

Stent-Assisted Coiling of Unruptured Intracranial Aneurysms with Wide Neck

Abstract

Objective: Morbidity and mortality in patients experiencing the rupture of intracranial aneurysm ruptures are high. We conducted a systematic review and meta-analysis to investigate the role of stent-assisted coiling (SAC) for unruptured intracranial aneurysms (UIAs) with wide neck. **Materials and Methods:** The current meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Pooled proportions with 95% confidence intervals (CIs) of ten outcomes of interest were calculated. **Results:** We finally reviewed 13 studies, including 976 patients. The technical success of the method was 98.43% (95% CI: 95.62–99.95). Early outcomes included total periprocedural obliteration with a rate of 50.20% (95% CI: 36.09–64.30) and periprocedural rupture with zero rate. During the follow-up period, ranging from 6 months to 2 years, the total postprocedural obliteration rate was 63.83% (95% CI: 45.80–80.18) and the overall late rupture rate was 0.41% (95% CI: 0.00–2.38). The pooled in-stent stenosis rate was calculated at 1.24% (95% CI: 0.02–3.63). We also estimated a pooled rate of 0.02% (95% CI: 0.00–0.51) and 4.33% (95% CI: 2.03–7.23) for total mortality and overall neurological complications, respectively. A pooled rate of 3.94% (95% CI: 1.48–7.33) was found for stroke. Finally, the recanalization rate was recorded at 7.07% (95% CI: 4.35–10.26). **Conclusions:** SAC of UIAs with wide neck seems to be a safe and acceptable alternative to surgical clipping. Although early results concerning total periprocedural obliteration may be modest, follow-up outcomes may be indicative of adequate occlusion of treated UIAs.

Keywords: Intracranial aneurysm, stent-assisted coiling, wide neck

Introduction

The incidence of cerebral aneurysms, although difficult to estimate, is reported around 0.2%–7.9% in autopsy data.^[1] The ratio of ruptured to unruptured (incidental) aneurysms is 5:3–5:6, making almost 50% of these aneurysm ruptures during life.^[1] Morbidity and mortality in patients experiencing significant intraoperative rupture are approximately 30%–35%,^[1] thus making this pathology rather challenging to treat. Risk for rupture for incidental findings depends on many factors. Among them, aneurysm diameter is mostly important, with an estimated annual risk for aneurysms of diameter <10 mm at 0.05% and more than 1% for those with diameters >10 mm.^[1]

The optimal treatment for unruptured intracranial aneurysms (UIAs) depends highly on the patient's general condition, the anatomy of the aneurysm, and the

surgeon's experience and must be weighed against the natural history of the condition. Treatment options include surgical clipping across the neck of the aneurysm or vascular bypass to maintain flow distal to trapped segment.^[1] At the same time, there have been considerable developments in the field of endovascular technology concerning various methods for the cure of intracranial aneurysms. What is more, the basic coil occlusion technique^[2] has expanded in terms of use through the evolution of the soft and three-dimensional coil technology, along with the Guglielmi coil first use in 1991.

The introduction of balloons and stents to the endovascular armamentarium^[2] has allowed better efficacy during endovascular coiling, not only on small-to-medium-sized aneurysms with narrow necks but also on wide-neck aneurysms' treatment. Stents with additional use of the coils reduce the

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possibility of dissection or vessel rupture. Implanting a stent across the neck area is used as a prop to the coil mass, thus collaborating to a change in the local hemodynamic parameters. This results in directing the flow and providing a substrate for endothelialization in that area,^[2] while it is obvious that a self-expanding stent can be easily positioned in the intracranial vessel.^[3] As far as wide-necked aneurysms are concerned (namely aneurysms with an aspect dome-to-neck ratio of <2 or with a neck size >4 mm), it should be noted that the latter has the possibility to be coiled with the assistance of balloon-assisted techniques or stent-assisted coiling (SAC).^[2]

The aim of this systematic review and meta-analysis was to investigate the clinical outcomes of SAC limited to the UIAs with wide neck. We explored the literature in terms of case series, concerning the mortality and the morbidity, the complications, the access, and the techniques of the method.

Materials and Methods

This meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Google Scholar, PubMed, and Cochrane Collaboration were systematically searched for relevant publications, while we followed a snowball process in the reference lists of the eligible articles to retrieve additional relevant articles.

We used the following terms for search purpose: stent-assisted coiling, intracranial aneurysm, and wide neck. We searched for all scientific papers, without gender or language restriction, until January 2019. We investigated studies focusing on SAC limited to the UIAs with wide neck, including aneurysms with an aspect dome-to-neck ratio of <2 or with a neck size >4 mm. Studies reporting on intracranial aneurysms without wide neck and on ruptured intracranial aneurysms with wide neck were excluded.

Data extracted from eligible studies included the first author's name, study year, country in which the study was conducted, total number of patients, number of male or female patients, follow-up (months), the mean age of patients, inclusion and exclusion criteria, vascular access (transfemoral), type of anesthesia applied, type of anticoagulation used, type of endograft used, and description of complications during follow-up.

We also extracted the number of patients with outcomes, which were thereafter described as early and late. Early outcomes were defined as outcomes during the periprocedural period and late ones as those ones occurring beyond this period. Outcomes of interest included the following: technical success, defined as stable device placement and adequate function on computed tomography angiography, total periprocedural obliteration, periprocedural rupture, total obliteration during follow-up,

overall late rupture, pooled in-stent stenosis, total mortality, any neurological complication, stroke, and recanalization.

Statistical analysis

The outcome rates in patients with SAC in UIAs with wide neck were estimated for each study and reported as the proportion of patients with the corresponding outcome among all patients with SAC in UIA with wide neck. Values of the concomitant outcomes were subsequently appropriately calculated, expressed as proportions and 95% confidence intervals (CIs), and thereafter transformed into quantities according to the Freeman–Tukey variant of the arcsine square-root transformed proportion. The pooled effect estimates were calculated as the back-transformation of the weighted mean of the transformed proportions, using DerSimonian–Laird weights of a random-effects model, and expressed as percentage proportions. One meta-analysis was conducted taking into account all case series.

Formal statistical test for heterogeneity using the I^2 test was performed. Publication bias was assessed using the Egger test for small-study effects as well as visual inspection of funnel plots. We used Stata statistical software version 14 (StataCorp LP, College Station, TX, USA) for the analyses.

Results

Study characteristics

We identified 886 potentially eligible studies after a literature search [Figure 1]. We excluded a total of 82 duplicate records, as well as 17 articles which were referred to *in vitro* experiments and *in vivo* ones based on laboratory animals. Further, 76 case reports and 3 articles were referred to children and were also excluded. Review of the titles and abstracts evidenced that 201 articles were irrelevant. We also removed 323 articles because they were reviews and not original articles or they did not refer to aneurysms with wide neck. A total of 184 articles were further evaluated. Among them, 130 and 28 articles including both ruptured and unruptured aneurysms with wide neck or only ruptured ones, respectively, were excluded. Finally, 26 articles were deemed relevant to be included in the systematic review. However, 11 articles were further excluded as they were referred to endovascular treatment of UIAs with wide neck using flow diverters or temporary stent, as well as 2 articles, because of overlapping population. Eventually, 13 articles participated in the meta-analysis,^[4–16] corresponding to a total of 976 patients who underwent SAC of their UIAs with wide neck [Supplemental Table 1].

The included eligible studies in the systematic review were published from 2005 to 2017. Among 976 patients included in our systemic review, 384 were females (72.6%). For another 447 patients, the gender was not specified. The access vessel was noted in 466 of 976 patients. Among them, the device delivery system was advanced

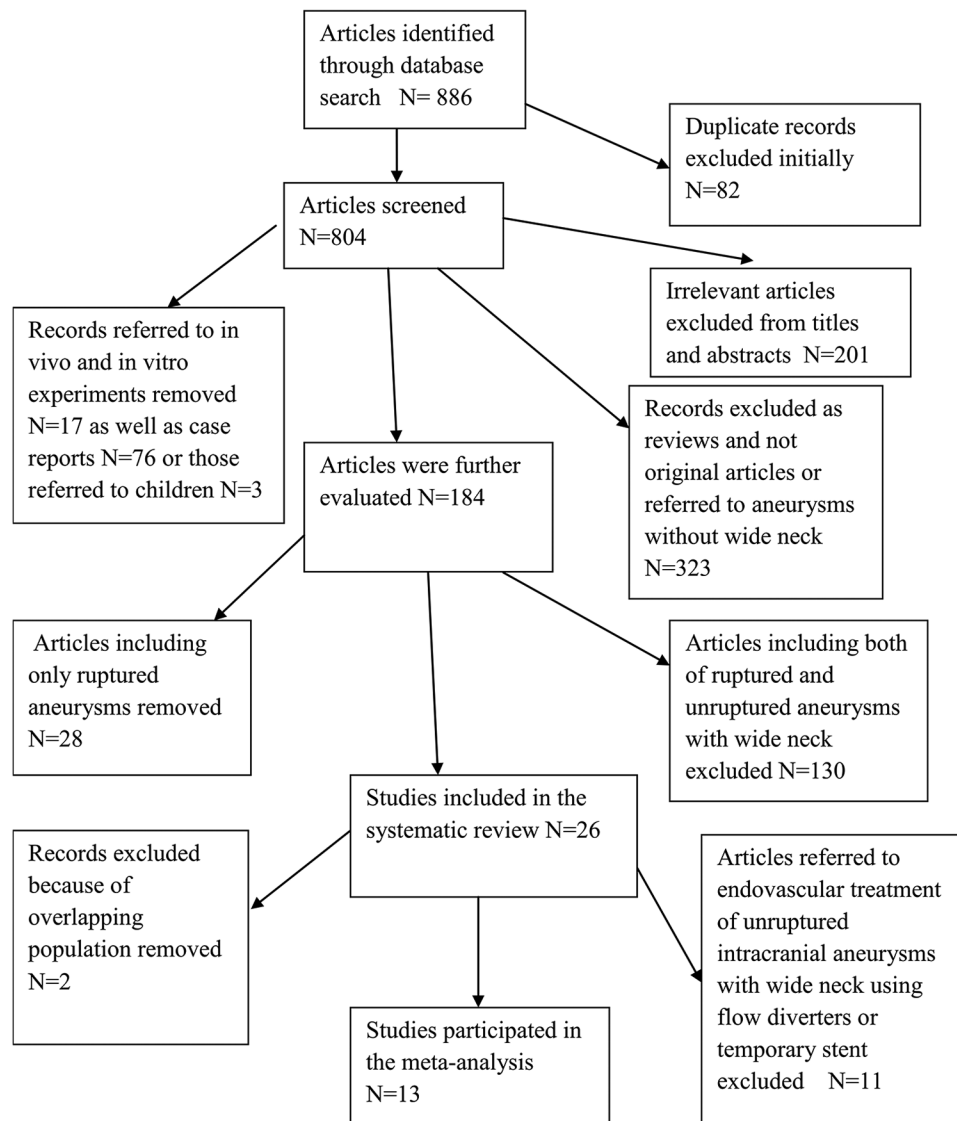


Figure 1: Flowchart of eligible studies

transfemorally. Neuroform and Enterprise devices were used in the majority of the patients. The procedure took place under general anesthesia in 460 cases (47.1%), whereas the type of anesthesia was not reported for the remaining patients. The age of the study sample ranged from 18 to 80 years, with an average age of 50 years, and the median follow-up ranged from 6 months to 2 years. The majority of the patients had also aneurysms placed in the anterior circulation. It is worth noting that the majority of the aneurysms in the posterior circulation were located on the basilar tip, while 69 patients with paraclinoid aneurysms were included in our review study. Studies on patients with blister aneurysms were excluded. Moreover, studies on fusiform ($n = 500$ patients), dissecting ($n = 384$ patients), mycotic/traumatic ($n = 116$ patients), or saccular ($n = 116$ patients) aneurysms were also excluded from our meta-analysis. Finally, antiplatelet drugs were routinely administrated during the periprocedural and

postprocedural period along with intravenous heparin during procedure.

Meta-analysis

Our meta-analysis found that the technical success of the method was 98.43% [95% CI: 95.62–99.95; Figure 2]. Among the other early outcomes, total periprocedural obliteration was at 50.20% [95% CI: 36.09–64.30; Figure 3], while periprocedural rupture was zero. The pooled rate for total obliteration during follow-up was 63.83% (95% CI: 45.80–80.18), while overall late rupture was estimated at 0.41% (95% CI: 0.00–2.38). However, this figure was estimated from only four studies,^[4,7,9,12] corresponding to only 4 events out of 365 patients, as these studies were the only which provided with corresponding data. Similarly, the pooled in-stent stenosis rate was 1.24% (95% CI: 0.02–3.63), and it was estimated from six studies,^[5,8,10,12,14,15] with 8 events out of 261 cases during follow-up.

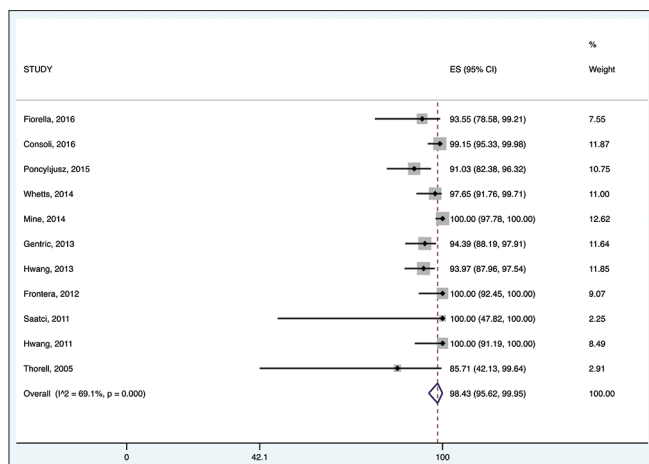


Figure 2: Forest plot presenting the meta-analysis of technical success based on event rates for the use of stent-assisted coiling of unruptured intracranial aneurysms with wide neck. Event rates in the individual studies are presented as squares with 95% confidence intervals presented as extending lines. The pooled event rate with its 95% confidence intervals is depicted as a diamond

Total mortality was estimated with a pooled rate of 0.02% (95% CI: 0.00–0.51). Any neurological complication and stroke rates were found to be 4.33% [95% CI: 2.03–7.23; Figure 4] and 3.94% (95% CI: 1.48–7.33), respectively. Finally, regarding recanalization, the pooled rate was 7.07% (95% CI: 4.35–10.26).

Discussion

The meta-analysis was derived from a comprehensive review of 13 case series and provided pooled outcome rates for patients treated with SAC for intracranial aneurysms with wide neck. Although high-risk patients constituted our study cohort, a high technical success rate of 98.4% was recorded.

Concerning anatomical results, our rate of immediate complete occlusion was lower (50.20%) than in a meta-analysis for stand-alone coiling (86.1%).^[17] This can be explained by the fact that coil packing after stent placement maneuverability and the use of dual antiplatelet therapy and heparin during the procedure may limit thrombosis around coil mass. The low rates of complete occlusion underline potential difficulties of SAC in relation to aneurysmal morphology, such as the size and localization. It was observed that, contrary to comparatively nonsatisfactory instant anatomical results, complete occlusion was achieved at follow-up reaching 63.83%. The thrombosis that is in progress could be further made clear through various speculations and theories. Primarily, certain computational and animal studies indicated that conventional self-expanding stents provoke a lessening of the flow velocity to the aneurysm and secondary wall shear stress.^[18-21] It is also noteworthy that an arterial angular remodeling with migration and narrowing of the flow impingement zone along with a decrease in apical pressure

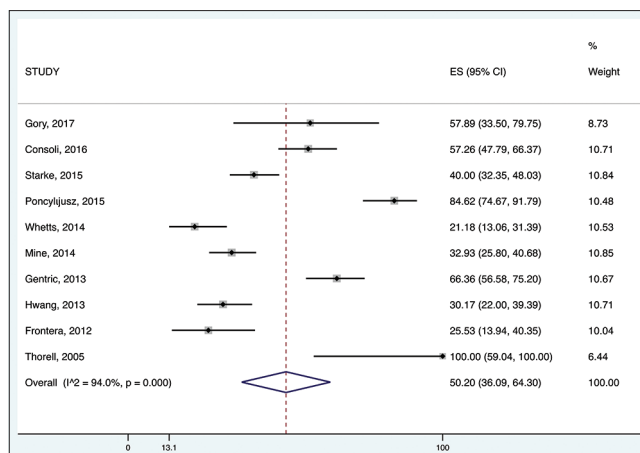


Figure 3: Forest plot presenting the meta-analysis of total periprocedural obliteration based on event rates for the use of stent-assisted coiling of unruptured intracranial aneurysms with wide neck. Event rates in the individual studies are presented as squares with 95% confidence intervals presented as extending lines. The pooled event rate with its 95% confidence intervals is depicted as a diamond

are caused by intracranial stents. Certain alterations to the inflow to the sac that might result in thrombosis^[22] could also be caused by the straightening. Finally, it should be highlighted that the stent struts that are connecting the aneurysmal neck might as well function as a bioactive scaffold for neointimal growth.^[22] For the same reasons that promote progressive aneurysm occlusion, the rate of recanalization of intracranial aneurysms by SAC is low, as also confirmed by our study (7.07%). This rate is also significantly lower than in meta-analyses for a stand-alone coiling (24.4%).^[17]

The mortality and neurological complication rates (0.02% and 4.33%, respectively) reported in our meta-analysis also compare favorably with those reported in the meta-analysis for stand-alone coiling (1.2% and 4.8%, respectively) and for clipping (1.7% and 6.7%, respectively),^[17,23] as well as with those mentioned in the studies for balloon-assisted coiling of intracranial aneurysms using the Eclipse 2L double-lumen balloon (0% and 3.2%, respectively) and for low rates of recanalization for wide-necked aneurysms treated with stenting after balloon-assisted coiling (4.6% and 2.3%, respectively). However, we should highlight that in the aforementioned studies for balloon-assisted embolization, the initial complete occlusion rate was approximately 95% higher than this in our study (50.20%). This may have resulted from balloon-assisted technique because the technique can enable denser packing of the aneurysm fundus and neck region or help mold the coil mass to improve its interface with the parent vessel.^[24,25]

Regarding the rate of stroke, this was almost 4%. Several factors may explain our low rate of stroke. Primarily, a tight antiplatelet protocol was pursued by the people in treatment. Furthermore, since a progressive thrombosis of the sac is anticipated because of a stent placement, we do not usually dare to acquire neither an immediate

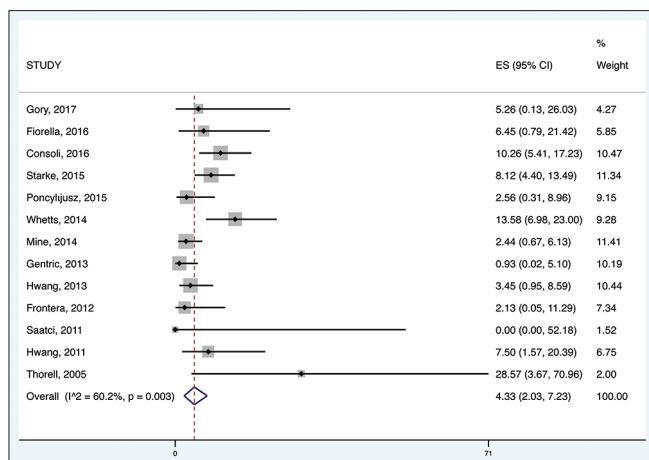


Figure 4: Forest plot presenting the meta-analysis of any neurological complications based on event rates for the use of stent-assisted coiling of unruptured intracranial aneurysms with wide neck. Event rates in the individual studies are presented as squares with 95% confidence intervals presented as extending lines. The pooled event rate with its 95% confidence intervals is depicted as a diamond

occlusion nor a very dense packing. As a third step, it should be mentioned that ruptured intracranial aneurysms with a high chance of being linked to an elevated stroke risk were not incorporated. The latter is due to the fact that ensuing subarachnoid hemorrhage induces vasospasm.^[2] In addition, the interventional neuroradiologists usually make an attempt to get a denser packing with a view to succeed in obtaining complete occlusion and further reduce bleeding chances. As a result, there is an elevated chance of coil protrusion at the area of the neck or in the parent artery than in unruptured aneurysms. The coil protrusion might end up in causing thromboembolic events (TEs). Finally, it should be noted that there is a possibility that the availability of the intracranial stents assists in the reduction of the percentage of symptomatic TE complications of coiling used as a rescue therapy to treat coil protrusion or instability and clot formation at the neck.^[26]

In our series, we did not observe intraprocedural aneurysmal ruptures, while this rate was 2.6% according to the meta-analyses for stand-alone coiling.^[17] The zero rate of aneurysmal rupture may be partially related to the fact that, when possible, the authors of studies in our review did not place the guidewire in the sac but tried to gently advance a microcatheter through the stent. It is worth noting that the overall late rupture was only 0.41%, which could be explained partially by the fact that additional treatment with coils was decided in some cases^[11] and the discontinuance of the antiplatelet therapy after some months according to the protocols.

A usual aggravation in-stent stenosis is atheromatous stenosis that is less important to endothelial and fibroelastic reaction. Despite the fact that not a major intimal damage could occur due to self-expanding stents used for stent coiling (SAC), the latter definitely takes place and most

possibly causes stability or improvement of the occlusion of intracranial aneurysms with SAC. What is more, this could further cause a certain kind of intrastent stenosis, something which was not common in our series (1.25%). This could be explained by the fact that surgeons administered routinely antiplatelet therapy including aspirin (325 mg the usual dose) and clopidogrel (75 mg the usual dose) mainly 5 days prior to surgery in combination with 5000 iu heparin intravenous bolus periprocedural which continued usually for additional 6 months for aspirin and 3 months for clopidogrel postprocedural since acute in-stent stenosis often elicits ischemic complications. However, as the premature or excessive prevention of in-stent stenosis may result in hemorrhagic complications before coil embolization, additional treatment for acute in-stent stenosis being delivered after its occurrence could be an option. It is also important to mention that in our study, even this negligible percentage for in-stent stenosis could be justified by aspirin or clopidogrel resistance. The platelet reactivity units should be measured as well as the appropriate dose of other drugs should be determined as an interaction is possible.

Among the SAC limitations are the necessity for double antiplatelet therapy, which is advisable to be kept for a period of 1 month at least. However, this might change in light of coated or absorbable stents.^[15] Our findings highlight that SAC is a considerable technical progress in the management of endovascular intracranial aneurysms. It is associated with low rates of morbidity, further enabling a safer treatment of wide-necked UIAs, which is supported by the large number of 976 patients who participate in our meta-analysis

Our study has some limitations. First, in the meta-analysis, we included mainly retrospective studies that did not directly compare different techniques. Second, follow-up images were homogeneous as they were mainly magnetic resonance angiography (MRA) and digital subtraction angiography. However, MRA has been reported to be highly effective and reliable for the follow-up of SAC.^[27] Third, heterogeneous aneurysm morphology and location can contribute to treatment bias since they are related to difficulties of endovascular techniques. Similarly, the modality of treatment including different choices of stents by physicians in different institutions is related to treatment bias. Other limitations of the eligible studies included in the meta-analysis were that not all patients complied with treatment during follow-up, along with the fact that some results were attributed to small number of cases, which were referred during follow-up. These two aforementioned limitations might have introduced an indirect publication bias in our study. Finally, in our series, morbidity was associated with TEs. This may have reflected the importance of adequate antiplatelet agent preparation before and even after the successful procedure. Practically, checking for antiplatelet agent resistance on a regular basis

would be helpful, but it was not available in the eligible studies.

Conclusions

Our review and meta-analysis pooled together outcome rates of relevant studies and highlighted the feasibility and safety of SAC of UIAs with wide neck. SAC is a relatively new technique, and we might need more experience before sound conclusions can be drawn. In spite of the fact that it might still be premature to make a generalization of the results, it seems that this technique might assist in the treatment of UIA with wide neck and SAC represents an acceptable alternative to surgical clipping.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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