

Providing Choice & Value

FRESENIUS KABI

Generic CT and MRI Contrast Agents



This information is current as of July 29, 2025.

Impact of Smoking on Recurrence and Angiographic Outcomes After Endovascular Treatment of Intracranial Aneurysms: A Systematic Review and Meta-Analysis

Sherief Ghozy, Seyed Behnam Jazayeri, Alireza Hasanzadeh, Julien Ognard, Hassan Kobeissi, Ali Ahmadzade, Ehsan Naseh, Mobina Motaghian Fard, Alzhraa S. Abbas, Rachana R Borkar, David F. Kallmes and Ramanathan Kadirvel

AJNR Am J Neuroradiol published online 21 February 2025 http://www.ajnr.org/content/early/2025/02/21/ajnr.A8712

SYSTEMATIC REVIEW/META-ANALYSIS

Impact of Smoking on Recurrence and Angiographic Outcomes After Endovascular Treatment of Intracranial Aneurysms: A Systematic Review and Meta-Analysis

Sherief Ghozy, ^{1,2, #,*}; Seyed Behnam Jazayeri, ^{3,#}; Alireza Hasanzadeh, ^{3, #}; Julien Ognard, ^{1, 4}; Hassan Kobeissi, ^{1,5}; Ali Ahmadzade, ³; Ehsan Naseh, ⁶; Mobina Motaghian Fard, ⁶; Alzhraa S. Abbas, ⁷; Rachana R Borkar, ⁸; David F. Kallmes, ¹; <u>Ra</u>manathan Kadirvel, ^{1,2}

ABSTRACT

BACKGROUND: Cerebral aneurysm recurrence serves as a significant endpoint for assessing the efficacy of various endovascular treatment strategies. The impact of smoking on outcomes such as aneurysm occlusion, recurrence, and recanalization remains unclear due to conflicting evidence.

PURPOSE: To systematically evaluate the role of smoking in influencing angiographic outcomes following endovascular treatment of intracranial aneurysms.

DATA SOURCES: Comprehensive searches were conducted in PubMed, Embase, Scopus, and Web of Science

STUDY SELECTION: This systematic review and meta-analysis followed PRISMA guidelines to identify relevant studies assessing smoking's impact on intracranial aneurysms following endovascular treatment.

DATA ANALYSIS: Studies were screened, selected, and assessed for risk of bias using appropriate checklists. Data on complete and adequate aneurysm occlusion, and recurrence/ recanalization rates were extracted. Random-effects meta-analyses calculated risk ratios (ORs) with 95% confidence intervals (CIs). Heterogeneity was measured using the I² statistic.

DATA SYNTHESIS: A total of 26 studies, encompassing 6,031 patients, met the inclusion criteria. Smokers had higher rates of complete aneurysm occlusion (RR 1.12, 95% CI 1.06-1.19; p < 0.01). Subgroup analysis revealed that smokers undergoing flow diversion exhibited a higher rate of complete occlusion (RR 1.14, 95% CI 1.07-1.21; p < 0.01). However, for patients undergoing coiling, there was no significant difference in complete occlusion rates between smokers and non-smokers (RR 1.00, 95% CI 0.83-1.20; p = 0.46). Recurrence/recanalization rates were similar between smokers and non-smokers: RR 1.17, 95% CI 0.93-1.47; p = 0.20, and the rate of aneurysm retreatment did not differ between the smokers and non-smokers: RR 0.82, 95% CI 0.59-1.13; p = 0.23.

LIMITATIONS: Heterogeneity in definitions of smoking status, variations in follow-up durations, short follow up, retrospective nature of studies.

CONCLUSIONS: Smoking status does not significantly impact aneurysm recanalization or retreatment after endovascular repair. However, the impact of smoking on complete occlusion rate might differ based on the type of device used for treatment. Histological and molecular factors may contribute to varied outcomes, highlighting the necessity for further research to understand smoking's role in aneurysm healing. Clinically, patients should be advised about the risks of smoking, though current evidence suggests that smoking cessation may not consistently affect treatment efficacy.

ABBREVIATIONS: sAH = subarachnoid hemorrhage; RROC = Raymond-Roy occlusion classification.

Received Nov 26, 2024; accepted after revision Feb 8, 2025.

From the Department of Radiology (S.G., J.O., H.K., D.F.K., R.K.) Mayo Clinic, Rochester, Minnesota, Department of *Neurologic Surgery* (S.G., R.K.), Mayo Clinic, Rochester, Minnesota, Tehran University of Medical Sciences, Tehran, Iran (S.B.J., A.H., A.A.), Department of Neuroradiology, Brest University Hospital, Brest, France (J.O.), Department of Neurosurgery (H.K.), Corewell Health William Beaumont University Hospital, Royal Oak, MI, Iran University of Medical Sciences, Tehran, Iran (E.N., M.M.F.), Evidence-based Practice Center, Kern Center for the Science of Healthcare Delivery (A.S.A.), Mayo Clinic, Rochester, MN, USA, and Department of Diagnostic Radiology (R.R.B.), Yale New Haven Health Bridgeport Hospital, Bridgeport, Connecticut

#Equal contribution

Disclosure of potential conflicts of interest: D.F.K. holds equity in Nested Knowledge, Superior Medical Editors, and Conway Medical, Marblehead Medical and Piraeus Medical. He receives grant support from MicroVention, Medtronic, Balt, and Insera Therapeutics; has served on the Data Safety Monitoring Board for Vesalio; and received royalties from Medtronic. R.K. has the following conflicts: Research support from: Cerenovus Inc, Medtronic, Endovascular Engineering, Frontior Bio, Sensome Inc, Endomimetics, Ancure LLC, Neurogami Medical, MIVI Biosciences, Monarch Biosciences, Stryker Inc, Conway Medical, Pireus Medical, and Bionaut Labs. He holds the following

research grants Research Grants: NIH (R01NS076491, R44NS107111, R43NS110114 and R21NS128199) and NSF (081215707).

Please address correspondence to Sherief Ghozy, MD. Mayo Clinic, Stabile Building 11-79, 150 3rd St SW, Rochester, MN 55902

Email:ghozy.sherief@mayo.edu Twitter (X) handle: @SheriefGhozy

Copyright 2025 by American Society of Neuroradiology.

INTRODUCTION

Cerebral aneurysm recurrence is the main endpoint when comparing the efficacy of different aneurysm treatment modalities¹. Regarding unruptured aneurysms, previous meta-analyses reported an annual bleeding risk of 0.2% after endovascular therapy and recurrences occurred in up to ~24 % of aneurysms, leading to retreatment in about 10% of cases² ³. The significantly described rates of recurrence of intracranial aneurysms introduce complex decision-making challenges in clinical practice. This is further amplified in the less-explored scenario of unruptured intracranial aneurysms, and underscores the need for innovative and effective treatment approaches⁴, as the decision to retreat recurrent aneurysms must balance procedural risks against the uncertain impact of retreatment on patient outcomes.

Several factors influence recurrence rates following endovascular aneurysm treatment, with smoking being a wellestablished risk factor for both aneurysm formation and rupture ⁵⁶. A large meta-analysis has demonstrated a 2.4% decrease in the global incidence of subarachnoid hemorrhage (sAH) for every percentage decrease in smoking prevalence⁷. However, the influence of smoking on the outcomes of endovascularly treated aneurysms remains ambiguous and has yielded contradictory results in the literature, possibly due to heterogeneity or lack of reporting of the smoking status among previous studies or heterogeneity in definition and assessment of the endpoints. Jin et al. in a meta-analysis⁸ found no significant association between smoking and recurrence after coil embolization for intracranial aneurysms whereas in the same year, Pierot et al. described current smoking as a risk factor of recurrent aneurysm after repair following sAH, when both explored risk-factors of recurrence⁹. Given these inconsistencies, we conducted a dedicated systematic review and meta-analysis to elucidate the role of smoking on the recurrence and outcomes of endovascularly treated intracranial aneurysms.

MATERIALS AND METHODS

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The supplementary materials include PRISMA checklists for both the abstract and main document. The Shiny app was utilized to generate a PRISMA 2020-compliant flow diagram and checklists. No protocol was registered for this review.

Search Strategy

A thorough literature search was performed without limitations on language, location, or time frame. We searched PubMed, Embase, Scopus, and Web of Science, on 25 Jun 2024, searching their records from inception. For PubMed, we used various Medical Subject Headings (MeSH) terms along with relevant titles and text words. The search syntax was customized for each database to fit their specific requirements. The full search syntax for all databases is available in the supplementary materials (Supplementary Table 1). Additionally, we manually performed bibliomining of included studies.

Eligibility criteria and selection process

Studies were included if they met the following criteria: (1) Design: Retrospective or prospective cohort or case-control studies (2) Population: Adult patients (\geq 18 years) with intracranial aneurysm who were treated with coiling, flow diversion, or a mixture of these methods (3) Exposure: smoking (4) Comparison: Patients with a history of smoking or current smoker vs never smokers (5) Outcome: Rates of aneurysm occlusion, recanalization and recurrence. The following studies were excluded: (1) Studies that did not mention the smoking status of patients, (2) Case series, conference abstracts, letters, editorials, book chapters, non-human studies, and reviews. Two authors (AH and AA) independently reviewed the titles and abstracts using eligibility criteria. If there was any disagreement, a third author (SG) was brought in to reach a consensus. The same two authors independently evaluated the full texts of all abstracts that fulfilled the inclusion criteria and performed hand searching. The included studies were reviewed to ensure institutional review board approval was obtained.

Data extraction

A standardized data collection form was designed, including the first author's name and year of publication, country and period of observation, smoking status of patients (current smoker, former smoker, non-specified smoker, non-smoker), baseline patient characteristics (age, sex, comorbidities, aneurysm location, size, and morphology), and treatments (coiling, clipping, flow diversion, other or mixed). Afterward, two authors (EN and JO) independently conducted data extraction. Any discrepancies or differences in data extraction were resolved through discussion and consensus.

Risk of Bias Assessment

Based on study design, two independent reviewers (SBJ and ASA) assessed the quality of studies using the Newcastle Ottawa Scale (NOS) for case-control and cohort studies or the JBI critical appraisal tool for case series ^{9 10}. Eight criteria were considered, each receiving 1 or 2 stars if the criterion was met and otherwise receiving no stars for a maximum possible score of 9. Studies scoring 8-9 were considered low risk, 6-7 indicated some concern, and scores 5 and lower were deemed high risk of bias.

Outcomes

Four endpoints were compared between smokers and non-smokers: (1) Rate of complete aneurysm (2) Rate of adequate aneurysm occlusion (3) Rate of aneurysm recurrence/recanalization, and (4) Retreatment. Complete occlusion was defined as Raymond-Roy occlusion classification¹¹ (RROC) grade I or 100% aneurysm occlusion in the follow up imaging. Adequate aneurysm occlusion was defined as complete or near complete aneurysm occlusion (RROC grade I and grade II or >90% occlusion in follow up imaging). Recanalization/recurrence was defined as inflow into a previously completely occluded aneurysm or growth of an incompletely occluded aneurysm. These endpoints were compared between smokers (current or former or non-specified) vs non-smokers (never-smokers). In cases where no definition for endpoints was provided, we adopted the authors' definitions of what constitutes a complete occlusion and what qualifies as recanalization/recurrence, using their reported terms as they are. Detailed definitions of study-reported endpoints are provided in supplemental materials (Supplementary Table 7 and Supplementary Table 8). When multiple reports of endpoints were available from different follow-ups, we collected the results from the last follow-up.

Statistical analysis

Meta-analyses were conducted using R software version 4.3.3 (R Project for Statistical Computing) meta package version 6.5-0 and metafor package version 4.4-0. We calculated risk ratios (RRs) and their corresponding 95% confidence intervals (CI) using a random-effects model: Generalized Linear Mixed Model (GLMM). Heterogeneity was assessed using the Q statistic and l^2 test, with l2 greater than 50% or P < 0.05 considered significant. In the case of significant heterogeneity, a sensitivity analysis was performed with the removal of outlier studies to bring the heterogeneity to an insignificant level. Outliers were detected using "influence" and "dmetar" packages consistent with the method previously described in the literature¹². A subgroup analysis was performed to assess the effect of different treatment methods (coiling, flow diversion or a mixture of different methods) on the specified endpoints. We did not include studies that used surgical clipping in the analysis because of low number of studies with appropriate outcome data (n=1). Publication bias was assessed using visual inspection of funnel plots for asymmetry and Egger's test with a value <0.1 considered significant. A meta-regression was performed to assess demographics on rate of aneurysm recurrence/recanalization. In our meta-regression we assessed effect of female gender, age, hypertension, aneurysm size, aneurysm location, aneurysm rupture, duration of follow up and publication year on the rate of aneurysm recurrence/recanalization. Publication bias and meta-regression analysis were not performed for aneurysm occlusion rate because of low number of studies (<10)¹³.

RESULTS

Search and Screening Results

The initial search retrieved 1,171 records including 284 duplicates. After removing duplicates, the title and abstracts of 887 remaining records were screened, of which, 818 were excluded and 69 full texts underwent further checks. Finally, 26 studies met the eligibility criteria^{14-37,74,75}, with 6,031 included patients (Figure 1). One study 36 reported aneurysm recurrence rate in patients who use tobacco, therefore it is not included in meta-analysis but the results are mentioned qualitatively.



FIG 1. PRISMA checklist of study selection.

Baseline study characteristics

A summary of study characteristics is presented in Supplementary Table 2. Supplementary Table 3 and Supplementary Table 4 details the characteristics of the treated aneurysms and treatment details.

Risk of Bias

Selection criteria, encompassing representativeness of the exposed cohort and ascertainment of exposure, were welladdressed in most studies, with frequent assignment of maximum scores. However, a few studies demonstrated limitations, particularly in defining the comparison groups or failing to fully describe their selection methods, reflected in lower scores for Selection 2. In the Comparability domain, most studies appropriately adjusted for confounders, earning two stars, though some scored lower due to inadequate adjustments or a lack of explicit confounder control. Outcome assessment, including adequate follow-up length and appropriate statistical analysis, was consistently strong across studies, often achieving maximum scores. Overall, the studies ranged from moderate to high quality, with total NOS scores clustering between 6 and 9. Additionally, the single study 38 evaluated using the JBI checklist scored 8/10, suggesting it was generally well-conducted but had some areas of unclear reporting (Supplementary Table 5).

Complete aneurysm occlusion

Seven studies, with 1,402 patients, were included in meta-analysis of complete aneurysm occlusion rate between smokers and non-smokers with a median follow up of 405 days (IQR: 325-678 days). The rate of complete aneurysm occlusion was higher among smokers compared with non-smokers (RR 1.12, 95% CI 1.06–1.19; p < 0.01) with no heterogeneity among studies (I² = 0%, p = 0.59) (Figure 2). In the subgroup analysis, which considered a median follow-up duration of 535 days (IQR: 371–700 days) for coiling and 405 days (IQR: 365–492 days) for flow diversion, a significant difference in the rate of complete occlusion was observed.

The rate of complete occlusion was higher among smokers compared with non-smokers who received flow diversion, (RR 1.14, 95% CI 1.07-1.21; p < 0.01). However, there was no difference in complete aneurysm occlusion rate among smokers and non-smokers who underwent coiling (RR 1.00, 95% CI 0.83-1.20; p = 0.46) (Figure 3). In three studies the status of smokers was specified as current smoker vs former smoker. We evaluated the effect of current vs past history of smoking in a separate subgroup analysis. The rate of complete aneurysm occlusion was comparable between all subgroups (Supplementary Figure 1).



FIG 2. Forest plot of complete occlusion rate

	S	moker	Non-st	noker			
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI
'Tx method' = Coiling					1		
Brinjiki, 2015	130	292	56	119		0.95	[0.75; 1.19]
Dabus, 2016	21	26	17	23		1.09	[0.80; 1.49]
Random effects model	151	318	73	142		1.00	[0.83; 1.20]
Heterogeneity: $l^2 = 0\%$, $t^2 =$	0, p = 0.	46					0201000-00000000
Test for effect in subgroup:	z = -0.04	(p = 0.9	97)				
'Tx method' = Flow Div	ersion						
Rouchaud, 2016	35	36	24	26		1.05	[0.93; 1.19]
Hussein, 2020	6	9	13	22		- 1.13	[0.63; 2.01]
Salem, 2023	69	81	188	250		1.13	[1.01; 1.27]
Adeeb, 2017	97	111	200	269		1.18	[1.06; 1.30]
Hanel, 2021	36	39	77	99		1.19	[1.03; 1.36]
Random effects model	243	276	502	666	•	1.14	[1.07; 1.21]
Test for effect in suboroup:	z = 4 36 (0 < 0.0	1)				
Test for subgroup difference	$r_{1,00}^{2} = 1$	83. df =	1 (p = 0.	18)		_	
	- 14			0.5	1	2	

Adequate aneurysm occlusion

FIG

Five studies, with 1,672 patients, compared adequate aneurysm occlusion rate between smokers and non- smokers with a median follow up of 193 days (IQR: 135-371 days). The rate of adequate occlusion was not different between the smokers and non-smokers (RR 0.97, 95% CI 0.93–1.01; p = 0.17), with no heterogeneity noted among studies (I² = 0%, p = 0.93) (Figure 4). Subgroup analysis showed no difference in rate of adequate occlusion between smokers and non-smokers in subgroups of coiling and flow diversion treatments (Supplementary Figure 2).



FIG 4. Forest plot of adequate occlusion rate

Aneurysm recurrence/recanalization

Seventeen studies, encompassing 3,748 patients, were included in a meta-analysis evaluating the recurrence/recanalization rates between smokers and non-smokers with a median follow-up of 649 days (IQR: 249-825 days). The rate of recurrence/recanalization was comparable between smokers and non-smokers(RR 1.17, 95% CI 0.93-1.47; p = 0.17), with high heterogeneity noted among studies (I² = 55%, p < 0.01) (Figure 5). Due to high heterogeneity, a sensitivity analysis was performed. One study was found to be as outlier (Morga, 2020). The results of the sensitivity analysis confirmed the finding of the main analysis which showed no significant difference between smokers and non-smokers in rate of aneurysm recurrence/recanalization (RR 1.10, 95%CI 0.88-1.38). Subgroup analysis showed no difference in rate of recurrence/recanalization among smokers and non-smokers in subgroups who were treated by coiling or mixed treatments (coiling and flow diversion embolization) (Supplementary Figure 3). There was no publication bias based on Egger's (intercept: -0.65, p = 0.44) and observation of the funnel plot (Supplementary Figure 4). The meta-regression analysis found no significant effect for any of the assessed factors for the rate of aneurysm recurrence/recanalization among smokers vs non-smokers (Supplementary Table 6).

	S	noker	Non-si	moker				
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
Stapleton, 2016	11	30	10	16		0.59	[0.32; 1.07]	6.7%
Yuan, 2023	4	37	8	55		0.74	[0.24; 2.29]	3.1%
Ji, 2016	1	15	12	135		0.75	[0.10; 5.37]	1.2%
Kim, 2021	6	24	47	147		0.78	[0.38; 1.63]	5.5%
Jang, 2020	15	115	23	145		0.82	[0.45; 1.50]	6.7%
Huang, 2017	19	162	64	496		0.91	[0.56; 1.47]	8.0%
Kim, 2023	2	11	5	25		0.91	[0.21; 3.99]	2.0%
Wu, 2022	14	57	31	115		0.91	[0.53; 1.57]	7.3%
Brinjikji, 2015	76	267	35	117		0.95	[0.68; 1.33]	9.8%
Park, 2019	5	20	39	151		0.97	[0.43; 2.17]	4.9%
de la Torre, 2018	10	35	15	61		1.16	[0.59; 2.30]	5.9%
Lecler, 2015	8	54	8	78		1.44	[0.58; 3.61]	4.1%
Pierot, 2022	152	415	110	448		1.49	[1.21; 1.83]	11.3%
Futchko, 2017	61	232	11	64		1.53	[0.86; 2.73]	6.9%
Jeon, 2016	5	9	19	56		1.64	[0.82; 3.26]	5.8%
Ortiz, 2008	35	61	11	49		2.56	[1.45; 4.49]	7.1%
Morga, 2020	8	12	4	34		5.67	[2.08; 15.46]	3.7%
Random effects model	432	1556	452	2192		1.17	[0.93; 1.47]	100.0%
Heterogeneity: $I^2 = 55\%$, τ^2	= 0.1084,	p < 0.0	01		01 05 1 0 10			
Test for overall effect: z = 1	.37 (p = 0	.17)			0.1 0.5 1 2 10			

FIG 5. Forest plot of recurrence/recanalization rate

Retreatment

Five studies, encompassing 971 patients, were included in the meta-analysis evaluating the retreatment rates between smokers and non-smokers with a median follow-up of 843 days (IQR: 787-972 days). All studies used coiling as the treatment method. The rate of retreatment was not different among smokers and non-smokers (RR 0.82, 95%CI 0.59-1.13, p = 0.23) with no heterogeneity among studies (I²=0%, p = 0.93) (Figure 6

	S	moker	Non-si	noker				
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	Weight
Stapleton, 2016	6	29	5	17		0.70	[0.25; 1.96]	10.1%
Brinjikji, 2015	51	267	29	117		0.77	[0.52; 1.15]	66.1%
Jang, 2020	4	115	6	145		0.84	[0.24; 2.91]	6.9%
Park, 2019	2	20	16	151	•	0.94	[0.23; 3.80]	5.5%
Ortiz, 2008	9	61	6	49		1.20	[0.46; 3.15]	11.5%
Random effects model Heterogeneity: $l^2 = 0\%$, $\tau^2 =$	72 = 0, p = 0.	492 93	62	479	, 	0.82	[0.59; 1.13]	100.0%
Test for overall effect: z = -	1.21 (p =	0.23)			0.5 1 2			

FIG 6. Forest plot of retreatment

Qualitative results

Youssef et al. (11) reported on a multicenter retrospective study of flow diversion with Woven EndoBridge (WEB) device for ruptured aneurysms, which inlcuded 45 patients with a tobacco use prevalence of 61.4%. Among baseline patient demographic factors, only tobacco use was associated with recurrent/residual aneurysm. Specifically, tobacco use was more common among patients with recurrent aneurysm

compared with those without recurrence at a median follow up of 5.5 months (88.9% vs 35.7%; p=0.012).

DISCUSSION

Our findings indicate that smoking status does not significantly influence recurrence/recanalization or need to retreatment following endovascular procedures. However, smoking was associated with higher probability of complete aneurysm occlusion. following endovascular procedures. Variability in outcomes across previous studies may stem from differences in endovascular devices used. Notably, our study found that smokers who underwent flow diversion treatment had a significantly higher rate of complete aneurysm occlusion compared to non-smokers. This may be attributed to the complex interplay between smoking-induced physiological changes and the mechanisms of healing related to flow diverters. While our study found that smokers treated with flow diversion had a significantly higher rate of complete aneurysm occlusion compared to non-smokers, this finding warrants further examination. The inherent higher occlusion rates associated with flow diverters relative to coiling may confound this result, potentially overshadowing the impact of smoking status. To better delineate the influence of treatment modality, future studies should consider comparative analyses that explicitly account for device-specific occlusion dynamics while controlling for confounding factors such as aneurysm size, location, and follow-up duration

The initial event following flow diversion treatment is adherence of clusters of inflammatory cells across the aneurysm neck. Endothelialization is relatively delayed and derived from cells in the adjacent parent artery ³⁹. Smoking-induced oxidative stress damages endothelial cells and this oxidative imbalance is compounded by increased levels of pro-inflammatory cytokines leading to chronic inflammation and disrupted vascular remodeling ⁴⁰. That's why the pro-thrombotic and inflammatory effects of smoking would have theoretically a more pronounced impact on the (negative) outcomes of flow diversion treatments compared to coiling ⁴¹. Unchanged outcomes associated with coiling procedures are also surprising, but the overall process may be potentially mitigated because the long-term impact of smoking on the vessel wall, particularly given the role of chronic inflammation in smoking-induced atherosclerosis is not fully assessed in our short term event collection ⁴².

The risk of rebleeding after endovascular treatment of ruptured aneurysms is 2.5% in the first year, but becomes negligible after six years ^{43 44}This decline correlates with the early mechanisms underlying late aneurysm recanalization, including poor thrombus organization or degradation⁴⁵. Nicotine has shown to increase plasminogen activator inhibitor-1 levels in brain endothelial cells, promoting a prothrombotic state by inhibiting fibrinolysis^{46 47}. Smoking also upregulates tissue factor, a key initiator of the coagulation cascade, while downregulating tissue factor pathway inhibitor-1, further predisposing individuals to thrombogenesis⁴⁸. The presence of an organizing luminal thrombus in cerebral aneurysm may favor the healing process^{45 49} by recruiting macrophages and neutrophils through chemotactic factors⁴⁹. Smoke particles have shown to activate mitogen-activated protein kinases (MAPK) and nuclear factor-κB (NF-κB) pathways⁵⁰⁻⁵³, which affect vascular stress responses, wall shear stress, blood viscosity and pro-inflammatory cytokine release^{54 55}. These processes can impair aneurysm wall integrity and upregulates the expression of matrix metalloproteinases, potentially promoting recanalization^{56 57}.

Favorable outcomes in smokers have been noted in other contexts, such as a reduction in the hospital stays and complications in patients with arteriovenous malformations with a documented smoking usage or better clinical outcomes and recanalization rates after intravenous thrombolysis for stroke^{58 59}. Similarly, potential confounding factors, including aneurysm size, shape, location, genetic predisposition and demographic influences, may play a significant role in recurrence risk after treatment. Further, genetic factors linked to smoking behavior may affect aneurysm morphology and recurrence, while polymorphisms in vascular integrity and nitric oxide production genes could amplify smoking-induced damage. Further, inconsistencies in defining smoking status, follow-up durations, imaging modalities, and treatment comparisons complicates the interpretation of results, emphasizing the need for standardized methods and consideration of confounders in future studies⁶⁰⁻⁶³.

The "smoker's paradox" phenomena, reported in some cardiovascular and neurovascular settings, post potential short-term benefits for smokers post-intervention ⁶³⁻⁶⁵ due to the anti-inflammatory and neurogenic vasodilatory effects that are mediated by nicotinic acetylcholine receptors ⁶⁶ on intracranial vessels. For instance, nicotine replacement therapy has been linked to reduced clinical vasospasm and better discharge scores ⁶⁷ and enhanced clopidogrel response in smokers may benefit certain interventions⁶⁸. However, smoking remains independently associated with higher all-cause mortality after percutaneous coronary intervention⁶⁹ and negatively impacts long-term outcomes after endovascular treatments, as demonstrated by Ahmad's analysis showing a 35% lower recovery rate among smokers⁷⁰.

Smoking is a well-established risk factor for aneurysm growth and rupture, yet the impact of smoking cessation or reduction on this risk remains underexplored⁵. While smoking is well-established to impair endothelial function, quitting does not consistently lead to improvement⁷¹.

Interestingly, our meta-regression analysis revealed that aneurysm rupture did not affect recanalization or recurrence rates. This is particularly notable given the common assumption that ruptured aneurysms might behave differently compared to unruptured ones during the healing process⁷². However, our finding aligns with the study by Cao et al., which demonstrated that, despite different endovascular approaches, ruptured and unruptured intracranial aneurysms exhibited comparable occlusion and recanalization rates⁷³. It is important to emphasize that our paper exclusively focuses on endovascular treatment and does not address surgical methods such as surgical clipping.

Smoking cessation should remain a cornerstone of preventive health strategies due to its well-documented benefits in reducing aneurysm rupture and systemic vascular risks. However, the lack of significant differences in angiographic outcomes between smokers and non-smokers suggests that cessation efforts should be framed around overall health benefits rather than specific improvements in aneurysm repair outcomes. This distinction may aid clinicians in setting appropriate patient expectations during counseling. Future studies should focus on unraveling the molecular pathways through which smoking modulates aneurysm healing processes, particularly in the context of endovascular device use. A deeper understanding of these mechanisms may pave the way for the development of targeted therapies or innovative coating materials for endovascular devices. These advancements could enhance healing, reduce recurrence rates, and improve overall treatment efficacy, particularly in high-risk populations, including smokers.

Limitations:

This study has several limitations. The heterogeneity in definitions of smoking status and recurrence outcomes across studies may have introduced variability, with inconsistent categorization of smokers complicating direct comparisons. Variations in follow-up durations, ranging from months to years, may have influenced the detection of late-occurring aneurysm recurrence or recanalization. The median follow-up time of 649 days for recurrence/recanalization is relatively short for evaluating aneurysm outcomes. Although a follow-up period of ~22 months offers some preliminary insights, it may not be adequate to fully assess the long-term efficacy and durability of the treatment^{74,75}. Additionally, reliance on retrospective studies, prone to selection bias, limited the control of confounders such as aneurysm characteristics, comorbidities, medications (e.g. antiplatelets) and genetic predispositions. Differences in imaging modalities and reporting standards further affected the comparability of outcomes. Due to the scarcity of data, we were unable to quantitatively assess the impact of smoking, such as in pack years. This study exclusively provides insights into endovascular treatment outcomes and does not extend to surgical aneurysm treatment methods, such as surgical clipping. The primary objective of this manuscript was to investigate the efficacy of the treatment rather than to assess periprocedural complications. Consequently, it does not provide data on periprocedural neurologic and non-neurologic complications.

CONCLUSIONS

Smoking status does not appear to significantly influence aneurysm recanalization or recurrence rates after endovascular treatment. However, our findings suggest that variations in angiographic outcomes may be partially attributed to differences in device types and the mechanisms of healing they promote. The observed heterogeneity across studies highlights the need for further research to elucidate the complex interplay between smoking-induced physiological changes, device-specific healing mechanisms, and patient outcomes. While smoking cessation remains critical for reducing the overall vascular risks and preventing aneurysm formation or rupture, the evidence suggests that cessation may not universally enhance the efficacy of endovascular treatments. These results emphasize the importance of systematic reporting of smoking status and treatment outcomes in future research to better understand the role of smoking in aneurysm healing. Clinicians should continue to counsel patients on the comprehensive health benefits of smoking cessation while managing expectations regarding its impact on aneurysm treatment efficacy.

ACKNOWLEDGMENTS

None.

REFERENCES

- 1. Zhang Z, Liu JY, Xing HS, et al. Microsurgical clipping and endovascular intervention for middle cerebral artery aneurysm: A metaanalysis. *Medicine* 2023;102(34):e34956.
- Ferns SP, Sprengers ME, van Rooij WJ, et al. Coiling of intracranial aneurysms: a systematic review on initial occlusion and reopening and retreatment rates. Stroke 2009;40(8):e523-e29.
- 3. Naggara ON, White PM, Guilbert F, et al. Endovascular treatment of intracranial unruptured aneurysms: systematic review and metaanalysis of the literature on safety and efficacy. *Radiology* 2010;256(3):887-97.
- 4. Habibi MA, Rashidi F, Fallahi MS, et al. Woven endo bridge device for recurrent intracranial aneurysms: A systematic review and metaanalysis. *The Neuroradiology Journal* 2024:19714009241247457.
- 5. Can A, Castro VM, Ozdemir YH, et al. Association of intracranial aneurysm rupture with smoking duration, intensity, and cessation. *Neurology* 2017;89(13):1408-15.
- 6. Chalouhi N, Ali MS, Starke RM, et al. Cigarette smoke and inflammation: role in cerebral aneurysm formation and rupture. *Mediators of inflammation* 2012;2012(1):271582.
- Etminan N, Chang H-S, Hackenberg K, et al. Worldwide incidence of aneurysmal subarachnoid hemorrhage according to region, time period, blood pressure, and smoking prevalence in the population: a systematic review and meta-analysis. JAMA neurology 2019;76(5):588-97.
- 8. Jin J, Guo G, Ren Y, et al. Risk factors for recurrence of intracranial aneurysm after coil embolization: a meta-analysis. *Frontiers in Neurology* 2022;13:869880.
- 9. Munn Z, Barker TH, Moola S, et al. Methodological quality of case series studies: an introduction to the JBI critical appraisal tool. JBI Evid Synth 2020;18(10):2127-33. doi: 10.11124/jbisrir-d-19-00099
- 10. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25(9):603-5. doi: 10.1007/s10654-010-9491-z [published Online First: 20100722]
- 11. Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. Stroke 2001;32(9):1998-2004.
- 12. Viechtbauer W, Cheung MWL. Outlier and influence diagnostics for meta-analysis. Research synthesis methods 2010;1(2):112-25.
- 13. Chandler J, Cumpston M, Li T, et al. Cochrane handbook for systematic reviews of interventions. Hoboken: Wiley 2019
- 14. Adeeb N, Moore J, Wirtz M, et al. Predictors of incomplete occlusion following Pipeline embolization of intracranial aneurysms: is it less effective in older patients? *American Journal of Neuroradiology* 2017;38(12):2295-300.
- 15. Brinjikji W, Lingineni RK, Gu CN, et al. Smoking is not associated with recurrence and retreatment of intracranial aneurysms after endovascular coiling. *Journal of neurosurgery* 2015;122(1):95-100.
- 16. Chen J-X, Lai L-F, Zheng K, et al. Influencing factors of immediate angiographic results in intracranial aneurysms patients after endovascular treatment. *Journal of neurology* 2015;262:2115-23.
- 17. Dabus G, Hacein-Bey L, Varjavand B, et al. Safety, immediate and mid-term results of the newer generation of hydrogel coils in the treatment of ruptured aneurysms: a multicenter study. *Journal of Neurointerventional Surgery* 2017;9(4):419-24.

- 18. de La Torre Y, Velasco S, Tasu J-P, et al. Impact of the global outflow angle on recanalization after endovascular treatment of middle cerebral artery bifurcation aneurysms. *Journal of NeuroInterventional Surgery* 2018;10(12):1174-78.
- 19. Futchko J, Starr J, Lau D, et al. Influence of smoking on aneurysm recurrence after endovascular treatment of cerebrovascular aneurysms. *Journal of neurosurgery* 2018;128(4):992-98.
- 20. Hammoud B, El Zini J, Awad M, et al. Predicting incomplete occlusion of intracranial aneurysms treated with flow diverters using machine learning models. *Journal of Neurosurgery* 2023;1(aop):1-10.
- 21. Hanel RA, Monteiro A, Nelson PK, et al. Predictors of incomplete aneurysm occlusion after treatment with the Pipeline Embolization Device: PREMIER trial 1 year analysis. *Journal of neurointerventional surgery* 2022;14(10):1014-17.
- 22. Huang D-Z, Jiang B, He W, et al. Risk factors for the recurrence of an intracranial saccular aneurysm following endovascular treatment. Oncotarget 2017;8(20):33676.
- 23. Hussein AE, Shownkeen M, Thomas A, et al. 2D parametric contrast time-density analysis for the prediction of complete aneurysm occlusion at six months' post-flow diversion stent. *Interventional Neuroradiology* 2020;26(4):468-75.
- 24. Jang CK, Chung J, Lee JW, et al. Recurrence and retreatment of anterior communicating artery aneurysms after endovascular treatment: a retrospective study. *BMC neurology* 2020;20:1-8.
- 25. Jeon J, Cho Y, Rhim J, et al. Fate of coiled aneurysms with minor recanalization at 6 months: rate of progression to further recanalization and related risk factors. American Journal of Neuroradiology 2016;37(8):1490-95.
- 26. Ji W, Liu A, Lv X, et al. Larger inflow angle and incomplete occlusion predict recanalization of unruptured paraclinoid aneurysms after endovascular treatment. *Interventional Neuroradiology* 2016;22(4):383-88.
- 27. Kim JH, Ko YS, Kwon SM, et al. Predictive factors of recurrence after endovascular treatment of unruptured vertebrobasilar fusiform aneurysms. *Clinical Neuroradiology* 2023;33(1):73-86.
- 28. Kim MJ, Chung J, Park KY, et al. Recurrence and risk factors of posterior communicating artery aneurysms after endovascular treatment. *Acta neurochirurgica* 2021;163(8):2319-26.
- 29. Morga R, Moskała M, Popiela T, et al. Recanalization of embolized endovascular intracranial aneurysms and changes in the blood viscosity: a pilot study. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research* 2020;26:e919059-1.
- 30. Ortiz R, Stefanski M, Rosenwasser R, et al. Cigarette smoking as a risk factor for recurrence of aneurysms treated by endosaccular occlusion. *Journal of neurosurgery* 2008;108(4):672-75.
- 31. Pierot L, Barbe C, Thierry A, et al. Patient and aneurysm factors associated with aneurysm recanalization after coiling. *Journal of NeuroInterventional Surgery* 2022;14(11):1096-101.
- 32. Rouchaud A, Brinjikji W, Cloft H, et al. Smoking does not affect occlusion rates and morbidity-mortality after pipeline embolization for intracranial aneurysms. *American Journal of Neuroradiology* 2016;37(6):1122-26.
- 33. Salem MM, Khorasanizadeh M, Nwajei F, et al. Predictors of aneurysmal occlusion following intracranial aneurysms treatment with pipeline embolization device. *Acta Neurochirurgica* 2023;165(10):2801-09.
- 34. Stapleton CJ, Kumar JI, Walcott BP, et al. The effect of basilar artery bifurcation angle on rates of initial occlusion, recanalization, and retreatment of basilar artery apex aneurysms following coil embolization. *Interventional Neuroradiology* 2016;22(4):389-95.
- 35. Wu D, Sheng B, Fang X, et al. Risk factors of recurrence after endovascular embolization of posterior communicating artery aneurysms. Interventional Neuroradiology 2022;28(5):562-67.
- 36. Youssef PP, Dornbos III D, Peterson J, et al. Woven EndoBridge (WEB) device in the treatment of ruptured aneurysms. *Journal of NeuroInterventional Surgery* 2021;13(5):443-46.
- 37. Yuan J, Huang C, Li Z, et al. Hemodynamic characteristics associated with recurrence of middle cerebral artery bifurcation aneurysms after total embolization. *Clinical Interventions in Aging* 2021:2023-32.
- 38. Dabus G, Hacein-Bey L, Varjavand B, et al. Safety, immediate and mid-term results of the newer generation of hydrogel coils in the treatment of ruptured aneurysms: a multicenter study. J Neurointerv Surg 2017;9(4):419-24. doi: 10.1136/neurintsurg-2016-012780 [published Online First: 20161018]
- 39. Kadirvel R, Ding YH, Dai D, et al. Cellular mechanisms of aneurysm occlusion after treatment with a flow diverter. *Radiology* 2014;270(2):394-9. doi: 10.1148/radiol.13130796 [published Online First: 20131028]
- 40. Dikalov S, Itani H, Richmond B, et al. Tobacco smoking induces cardiovascular mitochondrial oxidative stress, promotes endothelial dysfunction, and enhances hypertension. Am J Physiol Heart Circ Physiol 2019;316(3):H639-h46. doi: 10.1152/ajpheart.00595.2018 [published Online First: 20190104]
- 41. Ravindran K, Casabella AM, Cebral J, et al. Mechanism of action and biology of flow diverters in the treatment of intracranial aneurysms. *Neurosurgery* 2020;86(Supplement_1):S13-S19.
- 42. Ishida M, Sakai C, Kobayashi Y, et al. Cigarette smoking and atherosclerotic cardiovascular disease. Journal of Atherosclerosis and Thrombosis 2024;31(3):189-200.
- 43. Pierot L, Barbe C, Herbreteau D, et al. Rebleeding and bleeding in the year following intracranial aneurysm coiling: analysis of a large prospective multicenter cohort of 1140 patients—Analysis of Recanalization after Endovascular Treatment of Intracranial Aneurysm (ARETA) Study. Journal of Neurointerventional Surgery 2020;12(12):1219-25.
- 44. van Donkelaar CE, Bakker NA, Veeger NJ, et al. Predictive factors for rebleeding after aneurysmal subarachnoid hemorrhage: rebleeding aneurysmal subarachnoid hemorrhage study. *Stroke* 2015;46(8):2100-06.
- 45. Brinjikji W, Kallmes DF, Kadirvel R. Mechanisms of healing in coiled intracranial aneurysms: a review of the literature. *American Journal of Neuroradiology* 2015;36(7):1216-22.
- 46. Miller G, Bauer K, Cooper J, et al. Activation of the coagulant pathway in cigarette smokers. Thrombosis and haemostasis 1998;79(03):549-53.
- 47. Zidovetzki R, Chen P, Fisher M, et al. Nicotine increases plasminogen activator inhibitor-1 production by human brain endothelial cells via protein kinase C-associated pathway. *Stroke* 1999;30(3):651-55.
- 48. Barua RS, Ambrose JA, Saha DC, et al. Smoking is associated with altered endothelial-derived fibrinolytic and antithrombotic factors:

an in vitro demonstration. Circulation 2002;106(8):905-08.

- 49. Tulamo R, Frösen J, Hernesniemi J, et al. Inflammatory changes in the aneurysm wall: a review. *Journal of neurointerventional surgery* 2018;10(Suppl 1):i58-i67.
- 50. Gerzanich V, Zhang F, West GA, et al. Chronic nicotine alters NO signaling of Ca2+ channels in cerebral arterioles. *Circulation research* 2001;88(3):359-65.
- 51. Koide M, Nishizawa S, Yamamoto S, et al. Nicotine exposure, mimicked smoking, directly and indirectly enhanced protein kinase C activity in isolated canine basilar artery, resulting in enhancement of arterial contraction. Journal of Cerebral Blood Flow & Metabolism 2005;25(3):292-301.
- 52. Mayhan WG, Patel KP. Effect of nicotine on endothelium-dependent arteriolar dilatation in vivo. American Journal of Physiology-Heart and Circulatory Physiology 1997;272(5):H2337-H42.
- 53. Sandhu H, Xu CB, Edvinsson L. Upregulation of contractile endothelin type B receptors by lipid-soluble cigarette smoking particles in rat cerebral arteries via activation of MAPK. *Toxicology and applied pharmacology* 2010;249(1):25-32.
- 54. Mazzone P, Tierney W, Hossain M, et al. Pathophysiological impact of cigarette smoke exposure on the cerebrovascular system with a focus on the blood-brain barrier: expanding the awareness of smoking toxicity in an underappreciated area. *International journal of environmental research and public health* 2010;7(12):4111-26.
- 55. Singh PK, Marzo A, Howard B, et al. Effects of smoking and hypertension on wall shear stress and oscillatory shear index at the site of intracranial aneurysm formation. *Clinical neurology and neurosurgery* 2010;112(4):306-13.
- 56. Peterson JW, Kwun B-D, Teramura A, et al. Immunological reaction against the aging human subarachnoid erythrocyte: A model for the onset of cerebral vasospasm after subarachnoid hemorrhage. *Journal of neurosurgery* 1989;71(5):718-26.
- 57. Qi Y-X, Qu M-J, Long D-K, et al. Rho-GDP dissociation inhibitor alpha downregulated by low shear stress promotes vascular smooth muscle cell migration and apoptosis: a proteomic analysis. *Cardiovascular research* 2008;80(1):114-22.
- 58. Gajjar AA, Goyal A, Gill K, et al. Evaluating the effects of recreational drug use on ruptured cerebral arteriovenous malformation presentation and in-hospital outcomes: a national inpatient sample analysis. *Journal of NeuroInterventional Surgery* 2024
- 59. Kurmann R, Engelter ST, Michel P, et al. Impact of smoking on clinical outcome and recanalization after intravenous thrombolysis for stroke: multicenter cohort study. *Stroke* 2018;49(5):1170-75.
- 60. Bakker MK, van der Spek RA, van Rheenen W, et al. Genome-wide association study of intracranial aneurysms identifies 17 risk loci and genetic overlap with clinical risk factors. *Nature genetics* 2020;52(12):1303-13.
- 61. Cekirge H, Saatci I. A new aneurysm occlusion classification after the impact of flow modification. *American Journal of Neuroradiology* 2016;37(1):19-24.
- 62. McColgan P, Thant KZ, Sharma P. The genetics of sporadic ruptured and unruptured intracranial aneurysms: a genetic meta-analysis of 8 genes and 13 polymorphisms in approximately 20,000 individuals. *Journal of neurosurgery* 2010;112(4):714-21.
- 63. Slettebø H, Karic T, Sorteberg A. Impact of smoking on course and outcome of aneurysmal subarachnoid hemorrhage. Acta Neurochirurgica 2020;162:3117-28.
- 64. Cockroft KM. A smoker's paradox: does being a smoker really lead to a better outcome after aneurysmal SAH? *Journal of neurosurgery* 2017;129(2):442-45.
- 65. Dasenbrock HH, Rudy RF, Lai PMR, et al. Cigarette smoking and outcomes after aneurysmal subarachnoid hemorrhage: a nationwide analysis. *Journal of neurosurgery* 2018;129(2):446-57.
- 66. Kamio Y, Miyamoto T, Kimura T, et al. Roles of nicotine in the development of intracranial aneurysm rupture. *Stroke* 2018;49(10):2445-52.
- 67. Carandang RA, Barton B, Rordorf GA, et al. Nicotine replacement therapy after subarachnoid hemorrhage is not associated with increased vasospasm. *Stroke* 2011;42(11):3080-86.
- 68. Park KW, Park JJ, Jeon K-H, et al. Enhanced clopidogrel responsiveness in smokers: smokers' paradox is dependent on cytochrome P450 CYP1A2 status. Arteriosclerosis, thrombosis, and vascular biology 2011;31(3):665-71.
- 69. Gupta R, Kirtane AJ, Liu Y, et al. Impact of smoking on platelet reactivity and clinical outcomes after percutaneous coronary intervention: findings from the ADAPT-DES study. *Circulation: Cardiovascular Interventions* 2019;12(11):e007982.
- 70. Ahmad S. Clinical outcome of endovascular coil embolization for cerebral aneurysms in Asian population in relation to risk factors: a 3-year retrospective analysis. *BMC surgery* 2020;20:1-9.
- 71. Higashi Y. Smoking cessation and vascular endothelial function. Hypertension Research 2023;46(12):2670-78.
- 72. Britz GW, Salem L, Newell DW, et al. Impact of surgical clipping on survival in unruptured and ruptured cerebral aneurysms: a population-based study. Stroke 2004;35(6):1399-403. doi: 10.1161/01.Str.0000128706.41021.01 [published Online First: 20040429]
- 73. Cao R, Mattar A, Torche E, et al. Clinical and angiographic characteristics of ruptured and unruptured distal cerebral aneurysms: a review of a large series of cases in a high-volume center. *J Neurointerv Surg* 2024 doi: 10.1136/jnis-2023-021164 [published Online First: 20240305]
- 74. Lecler A, Raymond J, Rodriguez-Régent C, et al. Intracranial aneurysms: recurrences more than 10 years after endovascular treatment a prospective cohort study, systematic review, and meta-analysis. *Radiology*. 2015;277(1):173-180.
- 75. Park YK, Bae H-J, Cho DY, Choi JH, Kim B-S, Shin YS. Risk factors for recurrence and retreatment after endovascular treatment of intracranial saccular aneurysm larger than 8 mm. *Acta Neurochirurgica*. 2019;161:939-946.

SUPPLEMENTAL FILES

Supplementary Table 1. Search strategy

PubMed: 176

("Intracranial Aneurysm" [Mesh] OR (Cerebrovascular) OR (Intracranial) OR (Cerebral) OR (Brain) OR (Basilar) OR (Communicating) OR

(Berry) OR (cerebellar)) AND (aneurysm) AND ("Smoking"[Mesh] OR (smoking) OR (cigarette) OR (cigar) OR (tobacco)) AND ("Thrombosis"[Mesh] OR (thrombosis) OR (Occlusion) OR (recurrence))

Scopus: 610

(TITLE-ABS-KEY(Cerebrovascular) OR TITLE-ABS-KEY(Intracranial) OR TITLE-ABS-KEY(Cerebral) OR TITLE-ABS-KEY(Brain) OR TITLE-ABS-KEY(Basilar) OR TITLE-ABS-KEY(Communicating) OR TITLE-ABS-KEY(Berry) OR TITLE-ABS-KEY(cerebellar)) AND TITLE-ABS-KEY(aneurysm) AND (TITLE-ABS-KEY(smoking) OR TITLE-ABS-KEY(cigarette) OR TITLE-ABS-KEY(cigar) OR TITLE-ABS-KEY(communicating) OR TITLE-ABS-KEY(cigarette) OR TITLE-ABS-KEY(cigar) OR TITLE-ABS-KEY(cigarette) OR TITLE-ABS-KEY(cigar) OR TITLE-ABS-KEY(cigarette) OR TITLE

Embase: 264

(cerebrovascular OR intracranial OR cerebral OR 'brain'/exp OR brain OR basilar OR communicating OR 'berry'/exp OR berry OR cerebellar) AND aneurysm:ti,ab,kw AND (smoking:ti,ab,kw OR cigarette:ti,ab,kw OR cigar:ti,ab,kw OR tobacco:ti,ab,kw) AND (thrombosis OR occlusion OR recurrence)

Web of Science: 121

ALL=(Cerebrovascular OR Intracranial OR Cerebral OR Brain OR Basilar OR Communicating OR Berry OR cerebellar) AND ALL=(aneurysm) AND ALL=(smoking OR cigarette OR cigar OR tobacco) AND ALL=(thrombosis OR Occlusion OR recurrence)

	V		Detient	C	E1	Age		LITNI	D	A 41 1	Develiaidense
Study	r	Group	s	g (n)	e (n)	Mean/Medi an	SD/IQ R	(n)	M (n)	sis (n)	ia (n)
Occlusion											
CI	201	Adequate Occlusion	254	41	165	49.6	1.4	32	34	33	-
Chen	5	Incomplete Occlusion	275	52	173	49.8	1.6	45	28	25	-
	202	Complete Occlusion	19	6	3	53.4	42-69	10	-	-	4
Hussein	0	Incomplete Occlusion	12	3	3	65.5	41-79	8	-	-	7
D · ··1 ··	201	Complete Occlusion	371	261	-	-	-	-	-	-	-
Brinjikji	5	Incomplete Occlusion	40	31	-	-	-	-	-	-	-
	202	Complete Occlusion	113	36	101	53.6	11.2	-	-	-	-
Hanel	1	Incomplete Occlusion	25	3	20	59.9	10.4	-	-	-	-
Stapleto	201	Adequate Occlusion	22	14	17	54	-	14	-	-	-
n	6	Incomplete Occlusion	24	15	22	55.3	-	13	-	-	-
G 1	202	Complete Occlusion	257	69	206	57	47-65	80	-	-	-
Salem	3	Incomplete Occlusion	74	12	62	66	56-72	26	-	-	-
Rouchau	201	Complete Occlusion	109	58	-	-	-	-	-	-	-
d	6	Incomplete Occlusion	36	20	-	-	-	-	-	-	-
	201	Complete Occlusion	297*		255	-	-	-	-	-	-
Adeeb	7	Incomplete Occlusion	83*		66	-	-	-	-	-	-
Hammo	202	Complete Occlusion	470		400	55	48–64	208	-	-	-
ud	4	Incomplete Occlusion	146		113	58	50–71	89	-	-	-
DI	201	Complete Occlusion	41	21	-	-	-		-	-	-
Dabus	6	Incomplete Occlusion	14	5	-	-	-		-	-	-
Recurrence	e/recana	lization									
	201	Non-Recurrent/no recanalization	72	61	53	-	-	40	8	-	-
Futchko	7	Recurrent/Recanalizat ion	224	171	179	-	-	125	25	-	-
	202	Non-Recurrent/no recanalization	29	9	15	55.8	11	18	2	8	11
Kim	3	Recurrent/Recanalizat ion	7	2	2	55.3	15.7	2	1	1	1
Jang	202 0	Non-Recurrent/no recanalization	222	100	112	58.3	10.84	132	-	-	_

Supplementary Table 2. Summary of the included studies and baseline characteristics

		Recurrent/Recanalizat ion	38	15	14	53.58	11.7	25	-	-	-
	201	Non-Recurrent/no recanalization	575	143	363	-	-	495	18 0	-	-
Huang	7	Recurrent/Recanalizat ion	83	19	52	-	-	77	26	-	-
	202	Non-Recurrent/no recanalization	15	35.70%	9	61.3	16.9	66.70 %	-	-	66.70%
Yousef	0	Recurrent/Recanalizat ion	10	88.90%	8	55.2	8.9	57.10 %	-	-	14.30%
v	202	Non-Recurrent/no recanalization	80	33	7	58.83	6.56	7	3	3	2
Yuan	3	Recurrent/Recanalizat ion	12	4	54	55.11	10.21	29	10	13	19
	202	Non-Recurrent/no recanalization	127	43	76	-	-	41	31	-	-
wu	2	Recurrent/Recanalizat ion	45	14	29	-	-	18	17	-	-
17.	202	Non-Recurrent/no recanalization	118	18	101	62.3	10.6	57	15	-	49
Kim	1	Recurrent/Recanalizat ion	53	6	50	61.2	11.8	28	5	-	17
T .	201	Non-Recurrent/no recanalization	137	14	112	52.7	8.6	44	6	-	13
J1	6	Recurrent/Recanalizat ion	13	1	10	52.3	7.2	6	1	-	1
de la	201	Non-Recurrent/no recanalization	71	25	47	52	11	19	-	-	-
Torre	8	Recurrent/Recanalizat ion	25	10	17	53	10	14	-	-	-
T	201	Non-Recurrent/no recanalization	41	4	30	58.1	12	27	3	-	4
Jeon	6	Recurrent/Recanalizat ion	24	5	18	57.6	9.2	12	0	-	2
Stapleto	201	Non-Recurrent/no recanalization	25	19	20	52.8	-	16	-	-	-
n	6	Recurrent/Recanalizat ion	21	11	19	54.7	-	11	-	-	-
Marra	202	Non-Recurrent/no recanalization	34	4	28	58	15.26	14	-	6	4
Morga	0	Recurrent/Recanalizat ion	12	8	8	55.83	7.07	6	-	0	2
	200	Non-Recurrent/no recanalization	64	26	55	-	-	-	-	-	-
Ortiz	8	Recurrent/Recanalizat ion	46	35	32	-	-	-	-	-	-
	202	Non-Recurrent/no recanalization	666	263	-	53.5	12.5	-	-	-	-
Pierot	2	Recurrent/Recanalizat ion	279	152	-	51.7	12.1	-	-	-	-
D1	201	Non-Recurrent/no recanalization	127	15	104	58.0	51.0- 65.0	63	13	-	-
Park	9	Recurrent/Recanalizat ion	44	5	32	65.0	55.5- 71.0	25	5	-	-
Lecler	201 5	Non-Recurrent/no recanalization	60	-	-	-	-	-	-	-	-

Recurrent/Recana ion	ılizat 132	54	-	-	-	-	-	-	-
-------------------------	------------	----	---	---	---	---	---	---	---

HTN= Hypertension; DM= Diabetes Mellitus; * Number of aneurysms

Supplementary Table 3. Summary characteristics of the treated aneurysms

							Loc	ation				Siz	æ		N	eck	Morph	nology
Stud y	Y ea r	Group	Rup ture d	A C A	Ac o m	I C A	M C A	VB	Pc o m	Other	Micr o- Mini atur e	Mini atur e	La rg e	Othe r	W id e	Nar row	Regu lar	Irre gula r
Occlus	ion				1				1				1		1	1		1
Chen	20	Adequate Occlusion	179	1	05	8 2	35	32		-	41	181	32	-	25	229	212	70
	15	Incomplete Occlusion	225	1	17	8 6	42	30		-	15	208	52	-	53	222	205	42
Huss	20	Complete Occlusion	-	-	-	_	-	-	-	Caverno us: 3; Clinoid: 4; Ophthal mic: 8; SHA: 2; Others: 2	-	-	-	Mea n: 6.29			S: 16; F: 1	2
ein	20	Incomplete Occlusion	-	-	-	-	-	-	-	Caverno us: 3; Clinoid: 4; Ophthal mic: 4; SHA: 0; Others: 1	-	-	-	Mea n: 10.83			S:10; F: 1	1
Brinj	20	Complete Occlusion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
iki	15	Incomplete Occlusion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Hane 1	20 21	Complete Occlusion	0	-	_	_	-	-	_	Petrous: 1; Caverno us: 3; Clinoid: 10; Ophthal mic: 86; Commu nicating : 11; V4: 2	_		_	≤ 12m m	≥ 4 m m		S: 111; F: 2	_
		Incomplete Occlusion	0	_	-	_	_	-	_	Petrous: 0; Caverno us: 0; Clinoid: 1; Ophthal mic: 12;	-	_	-	≤ 12m m	≥ 4 m m	_	S: 23; F: 2	-

										Commu nicating : 8; V4: 4								
Stap	20	Complete Occlusion	6	-	-	_	-	All Ba sila r	-	-	19		3	small : <10; large : >10	-	-	S: 5; E: 14	Bi: 3
elton	16	Incomplete Occlusion	8	-	-	-	_	All Ba sila r	-	-	15		9	small : <10; large : >10	-	-	S: 11; E: 12	Bi: 1
Sale	20	Complete Occlusion	-	-	-	-	-	-	-	Post. Cir.: 22	-	-	-	6 [3.9- 10]	-	-	S: 234; F: 23	-
m	23	Incomplete Occlusion	-	-	-	-	-	-	-	Post. Cir.: 12	-	-	-	7 [5- 11.9]	-	-	S: 67; F:7	-
Rouc	20	Complete Occlusion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
haud	16	Incomplete Occlusion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Adee b	20 17	Complete Occlusion	-	-	-	-	_	-	-	Ant: 240, Post: 57	-	-	-	1–20 mm: 269, ≥ 21 mm: 21	-	-	S: 201, Blist er: 11, F: 76, Disse cting: 9	_
		Incomplete Occlusion	-	_	-	-	-	-	-	Ant: 56, Post: 27	-	-	-	1–20 mm: 21, ≥ 21 mm: 12	-	_	S: 56, F: 26, Disse cting: 1	_
Ham	20	Complete Occlusion	-	6	1	4 4 3	18	-	11	Post: 32	_	-	-	-	-	-	S: 447, Blist er: 5, F: 31, Disse cting: 28	_
d	24	Incomplete Occlusion	-	3	0	2 3 7	7	-	2	Post: 18	-	-	-	-	-	-	S: 122, Blist er: 1, F: 21, Disse cting: 1	-
Dab	20	Complete Occlusion	41	-	15	5	-	-	13	8	-	-	-	-	-	-	-	-
us	16	Incomplete Occlusion	14	-	8	-	1	-	1	4	-	-	-	-	-	-	-	-

Recurr	ence/r	ecanalization																
Futc	20	Non- Recurrent/n o recanalizatio n	20	-	_	-	-	-	_	High Risk (Acom, A2/Peri callosal, Pcom, Basilar) : 38	-	-	-	≥7: 51	-	_	-	_
hko	17	Recurrent/R ecanalizatio n	42	-	_	-	-	-	-	High Risk (Acom, A2/Peri callosal, Pcom, Basilar) : 114	-	-	-	≥7: 69	-	_	-	-
Kim	20 23	Non- Recurrent/n o recanalizatio n	0		-	-	-	All VB	-	-	-	-	-	7.76 (2.35)	-	-	F: 24; D: 4; T: 1	-
		Recurrent/R ecanalizatio n	0		-	-	-	All VB	-	-	-	-	-	12.41 (6.61)	-	-	F:3; T: 4	-
	20	Non- Recurrent/n o recanalizatio n	56		Al l Ac o m	-	-	-	-	-	-	-	-	5.17 (2.1)	-	-	-	-
Jang	20	Recurrent/R ecanalizatio n	21		Al l Ac o m	_	-	-	_	_	_	_	_	6.3 (3.0)	_	_	_	_
Hua	20	Non- Recurrent/n o recanalizatio n	479	41	12 2	_	75	-	16 0	Posterio r Circulat ion: 37	236	292	47	<5; 5-10; 10<	> 4: 17 1	404	S: all	-
ng	1/	Recurrent/R ecanalizatio n	77	2	35	-	17	-	15	Posterio r Circulat ion: 2	28	39	16	<5; 5-10; 10<	> 4: 57	26	S: all	-
Yous		Non- Recurrent/n o recanalizatio n	All	-	-	-	-	-	-	-	-	-	-	6.6 (2.6)	-	-	-	-
		Recurrent/R ecanalizatio n	All	-	-	-	-	-	-	-	-	-	-	5.9 (2.5)	-	-	-	-
Yua n	20 23	Non- Recurrent/n o recanalizatio n	-	-	-	_	80	-	-	-	-	-	-	5.23 (1.88)	-	-	S: 80	-
		Recurrent/R ecanalizatio n	-	-	-	-	12	-	-	-	-	-	-	5.75 (2.13)	-	-	S: 12	-
Wu	20 22	Non- Recurrent/n o	95	-	-	-	-	-	12 7	_	-	-	-	≥7: 31	29	98	S: 25	-

		recanalizatio n																
		Recurrent/R ecanalizatio n	35	-	-	-	-	-	45	-	-	-	-	≥7: 19	19	26	S: 18	-
	20	Non- Recurrent/n o recanalizatio n	31	-	_	-	-	-	A L L Pc o m		-	-	-	-	-	-	-	-
Kim	21	Recurrent/R ecanalizatio n	23	-	-	_	-	-	A L L Pc o m		-	-	-	-	-	-	-	-
Ji	20 16	Non- Recurrent/n o recanalizatio n	0	-	-	-	-	-	-	All Paraclin oid		-	-	6 (3.6)	12	1	-	-
		Recurrent/R ecanalizatio n	0	-	-	-	-	-	-	All Paraclin oid		-	-	9.9 (6.9)	10 2	35	-	-
de la Torr	20	Non- Recurrent/n o recanalizatio	38	-	-	-	-	-	-	_	-	-	-	8.9 (3.5)	-	-	-	-
e	18	Recurrent/R ecanalizatio n	18	-	-	-	-	-	-	-	-	-	_	6.2 (2.2)	_	-	-	-
Jeon	20 16	Non- Recurrent/n o recanalizatio n	-	-	-	-	-	-	-	-	-	-	-	6.3 (2.7)	-	-	-	-
		Recurrent/R ecanalizatio n	-	-	-	-	-	-	-	-	-	-	-	6.2 (4.1)	-	-	-	-
Stap	20	Non- Recurrent/n o recanalizatio n	7	-	-	-	-	All Ba sila r	-	-	22	-	3	small : <10; large : >10	-	-	S: 5; E: 17	Bi: 3
elton	16	Recurrent/R ecanalizatio n	7	-	-	-	-	All Ba sila r	-	-	12	-	9	small : <10; large : >10	-	-	S: 11; E: 9	Bi: 1
Mor ga	20 20	Non- Recurrent/n o recanalizatio n	0	-	17	1 4	2	5	-	-	-	-	-	5.82 (3.09)	-	-	27	11
		Recurrent/R ecanalizatio n	0	-	5	4	1	2	-	-	-	-	-	6.11 (2.84)	-	-	10	2
Ortiz	20 08	Non- Recurrent/n o recanalizatio	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

		n																
		Recurrent/R ecanalizatio n	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Piero	20	Non- Recurrent/n o recanalizatio n	418	-	-	-	13 0	-	-	536	-	-	-	<10: 600, ≥10: 66	37 8	288	204	462
t	22	Recurrent/R ecanalizatio n	196	-	-	-	68	-	-	211	-	-	-	<10: 216, ≥10: 63	17 9	100	65	214
	20	Non- Recurrent/n o recanalizatio n	14	-	18	8 5	8	6	-	10	-	-	-	Mea n: 9.5 [8.7; 11.2]	-	-	-	-
Park	19	Recurrent/R ecanalizatio n	15	-	5	2 5	5	3	-	6	-	-	-	Mea n: 13.1 [10.1 ;16.7]	-	-	-	-
Lecl	20 15	Non- Recurrent/n o recanalizatio n	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		Recurrent/R ecanalizatio n	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

ACA = Anterior Cerebral Artery; Acom = Anterior Communicating Artery; ICA = Internal Carotid Artery; MCA = Middle Cerebral Artery; VB = Vertebrobasilar; Pcom = Posterior Communicating Artery; NR = Not Reported; Post. Cir. = Posterior Circulation; Ant = Anterior; S = Saccular; F = Fusiform; E = Embolization; Bi = Bifurcation; T = Thrombosis; SHA = Superior Hypophyseal Artery; V4 = Fourth Segment of Vertebral Artery; Blister = Blister aneurysm; Dissecting = Dissecting aneurysm; Paraclinoid = Region adjacent to the clinoid process.

Supplementary Table 4. Treatment details

			Angiographic		Tre	eatment		Ray	mond-l	Roy
Study	Year	Group	Follow up duration	Coil	Stent- assisted	Baloon- assisted	Other	1	2	3
Occlusion										
CI	2015	Adequate Occlusion	Immediately	189	52	13	-	25	54	-
Chen	2015	Incomplete Occlusion	after EVT	226	37	12	-	-		275
Hussein	2020	Complete Occlusion	6 months	-	Flow diversion stent	-	-	000	Complet elusion:	e 19
Tussem	2020	Incomplete Occlusion	0 monuis	-	Flow diversion stent	-	-	In	comple lusion:	te 12
D · ····	2015	Complete Occlusion	24.22	371	-	-	-	186	185	-
Brinjiki	2015	Incomplete Occlusion	2.4 ± 2.3 years.	40	-	-	-	-	-	40
TT 1	2021	Complete Occlusion	10 1	-	-	-	PED	113	-	-
Hanel	2021	Incomplete Occlusion	12 months	-	-	-	PED	-	2	5
Stapelton	2016	Adequate Occlusion	Not specified	18	4	3	-	2	2	-

		Incomplete Occlusion		20	0	1	-	-	-	24
Salam	2022	Complete Occlusion	16.4 months	-	-	-	PED	0000	Complet lusion:	ie 257
Salem	2025	Incomplete Occlusion	16.4 months	-	-	-	PED	In occ	comple	ete 74
Developed	2016	Complete Occlusion	28.9 ± 23.7	-	-	-	PED	C occ	Complet lusion:	e 109
Rouchaud	2016	Incomplete Occlusion	months	-	-	-	PED	In	comple clusion:	ete 36
Alash	2017	Complete Occlusion	10.2 m antha	-	-	-	PED	C occ	Complet lusion:	.e 297
Adeeb	2017	Incomplete Occlusion	19.2 monuns	-	-	-	PED	In occ	comple clusion:	ete 83
Hommoud	2024	Complete Occlusion	6 months	57	21	-	clipping: 13, stenting: 2, Wraping: 2	C occ	Complet lusion:	e 470
Hammoud	Incomplete Occlusion		0 monuis	25	11	-	clipping: 3, stenting: 1, Wraping: 1	In occ	comple lusion:	ete 146
Dabus	2016	Complete Occlusion	6.8 months	28	2	12	-	41	-	-
Dabus	2010	Incomplete Occlusion	0.8 monuis	8	-	5	-	-	11	1
Recurrence/	recanaliz	ation			1	1	1			
Futchko	2017	Non-Recurrent/no recanalization	Smokers: 1.62 years	60	12	0	-	178	34	12
	2017	Recurrent/recanalization	Non-smokers: 1.72 years	168	54	2	-	36	26	9
W.	2022	Non-Recurrent/no recanalization	30.5± 29.2 months (range	-	21		Sole Stenting: 2; Parent Occlusion: 1; FDS: 5	24	2	4
KIM	2023	Recurrent/recanalization	2–127.8 months	-	3		Sole Stenting: 3; Parent Occlusion: 1; FDS: 0			
Jang	2020	Non-Recurrent/no recanalization	27 months	all	47		-	147	7	5
		Recurrent/recanalization	(range 1–110)	all	5		-	20	1	8
Huang	2017	Non-Recurrent/no recanalization	Follow-up: at least 6 months	all	212		-	-	-	-
		Recurrent/recanalization		all	15		-	-	-	-
Yousef	2020	Non-Recurrent/no recanalization	5.5 months	-	-	-	WEB	-	-	-
		Recurrent/recanalization		-	-	-	WEB	-	-	-
Yuan	2023	Non-Recurrent/no recanalization	6 (4, 7) months	all	-	-	-	80	-	-
		Recurrent/recanalization	6 (4, 10.75) months	all	-	-	-	12	-	-
Wu	2022	Non-Recurrent/no recanalization	11.4 ± 3.9	73	54	-	-	101	24	2
		Recurrent/recanalization	monuis	34	11	-	-	19	16	10
Kim	2021	Non-Recurrent/no recanalization	27.7 months (range: 3.5–	all	54	4	-	76	4	-2
		Recurrent/recanalization	78.6)	all	1:	5	-	24	2	9
Ji	2016	Non-Recurrent/no recanalization	7.4±2.8 months	all	117		FD: 5	93	42	2

		Recurrent/recanalization		all	11		FD: 0	1	9	3
de la	2018	Non-Recurrent/no recanalization	30 months	69	1		WEB: 1; WEB+Stent: 1	32	36	3
Torre		Recurrent/recanalization		22	0		WEB: 3	7	13	5
Jeon	2016	Non-Recurrent/no recanalization	24.8 ± 8.2	bioactive coil (>50%): 13	16	4	-	3	3	8
		Recurrent/recanalization	months	bioactive coil (>50%): 7	3	4	-	21		3
Stapelton	2016	Non-Recurrent/no recanalization	Not reported	19	5	1		13	4	8
		Recurrent/recanalization		19	2	0		1	4	16
Morga	Morga 2020 Non-Recurrent/no		6 months	all	-	-	-	-	-	-
		Recurrent/recanalization		all	-	-	-	-	-	-
Ortiz	2008	Non-Recurrent/no recanalization	24 months (range 18–30	all	-	-	-	-	-	-
		Recurrent/recanalization	months)	all	-	-	-	-	-	-
Pierot	2022	Non-Recurrent/no recanalization	12.6±3.9	367	-	299	-	368	29	98
		Recurrent/recanalization	months.	149	-	130	-	179	10	00
		Non-Recurrent/no recanalization	48.0 months [24.0-51.5]	85	42			92	3	5
Park	Park 2019 Recurrent/recanalization		32.0 months[18.5- 48.0]	34	10	-	-	19		.5
Lecler	2015	Non-Recurrent/no recanalization	more than 10 years	201	-	8	-	-	-	-
		Recurrent/recanalization			-		-	-	-	-

 $PED = Pipeline \ Embolization \ Device; \ FDS = Flow \ Diversion \ Stent; \ WEB = Woven \ EndoBridge; \ NR = Not$

Supplementary Table 5a. The Newcastle-Ottawa Scale for assessing the quality of the included studies

Study	Selection 1	Selection 2	Selection 3	Selection 4	Comparability	Outcome 1	Outcome 2	Outcome 3	Total
Adeeb	*	*	*	*	**	*	*	*	9
Brinjikji	*	-	*	*	**	*	*	*	8
Chen	*	-	*	*	**	*	*	*	8
de la Torre	*	-	*	*	**	*	*	*	8
Futchko	*	-	*	*	**	*	*	*	8
Hammoud	*	*	*	*	-	*	*	*	7
Hanel	-	-	*	*	**	*	*	*	7
Huang	*	-	*	*	**	*	*	*	8
Hussein	*	-	*	*	-	*	*	*	6
Jang	*	*	*	*	**	*	*	*	9
Jeon	*	-	*	*	**	*	*	*	8
Ji	*	-	*	*	**	*	*	*	8
Kim 2021	*	-	*	*	**	*	*	*	8
Kim 2023	*	-	*	*	-	*	*	*	6
Morga	*	-	*	*	-	*	*	*	6
Ortiz	*	-	*	*	**	*	*	*	8
Pierot	*	*	*	*	**	*	*	*	9
Rouchaud	*	*	*	*	**	*	*	*	9

Salem	*	-	*	*	**	*	*	*	8
Stapelton	*	-	*	*	**	*	*	*	8
Wu	*	*	*	*	**	*	*	*	9
Yousef	*	*	*	*	-	*	-	*	6
Yuan	*	-	*	*	-	*	*	*	6
Park	*	*	*	*	**	*	*	*	9
Lecler	*	-	*	*	**	*	*	*	8

Supplementary Table 5b. JBI Critical Appraisal Checklist for Case Series

Study	1	2	3	4	5	6	7	8	9	10	Total
Dabus	Yes	Unclear	Unclear	Yes	8						

Supplementary Figure 1. Subgroup analysis of complete occlusion rate based on smoking status

Subgroup analysis of complete aneurysm occlusion based on smoking status

Subgroup	Events	Total	Events	Total		RR [95% CI]
Current vs Former	Curr	rent	For	ner		
Rouchaud, 2016	50	58	39	49		1.08 [0.91, 1.29]
Salem, 2023	13	16	56	65	H-1	0.94 [0.73, 1.22]
Brinjiki, 2015	86	193	44	99	1-1	1.00 [0.76, 1.31]
RE Model for Subgroup					•	1.03 [0.91, 1.17]
Test for overall subgroup effect; Z=0.	43, P=0.665					
Former vs Never	For	mer	Net	/er		
Rouchaud, 2016	39	49	80	97		0.97 [0.82, 1.14]
Salem, 2023	56	65	188	250		1.15 [1.02, 1.29]
Brinjiki, 2015	44	99	56	119	144	0.94 [0.71, 1.26]
RE Model for Subgroup					•	1.04 [0.91, 1.20]
Test for overall subgroup effect: Z=0.1	61, P=0.544				100	
Current vs Never	Curr	rent	Ne	/er		
Rouchaud, 2016	50	58	80	97	•	1.05 [0.91, 1.20]
Salem, 2023	13	16	188	250	I- 1	1.08 [0.84, 1.38]
Brinjiki, 2015	86	193	56	119	+	0.95 [0.74, 1.21]
RE Model for Subgroup					•	1.03 [0.93, 1.15]
Test for overall subgroup effect: Z=0.	58, P=0.565					0.016530.201
Current + former vs Never	Current o	r Forme	r Ne	ver		
Rouchaud, 2016	89	107	80	97		1.01 [0.89, 1.14]
Salem, 2023	69	81	188	250		1.13 [1.01, 1.27]
Brinjiki, 2015	130	292	56	119	H.	0.95 [0.75, 1.19]
RE Model for Subgroup					•	1.05 [0.95, 1.16]
Test for overall subgroup effect: Z=0.	95, P=0.341					i erenterenterinet
RE Model						1.05 [1.00, 1.10]
Test for heterogeneity: t ² =0.00; χ^2 Test for overall effect: Z=1.98, P=	² =7.97, df=11, P=0 0.048).72; i ² ≈09	4			
						
					0 1 2 3 4 5 6	
					Risk Ratio (RR)	

Supplementary Figure 2. Subgroup analysis of adequate occlusion rate based on treatment method

	S	noker	Non-si	moker			
Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI
'Tx method' = Coiling					1		
Chen, 2015	41	93	213	436	· · · · ·	0.90	[0.70; 1.16]
Dabus, 2016	25	26	23	23		0.96	[0.89; 1.04]
Brinjikji, 2015	261	292	110	119	-	0.97	[0.91; 1.03]
Stapleton, 2016	14	29	8	17		- 1.03	[0.55; 1.93]
Random effects model	341	440	354	595	٠	0.96	[0.92; 1.01]
Heterogeneity: $I^2 = 0\%$, $\tau^2 =$	0, p = 0.9	96					
Test for effect in subgroup:	z = -1.54	(p = 0.1	(2)				
'Tx method' = Flow Div	ersion				200		
Hammoud, 2024	212	278	258	338		1.00	[0.91; 1.09]
Heterogeneity: $l^2 = 0\%$, $\tau^2 =$	0, p = 0.9	93					
Test for subgroup difference	es: $\chi_1^2 = 0$.	52, df =	1 (p = 0.4)	47)	0.75 1 1.5		

Supplementary Figure 3. Subgroup analysis of aneurysm recurrence/recanalization rate based on treatment

	S	moker	Non-si	moker										
Study	Events	Total	Events	Total		1	Risk	Rat	io			RR	9	5%-CI
'Tx method' = mix														
Ji, 2016	1	15	12	135	-		-	-				0.75	[0.10;	5.37]
Kim, 2023	2	11	5	25		3	-	-		6		0.91	[0.21;	3.99]
de la Torre, 2018	10	35	15	61			-					1.16	[0.59;	2.30]
Random effects model	13	61	32	221			<	\diamond	-			1.07	[0.59;	1.94]
Heterogeneity: $I^2 = 0\%$, $\tau^2 =$	= 0, p = 0.	89												
'Tx method' = Coil														
Stapleton, 2016	11	30	10	16		-		ł				0.59	[0.32;	1.07]
Yuan, 2023	4	37	8	55		ā		-	-			0.74	[0.24;	2.29]
Kim, 2021	6	24	47	147		-		-				0.78	[0.38;	1.63]
Jang, 2020	15	115	23	145		-	-	-				0.82	[0.45;	1.50]
Huang, 2017	19	162	64	496			-	-				0.91	[0.56;	1.47]
Wu, 2022	14	57	31	115			-	-				0.91	[0.53;	1.57]
Brinjikji, 2015	76	267	35	117			-	-				0.95	[0.68;	1.33]
Park, 2019	5	20	39	151		23		•	-			0.97	[0.43;	2.17]
Lecler, 2015	8	54	8	78			-	•				1.44	[0.58;	3.61]
Pierot, 2022	152	415	110	448				-	-			1.49	[1.21;	1.83]
Futchko, 2017	61	232	11	64			1	•	_			1.53	[0.86;	2.73]
Jeon, 2016	5	9	19	56			2	-				1.64	[0.82;	3.26]
Ortiz, 2008	35	61	11	49				- 7		-		2.56	[1.45;	4.49]
Morga, 2020	8	12	4	34								- 5.67	[2.08;	15.46]
Random effects model	419	1495	420	1971				٠				1.19	[0.92;	1.54]
Heterogeneity: $I^2 = 63\%$, τ^2	= 0.1360,	p < 0.0	01		12						123			
Test for subgroup difference	es: $\chi_1^2 = 0$.	10, df =	1 (p = 0.1)	75)	1	3	1	ł.	્ય		1			
					0.1	0	.5	1	2		10			



Supplementary Figure 4. Funnel plot of aneurysm recurrence/recanalization rate

Supplementary Table 6. Meta-regression of the effect of different factors on aneurysm recanalization/recurrence among studies. None of the evaluated factors was significant.

Recanalization/Recurrence rate	Tau ²	I ²	H ²	P value for moderator
Ruptured,%	0.1	60.1	2.5	0.3
Female,%	0.1	67.3	3.0	0.6
Age, mean	0.2	64.3	2.7	0.7
Mean follow up time, days	0.7	75.9	4.1	0.9
Aneurysm diameter, mm	0.2	60.7	2.5	0.5
Posterior circulation,%	0.07	43.1	1.7	0.1
Publication year	0.1	60.4	4.8	0.2
Hypertension,%	0.1	43.0	1.76	0.2

Supplementary Table 7. Definition of Recanalization or Recurrence by Studies

Study	Recanalization or Recurrence definition
Kim, 2021	Recanalization was defined as new or increased contrast
	filling of an aneurysm with or without aneurysm growth.
Ji, 2016	Recanalization was defined as any aneurysm remnant that had increased in size or contrast filling.
Wu, 2021	Those aneurysms appeared again while complete occlusion after 3month and/or residual aneurysm size had increased after incomplete occlusion were regard as recurrent aneurysm
Brinjikji, 2015	Aneurysm recurrence was defined as
	coil compaction, recanalization, or both.
Jeon, 2016	Recanalization was defined as contrast filling the aneurysm neck (minor recanalization) or dome (major recanalization) at follow-up imaging
Stapleton, 2016	Recanalization, or recurrence, was
	defined as an increase in opacification of the neck or
	dome of the aneurysm at the time of first and/or last
	angiographic follow-up as compared with the initial
	post-treatment cerebral angiogram
Morga, 2020	Each enlargement of the inflow of the aneurysm to the embolized aneurysm described by the radiologist was considered a recanalization
Ortiz, 2008	Aneurysm recanalization or regrowth was defined as an increase in inflow to the aneurysm in comparison with baseline
Pierot, 2022	Recanalization was defined as any increase of aneurysm contrast filling as depicted by the data coordinating center when directly comparing postoperative DSA and follow–up vascular imaging.
Futchko, 2017	Aneurysm recurrence was defined as inflow into a previously completely occluded aneurysm or growth of an incompletely occluded aneurysm (aneurysm recanalization)
Kim, 2023	Recurrence was defined as an increase in aneurysm contrast filling or shortened stasis, stabilization, unchanged volume of aneurysm filling
Jang, 2020	Recurrence was defined as any progression
	of Raymond-Roy class or increasing of aneurysmal
	flow.
Huang, 2017	Recurrence was defined as: Loosened or compressed spring coil, or contrast materials filling in the body or neck of the intracranial saccular aneurysm, which was not observed on the immediate postoperative angiogram, when compared with the immediate postoperative angiographic results.
Lecler, 2015	Increase in Raymond Ray Occlusion classification at long-term follow up.
Park, 2019	Recurrence was defined as coil compaction, recanalization through the coil mesh, aneurysm regrowth or neck enlargement.
Yousef, 2020	No definition is provided
Yuan, 2023	No definition is provided

de la Torre, 2018 No definition is provided

Study	Complete occlusion	Incomplete occlusion
Dabus, 2016	Complete occlusion (RR I)	Residual neck or residual aneurysm (RR>1)
Brinjikji, 2015	Complete occlusion (RR I)	Residual neck or residual aneurysm (RR>1)
Hanel, 2021	Complete occlusion (RR I)	Residual neck or residual aneurysm (RR>1)
Stapleton, 2016*	Complete occlusion or neck remnant (RR I or RR II)	Residual neck and partial remnant (RR III)
Chen, 2015*	Complete occlusion or neck remnant (RR I or RR II)	Residual neck and partial remnant (RR III)
Salem, 2023	Aneurysmal occlusion was classified into 3 categories: complete occlusion (100%), near complete occlusion (90–100%)	Both near-complete and partial occlusion were collectively defined as incomplete occlusion.
Adeeb, 2017	Occlusion was categorized as complete occlusion (100%), near-complete occlusion (90%–100%), and partial occlusion (<90%).	Both near-complete and partial occlusion were collectively defined as incomplete occlusion.
Rouchaud, 2016	Clinical assessment of follow up angiography	Clinical assessment of follow up angiography
Hammoud, 2024	Clinical assessment of follow up angiography	Clinical assessment of follow up angiography
Hussein, 2020	Clinical assessment of follow up angiography	Clinical assessment of follow up angiography
* These studies only provi RR: Raymond Roy Occlus	ded details for adequate occlusion (not complete occlusion).	

Supplementary Table 8. Definition of aneurysm occlusion by studies