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REVIEW ARTICLE

# Antiplatelet, anticoagulation, and elective aneurysm treatments in neurological patients

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## Abstract

Developing more specialized care for neurological disorders, such as aneurysms, arteriovenous malformations, and strokes, can revolutionize patient healthcare and outcomes. With the advent of surgical techniques such as flow diversion, non-stent- and stent-assisted coiling, and catheter embolization for elective aneurysm treatment in neurological patients, the adverse effects and morbidities associated with aneurysms can be reduced. This paper aims to highlight three specific strengths and weaknesses of the newly emerged techniques. Flow diversion devices involve placing a stent in the parent artery, whereas Woven EndoBridge embolization involves manipulation of the wall of the artery without the administration of dual-antiplatelet therapy. In addition to aneurysm treatment, the administration of antiplatelets and anticoagulants is helpful in disrupting the coagulation cascade. As stated in the new and enhanced guidelines released by the American Heart Association, the administration of dual anticoagulants is beneficial to the patients if they have low ischemic severity. Understanding the various benefits and complications associated with each treatment can allow clinicians to gain insight into the potential trajectory of treatment for different patients.

***Keywords:*** Aneurysm; Stent-assisted embolization; Antiplatelet therapy; Woven Endobridge embolization; Catheter embolization

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## 1. Introduction

In the realm of neurosurgical care, emerging approaches have opened up new frontiers and revolutionized the management of challenging neurovascular manifestations by offering patients minimally invasive treatments that come with exceptionally promising outcomes[1-3]. The field of neurovascular diseases encompasses a wide range of neurological disorders, such as intracranial aneurysms, acute ischemic strokes, cerebral arteriovenous malformations, and vascular growths, which require specialized expertise and thorough, comprehensive care. For instance, cerebral aneurysms — abnormal bulges that develop in the blood vessels of the brain — and arteriovenous malformations — tangled networks of abnormal blood vessels in the brain or spine — are both vascular conditions that

can disrupt the normal flow of blood in the brain[4]. These vascular anomalies pose a considerable threat of rupture, which can consequently result in severe neurological implications, including the onset of subarachnoid hemorrhage[4-6]. These challenges have driven the rapid development of vascular devices and surgical techniques, such as flow diversion, non-stent- and stent-assisted coiling (SAC), and catheter embolization[3,7], promoting the rapid evolution of the neurovascular surgery field.

Neurovascular disorders pose serious risks to heightened morbidity and mortality rates among the affected patients if such conditions are left uncontrolled, and thus, the management of these disorders has become an emerging area of concern in the field of neurology and neurosurgery, which has a bearing on the patients' quality of life[6]. In essence, the regulation of neurovascular diseases is a critical aspect of healthcare that emphasizes the minimization of thromboembolic events while ensuring adequate blood supply to the brain[8-10]. This, in particular, is a crucial area of research and clinical practice, as neurovascular conditions can have severe consequences for patients, such as cognitive impairments and, under serious circumstances, even death. To address these clinical issues, health-care professionals must employ a range of strategies that include not only surgical procedures but also pharmacological interventions. By implementing these approaches, health-care providers can help improve patient outcomes and reduce the burden of neurovascular manifestations on individuals and society as a whole.

The administration of antiplatelet and anticoagulant agents is a widely accepted approach to achieving therapeutic goals in patients with neurovascular disorders (Figure 1). Primarily, these agents are utilized to prevent the formation of blood clots, which could potentially lead to the development of severe complications, such as stroke, myocardial infarction, and pulmonary embolism[11]. Antiplatelet agents are widely utilized to prevent thrombus formation by inhibiting platelet aggregation[12]. Of interest, aspirin and clopidogrel are two commonly used drugs — efficacious in diminishing the risk for thrombosis[12,13]. Similarly, anticoagulant agents act by impeding the coagulation cascade, thereby inhibiting the formation of blood clots[14]. Warfarin and heparin are two commonly used anticoagulants that clinical studies have shown to be effective in preventing the formation of thrombi in vascular disease[15-17]. As such, the administration of antithrombotic agents is of paramount significance in patients with neurovascular disease, as they are at an increased risk of thromboembolic events[17,18]. However, the administration of the pharmacological agents mentioned above necessitates meticulous management, and their impact on bleeding and thromboembolic events must be closely monitored. The administration of antiplatelet and anticoagulant therapy is a crucial aspect of medical care that necessitates a personalized approach, contingent on the patient's symptoms and presentations, as well as the nature of the intervention being executed.

As of recently, the American Heart Association and the American Stroke Association have jointly released a revised set of management guidelines for the administration of antiplatelet and anticoagulant therapy in patients subjected to neurovascular procedures[19,20]. These guidelines cover a range of topics, including the selection of appropriate pharmaceutical interventions, the timing of therapy initiation and discontinuation, and the management of bleeding complications[19,20]. Ultimately, the purpose of this document serves to establish a uniform methodology for health-care practitioners to administer these treatments, with the aim of improving patient outcomes and minimizing the likelihood of unfavorable incidents[21]. Through dedicated adherence to these guidelines, health-care professionals can ensure that patients undergoing neurovascular interventions will receive optimal care and achieve the best possible outcomes. The efficacy and safety of these pharmaceutical agents have been rigorously scrutinized in several studies, which also further highlighted the significant role of these agents in the reduction of adverse outcomes in high-risk patient[22-24]. Therefore, the use of antiplatelet and anticoagulant agents remains a cornerstone of modern medical practice, but most importantly, in the world of neurovascular diseases.

## 2. Utility and efficacy of flow diversion

Flow-diverter devices (FDDs) are an emerging method for treating cerebral aneurysms. As seen in Figure 2, this method is performed by placing a stent in the parent artery where the aneurysm neck is located to disrupt intra-aneurysmal flow, favoring intra-aneurysmal thrombosis[25]. Using this device, the growth of endothelial cells over the neck of the aneurysm progressively excludes the aneurysm sac from circulation[26].

Specifically, the utilization of FDD promotes flow disruption and formation of a stable blood clot within the aneurysm, ultimately contributing to aneurysm occlusion. The endothelization process begins as soon as the FDD is deployed, and adhesion of undifferentiated cells occurs indiscriminately along the implanted stent[27,28]. Within 1 day of implantation, inflammatory cells cluster across the aneurysm neck. Compared to coil embolized aneurysms, the presence of tumor necrosis factor-alpha and monocyte chemoattractant protein-1 in FDD-treated aneurysms suggests that invading inflammatory biological units like macrophages may support healing following implantation

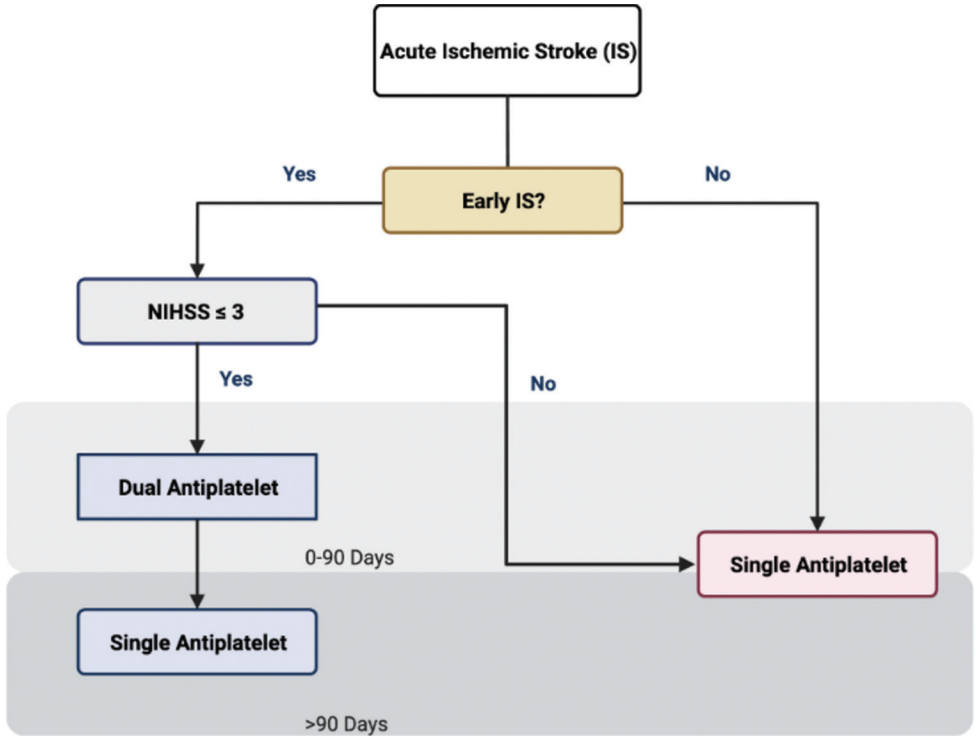



**Figure 1.** Acute ischemic stroke guidelines. Simplified, schematic representation of the 2021 revised American Heart Association/American Stroke Association recommendations for antiplatelet therapy in patients with acute ischemic stroke, a prevalent neurovascular disorder. NIHSS indicates National Institutes of Health Stroke Scale, an assessment of the severity of ischemic activity.

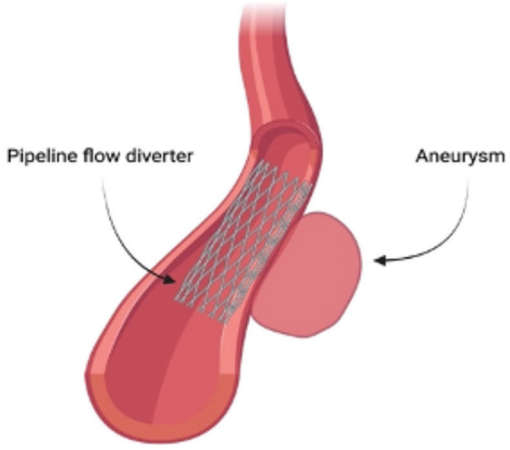



**Figure 2.** Flow diversion device following implantation.

of FDDs[29]. In addition, it has been shown that utilization of FDD in the treatment of aneurysms upregulates expression of apelin, cyclin B1, intercellular adhesion molecule 2, and CXCL8, key genes involved in endothelial function, mitogenic activity, cell cycle progression, and angiogenesis[30]. Thus, it is believed that due to enhanced gene expression, FDD intrinsically facilitates upregulated endothelization[26].

In addition, adhesion of differentiated smooth muscle cells results in the formation of a histologically visible initial neointima layer ~7 days after FDD implantation. At the ~8-week mark, $CD31^+$ endothelial cells appear over the neointimal layer of the smooth muscle antigen-positive cells[27].

Most current studies regarding intracranial aneurysm treatment utilized FDDs, pipeline embolization device, and silk embolization device[31,32]. In treatment of cerebral aneurysms, flow diversion has been shown to have a high success rate of 93 – 95% and a low complication rate of 2.3 – 5.6%[33]. Finally, a recent study has shown 83.5% and 85.2% occlusion rates for 1-year and 3-year follow-ups, and confirmed that FDDs are effective and safe in short-term and long-term follow-ups[34].

## 3. Flow diversion devices compared to traditional embolization techniques

Traditional methods for treating intracranial aneurysms include coil embolization (CE), stenting, and Woven EndoBridge (WEB) embolization (Figure 3).

CE involves the insertion of a microcatheter into the femoral artery before it moves to the site of the aneurysm for navigation. On reaching the aneurysm site, small

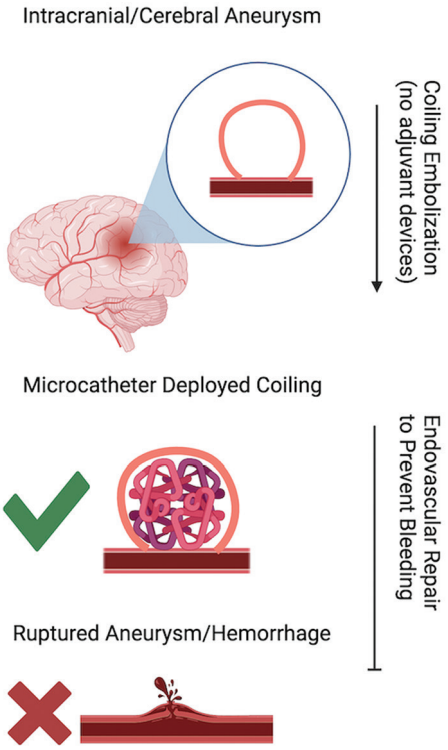



**Figure 3.** Impact of administering a microcatheter-deployed coiling to patients suffering from intracranial or intracerebral aneurysms.

helical platinum coils are deployed to fill the aneurysm and prevent further expansion[35]. Compared to FDD, CE devices have shown relatively low rates of complete occlusion but unfortunately are correlated with high rates of recurrence, especially when used to treat large intracranial aneurysms[36]. Stent-assisted CE has been shown to achieve more optimal outcomes compared to traditional CE but still faces high recurrence rates of 20 – 57% in treated patients[37,38].

On the other hand, WEB embolization is a device used to disrupt flow along the neck of the aneurysm[39]. This device functions as an intrasaccular flow diverter by placing a metabolic mesh along the wall of the aneurysm and the neck[39]. It is designed as a stand-alone therapy for the management of saccular aneurysms, unruptured or ruptured[39]. Other flow-disruption devices require the use of dual antiplatelet therapy (DAPT), while data suggest that the WEB device may be placed without the need for DAPT due to the high degree of neck coverage[39].

## 4. Protocol for antiplatelets and anticoagulant therapy

Although neurointerventional surgery offers benefits to patients with neurovascular diseases and stroke, the complications are difficult to avoid and ultimately diminish the efficacy of the intervention[40]. One possible complication that carries significant risk is the development of a thromboembolism[40]. Thromboembolisms are more inclined to attach to devices such as catheters due to repeated damage to the vascular walls[40]. Therefore, anticoagulation agents, such as heparin, and antiplatelet agents are commonly employed to decrease risk of thromboembolism. The use of antiplatelet agents before and during the procedure is deemed safe and efficacious in reducing the risk of a thromboembolism for unruptured aneurysms[40]. Antiplatelet agents, such as aspirin and clopidogrel, show evidence of reducing thromboembolism risk in coronary angiography and coronary endovascular interventions[41]. Aspirin works by irreversibly inhibiting the enzyme, cyclooxygenase-1 (COX1), preventing the conversion of arachidonic acid to thromboxane A2[42]. Conventionally, aspirin and clopidogrel are used in combination during aneurysm coiling and have shown to reduce thromboembolic events[43]. Heparin is an anticoagulant that is not traditionally used in diagnostic angiographic procedures but may be used in coiling procedures for patients with uninterpreted aneurysms[44]. Heparin use has shown to be efficacious in selected cases where there is cerebral ischemia or coil migration into the lumen of the parent vessel, but the use of heparin in ruptured aneurysms is not indicated[44]. Current guidelines recommend the use of DAPT for 3 – 6 months, but a meta-analysis published in 2021 found that single antiplatelet therapy involving aspirin reduced bleeding without raising the risk for stroke or death[45].

Abciximab is a Fab monoclonal antibody which blocks the IIb/IIIa receptor to inhibit platelet blockade[40]. Its effects occur within 10 min of administration and may persist for up to 48 h[46]. Abciximab inhibits platelets throughout the duration of intravenous infusion[47]. One study found that abciximab engendered a better response to clots in aneurysm coiling procedures, which were complicated by the formation of a thrombus[48]. Therefore, abciximab proves to be efficacious for intra-procedural thrombus formation. In addition, the risk of hemorrhagic complications is reduced in both unruptured and ruptured aneurysms[40].

## 5. Coiling

Endovascular coiling or embolization and open microsurgical clipping are considered the main standard non-conservative preventive treatment options in patients afflicted by unruptured cerebral aneurysms in addition to arteriovenous malformations[49]. In general, surgical clipping is commonly performed in younger patients, especially those admitted due emergency[50]. During the non-SAC process, a wired catheter is passed through the

femoral artery and is then threaded up to the affected artery with the aid of fluoroscopic guidance[51,52]. A microcatheter is then inserted through the original catheter, delivering soft platinum metal coils into the aneurysm space[53]. These initially straight-configured metal coils vary in sizes and, after detachment from the microcatheter by means of electrical induction, conform to various predetermined circular shapes[51]. Multiple coils may be deployed to sufficiently fill the aneurysm compartment[54,55]. Short-term success is indicated by coil-induced thrombus of the post-operative space shown on immediate angiography, resulting in an adequate seal from arterial blood flow[56].

Coiling without stent assistance is distinct in that a stent is not placed in the arterial space either before or after coil deployment into the aneurysm[57,58]. Intravascular tent assistance has been generally indicated based on aneurysm neck size. More specifically, stent use for cases of wide-necked aneurysms has been shown to provide structural scaffolding support for coiling integrity and density within the aneurysm sac[59]. However, ongoing studies have been aimed at establishing comparisons between coiling alone and coiling with stent assistance based on criteria including overall efficacy and safety in addition to solely anatomic parameters such as aneurysm diameter[60]. Both Hong *et al.* and Phan *et al.* conducted separate meta-analyses comparing the two aforementioned procedures with data analysis suggesting that SAC results in significantly higher progressive thrombosis rates and lower recurrent rates than coiling alone[61,62]. Conversely, immediate occlusion rates and complications including hematoma, dissection, perforation, stroke, and mortality were statistically similar between the two pooled groups[61,62]. As expected, mean aneurysm size was calculated to be slightly over 1 mm in the SAC cohort. Although both studies were based on retrospective cohort analysis, the evidence leads way to current and future randomized controlled trials to determine if standard intracranial aneurysm treatment should shift toward SAC, particularly if this option does not pose any significantly increased concern for complication. Endovascular coiling alone carries an approximately 25% recanalization rate, but technological advancements to coil properties have been made in an effort to reduce this trend[63]. Variation of coils in terms of shape, size, malleability, material, and detachment sites allows providers to employ more effective thrombotic structures for each intracranial aneurysm case. Moreover, adjunctive devices and techniques to coiling alone have been developed and extensively studied studied[64].

As previously mentioned, endovascular coiling of cerebral aneurysms presents as a relatively conservative treatment option, particularly in cases of unruptured aneurysm. Similarly, coiling alone entails similar rates of complication when compared to adjunctive coiling such as SAC. Thromboembolic events are one of the most significant, yet frequent (up to 8.2% rate), complications that can potentially arise from CE therapy[44,65]. Given the significant risk for neurologic impairment and/or death associated with thromboembolism, antiplatelet and anticoagulant therapy is a major point of concern in the therapeutic landscape of cerebral aneurysms. Moreover, ischemic event incidence in patients undergoing aneurysm intervention can range from 10% to 40% when detected with diffusion-weighted imaging techniques (DWI)[66,67]. Thrombus formation can stem from a number of different intraoperative interactions between devices and pre-existing aneurysm structure[40]. Mechanisms include vessel injury, coil migration, existing thrombus dislodgement, and incomplete aneurysm obliteration with subsequent thrombosis[68]. Intraoperative heparin loading is frequently utilized during aneurysm coiling as a preventive measure against the aforementioned thromboembolic complications[69].

With regards to endovascular coiling pre-operative standard of care in patients with unruptured aneurysms, antiplatelet therapy includes one dose of aspirin 81 or 325 mg either 1 day out from surgery or preoperatively on the same day. Of note, coiling alone does not necessarily indicate the administration of a second antiplatelet medication such as clopidogrel[36]. However, an aspirin 100 mg/clopidogrel 75 mg regimen may be recommended in some cases, more so when a stent is required[40]. Complicated aneurysm configuration requiring multiple catheters and challenging coiling may also indicate a pre-operative dual antiplatelet regimen. Interestingly, Hwang *et al.* observed no significant reduction in thromboembolism cases where only simple coiling from a single microcatheter was needed[43]. The evidence suggests antiplatelet therapy may or may not be critical to thromboembolic complication prophylaxis depending on the extent of coiling involvement. In addition to this finding, antiplatelet therapy was found to have no significant effect on hemorrhagic complications in cases of unruptured aneurysms[43]. Combining these two findings, it appears that dual, and even single, antiplatelet therapy may only have a beneficial effect on certain coiling procedures but administering either aspirin or an aspirin/clopidogrel combo as a pre-operative prophylactic measure renders no apparent harm. Although other studies have found slight nonsignificant trends in hemorrhagic complications after antiplatelet therapy, there is more evidence to suggest that the potentially significant reductions in thromboembolism outweigh the risks[70]. Given the possibility for hemorrhagic complications, a monotherapy dose of aspirin 81 mg or 325 mg shortly before coiling is generally a conservative measure, whereas DAPT is reserved for more complicated cases not consistently characteristic of endovascular

coiling alone. As aspirin only partially inhibits GPIIb/IIIa, it provides a low barrier effect on the risk of a thromboembolic event[71]. Postoperatively, coiling alone does not generally indicate prolonged antiplatelet or anticoagulant therapy, both mono and dual therapy, particularly after the point of discharge[72]. The addition of a stent may require an antiplatelet/anticoagulation therapy regimen postoperatively. Aside from prior medical histories such as atrial fibrillation that necessitates chronic medication; antiplatelet/anticoagulation therapy in cases of simple coiling is usually confined within the duration of a hospital course. Given resistance to antiplatelet agents may be a possibility, prolonged therapy that is not indicated for would not be a practical option[73]. The advantages and disadvantages of endovascular coiling for cerebral aneurysms are listed in Table 1.

In the case of ruptured aneurysm and subarachnoid hemorrhage, antiplatelet/anticoagulant therapy standards are distinct from the cases previously discussed, as subarachnoid hemorrhage was observed to be independently linked to thromboembolic complications associated with endovascular coiling[65]. In these cases, anticoagulant therapy can be initiated in the form of subcutaneous heparin approximately 12 h after CE. Supplemental aspirin administration may be flexible but has to be administered at the discretion of the neurointerventional provider[72]. More care must be taken to assess the appropriate antiplatelet therapy when dealing with CE of ruptured aneurysms. Patients with ruptured intracranial aneurysm are considered at significant risk for thromboembolism. Edwards *et al.* found that periprocedural monotherapy in the form of aspirin can significantly reduce periprocedural thromboembolic events without significantly increasing hemorrhage risk even in ruptured aneurysm and subarachnoid hemorrhage cases[74]. Of note, treatment cohorts received intraoperative aspirin at 650 mg near the end of the procedure. This group continued on aspirin 325 mg once daily for 2 weeks. In comparison, the control group received no aspirin or any other antiplatelet/anticoagulant agents[74]. Despite trends in randomized controlled trials, multiple factors, in addition to whether or not an aneurysm has ruptured, must be considered to provide the ideal antiplatelet/anticoagulant therapy mode for each patient undergoing endovascular coiling. Parameters include medical history, extent of procedure, recovery, follow-up status, and magnetic resonance angiography assessment. In less frequent cases suffering from intraoperative clotting despite having received antiplatelet therapy, glycoprotein IIb/IIIa inhibitors such as abciximab may prove effective in producing fast-onset platelet inhibition[40]. However, the safety and efficacy of these drugs must be further studied to determine accurate timing, dosing, and administration route for successful treatment in patients.

**Table 1. Advantages and disadvantages of endovascular coiling for cerebral aneurysm**

| Advantages | Disadvantages |
|---|---|
| Coiling alone | |
| Minimally invasive | Ruptured aneurysms cannot be treated with coiling alone; stent/balloon may be required |
| Quicker recovery | Requires blood thinners to prevent coagulation of coil |
| SAC | |
| Lower rates of aneurysm recurrence | Increased mortality rate |
| Can be used for wide-necked aneurysms | Difficulty visualizing aneurysms using fluorescence |
| WEB embolization | |
| Adaptable to wide-necked and bifurcation aneurysms | Not indicated for aneurysms that are not wide-necked |
| Reduced intraoperative time and long-term antiplatelet therapy; increased safety | Prevalence of recanalization postoperatively |

Abbreviations: SAC: Stent-assisted coiling; WEB: Woven EndoBridge.

## 6. SAC

Although coiling has been used successfully for aneurysm repair, it can prove to be a difficult process. Aneurysms can occur in numerous locations with a wide variety of shapes, dimensions, and rupture capacities[75]. Stabilizing the aneurysm is one way to minimize the risks of coiling without reducing its advantageous effects. This stabilization can be engineered by utilizing a stent. In SAC, a stent can be placed within an aneurysm to bolster its shape, allowing for secure coil deposition[76]. The endovascular technique used in SAC is minimally invasive, accompanied by a high success rate, and a reduced risk of complications in comparison to other options available for treating aneurysms. Hence, it has the potential to significantly improve outcomes in cerebral aneurysm coiling.

SAC was originally used to treat wide-necked aneurysms[58,59]. Not only did it provide structural support to bolster the coils in the wide aneurysm sac, but it also prevented the coils from protruding into the parent artery[77]. Coil migration affects 14% of patients undergoing aneurysm coiling, and its effects are relatively understudied and can range from life-threatening infarcts to no significant thromboembolic impact[78]. Using a mesh design for a stent helps maintain unobstructed blood flow while preventing the movement of coils out of the aneurysm sac. Further, the development of more flexible intravascular stents over

time has expanded the utility of SAC to improve outcomes for aneurysms in smaller vessels[79-81]. Hence, recent studies have explored utilizing SAC in patients with intracranial aneurysms.

The major complications of coiling aneurysms arise due to a lack of regulatory control over the migration and deposition of the coil. The wide variety of stents that can be used provides an additional level of modulation to have the optimal effect for each distinct aneurysm in every patient. Aneurysms with different proportions may require a different stent material or density to achieve the desired outcome. One study by Masuda *et al.* classified aneurysms by size and identified mesh wire densities that allowed for the greatest change in flow velocity through the aneurysm[82]. Aneurysm size can be classified into the following categories: small, medium, large, and giant[83]. Masuda *et al.* determined that a 46.2% mesh density led to the greatest change in blood flow for every aneurysm. This mesh density, however, had different effects on aneurysms of different sizes. Aneurysms smaller than 4.0 mm showed an 80% reduction in blood flow, whereas giant aneurysms greater than 25.0 mm showed a blood flow reduction of only 50%[81]. Hence, the mesh density can be changed to achieve the appropriate blood flow reduction in aneurysms with different dimensions. Another study by Piotin *et al.* found that stents with a higher packing density were associated with a lower rate of angiographic recurrence[60]. Hence, mesh density can be adjusted to create an optimal stent that allows for improved outcomes in coiling for aneurysms.

SAC, however, is not without risks. Accessing aneurysms surgically always carries a risk of morbidity due to procedure-related complications and the potential aneurysm rupture[84]. Possible complications of SAC include the piercing of vessels, thromboembolic events, and hemorrhaging[85]. An additional issue that can arise if the stent becomes occluded is in-stent stenosis, which contributes to blood flow reduction within the parent artery to the extent of pathological level[86]. These complications, however, typically have a prevalence of < 7%, and most of these risks can be attributed to aneurysm size, older patient age, sensitive aneurysm location, or issues from a previously coiled aneurysm[84].

In recent years, numerous studies analyzed the safety and efficacy of SAC with regard to complication rates. For instance, one retrospective study by Aguilar-Salinas *et al.* evaluated data from 124 patients with unruptured wide-necked intracranial aneurysms[85]. Only 3.3% of these patients experienced complications from the procedure, such as vessel occlusion or aneurysm rupture. These patients also had a low risk of severe in-stent stenosis and recanalization, which affect 1% and 6.6% of patients, respectively. The Glasgow Outcome Scale was used to analyze the extent of impaired consciousness in these cases. About 80.7% of patients had a score of 5 or above at a 30-day follow-up, which later increased to 83.9%[85]. With this data, the study concluded that SAC is an effective and safe way to treat wide-necked intracranial aneurysms, with lower risks of complications and higher rates of success. Another study by Chalouhi *et al.* analyzed 461 elective SAC procedures[84]. They found favorable outcomes in 99% of these patients. About 87% of patients were available for follow-up at 26 months, who had recanalization and retreatment rates of 12% and 6.4%, respectively[84]. Overall, both studies concluded that SAC is a safe and efficacious procedure with minimal complications that can significantly improve the prognosis of patients with aneurysms.

Numerous research studies have evaluated the prevalence of adverse effects following SAC compared to non-SAC procedures. The results of these studies are summarized in Table 2. Most studies noted no significant differences in adverse effects between SAC and non-SAC. Piotin *et al.*, however, reviewed 1049 cases of aneurysm coiling and found that SAC was associated with more adverse effects than non-SAC[60]. Patients undergoing SAC faced 4.6% of procedural complications and 7.4% of permanent neurological procedure-related complications compared to 1.2% and 3.8% of patients, respectively, with non-SAC[60]. One limitation of the study that must be taken into consideration is that around 40 – 50% of patients in both groups were lost to long-term follow-up; therefore, the conduction of more comprehensive studies is needed in the future to draw more definitive conclusions. In addition, different stent types were used in this study, including balloon-expandable models and self-expandable stents, but no significant difference was noted in their outcomes. Despite potential differences in conclusions regarding adverse outcomes, data from all of these studies show that SAC improved long-term outcomes for patients when compared to non-SAC. Multiple studies found lower rates of recurrence, reduced recanalization rates, and improvements in clinically acceptable levels of occlusion in patients who had undergone SAC. These large-scale studies imply that SAC has significant utility in the treatment of intracranial aneurysms. Despite the differences observed between SAC and non-SAC procedures, more studies are needed to validate these findings and analyze their impacts on patient's quality of life.

As safety and efficacy of SAC are continuously evaluated, the appropriateness of use for SAC changes over time. For instance, SAC is now regarded as a useful

**Table 2. An assessment of outcomes in patients treated with SAC compared to those treated with non-SAC**

| Study | Aneurysm type | Patients enrolled | Outcome |
|---|---|---|---|
| Zhang *et al.*, 2019[87] | Ruptured intracranial aneurysms | 1049 patients; SAC (*n*=499), non-SAC (*n*=409) | The SAC group had a lower recurrence rate and incomplete occlusion rate than the non-SAC group. There was no significant difference in mortality at discharge; there was no favorable clinical outcome at discharge or follow-up. |
| Yi *et al.*, 2022[88] | Ruptured intracranial aneurysms | 375 patients; SAC (*n*=101), non-SAC (*n*=274) | The SAC group had higher rates of complete occlusion, lower rates of recanalization, and lower need for treatment. There was no significant difference in periprocedural complications. |
| Piotin *et al.*, 2012[60] | Intracranial aneurysms | 1325 patients; SAC (*n*=216), non-SAC (*n*=1109) | The SAC group had a lower rate of angiographic recurrence, as well as higher rates of procedural complications and permanent neurological procedure-related complications. |
| Liu *et al.*, 2017[89] | Ruptured intracranial aneurysms | 279 patients; SAC (*n*=113), non-SAC (*n*=166) | The SAC group had better initial aneurysm occlusion status, implying better durability and safety. There was no significant difference in adverse outcomes, including permanent neurological deficits. |
| Zhang *et al.*, 2022[90] | Ruptured tiny intracranial aneurysms | 245 patients; SAC (*n*=93), non-SAC (*n*=152) | The SAC group had a higher complete occlusion rate, a lower recurrence rate, and a higher rate of hemorrhagic complications. There was no significant difference in mortality or other adverse effects. |
| Goertz *et al.*, 2021[91] | Ruptured intracranial aneurysms | 284 patients; SAC (*n*=64), non-SAC (*n*=220) | The SAC group had higher rates of complete occlusion and lower recanalization rates at 6-month follow-up. There were no significant differences in mortality or adverse effects. |
| Muller *et al.*, 2017[92] | Wide-necked aneurysms | 355 patients; SAC (*n*=33), non-SAC (*n*=322) | The SAC group had higher rates of complete and clinically acceptable levels of occlusion. |

Abbreviation: SAC: Stent-assisted coiling.

therapy for smaller berry aneurysms due to the improved long-term outcomes associated with SAC and the availability of stents that are effective in treating different sizes of aneurysms[60,61]. Considering that it was initially only used for wide-necked aneurysms, its implications are now countless. The adverse effects and long-term outcomes of SAC in comparison to non-SAC should be further researched, along with the impact of different sizes and densities of the stents that can be used in SAC. With future studies focusing on such topics, we believe that SAC can significantly contribute to harm reduction and better prognosis for patients with intracranial aneurysms.

## 7. WEB embolization

A trial known as the *International Subarachnoid Aneurysm Trial* has truly revolutionized our understanding of endovascular coiling in the treatment for ruptured aneurysms[93]. Since that trial, endovascular coiling has become one of the more prominent choices in the treatment of ruptured aneurysms[93]. While promising, endovascular coiling treating wide-necked bifurcating aneurysms (WNBA) remains a challenge due to the balance between preserving major vessels while properly occluding the aneurysm[94-97]. As the prevailing option for treating WNBAs, SAC has shown a ten-time higher risk in adverse events, which is largely caused by the requirement of DAPT post-procedure[94-99]. In addition, SAC poses durability concerns, exemplified by the frequent need for support from stents or flow diverters, and has limitations in safely achieving proper coil packing density[99,100].

The idea of the WEB was initially conceptualized in Aliso Viejo, California, USA in 2011 and is now FDA-approved. The WEB is a unique device that has a barrel-shape with a platinum core and nitinol mesh that employs intrasaccular flow disruption. The low porosity of the device causes disrupted flow at the aneurysm neck causing thrombosis and eventually occlusion[93,97]. The device allows for a seal of the aneurysm neck eliminating structural effects of the parent artery[101]. This, in combination with the WEB's lack of a metallic mesh, allows patients to avoid DAPT[93,99]. In addition, if the positioning of the deployed WEB is suboptimal, recapturing and resheathing can be performed to allow for better placement[102]. Further, devices employed in WEB have demonstrated an improved safety profile[102,103].

A prominent complication of WEB is the possibility of thromboembolic events[104]. Tau *et al.* conducted a meta-analysis by researching patients treated with unruptured aneurysms with WEB and found that 70% of periprocedural complications were thromboembolic[105]. It is theorized that this occurs for many reasons including lack of pre-treatment antiplatelet therapy, the thrombogenic state of the device, and the prothrombotic state of subarachnoid hemorrhage[93,106].

Typically, the WEB embolization procedure is performed by a neurointerventionalist and involves radial access.

Sizing of the WEB is selected according to measurements of the aneurysm on 2D digital subtraction angiography (DSA). The WEB should be oversized to properly fill the aneurysm sac while allowing it to completely cover its neck. Afterward, the device is delivered through a microcatheter[101,102].

A review published in 2021 by Crinnion *et al.*[93] summarized 11 articles encompassing 405 aneurysms in 398 patients diagnosed with ruptured aneurysms or subarachnoid hemorrhages that were treated with WEB embolization. Aneurysm characteristics included a range of 45%–92% anterior circulation and 7 – 56% with severe SAH. They found that the rate of success varied between 95.8% and 100%, and the number of aneurysms requiring additional techniques for occlusion was from 0% to 15%. Adequate occlusion was achieved in 71 – 96% of patients[107-114].

The safety profile of WEB embolization demonstrated that thromboembolic event rates range from 0% to 25% and overall, a thromboembolic event rate of 9.8% in all 398 patients. The authors cite two prominent studies, the CLARITY trial and the ARETA study which characterized thromboembolic event rates in CE. The CLARITY trial demonstrated a thromboembolic event rate of 20.8% for wide-necked aneurysms and the ARETA study showed a thromboembolic event rate of 10.4% in 753 aneurysms; both of the studies used coiling for treatment. Based on this, the TE rates of coiling and WEB embolization approaches are similar[93,115,116]. Other important safety endpoints included a 4% of morbidity, 1.8% of mortality, and rebleeding in 1.2% of patients. The authors concluded that WEB has proven to be safe and efficient in treating ruptured aneurysms when comparing it to other endovascular therapies[93].

In a retrospective review by Kabbasch *et al.* in 2019, around 66 patients that underwent WEB embolization were compared to 66 patients that underwent SAC. In the WEB group, 65 patients were treated with only WEB embolization, and the remaining one was treated with a combination of both WEB embolization and additional coiling. In the SAC group, both single stent and double stents were used in 80.3% and 19.7% of patients, respectively. Out of all of the patients, those that achieved complete occlusion immediately were 59.1% of WEB embolization patients and 92.4% of SAC patients. Halfway through their studies, complete occlusion was achieved in 83.3% of WEB embolization patients and 84.8% of SAC patients. Favorable outcomes were found in 86.4% of WEB embolization patients and 86.4% of SAC patients. The average treatment time was significantly longer for SAC when compared to WEB embolization. Complications occurred in 12.1% of the WEB embolization patients and 21.2% of SAC patients; however, these results were not statistically significant. Of note, 18.2% of SAC patients and 12.1% of WEB embolization patients developed thromboembolic complications. The authors conclude that WEB embolization is a viable alternative for the treatment of wide-neck bifurcation aneurysms, given that it limits long-term DAPT[101].

Another review performed in 2022 by Monteiro *et al.* analyzed nine articles with 377 acutely ruptured aneurysms treated with WEB embolization. Of the samples, 85.9% were anterior circulation aneurysms and 82.7% of them were wide-necked. Adequate occlusion occurred in 84.8% of cases and 4.5% of the patients required retreatment at follow-up. During catheterization, there were seven cases of perforation in the dome of the aneurysm. In all circumstances, once the WEB was deployed, the bleeding halted. The rate of post-procedural complications was 1% and was all thromboembolic[99].

A study performed by Stanca *et al.* characterized the long-term effects of WEB device. They included 35 ruptured WNBAs in 21 patients treated with WEB. They examined patients at the 3-year mark using DSA. After 3 years of follow-up, three death cases were recorded, which were not related to aneurysms. They also found complete occlusion in 61.1% of patients, 0% rebleeding rate, and 0% morbidity (no neurological signs). Although there was incomplete occlusion in 11.1% of patients, in this case, the neck showed no growth or minimal size increase (<2 mm); therefore, treatment was not required. The authors conclude that there is high stability 2 and 3 years after the procedure[117].

Overall, the WEB device demonstrates feasibility, a high rate of occlusions, and a low rate of complications. The clear advantages of this device include a reduction in long-term DAPT and fewer perioperative complications. The risk for thromboembolic events remains a challenge with using the WEB device, but compared with traditional coiling methods, the rates of these events are much lower. The WEB device should be considered a viable option in the treatment of WNBA.

## 8. Conclusion

For decades, numerous studies have contributed to diversifying treatment options of aneurysms. This review presents a detailed amount of information concerning the modern techniques of aneurysm treatment, including pharmaceuticals, SAC, coiling, and WEB embolization. Different techniques demonstrate varying levels of feasibility, safety, and patient satisfaction. The ability of WEB to disrupt intrasaccular flow is circumstantial evidence that it could be used to manage thrombotic

events. In comparison, the SAC method is rather complex due to a lack of regulatory control over the migration and deposition of the coil. In conclusion, this review provides details regarding various aneurysm treatments, and we believe a thorough understanding of these treatment methods could facilitate more personalized and monitored care.

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## Conflict of interest

The authors declare no conflicts of interest.

## Author contributions

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## Ethics approval and consent to participate

Not applicable.

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