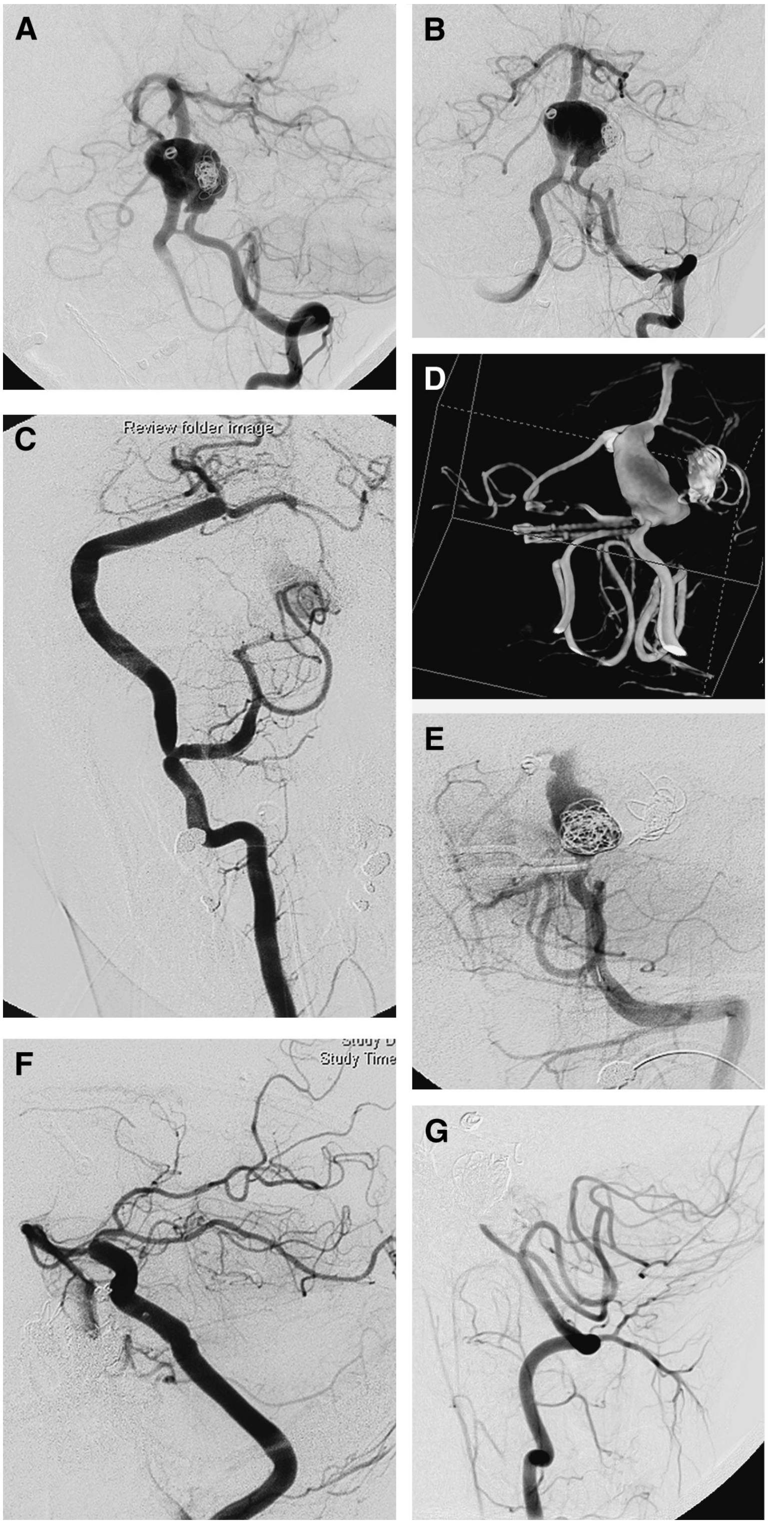

FIGURE 8. A and B, complex basilar trunk aneurysm filling predominantly through a right vertebral artery (VA) injection. C, postoperative angiogram showing VA to posterior cerebral artery bypass using a saphenous vein graft (SVG). D, postoperative 3-dimensional angiogram showing persistent filling of the aneurysm through the opposite VA. E, endovascular coiling of the residual aneurysm via the left VA. Note the coils placed. F, endovascular coiling of the residual aneurysm via the left VA. G, 1-year follow-up angiogram showing patent bypass graft and completely occluded aneurysm.

clotting time (ACT) >250sec. Both transcranial Doppler and cerebral angiography are performed preoperatively and during the procedure to study intracranial collateral circulation in both the presence and absence of induced relative hypotension. Balloon test occlusion for approximately 15 minutes is performed in each patient before permanent endovascular occlusion. A patient is considered to be a suitable candidate for permanent occlusion if the following

TABLE 7. Untoward Procedure Events of the SILK Trial[a] [95]

Poor SFD opening on deployment, n (%)	12 (7)
Partial or complete parent artery thrombosis, n (%)	7 (10)
Poor SFD positioning, n (%)	6 (8)
SFD migration, n (%)	4 (6)
Postprocedural extracranial hemorrhage, n (%)	3 (4)
Miscellaneous, n (%)	1 (1.5)
Total events, n/N (%)	20/68 (29.1)

[a]SFD, SILK flow diverter.

criteria are met: (1) No neurologic deficit develops during the balloon test occlusion; (2) angiographic evidence of intracranial collateral circulation is present; and (3) transcranial Doppler flowmetry demonstrates no greater than a 30% drop from baseline velocity in the ipsilateral middle cerebral artery during the test occlusion.[89]

Potential complications from proximal vessel sacrifice include transient ischemic attacks secondary to relative ischemia, thromboembolic strokes both immediately afterward or more delayed, and the late development of aneurysms.[90]

ENDOVASCULAR COILING OF GIANT ANEURYSMS

Endovascular coiling of giant aneurysms has a well-documented high risk of recurrence. When used without a stent, the coils frequently compact inside the aneurysm over time, necessitating subsequent retreatment. Nevertheless, in select cases, endovascular coiling may be a suitable treatment option. Furthermore, high-volume centers have demonstrated cases in which long-term coil occlusion, with or without stent assistance, has been durable. Some neurointerventionalists have used a liquid embolic agent, ONYX HD-500 (EV3, Irvine, California), to treat these aneurysms, either alone or in combination with coils. There is, however, a risk of distal embolic complications or recurrence of the aneurysms,[91-94] and this treatment has yet to become widely adopted. In all of these patients, the mass effect generated by coils filling the lumen of a giant aneurysm can have significant clinical implications. Finally, in some patients, both endovascular occlusion and bypass may be combined, although the senior author (L.N.S.) prefers to rely on a single-modality treatment whenever possible.

CASE EXAMPLE 5

This 10-year-old boy presented with a progressively enlarging basilar trunk giant aneurysm. The patient had previously undergone multiple episodes of endovascular coil obliteration of the aneurysm, but it was incomplete and the aneurysm continued to grow (Figure 8A). Consequently, the patient suffered from very severe and episodic headaches, hemiparesis, and neurogenic hypertension. Preoperative cerebral angiography revealed that the aneurysm was filling through both vertebral arteries with right-sided dominance (Figure 8A and 8B). Additionally, there was a fenestration of the basilar artery just proximal to the aneurysm. The right PICA was dominant, and a large anterior spinal artery was seen to be arising from the right vertebral artery. Preoperatively, stent-assisted coiling of the aneurysm was considered owing to the peculiar anatomy of the aneurysm and this patient's young age; he was not considered an optimal candidate for endovascular therapy. Therefore, a saphenous vein bypass graft followed by a proximal occlusion of the aneurysm was planned. The patient underwent a right-sided combined far lateral and transpetrosal approach, with a saphenous vein graft from the right V3 segment of the vertebral artery to the P2 segment of the posterior cerebral artery performed. Both vertebral arteries just proximal to the aneurysm were clip occluded (Figure 8C). Postoperative angiography revealed that the aneurysm was still filling (Figure 8D). The remainder of the aneurysm was obliterated with Guglielmi detachable coils (Figure 8E and 8F), with follow-up at 1 year showing no evidence of coil compaction or residual aneurysm (Figure 8G). The patient made a complete recovery, with an mRS score of 0.

FLOW-DIVERSION DEVICES

The introduction of flow-diversion devices was an exciting development in the treatment of cerebral aneurysms. Flow diverters are a new class of low-porosity metal stents intended to recreate an artificial endoluminal artery within the aneurysm itself that still preserves perfusion through associated perforator vessels.[66,73,86,95-104] The necessity of dual antiplatelet therapy for at least 6 months and aspirin indefinitely limits the utility of these devices in patients with ruptured aneurysms. Currently, the US Food and Drug Administration has approved the Pipeline (ev3 Endovascular, Inc, Plymouth,

TABLE 8. Overview of Published Clinical Results of Pipeline Embolization Device Treatment[a]

	PUFS Trial[b]	PITA Trial[99]	Buenos Aires Experience[73]	Budapest Experience[102]
Aneurysms, n	106	31	63	19
Patients, n	104	31	53	18
Mean aneurysm size, mm	18.2	11.5	11.1	16
Occlusion rate at 1 y, %	86	Not Reported	94	Not Reported
Recurrence rate, %	0	0	0	0
Major stroke or neurological death, %	5.6	6.5	0	5.3

[a]PUFS, Pipeline for Uncoilable or Failed Aneurysms; SFD, SILK flow diverter.
[b]Unpublished data.

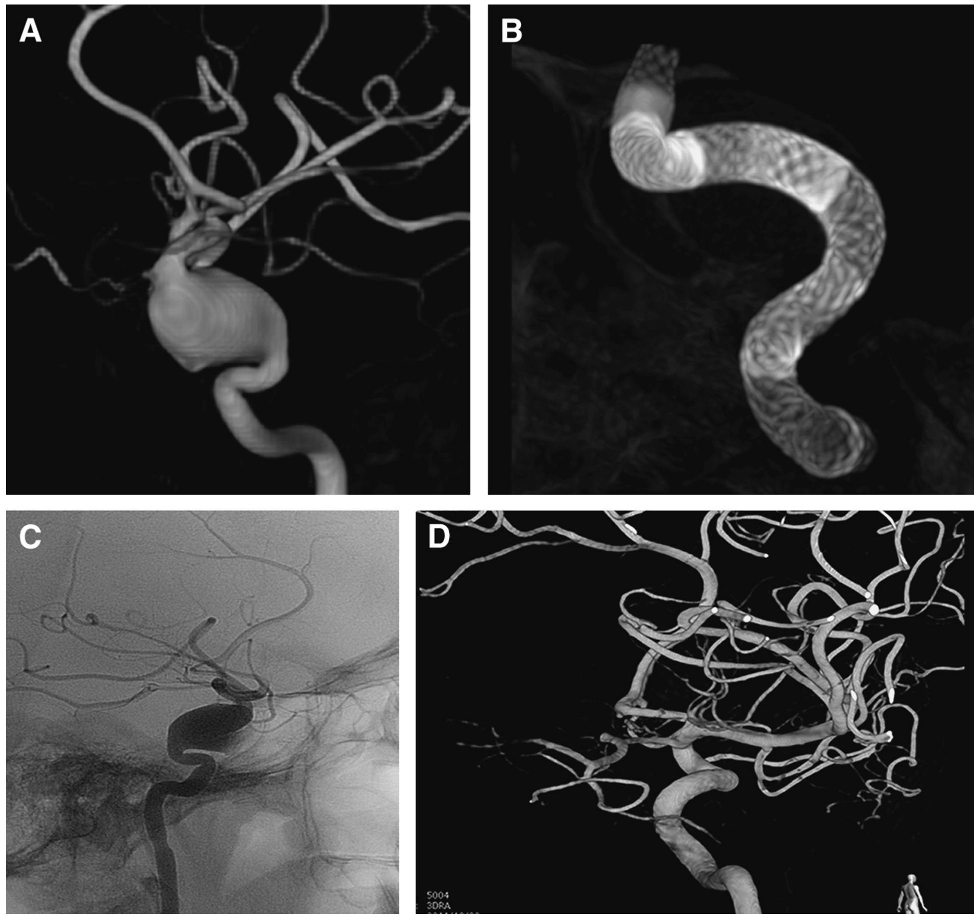

FIGURE 9. A, preprocedural angiogram revealing Fusiform right cavernous aneurysm measuring 1.4 × 1.8 cm in the greatest dimension. B, postdeployment angiogram showing the Pipeline Embolization Devices being deployed. C, postdeployment image showing stagnation of flow inside the aneurysm. D, 6-month follow-up angiogram showing complete obliteration of the aneurysm.

Minnesota) flow-diversion device to treat ICA aneurysms > 1 cm confined to the petrous, cavernous, and paraophthalmic segments of the ICA. Large and giant aneurysms in other locations have been treated, but this use is off-label. Another flow-diversion device, Silk (Balt Extrusion SA, Montmorency, France), has yet to receive Food and Drug Administration clearance, although it has been used in the United States on a compassionate care basis.[66]

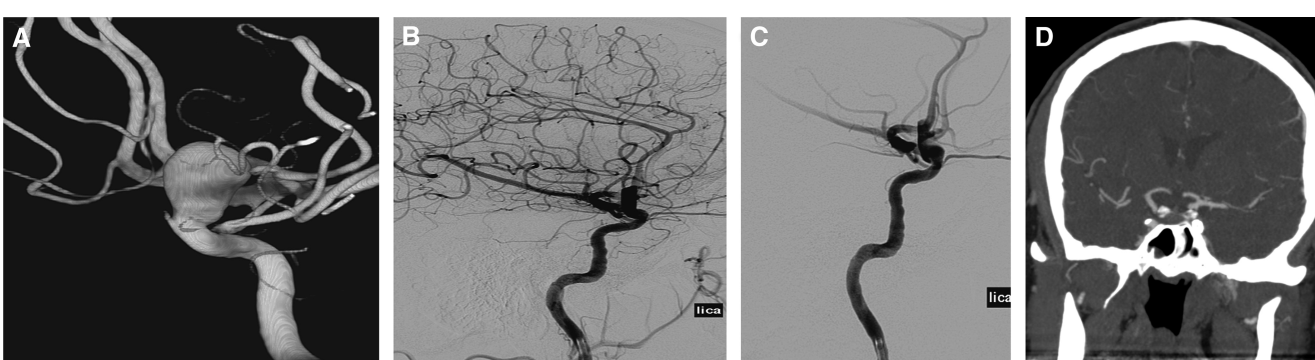

FIGURE 10. A, preprocedural angiogram showing left paraclinoid aneurysm measuring 13 mm in the greatest dimension and 8 mm in longitudinal extent and involving 180° of the circumference of the internal carotid artery. B and C, post-Pipeline Embolization Device deployment angiogram showing stagnation of the flow in the aneurysm and areas of partial thrombosis. D, 3-month follow-up 3-dimensional computed tomographic angiography showing the exclusion of the aneurysm from the circulation.

ANEURYSM TREATMENT WITH FLOW DIVERTERS: SILK

As of March 2010, > 1500 procedures with the Silk flow diverter (SFD) have been performed at multiple centers in Europe. The International SILK registry is an ongoing multicenter prospective study accruing patients that have received Silk stents. Preliminary data collected on 68 patients drawn from 18 centers have shown that ≥ 1 untoward procedural events were reported in 20 patients.[66] They included 12 (17%) poor SFD opening on deployment, 7 (10%) partial or complete parent artery thrombosis, 6 (8%) poor SFD positioning, 4 (6%) SFD migration, 3 (4%) postprocedural extracranial hemorrhages, and 1 (1.5%) complication related to another device (Table 7). No intracranial hemorrhage was reported in the 68 patients. In a recent study by Kulcsárz et al[96] involving 13 centers, 12 separate cases of delayed hemorrhage were reported. The cause was postulated to be thrombus-associated autolysis of the aneurysmal wall and delayed onset of hemorrhage. Rupture of previously unruptured aneurysms has also been reported in autopsy cases.[96] Furthermore, cessation of dual antiplatelet therapy in the periprocedural period has been associated with stent thrombosis.[66]

ANEURYSM TREATMENT WITH FLOW DIVERTERS: PIPELINE

The Food and Drug Administration approval of the Pipeline flow-diversion device was based on the results of the Pipeline for Uncoilable or Failed Aneurysms (PUFS) study, a multicenter, nonrandomized, single-arm study using historical control subjects with target accrual of 100 patients (unpublished data). There were 8 US and 2 international centers in the PUFS trial, which enrolled patients between 21 and 75 years of age who had a single target intracranial aneurysm with a size > 10 mm and a neck > 4 mm. Exclusion criteria included subarachnoid hemorrhage within the past 60 days, presence of an irreversible bleeding disorder, and presence of > 1 intracranial aneurysm requiring treatment in the next 6 months. The mean size of the aneurysms was between 10 and 36.1 mm, with only 1 aneurysm measuring 6.2 mm in size. The neck size of the aneurysms ranged from 2.1 to 36.1 mm. There were a total of 44 cavernous, 35 paraophthalmic, 10 superior hypophyseal, 9 supraclinoid, 4 petrous, 2 carotid cave, 2 lateral clinoid and 1 posterior communicating artery aneurysms in the study. Parent artery thrombosis with stroke, stenosis with stroke, hemorrhage, and neurological death of the patient were the major safety endpoint events. Ninety-six percent of the patients had a follow-up at 180 days. In this study, an 86% complete aneurysm obliteration rate was demonstrated. The aneurysms do not close immediately in most patients, with stasis of blood and clotting progressing to aneurysm occlusion during follow-up. Results are summarized in Table 8.

CASE EXAMPLE 6

This is a 32-year-old man who presented with left sided retro-orbital pain. He had a history of failed stent-assisted coil embolization of an unruptured right cavernous ICA aneurysm approximately 1 year previously. Angiography showed a fusiform-shaped aneurysm measuring 1.4 × 1.8 cm (Figure 9A), and CT demonstrated a peripheral rim of calcification. A total of 5 Pipeline flow-diversion devices were deployed under continuous fluoroscopy and roadmap guidance (Figure 9B). Postdeployment images showed flow stagnation within the lumen of the aneurysm. (Figure 9C). The CT angiography after 6 weeks and intra-arterial digital subtraction angiography after 6 months showed complete obliteration of the aneurysm (Figure 9D).

CASE EXAMPLE 7

A 51-year-old man with a history of blurry vision had a workup leading to the incidental discovery of an unruptured left paraclinoid aneurysm. Cerebral angiography revealed an unruptured paraclinoid aneurysm measuring 12 × 12 × 13 mm with an irregular contour and multiple focal out pouchings (Figure 10A). The neck was 8 mm along its long axis and encompassed 180° of the circumference of the ICA. He went on to undergo successful placement of the Pipeline Embolization Device. Follow-up imaging demonstrated flow stagnation in the aneurysm along with an area of partial thrombosis (Figure 10B, 10C). CT angiography at 4 months showed complete aneurysm obliteration.

COMPLICATIONS FROM PIPELINE DEVICES

The incidence of long-term complications for Pipeline flow diverters is not known, although thrombosis of the parent artery and hemorrhages have now been reported.[103,104] The intracranial bleeds have been noted to arise from the aneurysms themselves and remotely in the distal parenchyma. Persistence of a flow jet after stent placement presents the potential for aneurysmal rupture. Additionally, the required duration for the antiplatelet therapy after Pipeline deployment has not been established, although dual antiplatelet therapy has been used for a period of 6 months after the procedure.

CONCLUSIONS

Level III evidence has shown that giant aneurysms should be treated in large centers with multidisciplinary teams and expertise. What is clear is that no 2 giant aneurysms are necessarily alike and that the optimal treatment for a specific aneurysm can be delivered only when all treatment options are in the armamentarium of the treating team. Cerebrovascular microsurgery, skull base approaches, bypass techniques, and endovascular treatments (proximal occlusion, stents/coils, flow diversion) are fundamental tools in the armamentarium of cerebrovascular surgeons dealing with these complex lesions. DHCA has a limited role in the treatment of posterior circulation aneurysms. The role of the flow-diversion devices is evolving and merits further study based on the collective experience at multiple centers.

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REFERENCES

1. Locksley HB, Sahs AL, Sandler R. Report on the cooperative study of intracranial aneurysms and subarachnoid hemorrhage, 3: subarachnoid hemorrhage unrelated to intracranial aneurysm and A-V malformation: a study of associated diseases and prognosis. *J Neurosurg.* 1966;24(6): 1034-1056.
2. Sahs AL, Perret G, Locksley HB, Nishioka H. *Intracranial Aneurysms and Subarachnoid Hemorrhage: A Cooperative Study*. Philadelphia, PA: Lippincott; 1969.
3. Rosta L, Battaglia R, Pasqualin A, Beltramello A. Italian cooperative study on giant intracranial aneurysms, 2: radiological data. *Acta Neurochir Suppl (Wien).* 1988;42:53-59.
4. Matsumura K, Saito A, Nakasu Y, Matsuda M, Handa J, Todo G. Magnetic resonance imaging of large and giant intracranial aneurysms. *Neurol Med Chir (Tokyo).* 1990;30(6):382-388.
5. O'Neill M, Hope T, Thomson G. Giant intracranial aneurysms: diagnosis with special reference to computerised tomography. *Clin Radiol.* 1980;31(1):27-39.
6. Olsen WL, Brant-Zawadzki M, Hodes J, Norman D, Newton TH. Giant intracranial aneurysms: MR imaging. *Radiology*. 1987;163(2): 431-435.
7. Shi ZS, Ziegler J, Duckwiler GR, et al. Management of giant middle cerebral artery aneurysms with incorporated branches: partial endovascular coiling or combined extracranial-intracranial bypass: a team approach. *Neurosurgery*. 2009;65(6 suppl):121-129; discussion 129.
8. Fisher A, Som PM, Mosesson RE, Lidov M, Liu TH. Giant intracranial aneurysms with skull base erosion and extracranial masses: CT and MR findings. *J Comput Assist Tomogr.* 1994;18(6):939-942.
9. Nonaka T, Haraguchi K, Baba T, Koyanagi I, Houkin K. Clinical manifestations and surgical results for paraclinoid cerebral aneurysms presenting with visual symptoms. *Surg Neurol.* 2007;67(6):612-619; discussion 619.
10. Juvela S. Prevalence of and risk factors for intracranial aneurysms. *Lancet Neurol.* 2011;10(7):595-597.
11. Vlak MH, Algra A, Brandenburg R, Rinkel GJ. Prevalence of unruptured intracranial aneurysms, with emphasis on sex, age, comorbidity, country, and time period: a systematic review and meta-analysis. *Lancet Neurol.* 2011;10(7):626-636.
12. Amenta PS, Yadla S, Campbell PG, et al. Analysis of non-modifiable risk factors for intracranial aneurysm rupture in a large, retrospective cohort. *Neurosurgery*. 2012;70(3):693-699.
13. Herman JM, Rekate HL, Spetzler RF. Pediatric intracranial aneurysms: simple and complex cases. *Pediatr Neurosurg.* 1991-1992;17(2):66-72; discussion 73.
14. Meyer FB, Sundt TM Jr, Fode NC, Morgan MK, Forbes GS, Mellinger JF. Cerebral aneurysms in childhood and adolescence. *J Neurosurg.* 1989;70(3):420. Review.
15. Hetts SW, Narvid J, Sanai N, et al. Intracranial aneurysms in childhood: 27-year single-institution experience. *AJNR Am J Neuroradiol.* 2009;30 (7):1315-1324.
16. Hirasawa T, Tsubokawa T, Katayama Y, et al. Growth of a giant aneurysm following complete thrombosis by detachable balloon occlusion. *Surg Neurol.* 1992;38(4):283-286.
17. Pia HW, Zierski J. Giant cerebral aneurysms. *Neurosurg Rev.* 1982;5 (4):117-148.
18. Hahn CD, Nicolle DA, Lownie SP, Drake CG. Giant cavernous carotid aneurysms: clinical presentation in fifty-seven cases. *J Neuroophthalmol.* 2000;20(4):253-258.
19. Vasconcellos LP, Flores JA, Conti ML, Veiga JC, Lancellotti CL. Spontaneous thrombosis of internal carotid artery: a natural history of giant carotid cavernous aneurysms. *Arq Neuropsiquiatr.* 2009;67(2A):278-283.
20. Karamanakos PN, von Und Zu Fraunberg M, Bendel S, et al. Risk factors for three phases of 12-month mortality in 1657 patients from a defined population after acute aneurysmal subarachnoid hemorrhage [published online ahead of print November 9, 2011]. *World Neurosurg.* doi: doi:10.1016/j.wneu.2011.08.033.
21. Sato K, Yoshimoto Y. Risk profile of intracranial aneurysms: rupture rate is not constant after formation. *Stroke*. 2011;42(12):3376-3381.
22. Dengler J, Heuschmann PU, Endres M, et al; Giant Intracranial Aneurysm Study Group. The rationale and design of the Giant Intracranial Aneurysm Registry: a retrospective and prospective study. *Int J Stroke.* 2011;6(3):266-270.
23. Rahman M, Smietana J, Hauck E, et al. Size ratio correlates with intracranial aneurysm rupture status: a prospective study. *Stroke*. 2010;41 (5):916-920.
24. Wiebers DO, Whisnant JP, Huston J 3rd, et al; International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet*. 2003;362(9378):103-110.
25. Drake CG, Peerless SJ. Giant fusiform intracranial aneurysms: review of 120 patients treated surgically from 1965 to 1992. *J Neurosurg.* 1997;87(2):141-162.
26. Steinberg GK, Drake CG, Peerless SJ. Deliberate basilar or vertebral artery occlusion in the treatment of intracranial aneurysms: immediate results and long-term outcome in 201 patients. *J Neurosurg.* 1993;79(2):161-173.
27. Peerless SJ, Drake CG. Treatment of giant cerebral aneurysms of the anterior circulation. *Neurosurg Rev.* 1982;5(4):149-154.
28. Peerless SJ, Ferguson GG, Drake CG. Extracranial-intracranial (EC/IC) bypass in the treatment of giant intracranial aneurysms. *Neurosurg Rev.* 1982;5(3):77-81.
29. Drake CG. Giant intracranial aneurysms: experience with surgical treatment in 174 patients. *Clin Neurosurg.* 1979;26:12-95.
30. Leibowitz R, Do HM, Marcellus ML, Chang SD, Steinberg GK, Marks MP. Parent vessel occlusion for vertebrobasilar fusiform and dissecting aneurysms. *AJNR Am J Neuroradiol.* 2003;24(5): 902-907.
31. Darsaut TE, Darsaut NM, Chang SD, et al. Predictors of clinical and angiographic outcome after surgical or endovascular therapy of very large and giant intracranial aneurysms. *Neurosurgery*. 2011;68(4): 903-915; discussion 915.
32. Hanel RA, Spetzler RF. Surgical treatment of complex intracranial aneurysms. *Neurosurgery*. 2008;62(6 suppl 3):1289-1297; discussion 1297-1299.
33. Ponce FA, Albuquerque FC, McDougall CG, Han PP, Zabramski JM, Spetzler RF. Combined endovascular and microsurgical management of giant and complex unruptured aneurysms. *Neurosurg Focus.* 2004;17 (5):E11.
34. Spetzler RF, Riina HA, Lemole GM Jr. Giant aneurysms. *Neurosurgery*. 2001;49(4):902-908.
35. Lawton MT, Spetzler RF. Surgical strategies for giant intracranial aneurysms. *Neurosurg Clin N Am.* 1998;9(4):725-742.
36. Lawton MT, Daspit CP, Spetzler RF. Technical aspects and recent trends in the management of large and giant midbasilar artery aneurysms. *Neurosurgery*. 1997;41(3):513-520; discussion 520-521.
37. Javedan SP, Deshmukh VR, Spetzler RF, Zabramski JM. The role of cerebral revascularization in patients with intracranial aneurysms. *Neurosurg Clin N Am.* 2001;12(3):541-555, viii.
38. Spetzler RF, Fukushima T, Martin N, Zabramski JM. Petrous carotid-to-intradural carotid saphenous vein graft for intracavernous giant aneurysm, tumor, and occlusive cerebrovascular disease. *J Neurosurgery.* 1990;73(4):496-501.
39. Spetzler RF, Selman W, Carter LP. Elective EC-IC bypass for unclippable intracranial aneurysms. *Neurol Res.* 1984;6(1-2):64-68.
40. Spetzler RF, Schuster H, Roski RA. Elective extracranial-intracranial arterial bypass in the treatment of inoperable giant aneurysms of the internal carotid artery. *J Neurosurg.* 1980;53(1):22-27.
41. Spetzler RF, Roski RA, Schuster H, Takaoka Y. The role of EC-IC in the treatment of giant intracranial aneurysms. *Neurol Res.* 1980;2(3-4): 345-359.
42. Sundt TM Jr, Piepgras DG, Fode NC, Meyer FB. Giant intracranial aneurysms. *Clin Neurosurg.* 1991;37:116-154.
43. Sundt TM Jr, Piepgras DG, Marsh WR, Fode NC. Saphenous vein bypass grafts for giant aneurysms and intracranial occlusive disease. *J Neurosurg.* 1986;65(4):439-450.
44. Sundt TM Jr, Piepgras DG. Surgical approach to giant intracranial aneurysms: operative experience with 80 cases. *J Neurosurg.* 1979;51 (6):731-742.
45. Solomon RA, Smith CR, Raps EC, Young WL, Stone JG, Fink ME. Deep hypothermic circulatory arrest for the management of complex anterior and posterior circulation aneurysms. *Neurosurgery*. 1991;29(5): 732-737; discussion 737-738.

46. Solomon RA, Fink ME, Pile-Spellman J. Surgical management of unruptured intracranial aneurysms. *J Neurosurg.* 1994;80(3):440-446.
47. Connolly ES Jr, Solomon RA. Hypothermic cardiac standstill for cerebral aneurysm surgery. *Neurosurg Clin N Am.* 1998;9(4):681-695.
48. Lozier AP, Kim GH, Sciacca RR, Connolly ES Jr, Solomon RA. Microsurgical treatment of basilar apex aneurysms: perioperative and long-term clinical outcome. *Neurosurgery*. 2004;54(2):286-296; discussion 296-299.
49. Komotar RJ, Mocco J, Solomon RA. Guidelines for the surgical treatment of unruptured intracranial aneurysms: the first annual J. Lawrence Pool Memorial Research Symposium: controversies in the management of cerebral aneurysms. *Neurosurgery*. 2008;62(1):183-193; discussion 193-194.
50. Sughrue ME, Saloner D, Rayz VL, Lawton MT. Giant intracranial aneurysms: evolution of management in a contemporary surgical series. *Neurosurgery*. 2011;69(6):1261-1270; discussion 1270-1271.
51. Mirzadeh Z, Sanai N, Lawton MT. The Azygos anterior cerebral artery bypass: double reimplantation technique for giant anterior communicating artery aneurysms. *J Neurosurg.* 2011;114(4):1154-1158.
52. Sanai N, Zador Z, Lawton MT. Bypass surgery for complex brain aneurysms: an assessment of intracranial-intracranial bypass. *Neurosurgery*. 2009;65(4):670-683; discussion 683.
53. Sanai N, Tarapore P, Lee AC, Lawton MT. The current role of microsurgery for posterior circulation aneurysms: a selective approach in the endovascular era. *Neurosurgery*. 2008;62(6):1236-1249; discussion 1249-1253.
54. Lawton MT, Quinones-Hinojosa A, Sanai N, Malek JY, Dowd CF. Combined microsurgical and endovascular management of complex intracranial aneurysms. *Neurosurgery*. 2008;62(6 suppl 3):1503-1515.
55. Lawton MT, Quiñones-Hinojosa A. Double reimplantation technique to reconstruct arterial bifurcations with giant aneurysms. *Neurosurgery*. 2006;58(4 suppl 2):ONS-347-ONS-353; discussion ONS-353-ONS-354.
56. Quiñones-Hinojosa A, Du R, Lawton MT. Revascularization with saphenous vein bypasses for complex intracranial aneurysms. *Skull Base*. 2005;15(2):119-132.
57. Lawton MT, Raudzens PA, Zabramski JM, Spetzler RF. Hypothermic circulatory arrest in neurovascular surgery: evolving indications and predictors of patient outcome. *Neurosurgery*. 1998;43(1):10-20; discussion 20-21.
58. Kato Y, Sano H, Imizu S, et al. Surgical strategies for treatment of giant or large intracranial aneurysms: our experience with 139 cases. *Minim Invasive Neurosurg.* 2003;46(6):339-343.
59. Abdulrauf SI, Sweeney JM, Mohan YS, Palejwala SK. Short segment internal maxillary artery to middle cerebral artery bypass: a novel technique for extracranial-to-intracranial bypass. *Neurosurgery*. 2011;68(3):804-808; discussion 808-809.
60. Sano H, Kato Y, Shankar K, et al. Treatment and results of partially thrombosed giant aneurysms. *Neurol Med Chir (Tokyo).* 1998:38 (suppl):58-61.
61. Khandelwal P, Kato Y, Sano H, Yoneda M, Kanno T. Treatment of ruptured intracranial aneurysms: our approach. *Minim Invasive Neurosurg.* 2005;48(6):325-329.
62. Sano H. Treatment of complex intracranial aneurysms of anterior circulation using multiple clips. *Acta Neurochir Suppl.* 2010;107:27-31.
63. Hoh BL, Putman CM, Budzik RF, Carter BS, Ogilvy CS. Combined surgical and endovascular techniques of flow alteration to treat fusiform and complex wide-necked intracranial aneurysms that are unsuitable for clipping or coil embolization. *J Neurosurg.* 2001;95(1):24-35.
64. Chen L, Kato Y, Sano H, et al. Management of complex, surgically intractable intracranial aneurysms: the option for intentional reconstruction of aneurysm neck followed by endovascular coiling. *Cerebrovasc Dis.* 2007;23(5-6):381-387.
65. Loumiotis I, D'Urso PI, Tawk R, et al. Endovascular treatment of ruptured paraclinoid aneurysms: results, complications, and follow-up. *AJNR Am J Neuroradiol.* 2012;33(4):632-637.
66. Binning MJ, Natarajan SK, Bulsara KR, Siddiqui AH, Hopkins LN, Levy EI. SILK flow-diverting device for intracranial aneurysms. *World Neurosurg.* 2011;76(5):477.e1-477.e6.
67. Jahromi BS, Mocco J, Bang JA, et al. Clinical and angiographic outcome after endovascular management of giant intracranial aneurysms. *Neurosurgery*. 2008;63(4):662-674; discussion 674-675.
68. Wehman JC, Hanel RA, Levy EI, Hopkins LN. Giant cerebral aneurysms: endovascular challenges. *Neurosurgery*. 2006;59(5 suppl 3): S125-S138; discussion S3-S13.
69. Standard SC, Guterman LR, Chavis TD, Fronckowiak MD, Gibbons KJ, Hopkins LN. Endovascular management of giant intracranial aneurysms. *Clin Neurosurg.* 1995;42:267-293.
70. Guterman LR, Hopkins LN. Endovascular treatment of cerebral aneurysms: diagnosis and treatment [review]. *Clin Neurosurg.* 1993;40:56-83.
71. Wong GK, Kwan MC, Ng RY, Yu SC, Poon WS. Flow diverters for treatment of intracranial aneurysms: current status and ongoing clinical trials. *J Clin Neurosci.* 2011;18(6):737-740.
72. Thornton J, Dovey Z, Alazzaz A, et al. Surgery following endovascular coiling of intracranial aneurysms. *Surg Neurol.* 2000;54(5):352-360.
73. Lylyk P, Miranda C, Ceratto R, et al. Curative endovascular reconstruction of cerebral aneurysms with the pipeline embolization device: the Buenos Aires experience. *Neurosurgery*. 2009;64(4):632-643.
74. Lylyk P, Viñuela F, Campos J, et al. Diagnosis and endovascular therapy of vascular lesions in the cavernous sinus. *Acta Radiol Suppl.* 1986; 369:584-585.
75. Guglielmi G, Viñuela F, Duckwiler G, et al. Endovascular treatment of posterior circulation aneurysms by electrothrombosis using electrically detachable coils. *J Neurosurg.* 1992;77(4):515-524.
76. Snyder KV, Natarajan SK, Hauck EF, et al. The balloon anchor technique: a novel technique for distal access through a giant aneurysm. *J Neurointerv Surg.* 2010;2(4):363-367.
77. Batjer HH, Samson DS. Retrograde suction decompression of giant paraclinoidal aneurysms; technical note. *J Neurosurg.* 1990;73(2): 305-306.
78. Spetzler RF, Hadley MN, Rigamonti D, et al. Aneurysms of the basilar artery treated with circulatory arrest, hypothermia, and barbiturate cerebral protection. *J Neurosurg.* 1988;68(6):868-879.
79. Ponce FA, Spetzler RF, Han PP, et al. Cardiac standstill for cerebral aneurysms in 103 patients: an update on the experience at the Barrow Neurological Institute: clinical article. *J Neurosurg.* 2011;114(3):877-884.
80. Mack WJ, Ducruet AF, Angevine PD, et al. Deep hypothermic circulatory arrest for complex cerebral aneurysms: lessons learned. *Neurosurgery*. 2008;62(6 suppl 3):1311-1323.
81. Sullivan BJ, Sekhar LN, Duong DH, Mergner G, Alyano D. Profound hypothermia and circulatory arrest with skull base approaches for treatment of complex posterior circulation aneurysms. *Acta Neurochir (Wien).* 1999;141(1):1-11; discussion 11-12.
82. Kawaguchi T, Sekhar LN. The rubber dam interposition technique during intracranial aneurysm clipping under deep hypothermic circulatory arrest. *Surg Neurol.* 2000;53(2):146-149.
83. Sekhar LN, Chandler JP, Alyono D. Saphenous vein graft reconstruction of an unclippable giant basilar artery aneurysm performed with the patient under deep hypothermic circulatory arrest: technical case report. *Neurosurgery*. 1998;42(3):667-672; discussion 672-673.
84. Levati A, Tommasino C, Moretti MP, et al. Giant intracranial aneurysms treated with deep hypothermia and circulatory arrest. *J Neurosurg Anesthesiol.* 2007;19(1):25-30.
85. Schebesch KM, Proescholdt M, Ullrich OW, et al. Circulatory arrest and deep hypothermia for the treatment of complex intracranial aneurysms: results from a single European center. *Acta Neurochir (Wien).* 2010;152(5):783-792.
86. Kallmes DF, Ding YH, Dai D, et al. A second-generation, endoluminal, flow-disrupting device for treatment of saccular aneurysms. *AJNR Am J Neuroradiol.* 2009;30(6):1153-1158.
87. Ramanathan D, Ciporen J, Ghodke B, Ellenbogen RG, Sekhar LN. Treatment of coil embolization failed recurrent giant basilar tip aneurysms with bypass and surgical occlusion. *J Neurointerv Surg.* 2010;2(3):237-241.
88. Kellner CP, Haque RM, Meyers PM, Lavine SD, Connolly ES Jr, Solomon RA. Complex basilar artery aneurysms treated using surgical basilar occlusion: a modern case series: clinical article. *J Neurosurg.* 2011;115(2):319-327.

89. Lam AM. Intraoperative transcranial Doppler monitoring. *Anesthesiology*. 1995;82(6):1536-1537.
90. Arambepola PK, McEvoy SD, Bulsara KR. De novo aneurysm formation after carotid artery occlusion for cerebral aneurysms. *Skull Base.* 2010;20(6):405-408.
91. Jankowitz BT, Aleu A, Lin R, et al. Endovascular treatment of atypical posterior circulation aneurysms: technical results and review of the literature. *J Neuroimaging.* 2011;21(1):56-61.
92. Tevah J, Senf R, Cruz J, Fava M. Endovascular treatment of complex cerebral aneurysms with ONYX HD-500(®) in 38 patients. *J Neuroradiol.* 2011;38(5):283-290.
93. Simon SD, Reig AS, Archer KJ, Mericle RA. Biomechanical attributes of microcatheters used in liquid embolization of intracranial aneurysms. *J Neurointerv Surg.* 2012;4(3):211-214.
94. Simon SD, Eskioglu E, Reig A, Mericle RA. Endovascular treatment of side wall aneurysms using a liquid embolic agent: a US single-center prospective trial. *Neurosurgery*. 2010;67(3):855-860; discussion 860.
95. Bryne JV, Beltechi R, Yarnold JA, Birks J, Kamran M. Early experience in the treatment of intra-cranial aneurysms by endovascular flow diversion: a multicentre prospective study. *PLoS One.* 2010;5(9)pii: e12492.
96. Kulcsár Z, Houdart E, Bonafé A, et al. Intra-aneurysmal thrombosis as a possible cause of delayed aneurysm rupture after flow-diversion treatment. *AJNR Am J Neuroradiol.* 2010;32(1):20-25.
97. Gruber A, Killer M, Bavinzski G, Richling B. Clinical and angiographic results of endosaccular coiling treatment of giant and very large intracranial aneurysms: a 7-year, single-center experience. *Neurosurgery*. 1999;45(4):793-803.
98. Fiorella D, Lylyk P, Szikora I, et al. Curative cerebrovascular reconstruction with the pipeline embolization device: the emergence of definitive endovascular therapy for intracranial aneurysms. *J Neurointerv Surg.* 2009;1(1):56-65.
99. Nelsona PK, Lylykb P, Szikorac I, Wetzeld SG, Wankee I, Fiorella D. The pipeline embolization device for the intracranial treatment of aneurysms trial. *AJNR Am J Neuroradiol.* 2011;32(1):34-40.
100. Wong GK, Kwan MC, Ng RY, Yu SC, Poon WS. Flow diverters for treatment of intracranial aneurysms: current status and ongoing clinical trials. *J Clin Neurosci.* 2011;18(6):737-740.
101. Chestnut Medical FDA Panel presentation. Unpublished data through personal communication.
102. Szikora I, Berentei Z, Kulcsar Z, et al. Treatment of intracranial aneurysms by functional reconstruction of the parent artery: the Budapest experience with the pipeline embolization device. *AJNR Am J Neuroradiol.* 2010;31(6):1139-1147.
103. Chow M, McDougall C, O'Kelly C, Ashforth R, Johnson E, Fiorella D. Delayed spontaneous rupture of a posterior inferior cerebellar artery aneurysm following treatment with flow diversion: a clinicopathologic study. *AJNR Am J Neuroradiol.* 2012;33(4):E46-E51.
104. Hampton T, Walsh D, Tolias C, Fiorella D. Mural destabilization after aneurysm treatment with a flow-diverting device: a report of two cases. *J Neurointerv Surg.* 2011;3(2):167-171.

