

Review Article

Use of stent-assisted coil embolization for the treatment of wide-necked aneurysms: A systematic review

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Abstract

Background: The use of stent-assisted coiling (SAC) has been shown to be a treatment option for complex aneurysms. We reviewed systematically the immediate and mid-term angiographic results following treatment of wide-necked aneurysms with self-expanding stents and coils, as well as the peri- and postprocedural rate of complications.

Methods: A computerized database search was conducted from 01/2000 to 04/2011 using appropriate indexed terms on Pubmed. Inclusion criteria were: (1) homogeneous populations of ≥ 10 patients with wide-necked aneurysms; (2) use of a self-expandable neurovascular stent and coils for aneurysm treatment; (3) immediate and follow-up angiographic results; and (4) periprocedural and delayed thrombotic complications.

Results: Seventeen studies were included, containing retrospectively collected data on 656 patients/702 aneurysms. The target aneurysm was located on the anterior circulation in 78.4% of patients. The immediate rate of complete occlusion was 46.3%, (19.3-98.1%). The intra- and postprocedural rate of intrastent thrombosis or thromboembolic event was 4.6% and 4.3%, respectively. Complete occlusion was documented in 71.9% at last angiographic follow-up. The rate of recanalization was 13.2% of aneurysms (0-28.8%). Delayed in-stent stenosis occurred in 5.3% cases (0-20.6%).

Conclusion: SAC has been considered a treatment option for selected wide-necked aneurysms in some institutions. The use of intracranial stents should take into consideration the risk of ischemic complications, recanalization, delayed in-stent stenosis; and the currently unknown lifetime risks for stenosis, vascular injury, device failure, and aneurysm recurrence related to intracranial stenting. There is an evident need for a prospective multicenter registry for all treated patients with SAC.

Key Words: Aneurysm occlusion, complication, intracranial aneurysm, intracranial stent, wide neck aneurysm

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INTRODUCTION

Since the introduction of the Guglielmi detachable coil (GDC) system in the early 1990s, the criteria for

endovascular treatment have broadened. Embolization with GDCs alone is a recognized effective and durable treatment option in most small aneurysms with small necks. However, in the setting of wide-necked, large, or

giant aneurysm, important technical limitations in the GDC technology has prevented complete and durable aneurysm occlusion.^[19,65] In a study on 401 patients with 455 aneurysms treated with GDC coil published in 2000, complete coil occlusion of the aneurysm was achieved in 70.8% for small aneurysms (<10 mm) with small neck, 31.2% for small aneurysms with wide neck, 35% for large aneurysms (≥10 mm but ≤ 25 mm), and 50% for giant aneurysms (≥25 mm).^[19] Therefore the treatment of wide-necked aneurysms has remained a challenge for endovascular treatments.^[16,67] Numerous innovative devices and treatment strategies have been developed to render the endovascular treatment of wide neck aneurysms more effective and durable. New coils were developed to occlude the aneurysm including 3D coils, bioactive coils, hydrogel coils, and trispan coils.^[12,32,40] In addition, Onyx liquid embolic system has been used to occlude aneurysms unsuitable for coiling, or for recurrent aneurysms.^[61,73,85] The remodeling technique, also known as balloon-assisted coil embolization, has also contributed to extend the indications and feasibility of the endovascular treatment to broad-based aneurysms.^[64,70,71,83]

In the late 1990s and early 2000s, intracranial neurovascular stents were introduced to the armamentarium of endovascular surgery to treat wide-necked aneurysms.^[10,20,22,57] Stents have been proposed to have not only mechanical effects, but also hemodynamic and biological roles. Neurovascular stents were designed to act as a scaffold to prevent intrasaccular

coil protrusion into the parent artery lumen.^[95] They were also conceived to divert blood from the aneurysm inflow zone, and promote intraaneurysmal stasis and thrombosis, thereby preventing or reducing coil compaction by changing intraaneurysmal flow.^[33,95] In addition, stents appear to provide luminal matrix for orifice endothelialization.^[4,41,46,95]

Since their initial introduction, many improvements have been brought to the initial generation of neuroendovascular devices to improve their flexibility, maneuverability, and effectiveness [Table 1]. Although numerous groups have published their initial experience regarding initial occlusion rates and periprocedural complications, only a few studies have reported in a homogeneous aneurysm population their observations regarding durability of initial results, aneurysm recanalization, and in-stent stenosis. The mid-term impact of SAC on the outcome of embolized aneurysms and on patency of parent vessel has been published in a limited number of series. Long-term follow-up has not yet been extensively analyzed.

Furthermore, our impression in rendering second opinions for aneurysm treatment over the past 5 years is that SAC and also stents alone are increasingly being recommended not only for inoperable wide neck aneurysms, but also for many surgically treatable wide-neck aneurysms. This experience prompted our review of the literature regarding results of SAC. The intent of this review is to define the current state of understanding of success and

Table 1: Self-expanding neurovascular stents

Type of Stent	Structure	Properties	Advantage	Disadvantage
Neuroform (NF, NF2, NF2 Treo (NF2T), NF3)	Nitinol Open cell design 4 radiopaque markers on each end (more radiopaque and rounded as of NF2)	Radial force: 0.006 N/mm Vessel wall coverage: 9.5%	Stent stabilizer as of NF2 Decreased friction as of NF2 Can be used in small arteries (<2.5 mm)	Not retrievable Inadequate support with NF Difficult delivery with NF
Leo	Nitinol, braided wires Closed cell design 2 highly radiopaque wires that ensure visibility of both the diameter and length	Partially retrievable stent (1 st) Radial force: 0.004 N/mm (but described as high?) Vessel wall coverage: 12.8%	Good visibility Retrievable up to 90% is deployed Can be used safely in small arteries (<2.5 mm)	Unfixed gaps between the struts, potential of sliding of struts Need progressively larger and stiffer delivery catheters to place larger stents
Enterprise	Nitinol Closed cell design Small cell size Coated with Parylene C (smooth surface) Flared distal ends 4 radiopaque markers on each end	Partially retrievable stent (2 nd) Radial force: 0.008 N/mm Vessel wall coverage: 8.9%	Retrievable up to 70% is deployed	Relative poor visibility
Solitaire (SOLO first version)	Closed cell design Larger cell size 1 Proximal and 3 distal radiopaque markers	Completely retrievable stent Radial force: 0.011 N/mm Vessel wall coverage: 5.4%	Fully retrievable after complete deployment Coiling facilitated by larger cell design	Relative poor visibility Caution in arteries <2 mm (potential vasospasm)

NF: Neuroform

complication rates, to begin to define appropriate use, and to allow comparison with surgical results. As the new flow diverters, such as the Pipeline and Silk prototypes, constitute a distinct form of endoluminal reconstruction with still limited usage (i.e., indications with Food and Drug Administration [FDA]-approved indications), we have not included them in this review.^[7,69,99]

METHODS

Research method

A computerized database search was conducted from January 2000 to April 2011 using appropriate indexed terms on Pubmed including “intracranial aneurysm”, “treatment”, “stents”, “intracranial stent”. As of April 2011, the search resulted in 896 abstracts. All abstracts of manuscripts published either in English or in French were reviewed. We obtained the full manuscripts for all case series reporting clinical and/or radiological data following intracranial stenting for the treatment of cerebral aneurysms that included 10 or more patients, or controlled clinical trials, or prospective studies. In cases of doubt or if information was missing to determine eligibility, the entire article was obtained and reviewed. A total of 73 manuscripts were retained and reviewed thoroughly. Reference lists of all these articles were checked manually for additional potential eligible studies.

Inclusion/Exclusion criteria

Inclusion criteria were: (1) homogeneous populations of 10 or more patients with wide-necked aneurysms specifically in the report's methodology section; (2) use of a self-expandable noncovered neurovascular stent for wide-necked aneurysm treatment; (3) description of delayed angiographic follow-up (6 months) data analyzed in regards to initial postprocedure results; and (4) enumeration of intraprocedural and postprocedural thrombotic complications. Studies were not eligible if (1) they were case reports or small case series ($n < 10$); (2) their population was not homogeneously composed of wide-necked aneurysm; (3) the main stent used was either a coronary stent, covered stent, or balloon expandable stent; (4) use of flow diverters;^[7,66,71,87,99] (5) no clinical and/or radiological angiographic data were reported at midterm follow-up; (6) duplication of patient population reported in a larger series subsequently; and (7) studies were not yet published in full and only available as an Epub abstract.

Data extraction

From the included studies, the following data were extracted: (1) number of participating patients; (2) number of aneurysms treated; (3) location of aneurysms (anterior circulation vs posterior circulation); (4) type of stent used; (5) occurrence of intraprocedural events specifically intrastent thrombosis or thromboembolism (asymptomatic and symptomatic events); (6) procedure-related

mortality; (7) initial postprocedure angiographic result (complete occlusion rate); (8) postprocedural events, specifically intrastent thrombosis or thromboembolism (asymptomatic and symptomatic events); (9) follow-up angiographic results expressed as change in regards to the initial postprocedure result; (10) timing of follow-up angiography; (11) recanalization; (12) treatment required for recanalized aneurysm; (13) posttreatment in-stent stenosis (asymptomatic or symptomatic); (14) timing of diagnosis of in-stent stenosis; (15) treatment performed for in-stent stenosis.

Outcome measures

For the patient, the most important outcome is successful aneurysm occlusion. This includes complete (or near complete) occlusion at long-term follow-up, without significant recanalization, with no treatment-related symptomatic complications. Therefore, outcome was divided into three major components. The first outcome component is achievement of treatment goal – aneurysm occlusion. Most studies used the three point system developed by Roy, *et al.* to express the angiographic degree of aneurysm occlusion.^[79] Anatomical radiographic outcomes were defined as immediate occlusion (complete occlusion (100%), near complete occlusion or neck remnant ($\geq 95\%$ but $< 100\%$), subtotal occlusion or aneurysm residue ($< 95\%$).^[79] Immediate aneurysm occlusion was considered treatment success. The second outcome component is safety of treatment. This was assessed in terms of intraprocedural and postprocedural thrombotic events, either intrastent or thromboembolic, as well as procedure-related mortality. Although other factors pertaining to procedure safety could have been noted (e.g., femoral artery injury, contrast-related renal failure), they were not consistently reported throughout studies and therefore were not retained. The third outcome component is durability of treatment, which was assessed in terms of stability of initial radiographic results, recanalization, and development of in-stent stenosis. The majority of studies expressed the follow-up angiographic results in terms of change compared to immediate postprocedural results, and presence or absence of in-stent stenosis.

Statistical methods

Proportions of successes or failures were calculated for each qualifying publication without adjustment, as were aggregate proportions in each of the outcome domains. Confidence intervals (95% CIs) for each proportion were calculated using the mid-P exact method.^[1] Heterogeneity Index H was used to evaluate the total symmetry across sources within subsets. All analyses were conducted in R version 13.2 (R Core Development Group, Vienna, 2011).

RESULTS

A total of 656 patients with 702 aneurysms were collected from the 17 studies included in this systematic

review [Tables 2 and 3].^[4,14,25,28,34,35,44,48,54,80,81,92,94,96,102,103,106] SAC was performed to treat over 95% of these aneurysms. The rest were either treated with a stent only technique or completely failed attempted SAC or stenting alone. Overall, 34.3% of patients (225/656) were treated in the acute phase of a subarachnoid hemorrhage. Of the 17 studies, 2 included only unruptured aneurysms^[35,54] and 2 included only ruptured aneurysms.^[25,106] The distribution of aneurysms between the anterior and posterior circulation was detailed in 16 studies/648 aneurysm: 78.4% (508/648) were located on the anterior circulation and 21.6% (140/648) on the posterior circulation. Aneurysms included in these 16 studies (648 aneurysms) arose from the following arteries: 29 cavernous internal carotid artery (ICA) (4.5%); 13 superior hypophyseal (2%); 88 paraclinoid (13.6%); 101 carotido-ophthalmic (15.6%); 30 ICA bifurcation (4.6%); 68 posterior communicating artery (10.5%); 7 anterior choroidal artery (1.1%); 9 anterior cerebral artery (proximal and distal) (1.4%); 58 anterior communicating artery (9%); 111 middle cerebral artery (MCA) (17.1%); 86 basilar artery (BA) (apex and trunk) (13.3%); 18 vertebral artery (VA) (2.8%); 5 posterior cerebral artery (0.8%); 9 superior cerebellar artery (SCA) and SCA/BA (1.4%); 9 posterior inferior cerebellar artery/VA (1.4%).

Intraprocedural events including intrastent thrombosis and thromboemboli (TE) were reported in 16 studies (totaling 624 patients and 670 aneurysms), and were diagnosed in 4.6% of patients (29/624) and 4.3% of aneurysms (29/670). In these 29 patients with intraprocedural events, the majority had an intrastent thrombosis (22/29). The same 16 studies also reported their incidence of postprocedural stent thrombosis and TE events, resulting in 4.3% of patients (27/624) and 4.0% of aneurysms (27/670). The overall incidence of intrastent thrombosis and TE is 9.0% of patients (56/624) and 8.4% of aneurysms (56/670). The aggregate value of intraprocedural and postprocedural intrastent thrombosis and TE was, respectively, 0.0465 (95% CI: 0.0319-0.0652) [Figure 1] and 0.0417 (95% CI: 0.0280-0.0596) [Figure 1]. Of the 17 studies, 2 reported procedure-related mortality of 1.4 (1/71) and 8.7% (11/127) each, representing an overall rate of 1.8% (12/656).^[14,34] Procedure-related mortalities were due to intraoperative rupture in eight cases.^[14,34]

The completeness of aneurysm occlusion immediately after treatment was assessed in cases that underwent a SAC treatment performed in one procedure. Of the 17 studies, 1 did not detail the immediate angiographic results^[81] and another study used >95% occlusion as

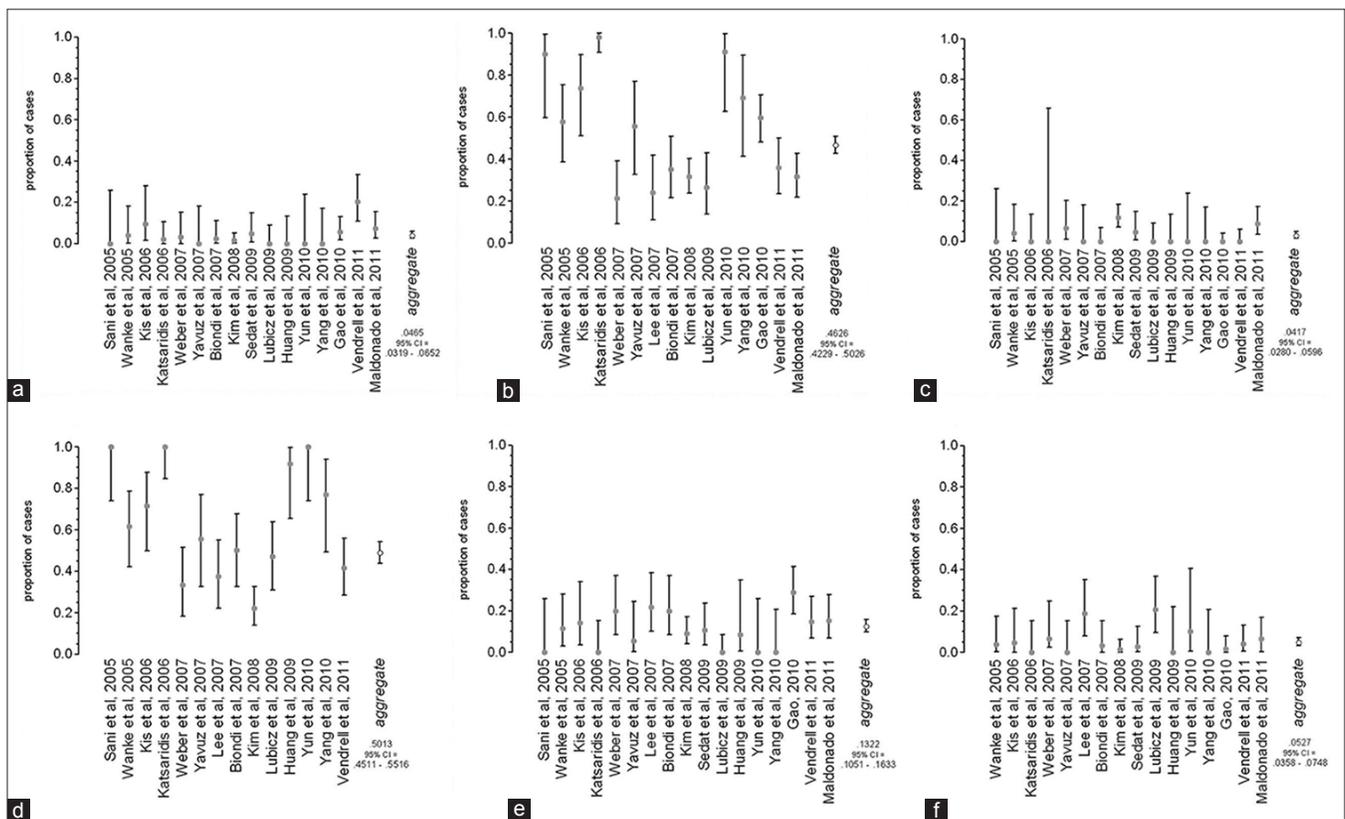


Figure 1: Schematic diagram of proportion of events from selected publications. Proportion of events (successes or failures) (solid symbol and 95% CI), by selected publication ordered by publication date, and by aggregate event (open symbol and 95% CI). (a) Intraprocedural thromboembolic event, (b) Initial aneurysm occlusion, (c) Postprocedural thromboembolic event, (d) No change of angiographic findings at follow-up angiography, (e) Recanalization, (f) Delayed in-stent stenosis. Aggregate value and confidence interval given for each graph

Table 2: Details of studies included in the review

Author/Yr	Nb pts/ Nb A	Pts with SAH	Ant circ/ Post circ	Type of Stent	Intra-procedural event	Post-procedural event	Immediate Angiographic results of SAC (nb pt)	Delayed Angiographic results (nb A; timing; result)	Delayed in-stent stenosis
Sani, 2005	10/10	3	9/1	NF 2T	IST: 0 TE: 0	ST: 0 TE: 0	C: 9/10	10A/6 mo Stable: 10; Recan: 0	N/M
Wanke, 2005	25/26	6	8/18	NF 2	IST: 1 TE: 0	ST: 0 TE: 1, AS	C: 15/26	26A/8mo Stable: 16; CThrombo: 4; Recan: 3	1, AS
Kis, 2006	21/25	0	18/7	Leo	IST: 1 TE: 1	ST: 1 TE: 0	C: 14/19	21A/mean 6 mo Stable: 15; Improved: 2 Recan: 3	1, AS
Katsaridis, 2006	44/54	33	N/S	NF2	IST: 1 TE: 0	ST: 0 TE: 0	C: 51/52	18A/after 6 mo Stable: 18; Recan: 0	0
Weber, 2007	30/31	13	25/6	Enterprise	IST: 1 TE: 0	ST: 1 TE: 1, S	C: 6/28	30A/6 mo Stable: 10; CThrombo: 14 Recan: 6	2 AS
Yavuz, 2007	15/18	1	16/2	SOLO	IST: 0 TE: 0	ST: 0 TE: 0	C: 10/18	18A/6 mo Stable: 10; CThrombo: 7 Recan: 1	0
Lee, 2007	32/32	4	21/11	NF	N/M	N/M	C: 7/32	32A/mean 6.1 mo Stable: 12; Improved: 13 Recan: 7	6
Biondi, 2007	42/46	5	39/7	NF: 7 NF 2: 17 NF 2T: 20 NF 3: 3	IST: 0 TE: 1	ST: 0 TE: 0	C: 14/40	30 A/mean 9 mo Stable: 15; Improved: 9 Recan: 6	1
Kim, 2008	127/ 136	50	93/43	NF	IST: 2 TE: 0	ST: 3 TE: 6 AS, and 6 S	C: 39/123	77A/mean 13.7 mo* Stable: 17; CThrombo: 40 Recan: 7	1, AS
Sedat, 2009	42/42	11	36/6	NF	IST: 1 TE: 1	TE: 2, S	N/M	38A/mean 42 mo C: 27; Recan: 4	1, AS
Lubicz, 2009	32/34	2	24/10	Leo: 14 Enterprise: 20	IST: 0 TE: 0	ST: 0 TE: 0	C: 9/34	34/mean 20 mo Stable: 16; Improved: 14 Recan: 0	7
Huang, 2009	21/21	21	21/0 AcoA	NF 2 or 3: 19 Leo 2	IST: 0 TE: 0	ST: 0 TE: 0	>95: 18	12A/median 5.6 mo Stable: 11; Recan: 1	0
Yun, 2010	11/11	11	11/0 AcoA	NF	IST: 0 TE: 0	ST: 0 TE: 0	C: 10/11	10A/6 and/or 12 mo Stable: 10; Recan: 0	1
Yang, 2010	16/16	10	16/0 MCA	NF: 12 Leo: 4 Enterprise: 1	IST: 0 TE: 0	ST: 0 TE: 0	C: 9/13	13A/mean 5.6 mo Stable: 10; CThromb: 3 Recan: 0	0
Gao, 2010	71/72	39	57/15	NF	IST: 0 TE: 4 (2S)	ST: 0 TE: 0	C: 43/72	59A/mean 43.2 mo N/M; Recan: 17	1, S
Vendrell, 2011	49/52	16	52/0 MCA	NF or Enterprise	IST: 10 (4S) TE: 0	ST: 0 TE: 0	C: 18/50	48 A/mean 14 mo Stable: 20; CThrombo: 21 Recan: 7	2, AS
Maldonado, 2011	68/76	0	68/8	NF: 1 NF2: 26 NF3: 49	IST: 5 (1S) TE: 0	ST: 1, S TE: 5, AS	C: 24/76	46A/mean 37.09 mo C: 26/46; Recan: 7 (at longest follow-up)	3, AS

A: Aneurysm, AcoA: Anterior communicating artery, AS: Asymptomatic, C: Complete occlusion, CThrombo: Complete thrombosis, IST: Intrastent thrombosis, MCA: Middle cerebral artery, Mo: months, NF: Neuroform, NF 2T: Neuroform 2 Treo, N/M: Not mentioned, Recan: Recanalization, S: Symptomatic, SAC: Stent-assisted coiling, SAH: Subarachnoid hemorrhage, ST: Stent thrombosis, TE: Thromboemboli

Table 3: Summary of results of the systematic analysis

	Number of studies reported	Minimum and maximum rate (%)	Overall rate in aneurysms (%)	Overall confidence interval
Intraprocedural events	16/17	0-19.2	4.3	0.0315-0.0652
Post-procedural event	16/17	0-8.8	4.0	0.0280-0.0596
Immediate complete occlusion	15/17	19.3-98.1	46.3	0.4229-0.5026
Unchanged FU angiographic studies	14/17*	22.1-100	50.1	0.4511-0.5516
Recanalization	17/17*	0-28.8	13.2	0.1051-0.1633
Delayed in-stent stenosis	16/17	0-20.6	5.3	0.0358-0.0748

*Studies presenting the FU angiographic results in comparison to the immediate post-procedural angiogram in terms of unchanged, completed or increased thrombosis, or recanalization

criteria for complete occlusion instead of 100% as did the other studies.^[25] Within the remaining 15 studies that documented immediate angiographic aneurysm occlusion as complete obliteration or class one of Roy classification, occlusion was documented in 46.3% of patients (278/601). Individual study rates of immediate complete occlusion vary from 19.3% to 98.1%. The aggregate value of this success was 0.4626 (95% CI = 0.4229-0.5026) [Figure 1]. If near-complete obliteration (95-99% occlusion or neck remnant/class 2 of Roy classification) is also included, 76.2% of patients (474/622) benefited of $\geq 95\%$ aneurysm obliteration after SAC treatment.

Follow-up angiography was performed in all 17 studies using solely digital subtracted angiography (DSA) in 15 studies and DSA or magnetic resonance angiography (MRA) in 2 studies.^[54,92] Overall, midterm angiogram was performed for follow-up in 74% of treated aneurysms (522/702), most commonly at 6 months (mean varying 5.6-43.2 months). Eleven of the studies had a mean follow-up period of less than 12 months. Of the six studies that reported a mean follow-up beyond 12 months, three had a follow-up greater than 24 months. Data regarding completeness of occlusion was extracted from 15 studies (totaling 431 aneurysms). Overall, 71.9% (310/431) of treated aneurysms were completely occluded at last angiographic follow-up. Fourteen studies (totaling 379 aneurysms) presented the follow-up angiographic results in comparison to the immediate postprocedural DSA in terms of unchanged, completed or increased thrombosis, or recanalization. Angiographic results were stable in comparison to the initial postprocedural images in 50.1% (190/379), with individual study rates varying from 22.1% to 100%. The aggregate value of this success was 0.5013 (95% CI = 0.4511-0.5516) [Figure 1]. Data regarding increased or completed thrombosis as documented on the angiographic follow-up could be extracted from 13 studies (totaling 302 aneurysms). A total of 31.5% (95/302) of aneurysms showed progressive thrombosis.

Recanalization was assessed on follow-up angiography in all studies. Overall 13.2% (69/522) aneurysms presented some degree of recanalization on the follow-up angiogram,

manifesting itself by a step-down on the three point aneurysm occlusion scale by Roy, *et al.*^[79] The individual study rate of recanalization varies from 0% to 28.8%. The aggregate value of this failure was 0.1322 (95% CI 0.1051-0.1633) [Figure 1]. If we consider only the studies with a mean follow-up ≥ 12 months that assessed recanalization, 15.6% of aneurysms had recanalized at long-term follow-up. Among the studies mentioning if further treatment had been required, 76.6% of recanalized aneurysms required additional endovascular treatment.

Presence or absence of delayed in-stent stenosis was clearly reported in 16 studies. The overall rate of delayed in-stent stenosis was 5.3% (27/512), with individual study rates varying from 0% to 20.6%. The aggregate value of this event was 0.05277 (95% CI: 0.0358-0.0748) [Figure 1]. Most cases of delayed in-stent stenosis were diagnosed on the follow-up angiographies performed around 6 months postprocedural. However, the diagnosis of in-stent stenosis was made more than 12 months after the SAC procedure in three patients (11%), specifically at 18, 15, and 13 months. These three patients belonged to studies with a prolonged mean angiographic follow-up time (9, 37, 43 months). The radiographic severity of the in-stent stenosis was not consistently reported throughout the studies, and when it was, was most often qualitatively described as mild, moderate, or severe. Only one patient was symptomatic with in-stent stenosis and was treated by angioplasty. Two additional asymptomatic cases were also treated: one medically and one with an angioplasty. Of note, two studies reported each a case of spontaneous in-stent stenosis resolution at 18 and 24 months.^[34,96]

DISCUSSION

Treatment options for wide-necked aneurysms

Treatment of wide-necked aneurysms has been challenging for neurosurgeons and interventional radiologists.^[16,67] Although direct aneurysm clipping is the most definitive and durable treatment for such aneurysms, it may be hazardous or impossible to safely clip the aneurysm because of difficult surgical access, incorporation of a parent vessel and/or perforators, tissue characteristics such as calcifications or atherosclerotic thickening, age or

medical condition of the patient.^[29,67-68,75] For unclippable aneurysms, proximal arterial ligation or trapping may be an option, with arterial bypass if collateral circulation is inadequate.^[55] Endovascular treatment has become an accepted alternative to surgical clipping. The International Subarachnoid Aneurysm Trial showed a significant 7.4% absolute 1-year disability free survival advantage, favoring coiling, which has persisted for 7 years.^[60,62] However, wide neck (>4 mm neck, or dome to neck ratio <2) aneurysms and fusiform aneurysms, were typically not included in this study.^[60] Sole embolization with GDCs has been problematic for wide-necked aneurysms given the instability of the coiling construct and the potential of coil protrusion in the parent artery. Most often, satisfactory occlusion has not been achieved due to loose packing, incorporation of the coils in the clot of large or giant wide-necked aneurysm, and compaction of coils.^[16,67] In order to circumvent this issue, balloon remodeling technique and new coils with bioactive properties and specific designs and configurations such as 3D shaped coils have been developed.^[64,95,98]

Evolution of intracranial stents

The earliest clinical reports of SAC of an intracranial cerebral aneurysm date to the late 1990s, by Higashida, *et al.* and Mericle, *et al.*^[22,57] Peripheral and coronary stents were initially used for SAC in intracranial vessels.^[3,47,57,82] These stents were relatively stiff and of large profile, limiting their navigation in the tortuous intracranial vessels. Since most stents needed balloon-assisted deployment, they carried a relatively high risk of dissection and/or rupture of the parent artery.^[22,31,52,88] A new generation of stents were specifically developed for intracranial use [Table 1]. The Neuroform stent (Boston Scientific, Natick, MA, USA) was the first self-expanding nitinol stent delivered through a microcatheter with an open cell design approved for use to treat wide-necked cerebral aneurysms.^[10,20,24] Although initial studies reported that its use was feasible and effective, various limitations were noted including deployment difficulty, low radial force, stent migration, dislocations of cells due to the open cell design, and lack of retractability [Table 1]. A subsequent generation of stents was developed to circumvent some of these limitations. The LEO stent (Balt Extrusion; Montmorency, France) was the first partially retrievable stent.^[35,50,74] Its major limiting characteristic was the need for progressively larger and stiffer delivery catheters to place larger stents. The Enterprise stent (Cordis Corporation; Miami, FL, USA) was the second partially retractable device.^[21,49,96] Although its navigation and positioning seemed the easiest, some authors noted its visibility to be suboptimal. The Solitaire stent (ev3, Irvine, CA, USA) was the first fully retrievable intracranial stent developed.^[36,37] Table 1 summarizes the characteristics of stents used in studies included in this analysis.^[24,36,38,51,74]

The initial studies assessing the use of each new stent have reported the feasibility of SAC for treatment of intracranial aneurysms. These studies from single institutions are numerous, and present results of small to medium size populations with various types of aneurysms including wide-necked, fusiform, and dissecting types.^[84] Few studies have described the anatomic durability of the SAC in a homogeneous aneurysm population, such as wide-necked aneurysms, with a mid-to-long angiographic follow-up.

Summary of findings and implications of results

From the 17 studies that met the inclusion criteria, data were collected on 656 patients/702 aneurysms [Tables 2 and 3]. The mean patient rate of intrastent thrombosis or TE event was 4.6% intraprocedural, and 4.3% postprocedural. Immediate complete angiographic occlusion was documented in an average of 46.3% of patients (278/601). Procedure-related mortality occurred in 1.8% of treated patients. A follow-up angiogram was performed in 54% of treated aneurysms (379/702), most commonly at 6 months (mean varying 5.6-43.2 months). The mean rate of angiographic occlusion was 71.9% (314/431). The mean rate of no angiographic change in comparison to the initial posttreatment images was 50.1% (190/379). The average rate of recanalization and in-stent stenosis was, respectively, 13.2% and 5.3%. If we define optimal clinically and anatomically successful treatment as complete immediate occlusion, no intraprocedural or postprocedural complication, no recanalization, and no in-stent stenosis, approximately 30-35% of the 702 aneurysms would be considered optimally treated successfully.

The statistical analysis of the described results is limited. All of the above subgroups showed significant indices of heterogeneity (H , $P < 0.001$), representing high levels of disagreement across the qualifying sources assessed in each of the separate key topic areas. In addition, the presence of multiple zero cell counts precludes computation of meaningful odds outcomes, the preferred statistical approach to understanding descriptive binary outcomes in noncontrolled studies. Aggregate confidence intervals are likely to be underestimated due to this same problem. Regrettably, none of the qualifying studies provided sufficient basis to compute odds ratios for more refined statistical appraisal of the topic areas.

Limitation of the study

A critical review of the current literature is important to determine the current understanding of safety and durability of SAC, and identify limitations preventing extrapolation of results.

Publication bias – A key limitation of any literature review is “publication bias”. Studies with positive results tend to be published more often than those with equivocal or negative results.^[8,26] We recognize that

for the interpretation of results presented in reviews, which are based mostly on small studies, bias should be carefully considered. Statistical tests for small study effect in meta-analysis and systematic analysis have been reported.^[9,86] However, their validity is limited when the analysis is based on a small number of small studies, and therefore such tests have not been applied in this review.^[9,86]

Type of studies included – The major limitation of this analysis refers to the retrospective nature of included studies, and the absence of a control group allowing comparison between SAC and traditional coiling. For the inclusion criteria detailed in this review, no prospective study or randomized trial was yet published in the literature. Even when considering other published series not included in the review, no study has yet determined superiority of SAC over traditional coiling or other treatment modality in terms of long-term durability.^[6,59]

Background of treating physicians – Although the inclusion and exclusion criteria were designed to obtain the most homogeneous study population possible, there are some physician-related factors that cannot be accounted for in the results such as each treating team's decision making process as well as their personal experience with stenting techniques.^[83]

Variety of stents and SAC protocols – Although most studies present results of the SAC using a specific type of stent, others included a variety of stents.^[25,48,54,102] Given that each stent has its own advantages and limitations, the choice of a specific stent for a given aneurysm may influence periprocedural morbidities and mortality as well as long-term efficacy. Different treatment sequences regarding timing of stenting and coiling, as well as various SAC techniques, including the parallel technique, jailing technique, and the sequential technique, may also contribute to the variability of results.^[4,23,25]

The pre- and postprocedural antiplatelet/anticoagulation protocol used by different institutions may also vary. The dual antiplatelet regiment of acetylsalicylic acid and clopidogrel has become a recommended regimen as they act synergetically to reduce the chances of TE events and stent thrombosis.^[18,100] However, the dosage and duration of each remains controversial. Furthermore, analysis of platelet function to identify low response or no response of individuals to platelet inhibitors is also important as some groups have noted ischemic complications and in-stent stenosis occurring while on antiplatelet medications.^[10,27,100,101,104] Indeed, the low response or no response to antiplatelet medication as well as interruption of antiplatelet therapy appears to influence development of delayed stenosis and/or thrombosis.^[58] In contrast, acute and delayed intracranial hemorrhages have been associated with antiplatelet therapy in SAC aneurysm.^[89,107] Furthermore, use of

dual antiplatelet treatment in SAC of acutely ruptured aneurysms has been associated with an increased risk of hemorrhagic complications following ventriculostomies and ventriculoperitoneal shunts.^[39,89] Prolonged postprocedural antiplatelet therapy may also potentially interfere with delayed aneurysm thrombosis.^[43]

Shortcomings in reporting of results – Data analysis is limited by the data collected and reported in each individual study. In most studies, no clear or standardized definition was given for the events tabulated.^[100] Use of standardized definitions may help to standardize data collection. Importantly, in all of the included studies, clinical and radiological results were assessed by the treating team, not by an independent evaluator. This is known to be associated with under-reporting of complications.^[56] Finally, other events in the periprocedural period, and mid- to long-term follow-up, would have been important to capture. These include technique-related complications^[13,53,93] and antiplatelet/anticoagulation-related complications, including femoral artery injury, leg embolism and distal ischemia, groin hematomas, retroperitoneal hematoma, stent migrations and fractures, intracranial bleeds, ventriculostomy-related hematomas, and aneurysm rupture during follow-up. Multiple other series, that did not meet the inclusion criteria, reported the occurrence of such complications.^[10,11,15,27,30,42,45,52,63,78,90,100,101,104] Table 4 summarizes the full spectrum of the types of reported

Table 4: Summary of reported complications occurring in the setting of stent-assisted coiling

Technique	Related to angiography: Femoral puncture Femoral artery injury, pseudoaneurysm Related to angiography: Catheter navigation Arterial dissection Arterial vasospasm Related to stenting Delivery or deployment failure Premature detachment or deployment Misplaced stent Stent protrusion in aneurysm Stent displacement or migration (acute vs chronic) Arterial injury (tearing, rupture) Inability to place coils through the stent Coil migration through the stent: Acute vs delayed
Vessel/stent	Thromboembolic event: Acute vs delayed In-stent stenosis: Acute vs delayed Occlusion of parent artery or branch
Aneurysm	Aneurysmal bleed/rebleed: Acute vs delayed Recanalization of the aneurysm
Bleeding (non aneurysmal)	Intracranial External ventricular drain-related hematomas Intracranial hemorrhage: Acute vs delayed Peripheral Groin hematoma Retroperitoneal hematoma Cervical hematoma (IV central line site) Gastric bleeding

complications occurring in the setting of SAC. Finally, there is limited data from mid-term angiographic follow-up, and almost none from long-term. The absence of angiographic follow-up may contribute to underestimating the rate of recanalization as well as delayed in-stent stenosis.

Although the underlying pathology of the arterial wall is distinct, the literature on the treatment of obstructive coronary disease with intraarterial stents has been a launching point for many of the hypothesis regarding stenosis of intracranial arterial stents. Specifically for in-stent restenosis following percutaneous coronary intervention, the rates have passed from 30% to 50% in patients that underwent angioplasty without stenting, to 10-30% in those treated with an intravascular stent.^[97] More recently the use of self-expanding coronary nitinol stents and drug-eluted stents have contributed to even further decrease the rate of restenosis.^[17,105] Although the rate is significantly less with intracranial stents, the extent of the phenomena and its future implications are not as well documented as in the cardiac literature and still need to be compiled.

Other large reports or reviews

Bodily, *et al.* reviewed the literature regarding SAC specifically in the context of acutely ruptured intracranial aneurysms.^[5] Details regarding the size and location of the ruptured aneurysms were not reported. All patients received heparin during the procedure and 96% received dual antiplatelet therapy after the procedure. Immediate complete aneurysm occlusion was reported in 63% of cases. A clinically evident intracranial hemorrhagic complication occurred in 8% of patients, whereas a clinically significant thromboembolic event occurred in 6% of patients.^[5] Importantly, a good clinical outcome was noted in only 81% of patients that presented in good clinical grade in this review. The authors cautioned that adverse effects appeared more common and clinical outcomes were worse with SAC than those achieved without stent assistance in the setting of ruptured aneurysms.^[5] Shapiro, *et al.* recently published a literature survey on SAC for complex aneurysm.^[84] Overall, 63% of the aneurysms measured <10 mm and 22% were treated in the setting of acute or recent subarachnoid hemorrhage. Despite the less stringent inclusion criteria and the resultant more heterogeneous global study population, they found that approximately 45% of aneurysms were completely occluded immediately after SAC, a result similar to our finding of 46.3% in a homogeneous population of wide-neck aneurysms. The rate of complete aneurysm occlusion was 61% at variable follow-up times, in comparison to the rate of 71.9% at last follow-up compiled in this review. The authors noted an overall complication rate of 19%, mainly from thromboembolic events, and concluded that the morbidity of SAC is higher compared with standard coiling.^[84] Piotin, *et al.* recently published their large experience with SAC

for intracranial aneurysms (sidewall and bifurcation) using mostly the neuroform stent but also other self expandable stents, balloon expandable stents, and flow diverters.^[72] Immediate complete aneurysm occlusion occurred in 46.3% of cases treated by SAC. Permanent neurological procedure-related complications occurred in 7.4% of procedures with stents. Procedure-related mortality occurred in 4.6% of procedures with stents.^[72] These three reports raise an important question as to whether the SAC may be used beyond its initial indication and also include relatively uncomplicated aneurysms amenable to direct or balloon-assisted coiling. The rates of aneurysm occlusion and of treatment complications presented in these studies as well as the current review suggest that surgical treatment may represent a safer and more durable treatment option for many wide neck aneurysms in medically stable patients.^[72,84]

Summary and implications for selection of stent therapy for aneurysms

This review has reported the range of results, and across-series aggregate results, for SAC for intracranial wide-necked aneurysms. Since there is, as yet, no information on long-term, lifetime risks of arterial injury or stenosis, aneurysm recurrence, stent fracture, or vessel erosion, use of intracranial stents should be employed very selectively for younger patients with a substantial life expectancy. Thus treatment decisions, and selection of a new technique (e.g., SAC), over an established technique (e.g., microsurgical clipping) should be made very cautiously, considering the documented limitations and complications, and unknown long-term results of the new technique – this is key particularly for optimal patient-centered care. Decision-making should not be based only on the results of the reports with the most favorable results – but should objectively consider the full range of reported results. Local decision-making should equally consider local results for the specific center where treatment is planned.^[2] Finally, treatment selection between several options should be based not on the newness of a particular choice, nor simply on the feasibility of a certain option, nor on any one aspect of a specific strategy (e.g., “non-invasiveness”), but rather on an objective consideration of all aspects of each treatment (short- and long-term efficacy, safety, discomfort, etc.) as they relate to the specific aneurysm in the specific patient.^[2]

The treatment of unruptured MCA aneurysms represents such an example. The presence of a wide neck and/or of an arterial branch originating from the aneurysm neck are two features that account for failure of standard endovascular techniques. In these circumstances, surgical clipping still represents the most efficient and durable treatment for unruptured MCA aneurysms.^[76,77,91] Will the SAC technique allow such MCA aneurysms to be treated effectively by endovascular means? In light

of the discussed results, this would probably not be recommended given the higher complication rate, more incomplete occlusion, higher recanalization rate, potential for stenosis, and absence of long-term data.

Further studies should take into considerations the discussed limits to help accurately define the role of SAC in the treatment of wide-necked aneurysms.^[95] Follow-up on more patients for a longer period after their treatment is necessary before this treatment approach can be recommended as an equivalent or preferred alternative to clipping for operable wide-neck aneurysms. There is an evident need for a prospective multicenter registry that will allow collection of long-term clinical results for all treated patients with SAC, and for similar patients treated with alternative techniques (e.g., simple coiling, surgical clipping).

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