

Endovascular Management of Cerebral Aneurysm: The Recent Trends

Vipul Gupta¹ Shrikant Londhe¹ Rajsrinivas Parthasarathy¹ Hilal Ahmad Ganaie¹

¹Department of Interventional Neuroradiology, Artemis Agrim Institute of Neurosciences, Gurgaon, Haryana, India

Address for correspondence Vipul Gupta, MD, Department of Interventional Neuroradiology, Artemis Agrim Institute of Neurosciences, Gurgaon, Haryana, India (e-mail: drvipulgupta25@gmail.com).

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Abstract

Cerebral aneurysm rupture is the leading cause of mortality and morbidity in patients with hemorrhagic stroke. Surgical clipping and endovascular coiling are the mainstay of management for securing the aneurysm. After International Subarachnoid Aneurysm Trial (ISAT) and Barrow Ruptured Aneurysm Trial (BRAT) results, worldwide trend has shifted gradually in favor of endovascular management. Nonetheless, endovascular management was faced with some limitations, especially while treating giant, wide neck bifurcation, blister, and small uncoilable aneurysm. The recent introduction of new devices such as flow diverter stents, microstents, bifurcation devices, double-lumen balloon catheters, and microcoils have proved to be effective in overcoming the limitations of traditional aneurysm coiling. The authors present a review of recent advances in the endovascular management of cerebral aneurysm.

Keywords

- cerebral aneurysm
- coiling
- flow diverter

Introduction

The first catheterization of brain arteries was described by Luessenhop and Velasquez in 1964.¹ Following that, another milestone in the form of detachable balloon was reported in cerebral aneurysm and carotid-cavernous fistulae.² Further improvements were sought since detachable balloon had its inherent problems while treating aneurysms and carotid-cavernous fistulae. Guglielmi, an endovascular neurosurgeon, devised controllable, retrievable, detachable platinum coils for a safer and effective treatment of brain aneurysm in 1989. First human application of these coils was done in 1990.³ Later, Moret et al reported balloon remodeling techniques that achieved more complete aneurysm occlusion and were found to be more effective than conventional aneurysm coiling.⁴ Thereafter, the concept of the intracranial stent assisted aneurysm coiling with parent artery reconstruction was introduced by Henkes et al.⁵

International Subarachnoid Aneurysm Trial (ISAT) and Barrow Ruptured Aneurysm Trial (BRAT) showed significant lower morbidity and better safety of the endovascular treatment than surgical clipping.⁶ However, in the ISAT and BRAT trials approximately 50% and 32% of patients,

respectively, were treated by endovascular approach.^{6,7} Long-term follow-up of ISAT trial showed decreased morbidity and dependency in the endovascular group compared with surgical group.⁸

Recent technical advances have enabled the possibility to treat majority of aneurysms, using endovascular means with significant reduction in recurrence rates. Management of the complex fusiform aneurysm, giant aneurysm, blister aneurysm, and small uncoilable aneurysm has been made possible by the recent introduction of flow diverter technology. Furthermore, endovascular treatment of the small distal branch wide neck aneurysms is now possible with introduction of intracranial microstents. Bifurcation devices have improved overall outcome of wide neck bifurcation aneurysm when treated using endovascular techniques. The authors present review of recent advances in endovascular treatment of cerebral aneurysm.

Flow Diverter Stents (Endoluminal Flow Diversion)

All flow diverters are braids with high pore density and low porosity (►Table 1). Flow diverter deployment modifies

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Table 1 Product summary of flow diverter devices available in India

Flow diverter	Available length (mm)	Available diameter (mm)	Design
Pipeline (Medtronic)	10–35	2.5–5	48 braided strands
Surpass (Stryker)	12–50	2–5	48, 72, and 96 braids—according to diameter of stent
FRED (MicroVention)	7–56	3.5–5.5	Outer 16 braids and inner 48 braids
SILK (Balt Extrusion)	15–40	2–5	48 braided strands
p64 (Phenox)	12–36	2.5–5	64 braided strands

the intra-aneurysmal blood flow while maintaining the laminar flow inside the parent artery. The resultant intra-aneurysmal stasis promotes progressive thrombosis within the aneurysm. Over a period of time, endothelium grows over the stent excluding the aneurysm completely with parent artery reconstruction and shrinking of aneurysm. Therefore, it leads to fewer recurrences when compared with traditional coiling.⁹ Flow diverter stents have transformed treatment of the giant aneurysm, which were managed with complex surgical techniques such as trapping and bypass (►Fig. 1).

Flow Diverters in Anterior Circulation

Pipeline embolization device was introduced in 2008 for treating intracranial aneurysm. Since then, to overcome the

shortcomings of the initial device, Pipeline Flex was introduced in 2014 with stiffer delivery wire and polytetrafluoroethylene (PTFE) sleeves instead of capture coil. Favorable outcomes with the device were noted in multiple studies. PUFFS (Pipeline for Uncoilable or Failed Aneurysms) study reported 93.4% and 95.2% complete aneurysm occlusion at the end of 3 and 5 years, respectively, with a good clinical outcome in 96.3% of patients.¹⁰

The PITA (The Pipeline Embolization Device for the Intracranial Treatment of Aneurysms) study again confirmed good occlusion rates (93%) at 6 months.¹¹ A meta-analysis revealed that flow diverters are particularly very effective in treating large and giant anterior circulation aneurysms with near-complete occlusion in 80% at 6 months. The early and delayed complication rates were 5.7% and 1.9%, respectively, with low retreatment rates.^{12,13}

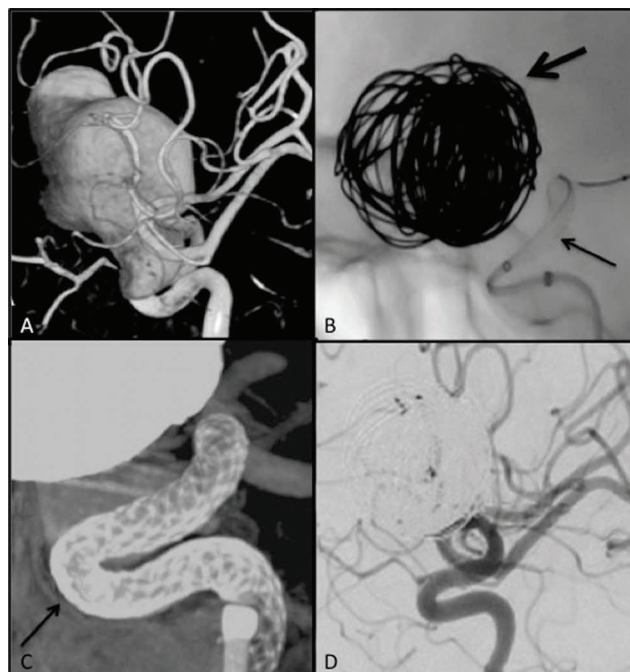


Fig. 1 A 35-year-old female patient presented with eye symptoms secondary to mass effect from the giant unruptured cavernous segment ICA aneurysm. 3D rotational angiogram surface shaded display image showing giant ICA aneurysm involving cavernous segment (A). Native image is showing flow diverter deployment (thin arrow in B) across the aneurysm after partial coil embolization (thick arrow in B) of the aneurysm sac. Vaso CT image post deployment showing well-apposed flow diverter even in curvature of cavernous segment ICA (arrow in C). Six-month follow-up angiogram showing complete occlusion of the aneurysm with parent artery reconstruction (D).

Flow Diverters in Blister Aneurysm

Surgical and conventional endovascular treatment (coils and parent vessel occlusion) had high complication rate for the treatment of the blister aneurysm. Flow diversion is now being increasingly used to treat blister aneurysm. Conceptually, flow redirection is better with flow diverters as compared with the traditional overlapping stents. Recent meta-analysis showed significant better outcome of flow diversion in blister aneurysms compared with surgical arm as well as other endovascular techniques such as coiling, stent-assisted coiling, and parent artery occlusion.^{14,15} The author's experience of flow diverters in ruptured blister aneurysm showed complete occlusion in 89% with no repeat treatment or rebleed.¹⁶ Single flow diverter device with good wall apposition and stent compaction in the region of aneurysm neck leads to complete occlusion of blister aneurysm without significant complications (►Fig. 2).

Flow Diverters in Posterior Circulation Aneurysm

Endovascular management of posterior circulation aneurysm using flow diverter stents is challenging because of the complex nature of disease and high risk of perforator ischemia. A meta-analysis of 225 posterior circulation aneurysm treated with flow diverter stents has showed procedure-related mortality rate of 15%, with higher rate of complications, especially in patients with giant aneurysms and basilar artery aneurysms. The rate of complete aneurysm occlusion at 6-month digital subtraction angiography (DSA) was 84%. Perforator occlusion accounted for 7% of all

ischemic strokes (11%).¹⁷ However, flow diverter is a viable option in the treatment of these aneurysms, allowing for vessel reconstruction and significantly better aneurysm occlusion (►Fig. 3).

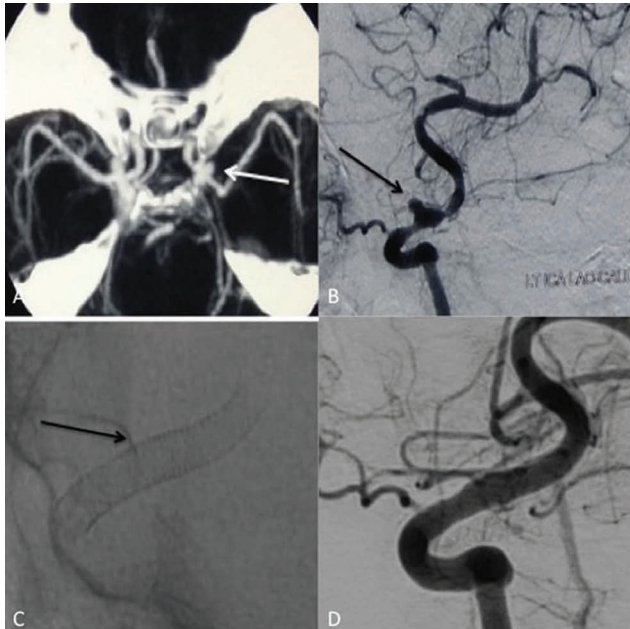


Fig. 2 A middle-aged woman presented with acute subarachnoid hemorrhage. CT angiography showing small aneurysm in left supraclinoid ICA (arrow in **A**). DSA confirmed the aneurysm in dorsal supraclinoid ICA (arrow in **B**)—typical location for blister aneurysms and interval size change compared with CT angiography. Distal intracranial arteries showed diffuse vasospasm. Flow diverter placement for the treatment of blister aneurysm with stent compaction near the aneurysmal segment of ICA (arrow in **C**). Six-month follow-up angiogram showing complete aneurysm occlusion with parent artery reconstruction (**D**).

Complications of Flow Diverters

The most common periprocedural complication in flow diverter treatment group is thromboembolic phenomenon. Using new antiplatelet agents such as Ticagrelor and Prasugrel has significantly reduced incidence of thromboembolic complications in our practice as these drugs have low probability of platelet resistance. Further, in a specific subset of patients in whom the aneurysm size is greater than 2.2 cm, delayed clinical deterioration due to a transient increase in the peri-aneurysmal brain inflammation has been noted.¹² Protective measures including prolonged steroid therapy and ventriculo-peritoneal (VP) shunt insertion in certain groups of patients proved to be beneficial. Finally, delayed aneurysm rupture has been noted following flow diverter placement, especially for large and giant aneurysm. The potential mechanisms of delayed rupture include persistent inflow jet after treatment, thrombosis with expansion of the aneurysm due to stagnation of flow, and thrombus-induced inflammation of the aneurysm wall.^{12,13} The RADAR (Retrospective Analysis of Delayed Aneurysm Ruptures after Flow Diversions) study reported a 2.1% risk of delayed ruptured for aneurysms larger than 10 mm in diameter, with a median time from treatment to rupture of 9 days. In the authors' experience, for large aneurysms of size greater than 10 mm, partial coiling can be done followed by the flow diverter placement to prevent thrombus-induced inflammation as coil mass helps fragment the thrombus.

New Advances in Flow Diverter Technology

Technical advancements in flow diverter are focused on the following issues:

1. Low-profile delivery system (FRED Jr. MicroVention and p48-Phenox) are compatible with small-diameter

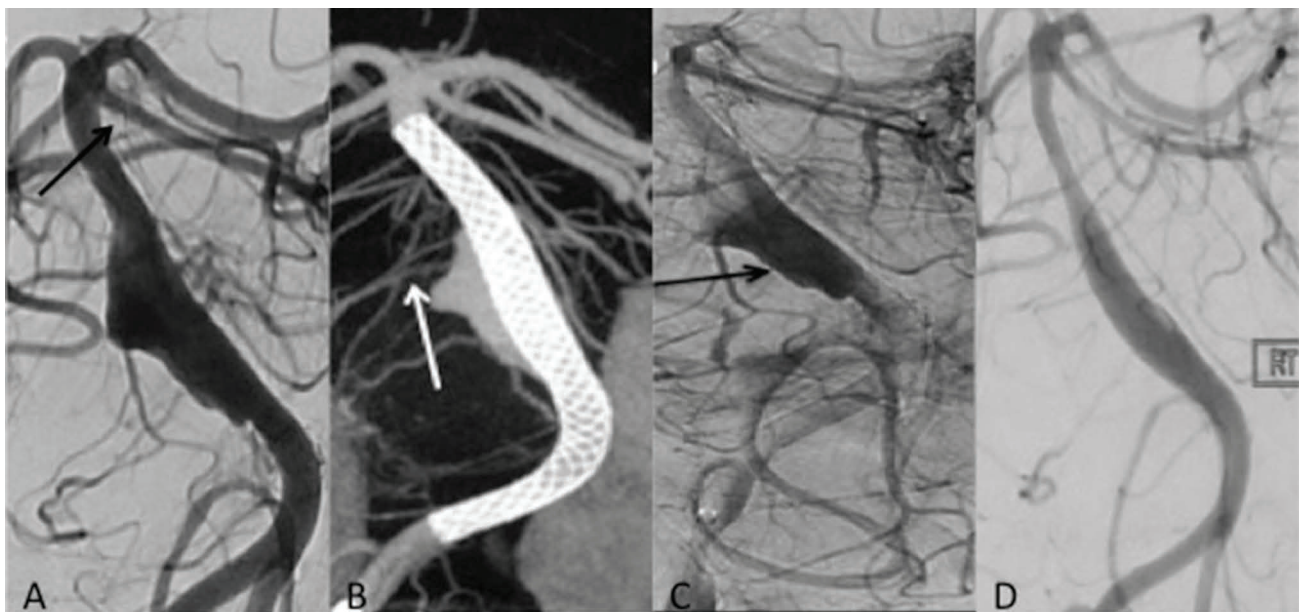


Fig. 3 A 45-year-old male patient presented with brainstem compression symptoms. DSA showed basilar artery fusiform aneurysm (arrow in **A**). Flow diverter was placed from right vertebral artery (V4 segment) to upper basilar artery across the fusiform aneurysm. Postprocedure Vaso CT showed good wall apposition of stent with maintained flow in the perforators from basilar artery even in aneurysmal segment (arrow in **B**). Postprocedure angiogram (late arterial phase) showed significant stasis inside the aneurysm sac (arrow in **C**). Follow-up angiogram after 6-month period showed complete aneurysm occlusion with parent artery reconstruction and maintained flow in branch arteries (**D**).

microcatheter that allows for easy navigation to small distal arteries.

2. The Pipeline Shield Technology is a modification of device in which a synthetic phosphorylcholine polymer is bonded to the pipeline braid to reduce thrombogenicity.¹⁸ Still further studies are necessary to analyze its clinical utility.

Intrasaccular Flow Diversion /Disruption

Flow diversion for wide neck bifurcation aneurysm is limited by thromboembolic complication and side branch occlusion. Therefore, intrasaccular device that enables reconstruction of the anatomy at the neck while providing a robust scaffold to the coil mass appears to be a welcome tool to treat bifurcation aneurysms (►Table 2). These devices are placed within the aneurysm leading to aneurysm occlusion and progressive thrombosis.

Woven EndoBridge

This was introduced in 2011 as first intrasaccular device for the treatment of bifurcation aneurysm. It consists of braided nitinol wires, which help maintain the globular shape of the device (►Fig. 4A, B). Total metal coverage provided is between 35 and 45% and intended to maintain good wall apposition along the aneurysm sac including the neck leading to inflow disruption. The WEB device comes in two configurations: standard (SL [single layer] and DL [double layer]) and spherical SLS [single-layer sphere]. The WEB SL-EV (enhanced visualization) is the latest version of these devices and delivered through 0.017-in ID microcatheter.¹⁹

In 2016, the WEBCAST (WEB Clinical Assessment of Intrasaccular Aneurysm Therapy) study reported successful treatment outcomes in 85% of patients. The rate of thromboembolic events was 17.6%, with a permanent deficit in one patient.²⁰ Meta-analysis of all the available series showed complete or near-complete aneurysm occlusion that was observed in 80% aneurysms at the end of 1 year.¹⁹

Luna Aneurysm Embolization System

The Luna AES (aneurysm embolization system) is a self-expanding double-layer nitinol mesh with platinum markers. It is delivered via a standard 0.027-in microcatheter and takes an ovoid shape within the aneurysm. Study conducted by Piotin et al showed 77% rate of complete or near-complete occlusion at the end of 1 year ($n = 44$). The authors concluded that the 12-month results demonstrated a good safety profile and good results on angiographic follow-up.²¹

Table 2 Overview of intrasaccular flow diversion/disruption devices

Device	Retrievable	Compatible microcatheter
WEB (Sequent Medical, Inc.)	Yes	0.027 in ID
LUNA (Nfocus Neuromedical)	Yes	0.027 in ID
Medina (Medtronic)	Yes	0.021 in ID

Medina

The Medina embolic device (Medtronic) is a three-dimensional (3D) coil made from shape-set core wire with outer filaments forming petals. The 3D petals constitute broader coil loops. This broader loop allows for stable anchoring of the coil mass within the aneurysm sac.²² Initial results in 11 unruptured aneurysms have showed complete or near-complete aneurysm occlusion in 10 patients and an enlarging neck remnant in 1 patient.²³ Lobulated aneurysms can be treated effectively with Medina and coils combinations to avoid recurrences.

Low-Profile Intracranial Stents

Braided Stent

LVIS, LVIS Jr (MicroVention), Leo Plus, and Leo Plus Baby (Balt Extrusion) are the available braided stents in India for the treatment of the cerebral aneurysm. These are self-expandable braided stents with closed cell construction and made of nitinol. The LVIS and Leo Plus stents are recommended for the larger vessels, whereas LVIS Jr and Leo

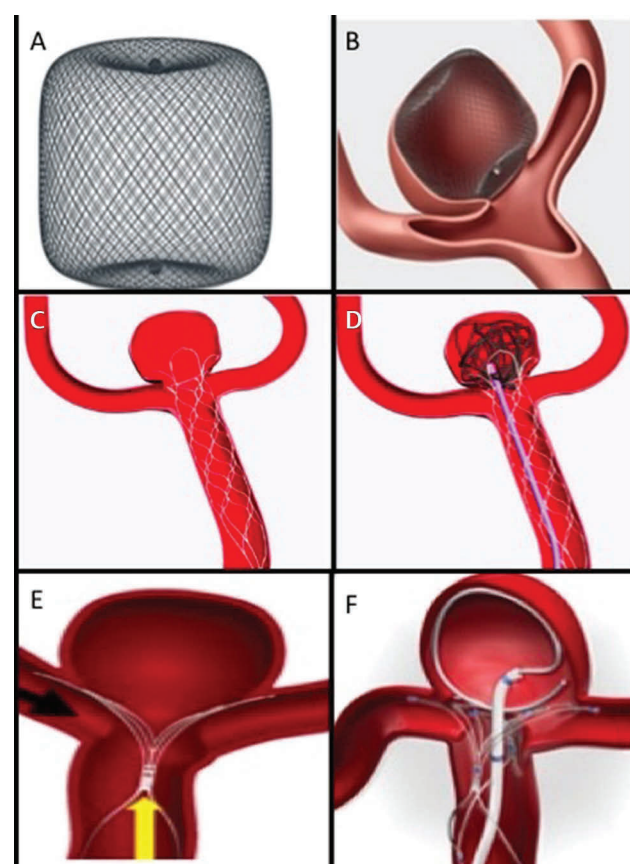


Fig. 4 Pictorial presentation of different bifurcation devices showing WEB intrasaccular (A), WEB deployed into the aneurysm sac (B, printed with permission from Sequent Medical), PCONUS with petals inside aneurysm sac (C), coiling microcatheter across the petals into aneurysm sac (D, printed with permission from Pulsar Vascular), PulseRider with both limbs in side branches (arrow in E), and coiling microcatheter inside the aneurysm sac through the device near neck (F, printed with permission from Phenox).

Plus Baby are for smaller vessel up to 2 mm in diameter. The later stents can be used with ease beyond the circle of Willis as they are compatible with smaller and more flexible microcatheter systems.²⁴ They have a relatively smaller cell size (~1.2 mm in Leo Plus, 0.9 mm in Leo Plus Baby, 1.0 mm in LVIS, and 1.5 mm in LVIS Jr), and therefore have high pore density and low porosity in comparison with conventional self-expandable intracranial stents. Furthermore, because the construct is a braid, it allows to create a shelf across the aneurysm sac and form an effective scaffold across the neck with a single device. The technique of “shelving” reduces the need for additional devices and consequently the complication rates. One study of 78 patients demonstrated 82% aneurysm occlusion at 6-month follow-up with only 3% of cases with TIA, which is better than other intracranial stents.²⁴ In authors' experience, using single microstents and shelving technique coil embolization of wide neck bifurcation aneurysm has shown good long-term occlusion rates (► Fig. 5).

Hybrid Stent

Neuroform Atlas (Stryker) stent has been approved by the Food and Drug Administration (FDA) for the treatment of the wide neck intracranial saccular aneurysm. The stent has unique combination of closed cell design at the proximal end and with open cell design at the distal end, and therefore offers distinct advantages of both stent designs. Conformability (vessel wall apposition), easy delivery, precise placement of stent, and easy microcatheter access to the aneurysm sac are the important advantages of this stent.

Double-Lumen Balloons Catheter

Single-lumen balloon catheters had certain technical challenges such as less torquability with 0.010-in microwire, poor stability, and difficult navigation, especially in tortuous anatomy. Further, development of double-lumen balloon catheters with 0.014-in microwire compatibility provided better wire torquability, thereby helping the catheterization of appropriate branches near the aneurysm neck (► Table 3).

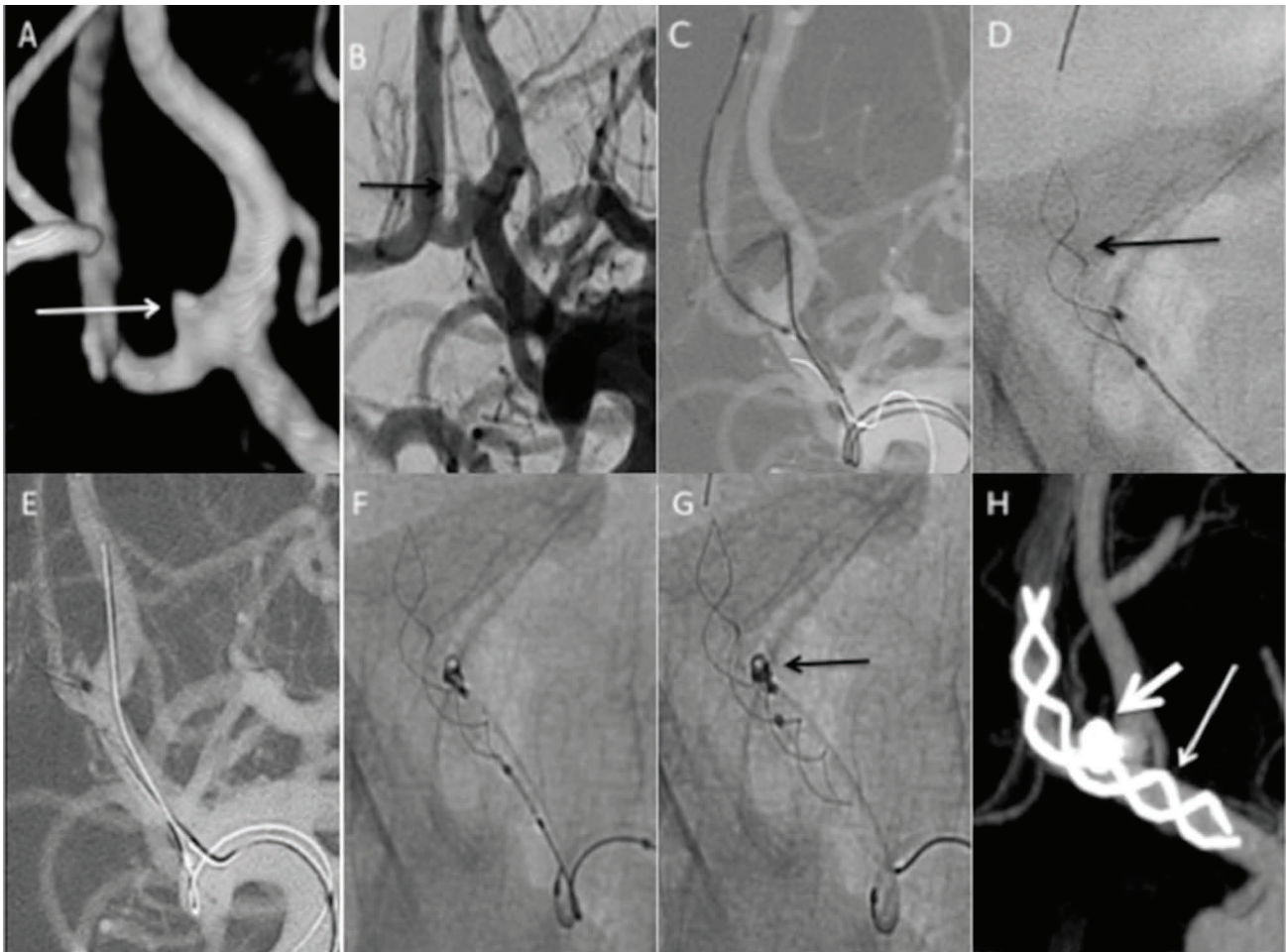


Fig. 5 A 48-year-old male patient presented with subarachnoid hemorrhage. Angiography showing small, sessile, broad-based anterior communicating artery (ACOM) aneurysm (perhaps a blister aneurysm) (arrows in **A**, **B**). Plan was to do stent-assisted coiling, with Leo Plus Baby stent. Stent microcatheter (Vasco 10) with microwire was placed in right A2 ACA from left A1 ACA. Due to small size of the aneurysm, it was difficult to have stable catheterization; hence, it was planned to partially deploy the stent with microcatheter in left A2 ACA (**C**). Aneurysm was later catheterized with the help of partially opened Leo stent (2.5 × 25), which acts as a scaffolding to support coiling microcatheter at the neck of the aneurysm (arrow in **D**). Aneurysm was then embolized using a 1.5-mm × 4-cm coil (**E**). Stent was then fully deployed, and coiling was completed (**F**, arrow in **G**). Poststenting Vaso CT showing well-opposed stent (thin arrow) along right ACA with coil in the aneurysm (thick arrow) (**H**).

Table 3 Technical details of available dual-lumen balloon catheters

Balloon	Guidewire (in)	Length of balloon (mm)	Diameter of balloon (mm)	DMSO compactible
Ascent (DePuy Synthes)	0.014	7, 9, 10, 15	4, 6	Yes
Scepter (MicroVention)	0.014	10, 15, 20/11	4	Yes
Eclipse 2L (Balt Extrusion)	0.014	7/9, 12, 20	6	Yes

Compared with single-lumen balloon catheters, double-lumen balloon offers other distinct advantages:

1. Ability to deploy the low-profile stent in case of bailout options
2. Injection of liquid embolic agents, if required
3. Simultaneous mechanical and chemical angioplasty of severe vasospasm following acute subarachnoid hemorrhage (SAH)²⁵

The Comaneci temporary bridging device (Rapid Medical) is a compliant radiopaque mesh, which temporarily bridges the neck of the aneurysm to support coil mass without compromising flow in the parent artery. One study reported on stable occlusion in 14 of 18 aneurysms treated using this device. Four patients required additional remodeling technique either stent or balloon. One patient had delayed parent artery occlusion probably owing to endothelial injury secondary to prolonged balloon inflation.²⁶

Smaller Coil

Hypersoft helical and 3D coils (Target Nano, Stryker; Blockade, Balt Extrusion; Hydro Coils, MicroVention; and Axium Prime, eV3), in particular those with 1 to 1.5 mm in diameter, achieve higher packing density in small aneurysms. These very soft platinum coils may offer the neurointerventionist the possibility to fill smaller spaces and allow for the improved packing in small aneurysm. However, the long-term follow-up of a large series of patients is necessary for evaluation of the improvement of the recanalization rate.²⁷

The authors' experience also showed improved packing density using these microcoils in small aneurysm as well as finishing coil in larger aneurysm.

Bifurcation Support Devices

Most of the bifurcation devices for wide neck aneurysm were only for the support of coil mass during the aneurysm treatment. Presently new devices offer the support as well as neck reconstruction in these aneurysm.

pCONus

The pCONus (Phenox GmbH) is a stent-like device with four petals at the distal end that rests on the inner wall of the sac. To create a scaffold that prevents coil prolapse, there is a meshwork at the base of the petals (►Fig. 4C, D). The aneurysm sac can be catheterized through the mesh at the base of the petals. The device is compatible with standard microcatheter with an inner diameter of 0.021 in.^{28,29} One retrospective study evaluated the safety and efficacy of pCONus with adjuvant coiling in unruptured wide neck bifurcation

aneurysm. At 12 months complete occlusion was noted in 75% of patients ($n = 12$). Two cases had embolic complications and out of this one was directly related to the pCONus device.²⁹ The latter generation pCONus 2 devices have six petals to provide a better scaffold at the level of the neck.

Pulse Rider

The Pulse Rider (Pulsar Vascular) is a bifurcation device—a self-expanding, nitinol implant that is available in both “T” and “Y” configurations, intended to fit the geometry of the daughter vessels arising at the bifurcation. The device is available in different diameters and lengths with the key benefit being that the daughter branches do not need to be accessed to deploy the device (►Fig. 4E, F). These petals offer neck protection regardless of whether they are positioned within the sac or daughter branches.³⁰

A prospective, nonrandomized, single-arm clinical trial showed near-complete occlusion in 87.9% and good outcomes in 94% of patients at 6 months.³¹ This device is not yet available in India.

Conclusion

Technological advancements in endovascular treatment methods have resulted in a sea change in the approach and treatment to cerebral aneurysms. Many of these novel devices represent new solutions to commonly encountered challenges in treatment of complex aneurysms, including giant aneurysm, blister aneurysm, nonsaccular posterior circulation aneurysm, and wide neck bifurcation aneurysm. Better safety profile and good long-term occlusion rates in multiple clinical trials have proved to be pivotal in the approval of new devices in the management of cerebral aneurysm.

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