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Stent-assistant versus non-stent-assistant coiling for ruptured and unruptured intracranial aneurysms: A meta-analysis and systematic review

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ABSTRACT

Background: Several different endovascular and non-invasive treatment methods are suggested for the various types of intracranial aneurysms including simple, balloon-assisted, and stent-assisted coiling (SAC). Previous studies investigated the safety and efficacy of SAC versus non-stent-assisted coiling (non-SAC) but the results were controversial. We aim to perform a systematic review and meta-analysis to compare the efficacy and safety of SAC with non-SAC technique in stratifying by the ruptured and unruptured aneurysms.

Methods: PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials were searched in April 2022 for studies investigated the efficacy and safety of SAC versus non-SAC.

Results: Overall, 26 studies entered into our qualitative and quantitative synthesis. We found that there was overall lower recurrence rate in SAC versus non-SAC significant (RR: 0.43, 95%CI: 0.33, 0.53). Furthermore, the comparisons were significant in unruptured (RR: 0.63, 95%CI: 0.40, 0.86), ruptured (RR: 0.29, 95%CI), and combination aneurysms (RR: 0.42, 95%CI: 0.30, 0.54). Also, we found higher risk of intraprocedural rupture for SAC versus non-SAC in unruptured aneurysms (RR: 1.40, 95%CI: 1.31, 1.50). Investigating hemorrhagic events risk showed that there was significant difference in ruptured (RR: 1.73, 95%CI: 1.12, 2.34) and combination aneurysms (RR: 0.60, 95%CI: 0.37, 0.82). There was no significant difference in immediate occlusion rate, complete occlusion, and risk of ischemic events in our analysis.

Conclusion: Overall, our findings demonstrated that SAC may have higher efficacy in term of recurrence rate, but also may have a higher risk of complications in the treatment of intracranial aneurysms. As there are several factors affecting the outcomes and safety of these interventions, further RCTs controlled for multiple factors are required better guide the neurointerventionists choose the best strategy.

1. Introduction

Intracranial aneurysms are a ballooning of the brain's blood vessels mostly located at branching points with the potential of rupturing and causing a hemorrhagic stroke.¹ Several different endovascular and non-invasive treatment methods are suggested for the various types of intracranial aneurysms including simple, balloon-assisted, and stent-assisted coiling (SAC).²

SAC was first introduced by Higashida et al in 1997³ as an endovascular method to treat complex IAs such as wide-necked, fusiform, and gigantic types which are now used for smaller berry aneurysms.⁴ Over time newer versions of stents have been developed such as laser-cut and braided stents.⁵ Due to the reopening and recanalization of aneurysms, conventional coiling does not apply to wide-necked or giant aneurysms,⁶ and considering the fact that stents prevent protrusion of coiling into the parent artery, SAC is a very efficacious technique in the treatment of complex intracranial aneurysms.⁵

Many studies already discussed the safety and complications of SAC but the results were controversial.^{7–9} Overall, SAC is considered safe and effective in the closure of aneurysms, even able to treat unruptured wide-necked aneurysms with a low rate of complication and stent-stenosis.¹⁰ Previously, Chalouhi et al investigated the safety of this technique in 508 patients treated by Neuroform and Enterprise stents and concluded that SAC provides durable closure of intracranial aneurysms.¹¹ Although several complications such as thromboembolism and postoperative aneurysm rupture were expected,¹² these results were mostly observed in the ruptured aneurysms.¹¹ According to Ho et al

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Abbrevia	ntions
SAC non-SAC CI RR I ² NOS PRISMA	stent-assisted coiling non-stent-assisted coiling confidence interval risk ratio I-squared Newcastle–Ottawa scale Preferred Reporting for Systematic Review and Meta-
	Analysis

despite the adverse events following the treatment of acutely ruptured aneurysms, SAC has been able to achieve good results and has been preferred to other endovascular treatment techniques.¹³

A previous meta-analysis compared the efficiency of SAC with conventional coiling in the treatment of intracranial aneurysms. In this study, SAC proved to have a lower recurrence but also a higher progressive thrombosis rate compared to non-stent-assisted coiling (non-SAC). However, the difference between the complications of the two methods was not significant.¹⁴ In line with these results, another study also found a lower recurrence rate in SAC compared with non-SAC.¹⁵ Although, both studies suggested further prospective studies might be needed to validate the angiographic outcomes of SAC compared to non-SAC.

Previous review studies investigated the safety and efficacy of SAC compared to non-SAC mainly without considering the type of aneurysms (ruptured or unruptured), though we aim to perform a systematic review and meta-analysis to compare the efficacy and safety of SAC with non-SAC technique in stratifying by the ruptured and unruptured aneurysms.

2. Methods and materials

We conducted this systematic review and meta-analysis based on the Preferred Reporting for Systematic Review and Meta-Analysis (PRISMA) checklist. 16

2.1. Search strategy

We performed a comprehensive literature search in four online databases including PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials in April 2022. The combination of the following terms was used in our search strategy: "intracranial aneurysms" or "cerebral aneurysms" and "stent" or "coil". Furthermore, one experienced investigator searched the reference list of previous review studies to identify additional relevant studies.

2.2. Eligibility criteria

The studies which investigated the efficacy and safety of SAC versus non-SAC were considered eligible if reported occlusion rate, complications, and aneurysms definition. Also, included studies must have an angiographic follow-up and sufficient data for comparisons. Case reports, case series, review articles, letters, conference papers, and non-English studies were excluded.

2.3. Study selection and data extraction

Two independent reviewers (F.N, P.V) first screened the title and abstracts and identified relevant studies. Next, the full text of the remained articles was reviewed and the eligible studies were selected. The same reviewers extracted the following information using a predefined datasheet: Study demographic, type of study, study period, non-SAC definition, type of aneurysms (ruptured or unruptured), the



Fig. 1. PRISMA flow diagram depicting the flow of information through the different phases of a systematic review.

Table 1
Characteristics of included studies.

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Author	Country	Type of study	Stent brand	Study period	non-SAC group definition	Ruptured or unruptured	SAC number	Non-SAC number	Age SAC	Age non- SAC	Women SAC	Women non-SAC	Size of aneurysms SAC (mm)	Size of aneurysms non-SAC (mm)	Hunt–Hess grade SAC	Hunt–Hess grade non- SAC	NOS
Cai et al 2016	China	Retrospective cohort study	NR	2011-2014	Balloon	Ruptured	65	32	56.6	56.5	49	22	5.1 ± 2.2	5.6 ± 2.2	Grade 1–3:60	Grade 1–3:32	9
Chalouhi et al 2012	USA	Retrospective cohort study	NR	2009–2010	Balloon	Combine (8 SAC, 21 non- SAC ruptured)	69	32	54	53	57	26	6.8	6.4	NR	NR	9
Chalouhi et al 2013	USA	Retrospective cohort study	Neuroform and Enterprise	2004–2011	Simple	Combine (35 SAC, 89 non- SAC ruptured)	88	147	56	54	69	108	7.9	8	NR	NR	9
Chung et al 2014	Korea	Retrospective cohort study	Neuroform and Enterprise	2008–2013	Multiple microcatheter and balloon	Combine (11 SAC, 19 non- SAC ruptured)	127	80	55	57	108	32	NR	NR	NR	NR	8
Colby et al 2011	USA	Retrospective cohort study	NR	1992–2009	Simple	Combine (2 SAC, 12 non- SAC ruptured)	30	60	53	52	27	55	7	8.8	Grade 1–3: 2	Grade 1–3: 10	9
Consoli et al 2014	Italy	Retrospective cohort study	NR	2004–2012	Balloon	Unruptured	122	164	NR	NR	80	108	NR	NR	Grade 1–2:121	Grade 1–2:98	8
Fan et al 2016	China	Retrospective cohort study	Neuroform, Enterprise, and Solitaire AB	2008–2015	Simple	Ruptured	63	159	53.7	53.9	29	79	6.2	5.2	NR	NR	9
Gao et al 2018	China	Retrospective cohort study	NR	2013-2015	Simple	Ruptured	33	42	52	55	10	15	NR	NR	Grade 1–2:30	Grade 1–2:36	9
Gordhan et al 2011	USA	Retrospective	Neuroform	2005–2009	Simple	Unruptured	26	12	61	64	20	7	11.5	8.1	NR	NR	9
Hetts et al 2013	USA	Clinical trial	Neuroform	NR	Simple	Unruptured	137	224	56	56	104	171	7.6	7.8	NR	NR	-
Hwang et al 2011	Korea	Retrospective cohort study	Neuroform and Enterprise	2003–2008	Multiple microcatheter and balloon	Unruptured	40	86	56	59	30	63	7.7	7.5	NR	NR	9
Jahshan et al 2013	USA	Prospective cohort study	NR	2004–2011	Simple	Combine (20 SAC, 191 non- SAC ruptured)	181	308	68	66	NR	NR	NR	NR	NR	NR	8
Kim et al 2010	Korea	Retrospective cohort study	NR	NR	Microcatheters and balloon	Combine (8 SAC, 8 non-SAC ruptured)	37	37	58	55	30	24	6.6	7	NR	NR	9
Kim et al 2017	Korea	Retrospective cohort study	NR	2005–2016	Simple	Combine (1 SAC, 12 non- SAC ruptured)	37	61	52	55	32	51	5.3	6.1	NR	NR	9
Liu et al 2014	China	Retrospective cohort study	Neuroform, Enterprise, and Solitaire AB	2004–2015	Simple	Combine (15 SAC, 165 non- SAC ruptured)	113	166	57	56	79	99	NR	NR	Grade 1–2:60	Grade 1–2:82	9
Ogilvy et al 2010	USA	Retrospective cohort study	Neuroform and Enterprise	NR	Simple	Combine (8 SAC, 2 non-SAC ruptured)	70	24	56	54	60	24	10.4	9.6	NR	NR	9
Ozretić et al 2015	Croatia	Retrospective cohort study	Neuroform, Leo, and Enterprise	NR	Simple	Combine (2 SAC, 116 non- SAC ruptured)	89	194	54	51	77	150	8.8	6	NR	NR	9
Piotin et al 2009	France	Retrospective cohort study	Neuroform and Enterprise	2002–2009	Simple and balloon	Combine (35 SAC, 549 non- SAC ruptured)	216	1109	51	50	163	746	9.3	7.1	NR	NR	9
Roh et al 2019	Korea	Retrospective cohort study	Enterprise and Cordis	2011-2017	Simple	Ruptured	38	64	57	57	29	43	NR	NR	NR	NR	8

(continued on next page)

Author Country Type of study															
	Stent brand	Study period	non-SAC group definition	Ruptured or unruptured	SAC number	Non-SAC number	Age A SAC n S	.ge W on- Sz AC	omen V AC n	Vomen on-SAC	Size of aneurysms SAC (mm)	Size of aneurysms non-SAC (mm)	Hunt-Hess grade SAC	Hunt-Hess grade non- SAC	SON
Satow et al Japan Retrospective 2020 cohort study	NR	2010-2014	Simple	Unruptured	1462	4942	61 6	1 N	R	R	NR	NR	NR	NR	8
Starke et al USA Retrospective 2014 cohort study	Neuroform and Enterprise	2006-2012	Dual microcatheter	Unruptured	120	60	57 5	8	4	0	NR	NR	NR	NR	6
Xue et al China Retrospective 2020 cohort study	NR	2013-2017	Simple	Ruptured	207	207	57 5	7 1	43 1	42	4.7	4.7	Grade 1–2:166	Grade 1–2:174	6
Yang et al China Retrospective 2015 cohort study	Enterprise and Solitaire	2013-2014	Simple	Ruptured	58	115	56.4 5	5.7 3.	9	4	8.4	5.5	Grade 1–2:33	Grade 1–2:35	6
Yao et al China Retrospective 2013 cohort study	Neuroform and Enterprise	2008-2011	Simple	Combine (35 SAC, 38 non- SAC ruptured)	58	56	60 5	8	4	4	5.4	5.6	NR	NR	6
Zhao et al China Retrospective 2016 cohort study	NR	2010-2012	Simple	Ruptured	23	108	56.7 5	4.2 9	Ω	2	6.3	5.7	NR	NR	80
Zuo et al China Retrospective 2018 cohort study NR: Not Reported, SAC: stent assistant coil	NR oiling, NOS: Newcas	2012–2014 stle-Ottawa Sco	Simple ale	Ruptured	133	289	58.1 5	6.2 9;	3 1	82	5.5	2	Grade 1–3: 120	Grade 1–3: 260	6

brand of the stent, number of aneurysms in each group, number of females, age, aneurysms size, Hunt–Hess grade, immediate occlusion rate, complete occlusion rate, recurrence rate, intraprocedural rupture, hemorrhagic events, and ischemic events.

2.4. Quality assessments

We used the Newcastle–Ottawa scale (NOS) to assess the quality of cohort studies which ranged between 0 to 9.1^{7}

2.5. Statistical analysis

The Stata 15.0 (College Station, TX) was used for statistical analysis. We calculated the risk ratio (RR) with a 95 % confidence interval (CI) and a random-effects model for comparisons between SAC and non-SAC. The publication bias was assessed using the Cochrane's Q test and I-squared (I²). The I² value > 75 % is an indicator of high heterogeneity among studies. All analyses were performed stratified based on the type of aneurysms (ruptured, unruptured, or combination) in entered studies.

3. Results

3.1. Search results

Our initial search and manual addition yielded 3464 studies after duplicate removal (Fig. 1). After title and abstract review, 3327 papers were excluded. In the end, after careful full-text evaluation, 26 studies entered into our qualitative and quantitative synthesis.^{18–42}

3.2. Characteristics and quality of included studies

A total of 12420 (SAC = 3642, non-SAC = 8778) with a mean age of 56.3 years were enrolled in our studies (Table 1). Overall, there were 3038 ruptured and 9382 unruptured aneurysms. Included studies mostly used Neuroform and Enterprise stents for SAC procedure. The aneurysms size ranged from 4.7 to 11.5 mm. Eight studies investigated only ruptured aneurysms, six studies only unruptured aneurysms, and twelve examined both unruptured and ruptured aneurysms. The detailed features of included studies are represented in Table 1.

All included studies were determined to be high quality with a mean NOS score of 8.76 (Table 1).

3.3. Efficacy analysis

To compare the efficacy of SAC versus non-SAC, immediate occlusion rate, complete occlusion rate, and recurrence rate were used. Our analysis showed that there was no significant difference in immediate occlusion rate between SAC and non-SAC (RR: 0.93, 95%CI: 0.85, 1.02; Q = 24.65, P = 0.22, I2 = 30.70 %) (Figs. 2 and 3). Furthermore, our sub-group analysis did not show significant difference in immediate occlusion rate for unruptured (RR: 0.96, 95%CI: 0.75, 1.17; Q = 5.67, P = 0.22, I2 = 38.71 %), ruptured (RR: 0.94, 95%CI: 0.81, 1.06; Q = 1.45, P = 0.84, I2 = 0.00 %), and combination aneurysms (RR: 0.94, 95%CI: 0.80, 1.07; Q = 17.18, P = 0.07, I2 = 47.43 %).

The difference in complete occlusion rate between two groups was not statistically significant (RR: 1.02, 95%CI: 0.91, 1.13; Q = 32.67, P = 0.40, I2 = 52.74 %) (Fig. 4). Moreover, there was no significant difference either in ruptured (RR: 0.97, 95%CI: 0.84, 1.11; Q = 5.64, P = 0.23, I2 = 37.74 %), unruptured (RR: 1.13, 95%CI: 0.87, 1.39; Q = 8.35, P = 0.08, I2 = 55.65 %), and combination aneurysms (RR: 0.93, 95%CI: 0.87, 1.07; Q = 9.98, P = 0.08, I2 = 10.94 %) between SAC and non-SAC.

We found that there was overall lower recurrence rate in SAC versus non-SAC significant (RR: 0.43, 95%CI: 0.33, 0.53; Q = 18.94, P = 0.06, I2 = 12.19 %) (Fig. 5). Furthermore, the comparisons were significant in unruptured (RR: 0.63, 95%CI: 0.40, 0.86; Q = 1.93, P = 0.75, I2 = 00.00

Study				RR W with 95% Cl	/eight (%)
Unruptured					
Consoli et al. 2014		-		1.06 [0.86, 1.26]	8.31
Gordhan et al. 2011		•		- 1.26 [0.16, 2.69]	0.32
Hetts et al. 2013		-		0.69 [0.42, 0.96]	5.90
Hwang et al. 2011				1.20 [0.63, 1.78]	1.79
Starke et al. 2014		_		1.00 [0.65, 1.35]	4.10
Heterogeneity: τ ² = 0.02, I ² = 38.71%, H ² = 1.63		•		0.96 [0.75, 1.17]	
Test of $\theta_i = \theta_j$: Q(4) = 5.67, p = 0.22					
Ruptured					
Cai et al. 2016				0.80 [0.38, 1.23]	3.00
Fan et al. 2016				0.89 [0.64, 1.15]	6.53
Yang et al. 2015				0.87 [0.57, 1.17]	5.08
Zhao et al. 2016		_		0.93 [0.57, 1.29]	3.94
Zuo et al. 2018				1.03 [0.82, 1.23]	8.32
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00		•		0.94 [0.81, 1.06]	
Test of $\theta_i = \theta_j$: Q(4) = 1.45, p = 0.84					
Combination					
Chalouhi et al. 2012		-		0.99 [0.78, 1.19]	8.20
Chalouhi et al. 2013	-	•	-	0.95 [0.31, 1.58]	1.50
Chung et al. 2014				1.08 [0.76, 1.40]	4.74
Colby et al. 2011				1.26 [0.46, 2.06]	0.97
Jahshan et al. 2013				1.18 [0.95, 1.41]	7.31
Kim et al. 2010				1.00 [0.64, 1.36]	3.95
Liu et al. 2014				0.86 [0.50, 1.21]	4.03
Ogilvy et al. 2010			_	1.07 [0.51, 1.62]	1.90
Ozretić et al. 2015	-	—		0.56 [0.29, 0.82]	6.11
Piotin et al. 2009		+		0.81 [0.67, 0.96] 1	1.42
Yao et al. 2013				0.92 [0.45, 1.38]	2.57
Heterogeneity: τ^2 = 0.02, I ² = 47.43%, H ² = 1.90		•		0.94 [0.80, 1.07]	
Test of $\theta_i = \theta_j$: Q(10) = 17.18, p = 0.07					
Overall		۲		0.93 [0.85, 1.02]	
Heterogeneity: τ^2 = 0.01, I ² = 30.70%, H ² = 1.44					
Test of $\theta_i = \theta_j$: Q(20) = 24.65, p = 0.22					
Test of group differences: $Q_b(2) = 0.04$, p = 0.98					
	0	1	2	3	

Fig. 2. Forest plot of immediate occlusion rate in SAC versus non-SAC.

%), ruptured (RR: 0.29, 95%CI: 0.13, 0.45; Q = 3.42, P = 0.49, I2 = 00.00 %), and combination aneurysms (RR: 0.42, 95%CI: 0.30, 0.54; Q = 7.81, P = 0.55, I2 = 00.00 %).

3.4. Safety analysis

We compared the safety of Sac and non-SAC in treatment of aneurysms using intraprocedural rupture, hemorrhagic events, and ischemic events. Our pooled analysis demonstrated that there was overall no

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Fig. 3. Visualization of Efficacy (A) and Safety (B) in SAC and non-SAC.

significant difference in intraprocedural rupture risk between SAC and non-SAC (RR: 0.95, 95%CI: 0.70, 1.19; Q = 52.82, P < 0.00, I2 = 66.73 %) (Fig. 6). However, we found higher risk of intraprocedural rupture for SAC versus non-SAC in unruptured aneurysms by pooling two studies (RR: 1.40, 95%CI: 1.31, 1.50; Q = 0.04, P = 0.85, I2 = 0.00 %). There was no difference in ruptured (RR: 1.02, 95%CI: 0.38, 1.66; Q = 11.08, P = 0.05, I2 = 63.50 %) and combination aneurysms (RR: 0.84, 95%CI: 0.65, 1.02; Q = 1.48, P = 0.83, I2 = 0.00 %).

Investigating hemorrhagic events risk showed that there was no significant difference among all included studies (RR: 1.11, 95%CI: 0.81, 1.40; Q = 38.78, P < 0.00, I2 = 68.03 %), but sub-group analysis for ruptured (RR: 1.73, 95%CI: 1.12, 2.34; Q = 18.65, P < 0.00, I2 = 64.21 %) and combination aneurysms (RR: 0.60, 95%CI: 0.37, 0.82; Q = 3.53, P = 0.62, I2 = 0.74 %) indicates statistically significant difference (Fig. 7). In addition, the risk of hemorrhagic events in SAC versus non-SAC did not differ for unruptured aneurysms (RR: 1.00, 95%CI: 0.82, 1.19; Q = 2.39, P = 0.30, I2 = 0.00 %).

The overall risk of ischemic events in SAC versus non-SAC was no significant (RR: 1.19, 95%CI: 0.94, 1.44; Q = 48.07, P < 0.00, I2 = 63.62 %) (Fig. 8). Moreover, we could not find higher or lower risk of ischemic events in unruptured (RR: 1.39, 95%CI: 0.81, 1.97; Q = 7.98, P = 0.05, I2 = 63.33 %), ruptured (RR: 1.18, 95%CI: 0.75, 1.61; Q = 19.40, P < 0.00, I2 = 70.49 %), and combination aneurysms (RR: 1.02, 95%CI: 0.74, 1.30; Q = 4.17, P = 0.53, I2 = 0.00 %).

4. Discussion

The present study is the first meta-analysis to comparatively assess the efficacy and safety of SAC vs. non-SAC for intracranial aneurysms in the ruptured and unruptured aneurysms. Since the ruptured or unruptured nature of the aneurysm and other morphological features affect the prognosis of the patient, a thorough understanding of the efficacy and safety of each of these interventions would help determine the best treatment plan. The results of our meta-analysis demonstrate that using stents is not associated with better immediate or complete occlusion rates in any of the sub-groups. However, our investigations demonstrate that using stents significantly reduces the recurrence rates of both ruptured and unruptured aneurysms. Interestingly, SAC is even more beneficial for those with ruptured aneurysms than those with unruptured ones. This finding is of great importance as ruptured aneurysms are reported to be associated with higher recurrence rates.⁴³ Furthermore, our safety analysis revealed no significant differences in risk for the three categories of complications studied (intraprocedural rupture, ischemic and hemorrhagic events) between the SAC and non-SAC groups. However, in the subgroup analysis, we observed a higher risk for intraprocedural ruptures in unruptured aneurysms and a higher risk for hemorrhagic events in ruptured and combined cases.

In comparisons between SAC and non-SAC, our findings regarding the immediate occlusion rates between the two techniques were in line with three previous meta-analyses.^{15,44,45} All previous meta-analysis studies have reported lower recurrence rates in SAC.^{15,44,45} Our study confirms their findings, adding that this effect is more pronounced in ruptured aneurysms. Findings of unchanged complication rates between the two groups have also been demonstrated in the previous studies.^{15,44}

As recurrence is frequent in endovascular treatments for intracranial aneurysms, with an incidence of almost 33 % percent in the first year,^{6,43} minimizing this probability is a crucial issue in the treatment of intracranial aneurysms. In fact, higher recurrence rates are one of the main disadvantages of coiling procedures, as recurrence is much less frequent in the other treatment method, surgical clipping.⁴⁶ The majority of studies on endovascular coiling determine recurrence rates based on angiographic recurrences, which are usually non-symptomatic and do not present with morbid conditions and, if indicated, can safely be retreated.⁴⁷ However, we should strive to reduce the chances of recurrence since it can cause both financial and psychological stress for patients.^{48,49}

Several risk factors have been introduced for higher recurrence rates, including larger aneurysm size and ruptured status with high odds ratios.^{43,50} Thus, reducing the probability of recurrence is even more critical in ruptured aneurysms. Several potential explanations have been suggested for the protective effect of stents. For instance, it has been proposed that stents can form a scaffold that promotes endothelization and supports fibroelastic tissue growth.^{44,51} Furthermore, using stents divert the blood flow away from the aneurysm, forming stasis in the

Churche		RR	Weight
		WITH 95% CI	(%)
Unruptured	•		0.00
	-	1.08 [0.85, 1.31]	9.66
Gordhan et al. 2011	.	0.72[0.11, 1.55]	1.58
Hetts et al. 2013	_ _	1.14 [0.81, 1.47]	6.64
Starke et al. 2014	_ _	1.04 [0.69, 1.38]	6.34
Satow et al. 2020	•	0.88 [0.81, 0.94]	15.44
Heterogeneity: τ ² = 0.01, I ² = 37.74%, H ² = 1.61	•	0.97 [0.84, 1.11]	
Test of $\theta_i = \theta_j$: Q(4) = 5.64, p = 0.23			
Ruptured			
Cai et al. 2016	-	1.10 [0.34, 1.86]	1.87
Fan et al. 2016	_	1.04 [0.49, 1.58]	3.29
Zuo et al. 2018	-	1.18 [0.94, 1.42]	9.30
Gao et al. 2018		0.78 [0.42, 1.13]	6.03
Xue et al. 2020	-\-	1.47 [1.15, 1.79]	6.92
Heterogeneity: τ ² = 0.05, I ² = 55.65%, H ² = 2.25	•	1.13 [0.87, 1.39]	
Test of $\theta_i = \theta_j$: Q(4) = 8.35, p = 0.08			
Combination			
Chalouhi et al. 2013	-	0.86 [0.58, 1.14]	7.98
Liu et al. 2014	·	2.33 [1.16, 3.50]	0.84
Ogilvy et al. 2010	_ -	0.95 [0.49, 1.40]	4.27
Ozretić et al. 2015		1.07 [0.77, 1.37]	7.47
Piotin et al. 2009		0.83 [0.66, 1.00]	11.91
Kim et al. 2017		- 2.14 [0.50, 3.78]	0.44
Heterogeneity: τ ² = 0.00, I ² = 10.97%, H ² = 1.12	•	0.93 [0.78, 1.07]	
Test of $\theta_i = \theta_j$: Q(5) = 9.98, p = 0.08			
Overall	•	1.02 [0.91, 1.13]	
Heterogeneity: τ ² = 0.02, I ² = 52.74%, H ² = 2.12			
Test of $\theta_i = \theta_j$: Q(15) = 32.67, p = 0.01			
Test of group differences: $Q_b(2)$ = 1.86, p = 0.40			
	0 1 2 3	4	
Random-effects			

Fig. 4. Forest plot of complete occlusion rate in SAC versus non-SAC.

sac.⁵² Along with the scaffold effect, the stasis facilitates thrombosis formation in the sac and obliteration of the aneurysm.^{44,53,54} A weaker scaffold effect is also observed in balloon-assisted aneurysm coiling procedures.⁵⁵

In the previous studies, SAC was generally associated with higher complications,^{15,44} especially ischemic events.⁴⁴ Furthermore, a higher ischemic complication rate was attributed to platelet aggregation on the stent and usage of double catheters.⁴⁵ In contrast, our study did not demonstrate any significant differences in complications except for the higher rupture rates in the unruptured subgroup and higher hemorrhagic event rates in the ruptured and combined subgroups. These observations can be justified by lower catheter flexibility and higher injury

to vessel walls.⁴⁵ However, some of these factors can be resolved by future technical improvements. For instance, formerly used balloon-expanding stents may have harmed vessel walls more than newer self-expanding stents, and self-expanding stents may have resulted in more positive safety records.⁵⁶

It is noteworthy that several factors other than the aneurysm rupture status affect the outcomes and complications, including aneurysm size, shape, location, and the dome-to-neck ratio.^{45,57,58} Stent-assisted methods are more frequently used in complicated aneurysms. This is a source of bias and can result in underestimation of the efficacy and safety of the stent-assisted interventions.^{45,59}

Study					with	RR 1 95%	CI	Weight (%)
Unruptured								
Consoli et al. 2014			•		0.53 [0.02,	1.08]	3.19
Gordhan et al. 2011	-		•		0.81 [0.00,	2.16]	0.56
Hetts et al. 2013		_	◆		0.58 [0.29,	0.86]	9.86
Hwang et al. 2011			•	_	0.86 [0.09,	1.63]	1.70
Starke et al. 2014		_	•		- 1.21 [0.19,	2.24]	0.97
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00			•		0.63 [0.40,	0.86]	
Test of $\theta_i = \theta_j$: Q(4) = 1.93, p = 0.75								
Ruptured								
Fan et al. 2016		•			0.26 [0.00,	1.26]	1.03
Roh et al. 2019			•		- 1.21 [0.16,	2.26]	0.92
Xue et al. 2020		-			0.25 [0.05,	0.44]	16.41
Yang et al. 2015			•		0.48 [0.01,	1.23]	1.79
Zuo et al. 2018		-	_		0.28 [0.06,	0.61]	7.72
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00		•	•		0.29 [0.13,	0.45]	
Test of $\theta_i = \theta_j$: Q(4) = 3.42, p = 0.49								
Combination								
Chalouhi et al. 2012		_	♦—		0.50 [0.17,	0.83]	7.88
Chalouhi et al. 2013		+			0.31 [0.01,	0.88]	2.97
Chung et al. 2014			•		0.73 [0.03,	1.49]	1.72
Colby et al. 2011			•		0.53 [0.02,	1.17]	2.43
Kim et al. 2010			•	_	0.81 [0.02,	1.64]	1.45
Kim et al. 2017					0.15 [0.00,	0.69]	3.28
Liu et al. 2014		•			0.37 [0.02,	0.84]	4.25
Ozretić et al. 2015		-	—		0.72 [0.37,	1.06]	7.36
Piotin et al. 2009		-4	-		0.39 [0.20,	0.57]	17.60
Yao et al. 2013			_		0.18 [0.01,	0.53]	6.92
Heterogeneity: τ^2 = 0.00, I ² = 0.00%, H ² = 1.00		•			0.42 [0.30,	0.54]	
Test of $\theta_i = \theta_j$: Q(9) = 7.81, p = 0.55								
Overall					0.43 [0.33,	0.53]	
Heterogeneity: τ^2 = 0.01, I ² = 12.19%, H ² = 1.14								
Test of $\theta_i = \theta_j$: Q(19) = 18.94, p = 0.46								
Test of group differences: $Q_b(2) = 5.78$, p = 0.06	ſ <u></u>				-			
	-1	0	1	2				

Fig. 5. Forest plot of recurrence rate in SAC versus non-SAC.

4.1. Limitations

There are certain limitations to the present study. First, most of the studies included in the meta-analysis were retrospective studies, and usually, more complicated cases were chosen for stent application. Thus, a patient selection bias might affect the findings. Second, as discussed earlier, there are several factors other than rupture status that can affect

success rates, but only a few studies have studied the effects of mentioned factors. Thus, they could not be included in the subgroup analysis of our meta-analysis. Third, some of the findings of our metaanalysis, especially findings of higher intraprocedural rupture complications in unruptured cases, are pooled from a minimal number of studies in the subgroup analysis, and more investigations are required to confirm these findings.

Study				RR with 95% CI	Weight (%)
Unruptured					()
Satow et al. 2020			•	1.40 [1.31, 1.50] 16.66
Gordhan et al. 2011			•	1.26 [0.16, 2.69] 2.45
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00			•	1.40 [1.31, 1.50]
Test of $\theta_i = \theta_j$: Q(1) = 0.04, p = 0.85					
Ruptured					
Cai et al. 2016		-	-	0.70 [0.35, 1.05] 12.50
Fan et al. 2016				— 2.47 [1.08, 3.85] 2.57
Xue et al. 2020			•	1.47 [0.01, 2.93] 2.35
Zhao et al. 2016			•	1.48 [0.00, 3.34] 1.52
Gao et al. 2018				0.09 [0.00, 0.82] 6.58
Roh et al. 2019			♦	1.10 [0.10, 2.10] 4.32
Heterogeneity: τ^2 = 0.35, I ² = 63.50%, H ² = 2.74				1.02 [0.38, 1.66]
Test of $\theta_i = \theta_j$: Q(5) = 11.08, p = 0.05					
Combination					
Chalouhi et al. 2012		-	-	0.97 [0.60, 1.33] 12.25
Chung et al. 2014		-4	-	0.86 [0.58, 1.15] 13.84
Liu et al. 2014			-	0.67 [0.21, 1.12] 10.65
Yao et al. 2013				0.97 [0.05, 1.99] 4.20
Chalouhi et al. 2013		-	_	0.69 [0.21, 1.17] 10.11
Heterogeneity: τ ² = 0.00, I ² = 0.00%, H ² = 1.00		•	•	0.84 [0.65, 1.02]
Test of $\theta_i = \theta_j$: Q(4) = 1.48, p = 0.83					
Overall				0.95 [0.70, 1.19]
Heterogeneity: τ ² = 0.09, I ² = 66.73%, H ² = 3.01					
Test of $\theta_i = \theta_j$: Q(12) = 52.82, p = 0.00					
Test of group differences: $Q_b(2) = 29.56$, p = 0.00					
	-2	Ó	2	4	

Fig. 6. Forest plot of intraprocedural rupture risk in SAC versus non-SAC.

5. Conclusion

This study investigated the efficacy and safety of SAC vs. non-SAC procedures in ruptured and unruptured intracranial aneurysms. In both subgroups, we observed no difference in occlusion rates between SAC and non-SAC. Stents were associated with lower recurrence rates in both subgroups. The protective effects of stents on the recurrence rates were more pronounced in ruptured aneurysms than in unruptured ones. As ruptured aneurysms are associated with higher mortality rates and complications, it is valuable to know that stent-assisted coiling is more beneficial in such cases. Furthermore, we observed higher rates of certain categories of complications in the stent-assisted group in subgroup analysis. Hemorrhagic events were more prevalent in SAC in the ruptured and combined aneurysms subgroups, and the risk of intraprocedural rupture was significantly higher when using stents in the unruptured subgroup. Thus, with a lower risk ratio for the protective effect of stents in ruptured aneurysms, patients with such aneurysms

benefit the most from stent-assisted procedures. However, with lower protective effects and chances of rupturing in unruptured aneurysms, these patients should undergo a more careful benefit-risk assessment to decide whether or not stents are indicated for them. Overall, our findings demonstrated that SAC may have higher efficacy in term of recurrence rate, but also may have a higher risk of complications in the treatment of intracranial aneurysms. As there are several factors affecting the outcomes and safety of these interventions, further RCTs controlled for multiple factors are required better guide the neurointerventionists choose the best strategy.

Declaration

Human and animal ethics

Not applicable.

Study			RR with 95%	CI	Weight (%)
Unruptured					
Consoli et al. 2014	♦		0.80[0.31,	1.28]	9.82
Hetts et al. 2013			- 5.96 [0.00,	13.69]	0.15
Satow et al. 2020	•		1.03 [0.83,	1.24]	12.48
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00	•		1.00 [0.82,	1.19]	
Test of $\theta_i = \theta_j$: Q(2) = 2.39, p = 0.30					
Ruptured					
Cai et al. 2016	•		0.78[0.41,	1.16]	10.93
Fan et al. 2016			1.53 [0.88,	2.18]	8.07
Roh et al. 2019	•		3.82 [0.87,	6.77]	0.94
Xue et al. 2020			2.70 [0.89,	4.51]	2.24
Yang et al. 2015	_		1.81 [0.33,	3.29]	3.08
Zhao et al. 2016			2.48 [1.37,	3.59]	4.66
Zuo et al. 2018	-		1.74 [0.89,	2.60]	6.34
Heterogeneity: τ^2 = 0.36, I ² = 64.21%, H ² = 2.79	•		1.73 [1.12,	2.34]	
Test of $\theta_i = \theta_j$: Q(6) = 18.65, p = 0.00					
Combination					
Chalouhi et al. 2012	+		1.61 [0.15,	3.38]	2.33
Chung et al. 2014	♦		0.43 [0.12,	0.74]	11.57
Colby et al. 2011	_		1.00 [0.10,	2.38]	3.42
Liu et al. 2014	♦		0.67 [0.21,	1.12]	10.11
Piotin et al. 2009	♦		0.74 [0.15,	1.33]	8.70
Yao et al. 2013	-		0.97 [0.05,	1.99]	5.16
Heterogeneity: τ ² = 0.00, I ² = 0.74%, H ² = 1.01	•		0.60 [0.37,	0.82]	
Test of $\theta_i = \theta_j$: Q(5) = 3.53, p = 0.62					
Overall	•		1.11 [0.81,	1.40]	
Heterogeneity: τ ² = 0.17, I ² = 68.03%, H ² = 3.13					
Test of $\theta_i = \theta_j$: Q(15) = 38.78, p = 0.00					
Test of group differences: $Q_b(2) = 15.14$, p = 0.00					
	ό Ś	10	15		

Fig. 7. Forest plot of hemorrhagic events risk in SAC versus non-SAC.

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Ethical approval

It does not include any research involving human or animal subjects.

Availability of supporting data and material

The datasets analyzed during the current study are available upon request with no restriction.

Consent for publication

This manuscript has been approved for publication by all authors.

Authors contribution

FN & PV: Designed the study, analyzed the data, and wrote the paper; FN & MB: collected data, analyzed and interpreted the data, and wrote the draft version of the manuscript. The manuscript was revised and approved by all authors.

Declaration of competing interest

The authors declare no conflict of interest regarding the publication

Study					RR with 95% CI		Weight (%)
Unruptured							()
Consoli et al. 2014	_		•	_	1.33 [0.00, 3.	78]	0.95
Hetts et al. 2013		-	-		0.92 [0.43, 1.	41]	8.76
Hwang et al. 2011			•		2.71 [0.20, 5.	22]	0.91
Satow et al. 2020			•		1.62 [1.47, 1.	77]	12.67
Heterogeneity: τ^2 = 0.16, I^2 = 63.33%, H^2 = 2.73					1.39 [0.81, 1.	97]	
Test of $\theta_i = \theta_j$: Q(3) = 7.98, p = 0.05							
Ruptured							
Cai et al. 2016		-	-		1.05 [0.60, 1.	50]	9.31
Fan et al. 2016			◆		1.67 [1.28, 2.	06]	10.03
Xue et al. 2020		-	-		1.18 [0.48, 1.	88]	6.44
Yang et al. 2015		-	▶—		1.31 [0.62, 2.	00]	6.58
Zhao et al. 2016		-			0.41 [0.03, 0.	86]	9.35
Zuo et al. 2018		-	•	_	2.05 [0.58, 3.	51]	2.36
Heterogeneity: τ^2 = 0.19, I^2 = 70.49%, H^2 = 3.39					1.18 [0.75, 1.	61]	
Test of $\theta_i = \theta_j$: Q(5) = 19.40, p = 0.00							
Combination							
Chalouhi et al. 2012		-	-		1.00 [0.54, 1.	47]	9.07
Chung et al. 2014		-	_		0.95 [0.37, 1.	54]	7.66
Colby et al. 2011		-			0.74 [0.18, 1.	30]	7.91
Liu et al. 2014		_	—		1.75 [0.87, 2.	62]	4.99
Ogilvy et al. 2010			•		1.30 [0.15, 2.	85]	2.15
Yao et al. 2013	-		•		1.82 [0.00, 4.	40]	0.86
Heterogeneity: τ^2 = 0.00, I^2 = 0.00%, H^2 = 1.00		•			1.02 [0.74, 1.	30]	
Test of $\theta_i = \theta_j$: Q(5) = 4.17, p = 0.53							
Overall					1.19 [0.94, 1.	44]	
Heterogeneity: τ^2 = 0.12, I ² = 63.62%, H ² = 2.75							
Test of $\theta_i = \theta_j$: Q(15) = 48.07, p = 0.00							
Test of group differences: $Q_b(2) = 1.37$, p = 0.51	-2	0	2	4	6		

Fig. 8. Forest plot of ischemic events risk in SAC versus non-SAC.

of this paper.

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