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Review Article

Endovascular Treatment of Wide-Neck Bifurcation Aneurysm: Recent Trends in Coil Embolization with Adjunctive Technique

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Wide-neck bifurcation aneurysms (WNBAs) are sometimes challenging to treat. During endovascular treatment, it is important to prevent coil deviation and preserve normal vessels. Adjunctive balloon- and stent-assisted techniques have been developed. A meta-analysis of endovascular treatments of WNBAs revealed that only 40% of patients had complete occlusion. Recently, novel devices have been developed to expand the range of treatment options. Flow-diverter stents and intra-aneurysmal flow disruption devices do not require coils; however, coil embolization remains the standard procedure used by many neurointerventionists. This review describes the recent trends in adjunctive techniques for supporting coil embolization for WNBAs. We referred to literature on balloon-assisted techniques, stent-assisted techniques, Y-stenting, PulseRider, Barrel stents, Comaneci temporary stents, pCONUS, and eCLIPs. These reports showed that adequate embolization rates were generally greater than 80%, and the complete occlusion rate was as high as 94.6%. All devices had a relatively high occlusion rate; however, it may be inaccurate to simply compare each device because of the heterogeneity of the studies. It is important to select the best treatment for each individual case by considering not only literature-based efficacy and safety but also patient background, aneurysm characteristics, and operator experience.

Keywords ▶ endovascular treatment, intracranial aneurysm, bifurcation aneurysm, coil embolization, adjunctive technique

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Introduction

The treatment of bifurcation aneurysms is sometimes difficult. Large aneurysms, particularly those with wide necks, are challenging to treat either surgically or endovascularly. In endovascular treatment (EVT), it is important to prevent coil deviation from a wide-necked aneurysm, preserve normal vessels branching from the neck, and follow up for recurrence (**Fig. 1A**). Adjunctive techniques such as double-catheter, balloon-assisted, and stent-assisted techniques have been developed. Various subtypes of these methods, including Y-stenting, X-stenting, and waffle cone methods, have been used for treatment. A meta-analysis of EVT for wide-neck bifurcation aneurysms (WNBAs) revealed that only 40% of cases were completely occluded.[1] Novel devices have recently been developed, which has expanded the range of available treatment optionss. In Japan, the W-EB (Microvention, Terumo, Aliso Viejo, CA, USA) and PulseRider (Cerenovus, Johnson & Jhonson Medical

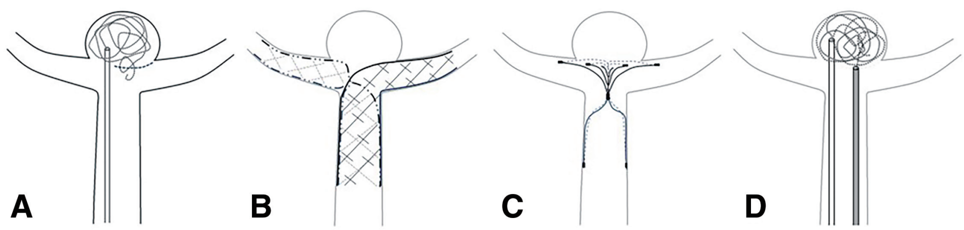

Fig. 1 Illustration of endovascular therapy for WNBAs. (**A**) The simple technique. Coils easily deviate into the parent vessel. (**B**) Y-SAC. Y-configuration double stent protects the parent artery and both side branches. (**C**) PulseRider. Bidirectional flexible leaflets provide a scaffold at the neck in an "extra-aneurysmal," "intra-aneurysmal," or "hybrid" fashion. (**D**) Double catheter technique. Simultaneous or alternating coil placement from two catheters allows coils to remain in the aneurysmal sac. WNBAs: wide-neck bifurcation aneurysms

Devices, New Brunswick, NJ, USA) have been introduced and are already in use at some facilities. The W-EB is an "intra-aneurysmal flow disruption device" that implants a basket of metal inside the aneurysm, while the PulseRider is a stent device that provides a scaffold for coil embolization at the neck of a bifurcation aneurysm. Flow-diverter stents and intra-aneurysmal flow disruption devices do not require coils; however, coil embolization remains the standard procedure used by many neurointerventionists. This review describes the recent trends in adjunctive techniques for supporting coil embolization for WNBAs.

Balloon-Assisted Coiling

Balloon-assisted coiling (BAC) provides temporary scaffolding to prevent coil protrusion into parent and branch arteries. Bulging neck plasty with a super-compliant balloon catheter is a technique that can sometimes be used to treat complex wide-neck aneurysms.[2,3] BAC also has a stabilizing effect on microcatheters used for coil embolization. Antiplatelet drugs being unnecessary in BAC is a major advantage over stent-assisted techniques, especially for the treatment of acutely ruptured wide-neck aneurysms. Previous reports have shown no increase in complications related to the use of BAC compared with the simple technique.[4]

A study using the Japanese Registry of Neuroendovascular Therapy 3 (JR-NET3), titled "The Dawn of the Stent Era," found that the use of stents increased significantly, with BAC being the most dominant treatment, accounting for 41%. A combination of BAC and other techniques was performed in 4.2% of the cases.[5] The study also reported an increase in the number of wide-neck aneurysms and a decrease in the percentage of complete occlusions. Although the study showed that BAC remains a useful and versatile technique, it also demonstrated that EVT of cerebral aneurysms faces greater challenges.

A report of 198 cases treated with the BAC technique within the last 10 years reported a technical success rate of 98.5%, with procedural thromboembolism in the parent vessel occurring in 14.1% of cases and symptomatic thromboembolism in 2.5%. The procedure-related mortality and morbidity rates were 1.6% and 4.3%, respectively. According to this report, intraprocedural rupture of aneurysms and thromboembolic events were more common in bifurcation than in sidewall aneurysms (6.5% vs. 2.2%, 15.7% vs. 12.2%, respectively).[6] In another report from the same period that explored the use of the simple technique or BAC, thromboembolic events were more common in middle cerebral artery aneurysms, and intraoperative rupture was more common in small size, anterior cerebral artery, and anterior communicating artery aneurysms.[7] It has been suggested that treating middle cerebral artery aneurysms with challenging features such as trifurcation and wide neck carries a high risk of thrombus formation due to inadequate neck coverage and coil protrusion.

A previous study on wide-neck aneurysms showed that complete occlusion was achieved in 46.7%, 75%, and 78.6% of patients in the balloon, double microcatheter, and stent groups, respectively.[8] Particularly, many cases of WNBA are difficult to treat using BAC alone, and various other methods have been developed, as described below.

Stent-Assisted Coiling

The use of stents for the treatment of intracerebral aneurysms was first approved in the United States in 2002 and Japan in 2010. Currently, three types of stents are available in Japan: the Neuroform Atlas (Stryker Neurovascular, Fremont, CA, USA), Enterprise 2 (Cerenovus), and LVIS

(Microvention). All stents are self-expanding, but each has unique characteristics. The Neuroform Atlas is the first low-profile laser-cut open-cell stent designed to allow delivery through a microcatheter with an inner diameter of 0.0165 inch. Enterprise 2 is also a laser-cut stent characterized by a closed-cell design that allows for re-sheathing. The LVIS exhibits flow-diversion-like effects owing to its braided structure, high metal coverage, and small cell size. The stent-assisted coiling (SAC) provides mechanical protection or coil protrusion into the parent and branching arteries. The intentional stent herniation technique is useful for treating complex wide-neck aneurysms.[9] SAC requires appropriate antiplatelet agents to be used but provides a more solid and stable scaffold without interrupting blood flow during the procedure. Several recent reports evaluating angiographic outcomes and safety in unruptured cases treated with SAC showed no difference when stratified by stent model.[10,11]

In a report on unruptured middle cerebral artery aneurysms, SAC significantly reduced the recurrence rate compared to simple coiling without increasing the risk of complications.[12] Although SAC has clearly improved the treatment of wide-neck aneurysms, it is not indicated for cases of acute rupture and its use is off-label. A decade ago, a review reported a higher complication rate after acute SAC than without stenting. Recently, it was reported that Neuroform Atlas may be suitable for acutely ruptured aneurysms owing to its low-profile design and reduced metal construction.[13] Similarly, its use in acute rupture cases has been reported, with a high rate of complete occlusion and a low rate of recanalization without increased procedural complications compared with simple coiling.[14] The study revealed that stent thrombosis was lower in cases using the Neuroform Atlas stent (Neuroform Atlas 2.8% vs. Enterprise 9.1% vs. LVIS and LVIS Jr 15.8%). A study on SAC versus coiling alone for ruptured anterior communicating artery aneurysms showed no significant differences in the incidence of complications, mortality, morbidity, midterm complete occlusion rate, or recurrence rate.[15] In another report on SAC with LVIS for ruptured bifurcation aneurysms, the rates of complete occlusion during the follow-up period, intraprocedural thrombosis, and intraoperative hemorrhage were 83.3%, 4.9%, and 2.4%, respectively.[16]

In the most recent report on SAC treatment for WNBAs, the rates of complete occlusion during follow-up and procedure-related permanent morbidity were 80.8%–90.9% and 1.5%–8.6%, respectively.[17–19] Although these studies have shown favorable results, treatment of WNBAs in which both branches are involved in the neck can be very difficult using a single stent. In such cases, developmental techniques such as the waffle cone technique or Y-stent-assisted coiling may be applied. Neck-bridging stents for coil embolization not only provide a mechanical scaffolding effect but also lead to the development of flow-diverter stents, focusing on the flow-diverting hemodynamic effect.

A flow diversion effect is expected for the braided stents. Previous reports on small aneurysms with stents implanted alone without coiling have shown a high rate of adequate occlusion. LVIS implantation is reportedly effective for bifurcation aneurysms of the superior cerebellar artery.[20] In a report on stent monotherapy with LEO (BALT Extrusion, Montmorency, France), a self-expandable low-profile braided stent for SAC, 73.7% complete occlusion was achieved with a single oroverlapping stent implantation without coiling in distally located, small, or difficult-to-coil aneurysms.[21] Another recent report showed that the rates of complete occlusion, permanent morbidity, and mortality were 90.4%, 2.0%, and 0%, respectively.[22] Neck-bridging stents or SAC continue to advance, leading to the development of novel therapeutic devices.

Y-SAC

Since the first report of coil embolization using a double-stent Y-configuration technique, several types of treatments using a combination of two stents have been developed (**Fig. 1B**). The basic Y-SAC technique is as follows: the first microcatheter is introduced into a branch of the parent artery. Next, the aneurysms are selected using a second microcatheter, and the first stent is placed across the neck of the aneurysm. The first microcatheter is navigated through the first stent strut into the other branch. Coil embolization is performed after the second stent is deployed in a Y-configuration. This technique is sometimes referred to as crossing Y-stenting. When one stent is placed parallel to another in the parent artery without crossing the other stent transcellularly, it is called kissing Y-stenting. When one stent is placed through the daughter branch to the parent artery, covering the neck, and the other is placed through the other daughter branch to the neck without overlapping with the first stent, it is called T-stenting.

Recently, new low-profile stents compatible with 0.0165-inch microcatheters have become available, making treatment with Y-SAC for distal wide-neck aneurysms safer, with improved procedural success rates and a reduced risk of intraoperative thromboembolism. Three recent reports of unruptured WNBAs indicate that angiography at follow-up shows complete occlusion in 73.3%–94.6%.[23–25] Particularly, Y-SAC with the new low-profile braided stents showed remarkable results with a modified Raymond–Roy classification (mRRC) I of 81.8%–94.6% and an mRRC I & II of 95.4%–99.1%.[23,24] No morbidity or mortality occurred in two of these reports.[24,25] However, intraprocedural in-stent thrombus formation that resolves asymptomatically and intraoperative rupture that does not result in morbidity have been reported as complications. A study evaluating patients with acutely ruptured WNBAs treated with Y-SAC documented mRRC I and II in 85.7% of patients and intraprocedural stent thrombosis in 16.6%.[26] In the report, intra-arterial injections of tirofiban were administered close to the thrombosis site, and complete or near-complete lysis was achieved in all cases; however, 40% resulted in symptomatic infarction and 40% in asymptomatic infarction. In the acute phase of rupture, when coagulability is elevated, the possibility of a high risk of thrombus formation should be considered. In a report of mostly unruptured aneurysms, mainly WNBAs, kissing Y-stenting showed cases of procedural failure and infarct complications, but there was no significant difference compared with crossing Y-stenting.[27] Since the use of novel devices such as the W-EB and PulseRider is limited to a few institutions and physicians, Y-SAC with conventional neck bridging stents may remain the first choice for WNBA treatment at the majority of institutions.

PulseRider

The PulseRider is a self-expanding nickel–titanium (nitinol) stent specifically designed to treat WNBAs (**Fig. 1C**). The instrument was designed using a concept similar to that of the waffle cone technique. The Adjunctive Neurovascular Support of Wide-Neck Aneurysm Embolization and Reconstruction (ANSWER) trial demonstrated its safety and efficacy for carotid terminal and basilar top aneurysms.[28] This device provides a scaffold for coil embolization by deploying bidirectional flexible leaflets at the neck, either inside or outside the aneurysm. It can be placed without catheter insertion in distal branch vessels, with less metal crossing normal vessels, reducing the amount and duration of antiplatelet drug use compared with conventional stents.

In the ANSWER trial, the PulseRider was successfully delivered and deployed in all patients. Immediate mRRC I or II occlusion was achieved in 82.4% of the cases and improved to 87.9%. A recent meta-analysis revealed that PulseRider-assisted coiling for the treatment of WNBAs had an adequate occlusion rate of 89% at six months (mRRC I, 64%; mRRC II, 25%).[29] The meta-analysis showed that complications occurred in 5% of patients, including intraoperative aneurysm rupture, thrombus formation, procedure-related infarction, vessel dissection, and delayed device thrombosis. No procedure-related deaths occurred. In a comparative study of the PulseRider with SAC, the complete obliteration rate was significantly higher with PulseRider-assisted coiling (88.2% vs. 41.4%).[30] However, compared with Y-SAC, complete occlusion at six months was significantly higher after Y-SAC (90.3% vs. 62.5%).[31]

PulseRider is also potentially useful in case of acute rupture, as its structure allows less metal to cross normal blood vessels normal vessels. Although only a few case series have been reported, good results have been obtained for basilar tip aneurysms in the acute phase of rupture.[32,33] Unfortunately, at the time of writing this review, the PulseRider is expected to be discontinued and no longer available.

Double Catheter Technique

The double catheter technique or dual microcatheter technique is sometimes used for wide-neck or complex-shaped cerebral aneurysms (**Fig. 1D**). Two microcatheters are implanted at different locations inside the aneurysmal sac. Embolization is performed with each microcatheter simultaneously or alternately, allowing the coils to remain in the aneurysmal sac. In a recent report comparing 34 patients treated with this technique to 35 patients treated with SAC for wide neck aneurysms, the complete or adequate occlusion rate and recurrence rate at follow-up and recurrence rate were superior for SAC.[34] Although the advent of neck-bridging stents has reduced the use of this technique, it may be considered in the acute phase of rupture.

Combination With EVT and Open Surgery

Complex intracranial aneurysms cannot always be adequately occluded using a single approach, either EVT or open surgery. One study reported EVT combined with extracranial-intracranial bypass for these lesions (**Fig. 2A**).[35] The basic concept of the method is to convert a bifurcation aneurysm into a sidewall aneurysm using bypass surgery followed by coil embolization. Hybrid surgery must be tailored to the wide variety of aneurysms and anatomical variations individually. In some cases, an IC–IC bypass, such as the A3–A3 bypass or PICA–PICA bypass, is performed. Endovascular procedures are performed using coil embolization, sparing the parent and daughter vessels with or without a stent. At our institution, the type of bypass surgery (single, double, or high-flow bypass) is based on the results of preoperative balloon test occlusion (BTO) using single-photon emission computed tomography or angiography-based BTO.[36] In one study, which included aneurysms with various morphology and mostly ruptured, the rates of complete occlusion, aneurysm-related morbidity, and mortality were 82.9%, 12.6%, and 6.8%, respectively. In a similar study that focused on ruptured fusiform aneurysms, treatment-related stroke was observed in 30% of patients.[37] A recent case report of a recurrent large complex middle cerebral artery aneurysm showed that staged hybrid techniques with a superficial temporary artery-M2 bypass, followed by flow-diverter deployment with coil embolization, resulted in complete occlusion without symptomatic complications (**Fig. 2B**).[38] Reports on these hybrid surgeries are limited and difficult to evaluate statistically. It is important that the treatment strategy is determined on an individual basis in collaboration with a multidisciplinary team when no other effective treatment options are available.

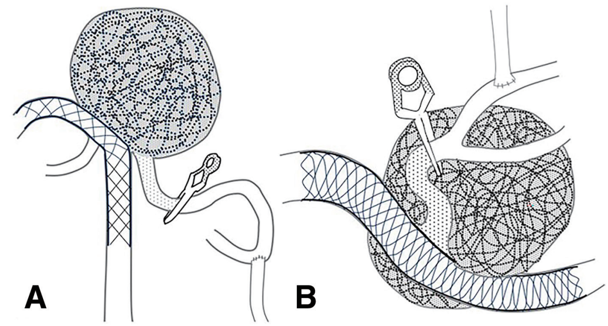

Fig. 2 Illustration of combination treatments with endovascular therapy and open surgery. (**A**) A case of basilar tip aneurysm reported by Sato et al.[35] (**B**) A case of middle cerebral aneurysm reported by Tanabe et al.[38]

Other Stenting Techniques

The Barrel vascular reconstruction device (Medtronic, Minneapolis, MN, USA) is an electrolytically detachable laser cut, closed-cell stent with a bulging central component (**Fig. 3A**). The bulged section protrudes into the aneurysmal neck, providing greater neck coverage. Three studies reported that the percentage of adequate occlusion at follow-up ranged from 78.9% to 100%, with mRRC I occlusion rates of up to 95%.[39–41] Complications included intraprocedural in-stent thrombus formation, intraoperative aneurysm rupture, delayed in-stent stenosis, or delayed infarction, with a permanent morbidity rate of 1.8%. Although several trials have been conducted abroad, the instrument has not yet been officially marketed.

The Comaneci (Rapid Medical, Yokneam, Israel) is an embolization-assisting device that can be temporarily deployed in the parent artery across the aneurysm neck without arresting blood flow (**Fig. 3B**). The Comaneci is not permanently implanted in the vessel, unlike other stents. The first retrospective case series with the Comaneci in 29 ruptured aneurysms reported that the rates of immediate complete occlusion and periprocedural complications were 100% and 3.44%, respectively.[42] A recent meta-analysis of treatments for acute subarachnoid hemorrhage from wide-necked aneurysms showed favorable embolization rates and safety compared to BAC or SAC.[43] Appropriate antiplatelet therapy and intravenous heparin administration are important to prevent thrombus formation inside the mesh of the Comaneci.[44] Treatment options in combination with BAC or SAC may be selected for difficult-to-treat WNBAs.

The pCONUS device (Phenox, Bochum, Germany) was designed using a concept similar to the waffle cone technique and eliminates the need to catheterize the daughter branches (**Fig. 3C**). It has a distal crown and petals that provide a bridging structure at the level of the aneurysmal neck, a stent-like structure for secure anchoring and long-term stability, and an electrolytic detachment system. The second generation "pCONUS2" has less metal shaft and six petals. This allows a more flexible fit to the neck and stronger support for coil embolization. The hydrophilic polymer coating (pHPC, Phenox) is a new glycan-based multilayer polymer that makes the coated device hydrophilic and less thrombogenic. There have been several reports on pCONUS2 and pCONUS2 HPC.[45,46] The unruptured cases received dual antiplatelet therapy, while ruptured cases received single antiplatelet therapy. The rate of complete occlusion at follow-up was 62.5%–68.8%, and intraprocedural thrombus formation occurred in 1.8% of patients.

The eCLIPs (Evasc Medical System, Vancouver, Canada) have a "spine-rib" design with 2 types of rib (**Fig. 3D**). The distal is a low-density anchor segment that secures the device to one of the daughter branches. The proximal

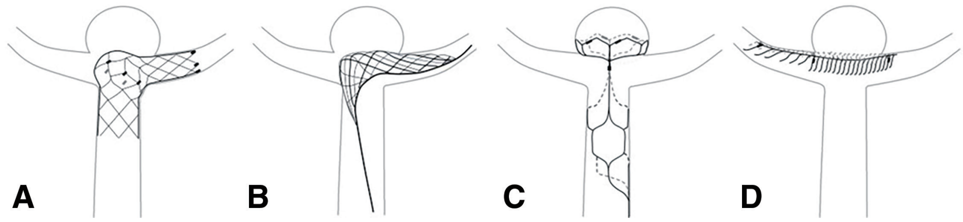

Fig. 3 Illustration of other stenting techniques for WNBAs. (**A**) Barrel. The bulged section protrudes into the aneurysmal neck, providing greater neck coverage. (**B**) Comaneci. It can be temporarily deployed in the parent artery across the neck without arresting blood flow. (**C**) pCONUS2. The distal crown and six petals provide a bridging structure at the neck. (**D**) eCLIPs. Low-density ribs are anchored in the side branch, and higher-density ribs cover the aneurysm neck. WNBAs: wide-neck bifurcation aneurysms

Table 1 Summary of recent endovascular treatment studies for wide-neck bifurcation aneurysms

Device/ technique	Reference	Aneurysm	Success rate (%)	Occlusion rate* (%) (follow-up period)			Morbidity (%)	Mortality (%)	Intraprocedural complication (%)
				I	II	III			
BAC	Vignesh et al.[6]	198, mostly ruptured	98.5	46.7			4.3	1.6	TEE 14.1, IOR 4.5
SAC	Hanel et al.[18]	35, unruptured	100	80.8	15.4	3.8 (12 months)	5.7	0	IOR 2.9, major infarction 5.7
			100	90.9	9.1	0 (4 months)	6.7	0	
	Çay et al.[17]	66, unruptured		89.4	9.1	1.5 (27.3 months)	1.5	0	
	Liu et al.[16]	41, ruptured	100	83.3	16.7	0 (13.9 months)	0	0	TEE 4.9, IOR 2.4
Y-SAC	Yıldırım et al.[26]	30, ruptured	90.9	71.4	14.3	14.3 (18.9 months)	6.6	0	TEE 16.6
	Endo et al.[24]	22, unruptured	100	81.8	13.6	4.5 (43.5 months)	0	0	TEE 4.5, IOR 4.5
	Kim and Chung[25]	15, unruptured	100	73.3	6.7	20 (12.3 months)	0	0	
	Suleyman et al.[23]	111, mostly unruptured	100	94.6	4.5	0.9 (6 months)	0	0.9	
PulseRider	Limbucci et al.[31]	32, unruptured		62.5	21.9	15.7 (6 months)	3.1	0	TEE 3.1
	Omodaka et al.[30]	17, unruptured		88.2	5.9	5.9 (6 months)	0	0	
Barrel	Gory et al.[40]	20, unruptured	95	63.2	15.8	21 (12 months)	5.3	0	IOR 5, minor stroke 5
Comaneci	Vinacci et al.[44]	14, mostly ruptured	86	76.9	15.4	7.7 (12–18 months)	0	0	TEE 21.4
pCONUS2 & pCONUS2 HPC	Yeomans and Sastry[45]	20, mostly unruptured	100	62.5	31.3	6.3 (6 months)	0	0	None
	Morales-Caba et al.[46]	56, unruptured	98.2	68.8	14.6	16.6 (12 months)	1.8	0	TEE 1.8, IOR 3.6
eCLIPs	Chiu et al.[49]	33, mostly unruptured	75.7	33.3	47.6	19 (8 months)	0	8 (delayed rupture)	TEE 4, vasospasm 12
	De Vries et al.[47]	24, unruptured	95.8	61.9	33.3	4.8 (15.8 months)	0	1 (vessel perforation)	TEE 4.2, vessel perforation 4.2
	de Vries et al.[48]	20, unruptured	90	66.7	22.2	11.1 (12 months)	5.6	0	

Occlusion rate* I: complete occlusion; II: neck remnant; III: body filling.
BAC: balloon-assisted coiling; IOR: intraoperative rupture; SAC: stent-assisted coiling TEE: thromboembolic event

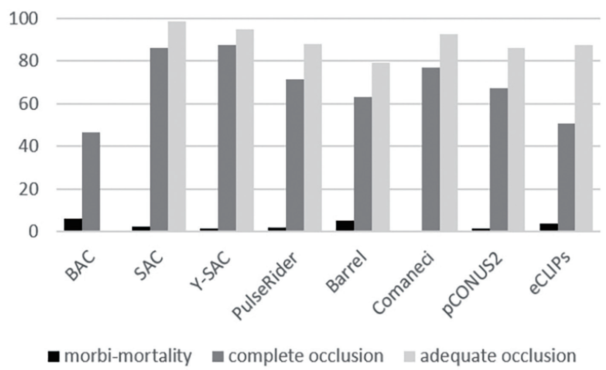

Fig. 4 Bar graph of radiological and safety outcome data. The mean values of morbi-mortality, complete occlusion, and adequate occlusion are shown, considering the specific population of each study. BAC: balloon-assisted coiling; SAC: stent-assisted coiling

segment with high-density ribs covers the neck of the aneurysm. It is called the "flow disrupting leaflet segment" and provides not only a scaffold for coil embolization but also a flow disrupting effect and endothelialization of the device. The eCLIPs can be delivered through a 0.034-inch microcatheter into one of the branch arteries. The device is fully unsheathed in the branch and partially unsheathed into the parent artery. Then, the guidewire is advanced into the contralateral branch artery. The ribs of the leaflet segment allow access for the microcatheter to the aneurysmal sac for coiling. In recent studies, complete occlusion and adequate obliteration were archived in 62%–67% and 85%–89%, respectively, during the follow-up period.[47,48] The technical success rate of deployment of the eCLIPs was 90%–96%. Procedure-related complications included subarachnoid hemorrhage due to guidewire perforation of the daughter branch, asymptomatic thrombotic events, and vasospasm or dissection due to an eCLIPs microcatheter. The unique design of the eCLIPs requires the insertion of a catheter or guidewire into both daughter branches. Therefore, it is important to consider vessel structure, including the diameter of the branch and the angle at which it forms with the parent artery. All patients were pre-treated with a dual antiplatelet therapy regimen. To the best of our knowledge, there are no reports examining the treatment outcomes for ruptured cases or the flow-diverting effect.

Conclusion

We summarized the treatment options for WNBA coiling based on recent studies (**Table 1**, **Fig. 4**). Not only the patient characteristics but also the morphology of cerebral aneurysms is remarkably varied. Since there is no one-size-fits-all device or technique, it is important to select the best treatment for each individual case by considering patient background, aneurysm characteristics, operator experience, and literature-based efficacy and safety. Additionally, combination therapies may be selected when no other effective treatments are available.

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Disclosure Statement

The authors declare that they have no conflicts of interest.

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